Preliminary Study on Tinnitus: Can we Control Ringing in the Ear?

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Preliminary Study on Tinnitus

Abstract

Objective: This preliminary study aimed to implement a new set of sound parameters in modified white noise to produce significant reductions in tinnitus amplitude. *Design*: This study was a single subject design in which subjects served as their own control. Each participant received treatment and changes were measured over time. *Sample*: Eight participants with tonal tinnitus underwent 3 months of tinnitus treatment. Participants were instructed to listen to an individualized notched white noise sound for 2 hours per day. Tinnitus mapping and the IOWA Tinnitus Handicap Questionnaire (THQ) were conducted at baseline (pre-treatment), and at a minimum of 1.5 and 3 months to measure treatment effects. *Results*: Data showed a significant decrease in tinnitus volume from the pre-treatment to post-treatment condition. There was also a significant improvement in the Q-Positive scores on the IOWA Tinnitus Handicap Questionnaire. *Discussion and Conclusion*: Individualized modified white noise therapy demonstrated a significant effect on reducing tinnitus amplitude. The negative effects of tinnitus on participants tended to decrease. These findings warrant further investigation of the potential long-term effects of this treatment, as well as factors related to maximizing its effectiveness.

Preliminary Study on Tinnitus: Can we Control Ringing in the Ear?

BACKGROUND

What is Tinnitus?

Tinnitus is often described as "ringing in the ears" (Langguth, Kreuzer, Kleinjung, & De Ridder, 2013) and is the conscious perception of sound in the absence of external auditory stimuli (Ariizumi, Hatanaka, & Kitamura, 2010; Baguley, McFerran, & Hall, 2013; Hobson, Chisholm, & Refaie, 2012). Subjective tinnitus is ringing in the ears heard only by the individual with tinnitus, and is the focus of this study. Objective tinnitus is not as common and can be heard by a clinician (Langguth et al., 2013). It is often classified as synchronous or asynchronous (Hobson et al., 2012). Synchronous tinnitus may be described as pulsatile due to its coherence to the individual's heart rhythm, indicating a vascular origin (Baguley et al., 2013; Sismanis, 1998). Asynchronous tinnitus is not synchronized to the rhythm of the heart and may be a result of myoclonus of the stapedius or palatal muscles (Baguley et al., 2013; Heller, 2003).

Tinnitus has been described as hissing, sizzling, ringing (Baguley et al., 2013), buzzing (Langguth et al., 2013), whistling, humming, indistinct music (Hobson et al., 2012), or indistinct voices without meaning (Baguley et al., 2013). It can present intermittently or be constant, and can consist of more than one type of sound (Baguley et al., 2013). Tinnitus can be heard bilaterally, unilaterally, or centrally within the head. It can develop abruptly, but is often gradual in onset. Due to the heterogeneous nature and high variability of tinnitus, uniform treatment and research can be challenging (Baguley et al., 2013; Hobson et al., 2012; Langguth et al., 2013). Currently, no treatment has ever succeeded in eradicating tinnitus completely (Ariizumi et al., 2010; Hobson et al., 2012).

How Many People are Affected?

Reports show that most people will experience tinnitus at some point in their life for short periods of time (Baguley et al., 2013). However, 10% to 15% of adults experience tinnitus long enough to require medical evaluation or intervention (Baguley et al., 2013; Heller, 2003; Langguth et al., 2013). Research has shown that up to 6% of those affected by tinnitus have incapacitating symptoms (Heller, 2003) and of these, 0.5 to 2.0% are so severely affected that it negatively impacts their ability to lead a normal life (Baguley et al., 2013; Davis & El Refaie, 2000; Heller, 2003; Langguth et al., 2013).

Tinnitus is more common with increased age, especially in those between 50 to 80 years. Within this age group, an estimated 30% of people suffer from tinnitus (Shargorodsky, Curhan, & Farwell, 2010; Sindhusake et al., 2003). It is more common in men than women (Heller, 2003; Langguth et al., 2013) and is more prevalent amongst those with lower incomes (Heller, 2003). Tinnitus is reported in North American, Asian, and European populations indicating this perception of non-acoustic sound is a global issue (Langguth et al., 2013). Adults are not the only ones affected. In a study of 2000 school-age children, 13% reported symptoms of tinnitus. Of these students, 43.9% also presented with otitis media and 29.5% with hearing loss (Heller, 2003).

How is it Caused?

Tinnitus can originate from numerous factors, including those that cause damage to any part of the auditory pathway (Langguth et al., 2013). Causes of tinnitus can include acoustic trauma (e.g., explosions, gunfire, loud music, city or occupation-related noise) (Baguley et al., 2013; Hobson et al., 2012; Langguth et al., 2013; Myers, et al., 2014; Naik & Pai, 2014; Vogel, van de Looij-Jansen, Mieloo, Burdorf & de Waart, 2014), vascular disease, tumours, and presbycusis (Langguth et al., 2013).

Individuals with hearing loss experience tinnitus more often than those without (Baguley et al., 2013; Heller, 2003). Tinnitus can also occur without hearing loss (Baguley et al., 2013; Hobson et al., 2012; Langguth et al., 2013), resulting from dead regions of outer hair cells in the cochlea, which are not severe enough to cause hearing loss (Langguth et al., 2013). In some cases of tinnitus, the cause is unknown. Possible risk factors include obesity, smoking, drinking alcohol, head injury, arthritis, and hypertension (Baguley et al., 2013). Ototoxic drugs can also trigger the onset of tinnitus (Cianfrone et al., 2011; Langguth et al., 2013).

What is Happening in the Brain?

Research exploring the neurological basis of tinnitus suggests it is a result of the plasticity of the brain compensating for a lack of acoustic stimulus (Baguley et al., 2013). It is often due to maladapted cortical plastic changes (Stracke, Okamoto, & Pantev, 2010). When the central auditory nervous system no longer receives neural input for a particular sound frequency (e.g., due to cochlear hair cell damage at the corresponding frequency), three phenomena are noted to happen: 1) remapping of neuron activity and tonotopy, 2) increased spontaneous firing rate of neurons, and 3) increased synchrony of neuronal firing (Baguley et al., 2013; Langguth et al., 2013; Pantev et al., 2014). This remapping and reorganization of neurons is similar to the phantom limb syndrome of amputees (Baguley et al., 2013; De Ridder, Elgoyhen, Romo, & Langguth, 2011).

Specifically, neurons that were once sensitive to a particular frequency no longer receive stimulation, and due to cortical plasticity and changeability, these neurons reorganize to a new frequency that neighbouring neurons are sensitive to. This is substantiated by the fact that this effect can be reversed by auditory treatment (Stracke et al., 2010). Neurons no longer receiving acoustic stimulation have no signal to inhibit their homeostatic activity, resulting in an increased spontaneous firing rate. This hyperexcitability of the neurons, as seen in increased gamma band activity in the auditory cortex (Musiek, Atcherson, Kennett, & Nicholson, 2012; Langguth et al., 2013), is a component of the subjective perception of tinnitus.

What are the Effects of Tinnitus on the Individual?

Tinnitus can be inconsequential or debilitating (Luxon, 1993). According to the neurophysiological model of tinnitus, if the tinnitus signal is processed by subcortical regions such as the limbic system (De Ridder et al., 2006; Jastreboff & Hazell, 2004), it can lead to a heightened perception of that signal (Hobson et al., 2012). Therefore, when symptoms of tinnitus are severe it may result in emotional distress (Pape et al., 2014).

Tinnitus can also affect attention and cognition. Jackson et al. found that the greater the severity of self-reported tinnitus, the greater the negative impact on executive attention (2014). There is also some evidence that suggests tinnitus negatively affects working memory (Mohamed, Hoare & Hall, 2015), and that irrelevant sounds have the highest influence on cognitive capacity by disrupting selective attention (Banbury, Macken, Tremlay & Jones, 2001). Tinnitus has been reported to lead to frustration, annoyance, irritability, difficulty concentrating, stress and hearing difficulties (Langguth et al., 2013). Anxiety, depression, hyperacusis, insomnia and hearing loss can also result from tinnitus (Baguley et al., 2013, Langguth et al., 2013), in addition to a decreased quality of life (Erlandsson & Hallberg, 2000).

How is Tinnitus Treated?

Some treatments can reduce the symptoms of tinnitus (Pantev et al., 2014; Stracke et al., 2010; Teismann, Okamoto & Pantev, 2011) but there is no known treatment that can cure it completely (Hobson et al., 2012). Commonly employed treatments include: habituation therapy (Jastreboff & Hazell, 2004), pharmaceuticals (Baguley et al., 2013), muscarinic affecters, antidepressants (Baldo, Doree, Molin, McFerran, & Cecco, 2012), hearing aids (Heijnemen, de Kleine, & van Dijk, 2012), transcranial magnetic stimulation (Teisman, et al., 2014), reflexology, hypnotherapy, acupuncture (Jeon, Kim, & Nam, 2012), cognitive therapy (Martinez-Devesa, Perera, Theodoulou, & Waddell, 2010), counseling (Baguley et al., 2013), masking (Hobson et al., 2012), notched white noise (Mahboubi, Ziai, & Djalilian, 2012; Okamoto, Stracke, Stoll, & Pantev, 2010; Stracke et al., 2010; Teismann et al., 2011; Teismann et al., 2014; Zhang, 2012), and notched music (Pantev et al., 2014; Stracke et al., 2010).

Research has found that the organization of the tonotopical sensory maps in the auditory cortex is not fixed in adults (Pantev, Wollbrink, Roberts, Engelien, & Lütkenhöner, 1999; Irvine, Fallon, & Kamke, 2006; Dietrick, Nieschalk, Stoll, Rajan & Pantev, 2001). Animal studies have shown that deafferentiated cortical regions can take over the functions of neighbouring areas, which have damage to their peripheral afferent sensory inputs (Dietrick et al., 2001). This can occur within hours in the auditory system (Robertson & Irvine, 1989). This research led to the idea that “functional” reversible deafferentiation (e.g., notched sound) may also result in the re-tuning of sensory neurons (Pantev et al., 1999).

Notched sound has been shown to reduce tinnitus in previous studies (Mahboubi et al., 2012; Okamoto et al., 2010; Stracke et al., 2010; Teismann et al., 2011; Teismann et al., 2014).

However, research has yet to be conducted using a customized bandwidth derived from the adjacent frequencies. Our research incorporates the use of customized notched white noise in which no auditory stimulation is present at the tinnitus frequencies based on the adjacent frequencies of the lower octave, lower half octave, upper octave, and upper half octave of the individual's tinnitus. The aim of the present study is to verify prognosis for this method of treatment. Using customized notched white noise, we expect to see a significant decrease in the volume of tinnitus.

METHODS

Participants

Participants were recruited to the study via a radio advertisement and flyers distributed to audiology clinics in the Edmonton area. Thirty-two individuals contacted researchers about participating; 15 of which did not meet criteria or did not respond to scheduling treatment sessions. Eight participants attended the first session where their tinnitus was matched but withdrew from the study thereafter (one of which came a second time to correct this initial tinnitus match and subsequently withdrew). The remaining 9 participants completed the three-month, 2-hour-a-day listening program, but one was later found to not meet the criteria for inclusion.

The inclusion criteria was as follows: 18 years or older, had suffered from tonal tinnitus for greater than 6 months, and the cause of their tinnitus had not been diagnosed. Exclusion criteria included: non-tonal tinnitus, severe hearing loss, unable to cease other current treatment, unable to use earphones, and significant depression. Ages ranged from 44-83 years old with an average of 60. Five males and 4 females participated as shown in Table 1 (pg. 23). Occupations included: hearing aid practitioner, maintenance worker, IT consultant, business owner, retired principal, heating plant electrician, and others. The Institutional Review Board approved the ethics of this study. Each participant gave written informed consent was made aware of all possible benefits and risks.

Design

This study was a single subject design in which subjects served as their own control. Each participant received treatment and changes were measured over time. In the pre-treatment session, all participants had their hearing tested at 500, 1000, 2000, 4000 and 8000 Hz. All participants' hearing thresholds were an average of 28.5 dB HL for right ears (SD: 16.48 dB HL), and an average of 35.75 dB HL for left ears (SD 17.00 dB HL), with the majority of hearing loss being mild to moderate-severe in the upper frequencies (following typical presbycusis and/or noise-induced hearing loss patterns). Participants also completed the IOWA Tinnitus Handicap Questionnaire and performed an audiological mapping of their tinnitus.

The tinnitus frequency, volume and adjacent frequencies at the lower and upper octave and half octave were mapped using a Lenovo IdeaPad U410 Ultrabook Laptop, and Bio-logic insert earphones with foam earphone tips. The computer program (*TNT: Generate Sound*) was created specifically for this study. It produces acoustic frequencies from 15-15,000 Hz as sine waves with a volume control of 0-100%. Participants matched the tone emitted from the computer software with the tone of their tinnitus (via scrolling with the mouse), in addition to the masking volume of the octave and half octave below and above their tinnitus frequency.

With these frequency and volume values, a notched white noise sound file was created unique to each individual based on the frequencies adjacent to their tinnitus. The second and third sessions (after approximately 1.5 months and 3 months of listening respectively) included the completion of the IOWA Tinnitus Handicap Questionnaire in addition to a remapping of their tinnitus. A new sound file was created after the 1.5-month visit using the new volume and frequency values. Previous tinnitus studies have used a t-test for statistical analysis. For this study the t-test was used to analyze the significance of the treatment effect pre-, mid, and post treatment. A p-value less than 0.05 will be regarded as significant.

RESULTS

All participants reported having tonal tinnitus and two of them reported hearing an additional hissing sound. Eight participants presented with bilateral tinnitus and one presented with unilateral tinnitus in the right ear. This participant reported the tinnitus to be heard centrally, but more intensely in the right ear and noted that it often presented as multiple tones. In this case the customized sound file was created based on the tinnitus tone that was most pronounced. No participants presented with unilateral tinnitus in the left ear. The average pre-treatment tinnitus frequency was 4139.7 Hz (SD: 2032.80 Hz). One participant presented with profound hearing loss in the tinnitus-adjacent frequencies but asked to remain in the study, as there are limited alternatives to treatment. Due to this degree of hearing loss, his data was excluded from the study.

This customized notched sound therapy has been reported to reduce the tinnitus volume in the majority of our participants as shown in Tables 2 and 3 (pgs. 24 and 25). Results of a paired-samples t-test showed that after 3 months of exposure to individualized notched-noise sound files, participants experienced a significant decrease in tinnitus loudness from the pre-treatment (M=43.39, SD=32.42) to post-treatment (M=22.48, SD=10.62) condition; t(14)=2.93, p=0.006. The average listening time was 185.06 hours (SD: 74.21 hours). Typically, improvement was gradual, based on a comparison among three sets of longitudinal data collected at baseline, at 1.5 months and at 3 months. The average decrease in tinnitus volume was 35% (SD=33.24). When participants were separated into two groups based on age, both groups experienced significant reductions in tinnitus amplitude as shown in Table 4 (p<0.05, pg. 26).

Of the 7 participants who reported bilateral tinnitus, 71% (n=5) showed a reduction in both ears and 29% (n=2) showed a reduction in one ear. The participant with unilateral tinnitus in the right ear experienced a 47% decrease in tinnitus volume from the first session to the second session but it increased 13% from the first to last session.

Seven participants also experienced a decrease in tinnitus frequency, however these results were not statistically significant. The average decrease in tinnitus frequency was 18% (SD=41.07). Of the 7 participants with bilateral tinnitus, 43% (n=3) showed a frequency reduction in both ears, 43% (n=3) in one ear, and 14% (n=1) experienced an increase in frequency in both ears. The participant with unilateral tinnitus also showed a reduction in frequency.

Q-Positive scores represent scores on the IOWA Tinnitus Handicap Questionnaire where values closer to 100 indicate tinnitus is not significantly impacting the participant's physical, social and emotional health. There was significant improvement from the first visit to the third visit in the Q-Positive survey questions (i.e., *I think I have a healthy outlook on tinnitus,* and *I* *have support from my friends regarding tinnitus*) ($p = 0.024$). The average Q-Positive scores increased from 50 (SD =37.35) in the pre-treatment session to 71.25 (SD=32.37) in the post-treatment session. For Q-Negative survey items, where scores closer to zero indicate tinnitus is not significantly affecting health, there was a decrease in scores but the difference was not significant. The average Q-Negative scores decreased from 32 (SD=23.60) in the pre-treatment session to 29 (SD=23.76) in the post-treatment session.

DISCUSSION

This study investigated the effectiveness of individualized notched white noise sound therapy on reducing the amplitude of subjective tinnitus. To the best of our knowledge, this study is the first to create individualized sound files based on the individual's tinnitus amplitude at the upper octave, lower octave, upper half octave and lower half octave of the frequencies adjacent to the tinnitus frequency.

Contributing Factors of Treatment Effectiveness

Optimal Listening Period. The data presented in this study suggests that listening to individualized, notched white noise sound files can significantly reduce tinnitus volume. Results were seen after the listening began during the first listening period, which ranged from 47 to 138 days. Within this period the ideal duration of listening presented as 2 hours per day over 50 days. However, further research is needed to determine the optimal listening duration of both the hours per day and number of days. For example, in this study one participant was able to achieve moderate results from listening 10 to 15 minutes per day for a total of 23 listening hours over 138 days. However, another participant who listened for a similar amount of time

(24 hours over 114 days) did not benefit to the same degree (this participant had profound hearing loss and his data had been excluded due to exclusion criteria).

The participants who experienced less success tended to have tinnitus for a greater period of time (10+ years) and a profound hearing loss in the tinnitus-adjacent frequencies, which may have decreased treatment effectiveness. Participants who listened to the sound file daily for a condensed period of time appeared to benefit most (e.g., 80-100 hours over 50 days). Listening for a period shorter than 2 hours daily, spreading listening times over longer periods, or listening for 2 hours a day for longer than 50 days (e.g., 168 hours over 84 days, 170 hours over 100 days, etc.) all appear to reduce treatment effectiveness.

Age and Degree of Hearing Loss. Other factors such as age, and the degree of hearing loss in adjacent frequencies were also possible contributors to treatment effectiveness. Those with moderate, moderate severe and severe hearing loss in frequencies adjacent to the tinnitus frequency still responded well to therapy. Those with profound hearing loss in adjacent frequencies did not appear to respond as well.

As shown in Table 4 (pg. 26), age was not a significant contributor to treatment effectiveness in this study. The mean tinnitus amplitude of older participants was greater than younger participants before treatment, and we found those with a greater tinnitus amplitude responded better to treatment than those with a weaker amplitude. More research with a larger sample size is needed to investigate this further. Tinnitus is characterized by hyperexcited neurons in the auditory cortex resulting from lack of auditory stimulation at select frequencies (often, but not always, related to hearing loss at those or adjacent frequencies) (Langguth, Kreuzer, Kleinjung, & De Ridder, 2013). We postulate that this customized sound treatment is effective by indirectly stimulating the neurons causing the tinnitus tone by delivering acoustic stimuli to the adjacent frequencies of the tinnitus.

Right Ear Versus Left Ear Response to Treatment. A number of participants (n = 5) had a greater amount of hearing loss in their left ear compared to their right ear. A general trend amongst participants was a greater responsiveness in their left ear toward treatment as is shown in the Figures 1 and 2 (pg. 28). This may be due to the increased neural input to the adjacent frequencies of the tinnitus. This would allow the adjacent frequencies to indirectly stimulate the tinnitus causing neurons, which would otherwise not receive the same degree of sensory input. However, many right and left ears had similar hearing loss in the frequencies adjacent to their tinnitus, yet as shown in Table 5 (pg. 27), the left still responded more effectively to the sound therapy than the right at all points in the study ($p < 0.05$).

Due to the organization of the auditory pathways, auditory information travels ipsilaterally and contralaterally to the auditory cortices from each ear. However, research suggests the contralateral pathways have a faster rate of transmission and more fibres (Majkowski, Bochenek, Bochenek, Knapik-Fijałkowska, & Kopeć, 1971). Zatorre and Poeppel have found that the left hemisphere of the brain is more suited to processing quicker auditory stimuli (e.g., speech phonemes), while the right hemisphere is more suited to processing longer auditory stimuli (e.g., intonation and tones of music) (Poeppel, 2003; Zatorre, Belin, & Penhune, 2002; Zatorre & Grandour, 2008). Due to the continuous nature of the individualized notched white noise, it is plausible the left ear (projecting to the right hemisphere) may have processed the auditory stimulus more efficiently than the right ear.

Lowering of Tinnitus Frequency. For those participants with greater hearing loss in the left ear (n = 5), the frequency of the tinnitus consecutively lowered with each visit. This was not true of all participants, yet is a trend noteworthy for future studies. Additionally some participants found this frequency lowering to be beneficial as it moved the tinnitus tone from speech sound frequencies to ranges that were outside, or on the border of speech frequencies. It is unknown whether the tinnitus is lowering in frequency due to treatment, or if it is due to the participant having multiple tinnitus frequencies in one ear. One could postulate that as the neural activity of one tinnitus frequency band decreased, another pre-existing frequency masked by the former becomes more apparent. This neuroplastic change of tinnitus perception from sound therapy suggests that the tinnitus frequencies may undergo remapping at the central cortical level (De Ridder et al., 2013).

Future research may also benefit from comparing pre-treatment and post-treatment audiograms. During our post-treatment audiological mapping of the tinnitus frequency and volume, some participants appeared to be more sensitive to certain sound frequencies previously not heard due to their tinnitus.

Subjective Survey Results. For the Q-Negative survey questions, scores decreased but statistical significance was not achieved. We have tried to evaluate it from another angle by testing its correlation with tinnitus reduction. Tinnitus amplitude reduction was significant as shown in our results. To avoid the effect of extremity in the correlation analysis of 8 subjects, we removed the case with the maximum reduction. The derived correlation is 0.87 (Pearson Product-Moment Correlation Coefficient), which indicates a strong positive correlation (i.e., the greater the decrease in tinnitus volume (%), the lower the Q-Negative scores). Three participants also reported that during the course of treatment they noticed their tinnitus would intermittently fade out and temporarily disappear.

There are a number of factors that may influence treatment effectiveness in addition to the length of time listened, brain hemisphere lateralization, and hearing loss level, which makes some of these observations more challenging. However, these findings are still noteworthy to consider for future research.

Limitations

Possible limitations of this study include the small sample size and lack of a separate control group. Also, there was a high amount of variability in participant listening duration. Although we instructed participants to set a comfortable sound volume, some found the sound difficult to tolerate. Others found the time commitment to be too large, although two hours has been a common formula used in many other tinnitus sound therapies.

Those who showed less improvement are associated with some negative factors, such listening to the prescribed sound fewer than study-required hours every day, smoking, taking medications, and having concurrent disorders or health problems (e.g., one participant suffered from Ramsay-Hunt syndrome and had seven ear operations as an infant, yet still benefited from treatment in the left ear). Also, there is evidence to suggest that those who report having tinnitus localized centrally within the head and present with multiple tones have more difficulties suppressing and masking their tinnitus (Erlandsson, Hallberg, & Axelsson, 1992). This may explain why the one participant in our study who reported hearing the tinnitus centrally with multiple tones did not experience significant treatment effects.

Some participants had difficulty hearing higher frequencies (e.g., near 10,000 Hz) due to hearing limitations (e.g., typical age-related hearing loss). This was not an issue for the lower frequencies, but may have affected the upper masking frequencies of some of the participants. Furthermore, tinnitus is highly variable and research on a variety of treatments has shown inconsistency in participant responsiveness (Baguley et al., 2013). Research with notched music therapy found there to be no general tinnitus loudness reduction trend over time (Pantev et al., 2014). Finally, as the current study was performed over a period of approximately 3 months, although the results show promise, further research is needed to investigate the long-term effects of such individualized sound therapy.

CONCLUSION

Individualized notched white noise therapy is effective in reducing the amplitude of subjective tinnitus. As research is relatively new in this specific type of therapy, many factors and possible outcomes relating to maximizing its effectiveness (e.g., length of listening time, lateralization, and level of hearing loss) all need to be considered in future studies. While results are promising and provide hope for those where treatment is not frequently offered, much is still yet to be discovered on individualized notched white noise therapy.

REFERENCES

Ariizumi, Y., Hatanaka, A., & Kitamura, K. (2010). Clinical prognostic factors for tinnitus retraining therapy with a sound generator in tinnitus patients. *Journal of Medical and Dental Sciences, 57*(1), 45-53.

Baguley, D., McFerran, D., & Hall, D. (2013). Tinnitus. *The Lancet, 382*(9904), 1600-1607.

Baldo, P., Doree, C., Molin P., McFerran, D., & Cecco, S. (2012). Antidepressants for patients with tinnitus. *The Cochrane Library, 9*, 1-34.

Banbury, S. P., Macken, W. J. Tremblay, S. & Jones, D. M. (2001). Auditory distraction and short-term memory: Phenomena and practical implications. *Human Factors, 43*(1), 12-13.

Cianfrone, G., Pentangelo, D., Cianfrone, F., Mazzei, F., Turchetta, R., Orlando, M.P., & Altissimi, G. (2011). Pharmacological drugs inducing ototoxicity, vestibular symptoms and tinnitus: A reasoned and updated guide. *European Review for Medical and Pharmacology Science, 15*(6), 601-636.

Davis A., & El Refaie, A. (2000). The epidemiology of tinnitus. In: R. Tyler (Ed.), *Tinnitus Handbook* (pp. 1-23). San Diego, CA: Singular.

De Ridder, D., Elgoyhen, A. B., Romo, R., & Langguth, B. (2011). Phantom percepts: Tinnitus and pain as persisting aversive memory networks. *Proceedings of the National Academy of Sciences, 108*(20), 8075–8080.

De Ridder, D., Fransen, H., Francois, O., Sunaert, S., Kovacs, S., & Van De Heyning, P. (2006). Amygdalohippocampal involvement in tinnitus and auditory memory. *Acta Oto-laryngologica, 126*(S556), 50–53.

De Ridder, D., Vanneste, S., Weisz, N., Londero, A., Schlee, W., Elgoyhen, A. B., & Langguth, B. (2013). An integrative model of auditory phantom perception: Tinnitus as a unified percept of interacting separable subnetworks. *Neuroscience and Biobehavioral Reviews, 44*, 16-32.

Dietrich, V., Nieschalk, M., Stoll, W., Rajan, R., & Pantev, C. (2001). Cortical reorganization in patients with high frequency cochlear hearing loss. *Hearing Research*, *158*(1), 95-101.

Erlandsson, S. I., Hallberg, L. R., & Axelsson, A. (1992). Psychological and audiological correlates of perceived tinnitus severity. *International Journal of Audiology*, *31*(3), 168-179.

Erlandsson, S. I., & Hallberg, L. R. (2000). Prediction of quality of life in patients with tinnitus. *British Journal of Audiology*, *34*(1), 11-19.

Heijnemen, K. M., de Kleine, E., & van Dijk, P. (2012). A randomized double-blind crossover study of phase-shift sound therapy for tinnitus. *Otolaryngology-Head and Neck Surgery, 147*(2), 308-315.

Heller, A. J. (2003). Classification and epidemiology of tinnitus. *Otolaryngologic Clinics of North America, 36*(2), 239-248.

Hobson, J., Chisholm, E., & El Refaie A. (2012). Sound therapy (masking) in the management of tinnitus in adults. *Cochrane Database of Systematic Reviews, 11*, 1-25.

Irvine, D. R., Fallon, J. B., & Kamke, M. R. (2006). Plasticity in the adult central auditory system. *Acoustics Australia/Australian Acoustical Society, 34(*1), 13.

Jackson, J. G., Coyne, I. J. & Clough, P. J. (2014). A preliminary investigation of potential cognitive performance decrements in non-help-seeking tinnitus sufferers. *International Journal of Audiology*, *53*, 88-93.

Jastreboff, P. J., & Hazell, J. W. (2004). *Tinnitus retraining therapy: Implementing the neurophysiological model*. New York, NY: Cambridge University Press.

Jeon, S. W., Kim, K. S., & Nam, H. J. (2012). Long-term effect of acupuncture for treatment of tinnitus: A randomized, patient-and assessor-blind, sham-acupuncture-controlled, pilot trial. *The Journal of Alternative and Complementary Medicine*, *18*(7), 693-699.

Langguth, B. Kreuzer P. M., Kleinjung, T., & De Ridder, D. (2013). Tinnitus: Causes and clinical management. *The Lancet Neurology, 12*(9), 920-930.

Luxon, L. M. (1993). Tinnitus: Its causes, diagnosis, and treatment. *BMJ*, *306*(6891), 1490-1491.

Mahboubi, H., Ziai, K., & Djalilian, H. R. (2012). Customized web-based sound therapy for tinnitus. *International Tinnitus Journal, 17*(1), 26-30.

Majkowski, J., Bochenek, Z., Bochenek, W., Knapik-Fijałkowska, D., & Kopeć, J. (1971). Latency of averaged evoked potentials to contralateral and ipsilateral auditory stimulation in normal subjects. *Brain Research*, *25*(2), 416-419.

Martinez-Devesa, P., Perera, R., Theodoulou, M., & Waddell, A. (2010). Cognitive behavioural therapy for tinnitus. *Cochrane Database of Systematic Reviews, 9.*

Mohamad, N., Hoare, D. J. & Hall, D. A. (2015). The consequences of tinnitus and tinnitus severity on cognition: A review of the behavioral evidence. *Hearing Research*, http://dx.doi.org/10.1016/j.heares.2015.10.001

Musiek, F., Atcherson, S., Kennett, S. W., & Nicholson, N. (2012). The dangers of edosing with binaural beats. *The Hearing Journal*, *65*(10), 9-10.

Myers, P. J., Griest, S., Kaelin, C., Legro, M. W., Schmidt, C. J., Zaugg, T. L., & Henry, J. A. (2014). Development of a progressive audiologic tinnitus management program for veterans with tinnitus. *Journal of Rehabilitation Research and Development, 51*(4), 609-622.

Naik, K., & Pai, S. (2014). High frequency hearing loss in students used to ear phone music: A randomized trial of 1,000 students. *Indian Journal of Otology, 20*(1), 29-32.

Okamoto, H., Stracke, H., Stoll, W., & Pantev., C. (2010). Listening to tailor-made notched music reduces tinnitus loudness and tinnitus-related auditory cortex activity. *Proceedings of the National Academy of Sciences, 107*(3), 1207-1210.

Pantev, C., Rudack, C., Stein, A., Wunderlich, R., Engell, A., Lau, P., ... & Shaykevich, A. (2014). Study protocol: Münster tinnitus randomized controlled clinical trial-2013 based on tailor-made notched music training (TMNMT). *BMC Neurology*, *14*(1), 40.

Pantev, C., Wollbrink, A., Roberts, L. E., Engelien, A., & Lütkenhöner, B. (1999). Short-term plasticity of the human auditory cortex. *Brain Research*, *842*(1), 192-199.

Pape, J., Paraskevopoulos, E., Bruchmann, M., Wollbrink, A., Rudack, C., & Pantev, C. (2014). Playing and listening to tailor-made notched music: Cortical plasticity induced by unimodal and multimodal training in tinnitus patients. *Neural Plasticity, 2014*(1), 1-10.

Poeppel, D. (2003). The analysis of speech in different temporal interaction windows: Cerebral lateralization as 'asymmetric sampling in time'. *Speech Communication, 41*(1), 245-255.

Shargorodsky, J., Curhan, G. C., & Farwell, W. R. (2010). Prevalence and characteristics of tinnitus among US adults. *The American Journal of Medicine, 123*(8), 711-718.

Sindhusake, D., Mitchell, P., Newall, P., Golding, M., Rochtchina, E., & Rubin, G. (2003). Prevalence and characteristics of tinnitus in older adults: The Blue Mountains hearing study. *International Journal of Audiology, 42*(5), 289-294.

Sismanis, A. (1998). Pulsatile tinnitus: A 15-year experience. *Otology & Neurotology, 19*(4), 472-477.

Stracke, H., Okamoto, H., & Pantev, C. (2010). Customized notched music training reduces tinnitus loudness. *Communicative & Integrative Biology, 3*(3), 274-277.

Teismann, H., Okamoto, H., & Pantev, C. (2011). Short and intense tailor-made notched music training against tinnitus: The tinnitus frequency matters. *PLOS ONE, 6*(9), e24685.

Teismann, H., Wollbrink, A., Okamoto, H., Schlaug, G., Rudack, C., & Pantev, C. (2014). Combining transcranial direct current stimulation and tailor-made notched music training to decrease tinnitus-related distress - A pilot study. *PLOS ONE, 9*(2), 1-11.

Vogel, I., van de Looij-Jansen, P. M., Mieloo, C. L., Burdorf, A., & de Waart, F. (2014). Risky music listening, permanent tinnitus and depression, anxiety, thoughts about suicide and adverse general health. *PLOS ONE, 9*(6), e98912.

Zatorre, R. J., Belin, P., & Penhune, V. B. (2002). Structure and function of auditory cortex: Music and speech. *Trends in Cognitive Sciences, 6*(1), 37-46.

Zatorre, R. J., & Grandour, J. T. (2008). Neural specializations for speech and pitch: Moving beyond the dichotomies. *Philosophical Transactions of the Royal Society B: Biological Sciences, 363*(1493), 1087-1104.

Zhang, M. (2012). Using notched or unnotched acoustic stimulation to treat tinnitus. *Abstract Association for Research in Otolaryngology, 35*, 300-301.

TABLES

Table 1

Clinical Characteristics of Research Participants

clinical variables		
gender	male (n = 5) female (n = 4)	
tinnitus duration	1-3yrs (n = 4) 5+yrs (n = 2) 10+yrs (n = 2)	
possible causes	presbycusis noise-induced psychological trauma middle ear infection Ramsay Hunt Syndrome hereditary unknown cause	
	mean	standard deviation
age (yrs)	60	12.88
hearing threshold (dB)	R: 28.5 L: 35.75	R: 16.48 L: 19.00
tinnitus frequency (Hz)	4139.7	2032.80

Table 2

Descriptive Statistics and t-test Results for Tinnitus Amplitude, Tinnitus Frequency (Hz), and THQ Scores

	Pre-test (1)		1.5 Months (2)		3 Months (3)		p-value		
Outcome	M	SD	M	SD	M	SD	1-2	2-3	1-3
Amplitude	43.39	32.42	25.83	12.73	22.49	10.62	*0.007	0.07	*0.006
Frequency	4139.68	1811.04	3766.11	2517.16	3653.96	2560.38	0.29	0.43	0.20
Q-Positive	50	37.34	59.37	38.86	71.25	32.27	0.10	0.06	*0.02
Q-Negative	31.93	23.59	30.40	24.71	29.33	23.76	0.33	0.24	0.20

*$p < 0.05$, one-tailed

Table 3

Descriptive Statistics and t-test Results for Tinnitus Masking Amplitude and Frequency (Hz)

	Pre-test (1)		1.5 Months (2)		3 Months (3)		p-value		
Outcome	M	SD	M	SD	M	SD	1-2	2-3	1-3
Lower Masking Amplitude	25.55	22.08	18.10	8.21	17.96	10.87	0.07	0.47	0.11
Lower Masking Frequency	2871	1563.02	2598.29	1613.81	2269.60	1485.03	0.37	0.08	0.06
Upper Masking Amplitude	55.97	35.85	46	34.63	41.31	29.92	0.05	0.13	*0.03
Upper Masking Frequency	6919.30	3332.68	6366.13	3644.95	5200.26	2747.25	0.50	0.05	0.06

*$p<0.05$, one-tailed

Table 4

Descriptive Statistics and t-test Results for Tinnitus Amplitude by Age

	Pre-test (1)		1.5 Months (2)		3 Months (3)		p-value		
Age Range	M	SD	M	SD	M	SD	1-2	2-3	1-3
44-63	23.18	11.45	18.72	13.39	16.96	9.43	*0.02	0.30	*0.01
64-83	61.07	34.99	32.06	11.32	27.33	9.59	*0.01	0.08	*0.01

*$p < 0.05$

Table 5

Descriptive Statistics and t-test Results for Right Ear and Left Ear Amplitude and Frequency (Hz)

	Pre-test (1)		1.5 Months (2)		3 Months (3)		p-value		
Outcome	M	SD	M	SD	M	SD	1-2	2-3	1-3
R Ear Amplitude	27.12	12.08	23.89	14.04	22.98	11.19	0.06	0.38	0.07
R Ear Frequency	3707.20	2013.33	3771.58	2954.37	3698.47	3050.12	0.90	0.32	0.98
L Ear Amplitude	62	39.07	28.06	14.10	21.93	19.80	*0.015	*0.006	*0.048
L Ear Frequency	4633.95	1545.81	3759.86	2145.02	3606.09	2106.40	0.07	0.06	0.61

*$p < 0.05$, one-tailed

Figures

Figure 1. Left Ear Tinnitus Mean Reductions.

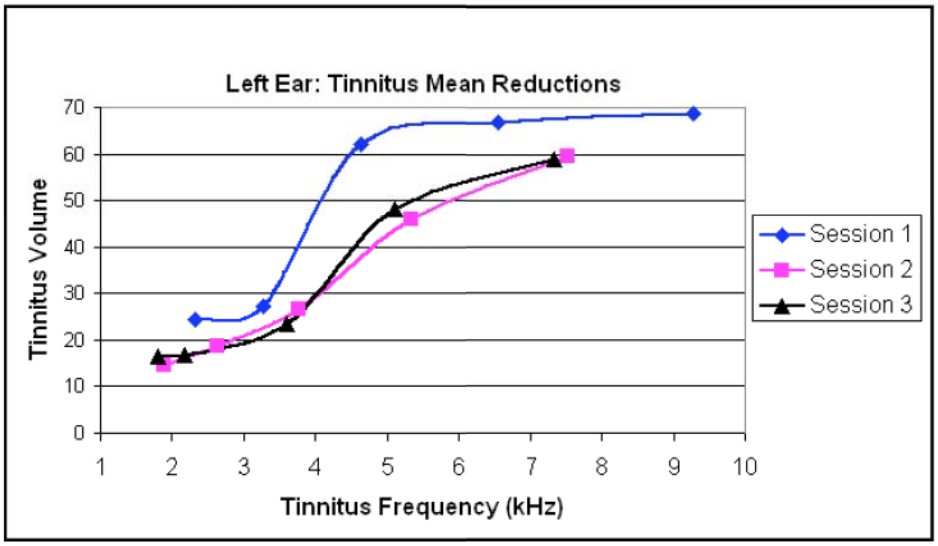

Figure 1. Visual representation of the mean right ear tinnitus changes in amplitude and frequency for sessions 1 to 3 across all participants. Two lower data points represent the lower octave and half octave means. Two upper data points represent the upper octave and half octave means. Midpoint represents the mean of the centre of the tinnitus tone.

Figure 2. Right Ear Tinnitus Mean Reductions.

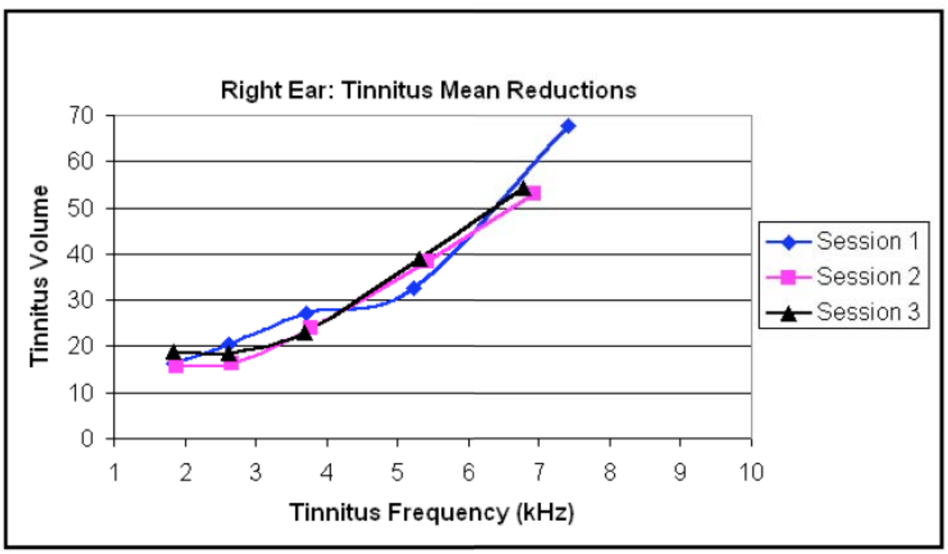

Figure 2. Visual representation of the mean left ear tinnitus changes in amplitude and frequency for sessions 1 to 3 across all participants. Two lower data points represent the lower octave and half octave means. Two upper data points represent the upper octave and half octave means. Midpoint represents the mean of the centre of the tinnitus tone.