Mice Exposed to Combined Chronic Low-Dose Irradiation and Modeled Microgravity Develop Long-Term Neurological Sequelae

Eliah G. Overbey[1,†], Amber M. Paul[2,†], Willian A. da Silveira[4], Candice G.T. Tahimic[2,5], Sigrid S. Reinsch[2], Nathaniel Szewczyk[6], Seta Stanbouly[7], Charles Wang[8,9], Jonathan M. Galazka[2], and Xiao Wen Mao[7]

1: Department of Genome Sciences, University of Washington
2: Space Biosciences Division, NASA Ames Research Center
3: Universities Space Research Association
4: Institute for Global Food Security (IGF), School of Biological Sciences
5: KBR, Moffett Field
6: MRC/ARUK Centre for Musculoskeletal Ageing Research & National Institute for Health Research Nottingham Biomedical Research Centre
7: Division of Biomedical Engineering Sciences (BMES), Department of Basic Sciences, Loma Linda University
8: Center for Genomics, School of Medicine, Loma Linda University, Loma Linda
9: Department of Basic Sciences, School of Medicine, Loma Linda University
† These authors contributed equally to this work.

Introduction

How rapidly do astronauts recover neurologically from spaceflight? Evidence suggests that astronauts can experience cognitive impairment while in space, but we don't know how long gene expression changes in brain tissue persist once returned to Earth. This study works towards the long-term goal of uncovering the length of time that astronauts need to in order to re-adapt to Earth after returning from their missions.

In our experiment, mice were exposed to modeled microgravity (hindlimb unloading) and low-dose radiation (cobalt plates). RNA sequencing data was collected from brain tissue and analyzed for differentially expressed genes and their corresponding functions.

Methods

Microgravity Model
Hindlimb unloading to create fluid-shift towards the head.

Low-Dose Radiation
Cobalt plates that release low-dose radiation (0.04Gy) as gamma rays.

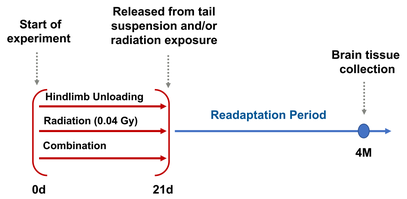
RNA-sequencing
Measures gene expression from brain tissue.

GeneLab computational pipeline
Processes RNA-sequencing data into differentially expressed genes.

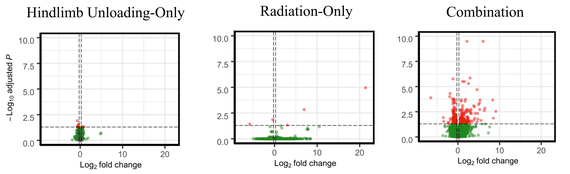
Higher-Order Analyses
Computational tools WebGestalt for gene ontology analysis and Reactome for pathway analysis

Results

Experimental Design

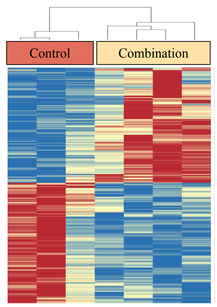


Differential Gene Expression Occurs Primarily with Combined Spaceflight Factors

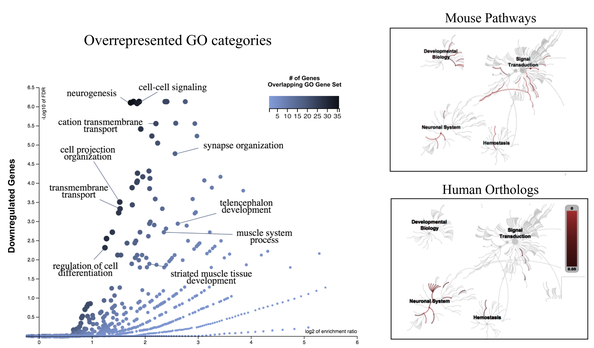


Each plotted point is a gene. Differentially expressed genes are in **red**, which means it has met the adjusted p-value and Log2 fold-change threshold for significance (p<=0.05, |log2FC| > 0.263). If it has only met the adjusted p-value threshold, it is in **green**.

Differentially Expressed Genes Profile for Combination Group



Gene Ontology (GO) and Pathway Analyses

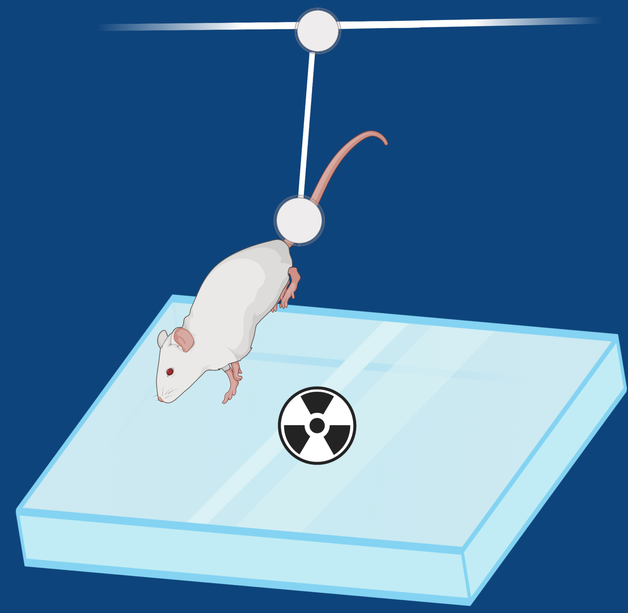


Discussion

- The combination group and each individual conditions **do not share** any overlapping differentially expressed genes. Each group had **a distinct set** of differentially expressed genes.
- Differentially expressed genes in the combination group suggest an **reduced transcriptional machinery, increased neurogenesis and neuropeptide production, dysregulated cell structure and cell signaling** at the 4 month timepoint.
- A subset of the differentially expressed genes in the combination group have orthologs in humans, particularly in **neurodevelopmental homeostatis and signal transduction pathways**. This provides neuro-related pathways that can be explored in future experiments on human cell systems.

A **combination** of spaceflight-relevant factors (**fluid-shift** and **radiation**) created a different **gene expression profile** than either factor individually.

Gene expression differences can persist for at least **4 months** after a **21-day exposure** to a combination of fluid-shift and radiation in the **brain tissue** of mice.



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