

The Combined Effects of a Typical American-Style Diet and Chronic Sleep Restriction on Anxiety-Like Behavior in Mice

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Alzheimer's disease (AD) currently afflicts well over six million people in the United States, and this number is projected to increase exponentially in the coming years. While much remains to be understood about the causes and pathogenesis of AD, two potential risk factors are chronic insufficient sleep and long-term consumption of an unhealthy diet. Both of these lifestyle factors are often studied separately, and evidence suggests that each has negative impacts on brain health and cognitive function, perhaps due to increases in inflammation, which itself is associated with increased anxiety and cognitive dysfunction. The current study investigated the combined effects of long-term consumption of a typical American-style diet (TAD) and six weeks of chronic sleep restriction on locomotor activity and anxiety-like behavior in male and female wild-type mice not otherwise predisposed to disease pathology. Female mice that underwent sleep restriction and consumed the TAD displayed greater anxiety-like behavior compared to mice that the TAD and did not undergo sleep restriction. This difference was not observed in male mice. Furthermore, male mice that underwent chronic sleep restriction displayed greater locomotor activity compared to controls. These differences were not observed in females. Given the prevalence of AD and the projected rise in AD cases, understanding how controllable lifestyle or environmental factors can increase AD risk is essential. Importantly, as AD is more prevalent in women compared to men, it is imperative that research efforts utilize male and female animals seek to understand the mechanisms driving this phenomenon.

Introduction

- Alzheimer's disease is a devastating neurodegenerative disease that disrupts cognitive function and memory
 - Cases: 44 million worldwide, 6 million+ Americans¹
 - Risk factors
 - Old age, genetics, chronic stress, unhealthy diet, irregular/inadequate sleep²
 - Poor Diet: heightened saturated fatty acids leading to inflammation⁴
 - Poor Sleep: sympathetic nervous system activated leading to inflammation³

Methods

Subjects: Wild-type C57BL/6J mice

Experimental Conditions	Home Cage Control (HCC)	Chronic Sleep Restriction (CSR)
Standard Diet (Std)	HCC/Std	CSR/Std
Typical American Diet (TAD)	HCC/TAD	CSR/TAD



Macronutrients (%kcal)	Standard Chow (Std)	Typical American Diet Chow (TAD)
Protein	21%	15%
Fat	14%	35%
Carbohydrate	65%	50%

Chronic Sleep Restriction

- Modified Multiple Platforms Method
 - 26.67 cm x 48.26 cm x 15.56 cm
 - 14 platforms
 - Water
 - To 1 cm below platform surface
 - 25 °C
- Ten Hours Daily (8am-6pm)



Open Field

- 10 minute session
- Locomotor Activity
 - Distance Traveled
- Anxiety-like Behavior
 - Time in Center



Results

Body Weight

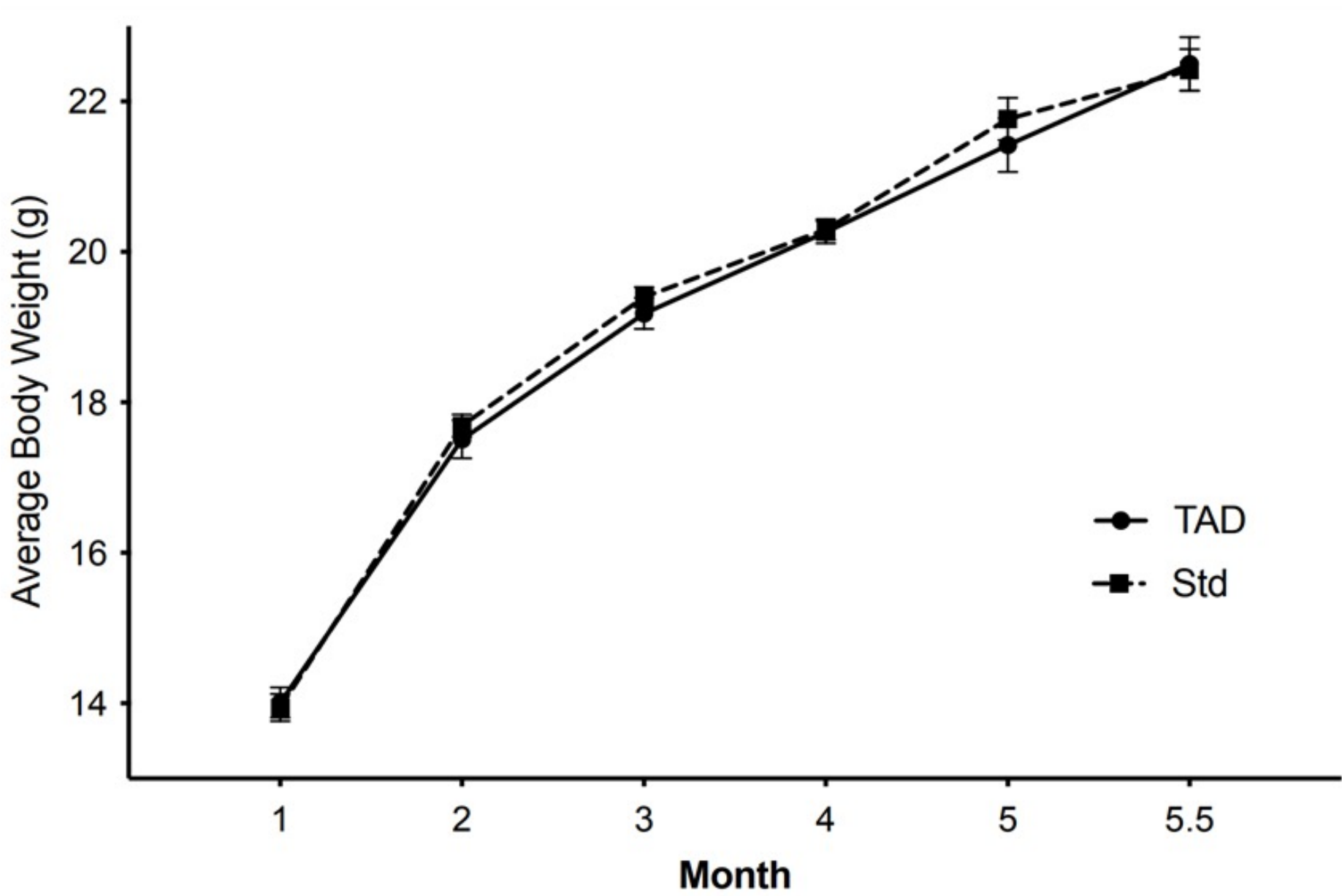


Figure 1: Female Body Weight

Repeated measures ANOVA revealed a significant effect of week such that all mice gained weight throughout the study. Bars represent +/- SEM. N's = 53-54.

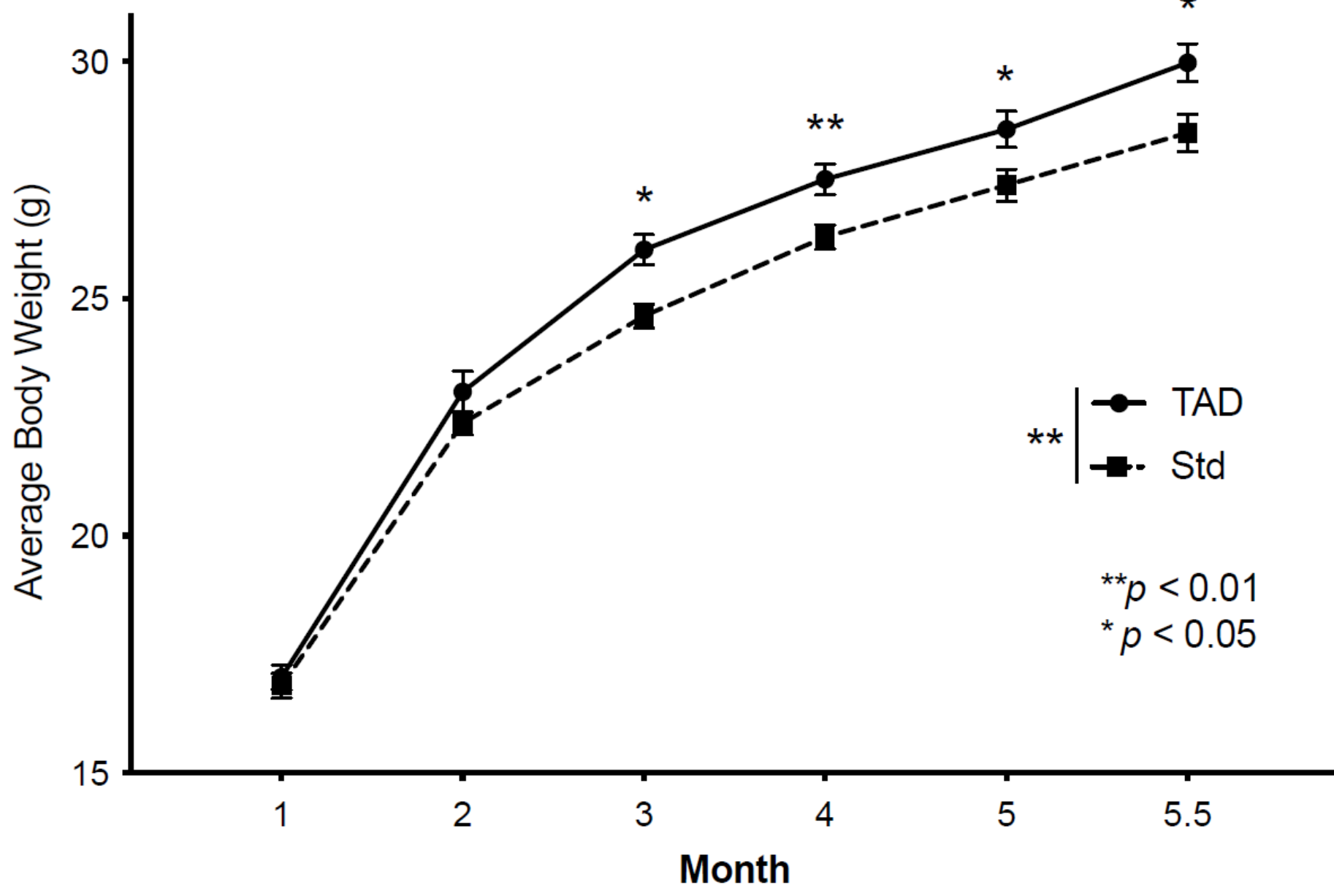


Figure 2: Male Body Weight

Repeated measures ANOVA revealed a significant main effect of diet such that the TAD mice gained more weight than Std mice. Bars represent +/- SEM. N's = 50-54.

Distance Traveled

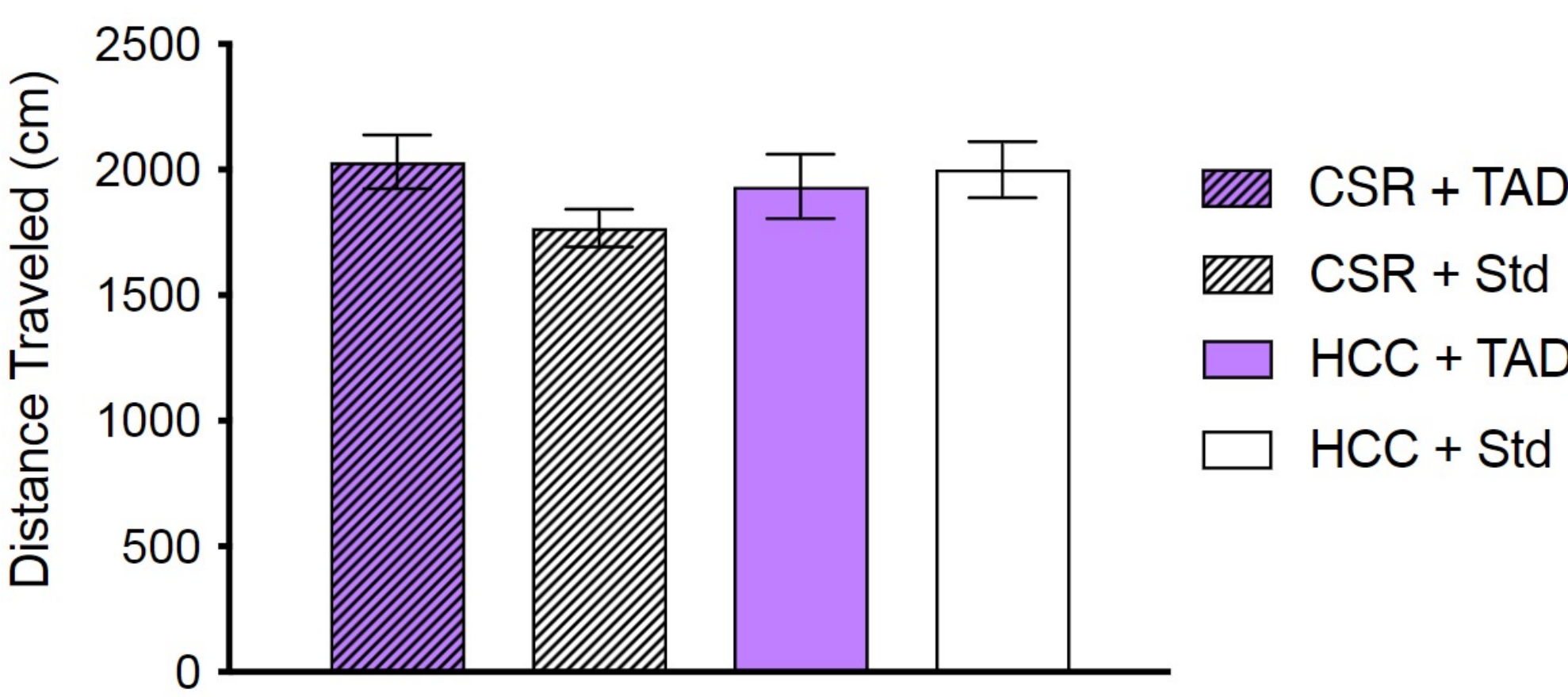


Figure 3: Female Open Field – Distance Traveled

Two-way ANOVAs revealed no significant effects. Bars represent +/- SEM. N's = 14-20.

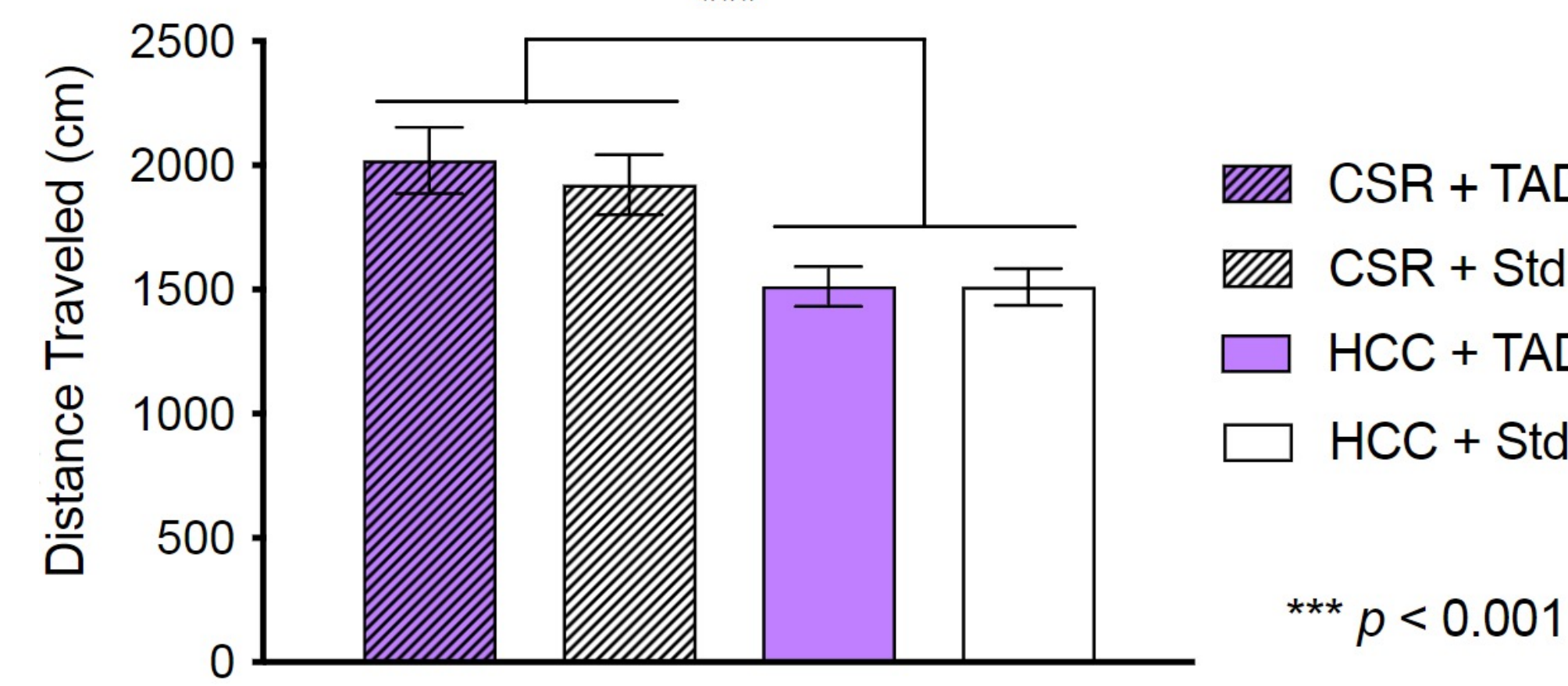


Figure 4: Male Open Field – Distance Traveled

Two-way ANOVAs revealed a significant main effect of sleep on distance. The CSR mice traveled farther than HCC mice. Bars represent +/- SEM. N's = 14-19.

Time in Center

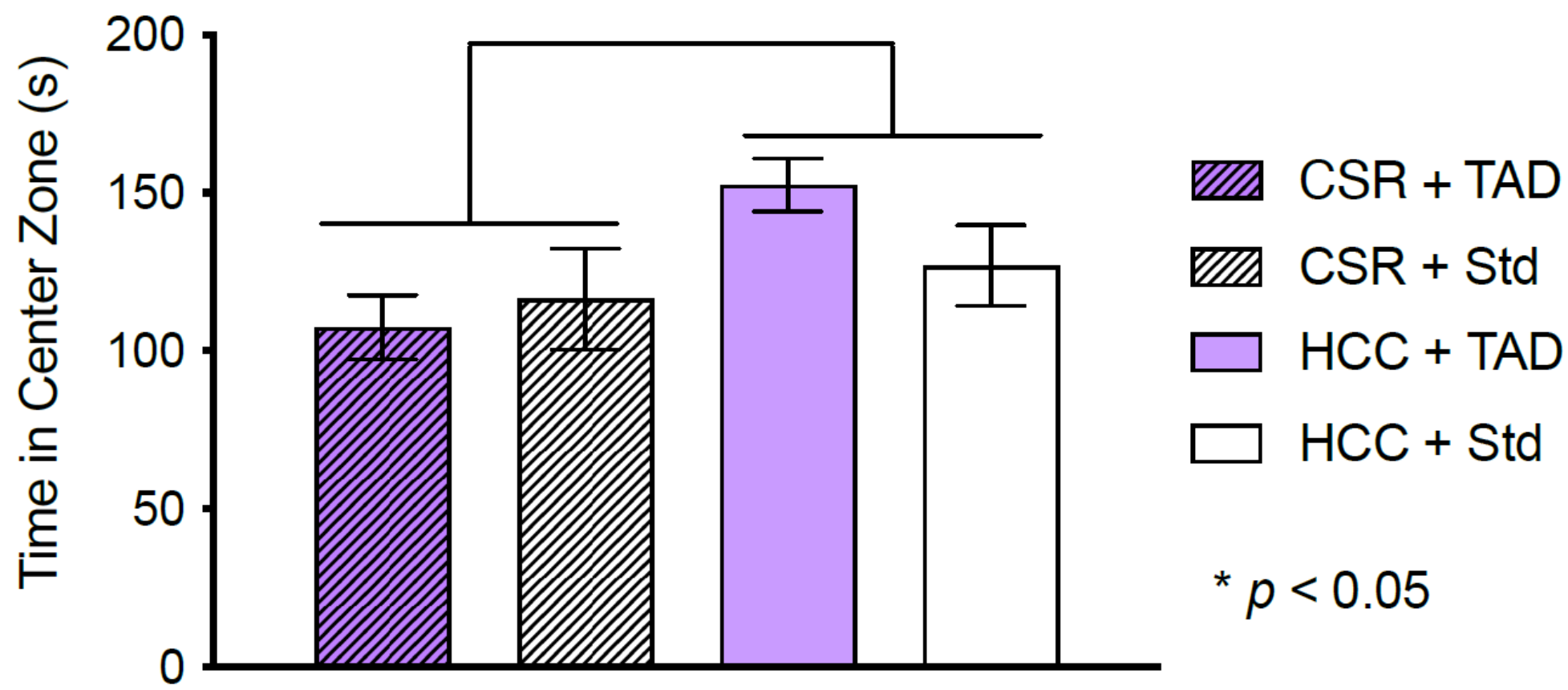


Figure 5: Female Open Field – Time in Center

Two-way ANOVAs revealed a significant main effect of sleep condition on time spent in the center zone. CSR mice spend less time in the center compared to HCC mice. Bars represent +/- SEM. N's = 14-20.

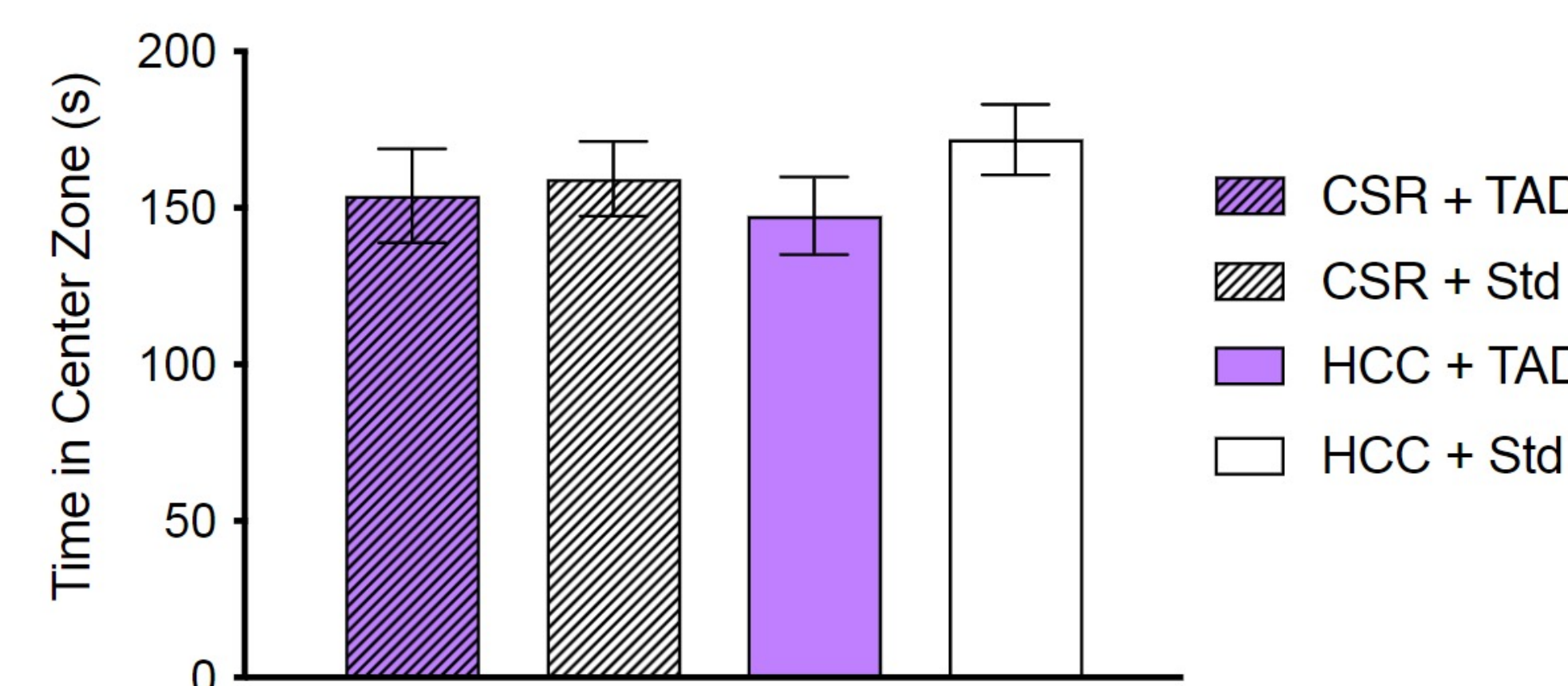
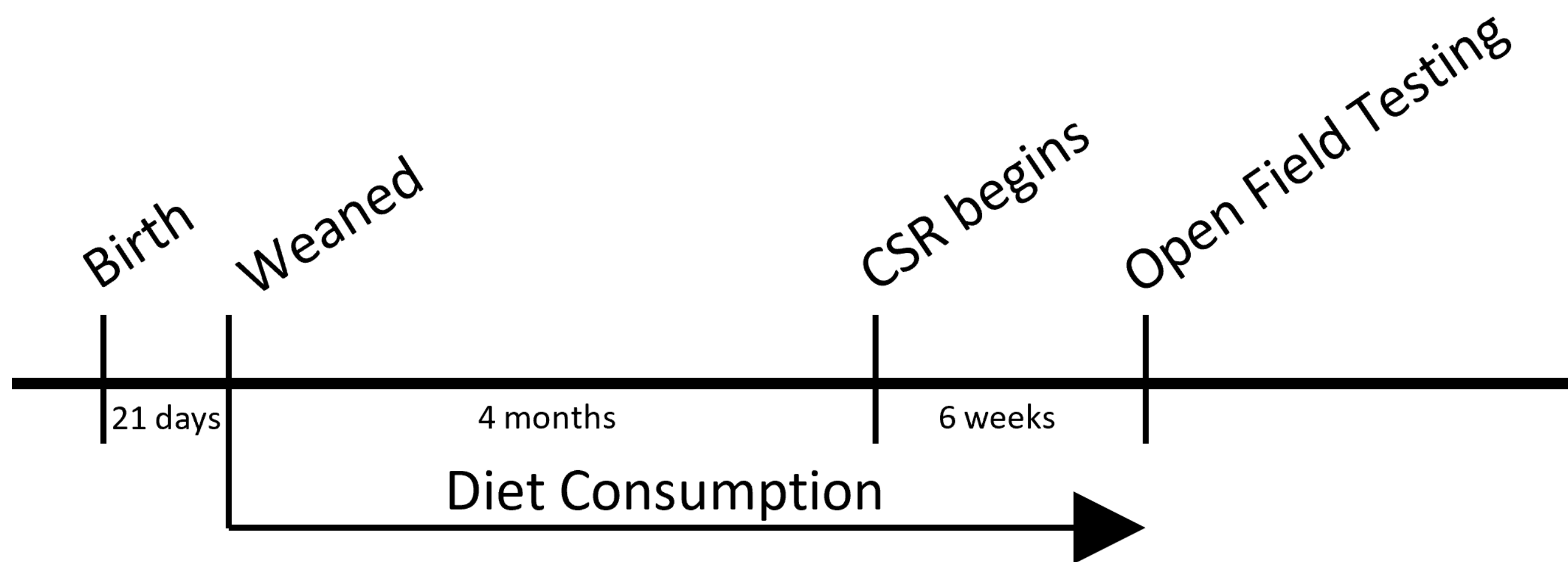


Figure 6: Male Open Field – Time in Center

Two-way ANOVAs revealed no significant effects. Bars represent +/- SEM. N's = 14-19.

Experimental Timeline



Conclusions

- Male mice gained weight on the TAD while female mice did not.
- Male CSR mice traveled farther compared to HCC mice. This was not observed in female mice.
- CSR was associated with anxiety-like behavior compared to HCC mice in female, but not male, mice.
- TAD did not appear to impact behavior in the open field test.
- Future research will investigate the combined effects of CSR and TAD consumption on body weight, anxiety, and Alzheimer's disease-like markers in a transgenic mouse with genetic risk factors for late-onset Alzheimer's disease.

Funding



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