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Effects of oxycodone self-administration on gene and microRNA expression

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The opioid epidemic has been exacerbated by the COVID-19 pandemic, highlighting the critical need to explore the neurobiological underpinnings of Opioid Use Disorder (OUD) and develop novel treatments to combat the opioid epidemic. Exposure to opioids modifies the expression of addiction-related genes in the nucleus accumbens (NAc). In our study, we hypothesize that microRNAs, small non-coding RNAs, regulate gene expression changes following oxycodone self-administration. We trained male Sprague-Dawley rats to self-administer oxycodone or saline, and sacrificed them 24 hours after their last session. Their brains were extracted, snap frozen, and the NAc was isolated and processed for small RNA and RNA sequencing. To validate our sequencing results and investigate microRNA expression changes across addiction cycle stages and potential sex-dependent effects, we analyzed male and female NAc samples from the “Oxycodone Biobank” at the University of California, San Diego (UCSD). These samples were collected at various time points following oxycodone self-administration. Our sequencing analysis shows that oxycodone self-administration significantly altered the expression of 42 genes and 15 microRNAs. Bioinformatic analysis revealed that opioid-regulated genes are predicted targets of differentially expressed microRNAs, suggesting that microRNAs can contribute to opioid-induced changes in the gene expression in the NAc. Validation in an independent cohort indeed confirmed that some microRNAs and genes have dynamically regulated expression during opioid withdrawal, pointing to their involvement in the addiction cycle. Collectively, our findings indicate that microRNAs could play a role in regulating opioid-induced gene expression and highlight their potential as therapeutic targets for OUD.