Evaluating effects of altered gravity on the nervous system using *D. melanogaster*

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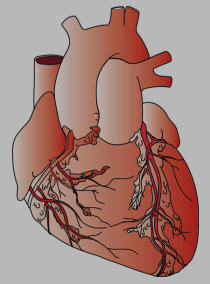
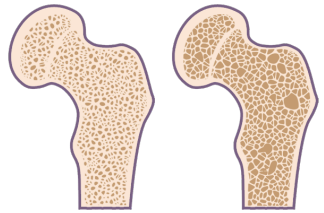
Physiological response to spaceflight

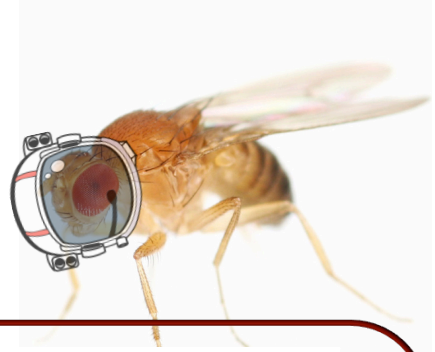


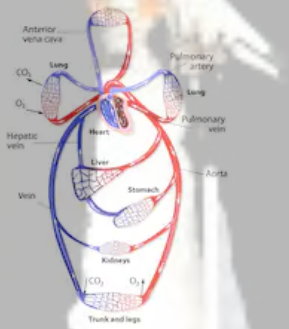
Cardiovascular deconditioning

Muscle atrophy

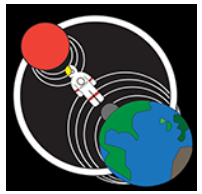


Bone loss





Fluidic shift

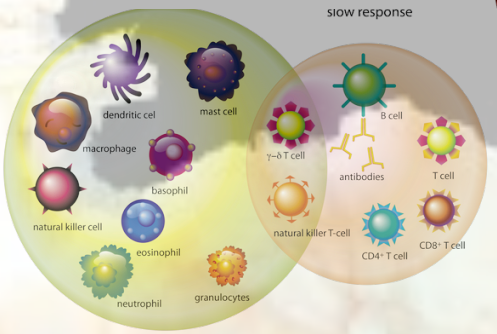


Microgravity (Lack of gravity)

Radiation

Social Isolation

Central Nervous system



Maladaptive immune system

Genetic changes - Telomeres

Drosophila melanogaster (fruit fly)

- ~75% of human disease-causing genes have a functional homolog in the fruit fly
  - Model for human innate immunity, circadian rhythms, development, neurobehavior etc.

- Amenable to experimental manipulation
  - Readily available genetic tools and fly lines
  - Well-annotated genome
  - Fast generation time
  - Low gene redundancy

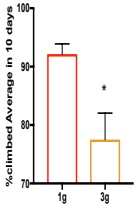
- Genetic manipulations and high throughput screening

- Small, convenient for ISS experimentation (requires little power, mass, volume) to get statistically significant sample sizes

Hypergravity – ground based altered gravity and stressor paradigm

- **Acute hypergravity (1.5hrs)**
- **Chronic hypergravity (15 days)**

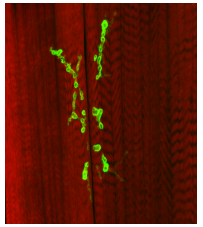
Neuro-behavioral assays

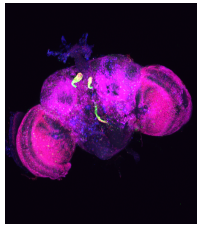


Climbing ability

Neural architecture and morphology

Glutamatergic synapses





Adult Brain

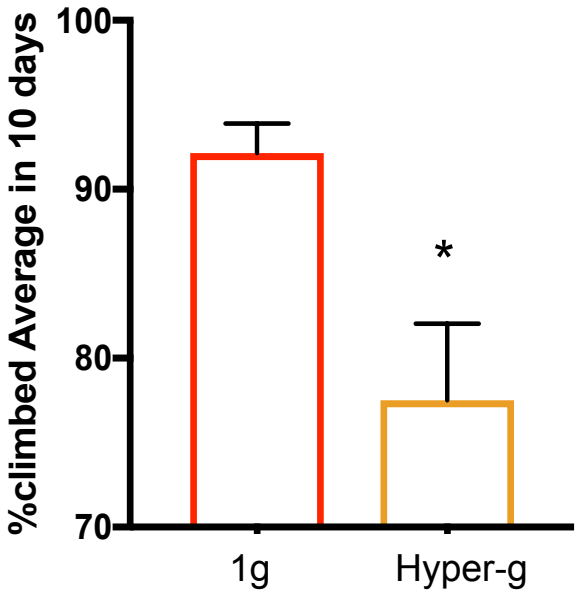
- Neuron
- Glia
- DA neurons
- Apoptosis
- Proliferation
- Oxidative stress markers

Biochemical assays

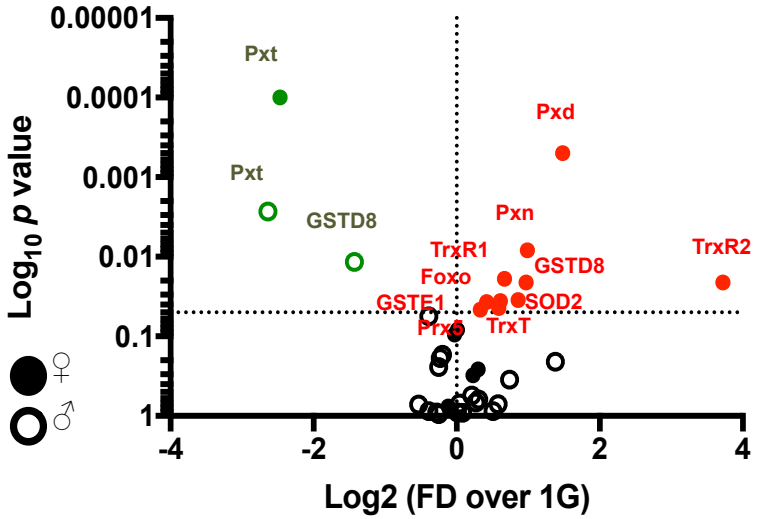
- Mitochondrial membrane potential
- ATP
- Western blot
- Colorimetric assays
- Gene expression

Hypergravity induces oxidative stress response genes

Neurobehavior

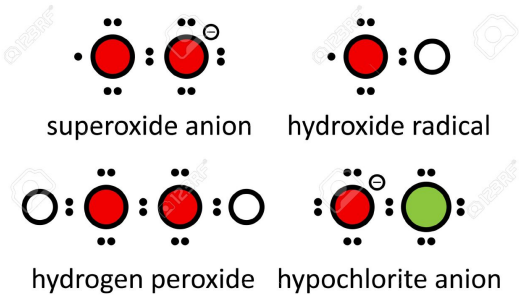


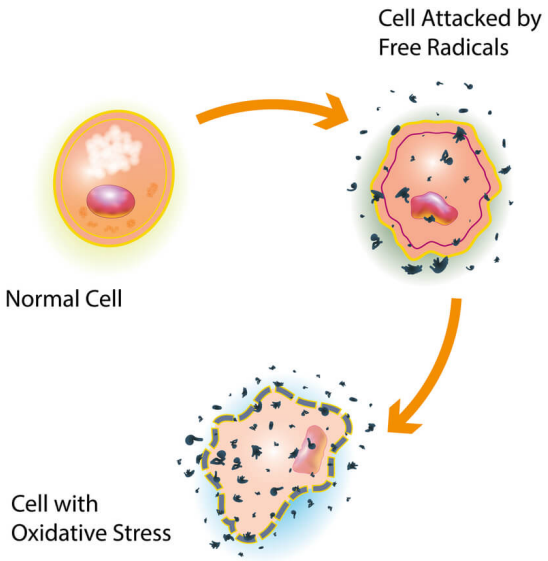
Oxidative stress genes

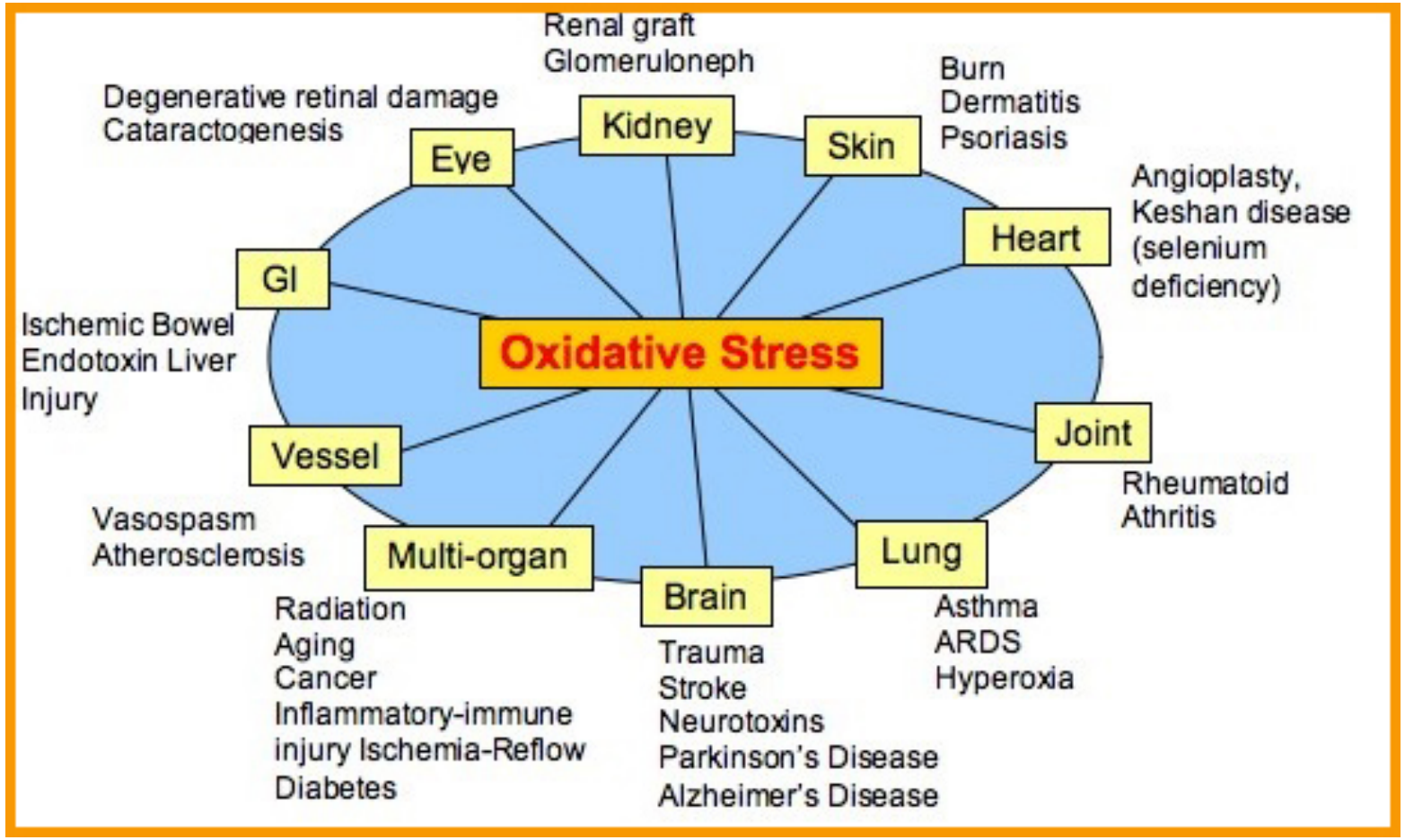


Hypothesis: Exposure to altered gravity triggers the oxidative stress response, leading to impairments in the nervous system.

What is oxidative stress?







https://www.123rf.com/photo_24396738_reactive-oxygen-species-ros-superoxide-anion-hydroxide-radical-hydroperoxide-and-hypochlorite-an.html

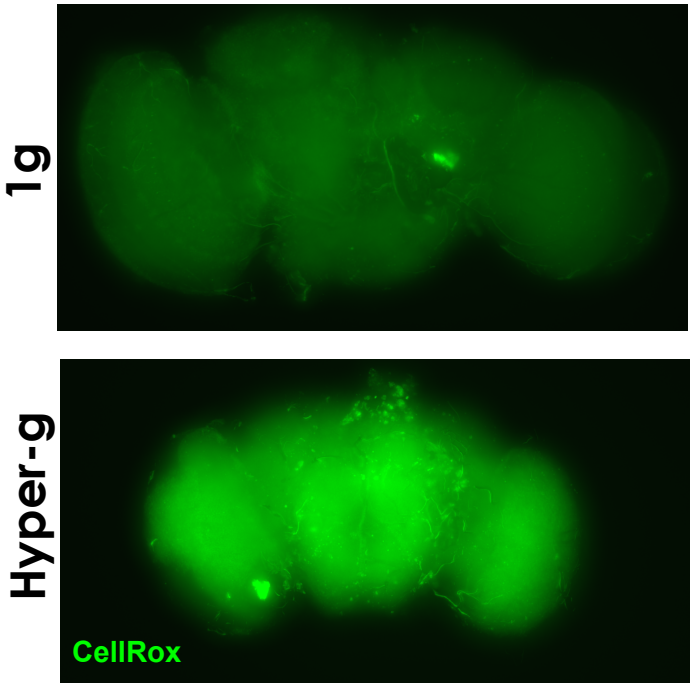
https://www.biovision.com/products/metabolism-assays/oxidative-stress.html?limit=20

Acute hypergravity – Increased ROS

Reactive Oxygen Species

Dopaminergic neurons

A



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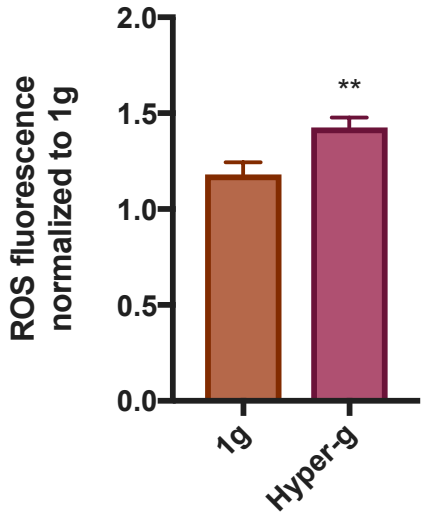

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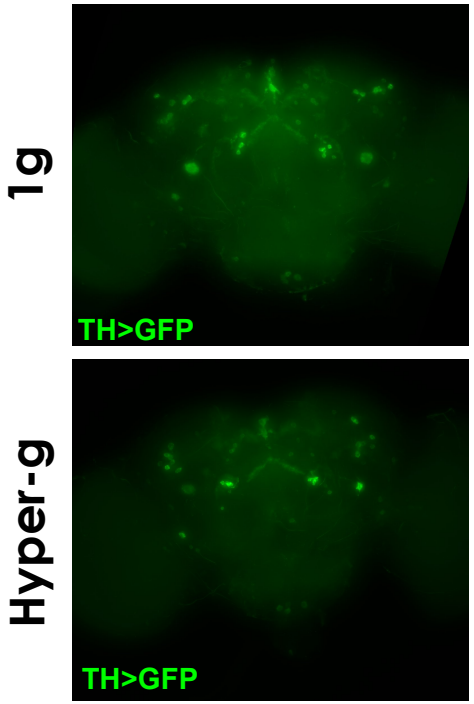

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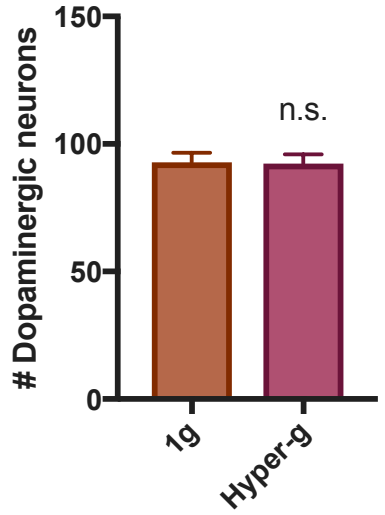
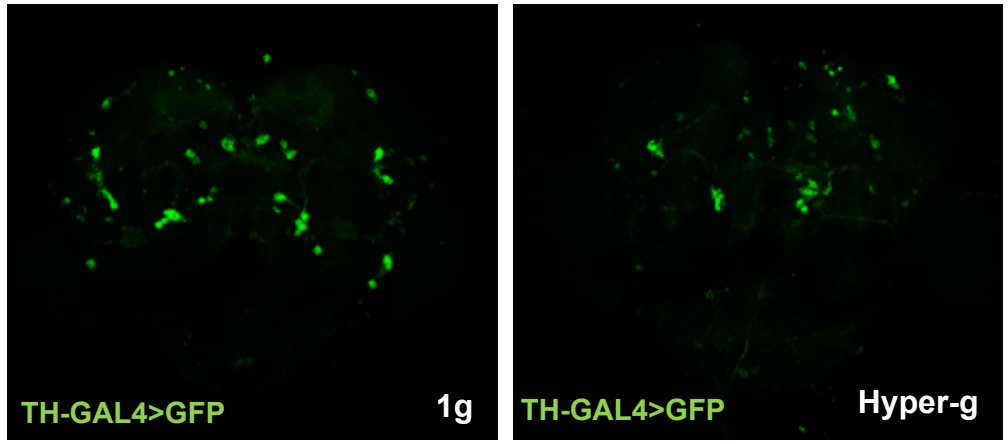
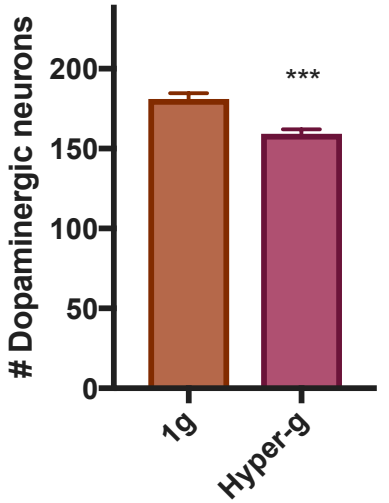


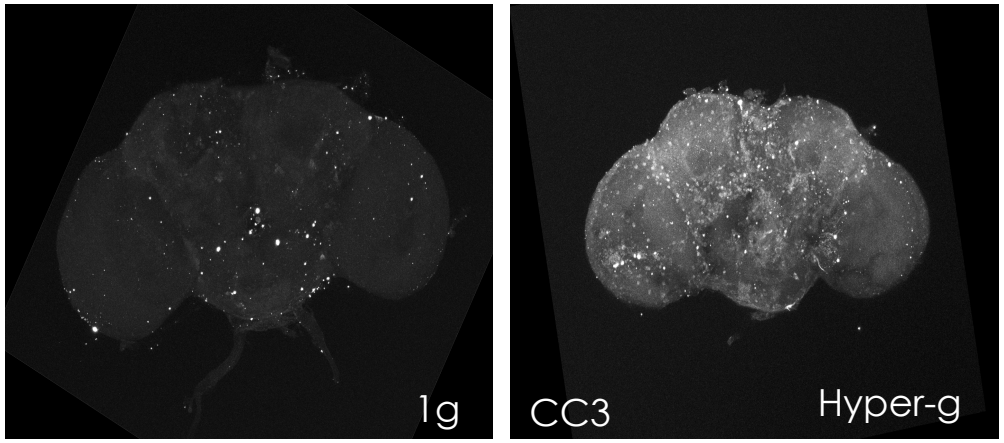
Chronic hypergravity – Neuronal loss

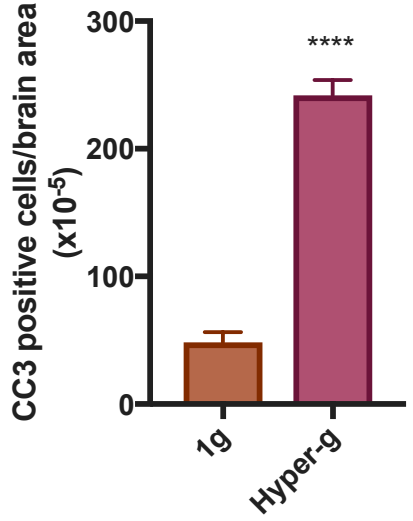
Dopaminergic neurons



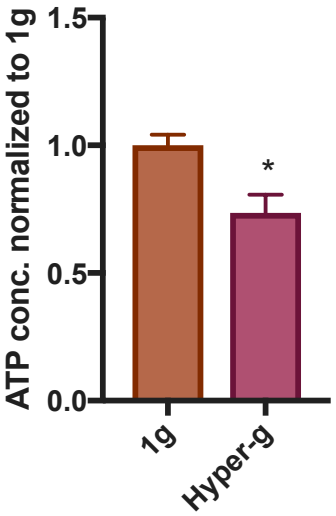


Pro-apoptotic cells



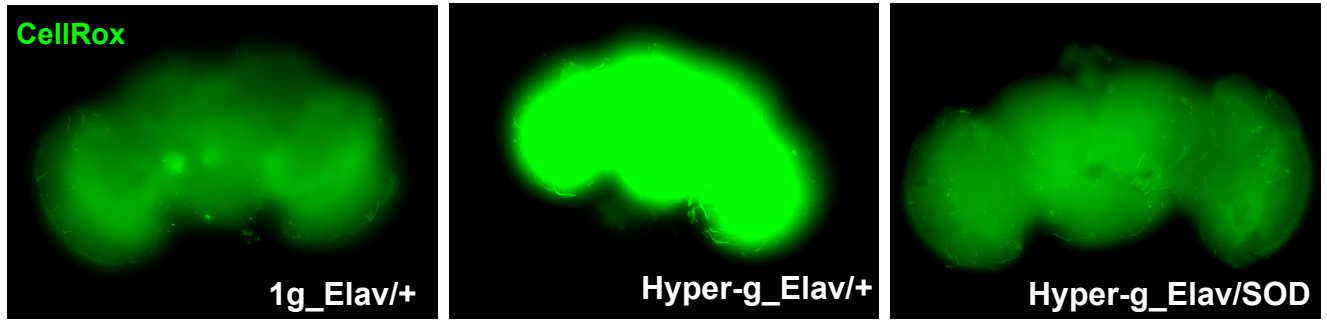


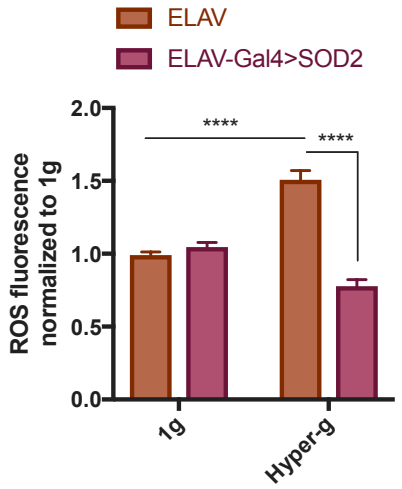
ATP levels



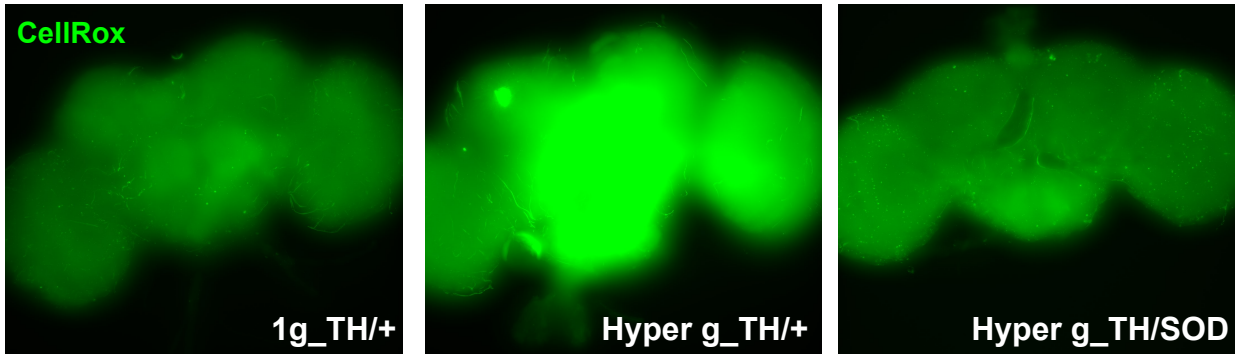
SOD2 overexpression suppresses ROS and neurobehavioral phenotype

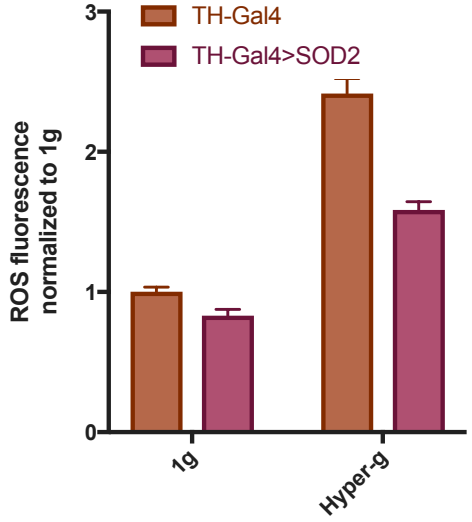
Pan neuronal SOD2 expression

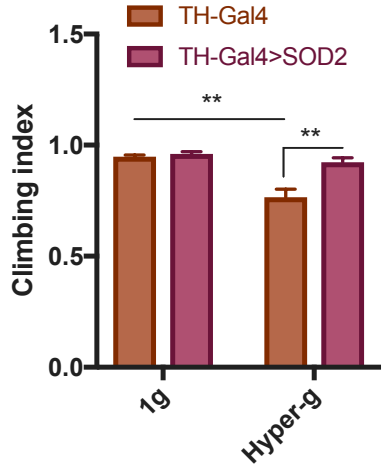




Dopaminergic SOD2 expression







Summary

- Hypergravity leads to increased ROS
- Increased ROS is causing loss of Dopeminergic neurons, similar to Parkinson's Disease
- Loss of neuronal cells
- Overexpression of antioxidant gene, SOD2 in neurons as well as dopaminergic neurons
- Hypergravity - ground based stressors and altered gravity model
- Fly hypergravity model for high throughput screening of putative genetic and therapeutic interventions

Acknowledgements

Bhattacharya Lab
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