

# The Effects of Social Stress on Voluntary Running Behavior in Female Mice.

C. Cattell, S. Coste

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

## Abstract

**Purpose:** Regular physical activity (PA) is well known to positively impact physical and mental health outcomes. However, there is a reciprocal relationship between these variables wherein stress significantly reduces healthy levels of routine PA. We showed previously that voluntary running behavior of male mice essentially ceases following exposure to a resident-intruder social stress that models human post traumatic stress outcomes. Here we sought to determine whether stress-induced inhibition of habitual voluntary running occurs in female mice. **Methods:** Five week old, C67BL/6J female 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  $6.86 \pm 2.5$  km. During the 9<sup>th</sup> week, stress groups were exposed to a single, 6 hr bout of a female specific, resident-intruder social stress. **Results:** Plasma corticosterone significantly increased following stress ( $34.56 \pm 13$  ng/ml basal to  $330.5 \pm 95$  ng/ml immediately post stress) while nightly running dropped significantly to  $1.72 \pm 0.9$  km. Unlike male mice where running levels were slow to recover, voluntary running in these female mice returned to near normal levels by the second night ( $5.01 \pm 2.5$  km). **Conclusion:** This study shows 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.

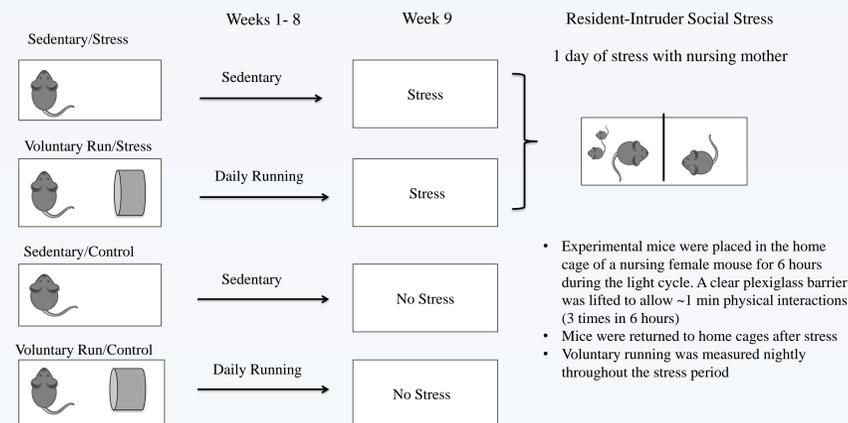
## Introduction

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). However, a reciprocal relationship between these variables exists, wherein stress exposure negatively impacts physical activity levels in human participants (4). We have begun studies using a mouse model to examine the mechanisms that underlie the decline in physical activity following stress exposure. We found that a posttraumatic-type stress significantly reduced habitual, voluntary wheel running activity in male mice. Running distance dropped from a daily average of  $4.75 \pm 1$  km to 0.31 km following stress exposure and running activity did not return to normal for several days. The purpose of this study was to examine whether female mice respond in a similar fashion. It is important to recognize that there are often significant sex differences in physiological responses to stress, and any potential differences need to be documented and explored, as the fundamental purpose of our animal studies is to guide human clinical studies for both sexes.

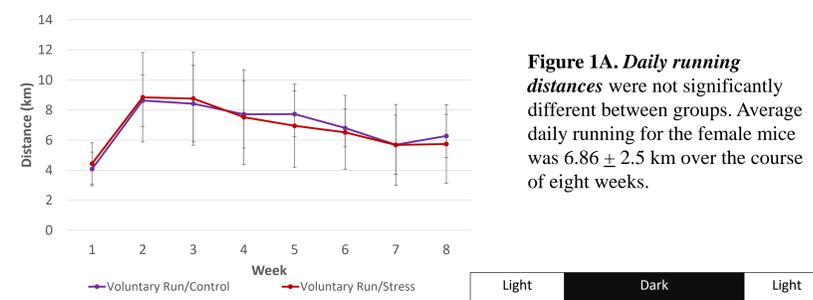
## Methods

C57BL/6J female 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 1 day female specific, resident-intruder social stress paradigm.

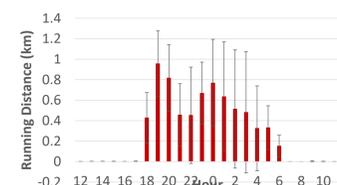
## Experimental Design



## Results

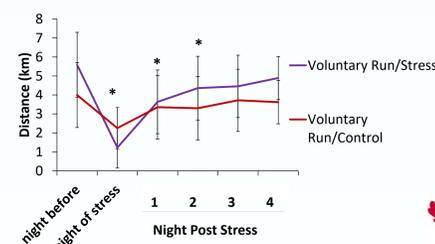


**B. Daily running occurrences** were consistent with the dark cycle of the room. The dark cycle began at 6pm and ended at 6am daily.

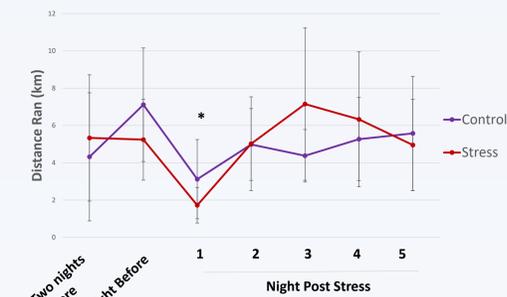


Food Intake (g)	Basal Average	Pre stress	day 1 post stress	day 2 post stress	day 3 post stress
Sedentary/Control	4.34 ± 0.62	4.33 ± 1.3	3.93 ± 0.97*	4.50 ± 0.79	3.78 ± 1.3
Voluntary Run/Control	4.76 ± 0.82	5.24 ± 1.3	4.16 ± 0.41*	4.59 ± 0.58	5.52 ± 1.2
Sedentary/Stress	4.32 ± 0.68	5.06 ± 0.91	4.13 ± 1.2*	4.33 ± 1.2	4.48 ± 0.45
Voluntary Run/Stress	4.91 ± 0.48	5.39 ± 1.1	4.41 ± 1.2*	4.91 ± 0.68	4.39 ± 0.69

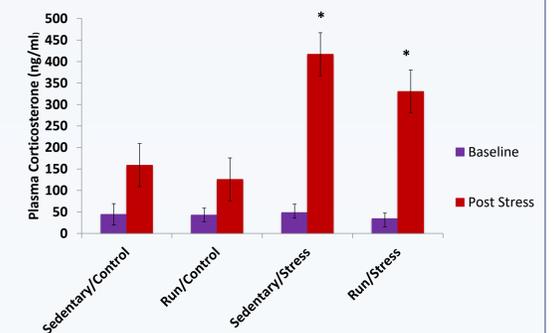
**Table 1. Basal food intake** showed voluntary running groups tended to eat more than sedentary groups, but there was no significant difference. Food intake was significantly lower the night following the 6hr stress in all groups (\*p<0.05).



A.



**B. Plasma corticosterone** was significantly increased by social stress. Blood samples were taken from the retro-orbital sinus at the end of the 6 hour social stress exposure. (\* p<0.05)



## Summary and Conclusion

- We found that mice in the voluntary running groups ran an average of  $6.86 \pm 2.5$  km each day. The majority of running occurred during the dark cycle between 6pm and 6am. These data are consistent with previous reports of running behavior in C57BL/6J female mice.
- We found that voluntary running behavior significantly decreased to  $1.72 \pm 0.9$  km and plasma corticosterone significantly increased in female mice exposed stress. Voluntary running behavior returned to normal levels the 2<sup>nd</sup> night post stress.
- Basal food intake for voluntary running groups was higher than for sedentary groups, but not significantly different. Food intake for all groups was significantly decreased the night after stress then returned to approximately normal levels This follows the same trend as the running the nights following stress.
- The female mice in this study recovered from 1 day of resident-intruder stress faster than male mice in previous studies.
- 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

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