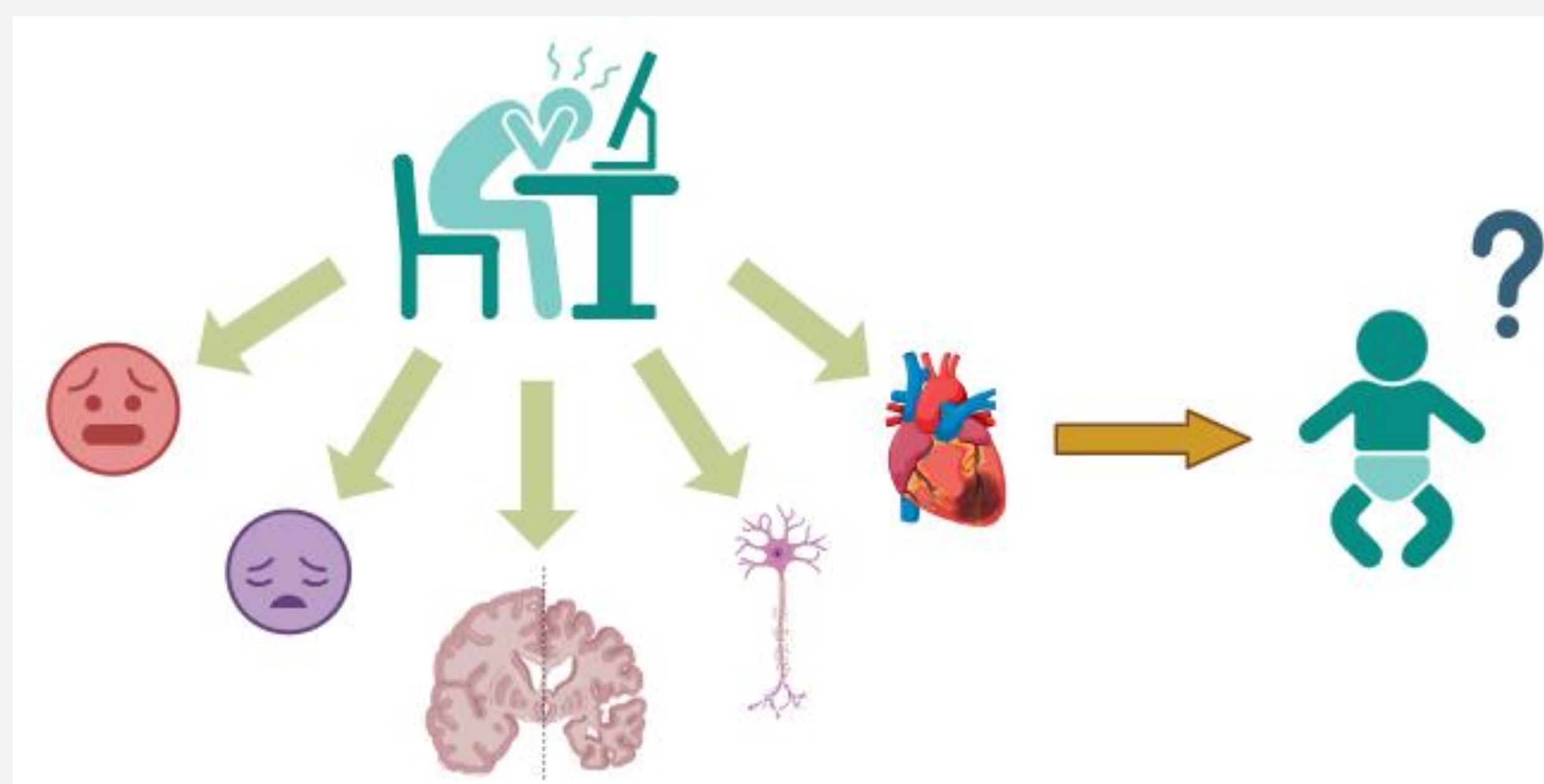


## Abstract

Chronic stress is increasingly common and may have consequences across generations. Paternal chronic stress has been shown to alter sperm small RNAs and influence offspring neurodevelopment and psychiatric disease risk. However, how stress signals from the brain reach the germline and how offspring respond to stress remains unclear. This study examines epigenetic inheritance of paternal stress and its effects on offspring stress responses. We compared offspring of chronically stressed and non-stressed sires and measured corticosterone following an acute stressor. Offspring of stressed fathers exhibited reduced corticosterone responses, with evidence of sex-specific differences in stress regulation.

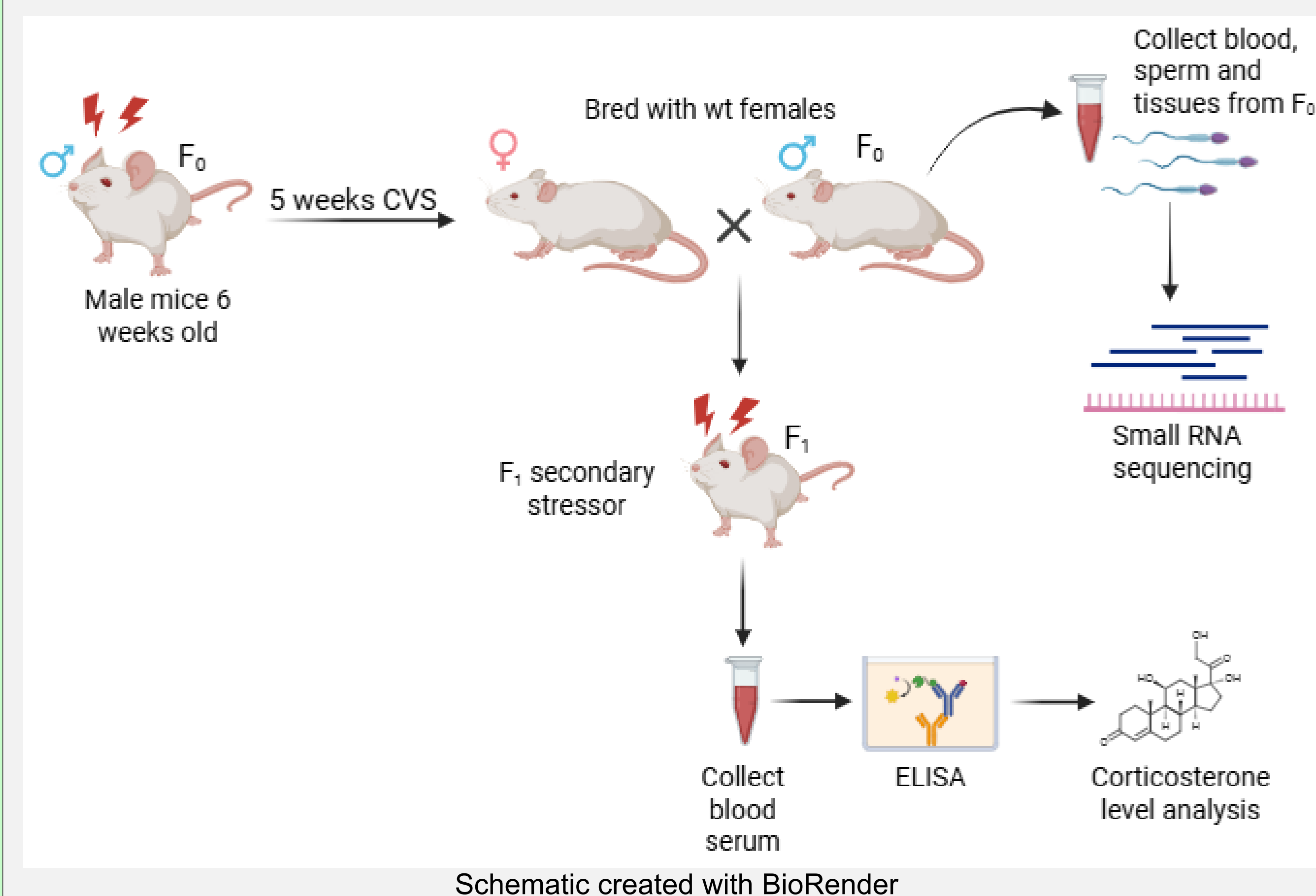


## Introduction

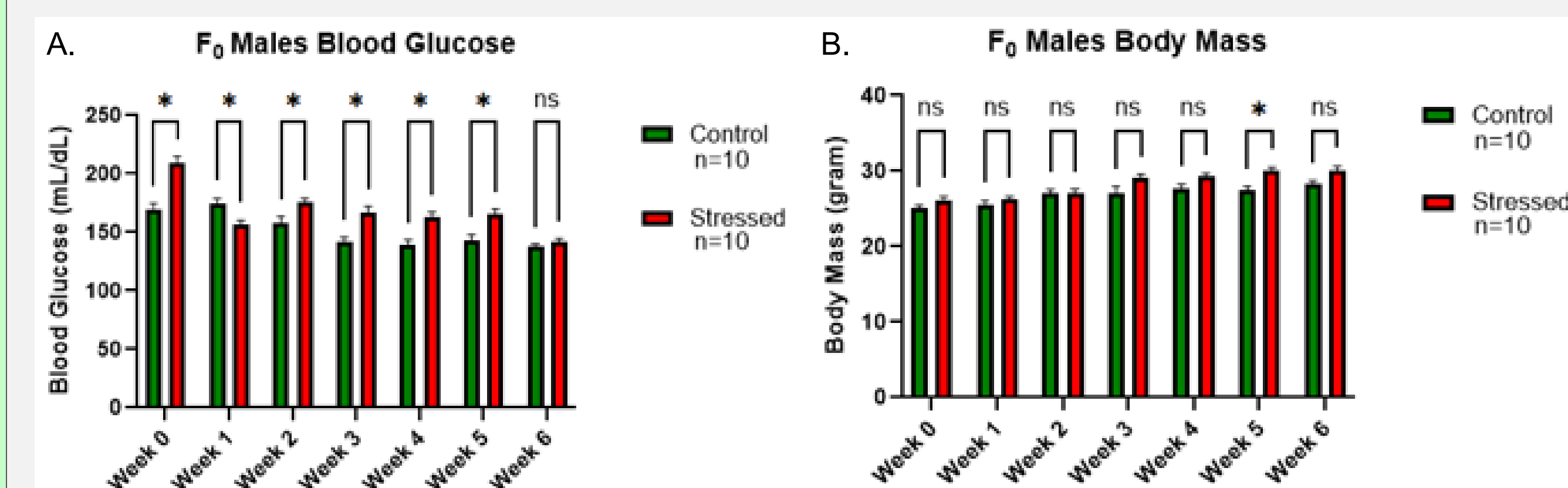
- Paternal chronic variable stress (CVS) causes stress dysregulation and risk of psychiatric disorders in offspring
- tRNA-derived fragments (tRFs) are found in high concentrations in the sperm of stress exposed fathers
- It is hypothesized that tRFs are communicated from the Central Nervous System to the germline via Extracellular Vesicles in blood circulation that fuse with sperm in the cauda region of the epididymis along the testis

**Goal: Assess stress response patterns of offspring from chronically stressed fathers and elucidate the mechanism of epigenetic inheritance.**

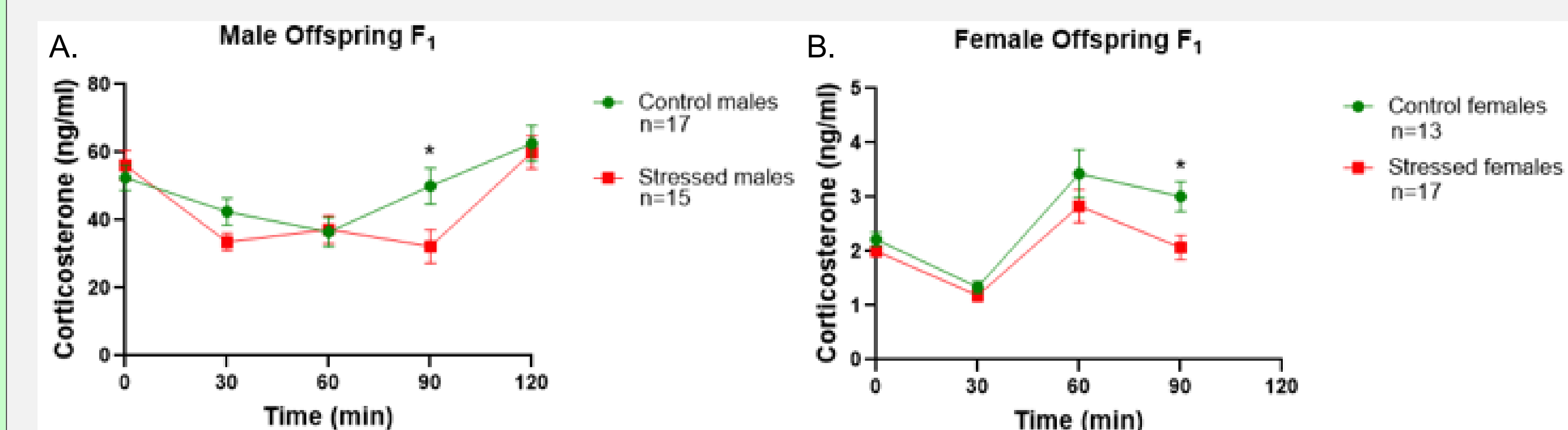
## Methods



## Results



**Fig 1. Chronic stress significantly affects blood glucose but not body mass index:** F<sub>0</sub> Male mice physiological observations during ongoing chronic variable stress (CVS). Stressed mice have significantly higher blood glucose levels but not notably higher body mass when compared to unstressed mice.



**Fig 2. Altered stress response and sexual dimorphism observed in offspring:** Male and Female offspring's stress response from stressed fathers after an acute stressor, compared to offsprings from unstressed control fathers. Mice were given stressor of restraint, then had a small volume of blood drawn every 30 minutes to test corticosterone levels. Males and females respond differently to stress as do offspring from stressed vs control sires.

## Discussion

- Corticosterone analysis revealed significantly altered stress response in offspring from stressed sires.
- Sexual dimorphism is observed in female vs. male stress response in offspring.
- Corticosterone release is lower in both male and female offspring from stressed sires, compared to offspring from control fathers.
- Corticosterone release variation is evident of stress dysregulation and increased risk of developing other neuropsychiatric disorders.

### Limitations:

- We did not test corticosterone levels during CVS in the F<sub>0</sub> generation males.
- We did not take baseline corticosterone levels prior to stress in the F<sub>1</sub> generation.

## Future Directions

- Sequence the RNA present in the F<sub>0</sub> generation blood to observe which small RNAs are upregulated in circulation.
- Sequence the RNA present in the F<sub>0</sub> generation sperm to confirm if these upregulated populations contain the same RNAs as present in the blood.

## Acknowledgments

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## Citations

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