

# Cessation of Nightly Voluntary Wheel Running Activity Following Exposure to a Mouse Model of Posttraumatic Stress

C. Stroh, E. Kinney, S. Coste

Department of Health, Human Performance & Athletics Linfield College – McMinnville, OR

## Abstract

Regular physical activity (PA) is well known to positively impact physical and mental health outcomes. In our work to examine cardiovascular benefits of PA in a mouse model of posttraumatic stress, we stumbled upon the reciprocal relationship between PA and stress exposure, wherein stress significantly reduced healthy levels of routine PA. The aim of the present studies was to define the parameters of our paradigm as first steps for its future use in examining mechanisms that underlie stress-induced declines in PA. Five week old, C67BL/6J male mice were divided into four groups (n=8/group); sedentary/ control, voluntary running/control, sedentary/stress and voluntary running/stress. Voluntary running groups were given 24 hr unlimited access to a running wheel in the home cage for 9 weeks. Mice ran a nightly average of  $4.75 \pm 1$  km. During the 9<sup>th</sup> week, stress groups were exposed to a 5 day resident-intruder social stress that models human post traumatic stress outcomes. Running behavior essentially ceased following stress. Running distance dropped to 0.31 km following the 1<sup>st</sup> stress day. Some habituation to stress occurred, as running distance increased to 1.12 km by the 5<sup>th</sup> day of stress but remained significantly lower than pre-stress running distances and distances recorded in non-stressed mice. A separate study examined a single exposure to resident-intruder social stress and found plasma corticosterone significantly increased ( $16.66 \pm 4$  ng/ml basal to  $496 \pm 155$  ng/ml immediately post stress) while nightly running dropped significantly from  $5.58 \pm 1.7$  km to  $1.22 \pm 1.1$  km, and returned to near normal levels ( $4.35 \pm 1.7$  km) by the 3<sup>rd</sup> night post stress. Food intake was moderately increased in the first 2 nights post stress, but also returned to normal by the 3<sup>rd</sup> night. These studies show the sensitivity of habitual running behavior to stress exposure and suggest the utility of this mouse model in exploring the means by which stress negatively impacts routine PA.

## Introduction

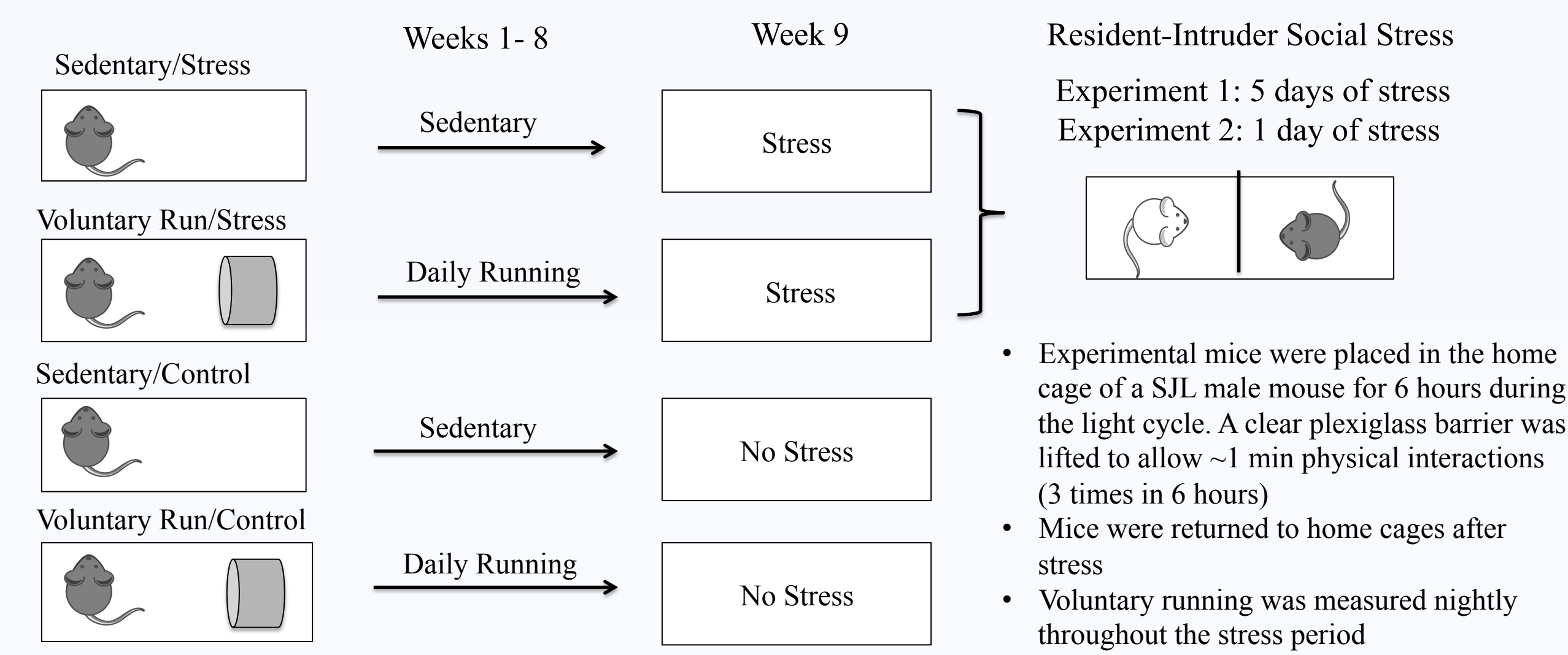
Regular physical activity is well known to positively impact physical and mental health outcomes. The incidence of cardiovascular disease, obesity, diabetes mellitus, certain types of cancer, depression and anxiety is lower in those who engage in physical activity (1, 2, 5). It is known that physical activity can reduce the physiological and behavioral responses to stress that contribute to the development and progression of various disease states (3). Indeed, research has focused on the duration, frequency and intensity of physical activity necessary to provide health benefits. In our work to examine cardiovascular outcomes of physical activity in a mouse model of posttraumatic stress, we stumbled upon the reciprocal relationship between physical activity and stress exposure. Specifically, we found that social stress significantly reduced habitual, voluntary wheel running activity. A recent meta-analysis of 168 research studies concluded that the majority of evidence to date indicates that stress negatively impacts physical activity levels in human participants. The authors point to a number of potential factors that may explain this effect, but indicate that more mechanistic research using animal models is needed (4). Thus, the purpose of the current studies was to define the parameters of our paradigm for use in future examination of the mechanisms that underlie the decline in physical activity following stress exposure



## Methods

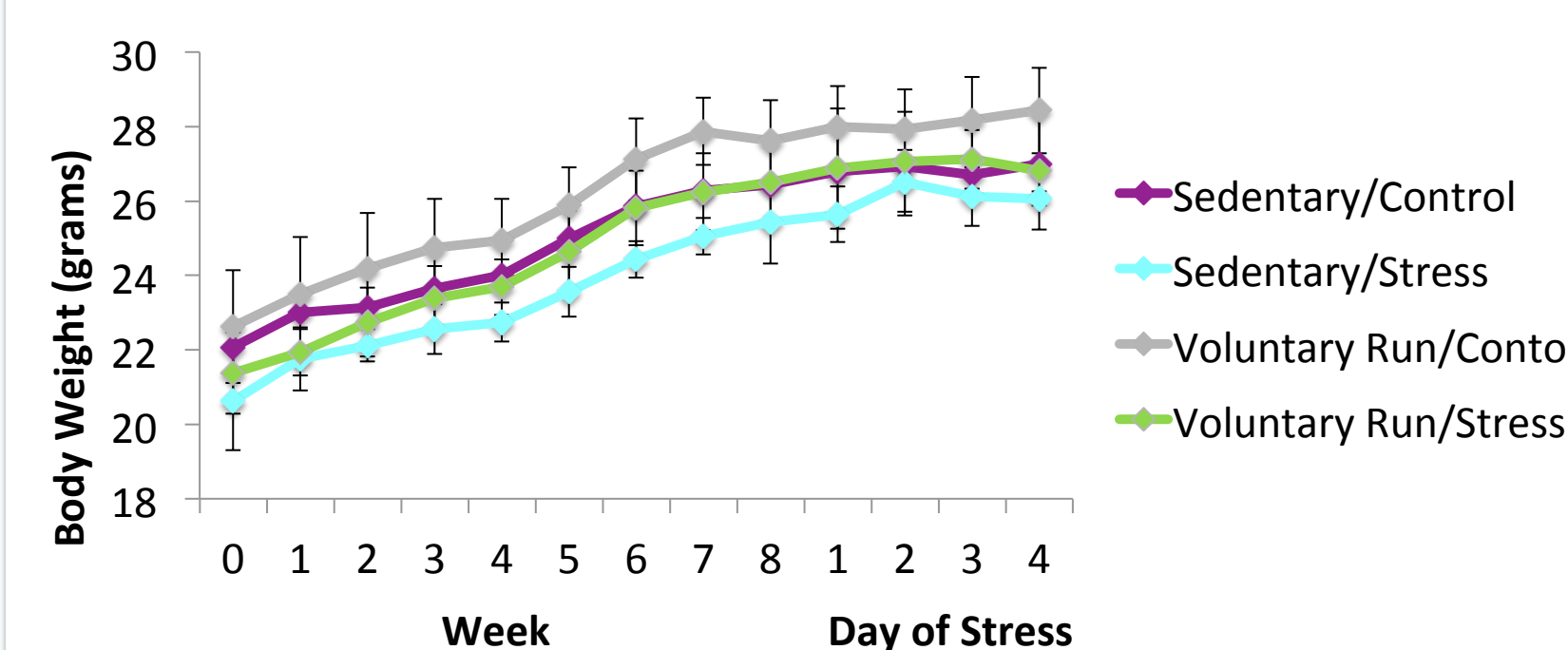
C57BL/6J male mice (5 weeks old) were divided into four groups (n=8/group); sedentary/control, voluntary running/control, sedentary/stress and voluntary running/stress. Mice in the voluntary running groups were given 24 hr unlimited access to a running wheel in the home cage for 9 weeks with wheel running activity recorded continuously. During the 9<sup>th</sup> week of running, mice in the stress groups were exposed to a 5 day resident-intruder social stress paradigm that is considered to model human post traumatic stress outcomes. In experiment 2, mice were exposed to only 1 day of the resident-intruder social stress.

### Experimental Design

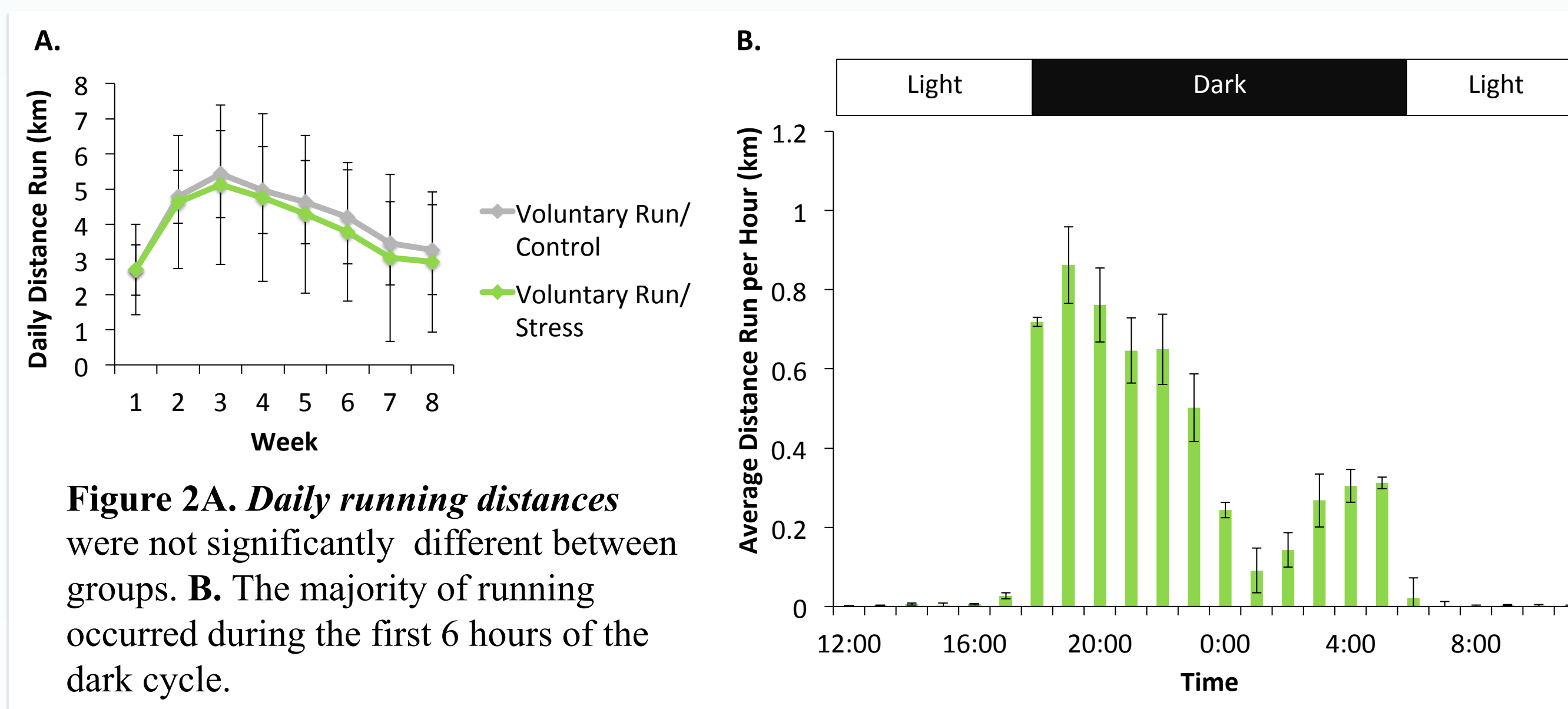


## Results

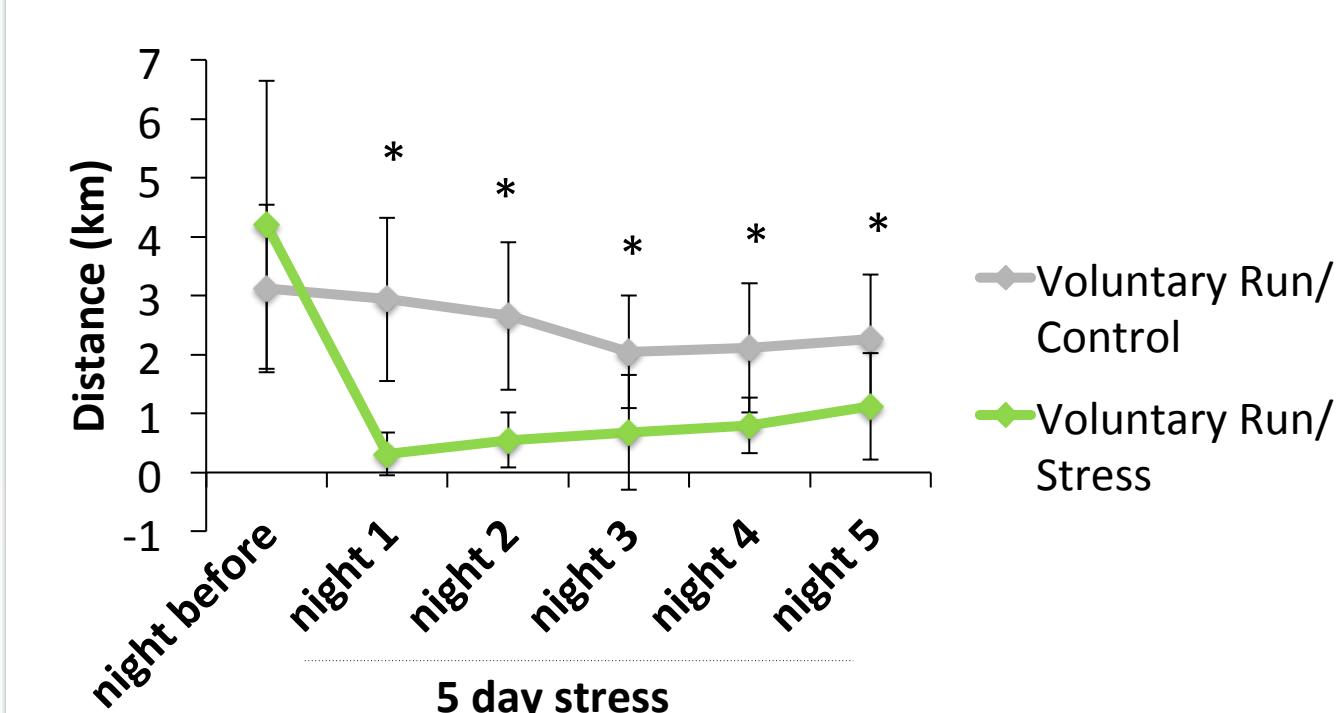
### Experiment 1



**Figure 1.** Body weight of mice increased from 5 to 14 weeks old due to natural maturation. There was no significant difference between groups. No change during stress week.

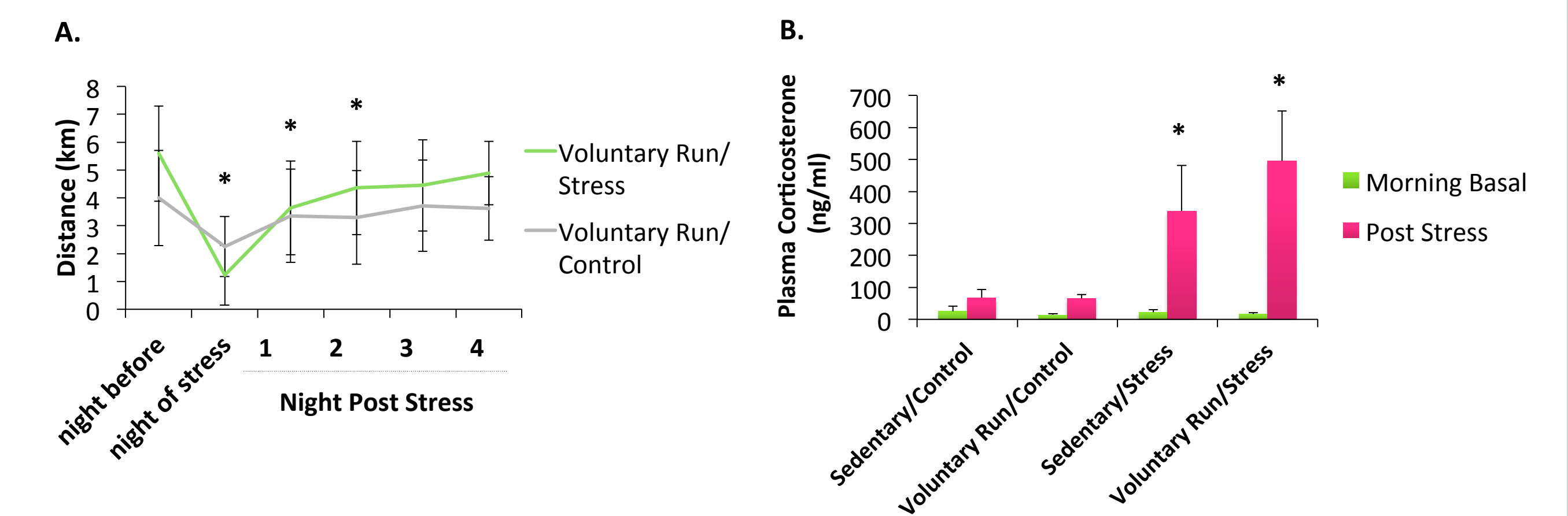


**Figure 2A.** Daily running distances were not significantly different between groups. **B.** The majority of running occurred during the first 6 hours of the dark cycle.



**Figure 3.** Voluntary running distance in the stress group decreased following the first day of stress and continued to be significantly lower than pre stress values and the distance of the non-stressed mice. Some habituation to the stress occurred as running distance began to increase across the 5 days of stress

### Experiment 2



**Figure 4A.** Voluntary running distance significantly decreased following stress. Distances returned to normal by the third night post stress. **B.** Plasma corticosterone was significantly higher in voluntary running groups compared to sedentary controls (\*p<0.05) following a single bout of social stress exposure. \* p<0.05

Food Intake (g)	3 day basal average	day 1 post stress	day 2 post stress	day 3 post stress
Sedentary/Control	3.92 ± 0.37	4.25 ± 0.9	4.60 ± 1.0	4.44 ± 1.3
Voluntary Run/Control	4.53 ± 0.81*	4.13 ± 0.9	4.61 ± 1.1	4.15 ± 0.9
Sedentary/Stress	3.80 ± 0.68	4.60 ± 1.1	5.10 ± 1.2	4.74 ± 1.4
Voluntary Run/Stress	4.81 ± 0.39*	5.80 ± 1.4*	5.29 ± 1.1	5.94 ± 2.6

**Table 1.** Basal food intake was significantly higher in voluntary running groups compared to sedentary controls (\*p<0.05) following a single bout of social stress, significantly in the voluntary run/stress group.

## Summary and Conclusion

- We found that mice in the voluntary running groups ran an average of  $4.75 \pm 1$  km each day. The majority of running bouts occurred within the first 6 hr of the dark cycle. These data are consistent with previous reports of running behavior in C57BL/6J male mice.
- Voluntary running behavior essentially ceased in mice exposed stress, as shown in both Experiment 1 and 2.
- Experiment 1 shows that some habituation to the stress occurred, as running distance increased by the 5<sup>th</sup> day of stress but was still significantly lower than pre-stress running distances and those recorded in non-stressed mice.
- In Experiment 2, we found that the reduction in voluntary running following a single 6 hour social stress exposure returned to near normal levels by the 3<sup>rd</sup> night post stress. The bout of stress significantly elevated plasma corticosterone, with some increase in food intake the first day post stress.
- These studies show the sensitivity of voluntary running behavior and the utility of this model to assess mechanisms that underlie the negative impact of stress on habitual physical activity.

## Selected References

- Cho et al. (2014) *Proceedings of the National Academy of Sciences*, 111(8), 3188-3193
- Costoli et al. (2004) *American Journal of Physiology*, 286, H2133-H2140
- Sasse et al. (2013) *Frontiers in Physiology*, 4, 1-11
- Stults-Kolehmainen (2014) *Sports Medicine*, 44, 88-121
- Turdi et al. (2012) *Physiology and Behavior*, 105, 498-509

## Acknowledgments

We would like to thank the following individuals for their help with this research project: Lee Bakner, Linfield College, Department of Psychology; Heather Long, Linfield College Department of Biology; and Susan Stevens, Oregon Health and Science University, Department of Molecular Microbiology and Immunology  
This research was funded by a Linfield Student –Faculty Collaborative Research Grant