

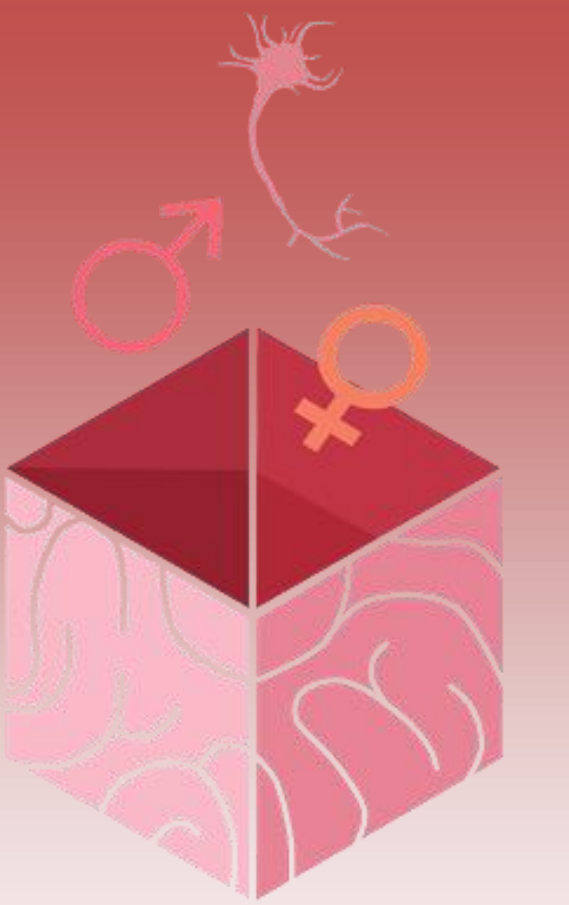


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The Long-Term Consequences of Pubertal Immune Stress on Learning and Memory

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Introduction

Puberty is a critical period for gonadal maturation and brain development (Sisk & Foster, 2004; Blakemore, Burnett, & Dahl, 2010)¹. The pubertal brain is also particularly vulnerable to damage, and early activation of the immune response from external stressors influences various aspects of brain functioning, including learning and memory (Ratnayake, Quinn, Walker, & Dickinson, 2013)². However, the enduring impact of a pubertal stressor, especially in the context of sex differences and gonadal status, is largely unknown.

Objectives:

Analysis of the long-term effects on learning and memory of pubertal immune stress as a function of treatment, sex, and gonadal status.

Hypotheses:

Learning and memory:

1. Outperformance of LPS-injected mice over their saline counterparts;
2. Outperformance of males over female regardless of treatment;
3. And, outperformance of gonadectomized females over sham-operated females.

Methods

3 weeks of age: Arrival of animals

Treatment (6 weeks old):

Single *i.p.* injection of LPS (1.5mg/kg) or 0.9% saline control (6 weeks of age). Sickness behaviours and weights were analyzed 48 hours post-injection.

Surgery (9 weeks old):

Gonadectomy (Gx) or sham-operations were performed on males and females.

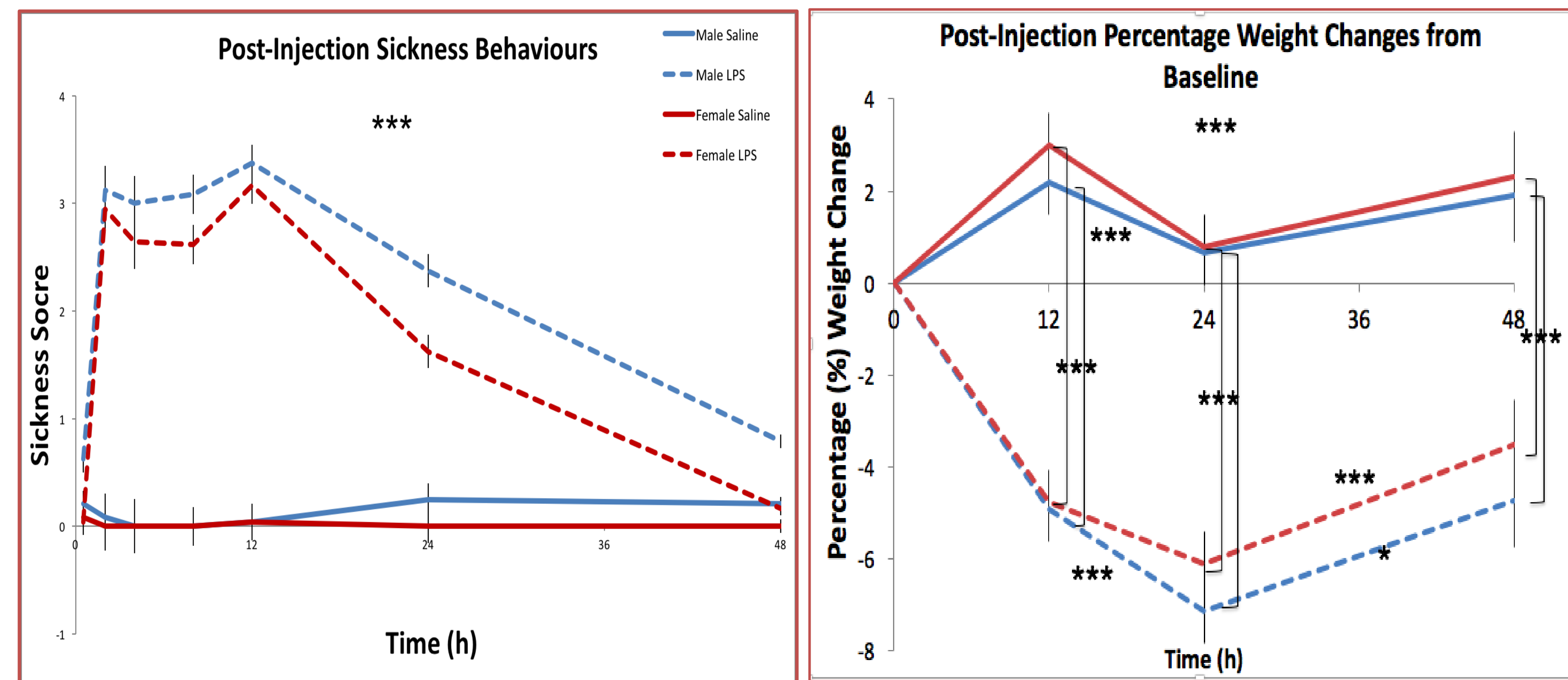
Behavioural Testing (13 weeks old):

Morris Water Maze: Analysis of short- and long-term visuospatial memory. A total of 16 60 s trials (four trials/day) were administered followed by a 60 s probe trial on the fifth day.

Sex	Males (n = 24)		Females (n = 24)	
	Saline (n = 12)	LPS (n = 12)	Saline (n = 12)	LPS (n = 12)
CD-1 Mice	Sham Operation (n = 6)	Gonadectomy (n = 6)	Sham Operation (n = 6)	Gonadectomy (n = 6)
	Sham Operation (n = 6)	Gonadectomy (n = 6)	Sham Operation (n = 6)	Gonadectomy (n = 6)

Results

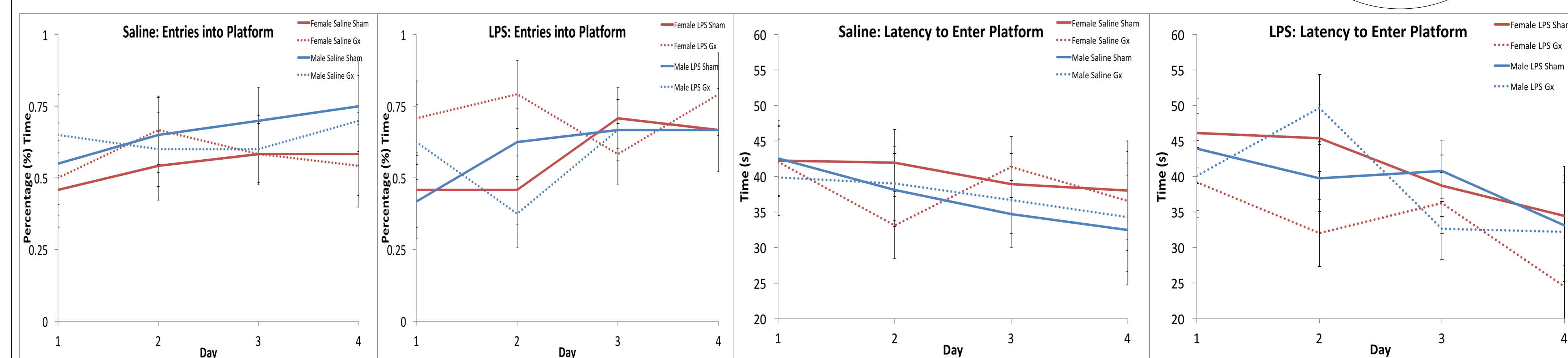
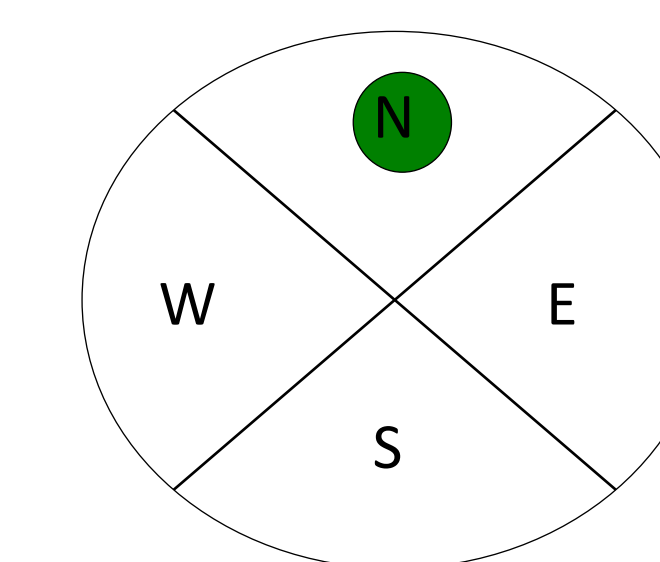
Post-Injection Sickness Behaviours and Weight Changes



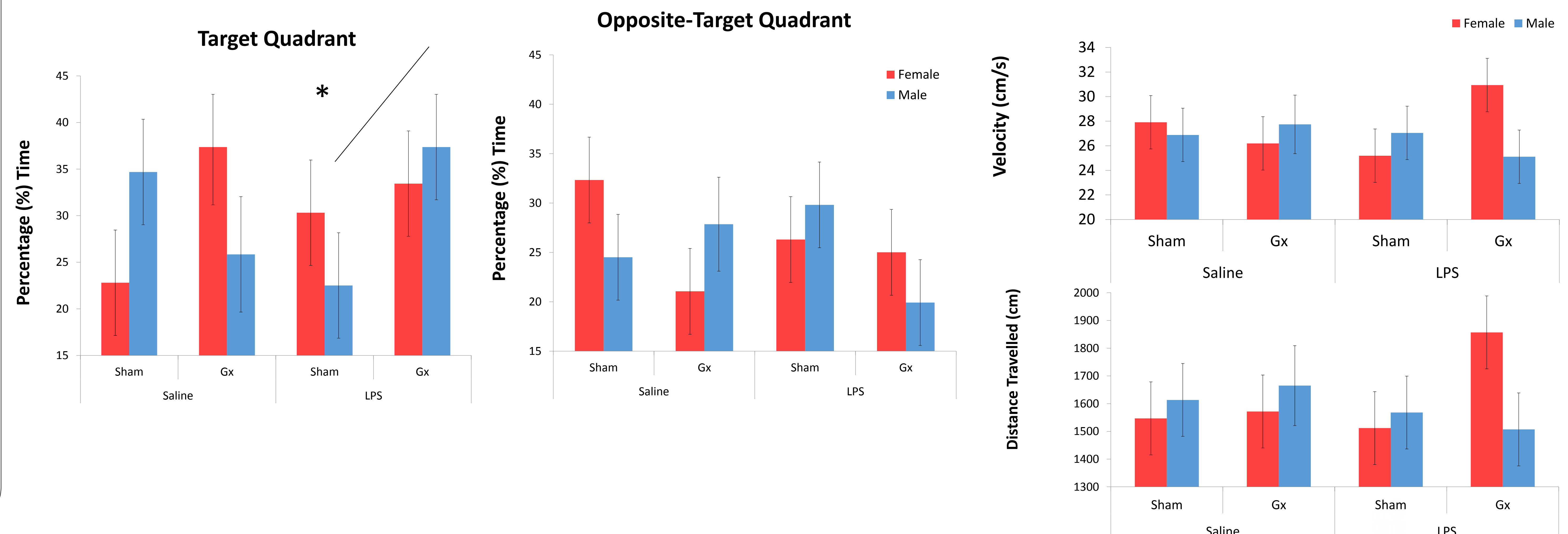
* $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$

Morris Water Maze

Learning Phase



Probe Phase



Discussion

Sickness behavior and weight change: Regardless of sex, LPS-treated animals displayed significantly more sickness behavior than those treated with the saline control. Overall, males tended to display more sickness behaviours than females.

Morris Water Maze: The lasting effects of LPS-induced pubertal immune stress is variable. In the learning phase of the Morris Water Maze, the time was significantly affected by sex, treatment and gonadal status. However, memory testing using probe trials revealed statistically non-significant differences in performance based on sex, treatment, and gonadal status.

Future Directions:

- Was there an effect of the estrous cycle on performance in females?
- Are there alternate cognitive paradigms that can be assessed?
- Does more severe sickness cause greater and more obvious impairments in learning and memory.

Acknowledgements

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References

- ¹Blakemore, S., Burnett, S., & Dahl, R. E. (2010). The role of puberty in the developing adolescent brain. *Human Brain Mapping, 31*, 926-933.
- ²Ratnayake, U., Quinn, T., Walker, D. W., & Dickinson, H. (2013). Cytokines and the neurodevelopmental basis of mental illness. *frontiers in Neuroscience, 7*(180), 1-9.
- ³Sisk, C. L., & Foster, D. L. (2004). The neural basis of puberty and adolescence. *Nature Neuroscience, 7*(10), 1040-1047.