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Differential Effects of Self-Administration of Opioid Receptor Agonists With Varying Potency on Exosomal Blood Serum and Orbital Frontal Cortex (OFC) Mirna Expression Patterns

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In the United States, opioid misuse has reached epidemic levels and poses significant public health challenges. Between 2016 and 2019, clinical studies reported over 115,000 overdose deaths linked to the synthetic opioid fentanyl. However, most preclinical studies have traditionally used the less potent opioid receptor agonists morphine or heroin and therefore few studies describe molecular alterations following fentanyl exposure. Our Lab previously reported that the brain microRNA profile is regulated by heroin and morphine in a dose-dependent manner and changes over time during abstinence from drug exposure. We hypothesized that fentanyl induces unique signatures of miRNA expression in the brain and blood that are distinct from opioids with less potency. This study aimed to examine a) the acute and long-lasting effects of fentanyl self-administration on exosomal blood serum and orbitofrontal cortex (OFC) brain miRNA expression and (b) compare the fentanyl-induced miRNA profiles to the less potent opioid heroin. This study will provide critical insight into both the immediate and long-lasting molecular consequences of fentanyl exposure to brain neurochemistry and identify miRNA-mediated pathways associated with opioid seeking, thus contributing to the broader understanding of the molecular mechanisms underlying opioid addiction and role of miRNAs in neuroplasticity and gene regulation