



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

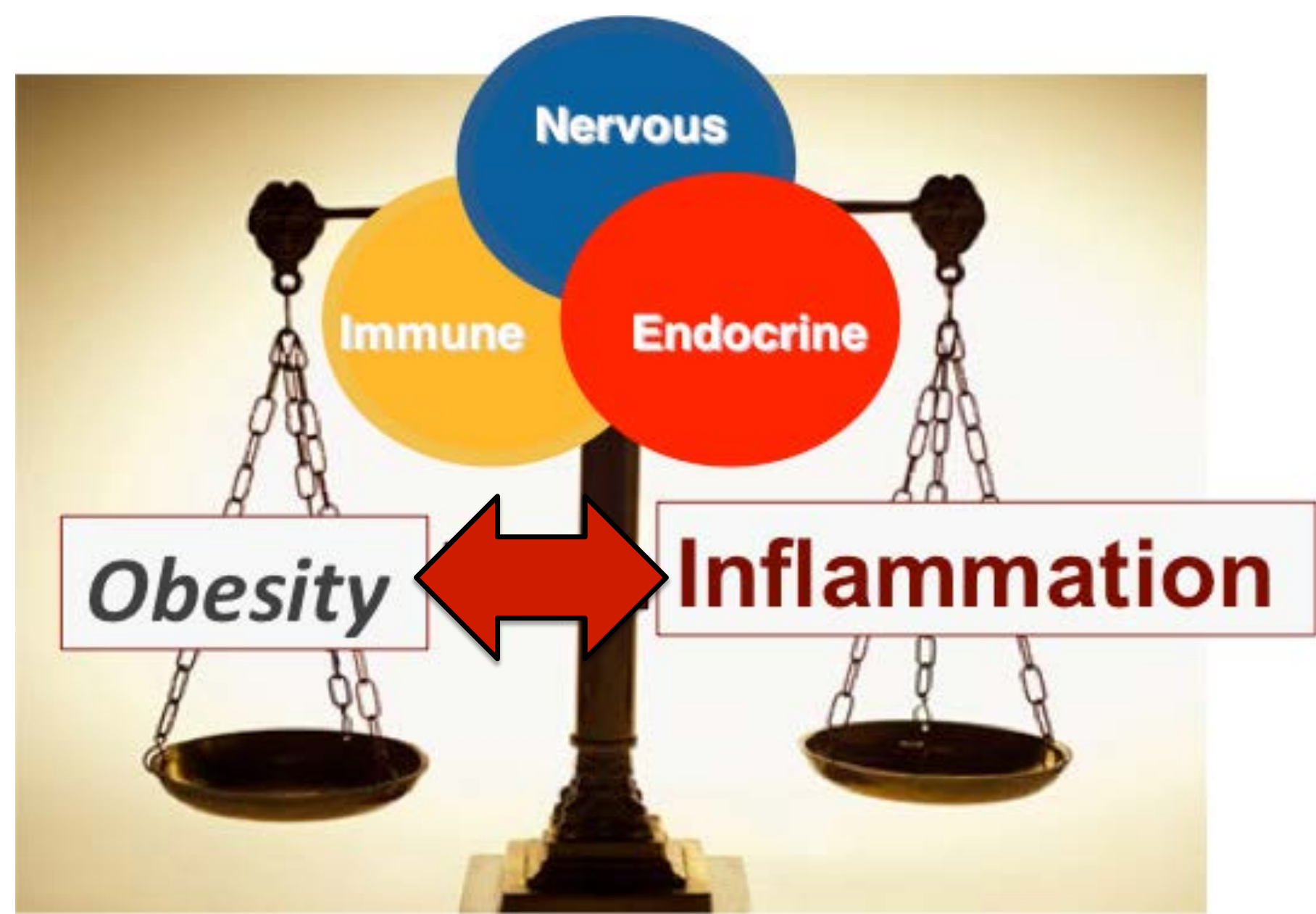
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## INTRODUCTION

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.

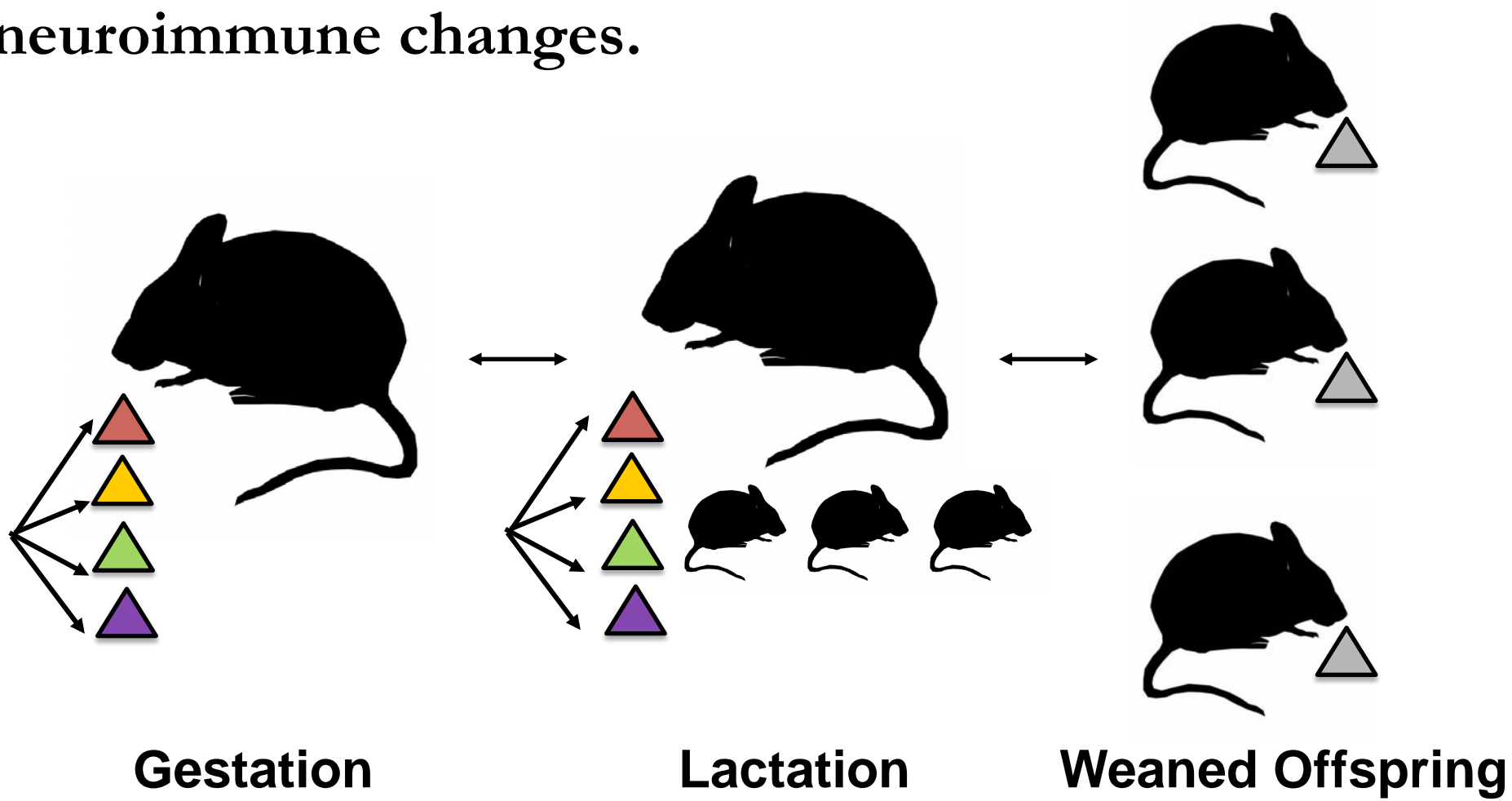


## METHODS

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:

$$\text{HFD/BCAA} > \text{HFD} = \text{LFD/BCAA} > \text{LFD}$$

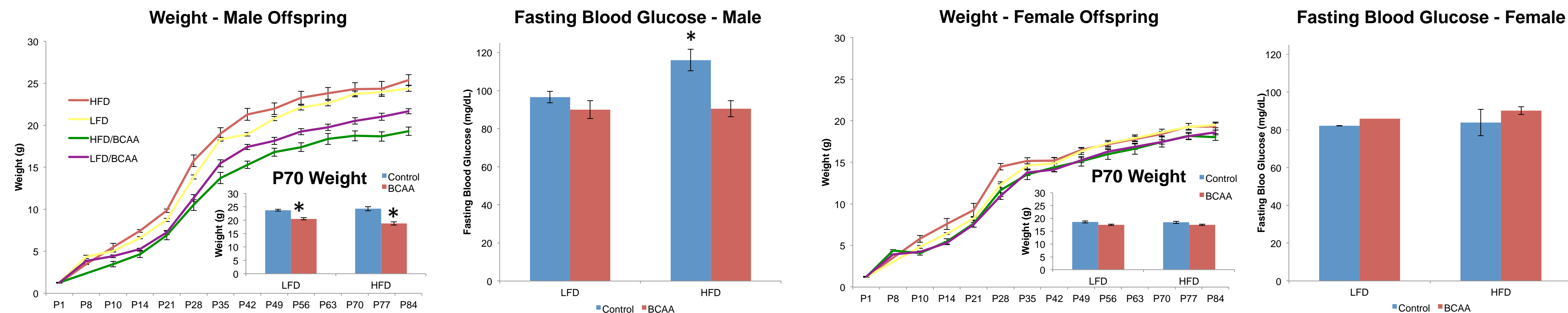
Offspring were fed standard chow after weaning (P28-adulthood) and assessed in adulthood (P60-P90) for behavioral, metabolic, and neuroimmune changes.



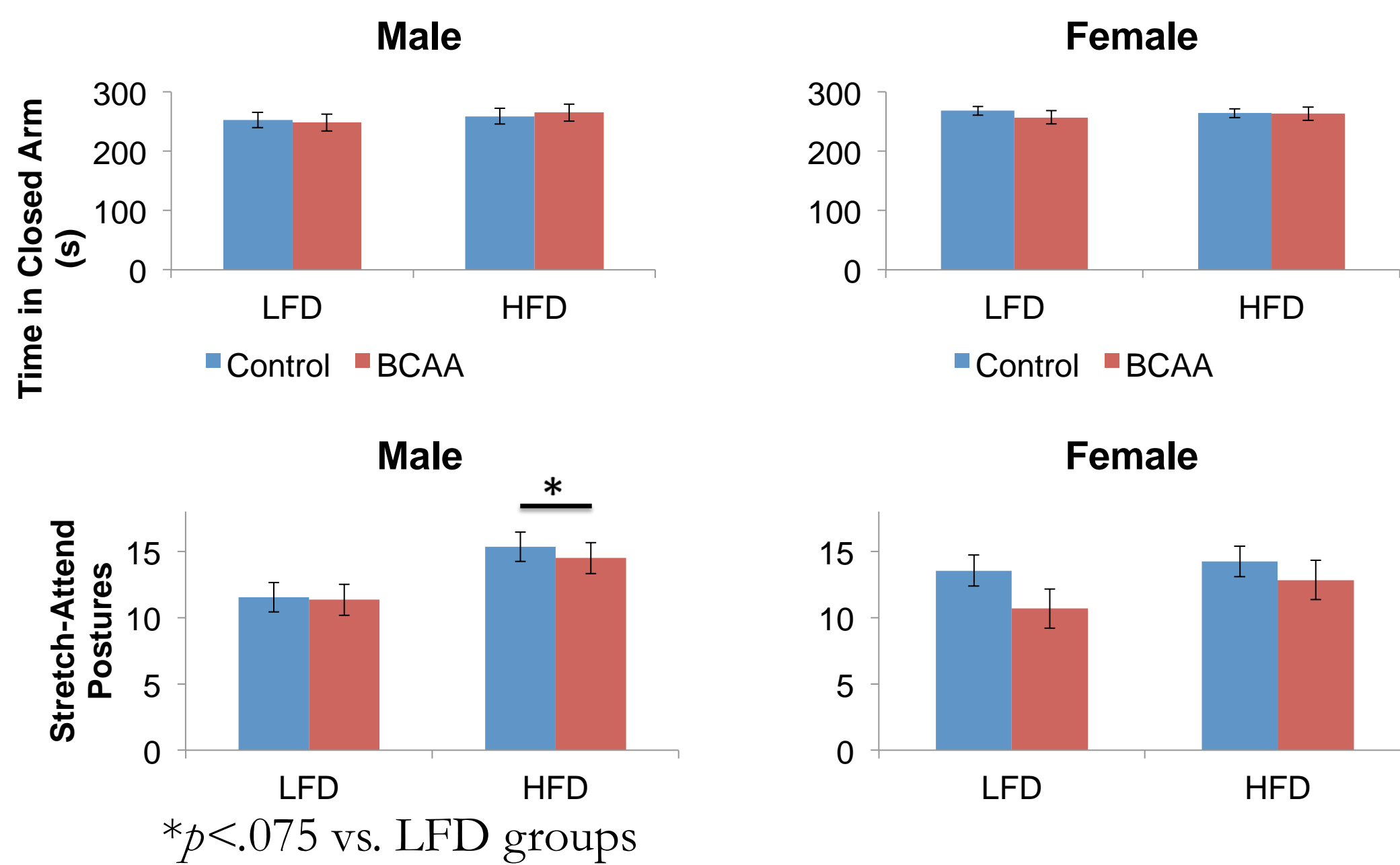
## PROJECT SUMMARY

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.

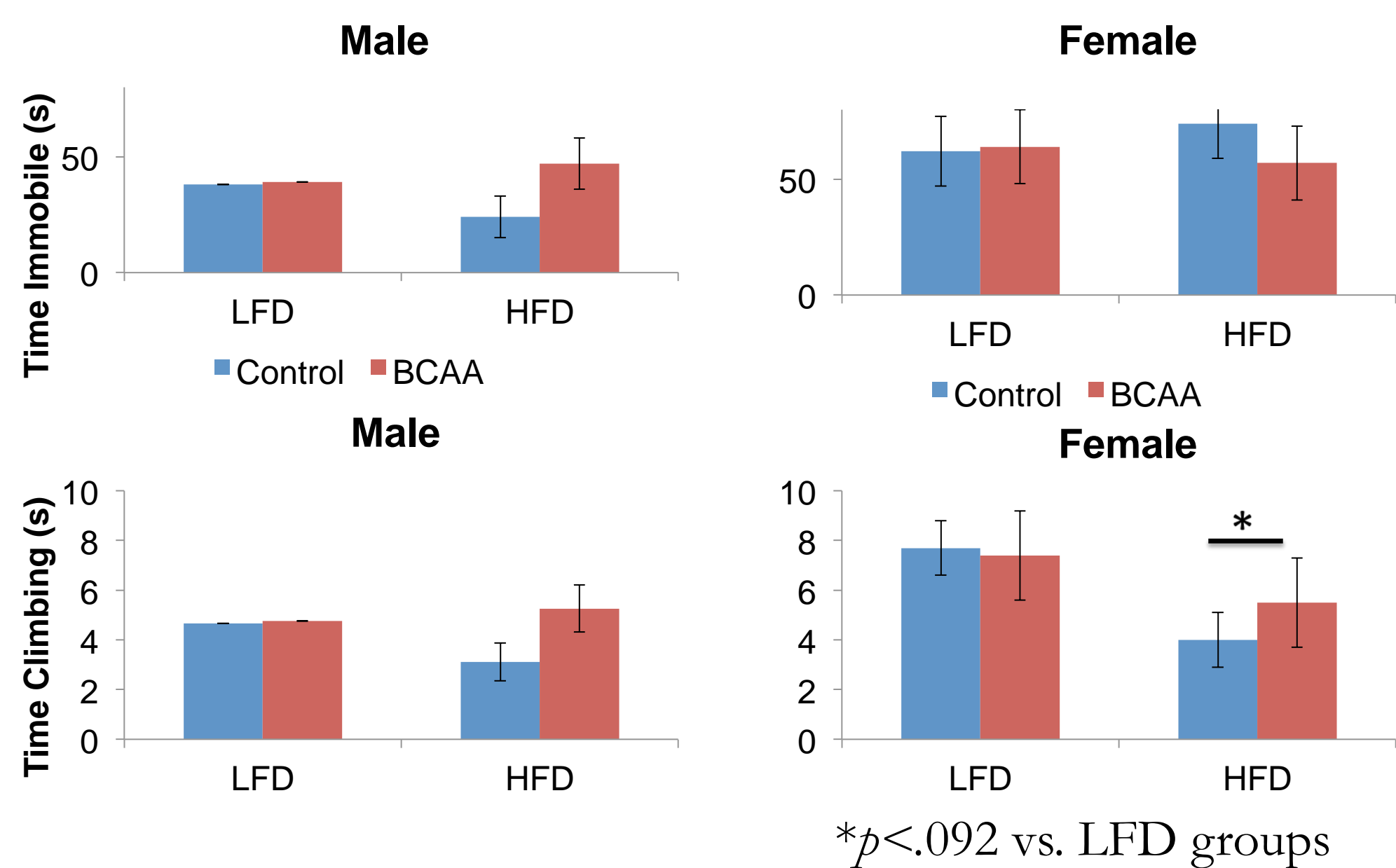
Male, but not female, offspring of BCAA-fed dams gain less weight than offspring of control-fed dams when fed standard chow after weaning. On the other hand, male offspring of HFD/Control-fed dams have increased fasting blood glucose.



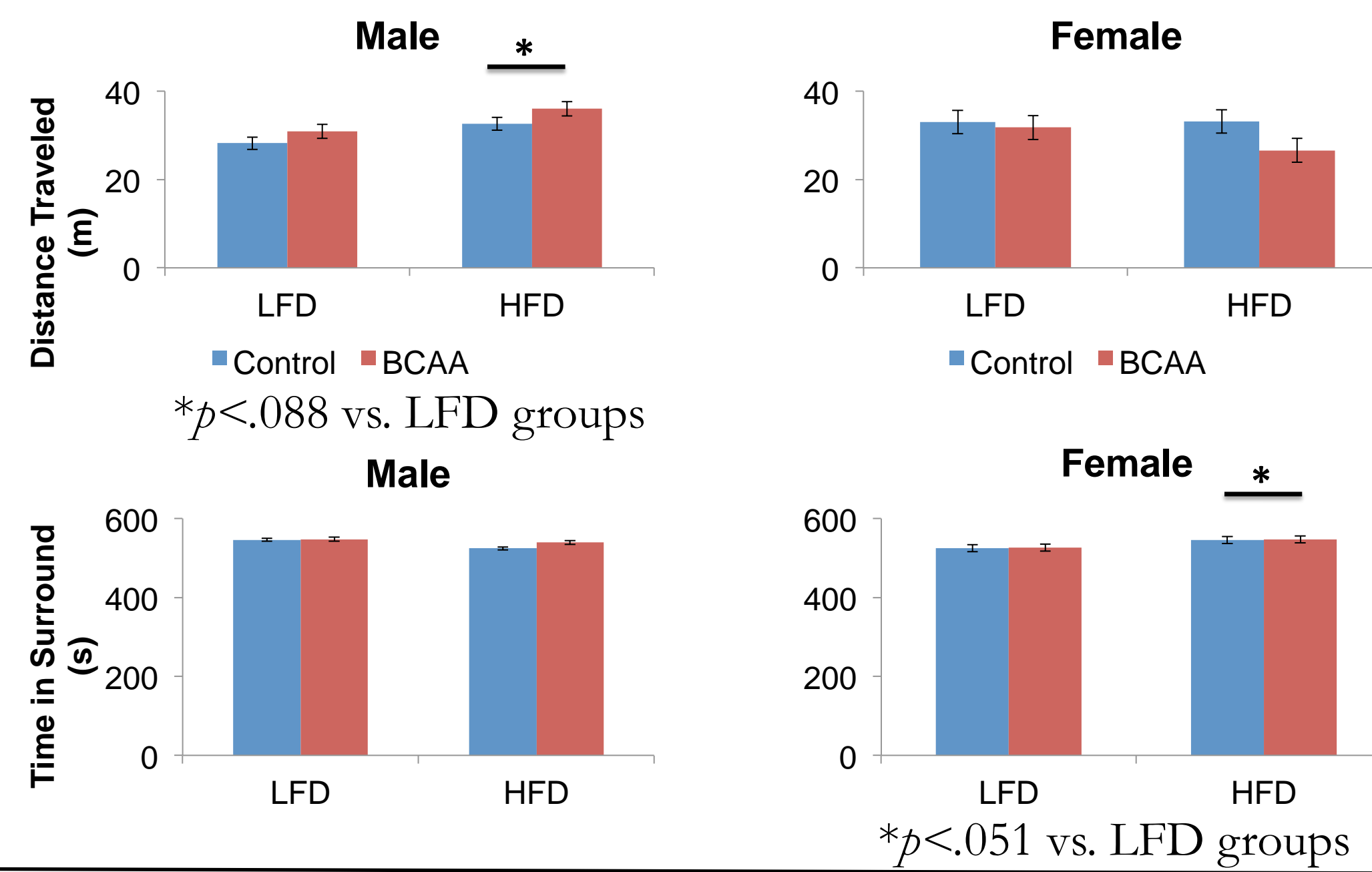
Male offspring of HFD-fed dams show more anxiety-like behavior in the elevated zero maze than LFD controls.



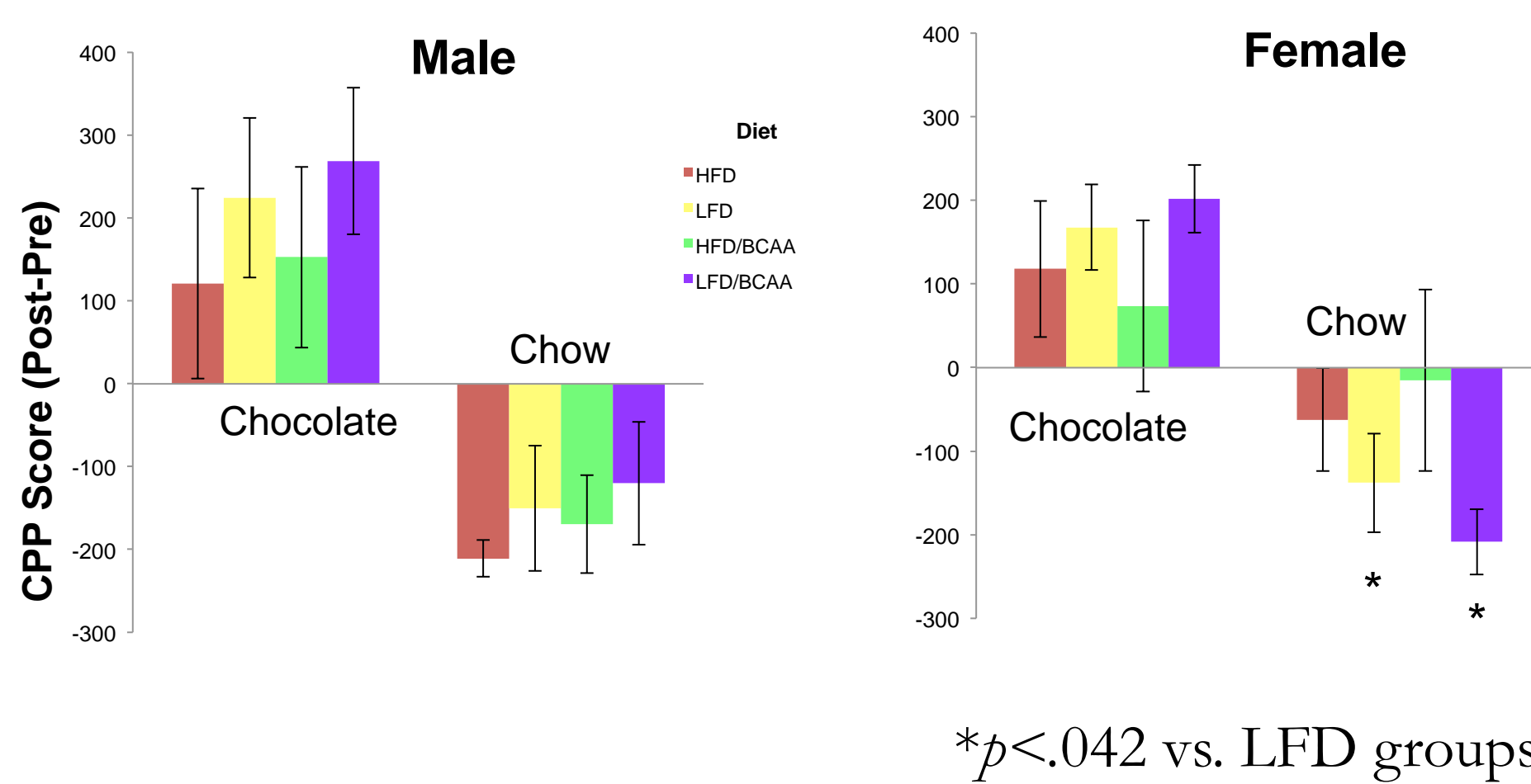
Female offspring of HFD-fed dams are less active in a forced swim test of depressive-like behavior than LFD controls.



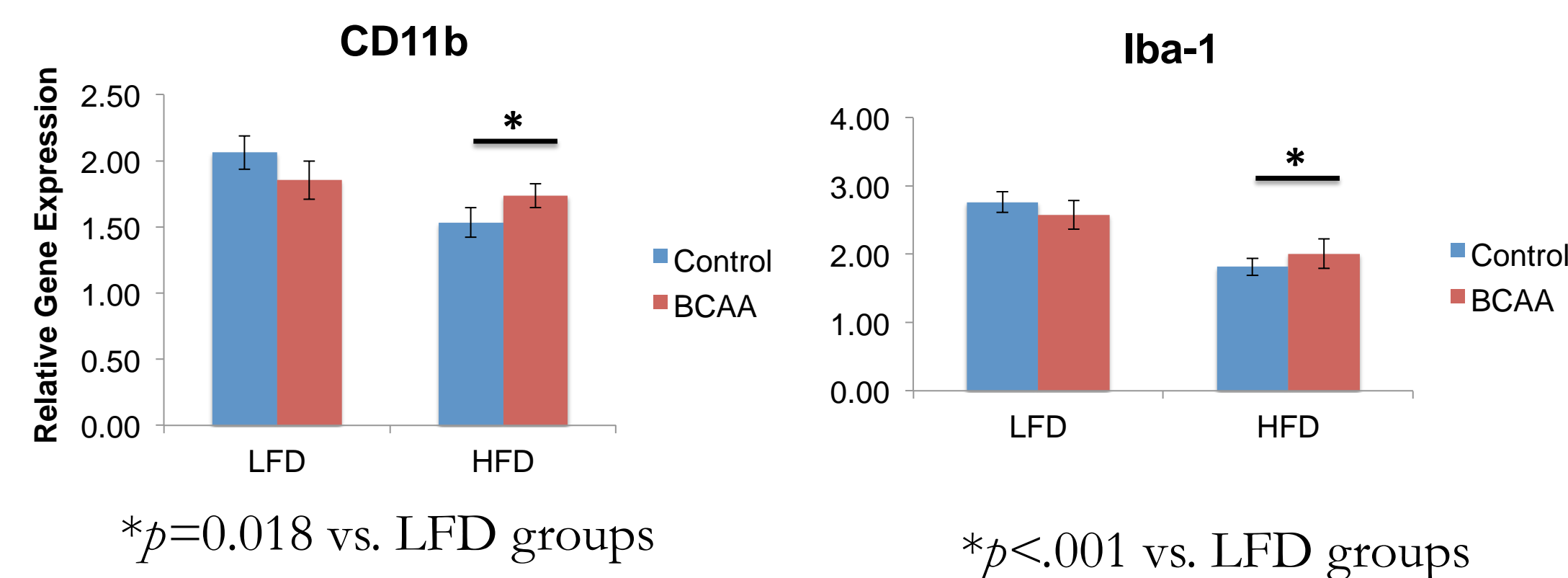
Male offspring of HFD-fed dams are more active, whereas females are more anxious in the open field than LFD controls.



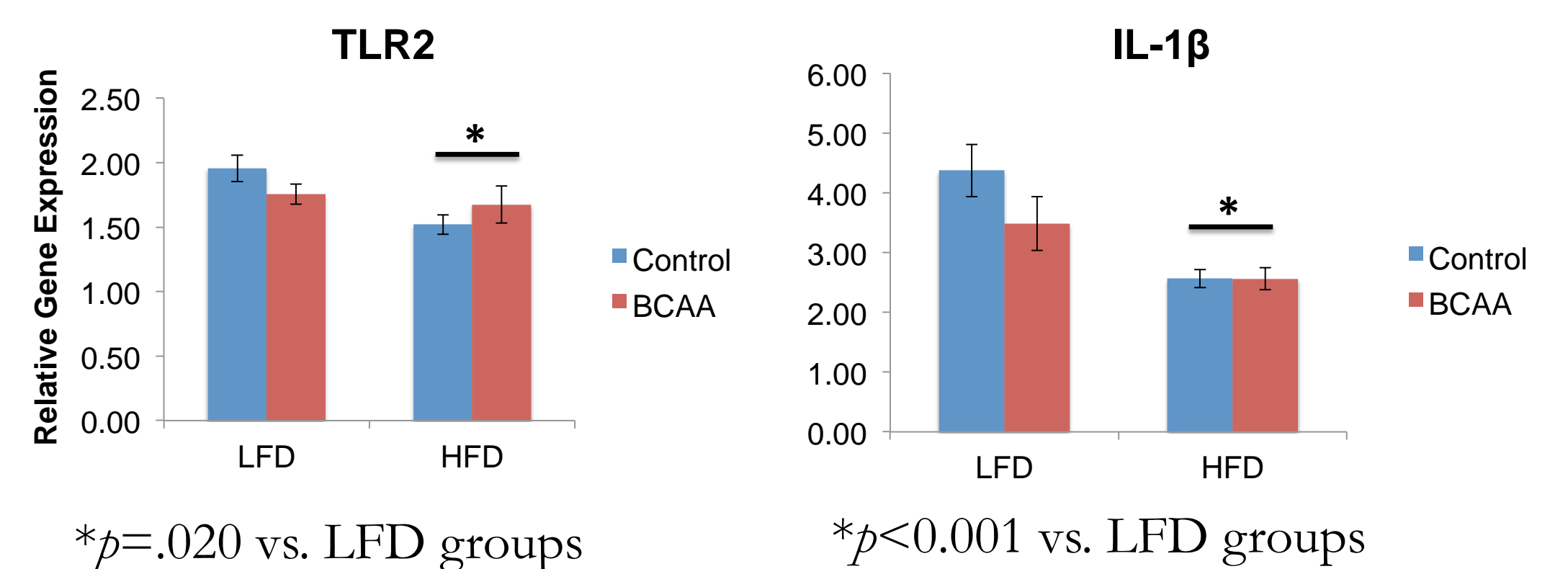
Female offspring of HFD-fed dams showed lower conditioned place preference (CPP) than LFD controls to a food reward.



Offspring of dams fed HFD express less Iba-1 and CD11b (microglial markers) in whole-brain samples at P1 than offspring of LFD-fed dams.



The inflammatory cytokine IL-1 $\beta$  and the innate immune receptor TLR2 are similarly reduced in whole-brain samples of P1 offspring of HFD vs. LFD dams.



## 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 increased activity in male offspring; increased anxiety-like behavior and altered context-dependent reward learning in females; and with a reduction of microglial markers at P1 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

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