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The effect of prenatal cannabinoid exposure on developing primate cerebrum

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As marijuana consumption increased among pregnant women, it is determinant to understand its effect on offspring's brain development. Cannabinoids act through the endocannabinoid signaling (ECS), whose dysregulation in the fetal brain, due to maternal cannabis abuse, is associated to increased risk for neuropsychiatric diseases in the child. However, which molecular mechanisms underlying the development of the neocortex, involved in our unique cognitive capabilities, are disrupted by maternal cannabinoid consumption remain elusive in human.

The effect of ECS perturbation on the molecular events regulating corticogenesis has been addressed mainly in rodents. However, primate's brain is more complex, raising the concern that our understanding of the effect of prenatal cannabinoid exposure on human subjects might be limited.

Here we employ rhesus macaques as animal model, which offers more translational advantages to humans. Using a large single-cell RNAseq dataset and electron microscopy data generated from fetal monkey brain, we describe the expression dynamics of relevant ECS genes in the cortical regions and neural cell types across the developmental phases. Moreover, we introduce an experimental approach to expose timed-pregnant monkeys to the cannabis psychoactive component Delta-9-tetrahydrocannabinol during distinct phases of corticogenesis, when different neurons are generated. Multi-omics, bioinformatics and cell imaging approaches will define how transcriptional and epigenetic landscapes of the developing primate cortex, as well as the migration pattern of the cortical neurons, change due to prenatal cannabis exposure. This study addresses the general interest to define the molecular mechanisms of primate fetal brain development affected by maternal cannabinoid exposure.