Effect of Perinatal Western Diet Exposure on Stress-Induced Neuronal Activation in Rats

Hanna Banfield, Giovanna Bettega Feitoza, and Linda Rinaman
Florida State University, Dept. of Psychology and Program in Neuroscience

Introduction

- The typical U.S. diet consists of high-fat, high-sugar foods known as the Western Diet (WD).
- WD exposure has been associated with cardiometabolic disease, cancer, and alterations in anxiety-related and neurodevelopmental outcomes[1].
- GLP1 neurons are located in the caudal nucleus of the solitary tract (cNTS) project to the paraventricular hypothalamus (PVH) and other regions that regulate eating behavior[2].
- Prior work in our lab suggests that perinatal WD exposure alters the structure of GLP1 circuitry; however, the functional impact of these alterations remains unclear.
- GLP1 neurons have also been implicated in stress regulation[3].
- This project will work to identify whether early life exposure to WD alters the acute stress-induced activation of GLP1- associated neurons in the NTS and target regions.

Question: How does perinatal WD exposure affect total body fat and stress responsesmediated by GLP1 neurons and their projections to target regions in offspring?

Hypothesis: We hypothesize that rats exposed perinatally to WD and rats weaned onto WD will develop higher total body fat and exhibit reduced cFos expression in the NTS and PVH following an acute stressor compared to rats exposed only to chow.

Methods

- Gcg-cre rats were used for this experiment to isolate and identify GLP1-producing neurons.
- These rats were assigned to 4 different dietary conditions: WD-reared and weaned to WD, WD-reared and weaned to chow, chow-reared and weaned to WD, and chow-reared and weaned to chow. All rats were weaned at age P21.
- All rats underwent EchoMRI scans at P23 and P60 to assess adiposity
- Just prior to P60, 24-hour food intake, including chow and WD where applicable, was measured for all animals.
- At age P70, rats received an intraperitoneal injection of saline, which serves as an acute stressor, before perfusion.
- Sections containing the NTS and the PVH were isolated and immunohistochemically labeled for cFos.
- Images of these regions were taken using a Keyence microscope.
- Using QuPath, a software optimized for quantitative analysis of histological images, all cFos-positive cells were quantified in the cNTS and in a series of sections through the PVH in order to assess the number of cells activated by the saline injection.
- Performed 2-way ANOVA statistical analysis (rearing diet x post-weaning diet) to assess the effect of these conditions on food intake and cFos in adult animals. Performed t-test to measure the effect on adiposity in adult animals under the same conditions.

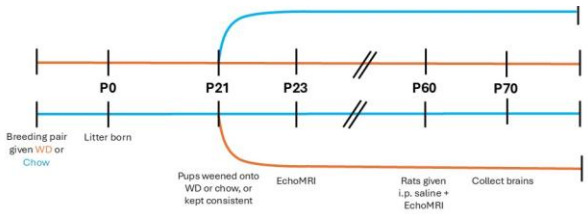

Figure 1. Timeline depicting rat litter lifetime, including rearing and weaning dates, EchoMRI's, and i.p. saline injections.

Results

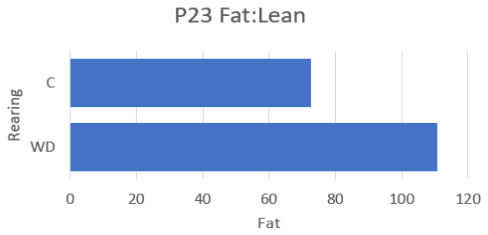

Figure 2. Effect of rearing diet on fat;lean ratio. Bar graph shows (insert unit here) for each rearing treatment, chow and WD 23 days after birth. P < 0.05.

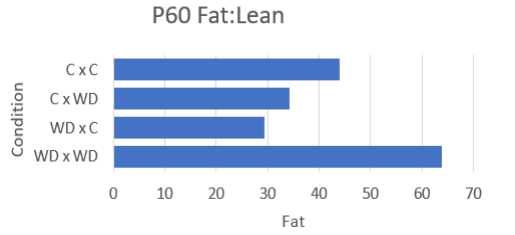

Figure 3. Effect of dietary condition, including rearing and weaning, on fat:lean ratio. Bar graph shows (insert unit here) for each assigned condition group 60 days after birth. P < 0.05.

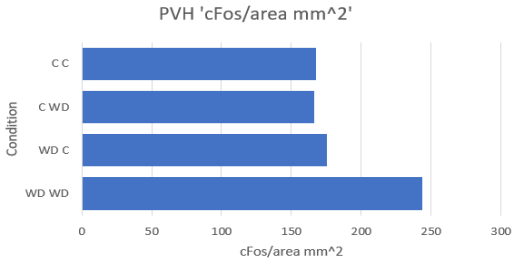

Figure 4. cFos quatification in PVH organized by dietary condition, controlling for each individual genotype. P > 0.05.

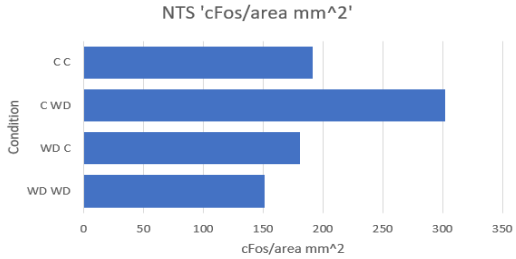

Figure 5. cFos quatification in NTS organized by dietary condition, controlling for each individual genotype. P > 0.05.

Interpretation:
Rats reared on WD developed higher total body fat relative to lean body mass than those reared on chow. However, rats weaned on WD having been reared on chow developed less total body fat than the control CxC group. Rats reared and weaned on WD developed the most total body fat.

Discussion

- WD-reared rats developed a higher fat:lean mass ratio than those reared on chow, possibly due to prenatal metabolic programming with reduced efficiency.
- Results depicted by Figure 2 are consistent with previous literature that suggest WD-reared rats weaned onto chow have reduced body fat mass due to metabolic adaptation that lowers their feed efficiency[4]
- No statistically significant differences (P > 0.05) were observed between diet conditions and cFos expression in the NTS or PVH following the acute stressor.
- These findings suggest that perinatal and post-weaning WD exposure did not produce the hypothesized effect on GLP1-associated neuronal activation in the NTS or PVH.
- However, genotype significantly influenced cFos expression in both of these regions.
- Future work should further investigate the mechanisms underlying these effects.
- There were no statistical significance (P > 0.05) between condition and cFos expression in the NTS and PVH following an acute stressor.

References

Research supported by NIH award DK059911 to A.R. and NSF award 1937954