

Name: Jose Martinez-Magana
PI Name: Janitza Montalvo-Ortiz
Presentation preference: Poster

Email: jose.martinez-magana@yale.edu
PI email: janitza.montalvo-ortiz@yale.edu

The prefrontal cortex transcriptomic landscape of the interaction between post-traumatic stress disorder and opioid misuse

Jose Jaime Martinez-Magana^{1,2}, John Krystal^{1,2}, Mathew Girgenti^{1,2}, Traumatic Stress Brain Research Group, and Janitza Montalvo-Ortiz^{1,2}

¹Department of Psychiatry, Yale University School of Medicine; ²National Center for Posttraumatic Stress Disorder, VA Connecticut Health Care System

Background: Opioid use disorder (OUD) is a chronic and relapsing disorder. OUD has a significant impact on public health burden and is the cause of more than 100,000 annual deaths worldwide. Mental health problems have been considered risk factors for opioid misuse, including post-traumatic stress disorder (PTSD). Nevertheless, the biological mechanism underlying this association remains underexplored. The prefrontal cortex is one of the brain regions involved in regulating stress and substance-related behaviors, and previous studies have shown transcriptomic changes associated with these phenotypes.

In this study, we evaluated transcriptomic interaction between PTSD and OUD in four prefrontal cortex (PFC) brain regions [dorsal anterior cingulate cortex (dACC), dorsolateral prefrontal cortex (dlPFC), orbitofrontal cortex (OFC), and subgenual prefrontal cortex (sgPFC)].

Methods: Postmortem tissue from four prefrontal cortex subregions was collected from 138 individuals. We analyzed transcriptomic interaction with RNASeq and linear models implemented in the DESeq2 package.

Results: In the combined analysis, we found differences in the expression levels of *HSPA6* in the sgPFC and dlPFC. In the OFC and sgPFC we found *HSPA7*, *SOX7*, and *SERPINH1* differentially expressed. For the previous genes, in the sex-stratified analysis, we found *HSPA6* and *HSPA7* differentially expressed in dlPFC, OFC, and sgPFC only in females. Noteworthy, *IL1B* is differentially expressed only on the OFC in females. Meanwhile, in males, we found *SOCS3* in dACC and 22 genes in OFC (*SOX7*, *PRX*, *EPAS1*, *SLCO4A1*, *COL6A1*, and others).

Discussion: Our cortical transcriptomic findings suggest an effect of genes in the immune and vascular system associated with the interaction between PTSD and opioid misuse.