WORKING MEMORY AND LOCOMOTOR ACTIVITY IN OLD AND YOUNG MICE FED A KETOGENIC DIET

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Background

- The ketogenic diet (KD), a high-fat, low-carb diet, has recently been used to treat disorders associated with an inflexibility of cognitive and behavioral routines, such as dementia and autism spectrum disorder. However, there has been little investigation into how KD's beneficial effects on cognitive behavior may change with age.
- Here, we fed some mice normal chow and some KD (see *Figure 1A & 1B)* and show the effects of KD on performance in a working memory task and locomotor activity in young and old C57BL6/J mice.
- In Experiment 1, we used a Barnes Maze (*see Figure 2*) to assess working memory. In the Barnes Maze, mice locate an escape box under a target hole by using spatial cues. Each day the target hole is moved to a new location.
- We found that mice on KD performed better, indicated by shorter latencies to find the target hole. However, only the young mice on KD made fewer errors.
- To check for differences in activity between mice on KD and mice fed a normal diet, experiment 2 employed a 1 hour locomotor test.
- KD increased horizontal activity in young and old mice.
- Thus, regardless of age, mice fed KD performed better in a working memory task and were more active.
- Findings may be useful for using KD as a form of therapy.

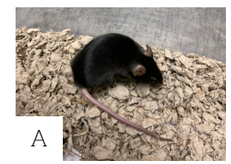

Figure 1A) depicts a mouse on the normal diet. *1B)* depicts a mouse on the KD diet

Figure 2. The Barnes Maze assessed working memory across 4 days, with 5 trials each day. The first day there is a visual cue indicating the target hole (Cue Day). The next 3 days working memory is assessed by moving the target hole to a different quadrant of the maze each day.

Experiment 1: Working Memory

- 14 old B6 mice (10-12 months) and 16 young B6 mice (4-6 months) were assessed in the working memory task.
- Latency to the target hole and the number of errors were compared between groups (see *Figure 3*).

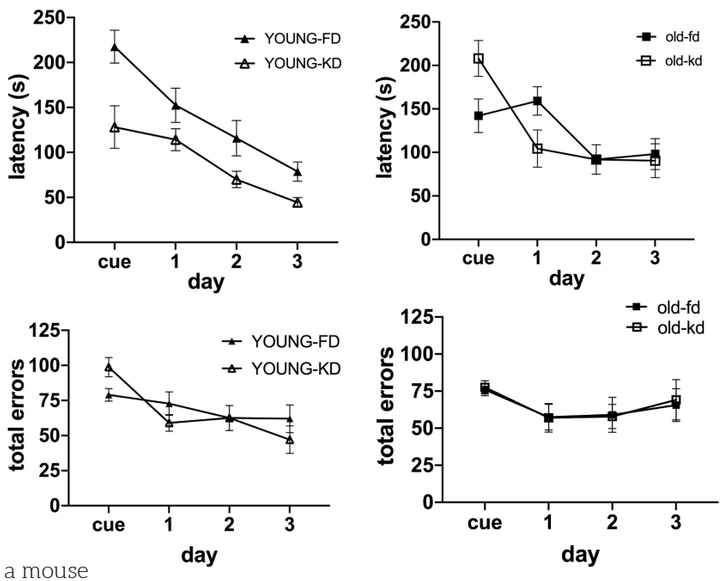

Figure 3. Mice fed KD performed better in a working memory task than controls (FD), as indicated by shorter latencies to find the target hole across sessions in A) young (RM ANOVA: Main effect of Diet: $F(1,14)=17.6$ $p=0.009$) and B) old mice ($F(3,36)=4.4$, $p=0.009$). C) Young mice fed KD made fewer errors overall (Time*Diet interaction $F(3,42)=2.7$, $p=0.056$) although D) errors made by old mice did not differ between groups.

Experiment 2: Locomotor Activity

- Locomotor activity was assessed in a 1 hour session using automated photo-beam breaks as an indication of activity (see *Figure 4A & 4B*).
- Specifically, we were interested in how KD affected horizontal activity.

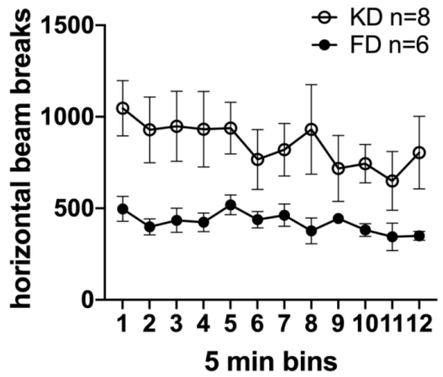

Figure 4A) KD increased locomotor activity in old B6 mice.

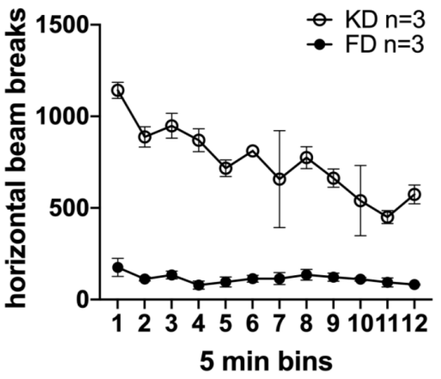

Figure 4B) KD increased locomotor activity in young B6 mice.

Discussion

- We found KD to improve performance in a working memory maze task.
- B6 mice on KD had shorter latencies to the target hole compared to control mice, and young mice on KD made fewer errors overall on the maze.
- KD also increased horizontal locomotor activity in both young and old B6 mice.
- KD is shortening latency times in old mice, while increasing locomotor activity in both young and old mice.
- Findings are of interest for the therapeutic benefits of KD in therapy for disorders associated with inflexibilities of cognitive and behavior routines.

Future Directions and Limitations

- Future research should further investigate the differences between the cognitive and behavioral benefits of KD on young and old mice.
- One limitation is that only one strain of mouse (B6) was used to track locomotor activity.
- The data for young mice in the locomotor test is preliminary and we are redoing it currently.
- Future research should replicate this experiment using other strains of mice, like FVB mice, because of the tendencies for these mice to exhibit repetitive stereotypic behaviors.