Examination of Age and Sex Differences in Sigma-1 Receptor Expression Following Pubertal Immune Stress

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INTRODUCTION

Background

- **Puberty** = sensitive period of neurophysiological development → neurological systems are highly vulnerable to external immune stressors
- **Sex-based differences in immune response following immune challenges also arise during puberty.**
- **Sigma-1 receptor (σ1-R)** = intracellular chaperone protein involved in neuroprotective functions within the brain that improve memory and cognition; found in high density in the **hippocampus** (region of brain involved in learning and memory)
- Lowered levels of σ1-R = predisposition to neurodegenerative conditions such as **Alzheimer's disease (AD)** → can there be age- or sex-based manifestations?
- **Pubertal immune stress may be an underlying factor in decreased σ1-R.**

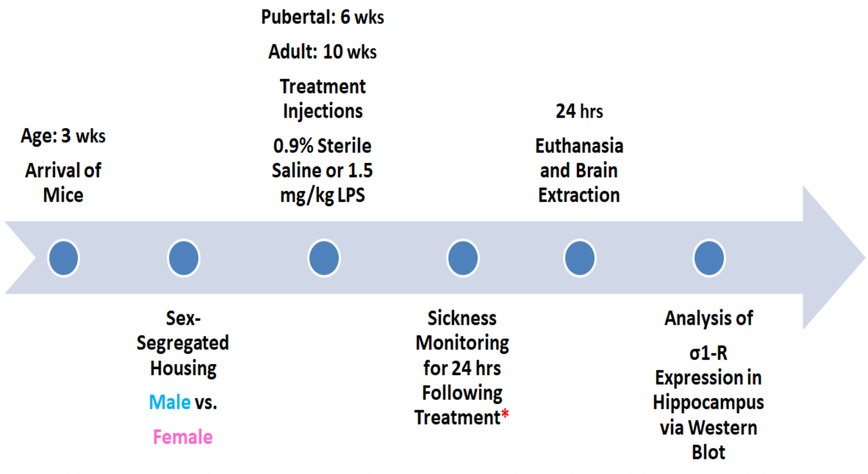
Objectives

- Examine age (pubertal vs. adult), sex (male vs. female), and treatment (saline vs. LPS endotoxin) effects on acute σ1-R expression following exposure to systemic immune stress.

Hypothesis

- Neuroinflammation induced by systemic LPS exposure is expected to reduce σ1-R expression among pubertal mice and among male mice vs. their respective counterparts.

METHODS



* Sickness monitoring was performed 2hrs, 4hrs, 8hrs, 12hrs, and 24 hrs post-treatment to observe changes in behavioural indicators of sickness.

N = 72 CD-1 Mice			
Pubertal		**Adult**	
♂ n_{LPS}= 8 n_{Saline}= 8	♀ n_{LPS}= 8 n_{Saline}= 8	♂ n_{LPS}= 8 n_{Saline}= 8	♀ n_{LPS}= 8 n_{Saline}= 8

RESULTS

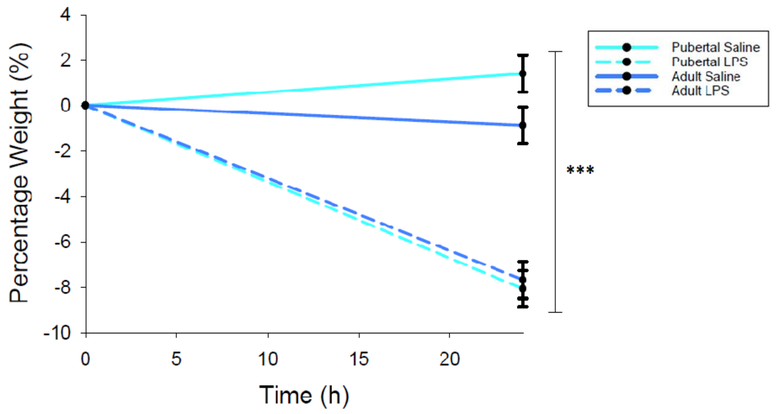


Figure 1. Mean percentage weight change in male CD-1 mice following 0.9% saline or LPS treatment.

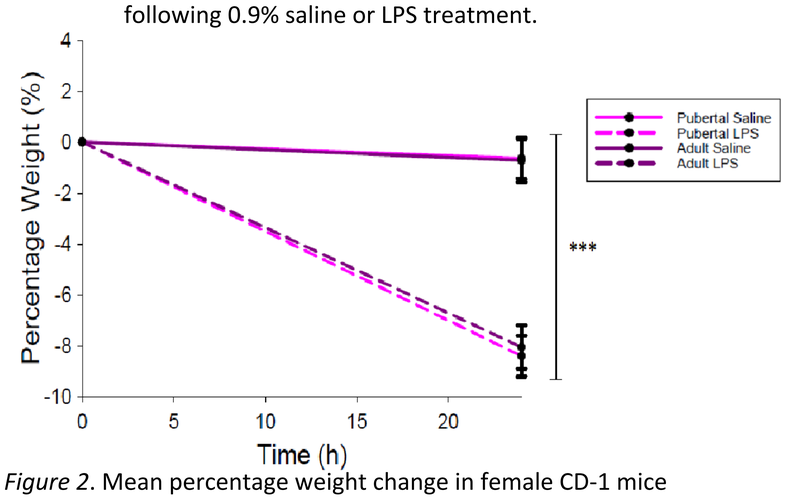


Figure 2. Mean percentage weight change in female CD-1 mice following 0.9% saline or LPS treatment.

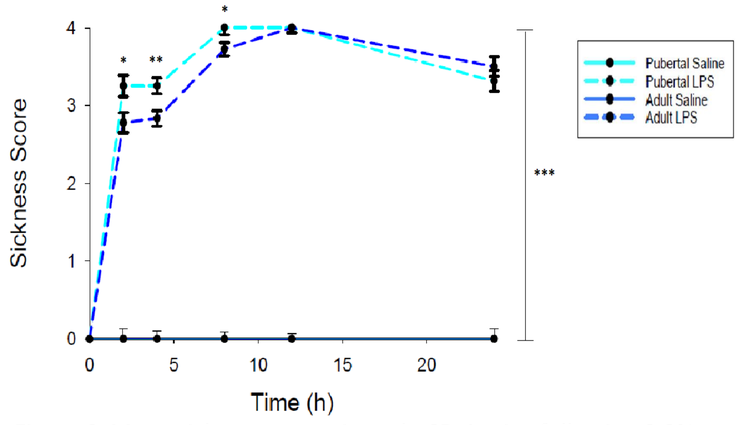


Figure 3. Mean sickness scores in male CD-1 mice following 0.9% saline or LPS treatment.

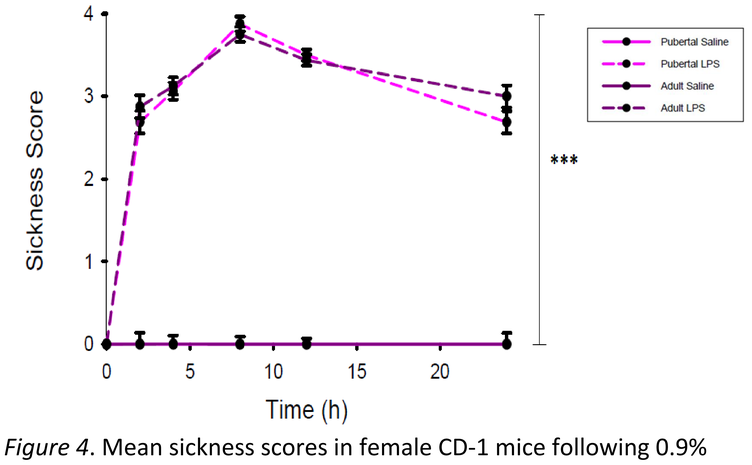


Figure 4. Mean sickness scores in female CD-1 mice following 0.9% saline or LPS treatment.

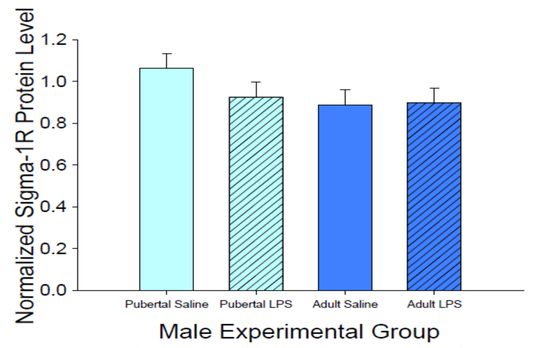


Figure 5. Normalized σ1-R levels in hippocampus of male CD-1 mice following 0.9% saline or LPS treatment.

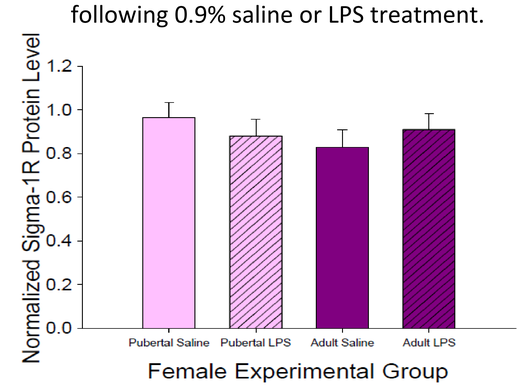


Figure 6. Normalized σ1-R levels in hippocampus of female CD-1 mice following 0.9% saline or LPS treatment.

Note: *= $p< 0.05$, **= $p< 0.01$, ***= $p< 0.001$

CONCLUSIONS

Sickness

- LPS **treatment** significantly decreased body weight and increased sickness behaviours compared to saline-treated mice.
- LPS-treated males had significantly higher sickness responses than female counterparts →**sex differences**
- Particularly in males , pubertal LPS-treated mice had significantly higher sickness responses than adult counterparts →**age differences**

σ1-R Expression

- No significant age, sex, or treatment differences in σ1-R expression 24 h after systemic LPS exposure.

Future Directions

- Examine age and sex differences in long-term changes in σ1-R expression following pubertal immune stress.
- Investigate age and sex differences in the development of related AD biomarkers and whether exposure to pubertal immune stress can effect the expression of these biomarkers.

Acknowledgements

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