Estrous Cyclicity of Mice During Simulated Weightlessness

Eric Moyer, Yuli Talyansky, Ryan Scott, Joseph Tash, Lane Christenson, Joshua Alwood, April Ronca

Presented at the 2017 meeting of American Society for Gravitational and Space Research
Motivation for studying estrous cyclicity in simulated weightlessness

- STS-131, STS-133, STS-135 revealed cessation of estrous cycle in female mice (Tash 2012 & Ronca 2014)
- Spaceflight leads to loss of corpora lutea and significantly reduced estrogen receptor mRNA levels in the uterus

Goals of this study
- Assess whether female endocrine signaling biomarkers are altered in simulated weightlessness via hindlimb unloading model in both reproductive and non-reproductive organs
Experimental Design

- Normally Loaded: n=10
- Hindlimb Unloaded: n=10
- Vivarium Control: n=10

Primary endpoints:
1. Did mice maintain/return to normal estrous cycling?
2. Were there structural changes to reproductive organs (ovaries, uterus, vaginal wall)?
Methods: Daily lavage and Imaging


Cora, Michelle C., Linda Kooistra, and Greg Travlos. "Vaginal cytology of the laboratory rat and mouse: review and criteria for the staging of the estrous cycle using stained vaginal smears." Toxicologic pathology 43.6 (2015): 776-793.
Methods: Cytology Analysis

• Translate qualitative data into an experiment timeline for each mouse defining Day 0 as start of treatment.

• Graph each animal’s estrous cycle in relation to other experiment landmarks

Hypothesis

• Hindlimb unloading will cause mice to arrest estrous cyclicity in the diestrous stage

<table>
<thead>
<tr>
<th>Experiment Landmark</th>
<th>Day</th>
</tr>
</thead>
<tbody>
<tr>
<td>HU Cage Acclimation Begins</td>
<td>-3</td>
</tr>
<tr>
<td>HU Treatment Begins</td>
<td>0</td>
</tr>
<tr>
<td>Euthanasia/Tissue Collection</td>
<td>11/12</td>
</tr>
</tbody>
</table>
Result: Pair-feeding/Cage effect observed
Result: Differences observed in HU reproductive organs and adrenals
Cytology Results

- Average cycle length of vivarium cage control animals was 4.7 days.
  - In line with reported literature\(^1,2\)
  - Suggests our technique did not impede normal cycling

- Normal cycling did not present in many animals during the acclimation to HU cages, or even throughout remainder of experiment.

- Some occurrences of cycling did return to HU cage mice.

- Infection-like symptoms resulted in missing data in HU mice.

Conclusions

• Cage effect/Pair Feeding effect present
• Validated model for observing estrous stage in VIV control
• Longer acclimation period may allow control cage animals to return to normal estrous cyclicity
• Longer HU period may allow HU animals to acclimate and return to normal estrous cyclicity
Thanks to those who contributed

NASA Ames Research Center
• Joshua Alwood
• Catherine Choi
• Parker Dubee
• Ayana Kishibuchi
• Eric Moyer
• Kotaro Okada
• Megan Pendleton
• April Ronca
• Ryan Scott
• Pantelis Solomides
• Brad Staten
• Yuli Talyansky
• Nicholas Thomas

Kansas UMC
• Lane Christenson
• Joseph Tash

This research was supported by NASA Space Biology Grant NNX15AB48G