R01 MH131532 (PI: Suarez-Jimenez) 12/6/2022 – 10/31/2027

Funding agency: NIMH
Total Award Amount (including Indirect Costs): $3,269,560
Title: Using novel virtual reality tasks to identify neural mechanisms of discrimination learning in PTSD

Abstract:
Post-traumatic stress disorder (PTSD) is a highly prevalent and debilitating disorder. Despite efforts to characterize PTSD pathophysiology, no biomarkers have been established to aid in diagnosis, treatment development, and prediction of treatment response. New evidence poses that PTSD is mediated by dysfunctional discrimination of context/cues in both threat and reward processing, involving the hippocampus, nucleus accumbens, amygdala, and prefrontal cortex. Still, the contextual component, or the formation of mental boundaries of the environment (mental representations) that delineate threat/safety and reward/non-reward cues/signals within a single environment, and the neural circuits of these processes are yet to be studied in PTSD where contextual processing is often impaired. I have developed two virtual reality (VR) tasks to examine threat and reward discrimination, to assess the underlying mechanisms of learning valence discrimination within an environment using location-specific information. Briefly, the task used for this study consists of neutral (CS-) and threat or reward (CS+) areas, within a single environment, and participants must use spatial information to learn to discriminate between both areas. The task is designed to reveal brain regions involved in learning locations predictive of environmental reward. This research proposal aims to investigate brain activity differences between patients with PTSD (n=80), trauma-exposed controls without PTSD (TE; n=80), and healthy controls (HC; n=80). Functional magnetic resonance imaging (fMRI) during the VR paradigm will be used to clarify the neural mechanisms underlying threat and reward learning and discrimination processing across groups. Multiple levels of assessment will include multimodal MRI, coupled with peripheral measures of arousal (e.g., Skin Conductance Response), eye-tracking, and subjective ratings of learning. This is a first step to clarify the process of threat and reward discrimination learning within an environment, particularly to elucidate if the neural signatures are specific to valence signaling or to PTSD psychopathology in general. In the long term, this research will shed light on the specific role of brain areas needed for discrimination learning within an environment which will advance the development of effective diagnostics and treatments for PTSD and other psychopathologies.

Zhu's Role: site-PI

The goal of this NIMH R01 is to perform two novel virtual reality (VR) tasks to determine how threat- and reward-related cognitive maps are created in 240 subjects, including 80 patients with PTSD, 80 trauma-exposed controls, and 80 healthy controls, over four years. The principal investigator of this subcontract is Dr. Xi Zhu. Dr. Zhu will provide expertise in multimodal neuroimaging analysis, machine learning analysis. She will provide help in training students and RAs on imaging data collection, and imaging analysis, preparations of the study instruments, and ensuring the integrity of all reporting activities.

Collaboration with University of Rochester
Benjamin Suarez-Jimenez, Ph.D:
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