

# The behavioral and molecular impact of binge-drinking alcohol

Eliyana Van Doren

Psychological and Brain Sciences, B.S.

Mentor: Leo Jimenez Chavez

PI: Dr. Karen Szumlinski

Psychology and Brain Sciences

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# What is binge-drinking and why is it a problem?

## WHAT IS BINGE DRINKING?

A pattern of drinking that brings blood alcohol concentration levels to 0.08 grams per deciliter.

**FOR WOMEN:**  four drinks  
in two hours

**FOR MEN:**  five drinks  
in two hours

- Among adolescents, alcohol is the most commonly abused drug in the US
- Females are more sensitive to the adverse effects of binge-drinking than males
- Withdrawal from binge-drinking in adults leads to increased anxiety

# Strong association between binge-drinking and anxiety

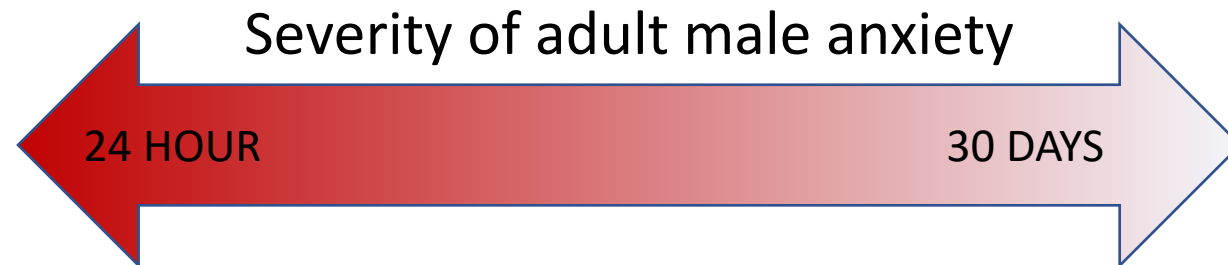
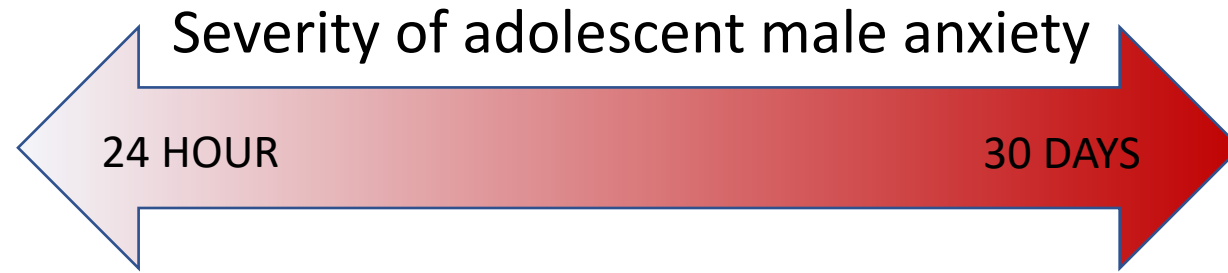


LONG TERM GOAL: understand biological mechanisms responsible for the different response to alcohol to develop targeted pharmacotherapies

SHORT TERM GOAL: examine sex x age differences in the expression of two proteins that are known to mediate addictive behaviors



# Extending male model of alcohol withdrawal induced-anxiety to include females

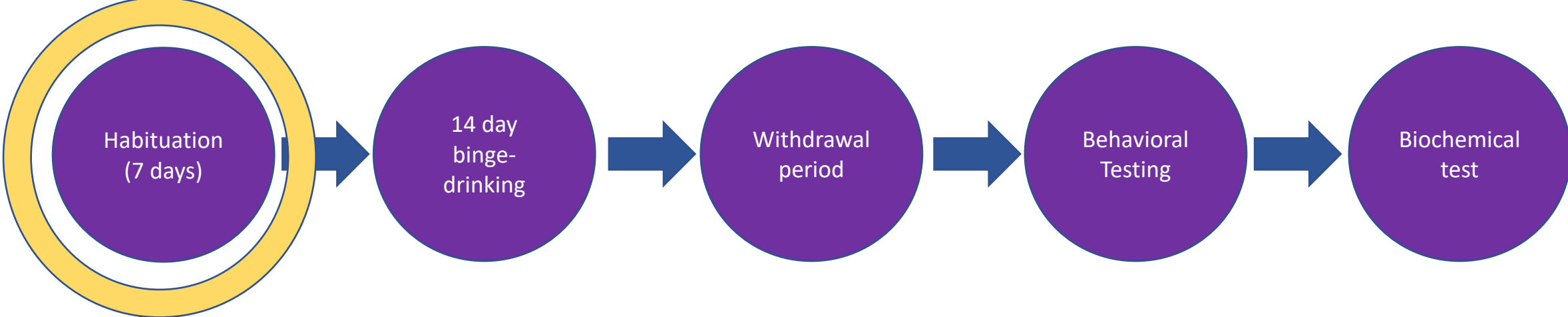


WATER-DRINKERS (n=160)

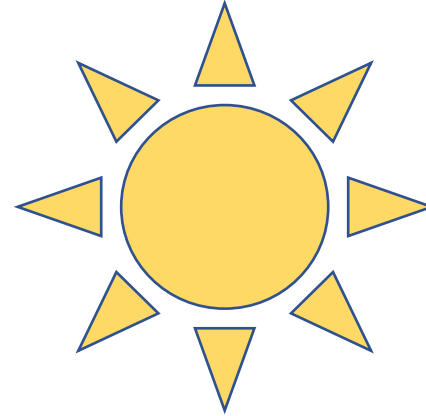
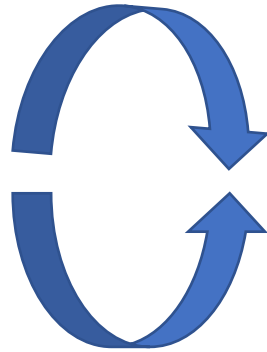


ALCOHOL-DRINKERS (n=187)

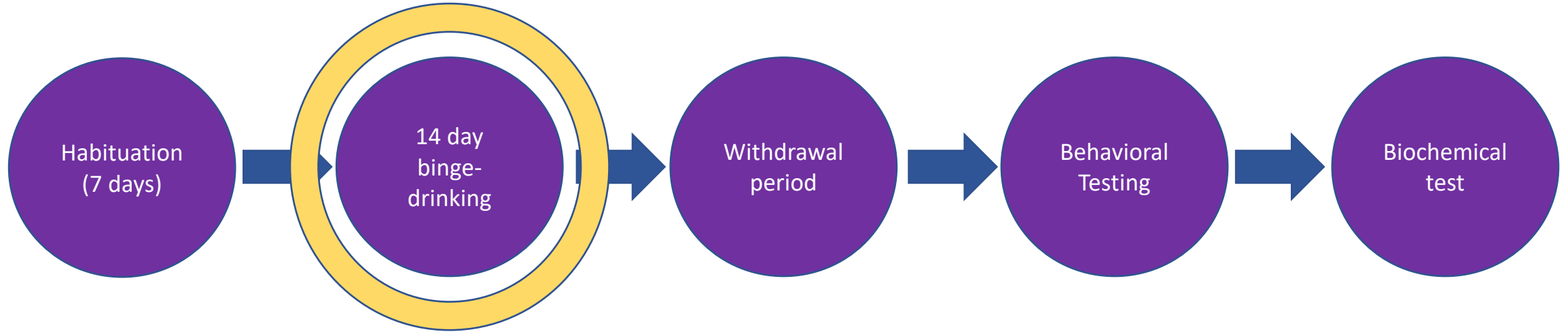




# Mice adjust to a new dark/light cycle 7 days prior to drinking



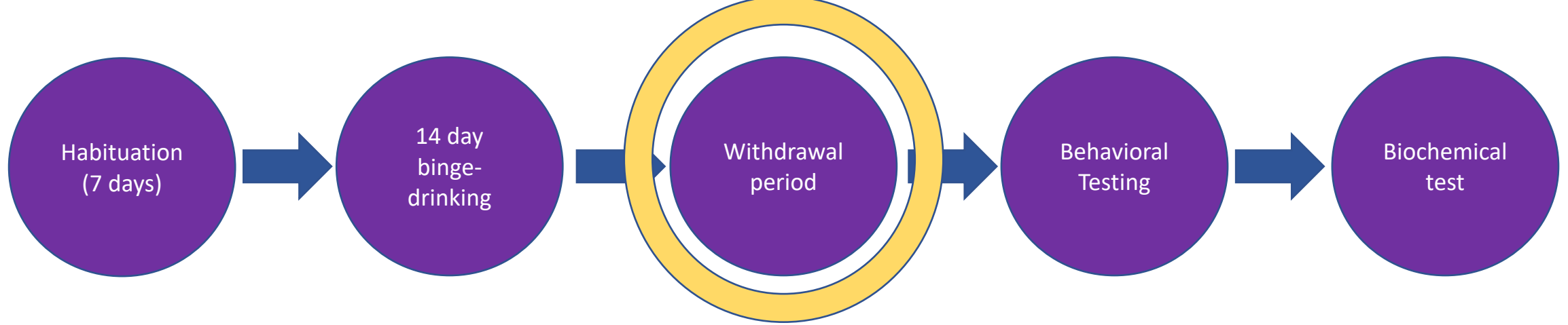
- Mice are normally nocturnal (sleep during the day)
- This makes researching them hard!
- We adjust them to a reverse light cycle



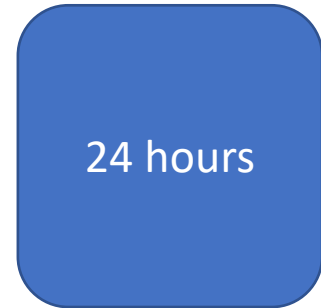


Mice are subject to 2-hour binge-drinking procedures for 14 days



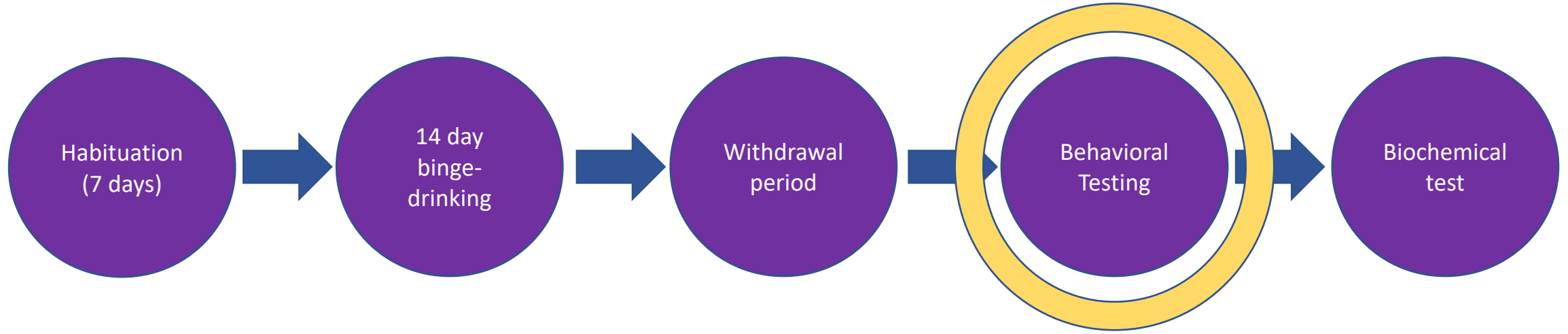


EARLY WITHDRAWAL

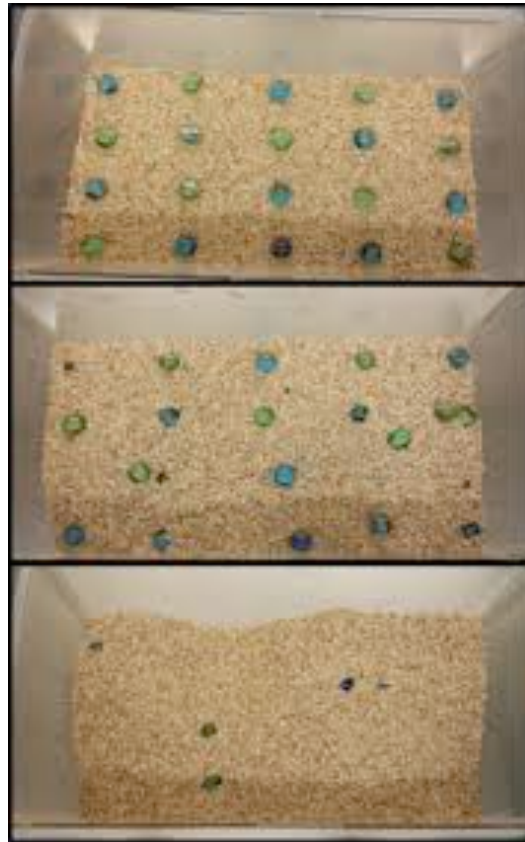


PROTRACTED WITHDRAWAL





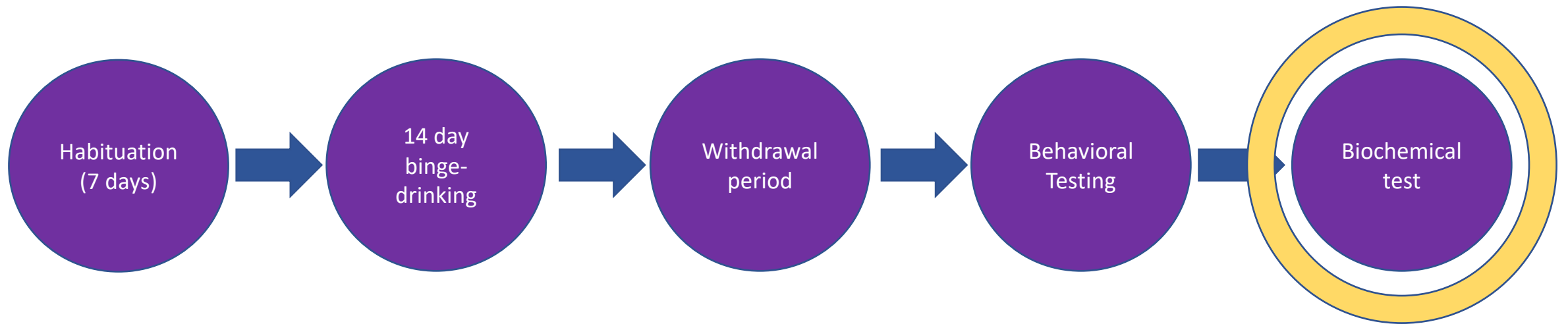
# After pre-determined withdrawal, mice run through behavioral tests



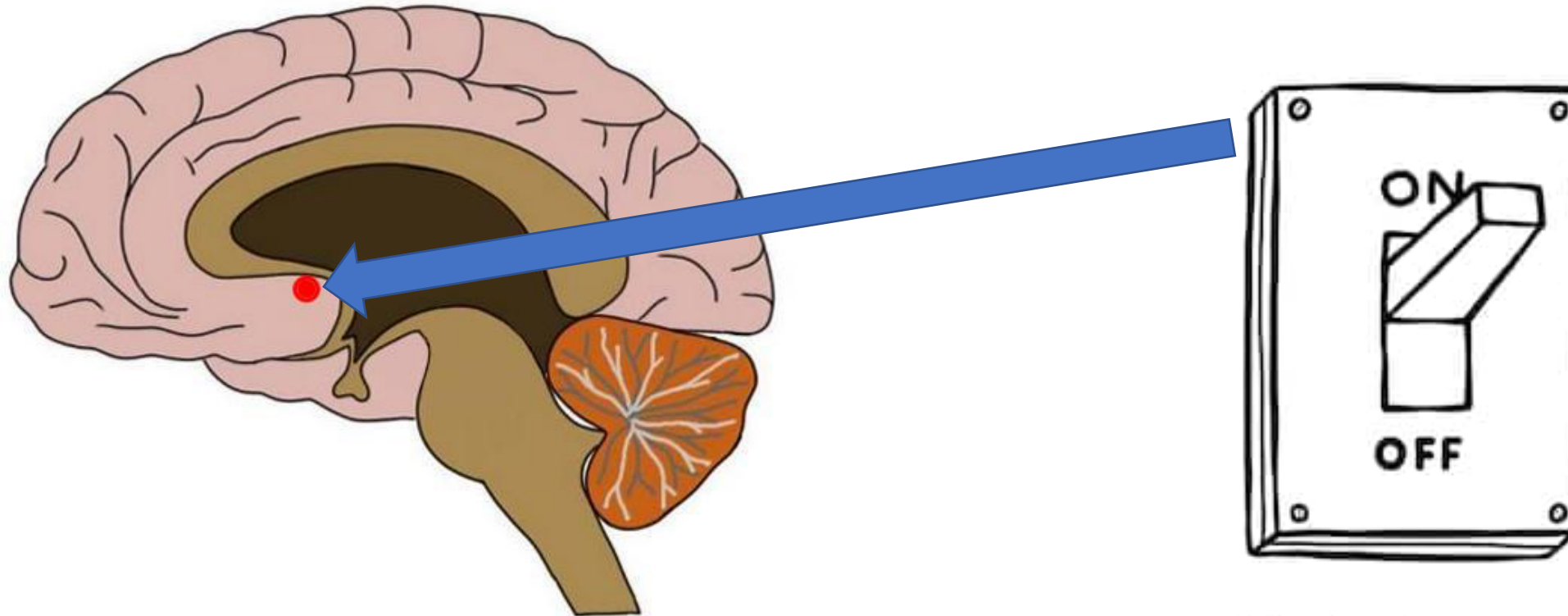
Marble-burying (15 mins)



Forced swim-test (6 mins)



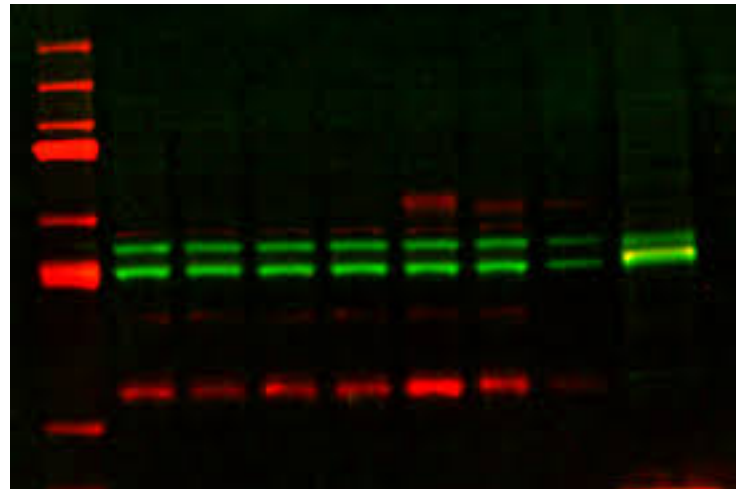
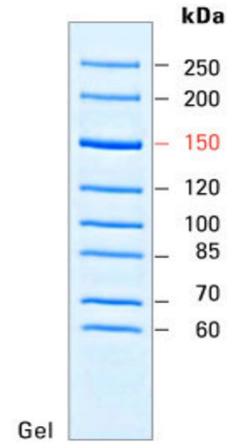
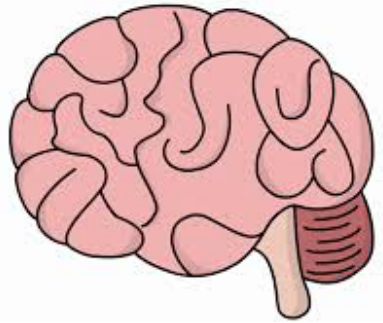
The Nucleus Accumbens (NA) is the brain's switch for addiction



High expression of homer 2 proteins in NA facilitate binge-drinking behaviors



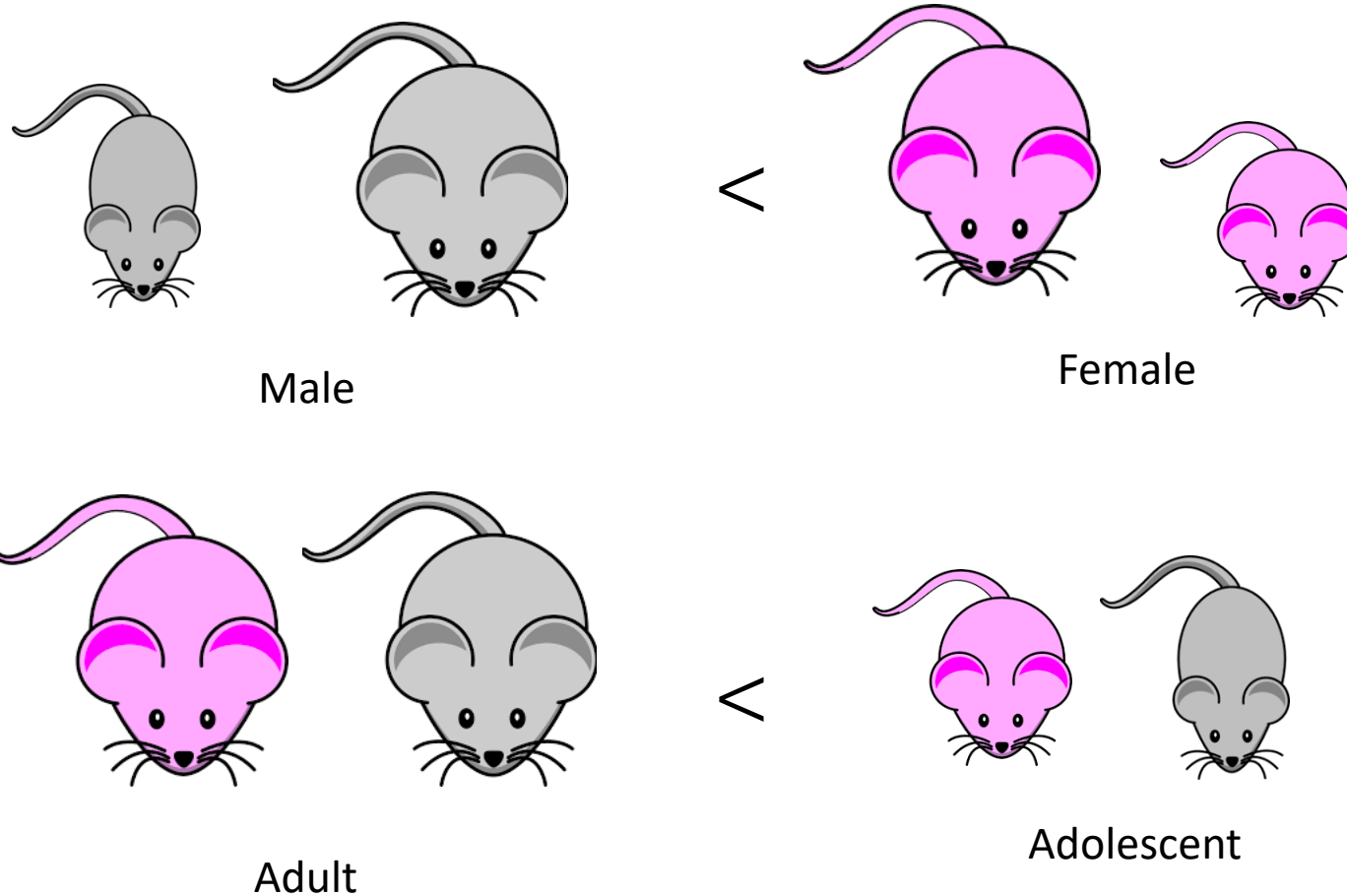
# Using western blots to image homer proteins





# Binge-drinking model mirrors human data

ALCOHOL INTAKE



Irrespective of sex, adolescent binge-drinkers displayed an increase in anxiety-like behavior in late withdrawal

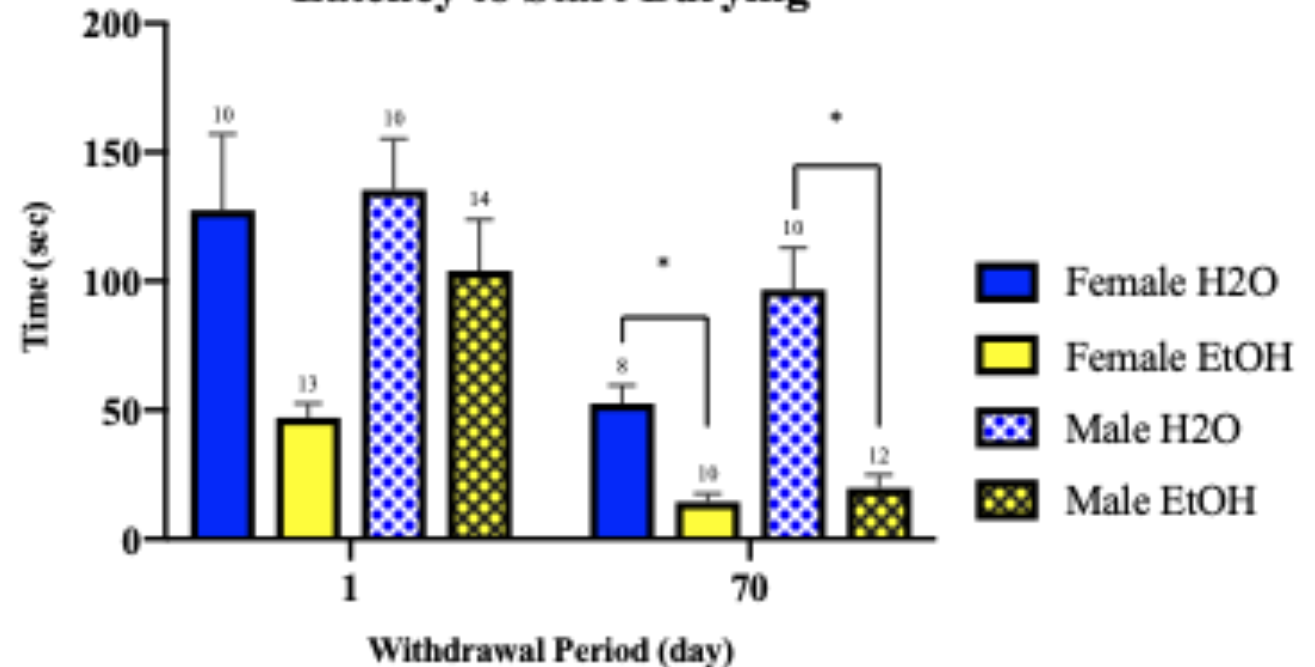
Typical behavior



Anxiety-like behavior



**Adolescent  
Latency to Start Burying**



# Binge-drinking adolescent males exhibit anxiety-like behavior in early withdrawal?



**Forced Swim Test**

- This result contradicts previous findings that adolescents are resilient to the effects of alcohol in early withdrawal
- Opposite-sex interaction is a novel variable in this experiment
- Exposure to female pheromones may have an effect on sex-naïve males

# Adult anxiety persists and incubates in late withdrawal

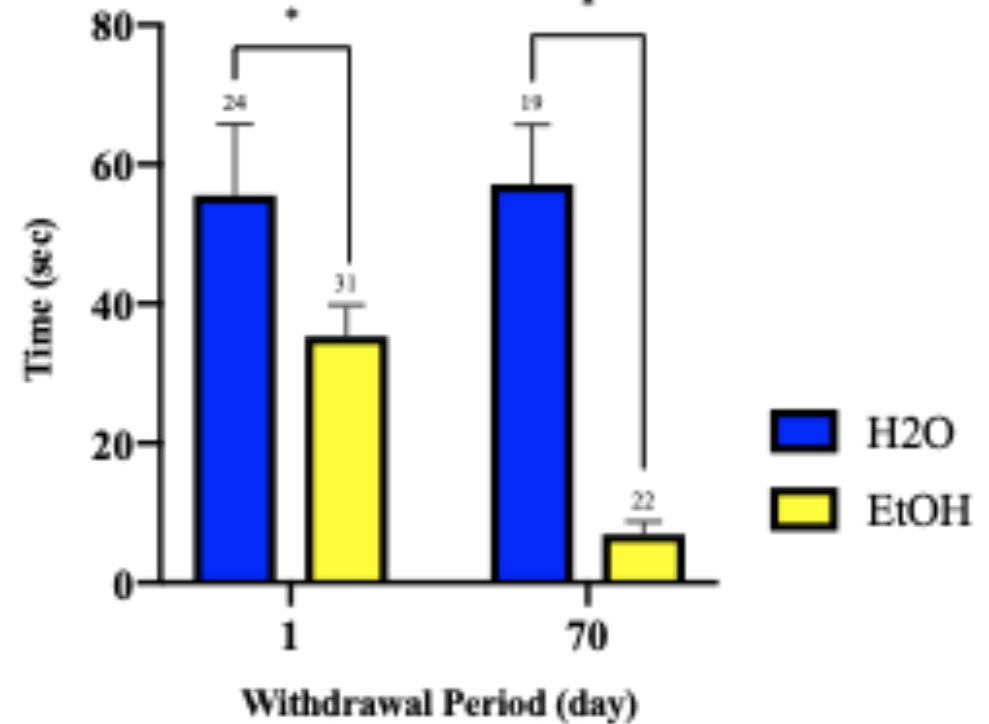
Typical behavior



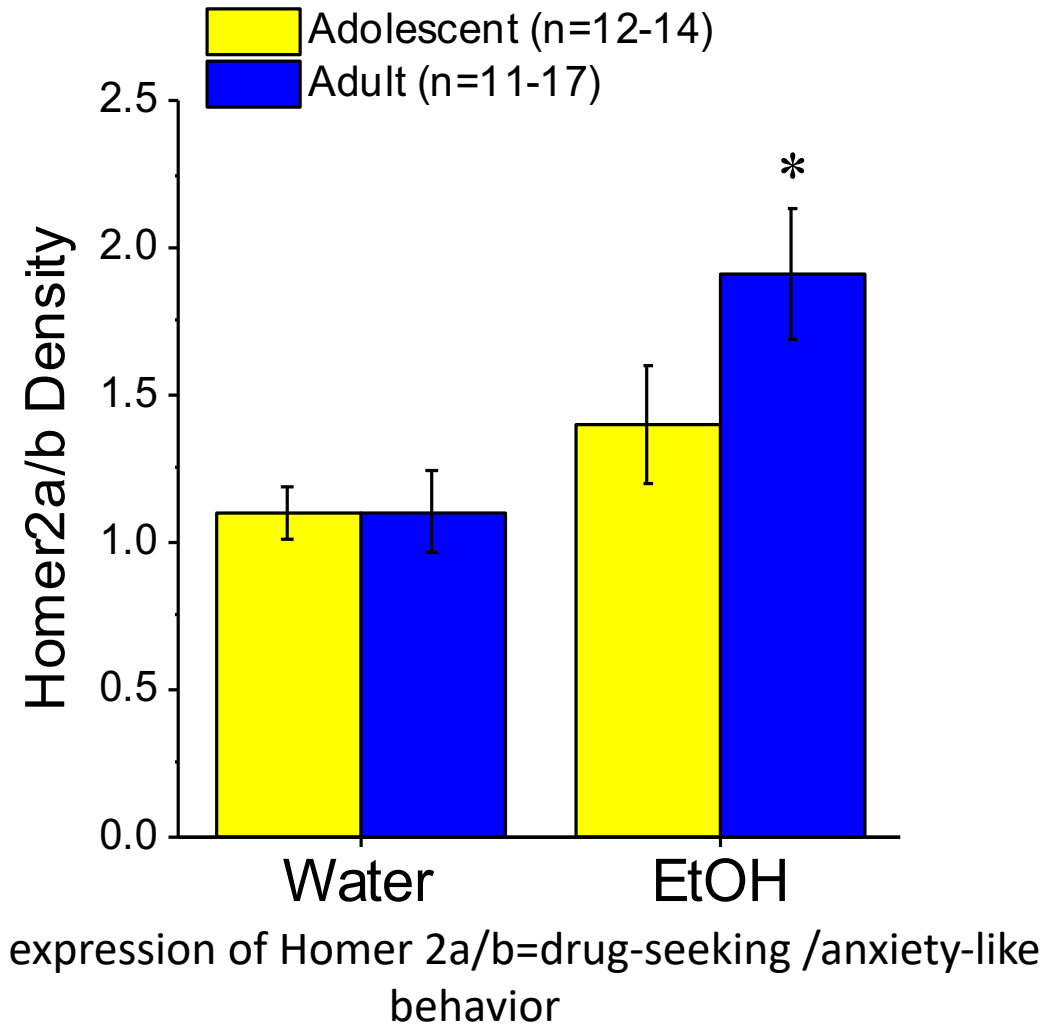
Anxiety-like behavior



**Adult  
Latency to Start Burying**



# Adult binge-drinkers on WD1 have a high density of Homer2a/b in the NA



# Conclusions

- Sex difference in alcohol intake was not an important variable of regulating withdrawal-induced anxiety
- Negative affect induced by a history of binge-drinking is age-related but not sex-specific
- Age of drinking-onset may not be a reliable predictor of when negative affect manifests
- Our model of binge-drinking is a valid one because it adheres to the standards set forth by the NIAAA

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Dr. Sammy Davis

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CSNI



# References

Blumenthal, Heidemarie et al. (2011) Anxiety Psychopathology and Alcohol Use among Adolescents: A Critical Review of the Empirical Literature and Recommendations for Future Research. *Journal of experimental psychopathology* vol. 2,3 : 318-353. doi:10.5127/jep.012810

CDC - Fact Sheets-Underage Drinking - Alcohol (2019). *Centers for Disease Control and Prevention*, Centers for Disease Control and Prevention, [www.cdc.gov/alcohol/fact-sheets/underage-drinking.htm](http://www.cdc.gov/alcohol/fact-sheets/underage-drinking.htm).

Lee KM, Coelho MA, McGregor HA, Solton NR, Cohen M and Szumlinski KK (2016) Adolescent Mice Are Resilient to Alcohol Withdrawal-Induced Anxiety and Changes in Indices of Glutamate Function within the Nucleus Accumbens. *Front. Cell. Neurosci.* 10:265. doi: 10.3389/fncel.2016.00265

Lee, Coelho, McGregor, Waltermire, & Szumlinski. (2015). Binge alcohol drinking elicits persistent negative affect in mice. *Behavioural Brain Research*, 291, 385-398.

Lee KM, Coelho MA, McGregor HA, Solton NR, Cohen M and Szumlinski KK (2016) Adolescent Mice Are Resilient to Alcohol Withdrawal-Induced Anxiety and Changes in Indices of Glutamate Function within the Nucleus Accumbens. *Front. Cell. Neurosci.* 10:265. doi: 10.3389/fncel.2016.00265

Lee KM, Coelho MA, Solton NR and Szumlinski KK (2017) Negative Affect and Excessive Alcohol Intake Incubate during Protracted Withdrawal from Binge-Drinking in Adolescent, But Not Adult, Mice. *Front. Psychol.* 8:1128. doi: 10.3389/fpsyg.2017.01128

Szumlinski, K., Coelho, M., Lee, K., Tran, T., Sern, K., Bernal, A., & Kippin, T. (2018). DID it or DIDn't it? Exploration of a failure to replicate binge-like alcohol-drinking in C57BL/6J mice. *Pharmacology Biochemistry and Behavior*, 12/2018.