Taylor F. Fitzpatrick-Schmidt
L2
LSU Health Sciences Center, New Orleans, LA

Mentors: Scott Edwards, PhD and Patricia Molina, MD, PhD
Louisiana State University Health Sciences Center, Department of Physiology; Comprehensive Alcohol-HIV/AIDS Research Center; Alcohol and Drug Abuse Center of Excellence

Neurobiological consequences of chronic binge alcohol exposure and ovariectomy on markers of hippocampal plasticity in SIV-infected rhesus macaques

Human immunodeficiency virus (HIV) infection has profound impacts on the central nervous system, including HIV-associated neurocognitive disorder (HAND). HIV-associated cognitive deficits can be further exacerbated by alcohol consumption[1]. With the rising prevalence of alcohol use disorder (AUD) in females, understanding the neurobiological impact of AUD and HIV infection in this population is increasingly important[2]. The hippocampus is part of the brain's limbic system and plays prominent roles in both cognition and affective regulation. Thus, investigating hippocampal neuroadaptations in the context of comorbid HIV infection and AUD is critical for understanding the mechanisms of neurocognitive and affective impairment in patients.

Three hippocampal signaling pathways of interest in our lab are glucocorticoids, estrogen, and brain-derived neurotrophic factor (BDNF). Glucocorticoids represent a major stress hormone class and are released as a result of chronic alcohol use and withdrawal, potentially facilitating the progression to AUD. In contrast, estrogen and BDNF are neuroprotective and may be decreased as a result of chronic alcohol use, resulting in cognitive deficits. We hypothesized that simian immunodeficiency virus (SIV)-infected, ART-treated female rhesus macaques with a history of chronic binge alcohol (CBA) administration and ovariectomy (OVX) would demonstrate decreases in hippocampal BDNF and estrogen signaling, along with increases in glucocorticoid signaling (n=7-8 per group).

Preliminary western blot analyses (n=3 per group) were performed to examine phosphorylation of proteins and changes in total protein levels in each signaling pathway. We found that CBA administration significantly increased phosphorylation of extracellular signal-regulated kinase (ERK; $p=0.0126$), a marker of neuronal plasticity associated with BDNF and other pathways. Additionally, we discovered a trend for increased phosphorylation of the glucocorticoid receptor in the CBA group ($p=0.0569$), indicating a potentiation of stress signaling. Ovariectomy did not significantly alter phosphoprotein levels in any pathway. Future directions include completion of western analyses, examination of additional proteins in these pathways, and analyzing data from novel object recognition experiments, an operant learning task that serves as a measure of cognitive function. Our preliminary findings illustrate the therapeutic potential for reducing stress-related glucocorticoid signaling to combat hippocampal deficits produced by chronic alcohol use in people living with HIV.

1. Molina PE, Bagby GJ, Nelson S (2014) Biomedical consequences of alcohol use disorders in the HIV-infected host. Curr HIV Res 12**:**265-275.
2. Grant BF, Chou SP, Saha TD, Pickering RP, Kerridge BT, Ruan WJ, Huang B, Jung J, Zhang H, Fan A, Hasin DS (2017) Prevalence of 12-Month Alcohol Use, High-Risk Drinking, and DSM-IV Alcohol Use Disorder in the United States, 2001-2002 to 2012-2013: Results From the National Epidemiologic Survey on Alcohol and Related Conditions. JAMA Psychiatry.