

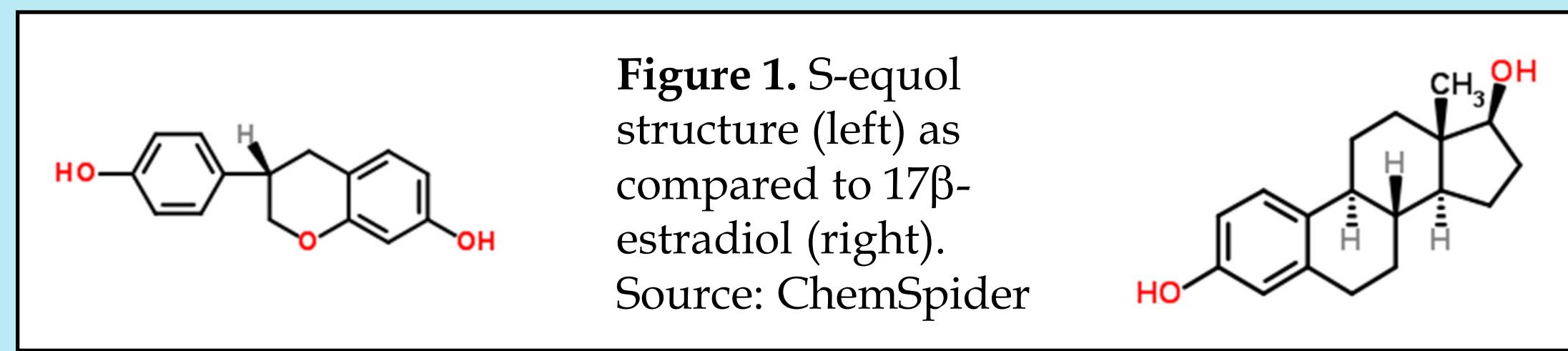
# Effects of S-equol on obesity-associated depression and anxiety in male and female mice

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## Introduction

S-equol is a non-steroidal estrogen metabolized from daidzein by intestinal microbiota. Previous studies attribute beneficial neurological and metabolic effects of this metabolite, including anti-depressive and anti-obesity effects<sup>1</sup>. A correlation exists between obesity and mood disorders<sup>2</sup>; therefore, the question remains whether S-equol (Figure 1), which has a similar chemical structure as 17 $\beta$ -estradiol (E2, Figure 1), can potentially mitigate the effects of obesity-induced depressive-like or anxiety-like behaviors. With both obesity and mood disorders on the rise, we sought to examine the potential ability of S-equol to improve depressive- or anxiety-like behaviors in a diet-induced mouse model of obesity (DiO).

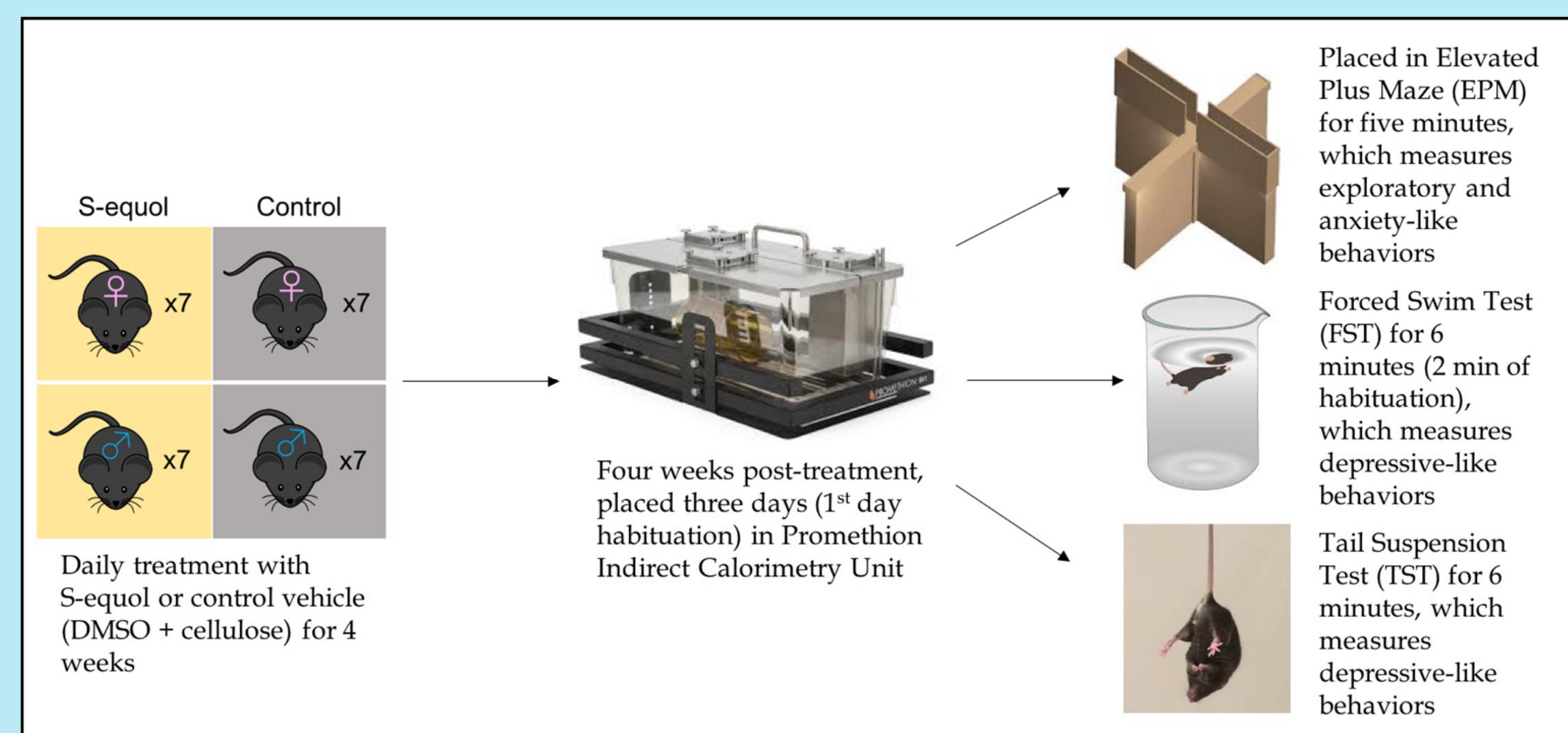


## Hypothesis

We hypothesized that mice treated with S-equol would have reduced depressive- and anxiety-like behaviors compared to those not receiving this supplementation.

## Methods

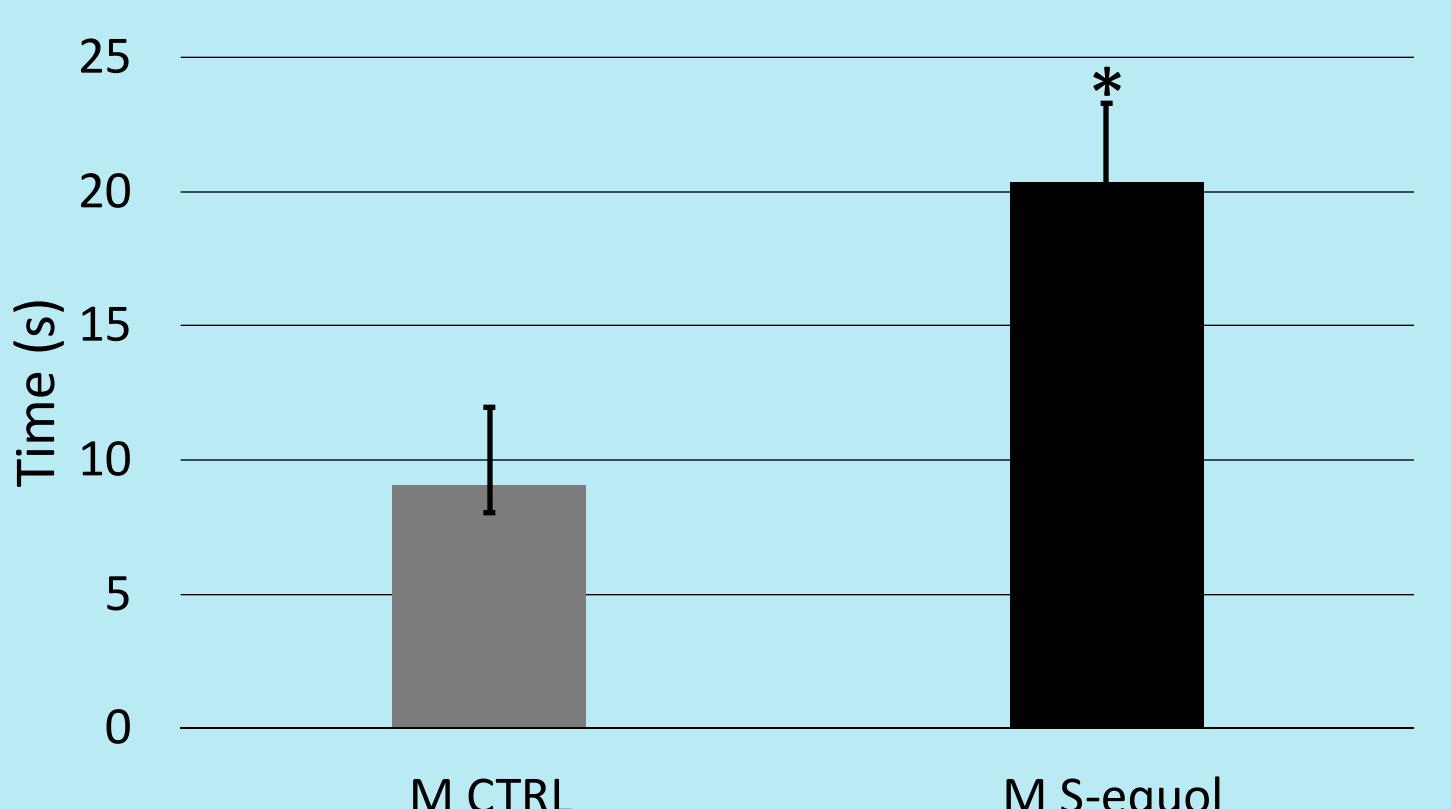
- Twenty-eight C57 mice were placed on a high fat diet (HFD) and randomly assigned to 4 groups: 7 females on S-equol, 7 females on control, 7 males on S-equol, and 7 males on control. The mice were six weeks old at start of studies.
- The mice were orally dosed (10 mg S-equol daily/kg body weight) for the total duration of the studies (8 weeks).
- Beginning at four weeks post-treatment, the following tests were performed: Metabolic Chamber, elevated plus maze (EPM), forced swim test (FST), and tail suspension test (TST) (Figure 2).



## S-equol Treatment Reduces Depressive- and Anxiety-like Behaviors

### Elevated Plus Maze Results

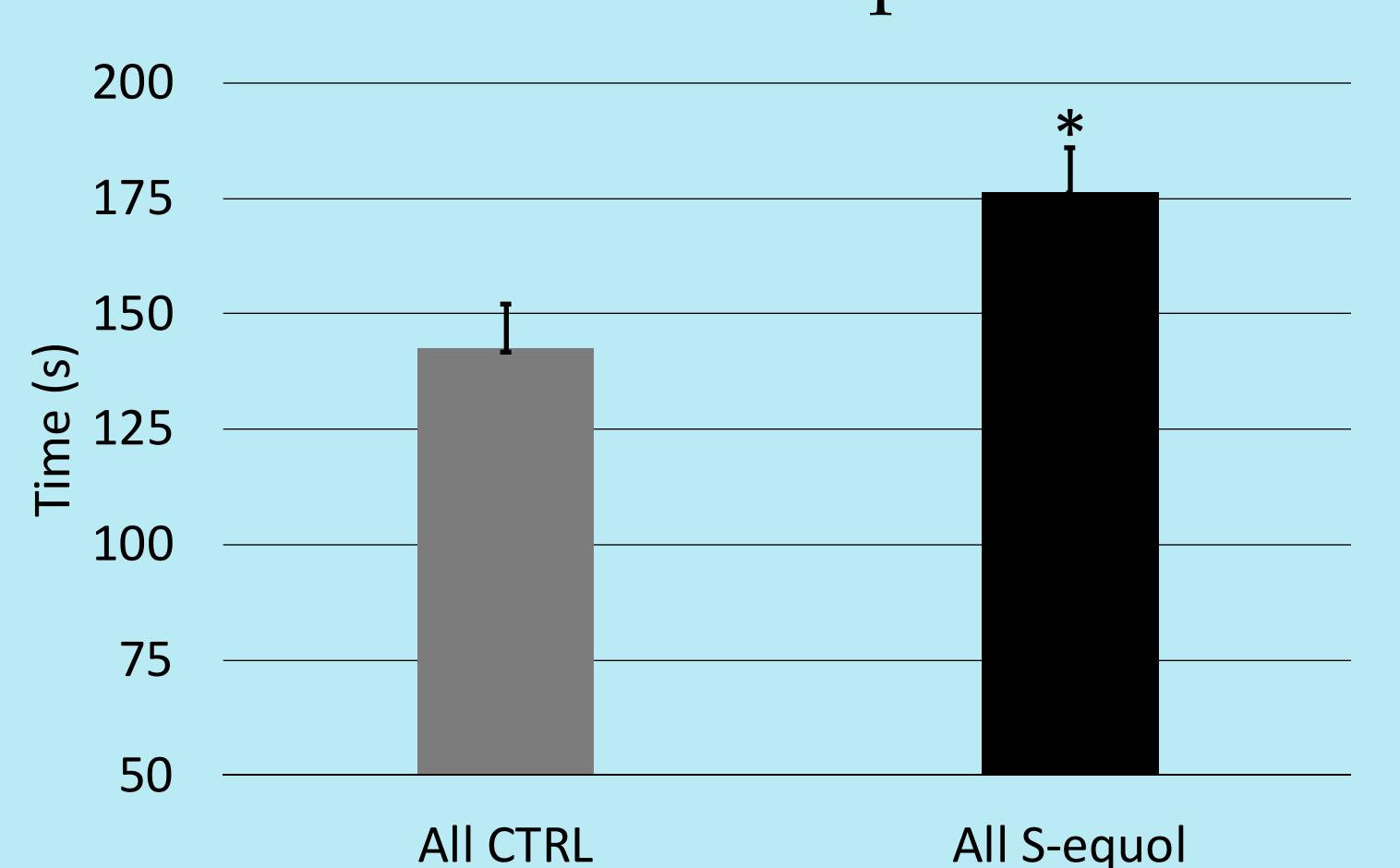
#### Duration of Exploratory Behavior



**Figure 3.** Male (M) S-equol mice had higher total exploratory behavior times (i.e. head dipping & rearing) than Male Control (CTRL) mice, suggestive of less anxiety during the maze testing. \*p=0.01.

### Tail Suspension Test Results

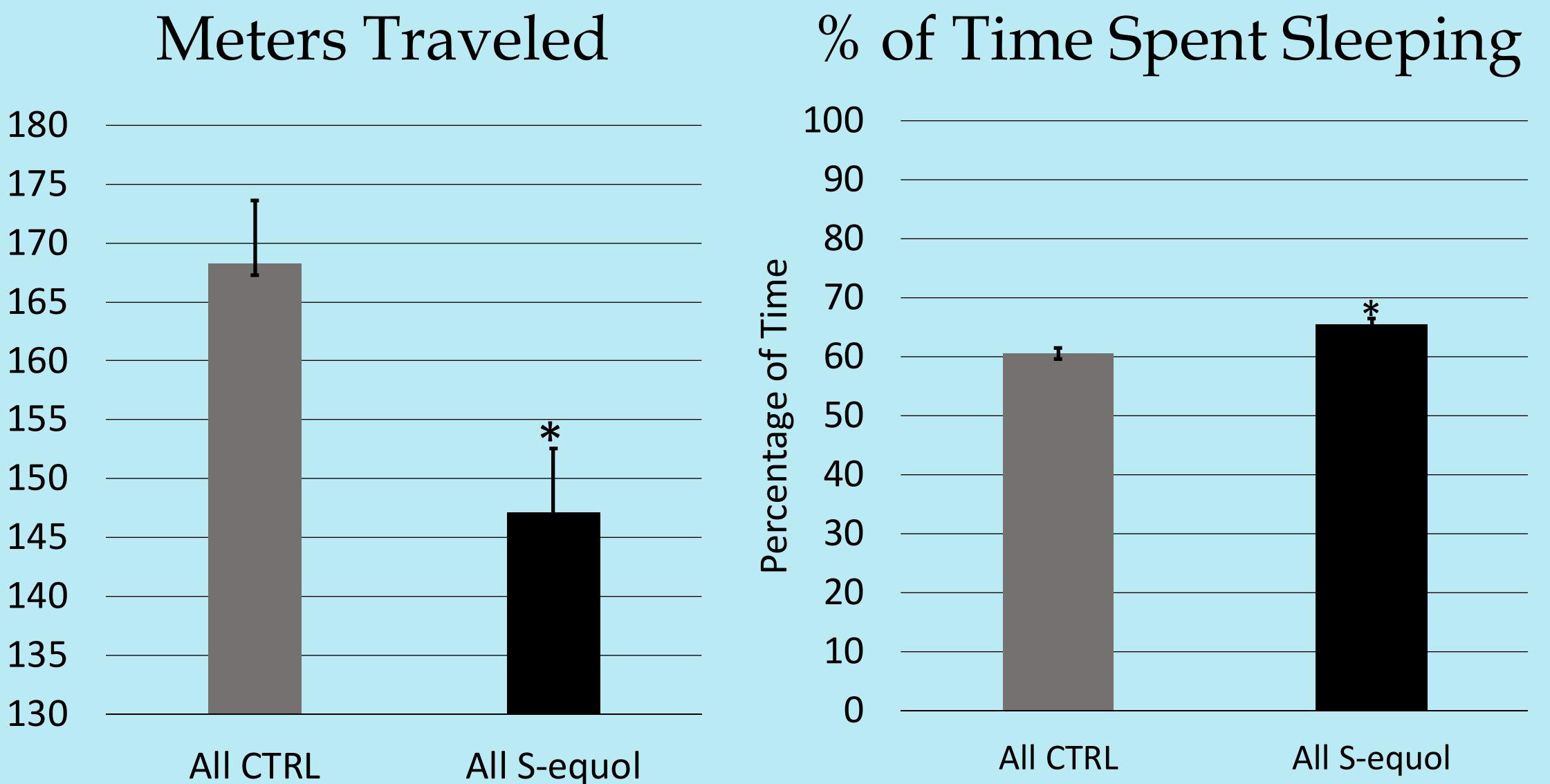
#### Duration of Time Spent Mobile



**Figure 4.** S-Equol mice (Males + females, M+F) spent more time mobile than Control mice (M+F), indicating reduced depressive-like behaviors. \*p=0.02.

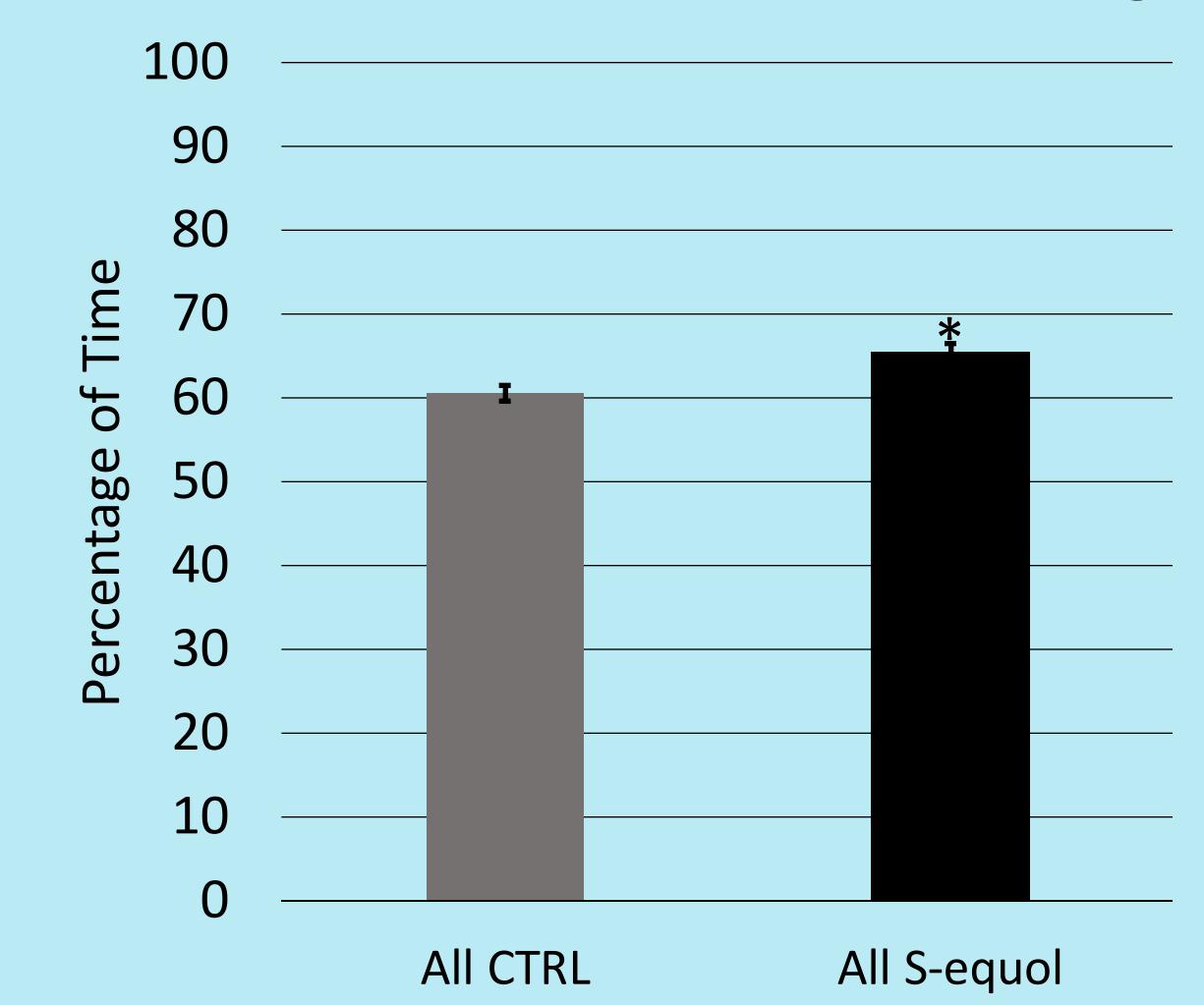
### Metabolic Chamber Results

#### Meters Traveled



**Figure 5.** Control mice (M+F) traveled more distance than S-equol mice (M+F) over the two-day period spent in the metabolic chamber. \*p=0.006.

#### % of Time Spent Sleeping



**Figure 6.** S-equol mice (M+F) spent more time sleeping than Control mice (M+F) over the two-day period spent in the metabolic chamber. \*p=0.0003.

## Conclusions & Future Aims

- The behavioral tests suggest that mice fed a HFD and treated with S-equol showed reduced anxiety-like behaviors as indicated by increased exploratory behaviors in a novel setting (EPM test), reduced depressive-like behaviors as evidenced by increased time spent mobile in the TST, and reduced anxiety-like behaviors as shown by percentage of time spent sleeping in the metabolic chamber.
- In contrast, mice fed a HFD and vehicle alone (CTRL) traveled more distance when tested in the indirect calorimetry unit, which approximates the homecage setting. Such behavior could, however, suggest increased overall anxiety-like behaviors.
- To test this possibility further, animals could be tested in an open field test, which also measures anxiety-like behaviors.
- Another possibility is that mice treated with S-equol are less active and correspondingly sleep more in the homecage setting, which may indicate such treatment affects their motivation to engage in voluntary physical activity.
- Future studies will also examine for gene expression differences in the amygdala, which regulates emotive behaviors, and nucleus accumbens, primary brain region mediating motivation to engage in voluntary physical activity.

## References

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