

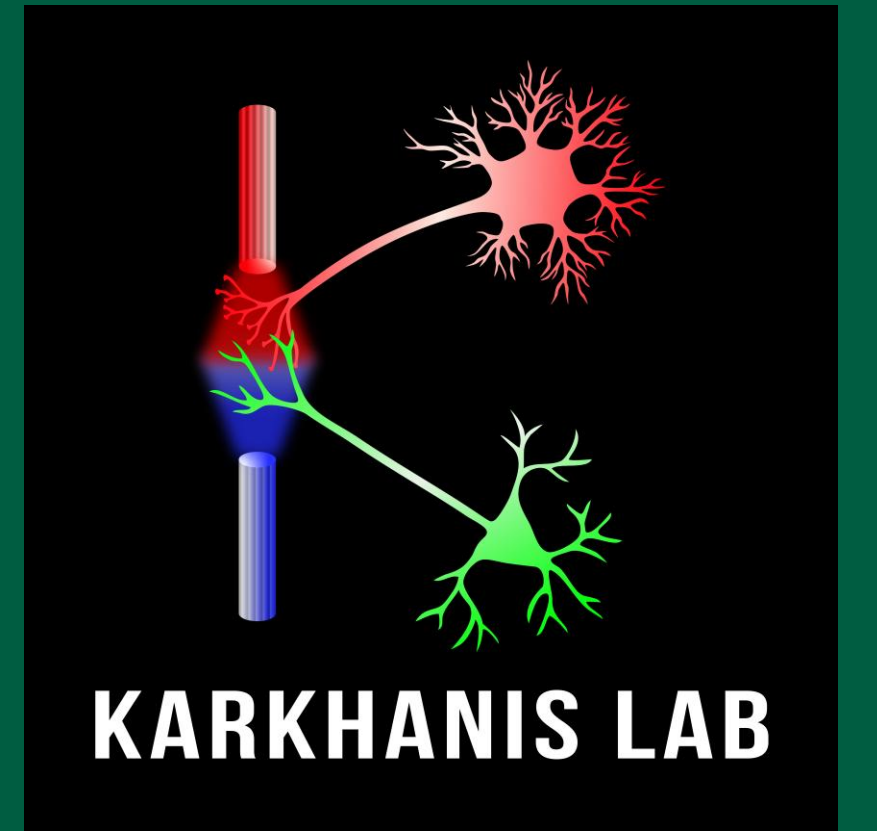


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The Effect of Prenatal Ethanol Exposure on Development and 24-Hour Ethanol Consumption During Adolescence

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Introduction

Alcohol is one of the most commonly consumed and misused substances among adults and youth in the United States; about 8.6% of underage youth and 14% of pregnant adults reported binge drinking in the last month. Prenatal ethanol exposure interferes with typical brain development, resulting in cognitive, emotional, and behavioral deficits later in life⁽¹⁾. Pre-clinical studies have shown that prenatal ethanol exposure increases risky drinking behaviors in adolescents and attenuates sensitivity to the aversive effects of alcohol⁽²⁾. This prenatal-exposure-associated-insensitivity to the aversive effects of ethanol during adolescence may result in an increased overall ethanol consumption and a greater propensity for developing alcohol use disorder (AUD).

This study investigates the effects of prenatal adolescent ethanol exposure (PAE) on adolescent drinking patterns, using a single-bottle-choice drinking paradigm in Long Evans rats. Observing the effects of PAE on drinking behaviors and development in rodents helps better inform treatment plans for youth and adults struggling with alcohol-abuse-related behaviors and disorders.

Methods

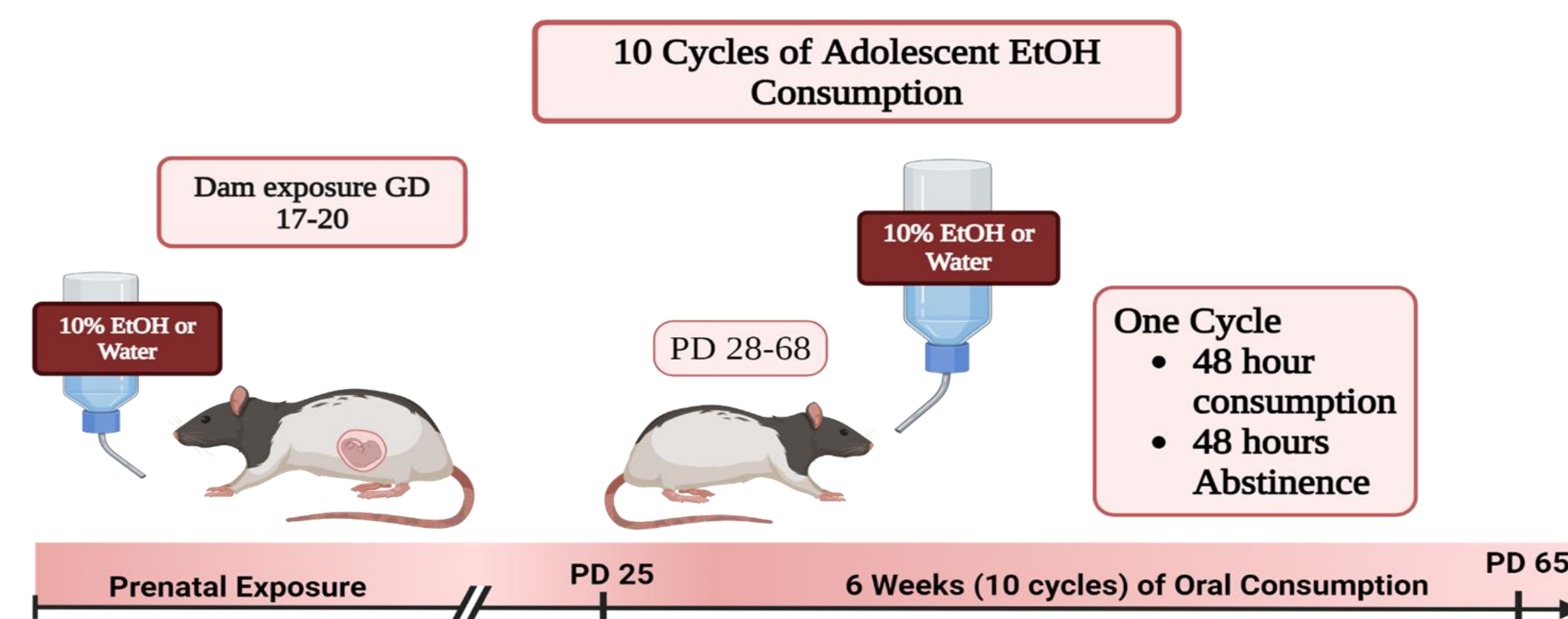
Animals:

Female (n=32) and male (n=32) Long Evans rats bred at Binghamton University were used within this study. Rats were paired-housed with same-sex cage-mates.

Ethanol and Water Oral Self-Administration during Adolescence :

It is important to note that these experiments were conducted in rats exposed to either ethanol or water in utero between gestation day 17 through 20 (GD 17-20).

Beginning postnatal day 28 (PD 28), rats were given access to either water or ethanol (10%, v/v, in tap water) for 48 hours, followed by 48 hours of access to tap water, constituting one cycle. Rats were exposed for a total of 10 cycles and weighed at the beginning of each cycle. Bottles were measured 3 hours prior to the start of the dark cycle every day.

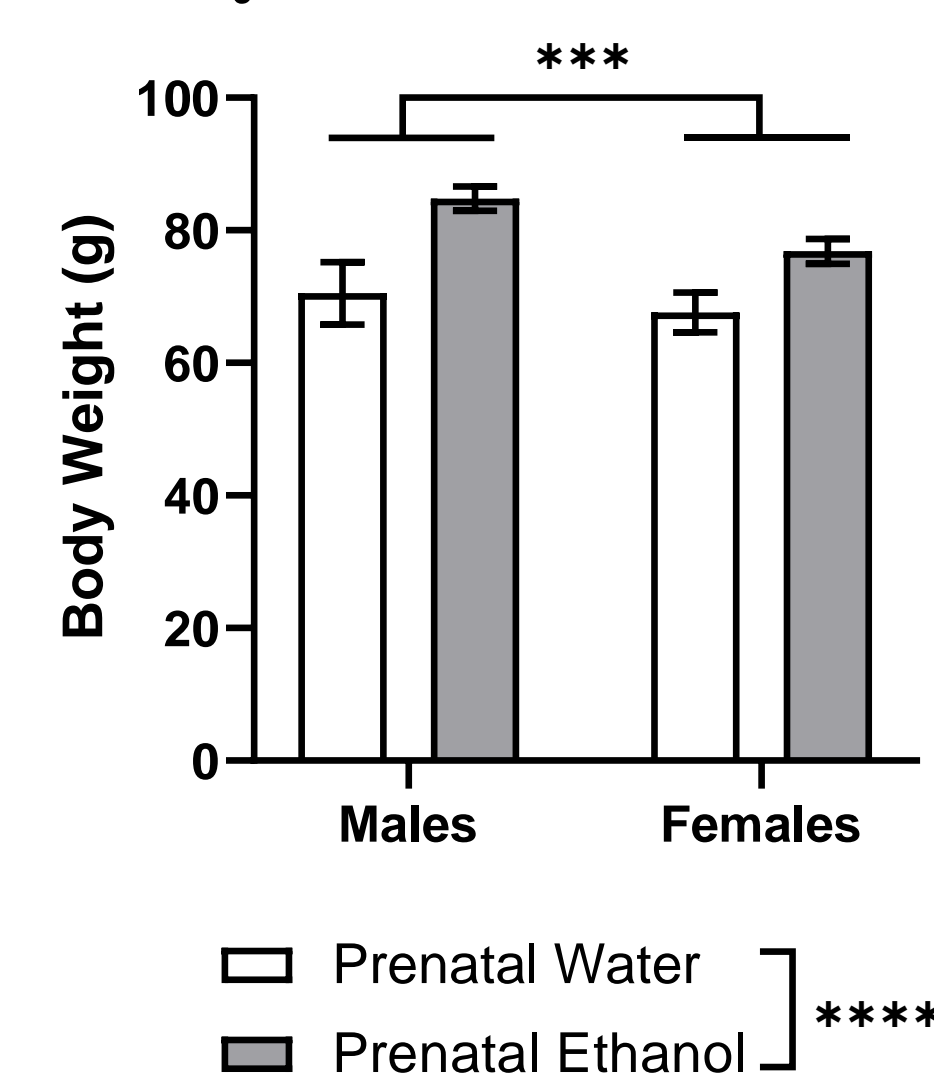


Statistical Analysis:

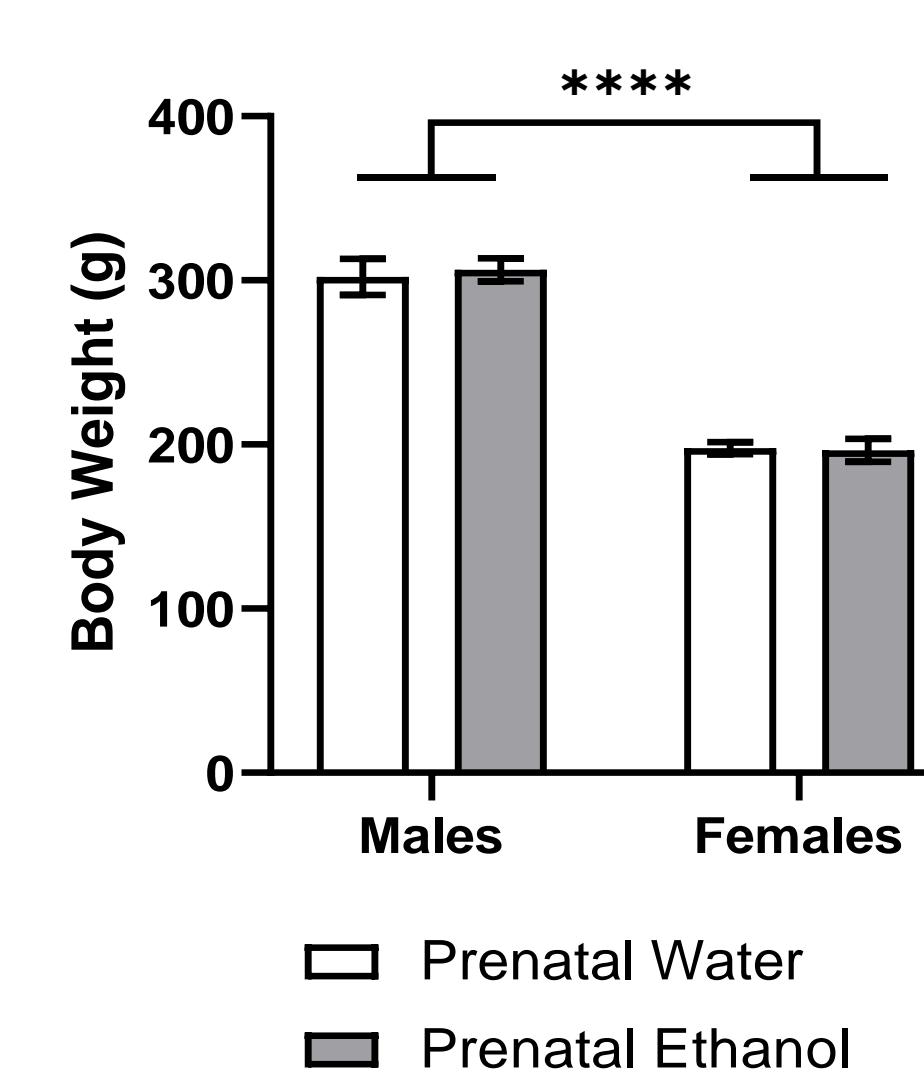
All statistical analyses in this experiment were completed using GraphPad Prism version 10. Data were analyzed using a repeated measure 2-way analysis of variance or a 3-way multivariate analysis of variance.

Prenatal exposure increases weight gain during early adolescence

Early Adolescence: PD 25

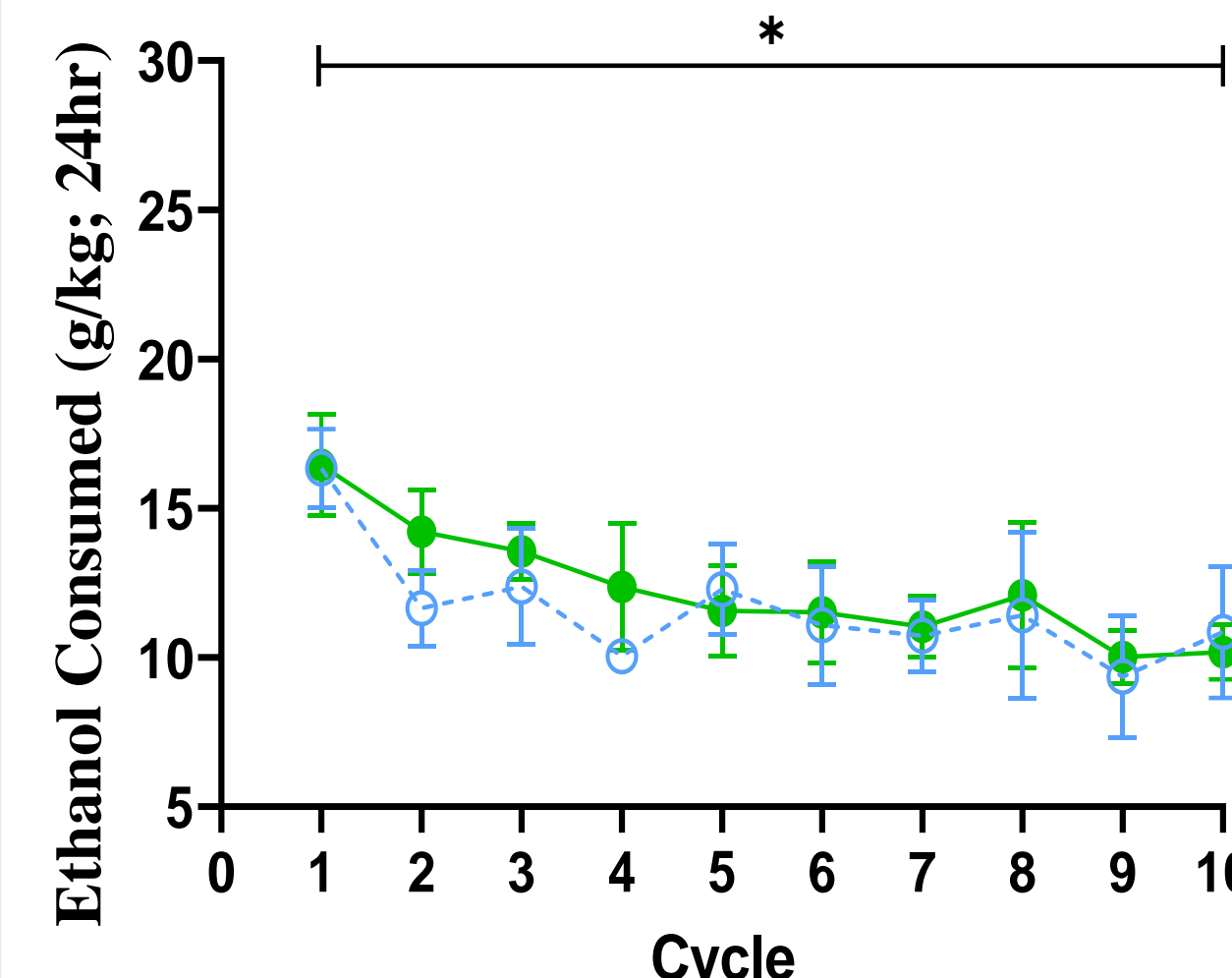


Late Adolescence: PD 61

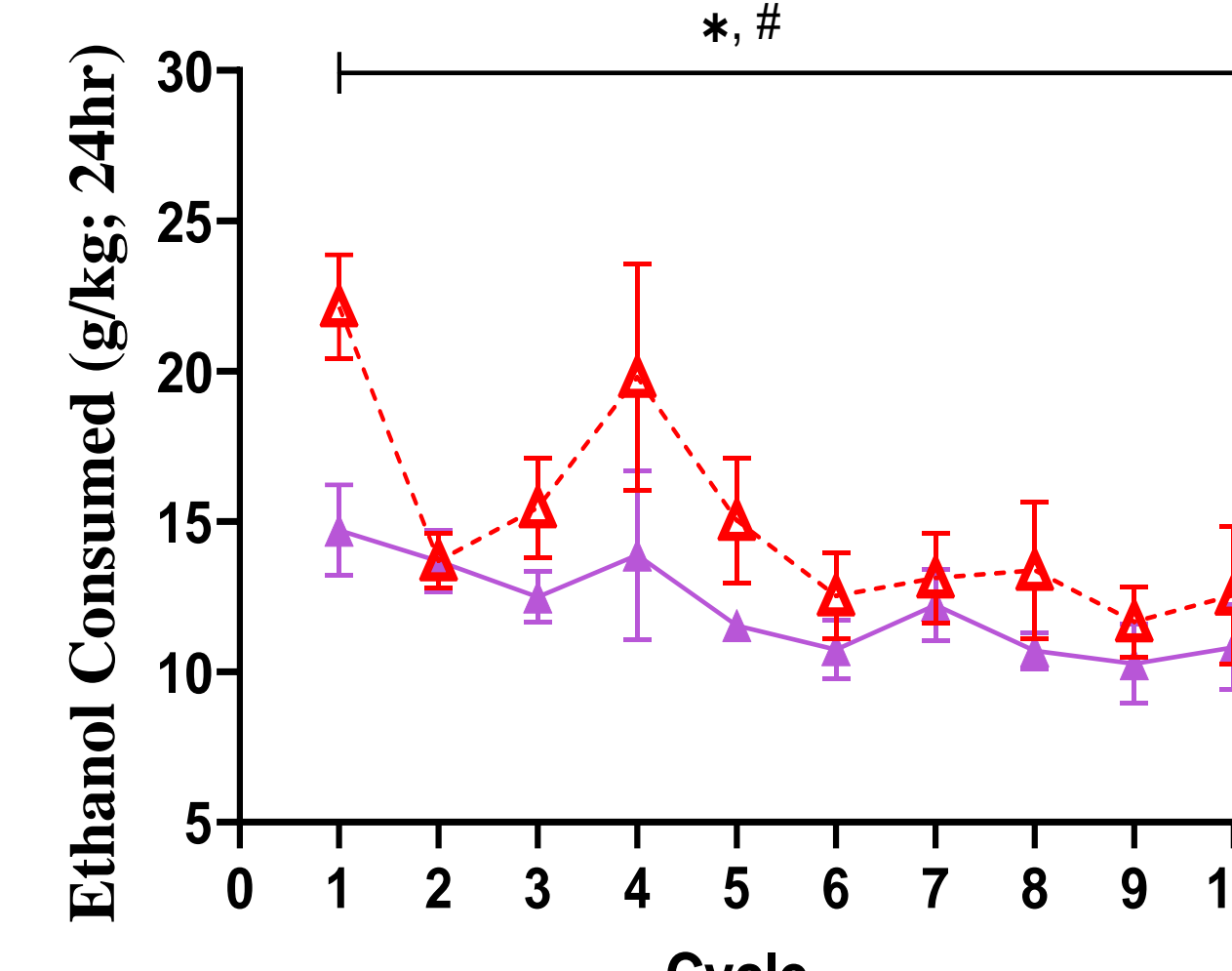


Prenatal exposure affects 24-hour ethanol consumption in a sex-dependent manner

Male

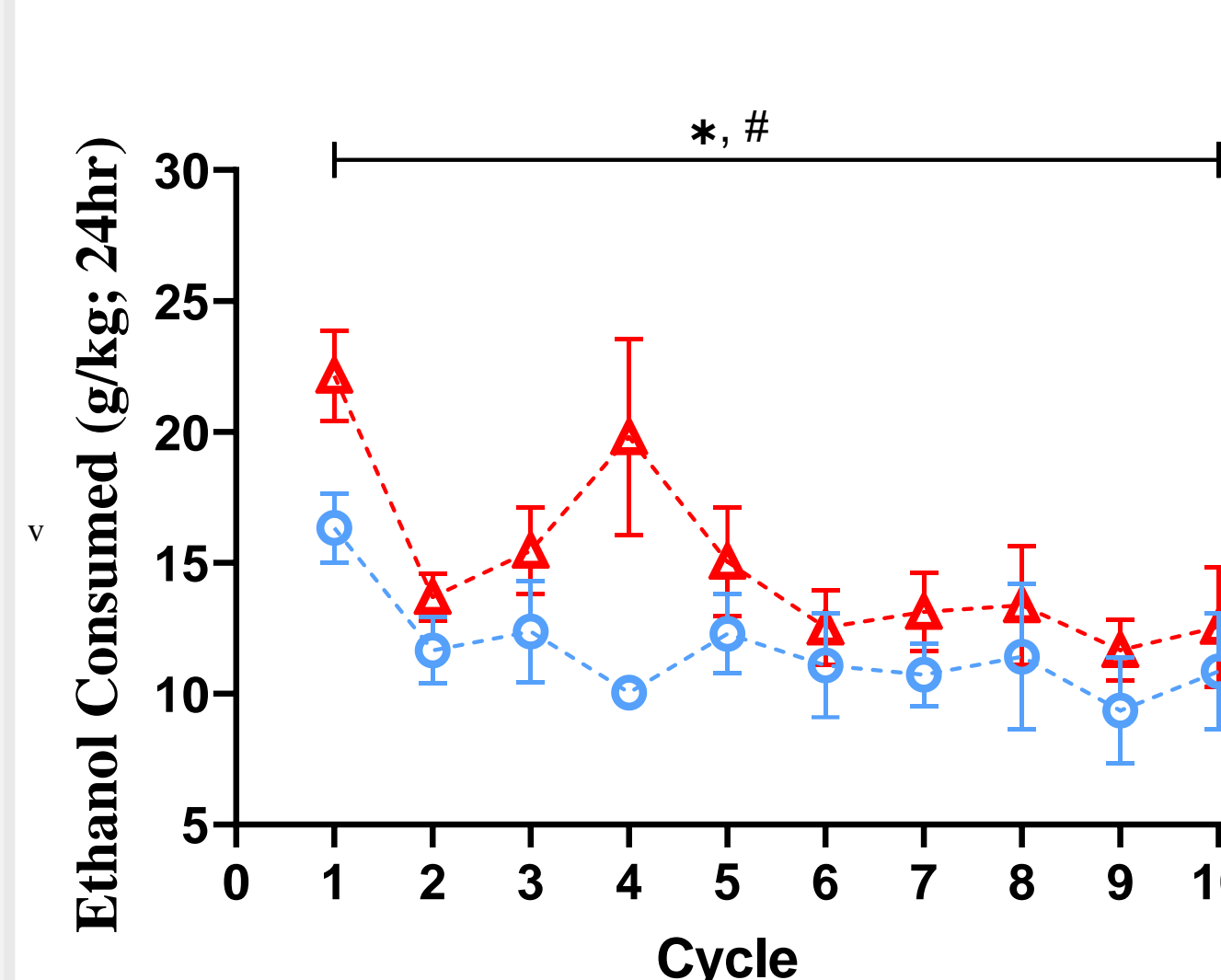


Female

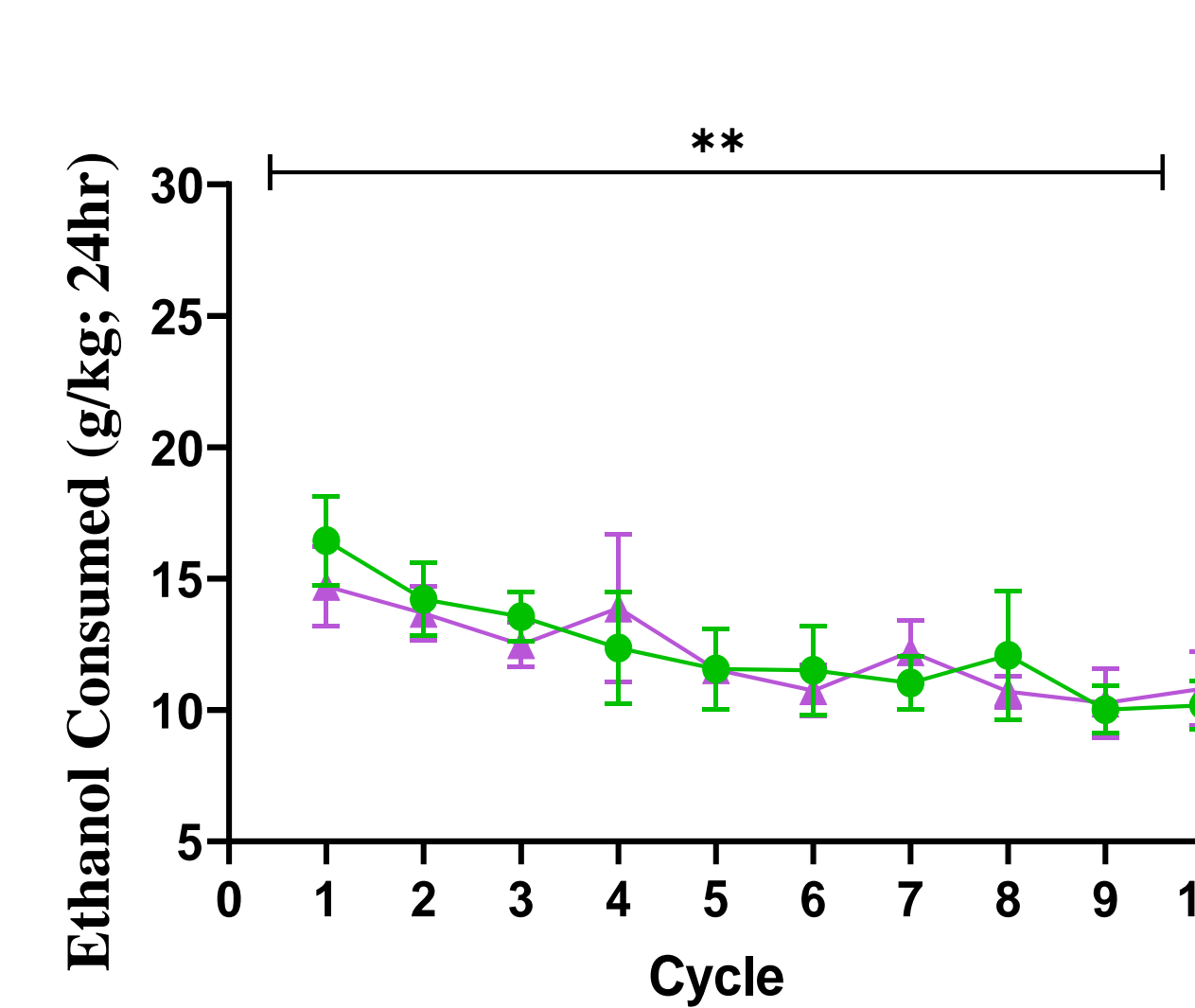


Interactions between PAE and sex on 24-hour ethanol consumption across 10 cycles

Prenatal Water



Prenatal Ethanol



Results

Age-Dependent Effects on Body Mass

- Early Adolescence (Cycle 1): PAE male and female rats had significantly higher average body masses compared to non-exposed sex and age matched counterparts
- Late Adolescence (Cycle 10): Significant differences in body mass diminished throughout adolescence, with no significant differences observed between same sex and age-matched groups by late adolescence.

Sex-Dependent Effects on Ethanol Consumption

- Non-PAE female rats consumed higher amounts of ethanol relative to body weight than PAE female rats ($F(1, 11) = 11.16, p = 0.0066$).
- There was a significant main effect of time on ethanol consumption in female rats ($F(9, 97) = 3.367, p < 0.0013$), with a spike in ethanol consumption observed during cycles 3-4, and a relative decrease in ethanol consumption compared to cycle 4 in cycle 5.
- PAE male rats and non-PAE male rats exhibited no significant differences in ethanol consumption. Consumption remained relatively constant across cycles.

Interactions between PAE and Sex on Ethanol Consumption

- There was a significant interaction effect. Female rats consumed more ethanol (relative to body weight) than male rats on average.
- Sex differences were particularly significant in the absence of PAE ($F(1, 194) = 9.63, P = 0.0027$). Non-PAE female rats drank significant more than non-PAE male rats, and PAE female rats.

Discussion

PAE and Body Mass

- This study suggests a temporal relationship between PAE and growth patterns, with PAE resulting in significantly increased body mass in early adolescence. Interestingly, body mass normalizes by late adolescence.

PAE and Ethanol Consumption

- Female rats consumed more ethanol per kilogram of body weight than male rats, aligning with previous literature suggesting increased female vulnerability to alcohol misuse
- PAE appears to reduce ethanol consumption in female rats only, while having no significant impact on ethanol consumption in male rats.
- PAE and non-PAE female rats exhibited time-dependent changes in ethanol consumption.

Future Directions

- This study highlights several areas that require further research to investigate and understand the mechanisms underlying these findings

Development:

- Temporal body mass differences potentially induced by PAE

Behavior:

- The observed sex differences in ethanol consumption.
- The time-dependent changes in drinking behavior in female rats.
- The specific impact, or lack thereof, of PAE on these behaviors.

Acknowledgements

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Citations

