

CLINICIAN SCIENTIST AWARD 2014-2017

"Multi-Sensory Modulation of Tinnitus Correlates in Primary Auditory Cortex"

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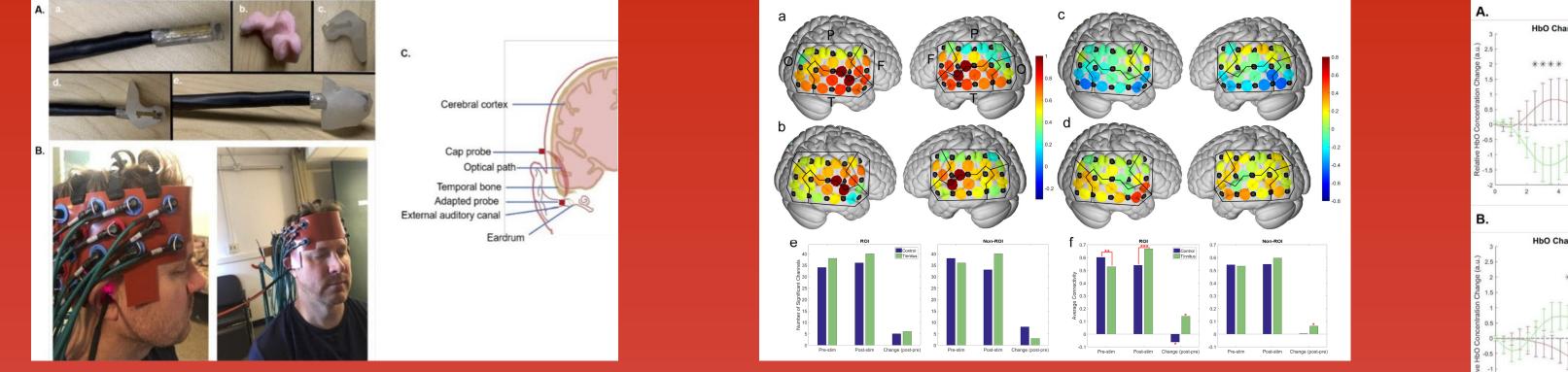
AMOUNT AWARDED BY AOS: \$240,000

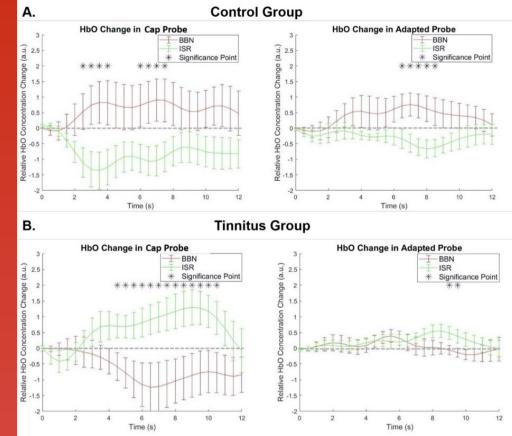
ONGOING FUNDING: National Institutes of Health R21-A1 5/1/2018-4/30/2020; \$411,211.00 No cost extension to 8/31/2020

PUBLICATIONS: Takacs J, Forrest T, Basura GJ. Noise Exposure Alters Long-Term Neural Firing Rates and Synchrony in Primary Auditory and Rostral Belt Cortices Following Bimodal Stimulation. *Hearing Research 356 (2017) 1-15.* Forrest TJ, Desmond TJ, Issa M, Scott PJH, and Basura GJ. Cholinergic Receptor Expression in Primary Auditory and Rostral Belt Cortices After Noise Damage. *Molecular Imaging 18 (2019) 1-11.*

RESEARCH SUMMARY: We demonstrated that auditory cortex (AC) neurons in an animal model of tinnitus can be regulated by spike-timing dependent plasticity. Specifically, if the somatosensory and auditory inputs into AC are paired, or staggered in input, the firing rates of AC neurons is changed and reflects the concepts of long-term potentiation and long-term depression. This suggests that tinnitus changes how AC are receptive to sensory inputs and depending on the timing of those inputs may influence neuron activity and possibly the contributions to phantom sound perception, subjective tinnitus.

OUTCOMES: Based on this fundamental basic science, funded by the AOS, I have transitioned these same questions into human translational work, whereby I am now measuring AC activity in human tinnitus using functional near infrared spectroscopy (fNIRS). This work has led to several key publications that show that we can use this tool to measure brain changes in human tinnitus that may be akin to those identified in the animal models noted above. As such, we have been able to replicate objective changes in human tinnitus in AC that may reflect the published spike-timing, or stimulus timing dependent plasticity in this case.





FURTHER FUNDING HAS ENABLED US TO EXPAND OUR RESEARCH TO: Tinnitus and Auditory Cortex; Using Adapted

Functional Near-Infrared Spectroscopy to Measure Neural Correlates in Humans (National Institutes of Health R21-A1).PI: Basura, Gregory; MD, PhD 5/1/2018-4/30/2020; \$411,211.00 No cost extension to 8/31/2020 Using fNIRS to study the human brain in tinnitus. Publications from this grant:

Zhai T, Ash-Rafzadeh A, Xiao-Su H, Kim, J, San Juan J, Filipak C, Islam M, Kovelman I, Basura GJ. Tinnitus and Auditory Cortex; Using Adapted Functional Near-Infrared-Spectroscopy to Expand Brain Imaging in Humans. *Laryngoscope Investigative Otolaryngology 16* (2020) 137-144.

San Juan J, Zhai T, Ash-Rafzadeh A, Hu X, Kim J, Filipak C, Guo K, Islam M, Kovelman I, Basura GJ. Tinnitus and Auditory Cortex; Using Adapted Functional Near-Infrared-Spectroscopy to Measure Resting State Functional Connectivity. *NeuroReport 32 (2021) 66-75*.

LAY SUMMARY OF FINDINGS AND IMPLICATIONS OF THIS RESEARCH: Using essentially pulse-oximetry for the brain (fNIRS); we have reliably objectified key neuron response patterns in the human AC in tinnitus that may, in part, contribute to phantom sound perception or tinnitus. The clinical implications of understanding where in the brain and to what extent objective neuron changes occur in human tinnitus is critical for designing possible therapies and future studies to better understand the etiology of this high debilitating problem.