

## INTRODUCTION

Cancer patients and survivors suffer numerous psychiatric comorbidities that are exacerbated by chemotherapy treatments. Anxiety is a prevalent comorbidity associated with chemotherapy treatment and can last years beyond the completion of treatment (Maas, et al., 2015). Chemotherapy treatments result in inflammation and an increase in pro-inflammatory signals (e.g., cytokines) within the brain.

Moderate exercise has been shown to ameliorate chemotherapy-induced anxiety in breast cancer patients and survivors (Zhu, et al., 2016), as well as alleviate neuroinflammation in non-cancer models (Zhang, et al., 2017). However, no studies have investigated the anti-inflammatory effects of exercise on chemotherapy-induced neuroinflammation and anxiety-like behavior.

## HYPOTHESIS

**Voluntary exercise decreases chemotherapy-induced anxiety-like behavior and expression of pro-inflammatory cytokines *Il1β*, *Icam1*, *Cxcl1* and *Tnfa* in the hippocampus, hypothalamus, and prefrontal cortex (brain regions that regulate sickness and anxiety-like behaviors).**

## METHODOLOGY

**Chemotherapy Treatment:** Non-tumor-bearing female C57/BL6 mice received 6 doses of 30 mg/kg paclitaxel chemotherapy or vehicle. The injections were 48 h apart.

**Wheels:** Healthy, female C57/BL6 mice were housed with a locked or unlocked running wheel for the course of the experiment.

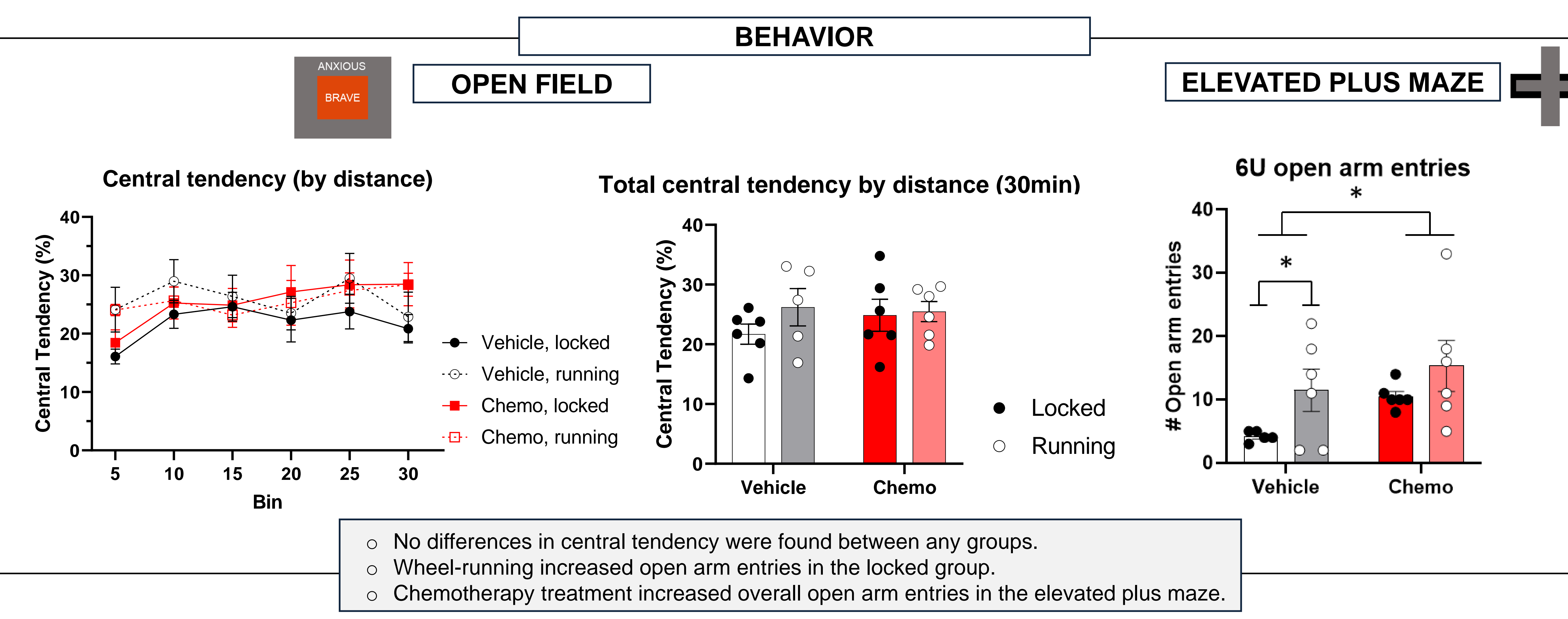
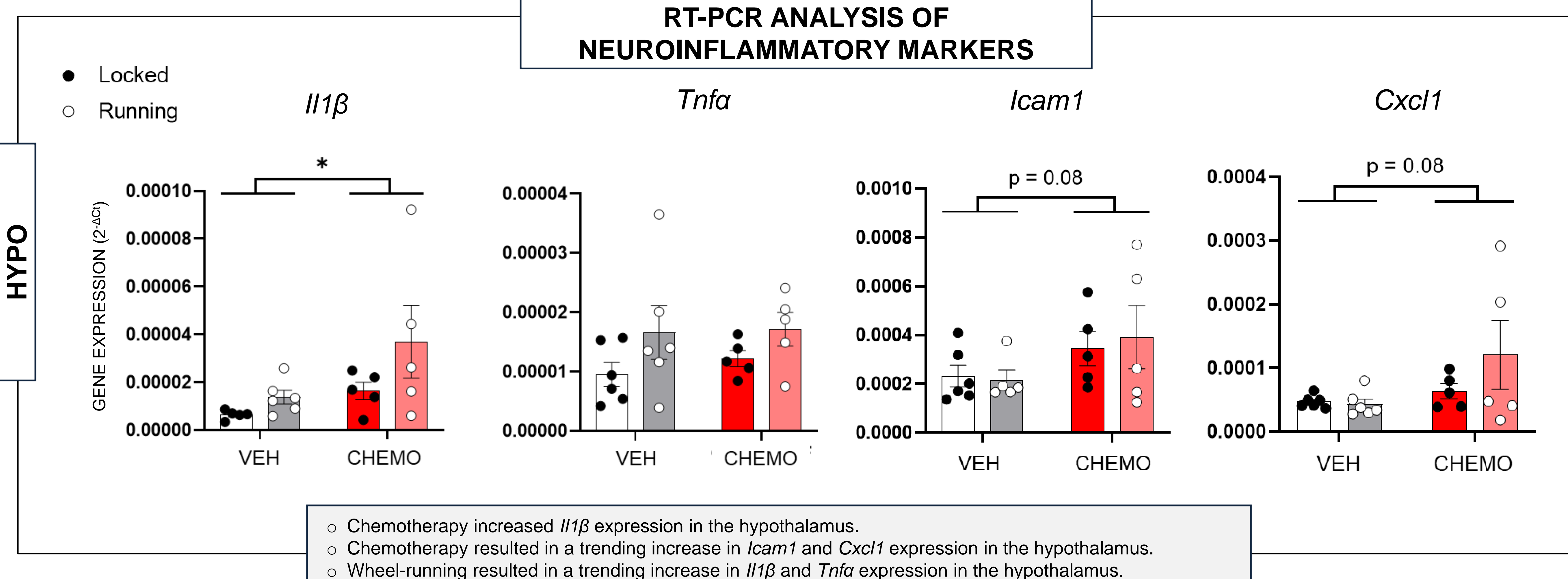
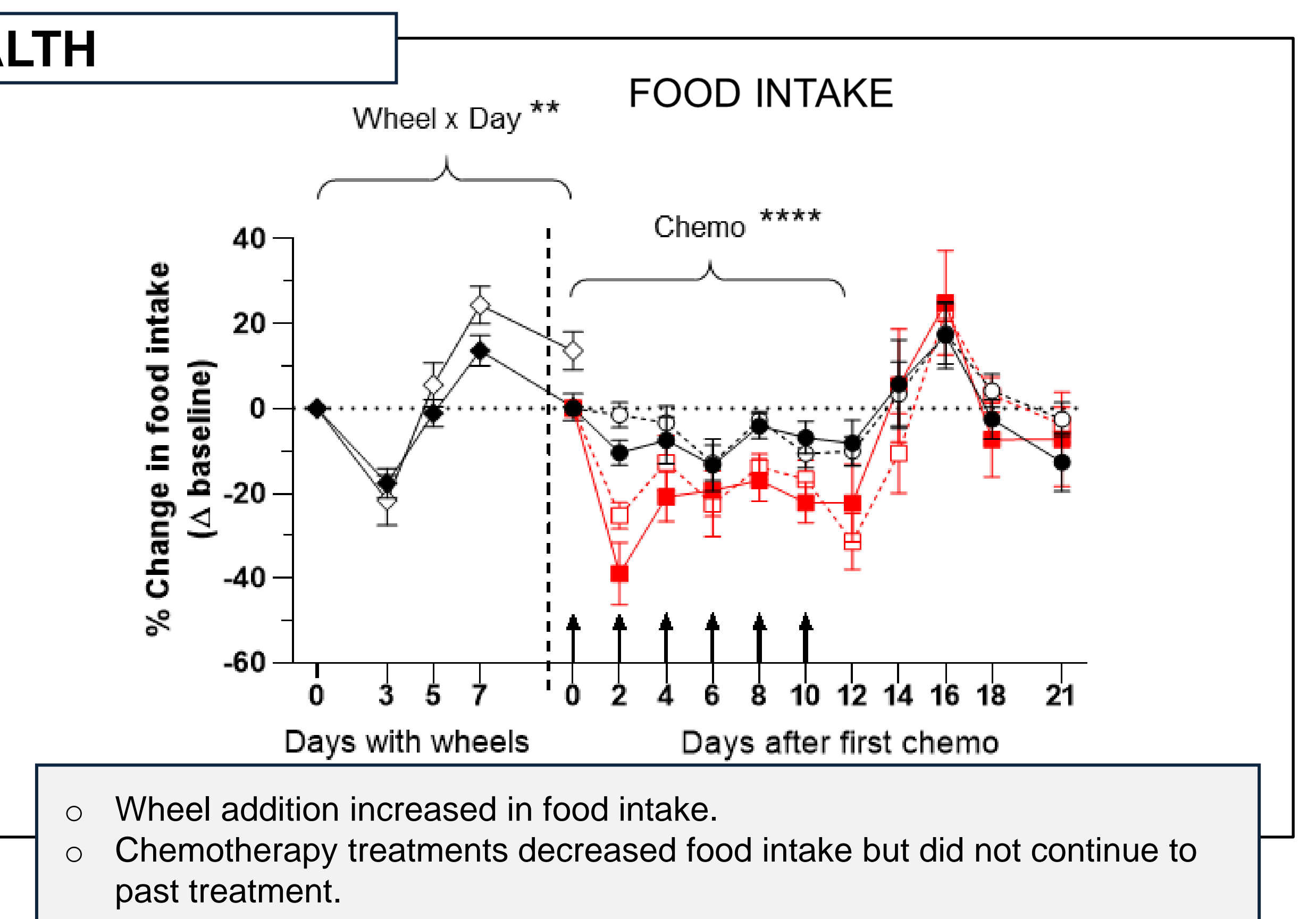
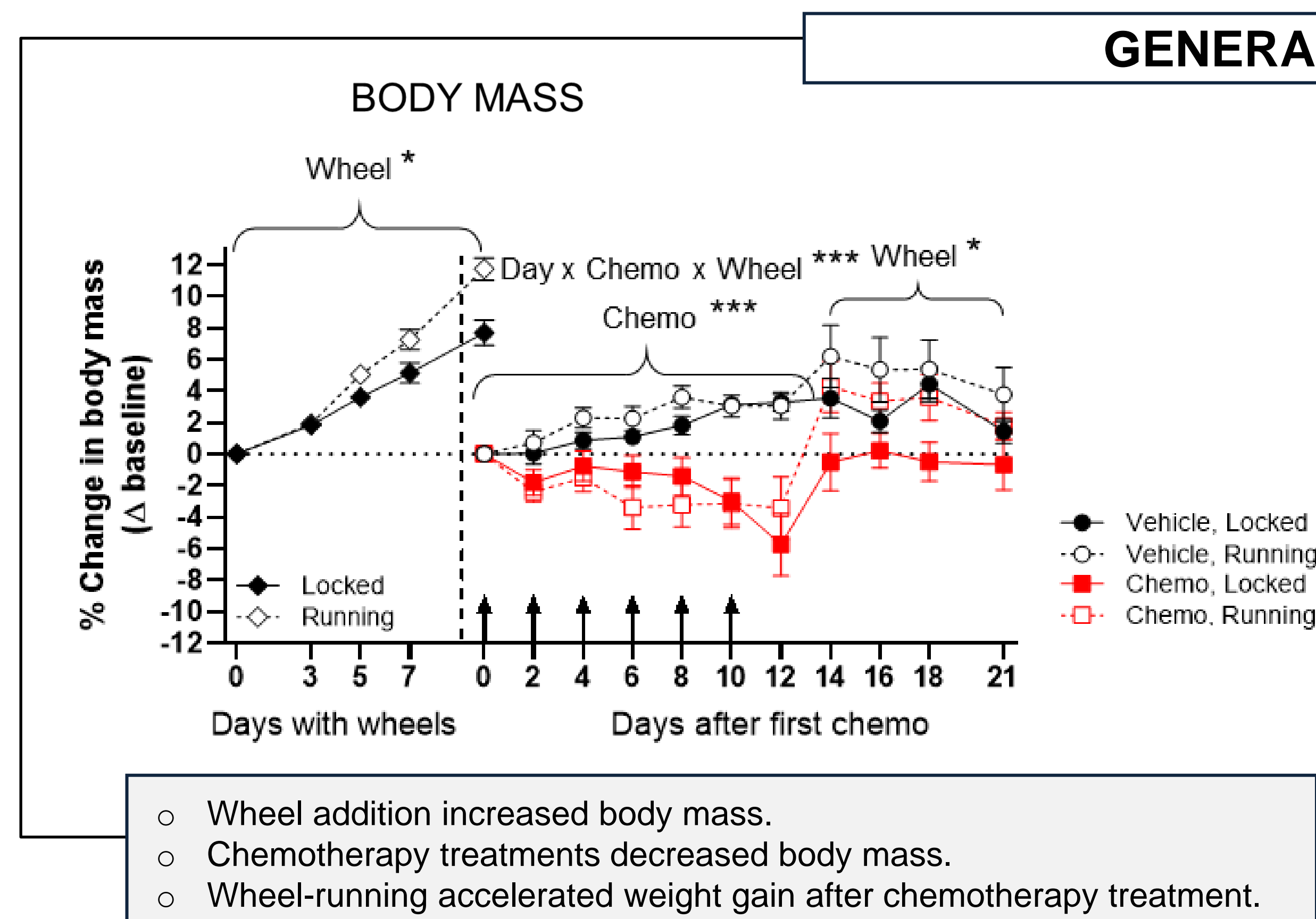
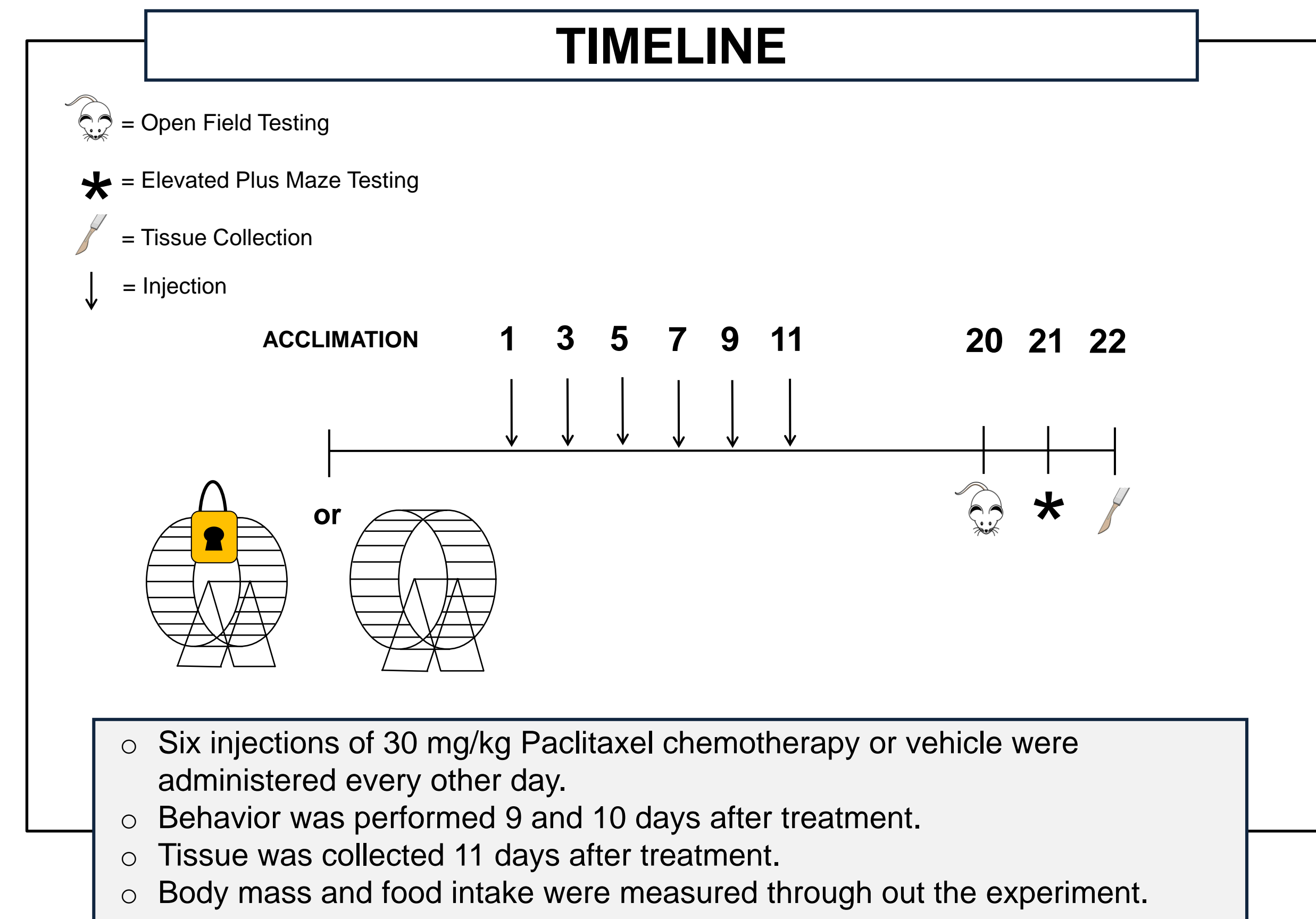
**Behavior:** **Open field** behavioral testing was performed 2 d prior to tissue collection to measure anxiety-like behavior. In this test, a mouse was placed in an open box, and locomotion and central tendency were recorded by a laser system (PAS). Each mouse spent 30 min in the apparatus. Locomotion and central tendency were averaged in bins of 5 min.

**Elevated plus maze** behavioral testing was performed 1 d prior to tissue collection to measure anxiety-like behavior. In this test, a mouse was placed in a “+” shaped apparatus consisting of two opposing closed and open arms. Open arm entries were recorded over a 5 min period.

**Tissue Collection:** Brains of mice were extracted 11 days post-chemotherapy treatment. The hypothalamus was manually dissected for mRNA isolation.

**RT-PCR:** mRNA was isolated from the hypothalamus to measure expressions of *Icam1*, *Il1β*, *Cxcl1* and *Tnfa*.

**Data Analyses:** GraphPad Prism software was used for all analysis.



## CONCLUSIONS

- Voluntary exercise may serve as a method of accelerating recovery from chemotherapy-induced cachexia as well as attenuating some anxiety-like behaviors.
- The intensity of exercise may impact inflammation measured in the brain.
- Attenuated anxiety-like behavior resulting from chemotherapy treatment may be due to an overcompensation by the mice during the recovery period.
- The measures of anxiety (central tendency and open arm entries) may not reveal every component of anxiety manifesting in patients.

## FUTURE DIRECTIONS

- Analyze behavior and cytokine expression at an earlier time point to investigate more acute interactions of voluntary exercise on chemotherapy-related anxiety-like behavior.
- Analyze neuroinflammatory markers in the hippocampus and prefrontal cortex to further investigate mechanisms of anxiety-like behavior.

## REFERENCES

○ Maass, S., Roorda, C., Berendsen, A., Verhaak, P., & Bock, G. D. (2015). The prevalence of long-term symptoms of depression and anxiety after breast cancer treatment: A systematic review. *Maturitas*, 82(1), 100-108.

○ Zhu, G., Zhang, X., Wang, Y., Xiong, H., Zhao, Y., & Sun, F. (2016). Effects of exercise intervention in breast cancer survivors: A meta-analysis of 33 randomized controlled trials. *OncoTargets and Therapy*, 2153. doi:10.2147/ott.s97864

○ Zhang, Q., Zhang, J., Yan, Y., Zhang, P., Zhang, W., & Xia, R. (2017). Proinflammatory cytokines correlate with early exercise attenuating anxiety-like behavior after cerebral ischemia. *Brain and Behavior*, 7(11). doi:10.1002/brb3.854

## ACKNOWLEDGEMENTS

We would like to thank Dr. Martha Belury, Lindsay Strehle, and Olivia Wilcox for technical assistance and advice.