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Mitochondria-Related Nuclear Gene Expression in Reward Related Brain Regions and Blood Mitochondrial Copy Number after Developmental Fentanyl Exposure in Adolescent Male and Female C57BL/6 Mice

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Rapid escalation in the use of the synthetic opioid fentanyl both clinically and recreationally has yielded increased exposure to the drug in the general population including in utero exposure to fetuses during pregnancy, although the long term consequences for this type of exposure are not fully understood. Previous work has shown that developmental exposure to fentanyl via dam access to drinking water during gestation and lactation is sufficient to impact body weight and anxiety-like behaviors in adolescent offspring in C57BL/6 mice. Further, this exposure leads to long-lasting impairments in somatosensory circuit function and behavior. The current study examines the effects on gene expression in reward related brain regions (nucleus accumbens). Specifically, we examine genes related to mitochondrial function, as neuronal mitochondria in the accumbens have been shown to be responsive to other drugs of abuse (cocaine), and the function and metabolic output of mitochondria help to regulate neuronal excitation and signaling. Additionally, we examine how peripheral mitochondria in blood leukocytes are impacted by perinatal fentanyl to determine if changes in circulating blood are correlated to changes in behavior or brain gene expression. Blood mitochondrial copy number is reduced in male, but not female adolescent mice that were perinatally exposed to fentanyl and is promisingly correlated with both behavioral and NAc gene expression changes. The impacts of developmental fentanyl exposure on mitochondrial function in both the brain and body may prime the brain for altered reward-related behavior in adolescence and adulthood.

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