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Neonatal Opioid Exposure Alters Epigenomic Regulations of Immune Response Genes in Mouse Brain

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Populations affected by the opioid epidemic include pregnant women and their offspring. Infants exposed to opioids in utero are at risk of developing Neonatal Opioid Withdrawal Syndrome (NOWS), a combination of acute somatic withdrawal symptoms. Rodent models of NOWS have recapitulated deficits in development and behavior, but few studies have examined alterations in immune functioning. We developed a mouse model of prenatal opioid exposure that encompasses the developmental equivalent of all three trimesters of human pregnancy. Mice receive morphine throughout gestation and the first two post-natal weeks— a period that is equivalent to the third trimester of human pregnancy and includes major developmental processes in rodents, including immune system consolidation. To determine if perinatal morphine exposure alters subsequent immune response, mice received an LPS challenge in adulthood. Using low-input technologies, we profiled epigenomes (H3K27ac) and transcriptomes in neurons from prefrontal cortex for both sexes. The data were examined using differential analyses and Taiji which conducts integrative epigenomic and transcriptomic data analysis to assess the involvement of transcription factors. In utero morphine exposure leads to suppressed immune response when mice are challenged by LPS in adulthood. Such suppression involves alterations in both epigenomic and transcriptional regulatory networks. These data indicate that early-life opioid exposure appears to impact neuroimmune response.