PROJECT SUMMARY (See instructions): **Title: Transcranial light therapy and imaging of prefrontal cognition in PTSD**

Post-traumatic stress disorder (PTSD) is a neuropsychiatric disorder that can develop after exposure to a traumatic event. PTSD has a lifetime prevalence of approximately 8% in the general US population. Patients with PTSD often suffer from neurocognitive impairments involving attention, working memory and executive functioning, suggesting a close interrelationship among prefrontal cortex-based cognition, neural alterations and PTSD. While a variety of pharmaceutical treatments are available, long-term side effects are hard to avoid. It is highly desirable to develop an integrated neurotechnology for diagnosis and treatment that can deliver a non-invasive, neurophysiology-based intervention. We propose such an approach with the ability to simultaneously image underlying brain alterations in PTSD and stimulate hemodynamic, metabolic activities in the brain, leading to a less-invasive and more-effective therapy for PTSD.

Recent human studies have documented that **transcranial laser stimulation** in the near-infrared (NIR) wavelengths non-invasively induces cognitive-enhancing and brain-stimulatory metabolic effects. Thus, transcranial laser stimulation may become an effective, therapeutic means for treating cognitive dysfunctions of patients with neuropsychiatric disorders, such as PTSD. Also, functional neuroimaging is recognized as an objective measurement tool in PTSD and thus has the potential to improve diagnostic evaluation, to monitor therapy, and to predict treatment responses. In particular, advances in **diffuse optical tomography** (DOT) using near-infrared spectroscopy have shown the ability to non-invasively image cortical activities associated with prefrontal memory functions. This proposed research plans to integrate these two promising NIR techniques (NIR transcranial laser stimulation for cortical stimulation and NIR DOT for cortical imaging), which enables treatment of memory impairments in PTSD and mapping corresponding improvements by the intervention. The research team consists of multidisciplinary expertise in bioengineering, neuroscience, neuropsychology, social work, and clinical psychiatry from three UT institutions.

Working hypothesis 1: Prefrontal memory activities and functional connectivity in PTSD are abnormal or suppressed, as identified and imaged by near-infrared diffuse optical tomography (NIR-DOT).

Aim 1: We will obtain volumetric DOT images of prefrontal memory functions and functional connectivity from patients with PTSD and age- and gender- matched controls using a multi-channel NIR-DOT brain imager and graph theory analysis (GTA). We will then identify DOT-derived metrics reflecting abnormal patterns and characteristics in brain activities and cortical networks in PTSD.

Working hypothesis 2: Transcranial laser stimulation by near-infrared illumination targeted at the prefrontal cortex improves memory functions in PTSD.

Aim 2: We will map cortical activities and networks by NIR-DOT during and after transcranial laser stimulation in PTSD and control subjects, followed by identification of alterations of DOT-derived metrics induced by the intervention. We will also perform independent neuropsychological evaluations before and after the laser therapy and then correlate the behavioral results with the DOT-derived metrics to show neuro-physiological alterations and improved memory functions after laser stimulation in PTSD subjects.

The outcome of this seed-funded study will not only demonstrate the initial feasibility of a new therapeutic approach to PTSD treatment, but also offer possible insights into the cerebral-hemodynamic and neuro-physiological mechanisms of treating cognitive impairments in PTSD by transcranial laser stimulation.

RELEVANCE (See instructions): This new project plan assembles a strong and multidisciplinary UT team: PI Liu from Dept. of Bioengineering, UT Arlington, co-I Gonzalez-Lima from Dept. of Psychology and Inst. of Neuroscience, UT Austin, co-I Woon, from Dept. of Psychiatry, UTSW, and co-I Smith-Osborne from School of Social Work, UT Arlington. PI Liu has advanced experience and expertise in NIR-DOT brain imaging, co-I Gonzalez-Lima is an international leader in brain metabolic research on learning functions and has a successful record using transcranial laser stimulation in animals and humans, and co-I Woon from UTSW is a clinician with research emphasis in neuropsychological and neuroimaging studies of PTSD.

The novelty of this project includes the concept, experimental implementation, data analysis, and significance of the integration of two non-invasive, promising NIR neurotechnologies for treating memory impairments in PTSD and mapping corresponding improvements by the intervention. For the first time, the treated prefrontal memory function will be monitored and mapped in humans before, during, and after the transcranial laser stimulation, providing direct information on neurophysiological metrics and neural circuits that can be correlated with behavioral, neuropsychological evaluations. The outcome of this seed-funded study will offer possible insight into the underlying mechanism of treating cognitive impairments in PTSD by NIR transcranial laser stimulation, leading to larger-sized NIH and DoD grant funding successfully.