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Unraveling Transcriptomic Dynamics: Interplay of Opioid Use Disorder and Early Life Adversity in Distinct Brain Regions

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Opioid use disorder (OUD) presents a significant public health challenge with increasing rates of morbidity and mortality. Despite considerable efforts, effective pharmacological interventions for OUD remain elusive, underscoring the imperative for a deeper comprehension of its molecular basis. While various brain regions have been implicated in addiction-related behaviors, the precise transcriptional alterations underlying OUD within distinct brain regions are poorly understood.

In this study, we performed bulk-tissue RNA sequencing from rats undergoing initial heroin self-administration (or yoked saline control), with an initial focus on the nucleus accumbens (NAc), basolateral amygdala (BLA), and prefrontal cortex (PFC). Our analysis, conducted on the largest and most diverse cohort of its kind to date, uncovered extensive transcriptomic changes associated with initial heroin self-administration in rats of both sexes. Employing co-expression network analyses, we identified specific gene networks activated by heroin intake, elucidating changes in several biologically relevant pathways. We validated findings by comparing rat data with human opioid studies, revealing parallels in addiction-related transcriptional alterations.

Our pilot study, using RNA-seq in rats exposed to heroin, showed significant gene expression changes in addiction-related pathways. These results pave the way for understanding molecular mechanisms in adversity-related disorders, like heroin addiction, and potential therapeutic targets.

In conclusion, our integrated transcriptomics approach provides novel insights into the transcriptional landscape of OUD, offering innovative strategies for OUD prevention and intervention.