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

Grace Lee, Emily Brocato, and Dr. Jennifer Wolstenholme

Medical Science Internship Program
Virginia Commonwealth University School of Medicine

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 28-42). Four hours and twenty-four hours after their last dose, prefrontal cortex tissue was collected. qPCR was utilized to determine the 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 28-42). 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 level of the genes. This study shows the immediate and long-term consequences of binge alcohol in adolescence on genes that regulate myelin.

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, Pdgfra, Akt2, Mal, Motp, Pip1, Mag, and Mbp

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 Pdgfra showed a trend for a decrease due to treatment after 3-way ANOVA statistical analysis, p-value <0.05.

Future Directions

- I would like to thank my mentor Emily Brocato for helping me with the research process.
- I would like to thank Dr. Wolstenholme as well as other lab members who allowed me to work in their lab.
- I would like to thank the MSIP co-directors for organizing this program.
- I would like to thank Dr. Whitehurst-Cook and Dr. Jackson for sponsoring this program.

Acknowledgements

References


