Why Mom Matters: Environmental Justice and the Early-Life Origins of Health Disparities

Dominic Le, Bailey Ryan, Sammie Truong, Tania Hassanzadeh, Jessica L. Bolton\textsuperscript{1}, Leigh Ann Simmons\textsuperscript{2}, Ph.D, MFT, and Staci D. Bilbo\textsuperscript{1}, Ph.D

\textsuperscript{1}Department of Psychology and Neuroscience, and \textsuperscript{2}Department of Nursing, Duke University

INTRODUCTION

The rising global obesity epidemic poses a major health concern, particularly in the context of maternal and child health. Exposure to poor maternal diet during early development may influence brain development via neuroimmune signaling, thereby predisposing offspring to negative health outcomes throughout life. Children of obese mothers are at higher risk for childhood obesity, insulin resistance, depression, anxiety, and autism (Sullivan, Nousena, & Chamloua, 2012). Intriguingly, dietary fat activates microglia, the primary immune cells of the brain, and maternal high-fat diet (HFD) has been shown to predispose offspring to obesity, anxiety, and an overactive immune response by “priming" hippocampal microglia (Bilbo & Tsang, 2010). More recently, the branched-chain amino acids (BCAA) have been proposed as a serum biomarker for obesity, insulin resistance, and postpartum depression; male rats fed BCAA also display increased anxiety-like behaviors (Coppola, et al., 2013; Bailara, et al., 2006).

We hypothesized that high-fat and BCAA-enriched maternal diets would modulate microglial activation in both mother and offspring, leading to increased depressive behavior in postpartum dams and to negative metabolic and behavioral outcomes in adult offspring.

PROJECT SUMMARY

Our Brain and Society team investigates the effect of perinatal nutrition on maternal health and offspring development. We are particularly interested in how diets high in fat and in branched-chain amino acids may influence risk for postpartum depression, developmental disorders, and metabolic syndrome, via nervous-immune-endocrine interactions in mother and child. Our work integrates behavioral, molecular, metabolic, and histological data from diet-manipulated mice with clinical data from early-postpartum women in the Durham area.

METHODS

We fed mouse dams low-fat (LFD) or high-fat (HFD) diets with or without supplemental BCAA, starting six weeks before mating and continuing through gestation and lactation. We observed the following weight gain prior to pregnancy:

HFD/BCAA > HFD = LFD/BCAA > LFD

Offspring were fed standard chow after weaning (P28-adulthood) and assessed in adulthood (P60-P90) for behavioral, metabolic, and neuroimmune changes.

DISCUSSION

Our study has uncovered interesting differences in the development of mice exposed to varying maternal diets. Maternal BCAA supplementation was associated with decreased weight. Maternal HFD was associated with increased fasting blood glucose, increased anxiety-like behavior, and decreased activity in male offspring; increased anxiety-like behavior and altered context-dependent reward learning in females; and a reduction of microglial markers at PI in both sexes.

Microglia are critical mediators of synaptic refinement and pruning, and early microglial function has wide-ranging implications for network formation and later-life cognition. Intriguingly, previous studies have found higher expression of microglial markers in males than in females perinatally, and this has been linked to male susceptibility to early-onset disorders such as autism. Similarly, we found disparate effects of maternal diet on male and female groups, with males most vulnerable to metabolic and behavioral changes.

We plan to continue our project with molecular and histological data from multiple timepoints; with analysis of serum levels of BCAA, serotonin and corticosterone; and with analysis of maternal as well as offspring outcomes. We will synthesize these data with a clinical study of postpartum women, which will examine many of the same response variables to produce a translational, interdisciplinary understanding of the impact of diet on maternal and child health.

ACKNOWLEDGEMENTS

We thank Jessica Bolton, Christine Belliveau, Melanie Wiley, Dr. Nicole Schramm-Sapyta, Dr. Leigh Ann Simmons, and Dr. Staci Bilbo for their guidance and mentorship. We thank the Bass Connections Program and the Bass Family for their generosity.