The Effects of Alcohol and Ketogenic Diet on Working Memory in Mice

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Background

- Working memory is defined as involvement of goal-directed behaviors where information is used for task execution. Working memory is important as it has been researched that it lays the foundation for many other cognitive controls in humans.
- Alcohol use disorder (AUD) is a chronic disease defined as an individual's loss of control over alcohol intake and consistent patterns of heavy alcohol consumption. Binge drinking is a common style of drinking seen in individuals diagnosed with AUD.
- AUD is shown to have association with long term cognitive deficits in the brain such as working memory.
- The ketogenic diet (KD) is a high fat, low carb diet that has become increasingly popular in research to improve working memory and reduce binge drinking.
- To model our research on AUD and working memory, we used a mouse model. We modeled AUD through studying binge drinking habits and modeled working memory through a task called Barnes maze.
- We hypothesized that mice on KD will consume less alcohol and find the target faster in the Barnes maze than those on the standard diet (SD).

Methods

- Our subjects included 14 mice, 7 mice experiencing the KD and 7 mice strictly on the SD. Figure 1 shows a timeline of diet for the mouse subjects.
- Mice went into the bar (Figure 2) for 2 hours a day, 3 times a week for a total of 8 weeks. Mice received 10% ethanol through their sippers also shown in Figure 2. To measure alcohol consumption, we measured pre and post volumes each trial day.
- After this 8 week period measuring diet and binge drinking, mice were introduced to the Barnes maze task to measure working memory.
- The task was measured over a 4 day period consisting of 5 trials per mouse each day. Cue day was the first day involving a small visual cue above the target hole. Days 1, 2, and 3 were then tested without the visual cue above the target hole.
- On each day, a new target hole was chosen and mice use their spatial and visual cues to find the target. Working memory is assessed in this task through latency times.

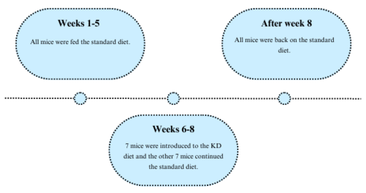

Fig. 1. Timeline of the SD and KD diets introduced to the mice subjects.

Fig 2. The bar including the sipper used for the 2 hour drinking periods for the mice.

Fig. 3. Mouse subject mid-trial peeking into one of the forty holes on the Barnes maze.

Results

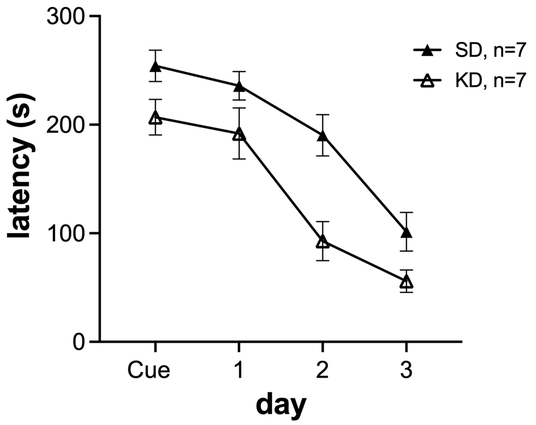

Fig. 4. Shows the latency for mice to reach the target platform using the spatial cues around the room. Mice found the target hole faster over time (Time: $F(3,30)=47.9$, $p = <0.0001$). Mice fed a ketogenic diet (KD) found the target hole faster than mice fed a standard diet (SD) (Diet: $F(1, 12) = 12.6$, $p = 0.003$).

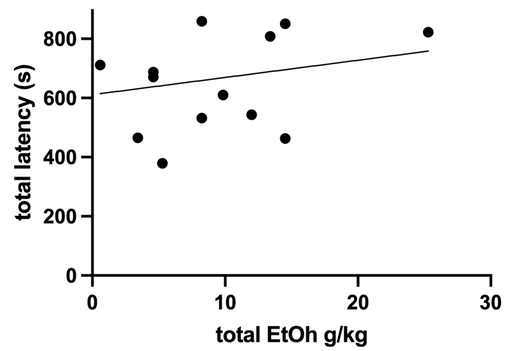

Fig. 5. There was no correlation between total latency of the maze performance and total alcohol consumption.

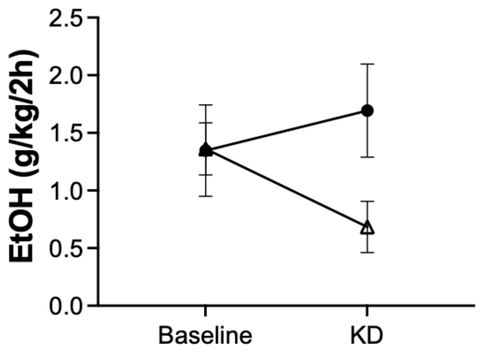

Fig. 6. The graph illustrates drinking patterns between subjects on the standard diet versus the ketogenic diet during baseline (Weeks 1-5) and after being introduced to the ketogenic diet. There is a significant interaction between time and diet ($p=0.0018$)

Discussion

- Figure 4 shows us that mice on the KD performed better on the Barnes maze through shorter latency times to the goal box than those on the SD on all four days of testing. The mice who were on the ketogenic diet were shown to have better performance of their working memory than those who were on the SD.
- Figure 5 shows no significant correlation between consumed EtOH over the 8 week period and latency times to the goal box. Our model shows that alcohol consumption did not have a significant interaction with performance of working memory.
- Figure 6 shows a significant correlation between diet and binge drinking patterns. Those on the KD drank less total amounts of alcohol than those on the SD showing a significant interaction between diet and binge drinking.

Future Directions/Limitations

- The first limitation in our study is our relatively small sample size. More research should be done in the future with more subjects to strengthen our results.
- The second limitation is that when we introduced subjects to the Barnes maze task, they were much older in their lifespan. We should consider the possibility in variations of results in terms of age in future research.
- The third limitation is that our study lacked investigating sex differences.
- In the future, in addition to looking at behavioral mechanisms, we could look at differences in neurobiology, more specifically changes in the hippocampus.
- Our research shows that diet is a promising possibility of treatment and prevention of cognitive decline in working memory of the brain and binge drinking.

References

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