

Voltammetric Analysis of Dorsal Striatal Dopamine Dynamics Following Chronic Ethanol Treatment in C57BL/6J Mice

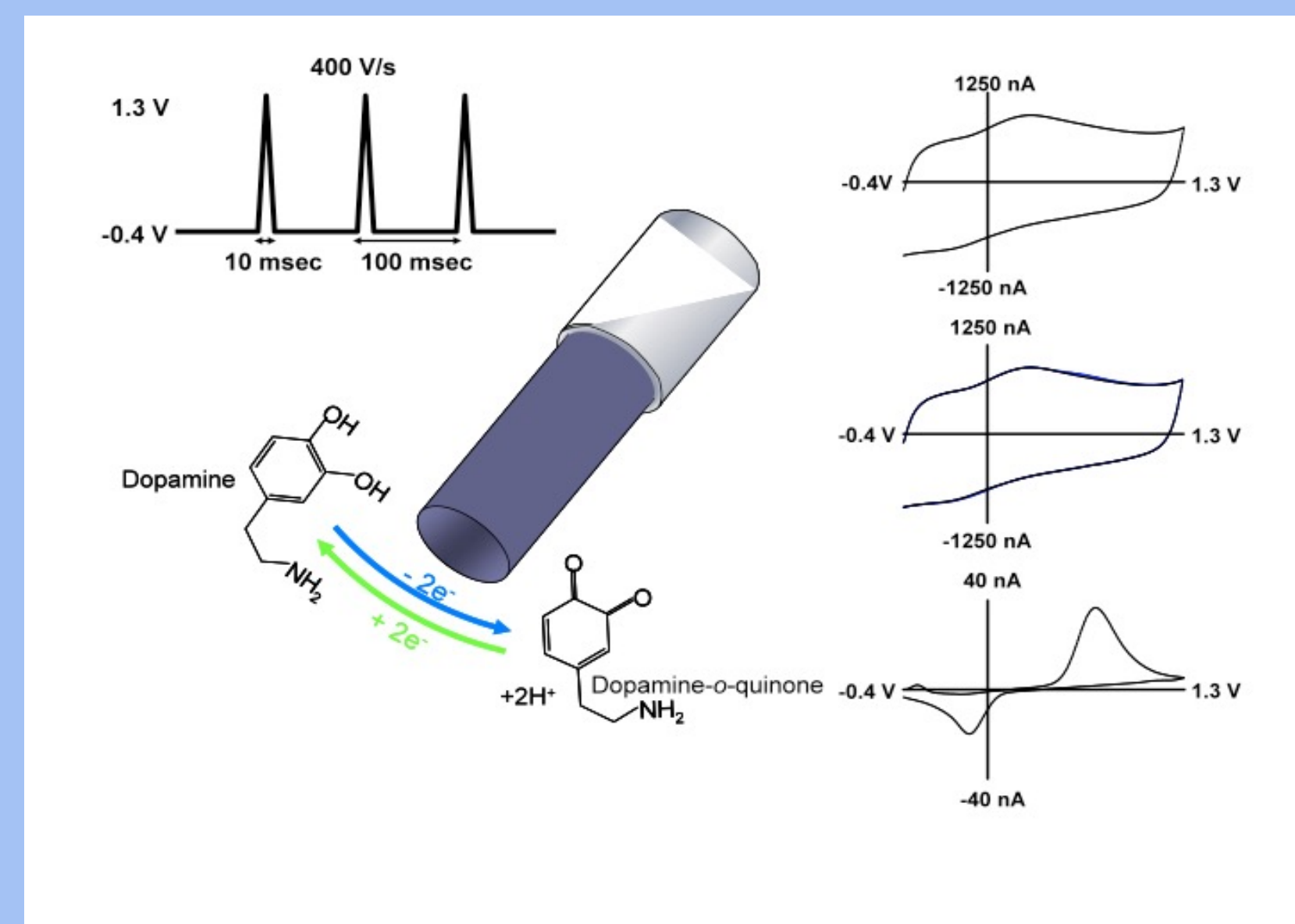
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Introduction

- Alcohol Use Disorder (AUD) is a chronic, progressive brain disease characterized by compulsive alcohol use, loss of control over alcohol intake, and a negative emotional state when not using. (NIAAA, 2020)
- AUD affects 29.5 million Americans aged 12+, causing 95,000 deaths and costing the nation \$249 billion in economic burden, annually. (NIAAA, 2024)
- Dorsolateral striatum (DLS), involved in habit and skill learning, receives inputs from sensorimotor and premotor cortices. (Janak, 2019)
- Dorsomedial striatum (DMS), involved in goal-direction action control, receives inputs from the prefrontal cortices. (Janak, 2019)
- Ethanol increases dendritic arborization and thus membrane capacitance in DLS neurons. (Holmes, 2013)
- Chronic ethanol treatment causes a greater reduction in dopamine release in DLS compared to the DMS.

Methods

Background-subtracted fast-scan cyclic voltammetry

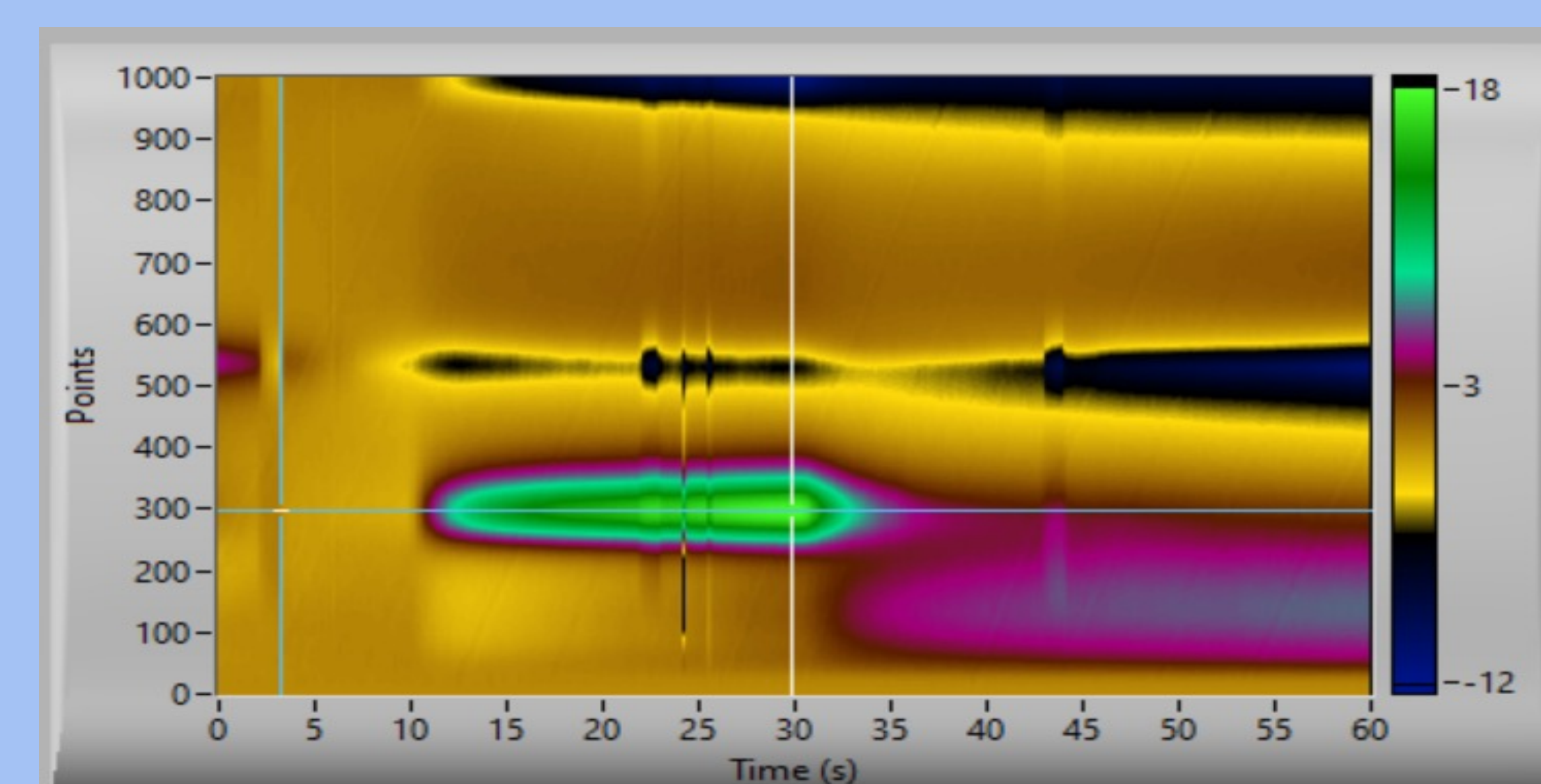
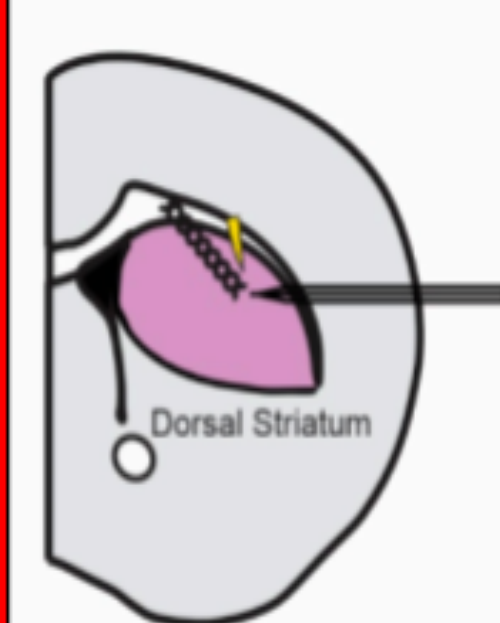


Chronic Ethanol Exposure Group
Daily intraperitoneal injection with 15% EtOH solution

Control Group
Daily intraperitoneal injection with saline

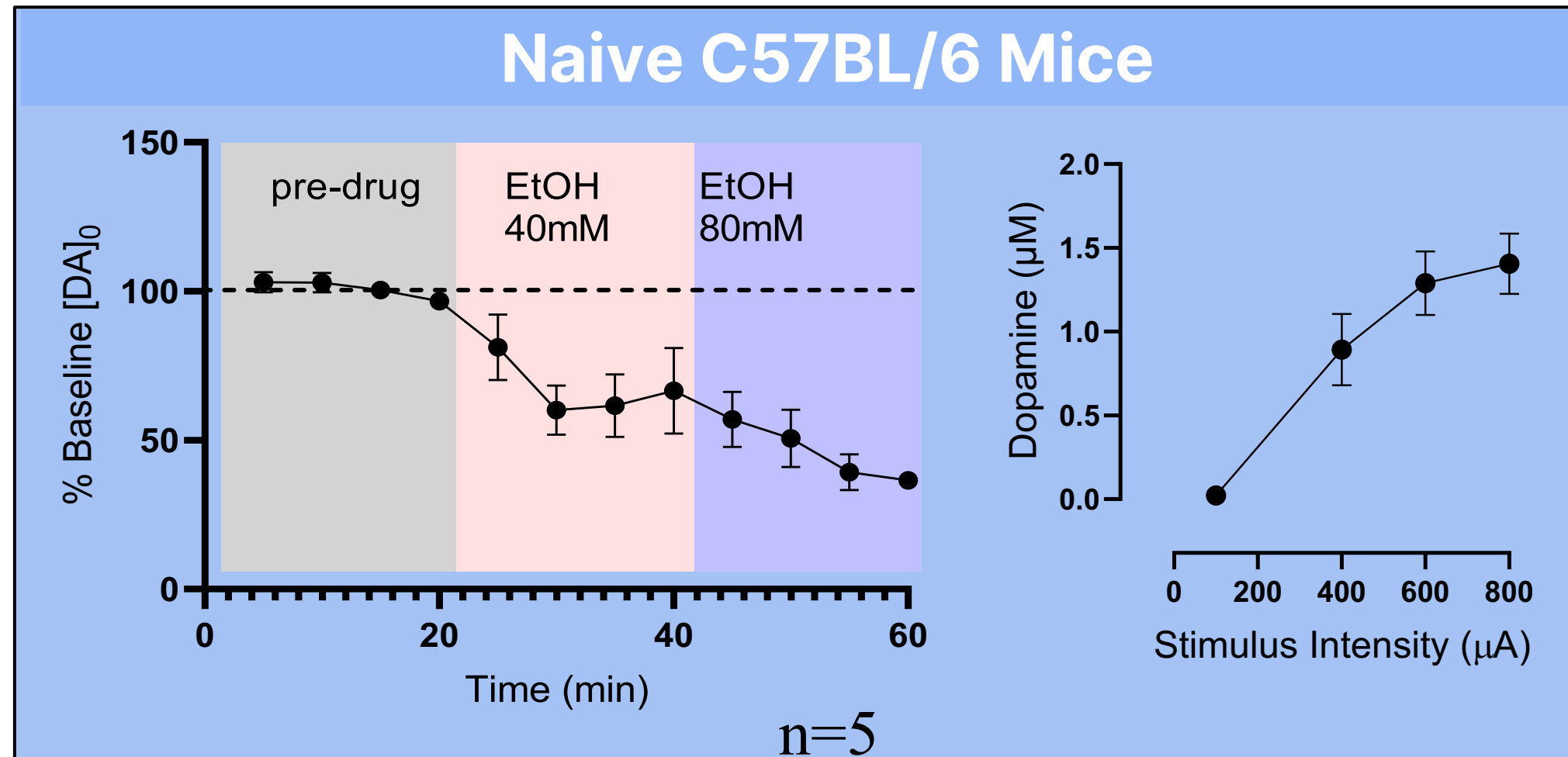
12 days

Sacrificed
24 hours
after last IP
injection



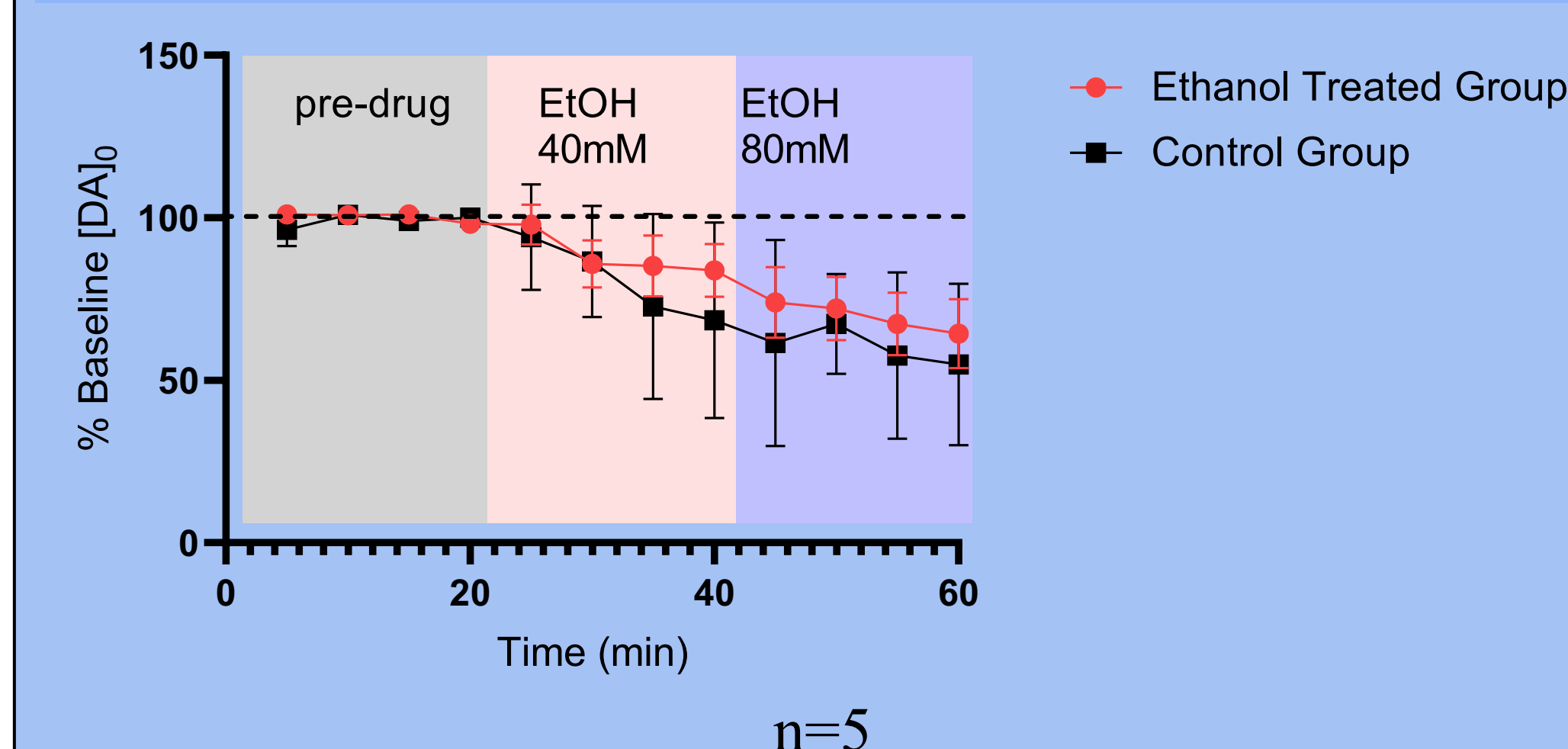
Results

Dorsolateral Striatum

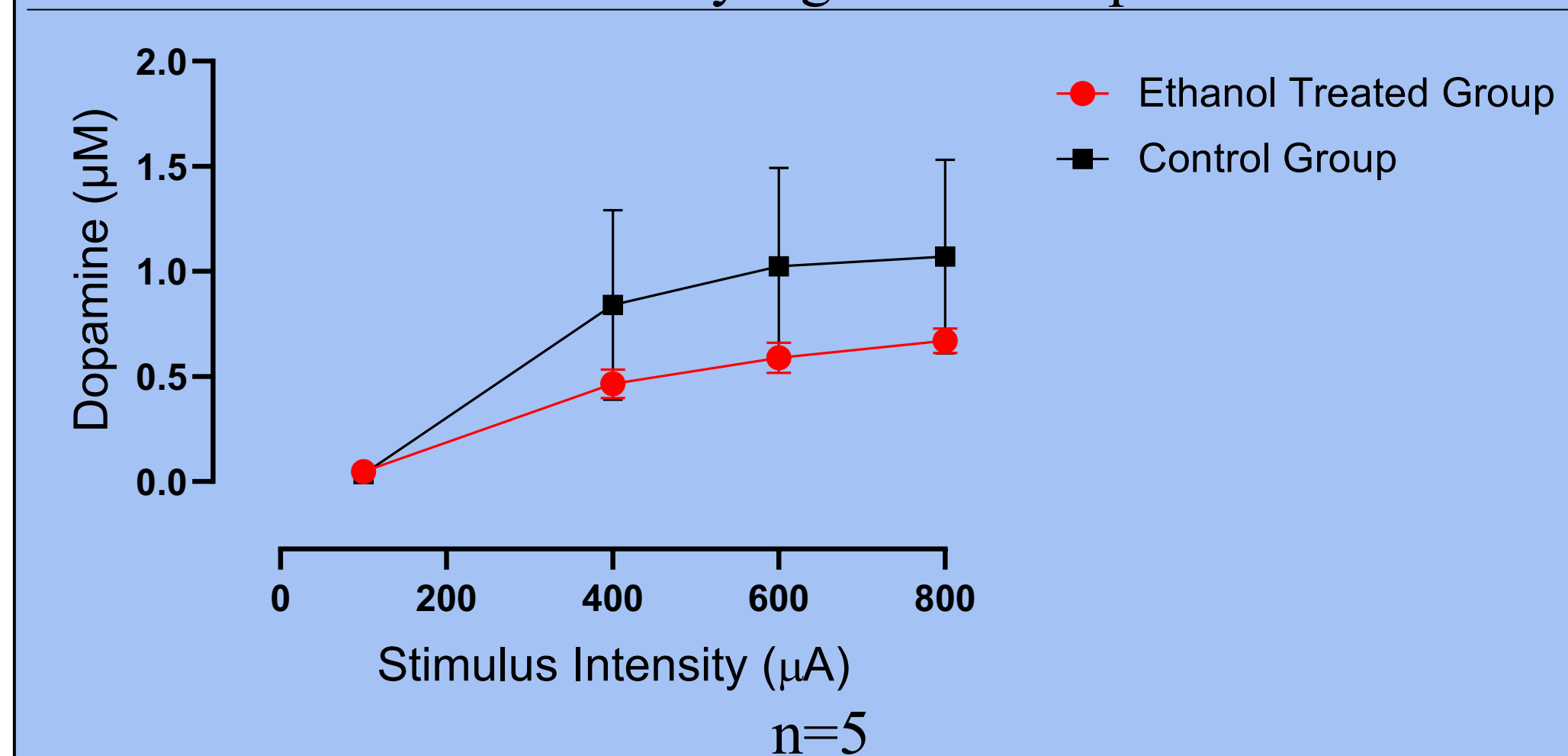


Higher ethanol concentration in DLS results in lower DA release. $p \leq 0.0001 < 0.05$ between pre-drug and EtOH 80mM readings.

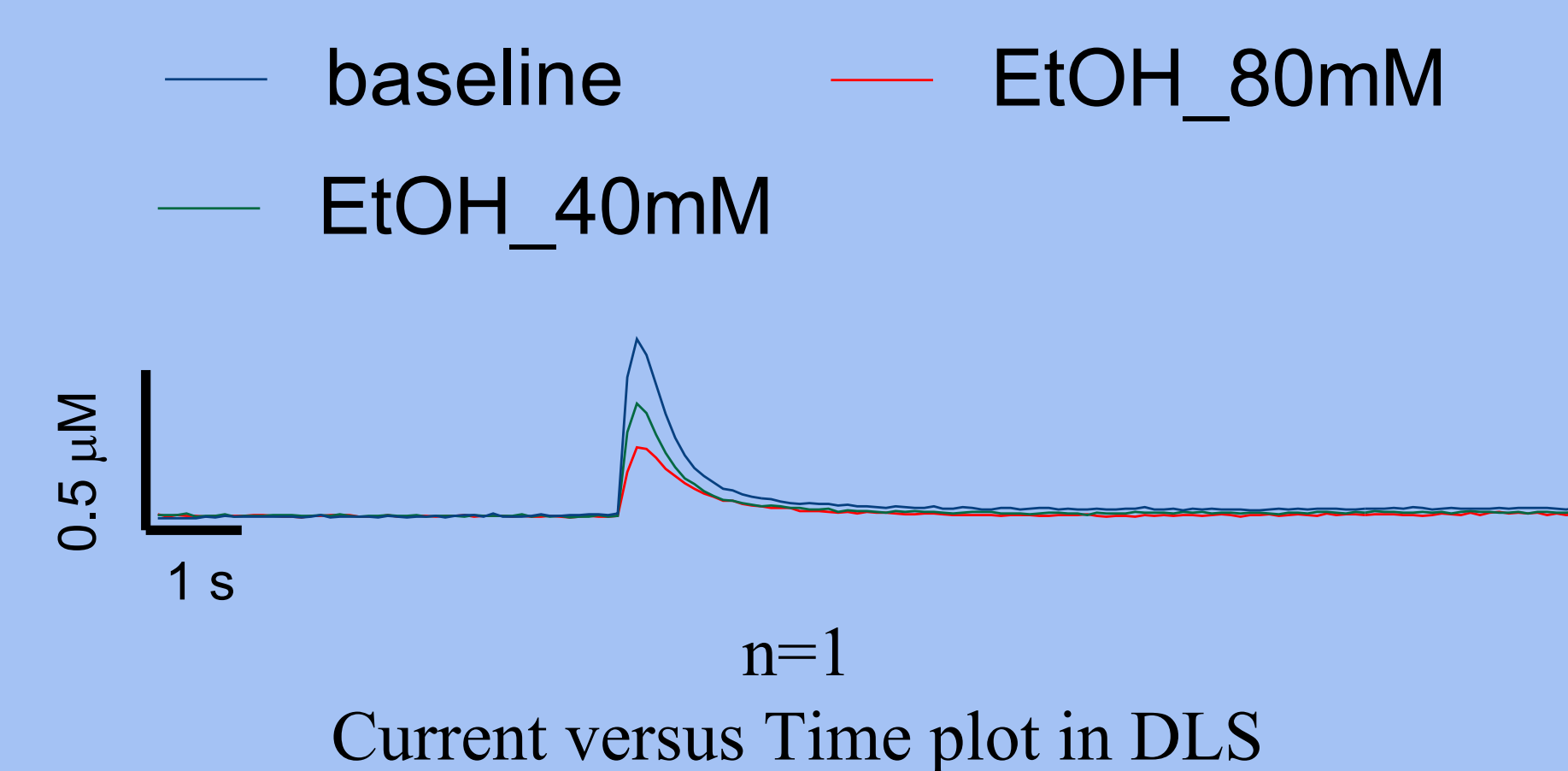
Ethanol Treated C57BL/6 Mice



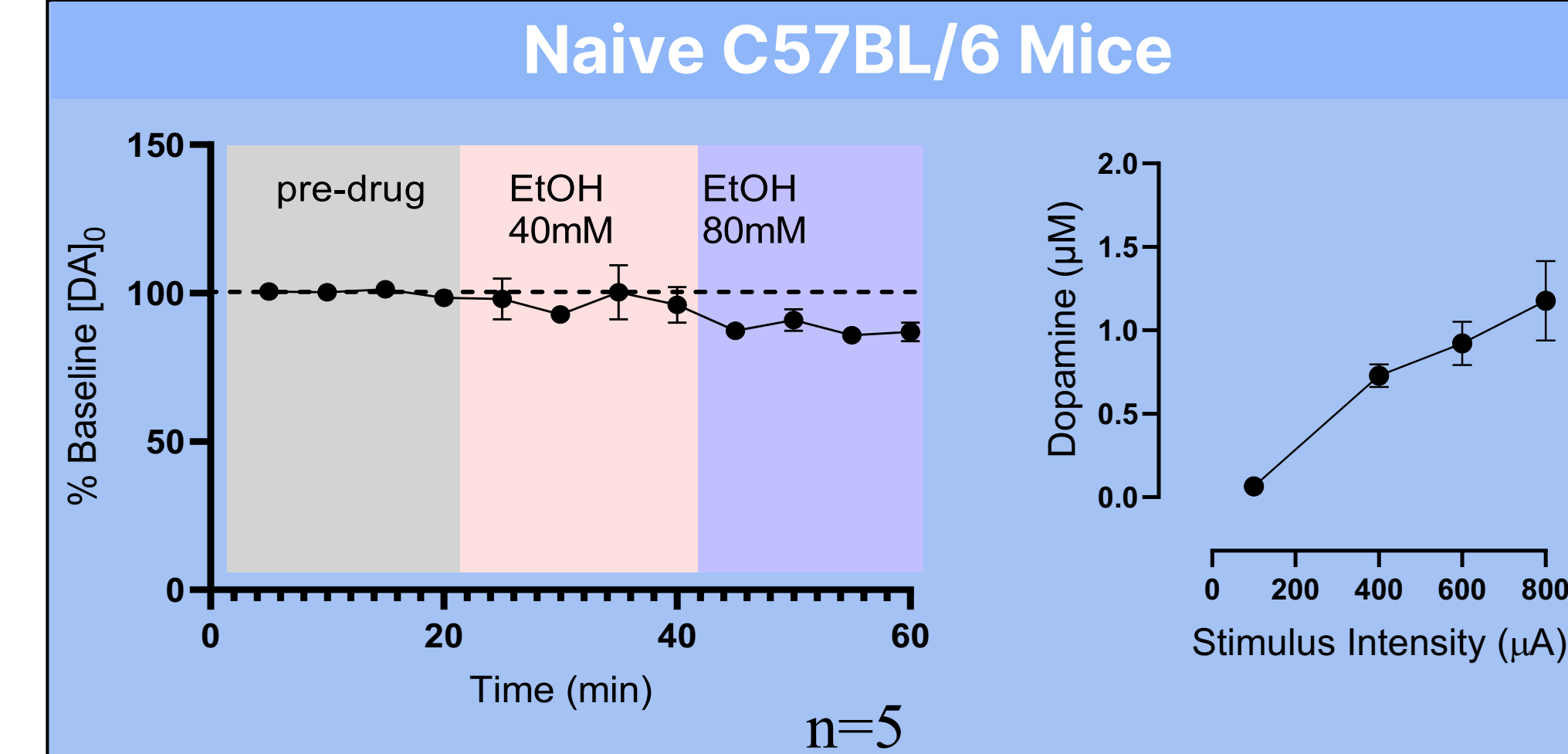
Two-way ANOVA was used to analyze differences in DA between the Ethanol Treated Group and the Control Group. Difference was statistically significant as $p = 0.0177 < 0.05$.



Two-way ANOVA was used to analyze differences in DA between the Ethanol Treated Group and the Control Group. Difference was statistically significant as $p = 0.0065 < 0.05$.

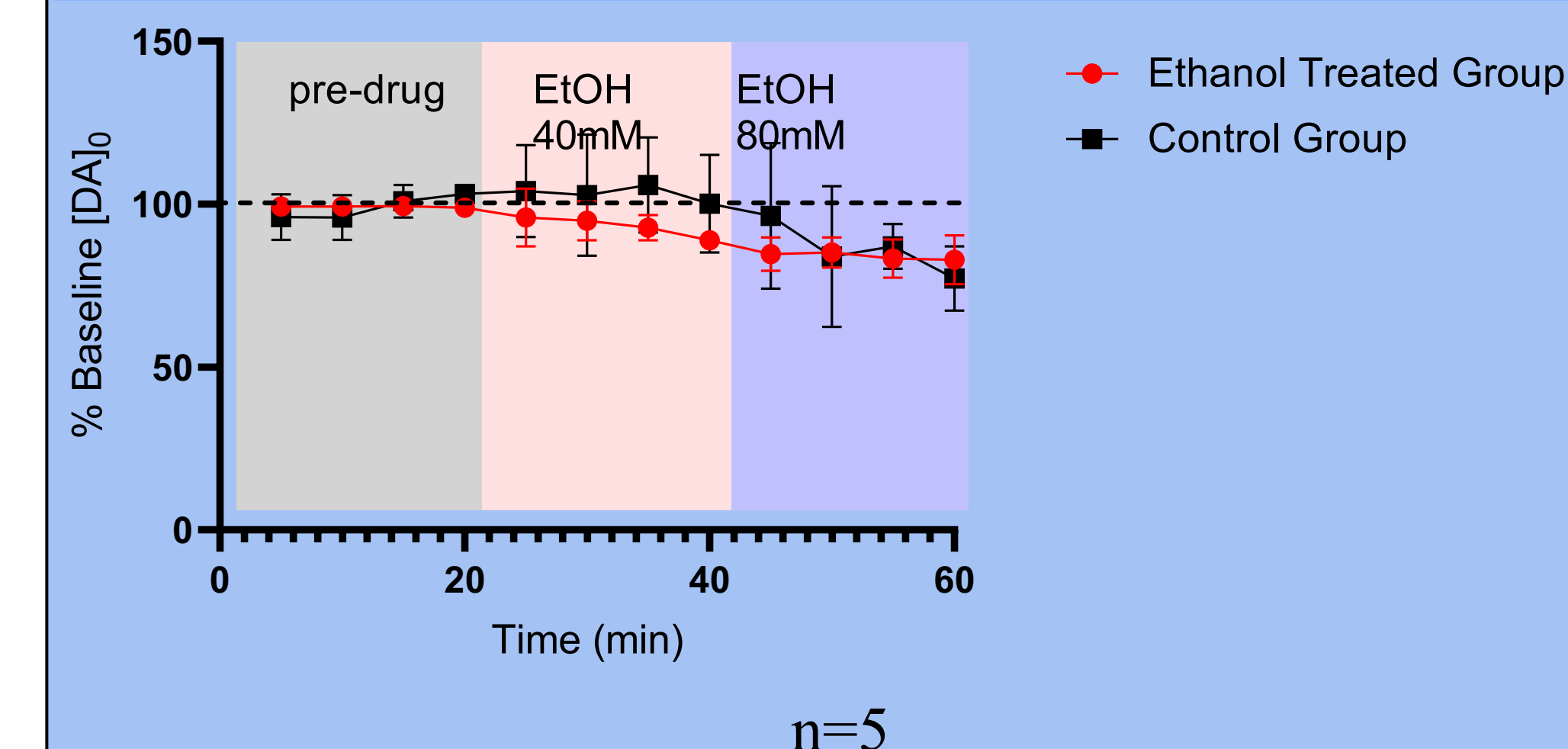


Dorsomedial Striatum

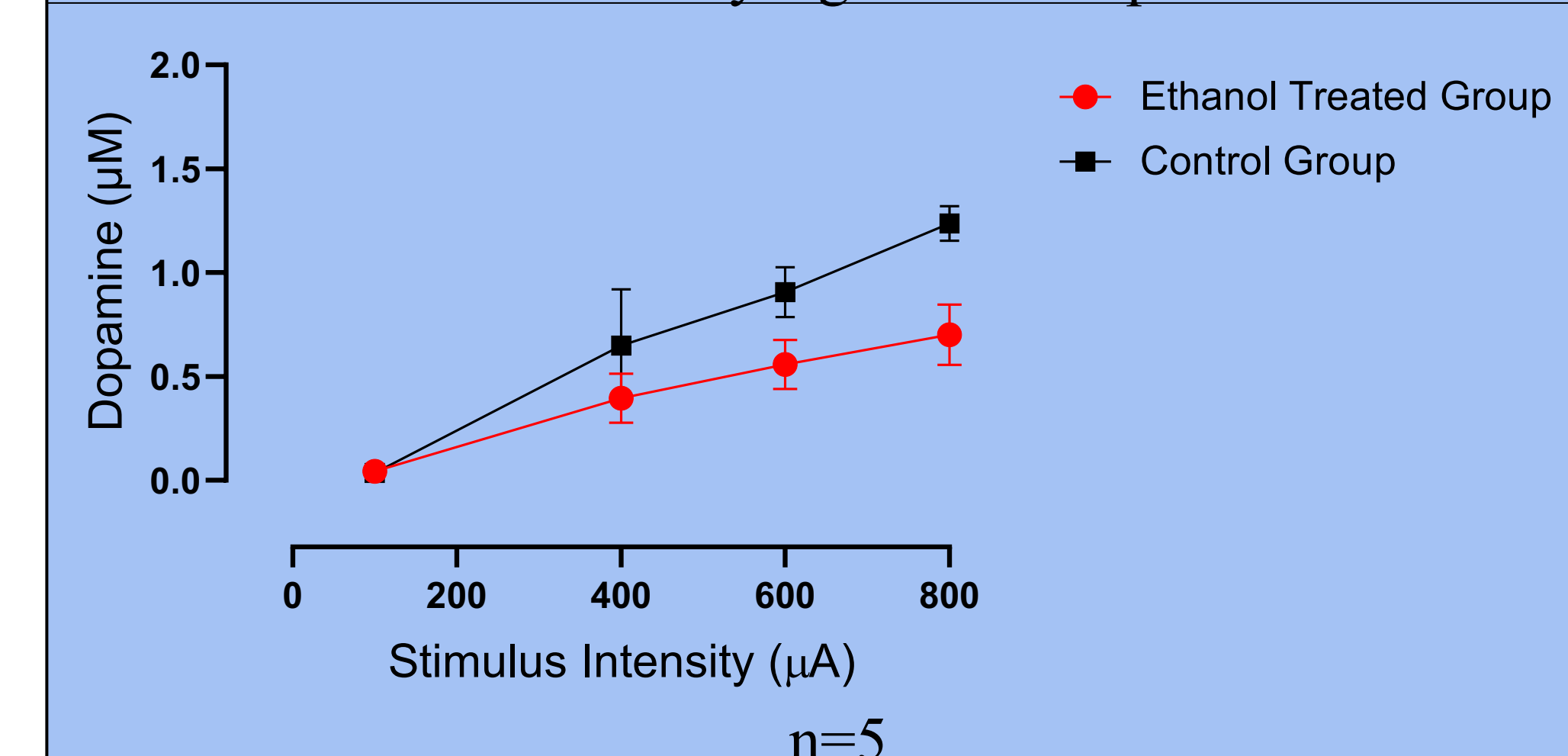


Higher ethanol concentration in DMS results in slightly lower DA release. $p \leq 0.0001 < 0.05$ between pre-drug and EtOH 80mM readings.

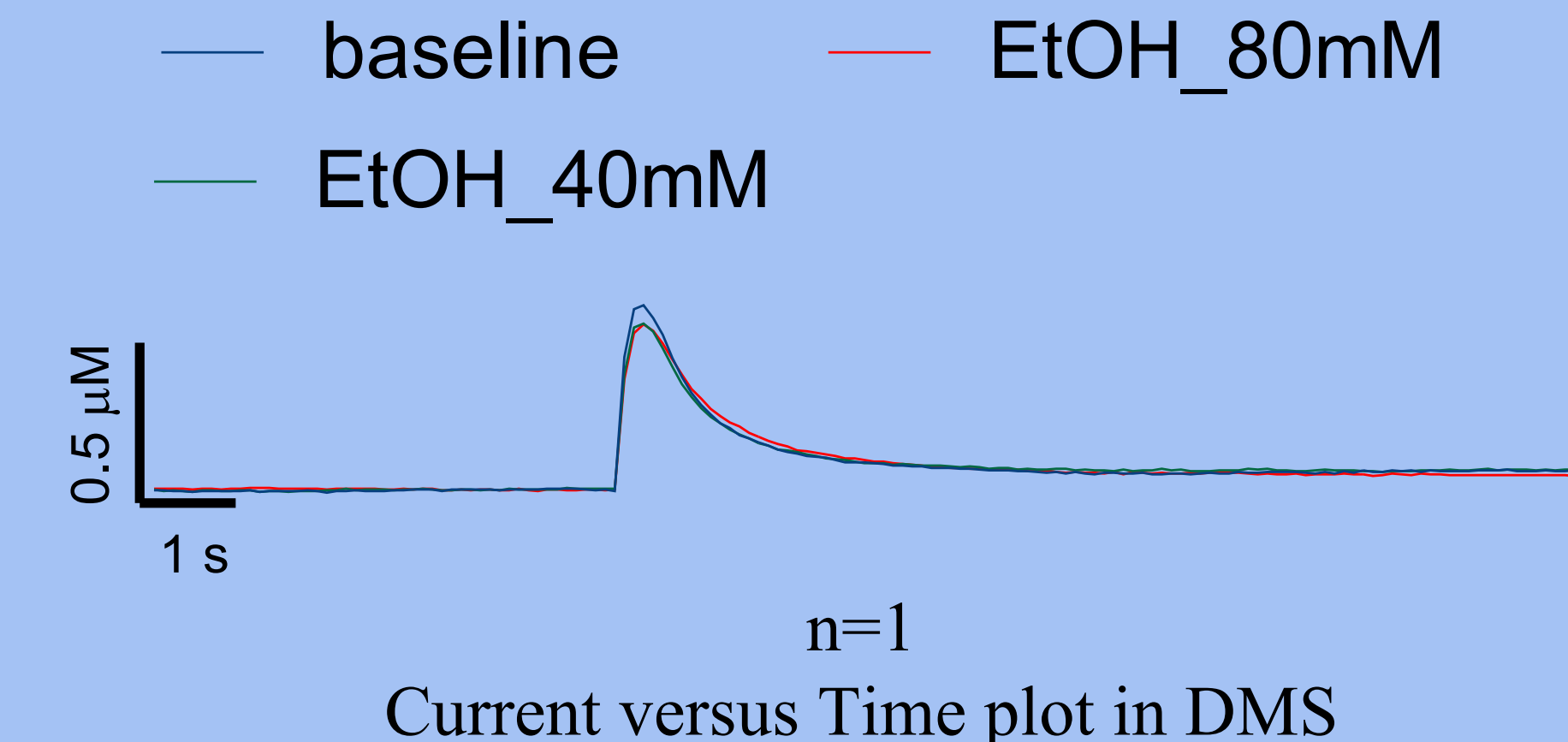
Ethanol Treated C57BL/6 Mice



Two-way ANOVA was used to analyze differences in DA between the Ethanol Treated Group and the Control Group. Difference was statistically significant as $p = 0.0053 < 0.05$.



Two-way ANOVA was used to analyze differences in DA between the Ethanol Treated Group and the Control Group. Difference was statistically significant as $p = 0.0084 < 0.05$.



Conclusions

- DLS experienced a more pronounced decrease in DA levels compared to DMS following increased ethanol treatment.
- Chronic ethanol exposure leads to a sustained reduction in dopaminergic signaling.
- Stimulus-response curves showed DMS retains a higher capacity for dopamine release in response to stimuli, when slice is treated with ethanol, whereas DLS shows a blunted response.
- Decrease in DA levels and altered stimulus-response characteristics in the DLS may contribute to the shift from goal-directed behaviors to habitual actions.
- DMS seems to retain a greater capacity for DA release, which may help preserve some goal-directed control.

Future Research

- Additional experiments in stimulus-response curves between a chronically ethanol treated group, acute ethanol treated group, and a control group in DLS and DMS.
- Measure changes in dendritic arborization and membrane capacitance between DLS and DMS neurons across genders following ethanol treatment.
- For measuring dendritic arborization, this may be possible through Confocal Microscopy, 3D Reconstruction, and Expansion Microscopy.
- For measuring membrane capacitance, this may be possible through Whole-Cell Patch-Clamp Electrophysiology and Current-Clamp and Voltage-Clamp Protocols can be used.

Acknowledgements

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