

Sex- and tissue- specific effects of binge levels of prenatal alcohol consumption on DNA methylation at birth: a potential link with FASD

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Issue: Binge level prenatal alcohol exposure (PAE) causes developmental abnormalities, which may be mediated in part by epigenetic mechanisms. In our well-characterised cohort, Asking QUestions about Alcohol in pregnancy (AQUA)^[1], one in five women binge drank (defined as ≥ 5 standard drinks per occasion) prior to pregnancy recognition in trimester one^[2], a period that is crucial for development of the nervous system^[3]. DNA methylation (DNAm) of cytosine at the CpG (cytosine-phosphate-guanine) dinucleotide, the most studied epigenetic mark, has been implicated as a mediator of the relationship between early life environment and risk of chronic disorders^[4, 5], including FASD^[6-9]. Despite this, few studies have characterised the association of binge PAE with DNAm in offspring.

Methods: We address this gap by measuring the association between binge drinking and genome-wide DNAm profiles in a sex-specific manner in neonatal cheek cells (n=154) and placental samples (n=105). Genome-wide DNAm data was obtained using Infinium HumanMethylation450K array platform. Sum-of-rank approach, which combines ranks of effect sizes and p-values were used to identify differentially methylated regions (DMR).

Results: We observed two DMRs with associations between binge-level PAE and DNA methylation, specifically in female offspring. DNAm in one of the DMR-associated genes, *ERICH1*, has been shown by two independent studies to be impacted by FASD and binge PAE in humans. The other gene, *SYBU*, is likely to play a role in neurodevelopment, cognition, and behaviour.

Conclusions: Our findings warrant further replication and highlight a potential epigenetic link between binge PAE and FASD.

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