bioRxiv preprint doi: https://doi.org/10.1101/2022.11.28.518290; this version posted November 29, 2022. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

Bimodal stimulation for the reduction of tinnitus using vibration on the skin

Michael V. Perrotta[1*], Izzy Kohler[1*], David M. Eagleman[1,2]

[1]*Neosensory, Palo Alto, CA*
[2]*Department of Psychiatry and Behavioral Sciences, Stanford University School of Medicine, Stanford, CA 94304*
[*] *these two authors contributed equally*

Abstract

Tinnitus (ringing in the ears) affects 1 in 10 adults in the United States, often with damaging psychological consequences. Currently, there exists no cure for most forms of tinnitus. Recently, bimodal stimulation – the pairing of sounds with haptic stimulation – has shown efficacy in reducing the symptoms of tinnitus. Previous bimodal stimulation approaches have used electrical shocks on the tongue, a technique that requires daily in-person sessions at an audiologist's office. We here show that excellent results can be achieved wearing a wristband with multiple vibratory motors. Tones are played and the wristband correspondingly vibrates the wrist of the user at different spatial locations depending on the frequency of the tone. We compared the experimental group with a control group who listened to the tones but did not wear the wristband. The tone frequencies were centered on each user's tinnitus frequency and the tones were randomized both in frequency and duration. 45 participants with Tinnitus Functional Index (TFI) scores of 25 and above were tested. Results show a significantly greater reduction in TFI scores for the experimental group compared to the control. Importantly, with higher baseline severity we find larger differences between the experimental and control groups, revealing greater symptom improvement for those with severe tinnitus. The therapeutic approach of combining sounds with spatially- and temporally-correlated vibrations on the wrist is found to be a simple, time-efficient, and effective procedure to lessen the symptoms of tinnitus.

Introduction

Tinnitus presents as a ringing in the ears. It can be underlain by various etiologies (such as noise-induced hearing loss, sinus infections, and Ménière's disease) and can express in different ways (ringing, static, pulsatile, etc). Tinnitus affects 21.4 million adults (9.6%) in the United States, a third of whom experience near-constant symptoms (Bhatt, Lin, and Bhattacharyya 2016). Tinnitus occurs in over 1 in 4 Americans between the ages of 65 and 85 (KochKin, Tyler, and Born 2011). Tinnitus is correlated with a variety of comorbidities, including hypertension and depression (Park et al. 2022). No treatment currently exists to completely remove tinnitus. Treatments which help alleviate the symptoms of tinnitus include counseling (e.g. cognitive behavioral therapy), pharmacological treatments (e.g. lidocaine), hearing aids, sound masking, and brain stimulation (e.g. transcranial magnetic stimulation) (Langguth et al. 2013).

Bimodal stimulation is a relatively new treatment used to alleviate the symptoms of tinnitus. Researchers demonstrated that pairing auditory tones with small shocks on the tongue reduced the symptoms of tinnitus (Marks et al. 2018; Riffle et al. 2021, Conlon et al. 2022). Shocks on the tongue were used based on the hypothesis that the key to bimodal stimulation was activity in the dorsal cochlear nucleus, where information from the ears first converges with haptic stimulation from the head and neck; therefore, tactile stimulation of the tongue seemed to be the appropriate haptic input. Next, other researchers demonstrated that bimodal stimulation works with a variety of timing characteristics between shock

bioRxiv preprint doi: https://doi.org/10.1101/2022.11.28.518290; this version posted November 29, 2022. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

and tone and that the treatment had high compliance and satisfaction rates (Conlon et al. 2020, 2022), although it should be noted that this paper did not present a control group.

We set out to determine whether tones combined with haptic stimulation – not on the tongue but on the skin of the wrist – would work just as well. If so, this would challenge the hypothesis that the bimodal signals need to converge at the dorsal cochlear nucleus, and would provide an easier treatment modality for the reduction of tinnitus.

Methods

We recruited adults in the United States via an online advertisement for a study investigating a new tinnitus treatment. Interested participants completed the Tinnitus Functional Index questionnaire (TFI) (Meikle et al. 2012; Henry et al. 2016) and were included if they scored 25 points or higher. A total of 45 participants were randomly assigned to the experimental condition (bimodal stimulation with tones + wristband) or a control condition (tones only).

Each participant completed ten minutes of daily treatment over the course of the eight-week study. The treatment included listening to tones and, unless in the control condition, feeling corresponding vibrations on the wrist. All participants completed the TFI questionnaire each week during the eight-week period.

Tones were presented from a phone app in a random order and with random timing. Each tone had a duration between 150 ms and 350 ms with an inter-tone silence of 0 ms to 500 ms. Each tone played without replacement before repeating the sequence in a newly shuffled order. The range of tone frequencies was set to be specific to the participant's main tinnitus frequency, which was collected in the app before the start of the study; their tinnitus frequency was set as the center of their individualized tone range. During treatment, 120 tones per minute were played at frequencies spread logarithmically between an octave above and below each participant's customized tinnitus frequency.

Treatment was administered through a phone app (sounds) and wristband (vibrations on the skin). Participants opened the app and listened to tones for ten minutes each day. Experimental participants listened to tones while feeling corresponding vibrations on their wristband (Figure 1). The app played the tones while sending spatially and temporally corresponding vibrations to the wristband via Bluetooth. These vibrations were spread evenly across the wrist in a logarithmic manner, such that an octave spanned the same spatial distance regardless of its frequency. Although the wristband has only four vibrating motors, frequencies were mapped onto one of 256 different spatial locations, accomplished by leveraging a haptic illusion (Alles 1970; Rahal, Cha, and El Saddik 2009; Luzhnica et al. 2017). Specifically, an illusory location is a point on the wrist that is felt by the wearer of the wristband even when a motor is not located directly at that point. We stimulate these illusion locations by turning on two motors, one on either side of the illusion location, at specific amplitudes such that the wearer feels as if a single point somewhere between the two motors is vibrating.

Figure 1. Bimodal stimulation. Tones are played from a phone app; a haptic wristband vibrates simultaneously with each tone. The location of the vibration is a function of the frequency of each individual tone, such that the frequency map is spread across the skin. Participants in the control condition listened to tones from the phone app but did not receive a wristband and were given no haptic stimulation.

bioRxiv preprint doi: https://doi.org/10.1101/2022.11.28.518290; this version posted November 29, 2022. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

The audio-only control participants did not receive a wristband and only listened to the tones without feeling any vibration.

Results

Participants in the experimental group (tones paired with simultaneous vibrations of the wristband) showed a clinically-significant average improvement in TFI scores of -17.9 (SD = 18.17, n = 22, p<.001, two-tailed t-test; **Figure 2A**). Interestingly, the audio-only control group also showed a significant difference from baseline of -7.5 (SD = 15.35; n = 23; p=.03, two-tailed t-test); however, it is important to note that a change in TFI score of less than -13 is not considered clinically significant (Meikle et al. 2012), so while the audio-only control showed a change, it was not clinically meaningful. The difference between the experimental and control groups was statistically significant (t(43) = 2.10, p=.04).

Importantly, participants who started the study with greater severity of tinnitus (as measured by their baseline TFI score) experienced greater improvement from the bimodal stimulation. The difference between experimental and control groups increased with higher baseline TFI scores: for baselines of 50 and above, the experimental group averaged -21.8 (SD=14.6; n=18; p<.001) while the control group averaged -4.6 (SD=15.0; n=18; p=.24); the significance of the difference increased to p=0.002 (two-tailed, t(32) = 3.39).

Meikle (2012) defined tinnitus as a “significant problem” in the TFI range from 25 to 50 and “severe” for any score above 50 points. In a more recent analysis of the TFI score distribution, "lower moderate" tinnitus was between 18 and 42 points, "upper moderate" was between 42 and 65 points, and "high" is any score higher than 65 points (Gos et al. 2021).

The correlation of a larger reduction with a higher TFI baseline can be seen by plotting improvement of each participant against baseline TFI score (**Figure 2B**). This effect is not present with the control group.

For participants with baseline TFI scores 50 or above, the weekly progression of their score is shown over 8 weeks in **Figure 3**. In the experimental condition, 91% of these participants showed improvements (in the negative direction) over the 8 weeks, and 64% of those improvements qualified as clinically significant (TFI score reduction of 13 points or greater; Meikle et al. 2012). In contrast, in the control group, 52% of the participants showed improvements (in the negative direction) over the 8 weeks, and 30% of those improvements qualified as clinically significant.

bioRxiv preprint doi: https://doi.org/10.1101/2022.11.28.518290; this version posted November 29, 2022. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

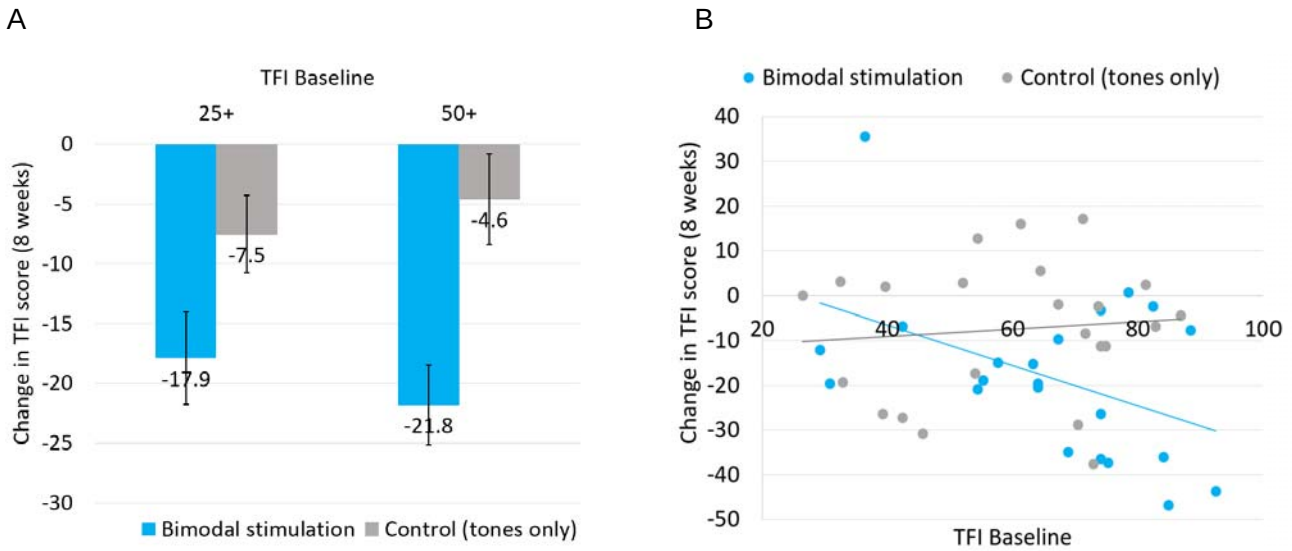

Figure 2. Bimodal stimulation with the wristband lowers tinnitus symptoms, especially for those with upper-moderate to severe tinnitus. (A) *The average change in TFI score after eight weeks of treatment was significantly greater for experimental participants when compared to tone-only control participants (left; p=.04). When performing this comparison only on participants with TFI scores greater than or equal to 50, the difference is greater and more statistically significant (right; p=.002). Error bars show SEM.* ***(B)*** *Change in TFI score after 8 weeks of treatment plotted against baseline TFI score. For the experimental group, a higher baseline TFI score predicts a larger improvement. The same correlation was not present in the control group.*

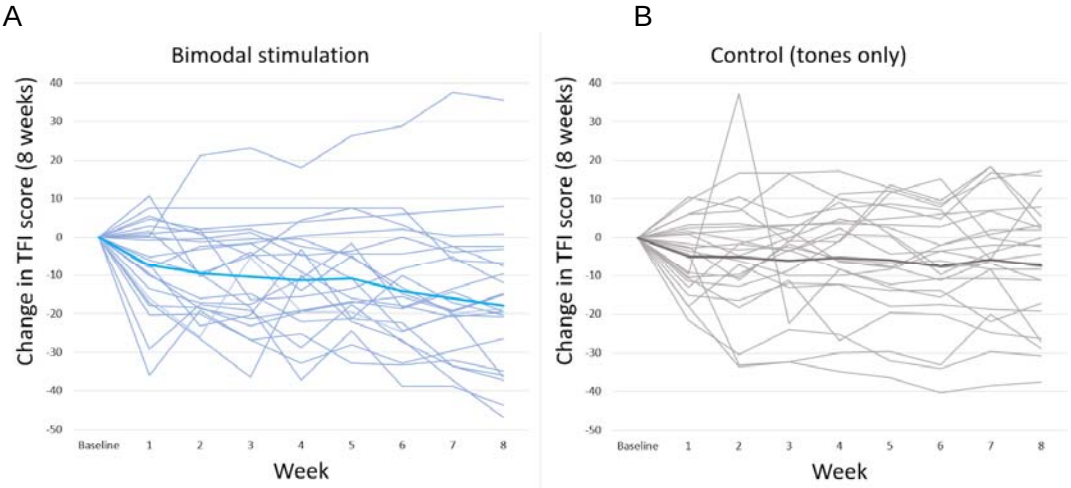

Figure 3. Changes from TFI baseline over 8 weeks for upper-moderate and severe tinnitus.
(A) Experimental group (tones + vibrations). (B) Control group (tones only). Shown in both panels are participants with a baseline TFI score 50 and above (scores were between 52.0 and 92.4). Individual participants are shown as thin lines and the average as thick lines.

We note that many participants in both the experimental and control groups had large variance in their TFI scores week to week. Presumably, this is at least partially a function of the broad range of tinnitus etiologies. Although we searched, we found no significant correlations between self-reported tinnitus etiology (or any other collected demographic data such as age, duration of tinnitus, or hearing loss) and TFI score change.

bioRxiv preprint doi: https://doi.org/10.1101/2022.11.28.518290; this version posted November 29, 2022. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

Discussion

We found improved TFI scores for both the experimental (tones and vibration) and control (tones only) groups. However, only the experimental group's average TFI improvement was clinically significant (greater than 13 points).

Importantly, individuals with a greater severity of tinnitus at baseline experience a larger improvement in their tinnitus with bimodal treatment (**Figures 2 and 3**). For example, participants starting at a baseline TFI score of 50 or above demonstrate an almost five-fold greater improvement than those treated with tones only.

It is worth noting the size of the effect in the audio-only control experiment. It has long been known that there is a placebo effect in tinnitus treatments (Duckert and Rees, 1984), and our control-group results are presumably an expression of that. However, despite the effect of tones alone, the result was not clinically significant, and it was significantly smaller than tones-plus-haptics.

The experimental group showed improvements in their TFI score that match or exceed previous research employing electric shocks on the tongue instead of vibrations on the wrist. Conlon et al. (2020, 2022) found TFI improvements at week 12 between -10 and -15 points for three experimental groups, while Marks et al. (2018) found an average TFI improvement of -8 points over 4 weeks. In comparison, our experimental group showed improvement of -14.3 for all participants, and -21.8 for those with moderate to severe tinnitus (baseline TFI score 50+).

Among other things, these results suggest that convergence of neural signals at the dorsal cochlear nucleus (where auditory signals first converge with haptic signals from the head and neck) is not the site of action of the improvement, as the same average TFI improvement is found with stimulation at the wrist. Thus, the current findings open the door to an easier and less expensive method of tinnitus treatment.

Conclusion

We have demonstrated that bimodal stimulation using audio tones (individualized to a participant's tinnitus frequency) combined with spatially-corresponding vibrations on the wrist can significantly reduce the symptoms of tinnitus more than a control treatment of tones alone. Those with more severe tinnitus at baseline experience larger improvements, almost five times that of the control group.

References

Alles, David. 1970. "Information Transmission by Phantom Sensations." *IEEE Transactions on Man Machine Systems*. https://doi.org/10.1109/tmms.1970.299967.

Bhatt, Jay M., Harrison W. Lin, and Neil Bhattacharyya. 2016. "Prevalence, Severity, Exposures, and Treatment Patterns of Tinnitus in the United States." *JAMA Otolaryngology--Head & Neck Surgery* 142 (10): 959–65.

Conlon, Brendan, Berthold Langguth, Caroline Hamilton, Stephen Hughes, Emma Meade, Ciara O. Connor, Martin Schecklmann, et al. 2020. "Bimodal Neuromodulation Combining Sound and Tongue Stimulation Reduces Tinnitus Symptoms in a Large Randomized Clinical Study." *Science Translational Medicine* 12 (564). https://doi.org/10.1126/scitranslmed.abb2830.

Conlon, Brendan, Caroline Hamilton, Emma Meade, Sook Ling Leong, Ciara O Connor, Berthold Langguth, Sven Vanneste, Deborah A. Hall, Stephen Hughes, and Hubert H. Lim. "Different bimodal neuromodulation settings reduce tinnitus symptoms in a large randomized trial." *Scientific reports* 12, no. 1 (2022): 1-18.

Duckert, Larry G., and Thomas S. Rees. 1984. "Placebo Effect in Tinnitus Management." *Otolaryngology–Head and Neck Surgery*. https://doi.org/10.1177/019459988409200618.

Gos, Elzbieta, Joanna J. Rajchel, Beata Dziendziel, Justyna Kutyba, Katarzyna Bienkowska, Weronika Swierniak, Maria Gocel, Danuta Raj-Koziak, Piotr H. Skarzynski, and Henryk Skarzynski. 2021. "How to Interpret Tinnitus Functional Index Scores: A Proposal for a Grading System Based on a Large Sample of Tinnitus Patients." *Ear and Hearing* 42 (3): 654–61.

Henry, James A., Susan Griest, Emily Thielman, Garnett McMillan, Christine Kaelin, and Kathleen F. Carlson. 2016. "Tinnitus Functional Index: Development, Validation, Outcomes Research, and Clinical Application." *Hearing Research* 334 (April): 58–64.

KochKin, Sergei, Richard Tyler, and Jennifer Born. 2011. "MarkeTrak VIII: The Prevalence of Tinnitus in the United States and the Self-Reported Efficacy of Various Treatments." *Hear Rev 18.12* 18 (12): 10–27.

Langguth, Berthold, Peter M. Kreuzer, Tobias Kleinjung, and Dirk De Ridder. 2013. "Tinnitus: Causes and Clinical Management." *Lancet Neurology* 12 (9): 920–30.

Luzhnica, Granit, Sebastian Stein, Eduardo Veas, Viktoria

bioRxiv preprint doi: https://doi.org/10.1101/2022.11.28.518290; this version posted November 29, 2022. The copyright holder for this preprint (which was not certified by peer review) is the author/funder. All rights reserved. No reuse allowed without permission.

Pammer, John Williamson, and Roderick Murray Smith. 2017. "Personalising Vibrotactile Displays through Perceptual Sensitivity Adjustment." *Proceedings of the 2017 ACM International Symposium on Wearable Computers*. https://doi.org/10.1145/3123021.3123029

Marks, Kendra L., David T. Martel, Calvin Wu, Gregory J. Basura, Larry E. Roberts, Kara C. Schvartz-Leyzac, and Susan E. Shore. 2018. "Auditory-Somatosensory Bimodal Stimulation Desynchronizes Brain Circuitry to Reduce Tinnitus in Guinea Pigs and Humans." *Science Translational Medicine* 10 (422). https://doi.org/10.1126/scitranslmed.aal3175.

Meikle, Mary B., James A. Henry, Susan E. Griest, Barbara J. Stewart, Harvey B. Abrams, Rachel McArdle, Paula J. Myers, et al. 2012. "The Tinnitus Functional Index: Development of a New Clinical Measure for Chronic, Intrusive Tinnitus." *Ear and Hearing* 33 (2): 153–76.

Park, Hye-Min, Jinsei Jung, Jong-Koo Kim, and Yong-Jae Lee. 2022. "Tinnitus and Its Association With Mental Health and Health-Related Quality of Life in an Older Population: A Nationwide Cross-Sectional Study." *Journal of Applied Gerontology: The Official Journal of the Southern Gerontological Society* 41 (1): 181–86.

Perrotta, Michael V., Thorhildur Asgeirsdottir, and David M. Eagleman. 2021. "Deciphering Sounds Through Patterns of Vibration on the Skin." *Neuroscience* 458 (March): 77–86.

Rahal, Lara, Jongeun Cha, and Abdulmotaleb El Saddik. 2009. "Continuous Tactile Perception for Vibrotactile Displays." *2009 IEEE International Workshop on Robotic and Sensors Environments*. https://doi.org/10.1109/rose.2009.5355986.

Riffle, Travis L., David T. Martel, Gerilyn R. Jones, and Susan E. Shore. 2021. "Bimodal Auditory Electrical Stimulation for the Treatment of Tinnitus: Preclinical and Clinical Studies." *Current Topics in Behavioral Neurosciences* 51: 295–323.