

DRK Progress Report 3 (2020)

Grant Title: Photoneuromodulation: A Novel Therapy for Mild Cognitive Impairment

PI: Andreeana Haley, Ph.D., Associate Professor, The University of Texas at Austin, Austin, TX; **Co-I:** Francisco Gonzalez-Lima, Professor, The University of Texas at Austin, Austin, TX

A. Significance

This is a mechanism-driven translational research project to test the efficacy of a new intervention, photoneuromodulation through non-invasive transcranial infrared laser stimulation, to enhance brain function in older adults with Mild Cognitive Impairment (MCI). MCI is widely regarded as a transitional phase between normal cognitive aging and dementia with MCI patients converting to dementia at rates much higher than the general population (10-15% per year vs. 1-2% per year) (Petersen et al., 2001). Among patients with MCI, adults with impairments in multiple domains (e.g., memory + attention, executive, or psychomotor deficits) appear to be most vulnerable to further cognitive decline (Belleville et al., 2007; Broster et al., 2013; Mitchell et al., 2009). Considering the current lack of dementia cures, and the fact that cognition is the most important determinant of quality of life and functional ability in older age (Gaugler et al., 2009), it is critical to seek new treatments to prevent or delay severe cognitive impairment in this particularly vulnerable population.

B. Specific Aims

Aim 1: To determine if non-invasive transcranial infrared laser stimulation to the forehead can boost neurocognitive function in older adults with multi-domain MCI.

Aim 2: To test if the cognitive benefits of transcranial infrared laser stimulation in adults with multi-domain MCI are mediated by treatment-related changes in cerebrovascular response to a cognitive challenge.

These aims have not been modified from the original application.

C. Studies and Results

Status: The project is ongoing with target completion date September 2020.

Preliminary Findings: Preliminary analyses of the pilot data revealed improved neurocognitive performance in older adults following a single transcranial laser treatment as well as repeated treatments. These changes were accompanied by reduced cerebrovascular response during a working memory task in the frontal lobe, possibly indicating increased oxygen extraction. Our preliminary findings have been presented during a symposium highlighting *Neuromodulation of Cognition, Emotion and Behavior* at the annual meeting of the American Psychosomatic Society, at the Texas Alzheimer's Research and Care Consortium (TARCC) meeting at the University of Texas as well as at the Texas Academy of Science (TAS), the Society for Advancement of Chicanos/Hispanics and Native Americans in Science (SACNAS) and the International Behavioral Neuroscience Society (IBNS). They were included in a manuscript published in the journal of Lasers in Medical Science.

Current Project Findings: Since the project was double blind during data collection (neither researcher, nor participant were aware of their treatment group assignment), we have only just begun analyzing the newly collected data including the participants with Mild Cognitive Impairment. The results are very exciting. We found that functional connectivity in the default mode brain network significantly increases after six weeks of laser therapy, relative to each participant's own baseline (this is not the case for the participants in the placebo condition). Evidence of disruptions in this large-scale network of interacting brain regions is reported in people with Alzheimer's disease. Our results indicate potential for improving vulnerable networks function with laser therapy in individuals with Mild Cognitive Impairment who are at increased risk for developing dementia. These results will be presented at the mid-year meeting of the International Neuropsychological Society (INS) in Vienna in June, 2020. Follow up analyses are planned to explore which areas of cognitive function are improved by this physiological change, whether these changes are clinically meaningful, whether initial network organization can predict treatment response, and whether treatment effects last beyond therapy discontinuation.

The support of the DRK for this project was acknowledged in each presentation/publication.

Publications:

1. Vargas, E., Barrett, D., Saucedo, C., Huang, Li-Da, Abraham, J.A., Tanaka, H., Haley, A.P., Gonzalez-Lima, F. (2017). *Beneficial neurocognitive effects of transcranial laser in older adults*. Lasers in Medical Science, 32(5), 1153-1162.

Oral and Poster Presentations:

1. Foret, J.T., Saucedo, C., Alexander, C., Weng, T., Hickson, B., Craddock, C., Gonzalez-Lima, F., Haley, A.P. (2020). Submitted to the mid-year meeting of the International Neuropsychological Society (INS), Vienna, Austria.
2. Haley, A.P., Barrett, D., Vargas, E., Pasha, E., Tanaka, H., Gonzalez-Lima, F. (2017). *Neuromodulation of Cognition through Transcranial Laser Stimulation*. American Psychosomatic Society (APS), 75th Annual Meeting, Seville, Spain
3. Saucedo, C., Alexander, C, Barrett, D.W., Gonzalez-Lima, F. (2018). *Laser-Enhanced Sustained Attention and Working Memory in Neurocognitive Disorders*. Behavioral Neuroscience Seminar, UT Austin, Austin, TX
4. Saucedo, C., Alexander, C, Barrett, D.W., Gonzalez-Lima, F. (2018). *Laser-Enhanced Sustained Attention and Working Memory in Neurocognitive Disorder*. Texas Academy of Science (TAS), Midland, TX
5. Saucedo, C., Alexander, C, Barrett, D.W., Gonzalez-Lima, F. (2018). *Infrared Laser Stimulation Enhances Sustained Attention and Working Memory*. International Behavioral Neuroscience Society (IBNS), Boca Raton, FL
6. Saucedo, C., Alexander, C, Barrett, D.W., Gonzalez-Lima, F. (2018). *Reversal of Age-Related Neurocognitive Decline by Transcranial Infrared Laser Stimulation*. Society for Advancement of Chicanos/Hispanics and Native Americans in Science (SACNAS), San Antonio, TX
7. Gonzalez-Lima, F, Saucedo, C., O'Donnell, C, Haley, A.P. (2019). *Augmentation of Cognitive Brain Functions with Transcranial Infrared Laser Stimulation*. Texas Alzheimer's Research and Care Consortium (TARCC), Austin, TX