

# Unpredictable Variable Prenatal Stress Programs Expression of Genes Involved in Appetite Control and Energy Expenditure

EL Moyer<sup>1</sup>, B. Al-Shayeb<sup>1</sup>, L.A. Baer<sup>2</sup>, A.E. Ronca<sup>1,3-5</sup>.

<sup>1</sup>Space Biosciences Division, NASA Ames Research Center, Moffett Field, CA; <sup>2</sup>Surgical Sciences, University of Texas Medical Center, Houston, TX;

<sup>3</sup>Obstetrics and Gynecology; <sup>4</sup>Program in Neuroscience; <sup>5</sup>Molecular Medicine & Translational Science, Wake Forest School of Medicine, Winston-Salem, NC.

## Introduction:

Exposure to stress in the womb shapes neurobiological and physiological outcomes of offspring in later life, including body weight regulation and metabolic profiles. Our previous work<sup>1</sup> utilizing a centrifugation-induced hyper-gravity demonstrated significantly increased (8-15%) body mass in male, but not female, rats exposed throughout gestation to chronic 2-g from conception to birth. We reported a similar outcome in adult offspring exposed throughout gestation to Unpredictable Variable Prenatal Stress (UVPS). Here we examine gene expression changes and the plasma of animals treated with our UVPS model to identify a potential role for prenatal stress in this hypergravity programming effect. Specifically we focused on appetite control and energy expenditure pathways in prenatally stressed adult (90-day-old) male Sprague-Dawley rats.

## Hypothesis

Pre-natal stress caused by unpredictable, variable, sources exhibits similar physiological effects to those observed during gestation under hyper-gravity.

## Methods:

- Time-mated female rats were exposed throughout their 22-day pregnancy to UVPS consisting of white noise, strobe light, and tube restraint individually once per day on an unpredictable schedule for 15, 30 or 60 min.
- To control for potential changes in postnatal maternal care, newborn pups were fostered to non-manipulated, newly parturient dams.
- At 90-days of age, we collected plasma and tissue from both the brain and fat depots located in males (epididymal fat)
- We determined the concentrations of glucose and corticosterone within the plasma samples.

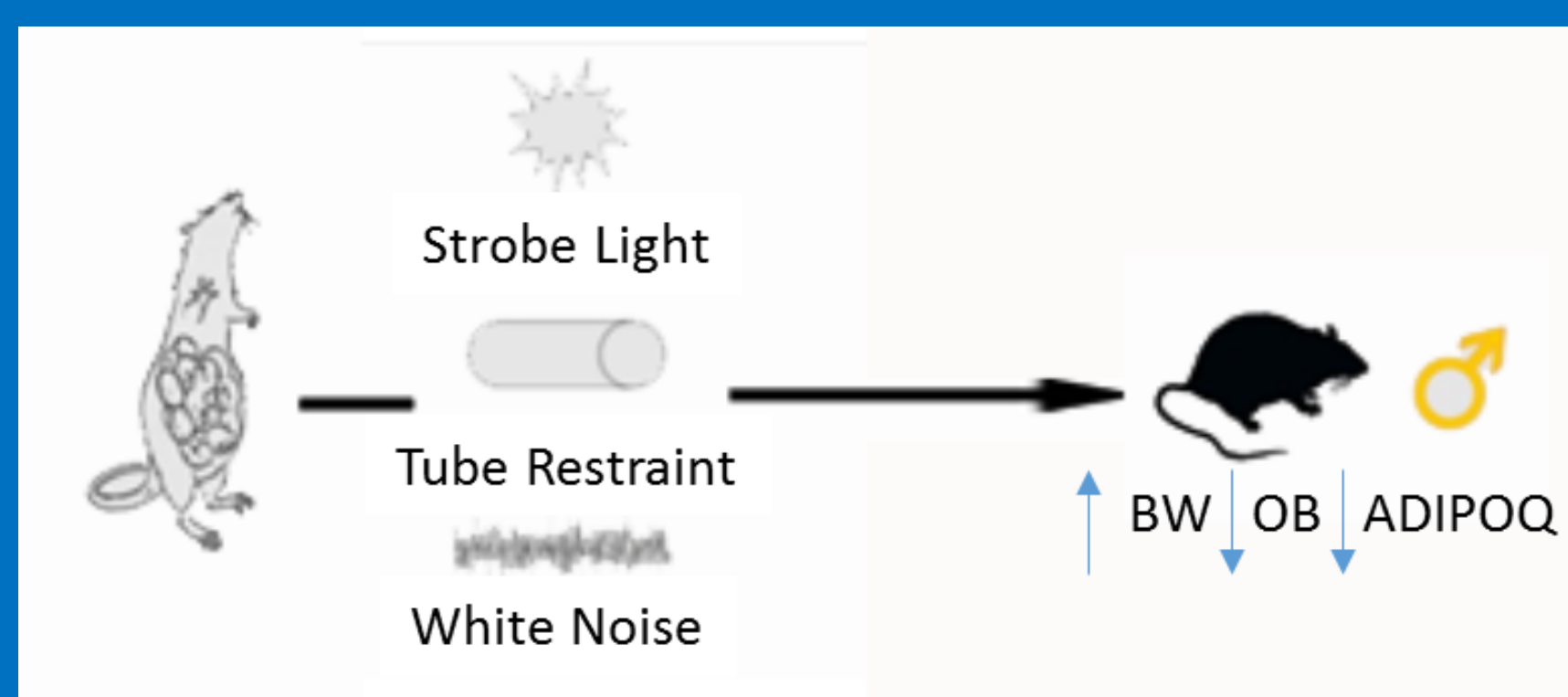


Figure 1: Summarizes treatment and the previously reported results

## Previously Reported Data

- Previous results (B. Al-Shayeb et al, ASGSR 2015) suggested that the energy expenditure pathway is augmented as an effect of UVPS in males. Specifically, the stressed animals demonstrated a lower mRNA expression for genes that both inhibit hunger (OB) and increase regulation of energy expenditure (ADIPOQ).
- Previous data showed increased expression of leptin (OB) and adiponectin (ADIPOQ) as a result of UVPS in males (Figures 2 and 3, respectively)

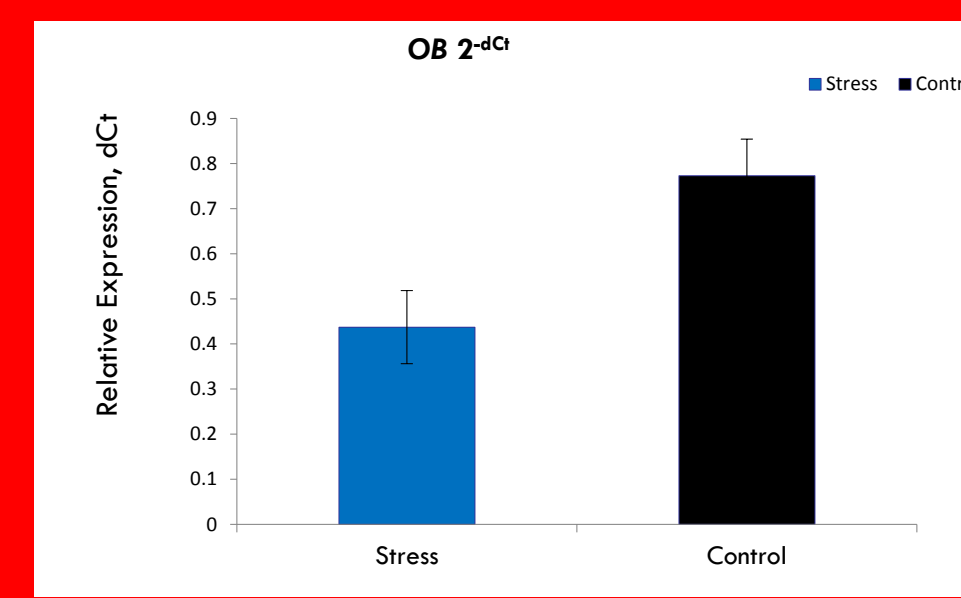


Figure 2: Modulation of fat pad leptin in adult male rats

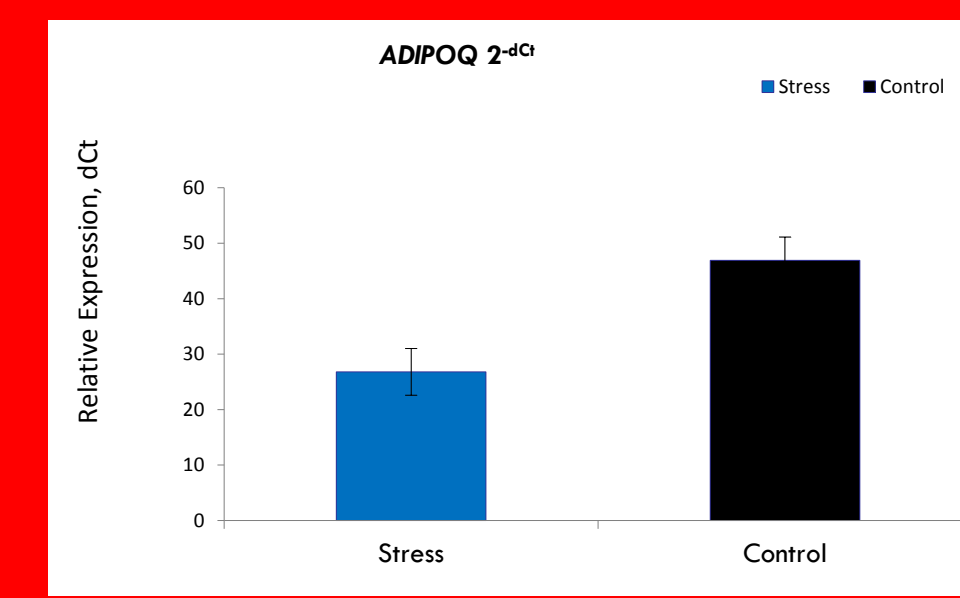
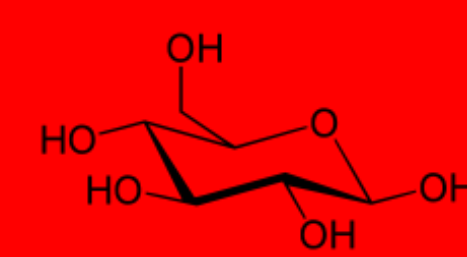


Figure 3: Modulation of fat pad adiponectin in adult male rats

## Newly Presented Data:

### Glucose Plasma Concentrations in Male and Female



- Glucose is a sugar which circulates within the blood and is a common source of energy within the mammalian body. An elevated concentration can be a sign of diabetes or other metabolic affliction
- Results of plasma analysis of both the adult male and adult female offspring showed no stress effect and no sex effect (Figure 4)

### Corticosterone Plasma Concentrations in Male and Female



- Corticosterone is a steroid which circulates in the blood and is regulation of energy and the stress response. Elevated levels are associated with increased stress.
- Results of plasma analysis of both the adult male and adult female offspring demonstrated similar effects (Figure 5). In both instances, stress exposure in the womb decreased adult plasma concentrations. There was no sex effect or interaction effect between the two variables (determined by two-way ANOVA).

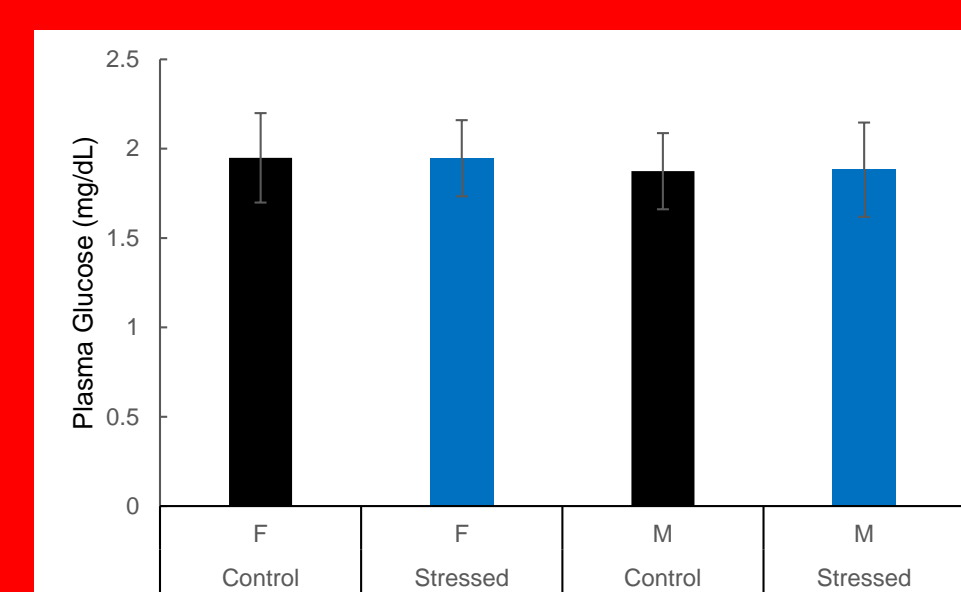


Figure 4: Modulation of plasma glucose in adult male rats

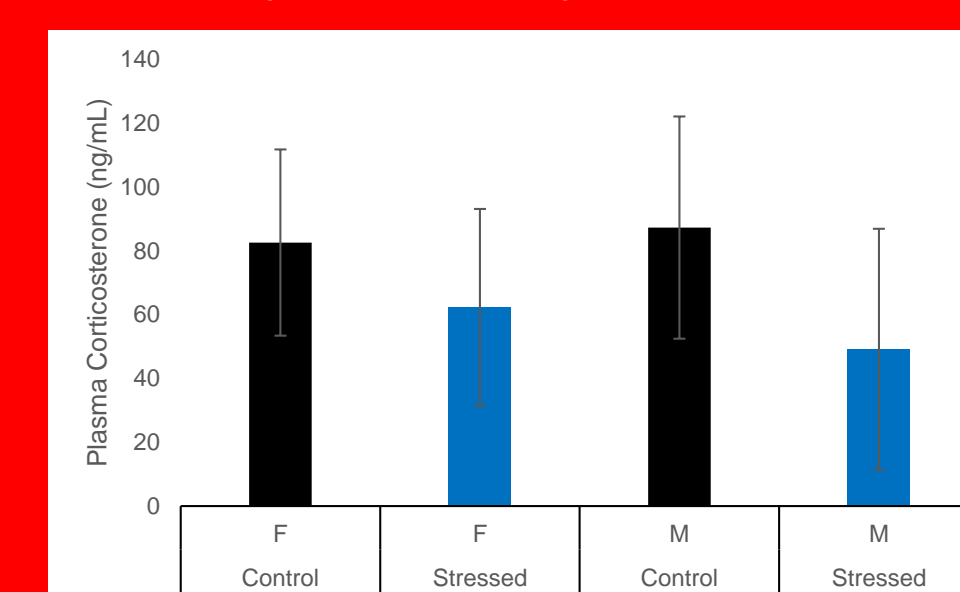
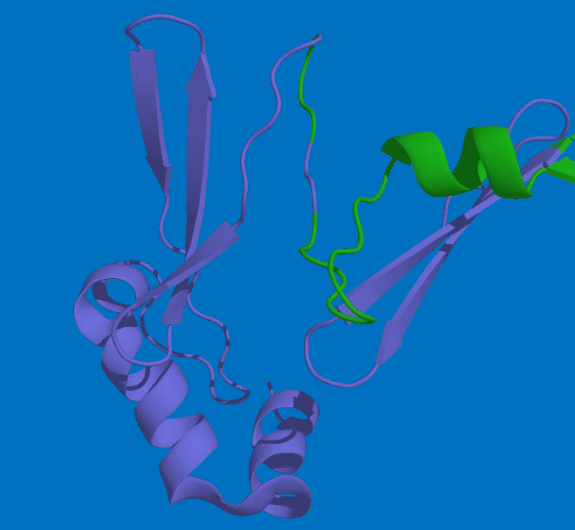


Figure 5: Modulation of plasma corticosterone in adult male rats

## Future Work

### Fat pad Ghrelin mRNA Expression



- Ghrelin is a protein involved in the energy regulation pathway which functions by modulating the sense of hunger with the Central Nervous System via the hypothalamus, and also acts on the distribution and rate of energy use. Typically it functions in an inverse relationship with leptin, and so analysis of this pathway could further support those results previously reported.

### Correlation Analysis

- To date, this study has produced an immense amount of data from both the mothers exposed to prenatal stress and the offspring. A correlation analysis between these datasets may yield interesting new avenues for future studies.

## Conclusions

- Exposure to prenatal stress did not alter the concentration of adult plasma glucose, suggesting that the increased body weight observed in males is not being stored as excess energy reserves within the body, despite mRNA analysis of fat pad tissue showing a decrease in the transcription of genes involved in both hunger inhibition (OB) and regulating energy expenditure (ADIPOQ).
- Prenatal exposure to stress elevated the baseline levels of corticosterone within both the adult male and female blood. This demonstrates a significant implications that the developmental environment exhibits on future physiological homeostasis. This elevated levels of corticosterone in the blood could indicate a hypersensitivity to stress, but future analysis would need to be done to investigate that theory.

## Acknowledgements:

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