Critical Review: Efficacy of Notched-Sound Therapy for Neural Plasticity Mediated Tinnitus Treatment

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About the Author

Mark Bennett was born and raised in Brantford, Ontario. He developed a passion for community health while pursuing a bachelor's degree in physiological psychology from Brock University. Here, he taught undergraduate health psychology seminars and helped establish rehabilitation programs for the Ontario March of Dimes in the Niagara region.

Mark graduated from The University of Western Ontario with a Master's of Clinical Science in Audiology. He has worked in multiple private hearing clinics across Canada in both adult and pediatric settings.

Most recently, Mark founded and runs the Cobourg Hearing Centre - a comprehensive hearing clinic serving the Northumberland community. His current clinical and research interests are adult hearing-impaired treatment programs, aural rehabilitation, and management programs for tinnitus.

This critical review examines the effects of notched-sound therapy on the human auditory system and its' potential as a novel and effective treatment option for tinnitus. Studies evaluated consisted of one mixed groups randomized clinical trial, two mixed groups pseudorandomized clinical trials, and two mixed groups non-randomized clinical trials. Analyses of these studies revealed moderate evidence for notched-sound's ability to induce changes in the auditory cortices and reduce tinnitus-related symptoms. Future research directions and clinical applications shall be discussed.

INTRODUCTION

It is well documented that the tonotopically-arranged sensory maps in the human auditory cortex are neither static nor permanent in their functional organization. For instance, animal models have demonstrated that damage to peripheral afferent sensory inputs results in deafferented cortical regions taking over and resuming functions for neighboring cortical sites.[1] This induced deafferentation of auditory pathways results in cortical neurons to shift and broaden their receptive fields outside of the damaged area within hours.[2] It has been demonstrated in other sensory systems that such cortical plasticity is not limited to cases of permanent lesions or long term sensory deprivation. For instance, restructuring of sensory neurons in the visual system has been documented after reversible "functional" deafferentations whereby the field of vision is temporarily restricted.[3] It is proposed that such neural retuning, as a result of either permanent or functional deafferentation, occurs due to several plasticity-based changes in the sensory system. These changes include: the unmasking of existing cortical connections, lack of local inhibitory connections, alterations in cell membrane excitability and synaptic efficacy.[4]

Subjective tinnitus, the percept of sound in the absence of external acoustic stimuli, affects 5–15% of the human population and is one of the most prevalent symptoms of hearing impairments.[5] Tinnitus has been shown to be loud and chronic enough to drastically influence quality of life.[5] In severe cases, it can have negative psychophysiological impacts that result in anxiety, depression, and insomnia.[6] An effective, universally accepted treatment approach that objectively reduces tinnitus symptoms does not exist. Studies have shown that the perception of tinnitus rises from the auditory cortex and the generation and persistence of tinnitus is related to maladaptive auditory cortex reorganization.[5] It is therefore speculated that such maladaptive neural structuring may be reversed by some form of functional deafferenatation.

OBJECTIVES

The overlying objective of this critical review is to determine if there is evidence to support that notched-sound therapy is an effective and practical treatment option for tinnitus. Thus, evidence evaluating whether exposure to notched-sound can induce plasticity-based alterations in the human auditory system, and whether such exposure affects tinnitus-related symptoms shall be reviewed.

METHODS

SEARCH STRATEGY

Computerized databases, including, Pubmed, CINHAHL, and Scopus were searched using the following strategy:

a ((noise) OR (sound) OR (music)) AND ((notched) OR (filtered) OR (windowed)) AND (tinnitus))
b ((noise) OR (sound) OR (music)) AND ((notched) OR (filtered) OR (windowed)) AND (human auditory cortex))

The results of these two search strategies were combined for evaluation of selection criteria and acceptance into this critical review. The search was limited to articles written in English and those studying humans only.

SELECTION CRITERIA

Studies selected for inclusion in this critical review paper were required to either investigate the impact of notched sound (digitally filtered at a specified frequency band) on the human auditory system and/or on tinnitus-related symptoms. Limitations were not set for which level of the auditory system was being evaluated (peripheral systems to cortices) or on a particular population of tinnitus sufferers. No limits were set on the demographics of research participants (aside from being human) or outcome measures.

DATA COLLECTION

Results of the literature search yielded the following 5 articles congruent with the aforementioned selection criteria: mixed groups randomized clinical trial (1), mixed groups pseudo-randomized clinical trial (2), mixed groups non-randomized clinical trial (2).

RESULTS AND DISCUSSION

RANDOMIZED CLINICAL TRIAL

Study #1: Lugli and colleagues performed a study evaluating the effects notched noise stimuli on patients' subjective ratings of tinnitus loudness (dB).[7] Participants recruited were unilateral and bilateral tinnitus patients with high frequency hearing loss of both gender ($n = 43$). Participants were randomly assigned to one of three auditory stimulation regiments: (1) broadband noise containing a notch centered at the individual's tinnitus frequency (WWN); (2) non-notched broadband noise (WN); (3) waterfall noise (Wa). Participants listened to their assigned auditory stimulation for 1.5–3 hours/day over a 1 year span.

Absolute and percentile changes of tinnitus loudness from baseline measures across groups were examined using the Kruskal-Wallis non-parametric analysis of variance. When significant differences between means were found, a multiple-comparisons procedure of the Kruskal-Wallis test was used to test the difference of mean values between pairs of treatments. Results showed that the mean final absolute change of tinnitus loudness between the three groups differed significantly ($H = 15.6$, $p < 0.001$). Multiple comparisons analyses revealed that final absolute change of tinnitus loudness was significantly larger in the WWN group than in the two controls ($p < 0.5$). There was not a significant difference between the two control groups. The final absolute tinnitus loudness decreased significantly by roughly 12 dB from baseline in the WWN group and non-significantly by roughly 2 dB in the two control groups. Importantly, upon completion of the treatment the perception of tinnitus was entirely eliminated in four of the twenty participants in the WWN group. None of the participants in either control group completely recovered.

Overall, the results of this study provide moderate support for a notched sound exposure as a potential treatment option for tinnitus sufferers and warrants future search in this area. However, the results fail to explain the underlying mechanisms of tinnitus loudness reduction or answer the current research questions. A lack of neurophysiological data limits the ability to correlate a reduction of tinnitus sensation to changes in the neurophysiology of the human auditory system. Moreover, a major limitation to the methodology of the study was that it failed to follow the participants longitudinally posttreatment. Therefore, it is unclear whether the reduction of tinnitus loudness is maintained, and to what degree, after prolonged exposure has ceased.

PSEUDO-RANDOMIZED CLINICAL TRIALS

Study #2: Okamoto et al conducted a study evaluating the effects of notched music on subjective tinnitus loudness and evoked activity in the auditory cortex.[8] The participants (n = 23) matched the following inclusion criteria: (1) chronic tinnitus; (2) unilateral/strongly lateralized tinnitus; (3) tonal tinnitus; (4) tinnitus frequency < 8kHz; (5) no severe hearing impairment; (6) no neurological or psychiatric complications.

Participants willing to participate in music training therapy were pseudo-randomly assigned to one of two notched music exposure groups: (1) target notched music, which was filtered centered at the participants' individual tinnitus frequency (n = 8); (2) placebo notched music, which was had a moving filter that avoided the individuals' tinnitus region (n = 8). Those unwilling to participate in music therapy due to time constraints were assigned to a monitoring group and received no treatment (n = 7).

Participants listened to notched music daily for 1 year. Listening times were recorded daily and approximated at 2 hours/day. Tinnitus loudness and magnetoencephalography (MEG) measures were taken at baseline and periodically throughout the study. MEG recordings used both a test stimulus frequency corresponding to the participants' individual tinnitus frequency and a control stimulus of 500 Hz; both N1m and auditory steady state (ASSR) measures were taken.

Methods of statistical analyses are not reported by the authors. The target group showed a significant reduction in tinnitus loudness after 12 months of treatment compared to baseline (F [1,7] = 26.1, P = 0.001). Also, there was a significant interaction between group (target vs. placebo) and time of measurement (baseline vs. average across 7–12 months) (F [1,14] = 5.9, P =0.030). However, the placebo and monitoring groups did not significantly differ from baseline measures of tinnitus loudness.

In the target group, both ASSR and N1m source strength ratios were significantly reduced after 12 months compared to baseline (ASSR: F [1,7] = 5.9, P = 0.045); N1m: F[1,7] = 24.6, P = 0.002). There was also a significant interaction between group (target vs. placebo) and time of measurement (baseline vs. month 12) for both ASSR (F [1,14] = 6.1, P = 0.027) and N1m (F [1,14] = 13.1, P = 0.003). There was not a significant difference between baseline and at 12 months for either the placebo or monitoring group for ASSR or N1m signal strength ratios. Reductions of all outcome measures (tinnitus loudness, ASSR, N1m) found in the treatment group were also significant by 6 months. Finally, there was a significant correlation between tinnitus loudness change and auditory evoked response ratio change of the ASSR (r = 0.69, p = 0.003), but not for the N1m.

In summary, the treatment group showed significant reductions in both tinnitus loudness and auditory cortex evoked activity relative to baseline. Such results appear to provide plausible evidence for the current research question. The authors conclude that the decreased evoked cortical activity, as represented by the MEG recordings, reflects a reduction of pathological auditory neural activity corresponding to the tinnitus frequency. Such a reduction subsequently led to reduced tinnitus loudness. The authors do however fail to speculate on nonsignificant correlation between tinnitus loudness and the N1m measures.

Despite these positive findings, the results should be interpreted cautiously. The authors failed to utilize a randomized clinical trial and due to participant refusal, used a monitoring group. Moreover, they fail to specify how the participants were pseudorandomly designated to either the treatment or placebo group. Therefore, possible confounding variables are left unknown and we are forced to render their control groups as meaningless. The authors also failed to provide any description of statistical analyses used. It is also curious that they omitted any reference to data concerning the control carrier frequency of 500 Hz used in the MEG recordings.

Study #3: A paper by Stracke and colleagues presents data that went unpublished from their original paper: the aforementioned Study # 2.[9] This publication presents the effects of notched music on the perceived annoyance and handicap of tinnitus. As in Study #2, the methods of statistical analyses are not provided by the authors. Compared to baseline, the target group reported significantly less tinnitus annoyance and tinnitus-related handicap upon completion of therapy. Those in the placebo and monitoring groups did not report a significant reduction of these two measures.

In summary, the participants in the treatment group from Study #2 not only had reduced auditory cortical activity and tinnitus loudness, they also reported less annoyance and handicap experienced by the tinnitus. This supports that such treatment may be effective at improving tinnitus symptoms on a global scale and lends support to such a regiment as a possible form of tinnitus management. Moreover, it also strengthens the association between cortical activity and tinnitus perception. However, these results remain questionable for the aforementioned methodological limitations discussed in Study # 2.

NON-RANDOMIZED CLINICAL TRIALS

Study #4: Teismann, Okamoto, and Pantev (2011) evaluated the effects of notched music on subjective tinnitus loudness, tinnitus-related distress, and cortical evoked activity.[10] Moreover, the study assessed whether the perceived pitch of tinnitus affects the efficacy of notched music therapy based on the above outcome measures.

Participants (n = 20) with chronic, tonal tinnitus who did not have severe hearing losses were recruited for the study. Participants were separated into a low tinnitus frequency group (<8 kHz) and a high tinnitus frequency group (>8kHz) based on pitch matching tasks. Participants were exposed to music notched at their individual tinnitus frequencies. They were instructed to listen for three hours on day 1 and 5 and for six hours on days 2–4. MEG recordings (both ASSR and N1m source strength ratios) were taken using a carrier stimulus corresponding to the participants' individual tinnitus frequency and a 500 Hz control stimulus. For patients with tinnitus frequencies above 8 kHz, auditory evoked fields could not be measured with sufficient quality and were thus not included in statistical analyses.

Planned t-tests were used to compare outcome measures from baseline to specified intervals posttreatment within each group. For the low frequency group, significant reductions were found in at least one outcome measure at all intervals post-treatment. At 3 hours post-treatment there was a significant reduction in tinnitus loudness (t = –2.3, p < 0.03), but no other outcome measure. At 3 days post-treatment there was a significant difference reduction in N1m ratios (t = –2.14, p < 0.02). There was no significant change in tinnitus loudness, tinnitus-related distress, or ASSR ratio. At 17 days post-treatment there were significant reductions in tinnitus-related distress (t = – 2.11, p < 0.02), tinnitus loudness (t = -2.15, p <0.02), and N1m ration (t = -1.97, p < 0.03). There was not a significant difference in ASSR ratio. At 31 days post-treatment there was a significant reduction in tinnitus-related distress (t = 2.38, p < 0.01), but not in any other outcome measure. For the high frequency group, there was not a significant change in tinnitus-related distress or tinnitus loudness at any of the four points measured compared to baseline. A possible reason for the null results in this group, suggested by the authors, is that the music contained little high frequency energy. Future research with this population should include high frequency enriched stimuli.

It is evident from results across the follow-up measurements post-treatment that both the subjective ratings of tinnitus symptoms and MEG measures are inconsistent across days. The authors speculate that tinnitus loudness reduction did not persist past 3 days because the treatment program was uniquely short. Thus, the neuronal activity reduction, observed by the N1m, was merely functional and thus only temporary. They go on suggest permanent structural changes may require extended treatment periods. This is supported by evidence from treatment programs for other diseases associated with maladaptive brain plasticity such as phantom limb pain. Whether such permanent neural changes can occur through notched sound exposure can occur in the human auditory system remains unanswered. Importantly, whether such structural changes correlate to a reduction in tinnitus-related symptoms remains to be seen. Thus, although the results of this study warrants future research into the relationships between neural reorganization, the auditory cortical tonotopic map, notched sound, and tinnitus treatment, they provide only plausible evidence at this time. Moreover, the study has several limitations such as failure to utilize a randomized, double-blind procedure with a control group and small sample size relative to the large percentage of tinnitus sufferers in the population.

Interestingly, the authors also speculate on the lack of ASSR reduction in all post-treatment measurements. ASSR source strengths were found to decrease after a more lengthy notched sound treatment in study # 2. Therefore, it the primary auditory cortex (ASSR) may require longer periods of treatment for plastic changes to be observed compared to the non-primary auditory cortex (N1m). What is evident from this prediction is that the plastic nature of the human auditory system is not yet well understood. More research is needed addressing the precise neural changes as a result of notched sound exposure, and what changes, if any, are most associated with the perception of tinnitus.

Study #5: Pantev et al examined the effects of notched music on cortical neural activity.[11] Participants (n = 10) between the ages of 25–50, with normal hearing and no history ontological or neurological disorders were recruited. Participants listened to 3 hours of music notched at 1 kHz. Immediately before and after music exposure, MEG recordings were taken using both a test stimulus of 1 kHz and a control stimulus of 500 Hz. This procedure was repeated on three consecutive days. Both the global source power averaged over the sensory array (RMS) and the dipole moment (Q) were the principal parameters used in this study.

An analysis of variance evaluated main effects of the variables days (1–3), stimuli (test/control), before/after functional deafferentation. The RMS field values and dipole moment were assessed using pre-planned *t*-tests contrasting test and control stimuli before and after listening to notched music. There was a significant interaction of before/after with stimulus (test/control) was found for Q (F[1,9] = 6.71, P = 0.029) *T*-tests of measurements taken before and after notched music were not significant for the control stimulus when applied to Q (t[9] = 0.894, p = 0.394) or RMS (9t[9] = –0.447, p = 0.665). For the test stimulus, Q diminished significantly after listening to notched music (t[9] = –3.30, p 0.009). Similar results were also significant for RMS, but only after applying higher significance levels ($p < .10$). For the test stimulus there was also a significant interaction between days and before/after F(2,18) = 3.76 (p = 0.043). It was discovered that the RMS measures decreased after the second and third days of music exposure, but not the first. There were no significant main effect or interactions concerning days and before/after for the control stimulus. Finally, upon completion of this study, two participants repeated the same study except that the control and test frequencies had been reversed. There were no significant effects.

The authors were able to use MEG recordings to measure short-term plastic changes after periods of brief functional deafferenation. These results were both cumulative and temporary. The reduction of cortical activity was more pronounced on days two and three of exposure; however, after each 24 hour period, values returned to baseline. These results are only suggestive and do not provide strong evidence that notched music treatment can induce permanent neural reorganization; or if such reorganization has any impact on tinnitus symptoms. Finally, their null results in experiment two is not surprising due to the number of participants. However, to be considered a treatment options, the method must be flexible to a variety of individual tinnitus frequencies. A counterbalanced, crossover, randomized, controlled study, which uses multiple test frequencies is needed.

CONCLUSION AND CLINICAL IMPLICATIONS

The underlying rationale behind the studies under review are that by targeting auditory cortex neurons that code for tinnitus frequencies, through customized notched sounds, maladaptive neural structuring that is causing tinnitus perception may be remedied. Indeed, where applicable, the authors of these studies attribute their positive to results to the ability of notched sound to reduce the excitability of hyperactive auditory neurons. This reduction would be caused by strengthening weakened inhibitory networks in the critical tinnitus frequency band. Such suggestions remain purely speculative and rest heavily on studies of animals and other sensory systems. Although these studies provide some evidence that notched sound exposure can reduce auditory cortex activity, MEG measurements represent large areas of the nervous system and should be interpreted with caution. The MEG results across studies were inconsistent. In the studies of notched sound exposure lasting only several days, such reductions in cortical activity were not maintained and in some cases not measurable. In both studies of 1 year, an adequate assessment of cortical activity post-treatment was not obtained. Therefore, it remains unclear whether such reductions can be sustained. Similar to the neurophysiological results, the subjective ratings of tinnitus symptoms were inconsistent across studies and whether a reduction of symptoms in these participants was maintained is unknown. It is also important to consider the overt methodological limitations, which were largely consistent amongst the studies under review. The lack of longitudinal randomized controlled studies, disclosure of statistical methods, and omission of many important statistical data renders the results of these studies questionable.

Indeed, a customized notched sounds treatment, if feasible, would be a cost effective and perhaps even enjoyable (music) form of tinnitus treatment. However, there is not yet enough evidence to support that such a form of treatment is ready for clinical implication. The studies that have attempted to study the efficacy of such a treatment remain too few and inconsistent. The studies under review differed in many ways including: forms of notched sound (noise vs. music), tinnitus loudness and frequency matching, length of exposure, outcome measures, and participant inclusion (hearing thresholds, tinnitus characteristics, and age). The latter point is significant clinically as what population such a treatment option would be successful for, if at all, remains unknown. Important to the audiology profession, if those with both and hearing impairments and tinnitus could benefit from this treatment is important. Whether or not such treatment could be used while wearing hearing aids is also an avenue for future research. This of course after the more conclusive evidence to suggest that notched sound can indeed restructure maladaptive neural networks associated with the perception of tinnitus.

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