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Association of cord blood DNA methylation patterns and scores with prenatal exposure to opioids, cannabis, and polysubstances

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Background: Substance use (such as opioids) during pregnancy can be subject to bias when assessed through self-report. Leveraging biomarkers of substance use can aid in identifying exposure. Epigenetic changes for maternal tobacco and alcohol use has been demonstrated, however, but is not well characterized in opioids, cannabis, or polysubstance use during pregnancy.

Methods: Using data from the Boston Birth Cohort collected from 1998 to 2020, we examined cord blood epigenome-scale DNA methylation levels for association with prenatal exposure to maternal opioids, cannabis, or polysubstance use (defined as exposure to at least 2 or more substances). We generated DNA methylation scores using summary statistics and tested predictive exposure accuracy using 4-fold cross-validation, receiver operator characteristic curves, and regression to understand score specificity.

Results: We identified cord blood methylation changes at 74 and 21 novel loci showing evidence of association with prenatal exposure to opioids and cannabis, respectively, at the epigenome-wide statistical significance level. We investigated prenatal exposure to more than 1 substance, i.e., polysubstance exposure, and found 1 associated locus. We built methylation scores that are highly predictive of prenatal exposure to these substances and found area under the curve (AUC) for our opioid (AUC=0.91) and cannabis-specific (AUC=0.90) substance scores.

Conclusion: In this sample, we identified novel neonate methylation changes and using these loci generated the first DNA methylation score reflecting prenatal opioid, cannabis, and polysubstance exposures. These findings have implications for biologic targets related to prenatal substance exposures and provide biomarkers that can be used to advance epidemiological research.