The Impact of Binge Ethanol During Adolescence on Myelin Related Gene Expression

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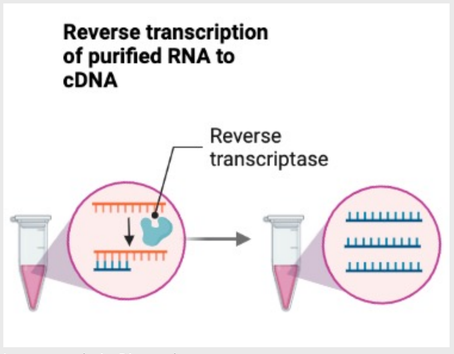
Abstract

Adolescents tend to consume alcohol in binges. The earlier one begins to drink, the higher risk they have of developing an alcohol use disorder. Brain development is ongoing throughout adolescence, and consuming ethanol in the early stages of life can have a long-term negative impact. Specifically, decreases in myelin and white matter in the frontal cortex have been shown following binge ethanol in adolescence, which may cause cognitive deficits. In this study, different genes were studied to detect if adolescent ethanol treatment had an impact on myelin-related gene expression. RNA expression level of genes important to the maturation of oligodendrocytes, which form myelin sheaths, were measured. The hypothesis was that ethanol treatment will decrease expression of these genes and therefore negatively affect myelin and the maturation of oligodendrocytes. Ethanol (4 g/kg) or water was provided to adolescent male and female mice during adolescence (postnatal day 29-42). Four hours and twenty-four hours after their last dose, prefrontal cortex tissue was collected. qPCR was utilized to determine the expression level of the genes. This study shows the immediate and long-term consequences of binge alcohol in adolescence on genes that regulate myelin development and its effect on the prefrontal cortex. In the future, additional time points such as eight hours and sixteen hours can be incorporated to examine the course of the change in the gene expression levels.

Methods

- DBA/2J Mice were dosed with H2O or ethanol (4g/kg), and PFC tissue was collected after 4 hours and 24 hours of dosing ethanol
- Primers were designed and had efficiencies between 80% - 110%
- RNA was isolated from PFC tissue, and cDNA was made
- qPCR was utilized to amplify specific mRNA sequences and determine the level of gene expression of myelin-related genes
- Following genes are structural components of myelin or involved in oligodendrocyte differentiation: *Olig1, Sox10, Pdgfrα, Akt2, Mal, Mobp, Plp1, Mag, and Mbp*



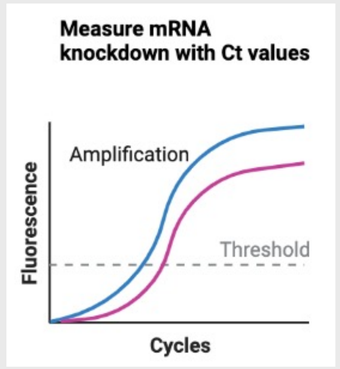
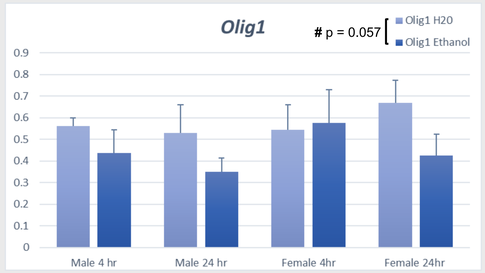
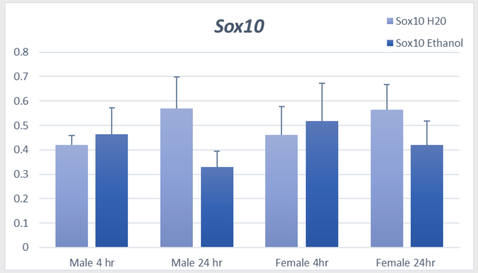
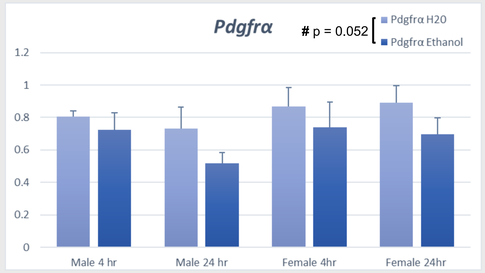


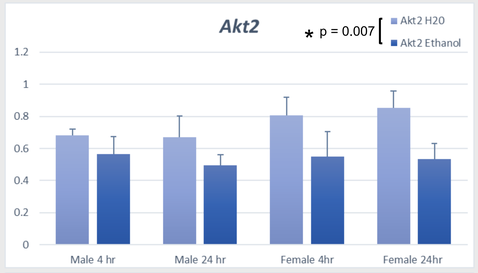
Image made in Biorender

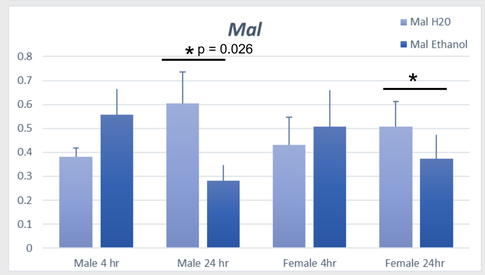
qPCR Results

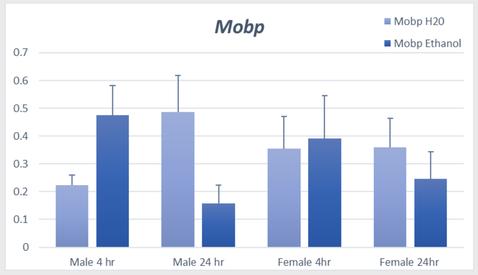


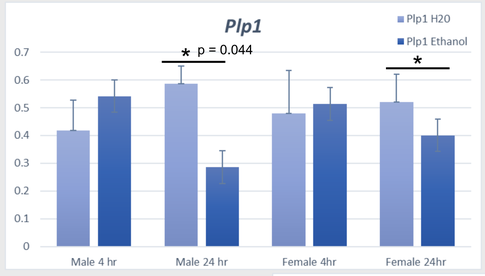


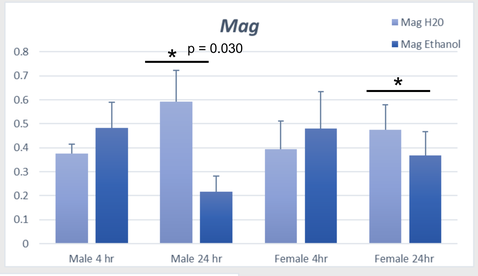


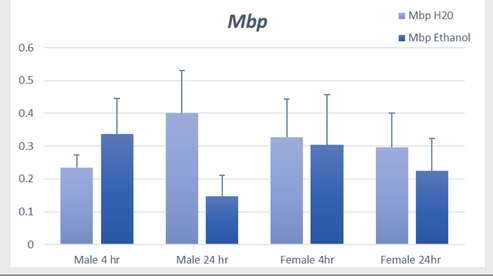












Conclusion

The qPCR results demonstrate a decrease in myelin-related gene expression in the prefrontal cortex after adolescent binge ethanol use. The effect is stronger at the 24-hour mark, which indicates that gene expression shifts over time. In the analysis, effects of ethanol treatment, sex, and timepoint on myelin related gene expression were evaluated. *Mag*, *Mal*, and *Plp1* showed significant treatment and timepoint interactions within the 24hr timepoint. *Akt2* showed significant decrease due to treatment, and *Olig1* and *Pdgfrα* showed a trend for a decrease due to treatment after 3-way ANOVA statistical analysis, p-value <0.05.

Future Directions

Primers to assess additional myelin-related genes were designed and had sufficient efficiency but could not be incorporated in this experiment. In the future studies, these genes could be tested to see if there are any changes to the expression levels after ethanol treatment.

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