Submitter Name: Drew D. Kiraly. Submitted Email: dkiraly@wakehealth.edu

Gut-brain signaling as a modulator of brain chromatin structure and gene expression in models of substance use disorder.

Drew D. Kiraly

Departments of Translational Neuroscience & Psychiatry, Wake Forest University School of Medicine, Atrium Health Wake Forest Baptist, Winston-Salem, North Caroliina 27104

Pathological substance use disorders lead to tremendous levels of morbidity and mortality worldwide. Despite extensive research into the neurobiology and pathophysiology of these conditions, treatment options remain limited, and those that do exist are ineffective for many. The need to identify novel strategies for treatment development for these conditions remains great. In recent years, there has been a growing body of evidence demonstrating that the resident flora of the gastrointestinal tract, collectively the gut microbiome, can play a key role in mediating the development of addiction-like behaviors in animal models of substance use disorders. This early evidence suggests that targeting the gut microbiome and its molecular byproducts may be a high value translational research strategy in the substance use disorder arena. This talk will highlight the ways in which manipulations of the gut microbiome affect similar measures of drug intake and seeking in models of cocaine and opioid use disorders. Depletion of microbial diversity with broad spectrum antibiotics leads to increased intake of low dose drug, increased effort to obtain drug, and increased seeking after abstinence. These behavioral findings will be coupled with detailed transcriptomics analyses highlighting microbiome effects on gene expression in the brain in response to drugs of abuse. Finally, mechanistic data highlighting microbial byproducts that can account for these effects will be discussed. Taken together, these findings will establish commonalities in microbiome effects on drug taking and seeking and will discuss potential paths forward for utilizing the microbiome as a translational research approach in substance use disorders.