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# Prenatal THC Exposure Alters the Offspring Methylome, Neurodevelopment, and Emotional Behavior

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Cannabis is commonly used in pregnancy, but currently there is insufficient evidence to establish a direct association between maternal THC use and offspring outcomes. The objective of this study was to examine the impact of chronic perinatal THC exposure on neonatal and infant neurodevelopment and behavior in a rhesus macaque model. Female rhesus macaques (n=8) were divided into 2 groups, control (CON, n=4) and THC-exposed (n=4), through a daily THC edible (2.5mg/7kg/day, ~ heavy medical cannabis dose). All animals underwent time-mated breeding and were delivered naturally at term. Infant neuroimaging was performed on postnatal day (P)30 and P180, behavioral testing (motor and emotional assessments) was performed on P30 and P120, and necropsy and brain tissue collection for whole genome bisulfite sequencing and RNA-sequencing was performed on P180. Infants exposed to THC *in utero* displayed signs of increased stress and anxiety, including higher cortisol levels, significantly greater vocalizations in response to novel stimuli ($p=0.0017$), and difficulties with parental separation. Brain MRI revealed higher fractional anisotropy in the corpus callosum and centrum semiovale in THC-exposed infants ($p<0.05$). In our rhesus macaque model, prenatal exposure to THC was associated with an adverse effect on infant emotional behavior including greater anxiety and decreased independence, altered fetal brain DNA methylation at genes involved in neurodevelopment, and changes in brain microstructure seen in individuals with autism spectrum disorder that may have long-term implications for offspring outcomes. Further studies are needed to determine whether these findings in early childhood correlate with long-term neurodevelopmental health.