THE EFFECT OF AN ADENOSINE RECEPTOR AGONIST ON STEREOTYPY IN MICE

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Introduction

- In the US presence of autism spectrum disorder (ASD) is rising. A main symptom of ASD is stereotypic behavior, which is rigid, repetitive, and functionless. Despite its potential to disrupt daily functioning and routines, there is no effective treatment.
- The keto diet (KD), a low-carb high-fat diet, has gained increased efficacy in treating ASD.
- FVB mice are genetically predisposed to perform stereotypic behavior manifested in a circling movement pattern.
- Adenosine is involved in energy regulation and typically inhibits motor activity. Adenosine 2A (A2A) receptors are expressed in the indirect basal ganglia pathway. Here, we hypothesized administration of an A2A receptor agonist would decrease repetitive circling.

Methods

- Mice were used from an earlier study analyzing the effect of KD on locomotion. Here, mice remained in their previous diet group and were again fed either KD or a standard diet (SD).
- Stereotypic behavior was recorded weekly through an automated locomotor test, consisting of a 20 minute habituation period, 30 minute baseline followed by a 60 minute test.
- During week 1, pre-experimental conditions (Before KD & adenosine) were recorded. Accordingly, KD and adenosine were not employed. Mice were instead given a 0.2 mg peanut oil injection following the baseline measurement.
- On weeks 2, 3, & 4, half of the mice began KD while the others remained on SD. After the baseline, an A2A receptor agonist was administered at 1 ml/g, and movement was recorded.
- For week 5, all the mice returned to SD, and a peanut oil injection was administered after the baseline measurement.
- Throughout each week, the weight of the mice was monitored due to the potential effect of diet.

Figures

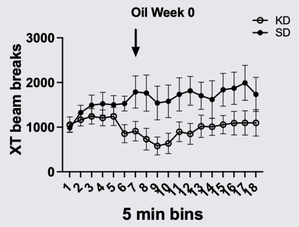

Figure 1. Baseline locomotor activity prior to the introduction of adenosine and diet change. Mice previously on KD showed reduced activity, as indicated by fewer beam breaks.

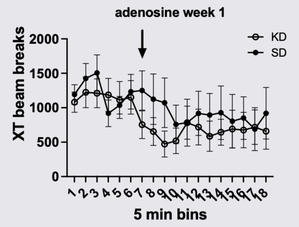

Figure 2. Adenosine reduced locomotor activity in both groups. KD mice had decreased locomotion activity compared to the SD group.

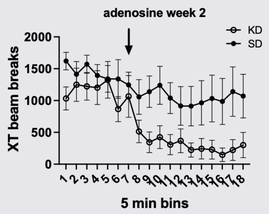

Figure 3. Adenosine reduced locomotor activity in both groups. There was diet differences between groups, as KD mice had significantly reduced locomotion activity compared to the SD group.

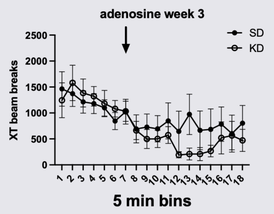

Figure 4. Adenosine collectively decreased locomotion activity, and KD mice had reduced movement compared to SD mice

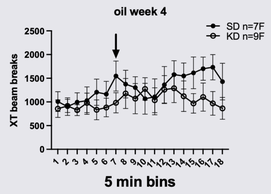

Figure 5. After removing KD and injecting with peanut oil, locomotor activity increased for both groups; however, mice previously on KD remained less active than SD mice

Results

- During week 1 (baseline), stereotypic behavior was lower in mice previously on KD compared to those never on KD.
- Group differences show the persistent effect of KD on lessening repetitive behaviors.
- After the A2A receptor agonist injection, locomotion for all mice decreased.
- During week 2 there were differences due to diet.
- Results indicate that the A2A receptor agonist reduces repetitive behavior but does not synergistically interact with KD.

Limitation/ Future Directions

- Future directions include repeating our study using the same conditions to increase the validity of results and further assess which mechanisms in the brain allow for adenosine and KD to attenuate stereotypic behavior.
- All conditions should remain the same except for the subject group. In order to assess for sex differences, a larger sample size should be utilized.
- We would like to investigate both the adenosine A1 and 2A receptor agonists, which have previously been shown to reduce spinning with coadministration.
- Potential to reevaluate/ experiment with different drug administration dosages.