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Multi-omic long-term reprogramming after perinatal opioid exposure across brain regions: a hypothesis-generating study

Infants exposed to opioids in utero are at risk of developing Neonatal Opioid Withdrawal Syndrome (NOWS). Rodent models of perinatal opioid exposure can reliably recapitulate acute withdrawal and developmental deficits exhibited in clinical NOWS, but few persisting phenotypes are consistently observed between studies due to methodological variability. Our state-of-the-art methodology enabled low-input, high-throughput epigenomic profiling to conduct an unbiased screen for potential NOWS-related phenotypes. We integrated RNA-seq and ChIP-seq methods to translate high-resolution epigenomic data into functional context across development. Epigenomic data revealed alterations in immune and metabolic function and was highly correlated with molecular and behavioral data. We found decreased levels of brain and peripheral cytokines in opioid-exposed mice, both in early life and in adulthood. When exposed to a future immune challenge, these mice showed displayed a blunted behavioral sickness response. Several metabolic properties, including changes in weight and basal body temperature, were also altered. This is the first study to comprehensively characterize the long-term impacts of perinatal opioid exposure across multiple biological levels within the same drug exposure framework and addresses broader fundamental questions regarding how early environments shape lifelong health outcomes.

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