Space Biosciences
NASA AMES RESEARCH CENTER

Social isolation impacts select responses to simulated weightlessness

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Overall goals

1. Gain better understanding of HU model
   - *better extrapolate to human responses*

2. Determine contribution of social isolation to HU responses
   - *gain insight on combined effects of spaceflight factors*

Rodent hindlimb unloading (HU) as a ground-based analog for weightlessness

- Analog for musculoskeletal disuse and cephalad fluid shift observed in spaceflight (Morey-Holton, Bikle and Globus 1984)

- Non-invasive tail traction to elevate hindlimbs; single housing

- Variations
  - Partial unloading (Wagner et al 2010 J Appl Phys)
  - Tail piercing at intervertebral disc space; single or group housing (Ferreira et al 2011 J Vis Exp)

Our goal: Develop social housing HU system; retain non-invasive tail securement, 360^{o} range of motion + uniaxial movement

Rationale for group housing during HU

- Rodents are **social** animals
- Better simulation of housing conditions in **ISS** (NASA Rodent Research animal habitat)
- Apply **refinement** principle

Social housing versus single housing HU models

- Standard tools and COTS materials
- Portable
- Individual treatments in food and water
- Easy cleaning

Environmental stressors during spaceflight

- **Microgravity**
- **Isolated environment**
- **Ionizing radiation**

Social isolation profoundly impacts physiology of social species

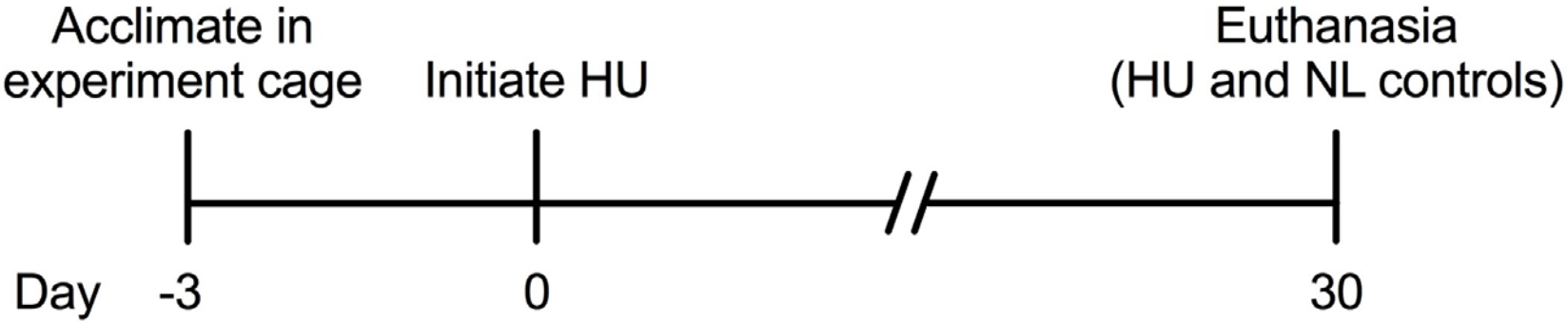
Astronauts not in solitude but experience a sense of isolation

Study combined effects of microgravity and social isolation in HU model

Hypothesis

Social isolation exacerbates tissue deficits caused by simulated weightlessness.

Experiment design

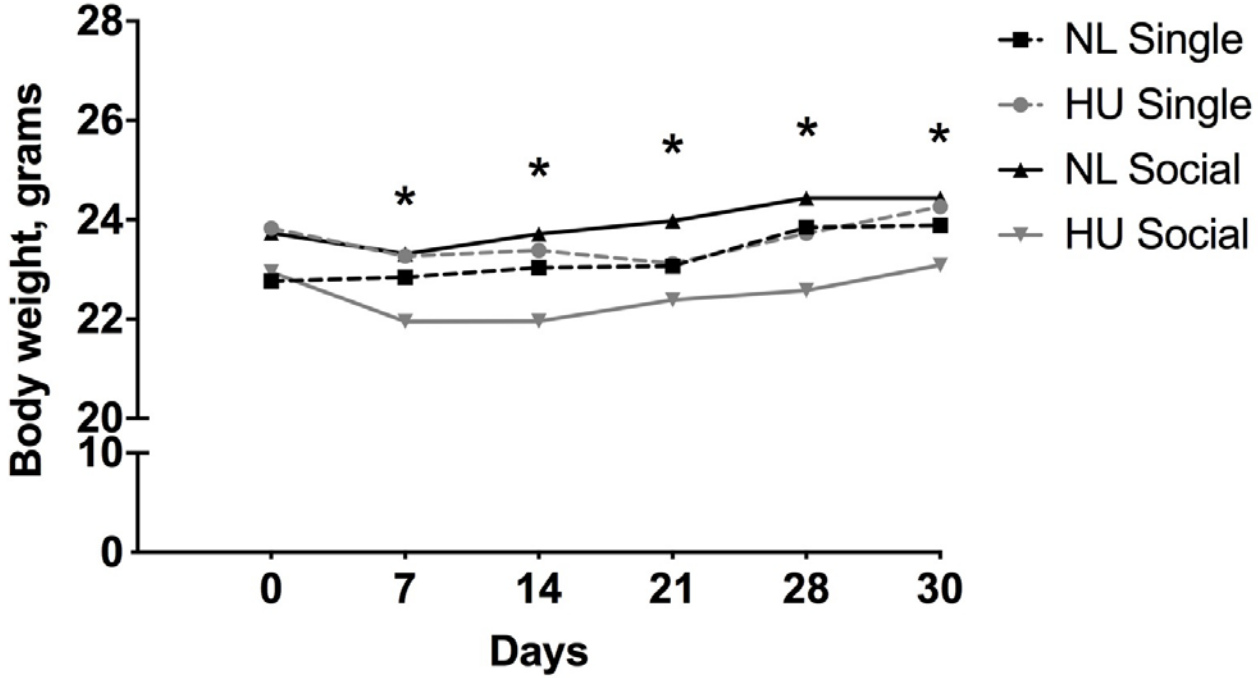


Study A (C57BL6/NJ) **16-17 week old females**

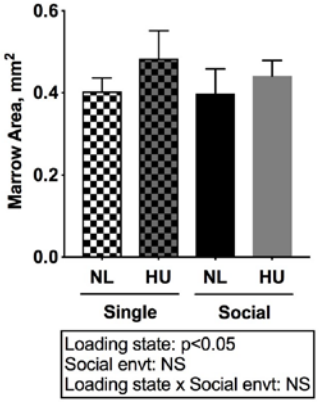
Social-housed NL control	Single-housed NL control
Social-housed HU	Single-housed HU

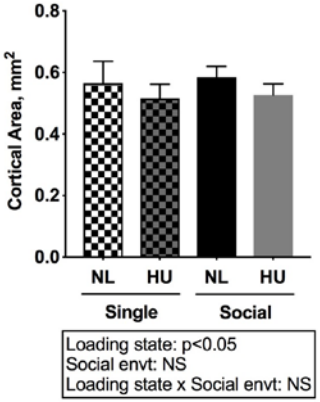
IACUC approval obtained prior to any animal experiments.

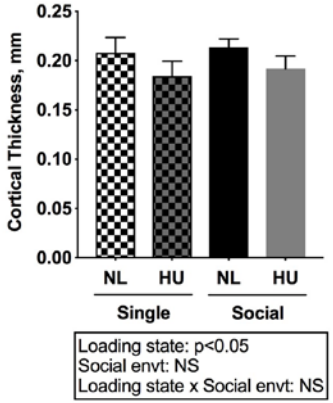
Body weights

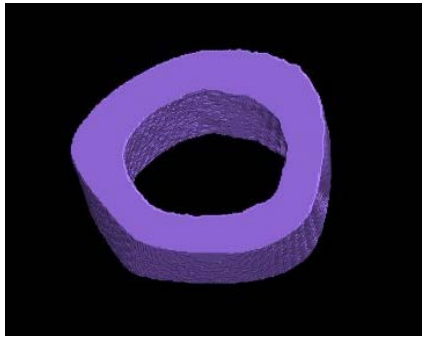


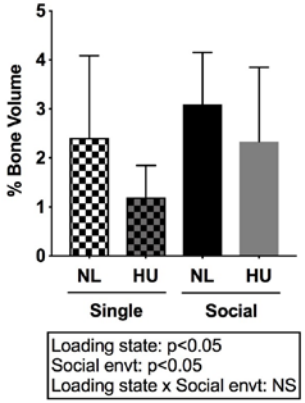
Social isolation contributed modestly to skeletal structural deficits caused by HU

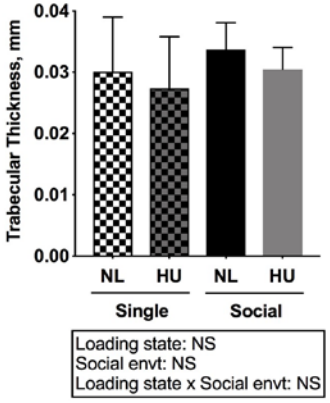


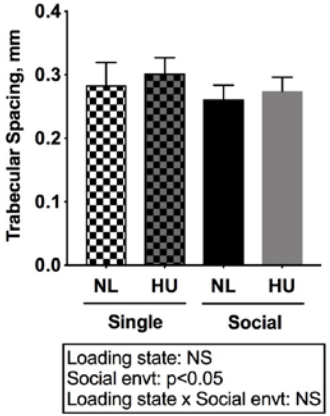


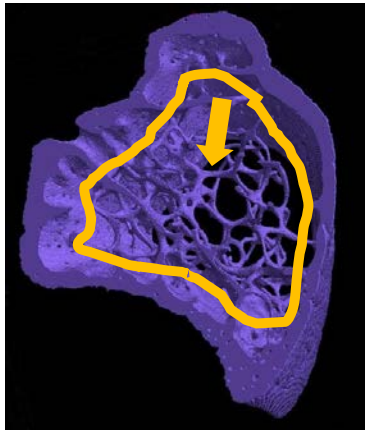




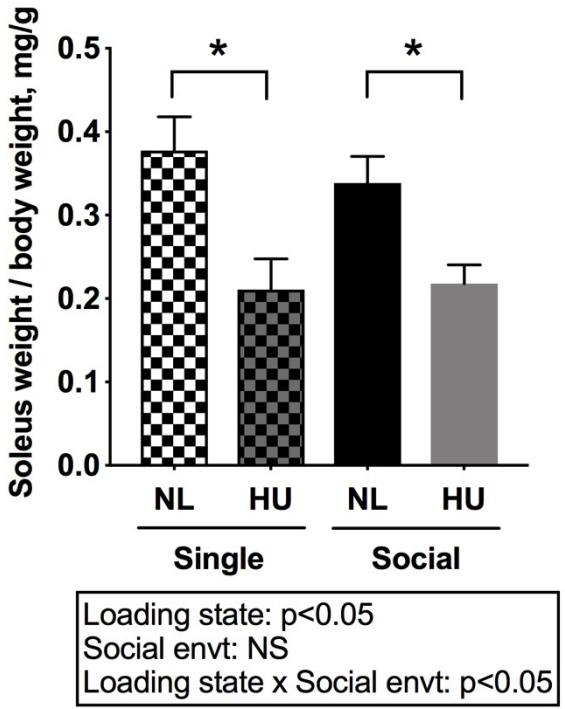




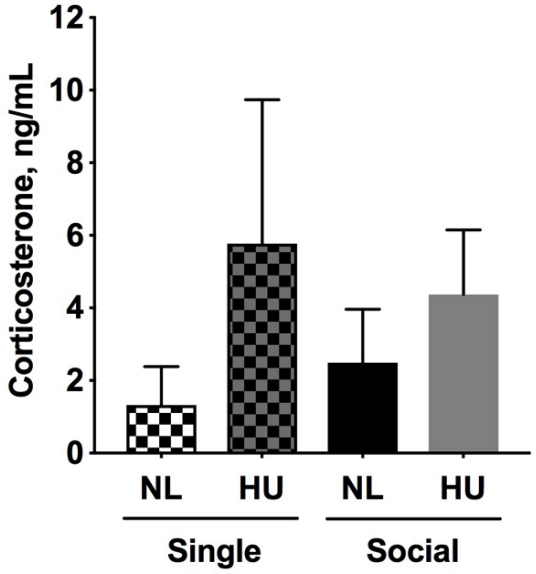




Social isolation did not impact soleus atrophy during HU



Neuroendocrine response was differentially affected by social environment



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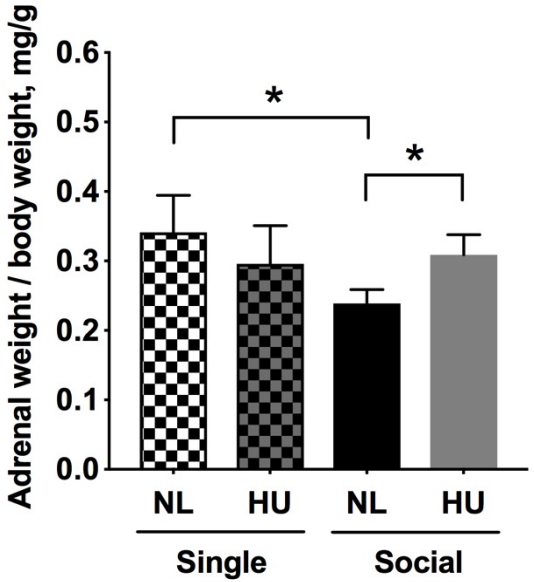

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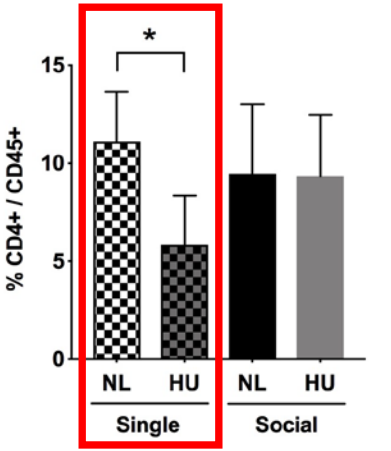
Social isolation during HU leads to decreased neutrophil populations



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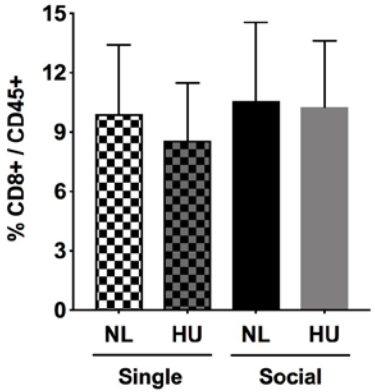

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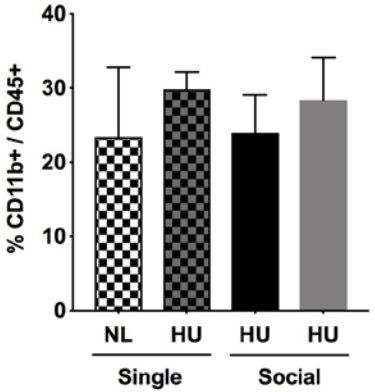

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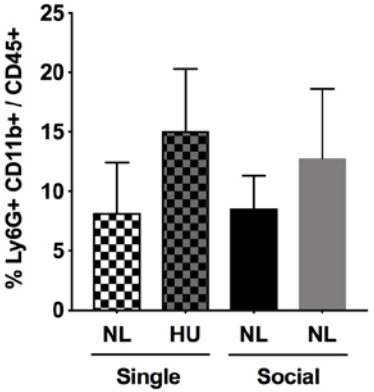

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Summary

- Deficits in musculoskeletal structure: comparable in social versus singly housed HU animals
  - *HU-induced musculoskeletal decrements mostly attributed to altered mechanical load (minor contribution of social isolation)*
- Social isolation can potentially mask some aspects of the neuroendocrine response to HU
  - *Effect of HU and social isolation on some aspects of neuroendocrine stress response may not be additive*
- Some immune outcomes (e.g. neutrophils, cytokines) are sensitive to the social environment during HU

Impact of social isolation must be taken into account in interpreting data from traditional HU model

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Social housing HU model