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The effects of maternal cocaine use during pregnancy in pediatric epigenetic clocks and methylation risk scores in humans

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Introduction: The investigation of the effects of maternal cocaine use exposure during pregnancy (MCU) on offspring has been inconsistent, with few studies investigating biological outcomes in humans. Here, we profiled genome-wide DNA methylation (DNAm) of umbilical cord blood (UCB) from newborns exposed (n=35) and not exposed (n=47) to MCU. We used DNAm data to (1) assess their developmental maturity at birth and (2) to build an individual's risk of adult life disorders. Methods: we generated gestational epigenetic age estimates (DNAmGA) based on Knight and Bohlin pediatric epigenetic clocks. We also investigated the association between DNAmGA with UCB serum levels of BDNF. Considering the large-scale DNAm data availability and existing evidence regarding MCU as a risk for health problems later in life, we generate methylation risk scores (MRS) for tobacco smoking, schizophrenia, diabetes, and obesity. We performed a gene ontology (GO) enrichment analysis on the CpGs included in the MRS with group differences. Results: MCU was associated with lower DNAmGA in newborns and this effect remained significant when controlling for potential confounders, such as blood cell type composition predicted by DNAm and obstetric data. DNAmGA was negatively correlated with BDNF levels in the serum of UCB. Higher tobacco smoking, schizophrenia, and diabetes MRS were found in the MCU group. The GO analysis revealed GABAergic synapses as a potential pathway altered by MCU. Conclusion: Our findings of decelerated DNAmGA and risk scores for adverse phenotypes suggest the effects of MCU on the epigenetic landscape of newborns are capable of being detected at birth.