**GUT MICROBIOTA AND IMMUNE PROFILES UNDERLYING RISK AND RESILIENCE TO EMOTIONAL DYSREGULATION FOLLOWING PRENATAL ALCOHOL EXPOSURE**

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Objectives: Impaired emotional processing and social behavior problems are among the many disabilities experienced by individuals with Fetal Alcohol Spectrum Disorder (FASD), a finding supported by evidence from animal models. The underlying biological mechanisms of emotional dysregulation following prenatal alcohol exposure (PAE) are still being uncovered. Increasing evidence highlights the role of gut microbiota-immune system interactions in regulating emotional processes. Recent studies using animal models have shown that PAE alters both the gut microbiota and immune function. However, no study has examined the contribution of gut microbiome and immune function to PAE-induced emotional dysregulation. The overall objective of this study is to examine how PAE-induced changes in the gut microbiota and immune function contribute to risk and/or resilience to emotional dysregulation.

Methods: Pregnant rat dams were randomly assigned to: PAE – liquid ethanol diet *ad libitum* or Control – pelleted control diet *ad libitum*. Adult male and female rats (n=48 per/group/sex) were evaluated for anxiety-like behavior through the open field and dark-light emergence tests, depressive-like behavior through the sucrose preference test, and social behavior through the social interaction test. These scores for each test were compiled into a single emotionality score, and the 10 animals from each group with the highest (risk) and lowest (resilience) scores were selected for assessment of gut microbiome composition (16S rRNA sequencing of fecal samples) and immune function (cytokine levels in blood and brain tissues).

Results: Analysis of the gut microbiome indicates that, although no significant differences in diversity or community structure were observed between risk and resilient animals in either control or PAE groups for both sexes, there is a trending difference in community structure between risk and resilience in PAE females but not in control females. Also, exclusively in PAE females, risk animals have increased abundance of *Lactobacillus* genus compared to resilient animals. In control males but not PAE males, risk animals have increased abundance of Actinobacteria phylum. The immune profiles were drastically different between risk and resilience animals, along with few alterations due to prenatal treatment. In males but not females, risk animals had lower serum IFN-γ, IL-1β, Il-10, and IL-4 levels compared to resilient animals. In males but not females, IL-6 levels in the hypothalamus were higher in risk compared to resilient animals. In females but not males, IL-10 levels in the dorsal hippocampus were lower in PAE animals compared control animals.

Discussion/Conclusion: The results in this study are still preliminary, but differences in the abundance of bacterial taxa and cytokine levels have already been observed across prenatal treatment groups and emotionality scores, with many of these differences being sex-specific. Ongoing analyses will allow us to identify gut microbiota and immune markers underlying the increased risk and/or resilience for emotional impairments and if these changes are interacting, or not, with prenatal treatment.

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