

# Ketogenic Diet and Social Behavior in a Mouse Model of Autism Spectrum Disorder

Macy Kuebler, Abigail Grzeskowiak, Emily Trabulsi, Abigail Schwartzman, Gabrielle Skiba & Allison R. Bechard

State University of New York at Geneseo, Departments of Psychology and Neuroscience



GENESEO

## Background

- Three key criteria for Autism Spectrum Disorder (ASD) include repetitive behavior, impaired communication skills, and impaired social interaction (Yang et al., 2016).
- Ketogenic Diet (KD), a high-fat and low carb diet, is noninvasive and proven to help many neurological issues in humans and reduce repetitive behavior in the mouse model. (Jagadish et al., 2018; Ruskin et al., 2013, Brady et al. 2022)
- Current research has found that KD increases sociability and helps other symptoms of ASD (Ruskin et al., 2017).
- Animal models are useful for studying behaviors in ASD and associated neurobiology.
- We hypothesized that 3 weeks of KD would improve social abilities and motor performance in a mouse model of ASD. We studied both older (+1year) and younger (4-6mos) mice.
- A lack of literature on the estrous cycle and its role as an experimental variable is ongoing. Thus, we monitored estrous cycle in our female subjects and stranger mice.
- The goal of this study is to search for the role of KD compared to standard diet (SD) in sociability and also examine the estrous cycle relative to social behaviors

## Methods

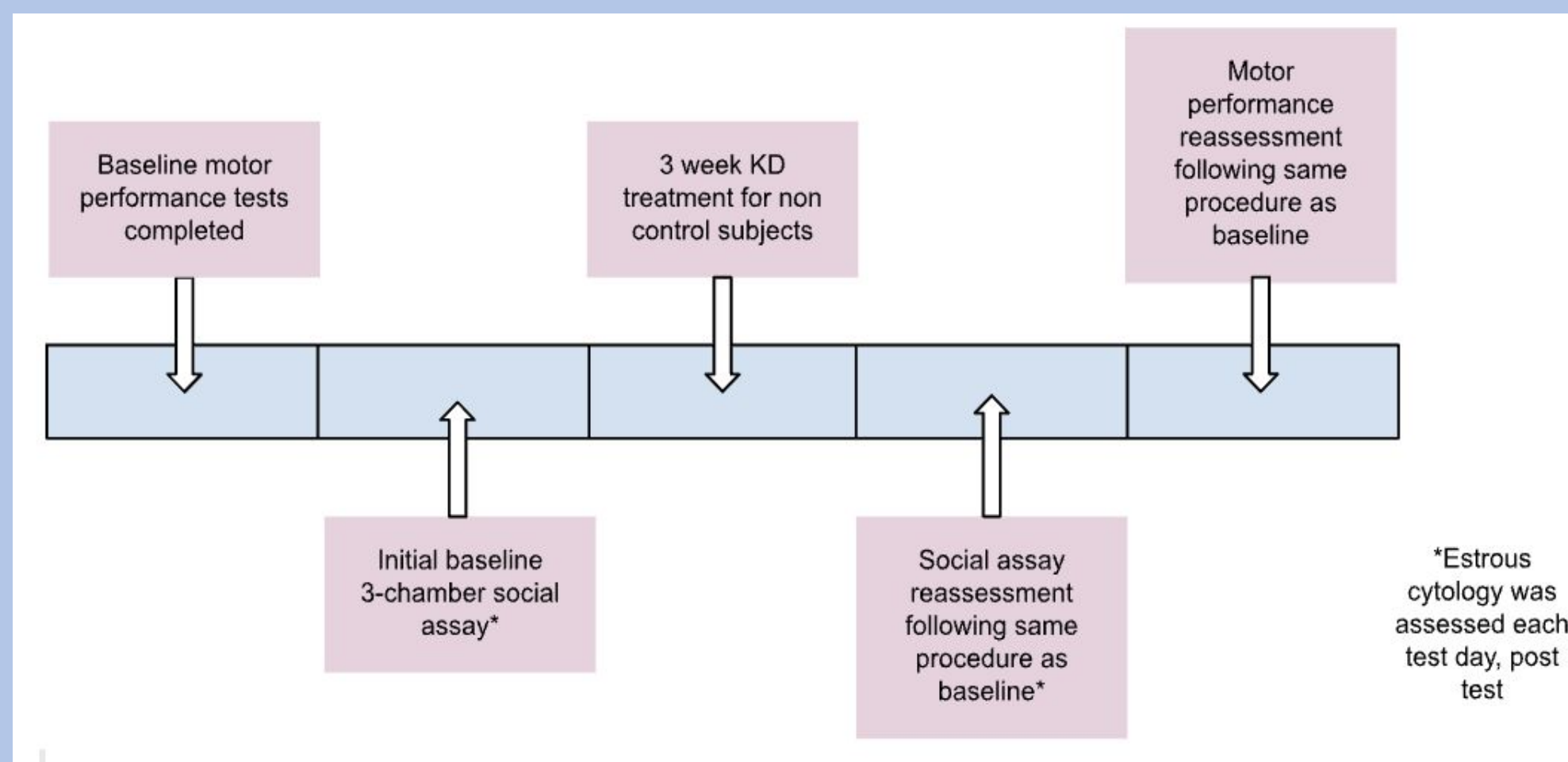


Figure 1: Timeline for social assay and motor tests.

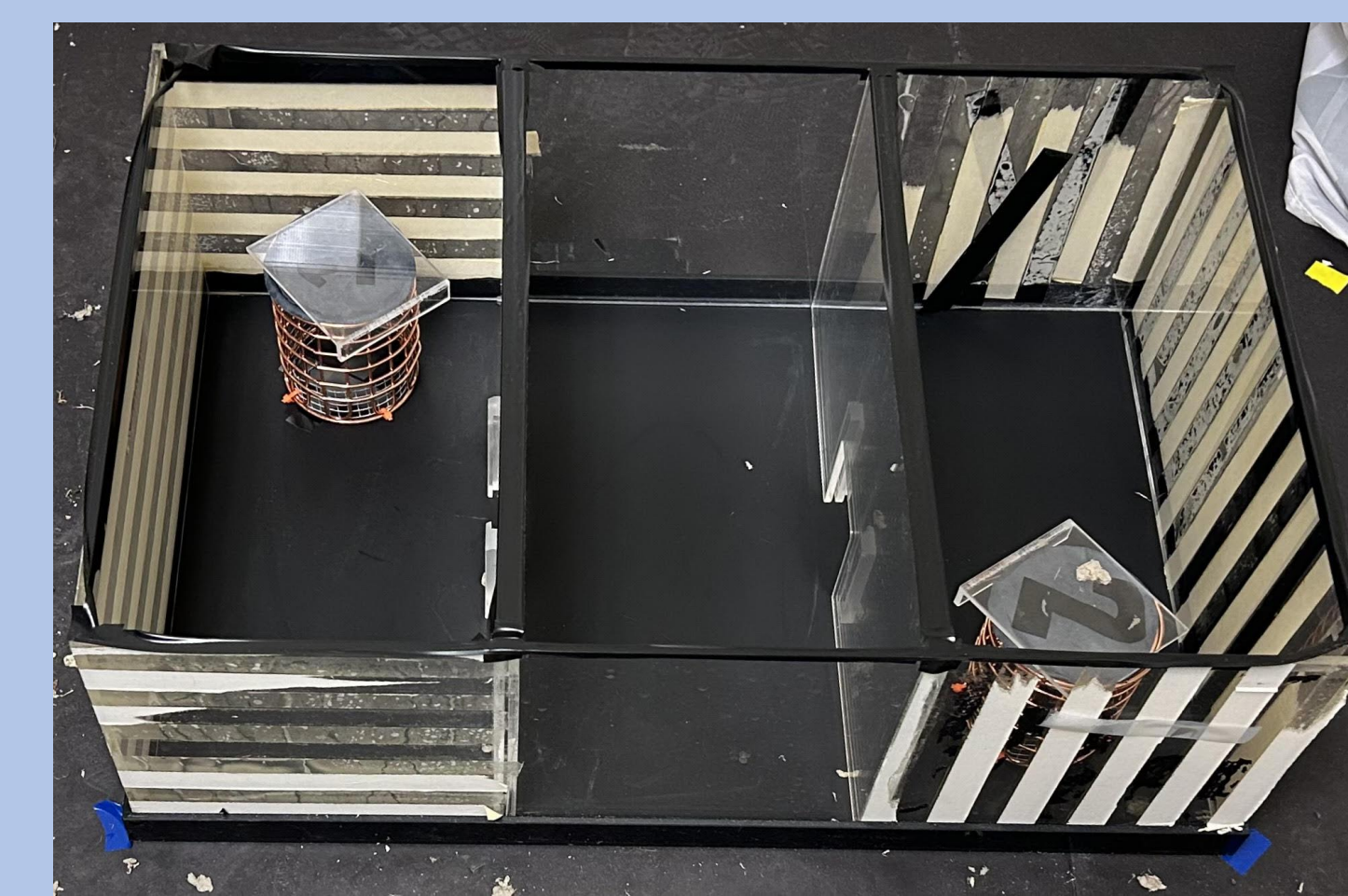


Figure 2. 3 chamber testing set up for social assay used to test sociability in mice with repetitive behaviors.

For this experiment, a 3 chamber social assay was used to complete a 30 minute novel object task where 2 stranger mice (ST1 and ST2) represented the novel or familiar object.

- The three trials were:
  - **Trial 1:** Empty (No ST1/ST2); 10-min.
  - **Trial 2:** ST1 mouse placed; 10 min.
  - **Trial 3:** ST1 and ST2 mouse placed: 10 min.

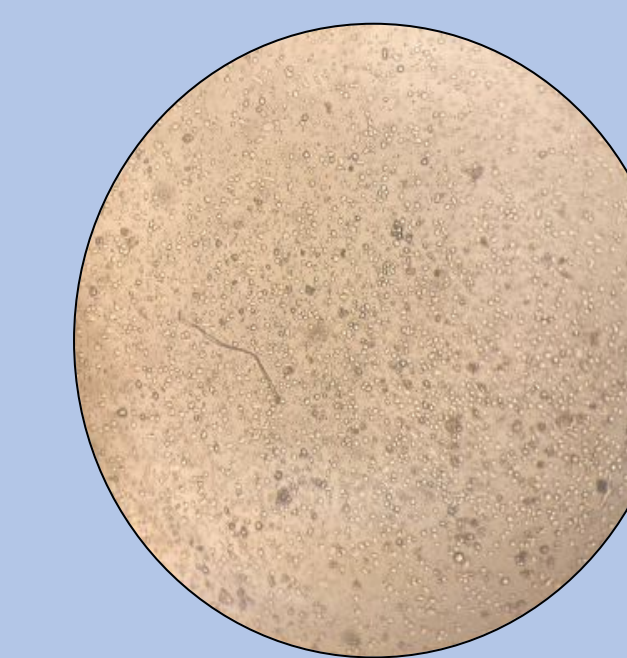


Figure 3: The image above is a sample of an estrous cytology taken.

## Discussion and Future Directions

- We did not find strong effects of KD on social behavior in older mice. However, young mice fed KD were more likely to spend time with a stranger mouse (figure 4). Increased social interactions in females fed KD fits with previous findings (Ruskin et al., 2017).
- We did not find a reduction in stereotypic locomotor activity after KD (figure 5). This was unexpected, as we have found this several times previously (Brady et al. 2022).
- We did find that KD increased grip strength in older but not younger mice.
- Findings suggest that KD may interact with age, and be most beneficial for motor performance in older mice.
- Future directions involve neurobiology of KD effects and increasing number of male and female subjects.

## Results

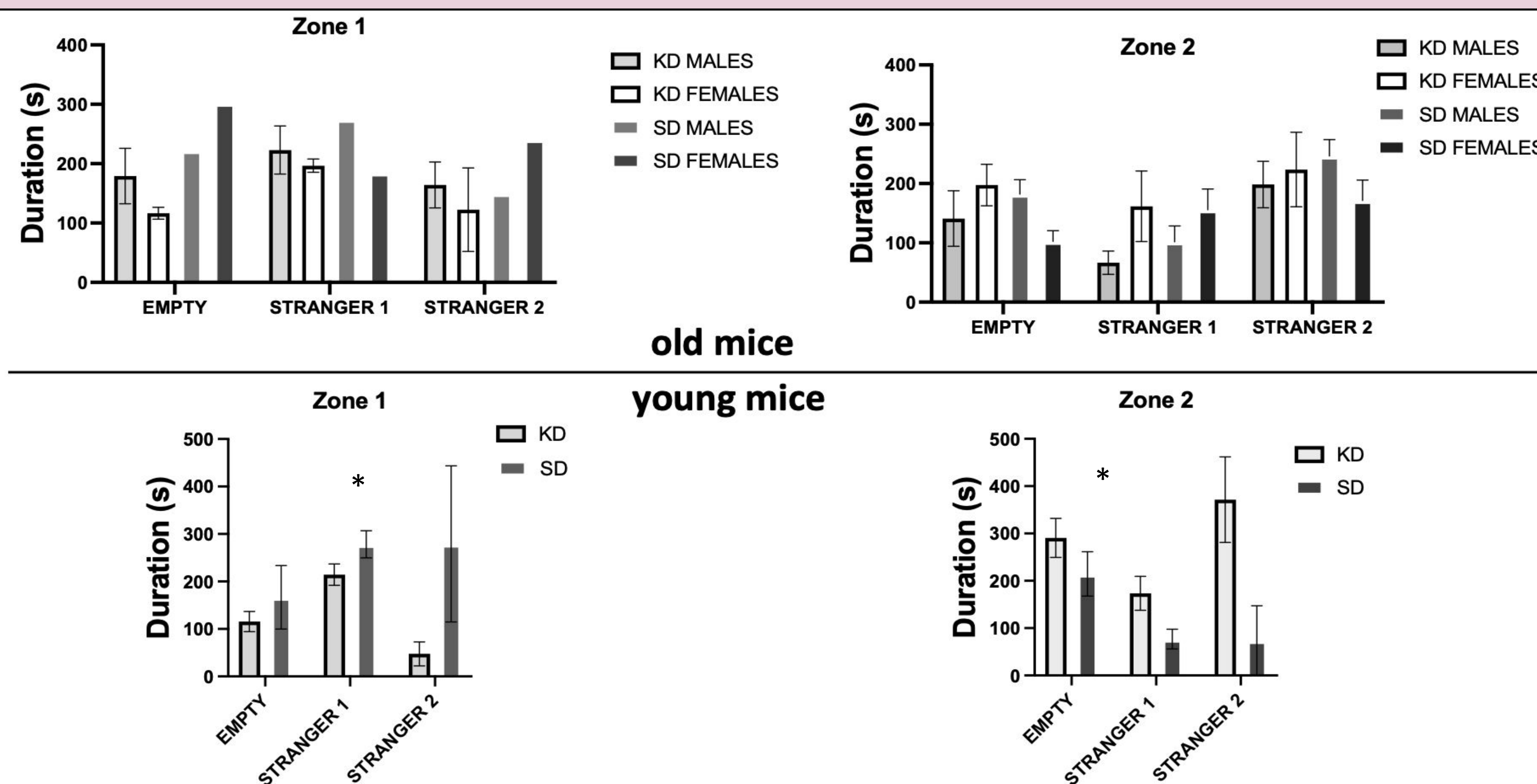


Figure 4. Social behavior in a 3-chambered test.

- In older mice, the time spent a) in Zone 1 (Time:  $F(1, 28) = 6.16, p = 0.006$ ), and b) in Zone 2 ( $F(1, 28) = 8.3, p = 0.001$ ) is dependent on the session (Sessions 1, empty; 2, Stranger 1; and 3 is Stranger 2).
- In younger mice c) the duration spent in Zone 1 differed by diet, as females fed KD were more social with a stranger mouse ( $F(1,4) = 7.0, p = 0.05$ ). d) females fed KD were also more social with a new stranger mouse compared to standard fed control females ( $F(1,4) = 20.1, p = 0.011$ ).

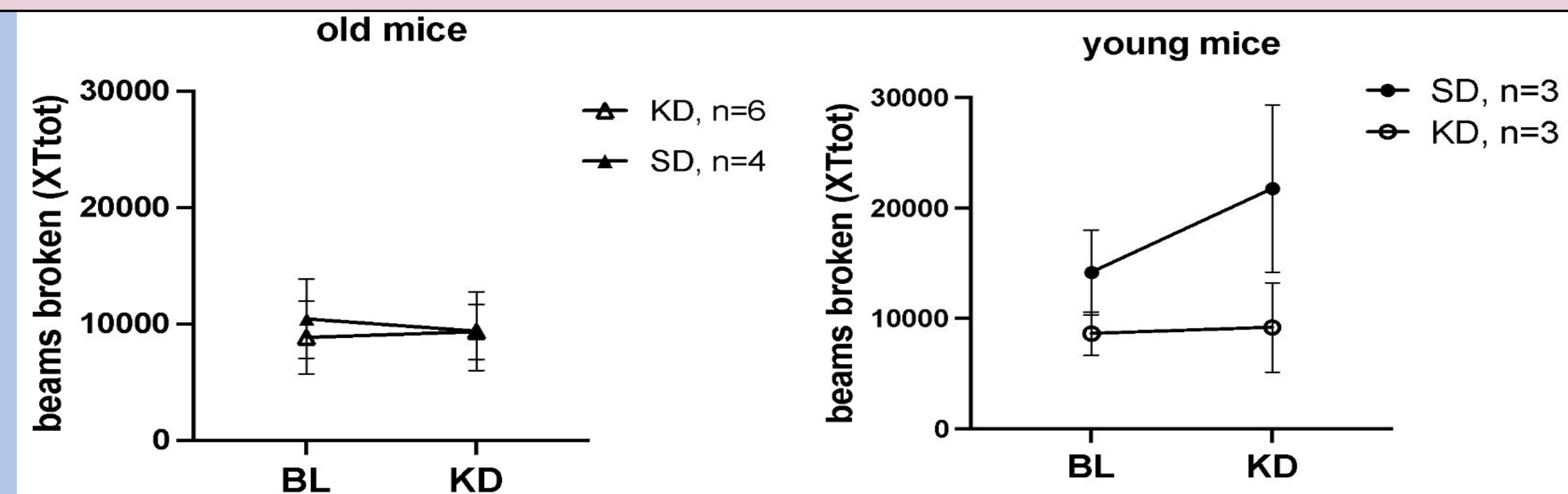


Figure 5. Locomotor data for old vs young mice. No significance for old or young mice.

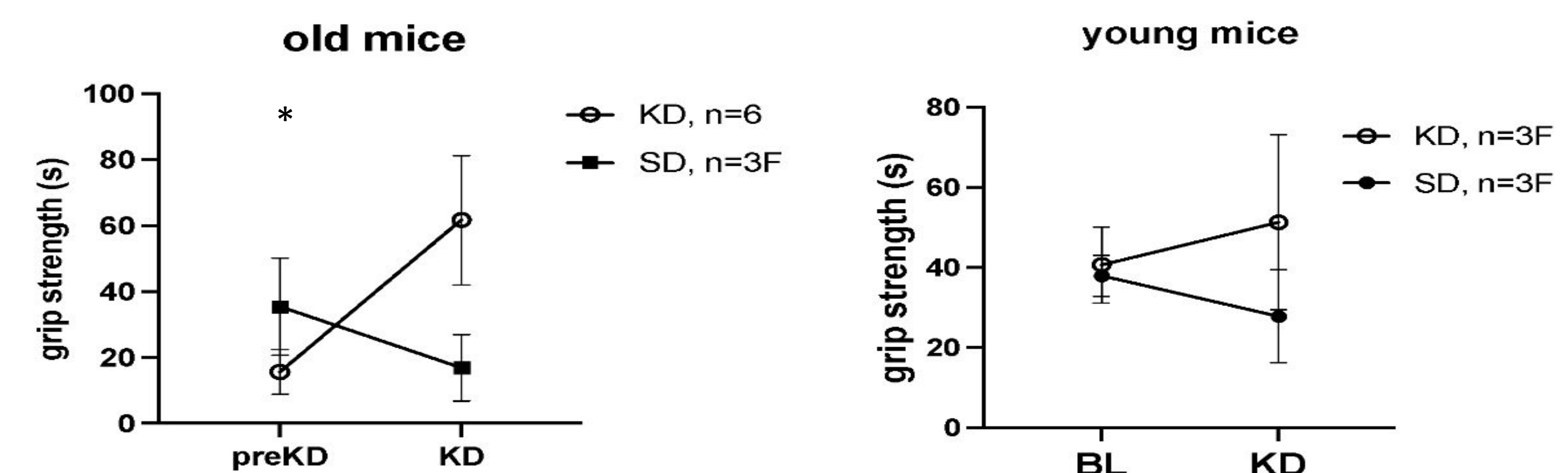


Figure 6. Grip strength of old mice shows a time x diet interaction Mice fed KD held on to a wire for longer (Time x diet:  $F(1, 7) = 7.0, p = 0.032$ ).

Grip strength of young mice. No effects of diet in young mice.