Elucidating Metabolic Connection Between Liver and Brain via Metabolomics and Integration Modeling in Epilepsy

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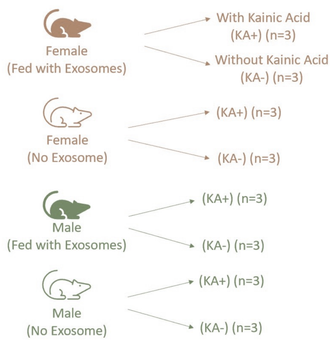
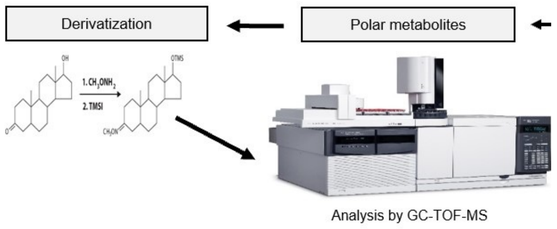
Introduction

Epilepsy is the fourth most common neurological disorder in the US impacting ~1% of the population and of those, 30% are resistant to traditional drug treatments, a condition known as refractory epilepsy. One of the oldest alternative treatment options is the Ketogenic diet (KD). The specific mechanism behind the KDs success remains ambiguous, however current research suggests it functions through a metabolic switch of the main fuel sources from carbohydrates to fatty acids. The findings of this study further support the importance of considering liver metabolism as the metabolic dynamics of epilepsy continue to be studied and may uncover metabolic targets which could be used to develop more effective treatment options for refractory epilepsy.

Methods



Liver samples were extracted from mice in the conditions displayed to the left, and then analyzed using GC-TOF-MS. Mice were feed milk derived exosomes in accordance with their group



Results

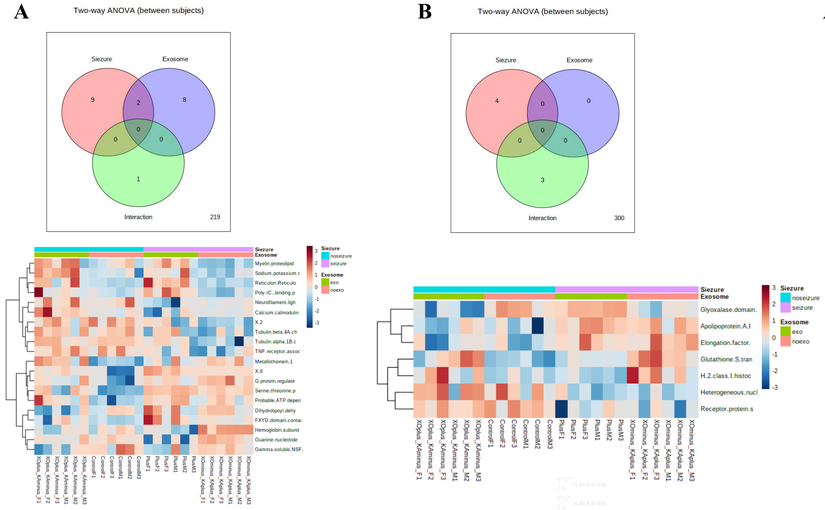


Fig.1. Ven diagram showing ANOVA results considering interactions (top) and the corresponding heatmap results (bottom) for both brain (A) and Liver (B) analysis.

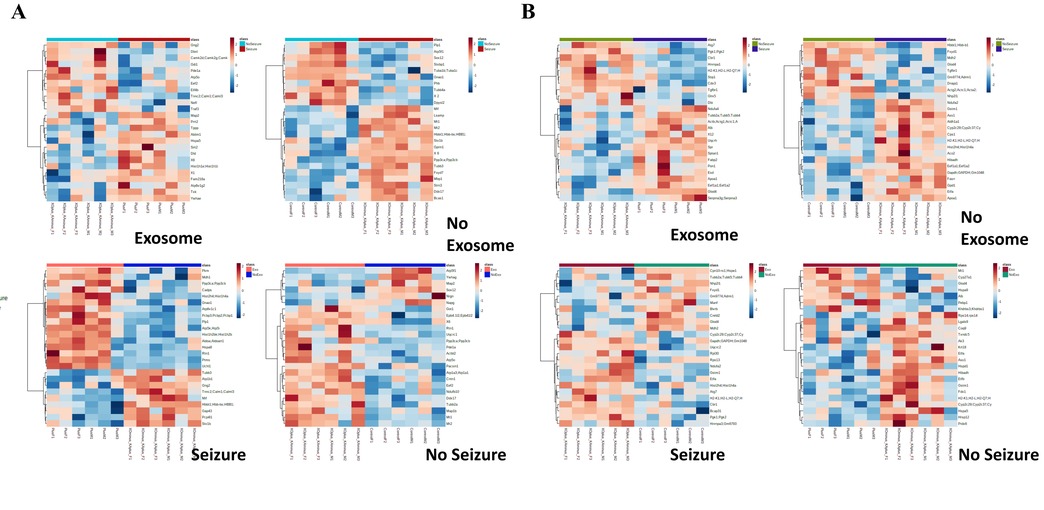
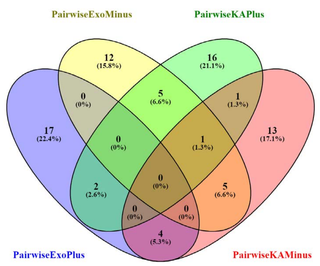


Fig.2. Heatmap results for pairwise analysis of brain (A) and liver (B) data. Variable controlled stated in lower right-hand corner of each heatmap (4 for each organ). Heatmap results based on T-Test analysis results.

3. Ven Diagram Brain



Gene Names

Significant between all analysis

None

Significant between Exo based Analysis

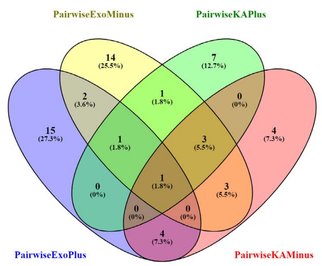
None

Significant between KA based analysis

Rtn1

Fig.3. Ven diagram taking into account top 25 significant proteins detected by each individual pairwise analysis and comparing results across all four analyses. The table lists the gene names for significant proteins in analysis comparison. (Seizure/ NoSeizure) ; (Exo/NoExo), value threshold < .05, FDR threshold < 0.2.

4. Ven Diagram Liver



Gene Names

Significant between all analysis

Glod 4

Significant between Exo based Analysis

Apoa1

Eef1a1;Eef1a2

Significant between KA based analysis

None

Fig.4. Ven diagram taking into account top 25 significant proteins detected by each individual pairwise analysis and comparing results across all four analyses. The table lists the gene names for significant proteins in analysis comparison. (Seizure/ NoSeizure) ; (Exo/NoExo), value threshold < .05, FDR threshold < 0.2.

Conclusions

- Our analysis demonstrates significant changes associated with seizure presence across liver and brain samples
- Results of comparison across pairwise results reveal proteins of high interest for focused analysis
- These results indicate possible presence of metabolic targets for future analysis
- Future research will continue with pathway analysis of current results
- Future research will also compare previous metabolic analysis with current proteomic analysis
- Future research could further investigate these metabolic targets for development of new treatment options