Downregulation of Clock Genes in the Accumbal Shell Reduces Binge Drinking in Mice.

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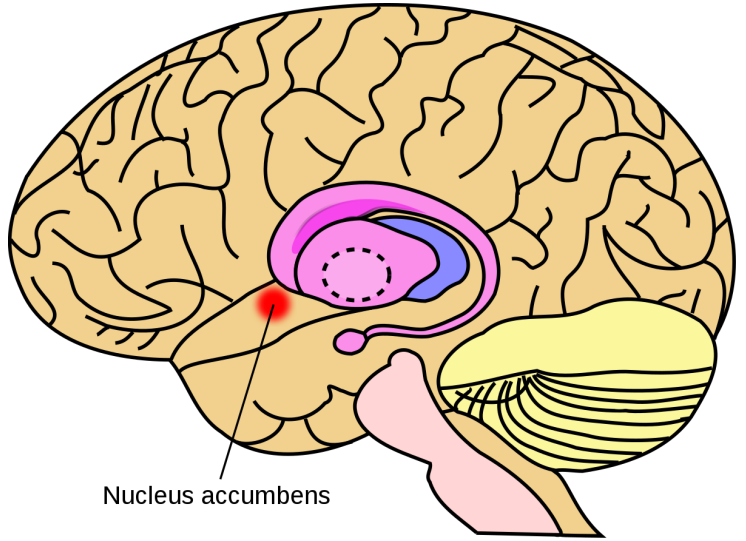
University of Missouri

Faculty Mentor: Dr. Mahesh Thakkar

INTRODUCTION



HYPOTHESIS

- We hypothesized that circadian genes in the NAcSh regulates chronic excessive alcohol consumption in mice.

METHODS

Experiment 1

- **Animals**: C57BL/6J mice;
- **Surgeries**: None;
- **Alcohol/Sucrose consumption**: Using Drinking in Dark (DID) paradigm, animals were exposed to alcohol (20%) /sucrose (10%) for 2 hours on Days 1-3 and for 4 hours on Day 4.
- **Circadian Gene expression**: After 4 hours of alcohol/sucrose consumption, animals were euthanized and their brain isolated, NAcSh and SCN dissected out and processed for RT-PCR.

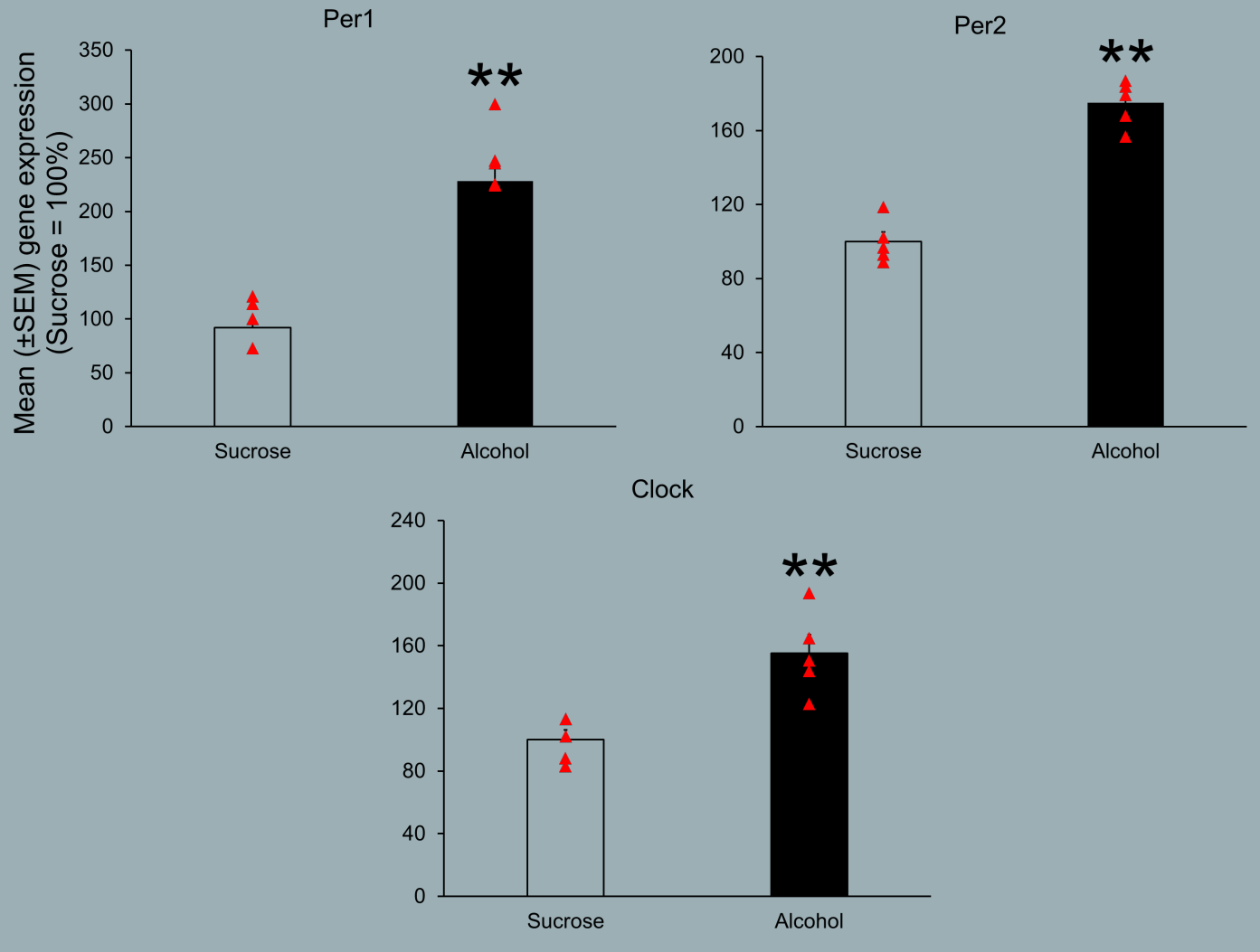
METHODS

Experiment 2

- **Animals**: C57BL/6J mice;
- **Surgeries**: Implantation of bilateral guide cannula above the NAcSh;
- **Alcohol/Sucrose/water consumption**: As in Experiment 1; On Day 4, one hour prior to the onset of alcohol/sucrose/water exposure, mice were bilaterally infused with either a mixture of Clock, Per1, and Per2 antisense oligodeoxynucleotides (AS-ODNs; Antisense group) or nonsense/random ODNs (R-ODNs; Control group) into the NAcSh. Blood alcohol concentration was measured to confirm binge drinking.

DATA

Alcohol consumption increases expression in circadian genes

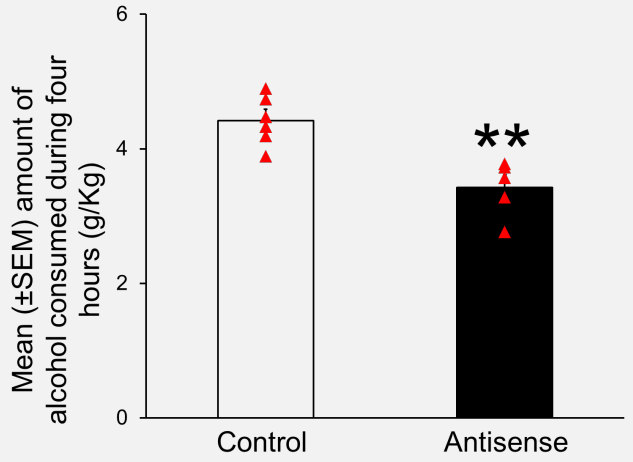


DATA

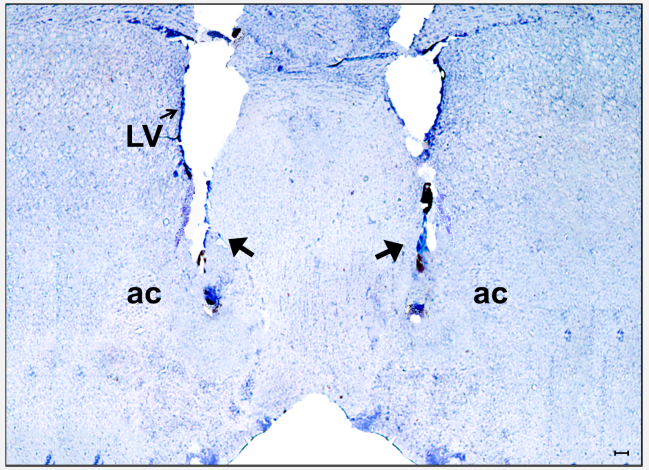
Antisense induced downregulation

(A) Mice in the Antisense group showed significant reduction in alcohol consumption
(B)Photomicrograph depicting bilateral injection sites in the NAcSh

A



B



FINDINGS

Conclusion:

- **Clock genes in the NAcSh play a crucial role in binge drinking and antisense downre**

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