



Delineating sex-specific mechanisms of impaired vasoreactivity in thermoneutrality

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Background

- Cardiovascular disease (CVD) is a leading cause of hospitalization and death.
- CVD is characterized by impaired vasoreactivity and mitochondrial dysfunction.
- Perivascular adipose tissue (PVAT), considered brown adipose tissue (BAT), regulates vasoreactivity
- In a previous experiment with rats housed at either their thermoneutral (TN, 30°C) or room temperature (RT, 22°C), TN-housed rats showed diminished vasodilation as well as less mitochondrial respiration in aorta.

Hypothesis: remodeling of PVAT phenotype from BAT to white adipose tissue (WAT) alters mitochondrial lipid utilization causing vasoreactivity dysfunction.



Lipid count Lipid/Tissue Ratio

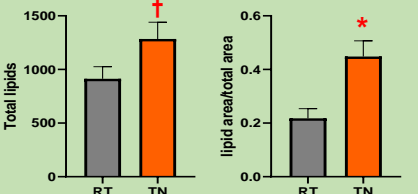
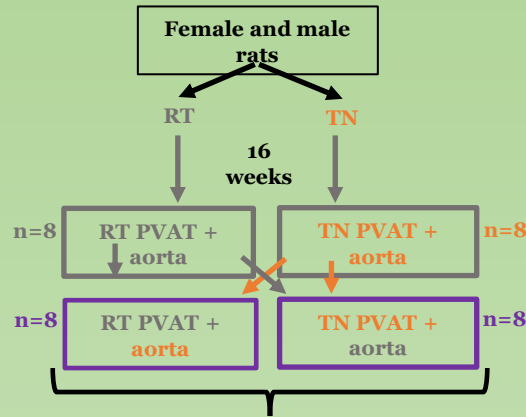


Figure 1. Lipids in PVAT from RT and TN-housed rats, stained with H&E.

Methods



Vasoreactivity and mitochondrial measurements

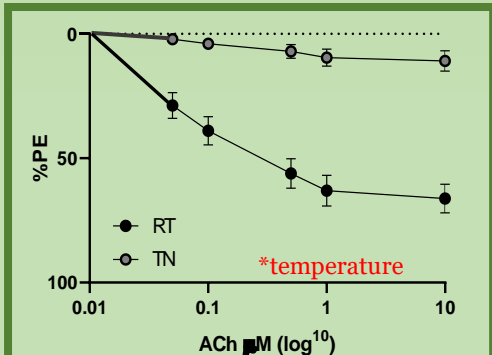


Figure 2. Background data showing vasodilation of male rat aorta without PVAT at RT or TN housing. *temperature

Results

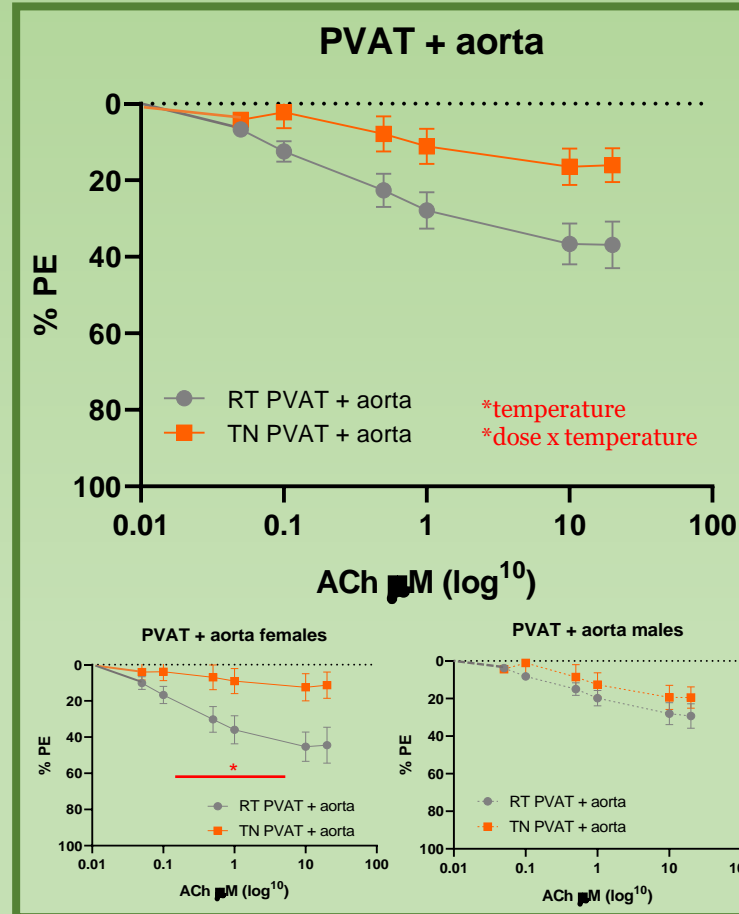
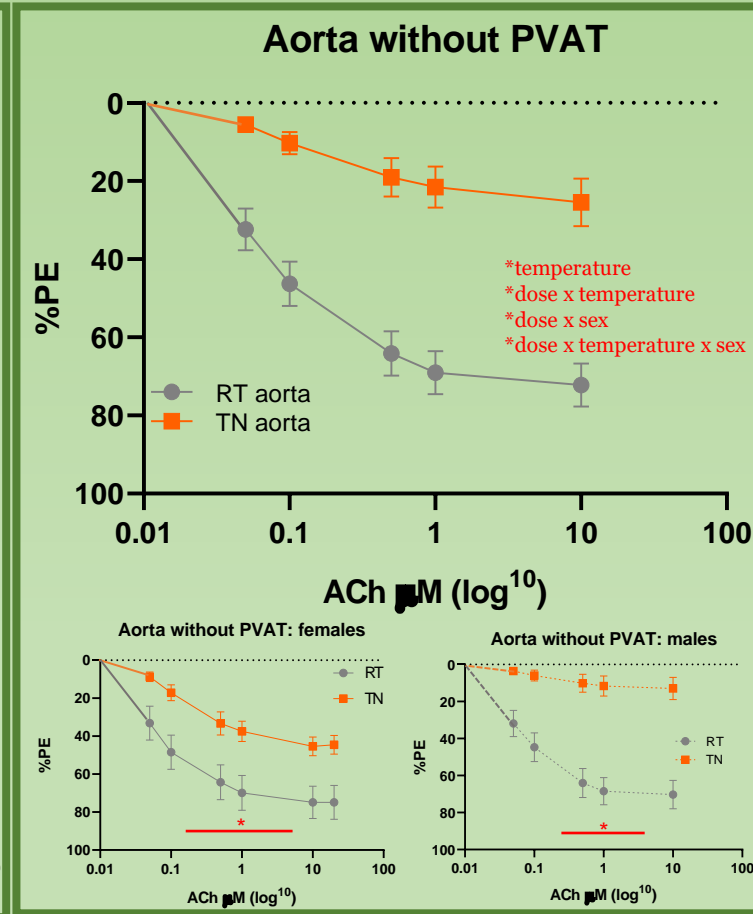


Figure 3. PVAT + aorta and aorta without PVAT response to ACh. All animals are combined according to housing temperature in upper graphs and split into graphs to show sex differences. *p<0.05, †p<0.08, three-way ANOVA or Student's t-test, sexes alone. Data are mean ± SEM.



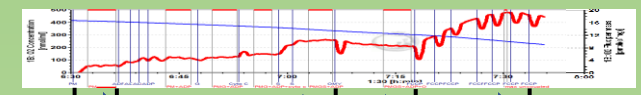
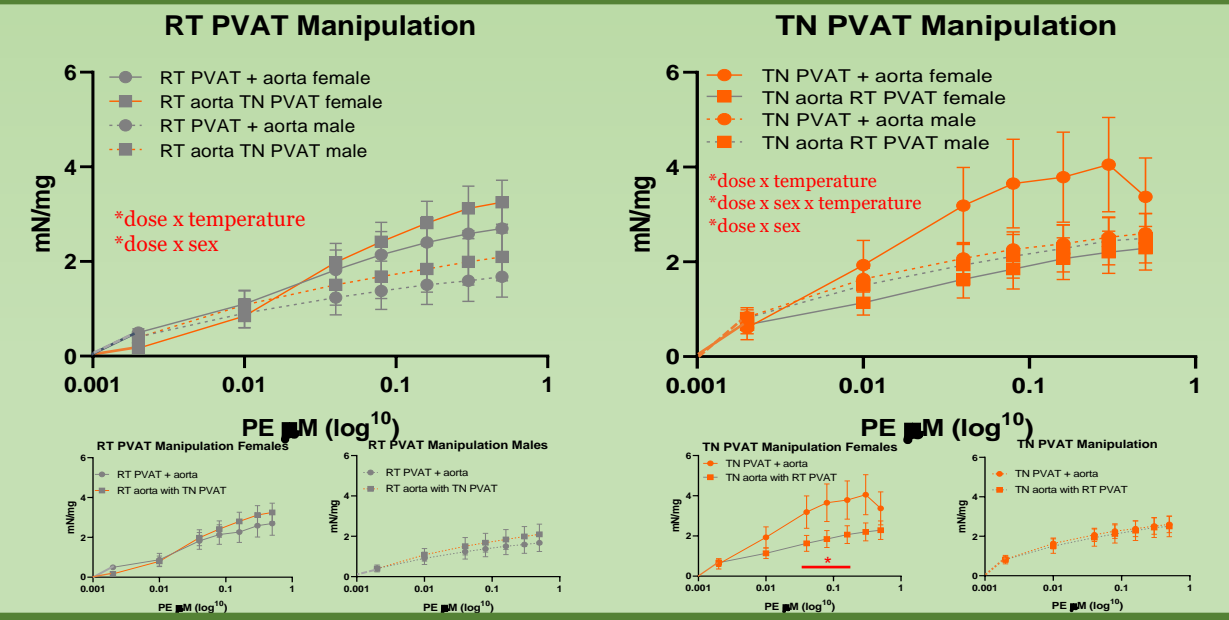
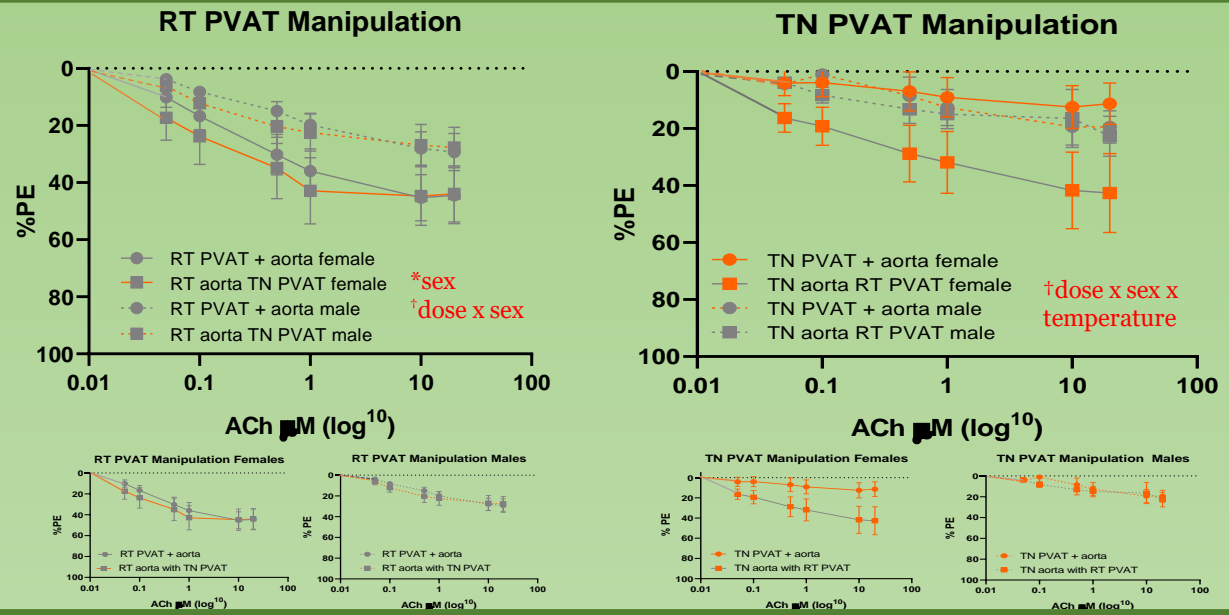
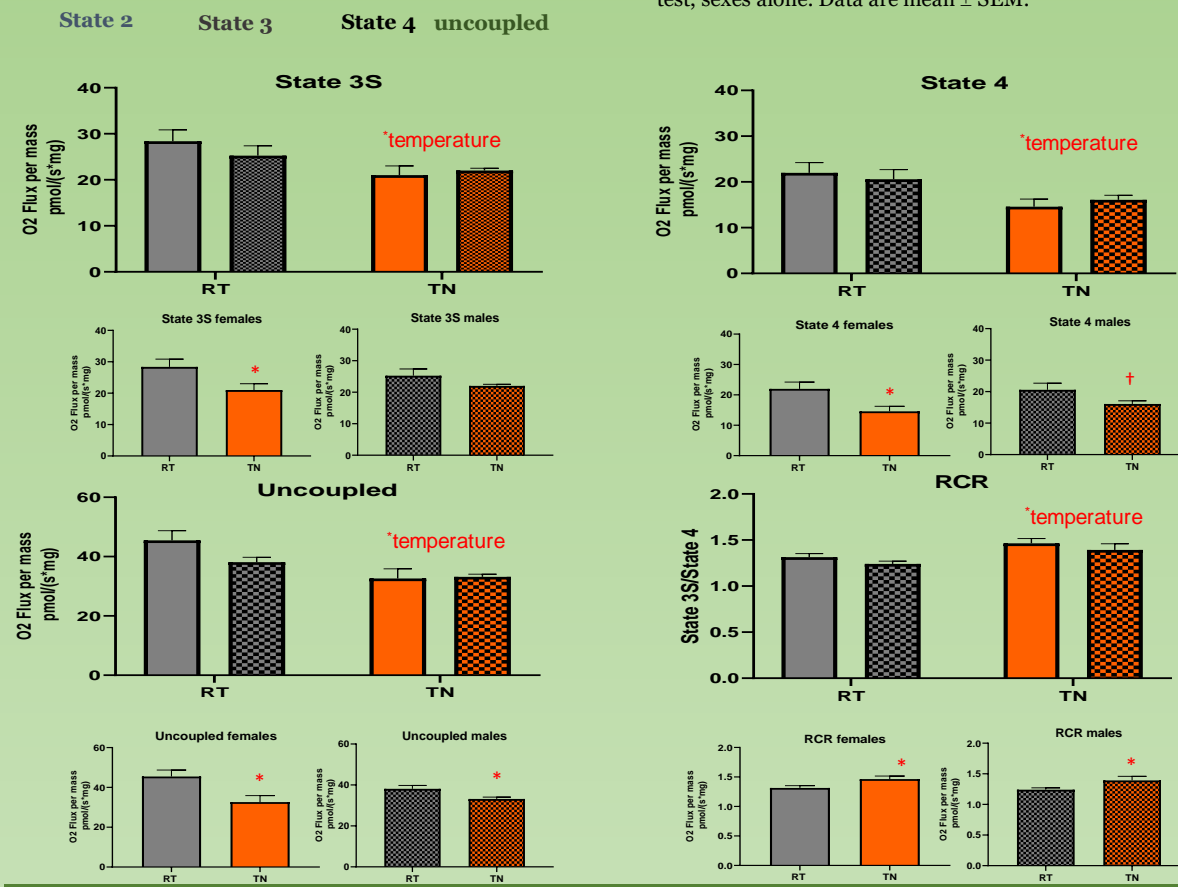


Figure 5. Lipid aorta mitochondrial respiration. Tissue was permeabilized and exposed to substrates mimicking lipid respiration (example trace, left). *p<0.05, two-way ANOVA or Student's t-test, sexes alone. Data are mean ± SEM.



Summary and conclusions

- Our data support that TN alters PVAT phenotype in a sex-dependent manner, resulting in dysfunctional vasoreactivity and diminished lipid mitochondrial metabolism.
- By utilizing TN housing, it is our objective to characterize the pathology of vascular disrepair along with mitochondrial dysfunction and address these pathologies and underlying sex differences.
- These targetable aspects of CVD in both male and female animals are exciting avenues for novel therapeutics.

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Figure 4. RT and TN PVAT Manipulation, ACh response (above) and PE response (below). Aorta were tested for ACh response or PE response with either their own PVAT or that from oppositely-housed rats. *p<0.05, †p<0.08, three-way ANOVA or Student's t-test, sexes alone. Data are mean ± SEM.