Synchronized Body and Acoustic Stimulation Induces Auditory Plasticity: Implications for a New Noninvasive Tinnitus Treatment

Cory D. Gloeckner, Benjamin T. Smith, Craig D. Markovitz, and Hubert H. Lim, *Member, IEEE*

Tinnitus, a neurological disorder in which a phantom sound is generated within the brain in the absence of an external sound source, affects about 250 million people worldwide and is debilitating for about 1% of the world population [1,2]. Tinnitus is caused by abnormal neural plasticity that occurs throughout the auditory system and has been linked to tonotopic reorganization, hyperactivity, and hyper-synchrony across neurons [2]. Currently, noninvasive treatments show mixed results across patients. Recent developments use invasive cortical, deep brain, and vagal nerve stimulation to modulate the neurons driving the tinnitus percept [3,4]. However, these treatments are available only to a subset of patients due to the surgical risks and costs associated with device implantation. We propose a new tinnitus treatment using noninvasive brain activation that targets specific neural populations in the auditory system through multimodal integration and can be implemented with a simple, low-cost device. Our approach, which we call Multimodal Synchronization Therapy (MST), utilizes electrical stimulation of different body regions synchronized with acoustic stimulation to induce auditory plasticity that could potentially fix tinnitus-affected neurons. To assess the feasibility of MST, we investigated the activation and plasticity effects of body and acoustic stimulation within the central auditory system in ten ketamine-anesthetized guinea pigs.

We positioned 32-site electrode arrays in different locations throughout the auditory midbrain (AM) and auditory cortex (AC), both of which have shown abnormal neural activity in tinnitus [2]. We recorded the activity within the AM and AC in response to electrical stimulation of different body regions with and without acoustic stimulation (broadband noise or pure tones; 50 ms duration) in a sound-attenuating electrically-shielded booth. Body stimulation consisted of biphasic electrical pulses (205 μs/phase, cathodic-leading) delivered through subcutaneous needle electrodes on the tongue, left & right mastoids, neck, left & right shoulders, back, left & right hind legs, and genital area. Following experiments, we performed histology and generated 3-dimensional computer reconstructions of our recording sites across the AM and AC. Signals were bandpass filtered (300-3000 Hz) for multiunit spikes, and Signal Detection Theory (d'=1) was used to test for significance.

Unexpectedly, we discovered a somatotopic map within the AM in which different body regions predominantly activate different AM regions in a systematic fashion. These findings suggest that we could potentially activate different body regions to modulate and alter different central auditory neurons. By combining body and acoustic stimulation, we were able to induce plasticity within different regions of the AM and AC including changes in spiking activity, neural synchrony, and tonotopic organization, which are all features that have been linked to tinnitus. In addition, we can alter the neural coding patterns by varying the time delay between the body stimuli and acoustic stimuli and by selecting different body stimulation locations.

Our discovery of a somatotopic map and the ability to modulate the auditory system through somatosensory activation is consistent with previous studies [2,5,6], and opens up an exciting opportunity for using MST to potentially treat tinnitus. Further studies are needed to assess how varying parameters can alter and suppress neurons actually driving the tinnitus percept. Since MST is noninvasive, we can potentially test its effects and optimize parameters directly in tinnitus patients.

REFERENCES

[1] ATA. American Tinnitus Association. http://www.ata.org/research/resources-researchers.

[2] A.R. Moller, B. Langguth, D. De Ridder, and T. Kleinjung. *Textbook of Tinnitus*, New York, NY: Springer Science+Business Media, 2011.

[3] S. Vanneste, and D. De Ridder. "Noninvasive and invasive neuromodulation for the treatment of tinnitus: an overview," *Neuromodulation*, vol. 15, pp. 350-360, 2012.

[4] N.D. Engineer, J.R. Riley, J.D. Seale, W.A. Vrana, J.A. Shetake, S.P. Sudanagunta, M.S. Borland, and M.P. Kilgard. "Reversing pathological neural activity using targeted plasticity," *Nature*, vol. 470, pp. 101-104, 2011.

[5] R.F. Huffman, and O.W. Henson. "The descending auditory pathway and acousticomotor systems: connections with the inferior colliculus, *Brain Res Rev*, vol. 15, pp. 295-323, 1990.

[6] S. Dehmel, S. Pradhan, S. Koehler, S. Bledsoe, and S. Shore. "Noise overexposure alters long-term somatosensory-auditory processing in the dorsal cochlear nucleus-possible basis for tinnitus-related hyperactivity?" *J Neurosci*, vol. 32, pp. 1660-1671, 2012.

This work was supported by start-up funds from the University of Minnesota (Institute for Translational Neuroscience and College of Science & Engineering), MD5M Lions Hearing Foundation, NSF IGERT DGE-1069104, and the Frieda Martha Kunze Fellowship.

C. D. Gloeckner is with the Biomedical Engineering Department, University of Minnesota, Minneapolis, MN 55455 USA (phone: 612-624-7342; e-mail: gloe0027@umn.edu).

B. T. Smith was with the Biomedical Engineering Department, University of Minnesota, Minneapolis, MN 55455 USA. He is now with the Medical School at University of Minnesota (e-mail: smit4283@umn.edu).

C. D. Markovitz is with the Biomedical Engineering Department, University of Minnesota, Minneapolis, MN 55455 USA (e-mail: mark0561@umn.edu).

H. H. Lim is with the Biomedical Engineering Department, Otolaryngology Department, and Institute for Translational Neuroscience, University of Minnesota, Minneapolis, MN 55455 USA (e-mail: hlim@umn.edu).