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Dissection of Gut-Brain Signaling Pathways in Models of Cocaine Use Disorder With Single Cell Resolution

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Pathological substance use disorders are a set of recalcitrant neuropsychiatric conditions that 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. In particular, we have found that depletion of the gut microbiome results in increased cocaine intake and increased cocaine seeking behavior in models of relapse. Additionally, we have found that mice with depleted microbiota have markedly altered transcriptomic responses to cocaine in the key brain reward structure the nucleus accumbens.

In this presentation, we will present our newest data using single nucleus sequencing of the nucleus accumbens in control mice and those with their microbiome depleted with antibiotics after cocaine treatment. We find significant interactions in synaptic plasticity pathways in multiple neuronal populations, and also identify significant alterations in microglial activity markers. Altered transcriptomics will be related to behavioral findings, and mechanistic targeting of these pathways discussed. These findings will provide important mechanistic data that build on our previous behavioral and bulk transcriptomic work, and will seek to provide further mechanistic insight into critical gut-brain signaling pathways.

Hyperlink to relevant publication: https://pubmed.ncbi.nlm.nih.gov/37528220/

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