The behavioral and molecular impact of binge-drinking alcohol

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

- 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

Severity of adolescent male anxiety

Severity of adult male anxiety

24 HOUR 30 DAYS

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WATER-DRINKERS (n=160)

ALCOHOL-DRINKERS (n=187)
Habituation (7 days) → 14 day binge-drinking → Withdrawal period → Behavioral Testing → Biochemical test
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
Habituation (7 days)

14 day binge-drinking

Withdrawal period

Behavioral Testing

Biochemical test
Mice are subject to 2-hour binge-drinking procedures for 14 days
Habituation (7 days)

14 day binge-drinking

Withdrawal period

Behavioral Testing

Biochemical test

EARLY WITHDRAWAL

PROTRACTED WITHDRAWAL

24 hours

70 days
Habituation (7 days) -> 14 day binge-drinking -> Withdrawal period -> Behavioral Testing -> Biochemical test
After pre-determined withdrawal, mice run through behavioral tests

Marble-burying (15 mins)  Forced swim-test (6 mins)
Habituation (7 days) -> 14 day binge-drinking -> Withdrawal period -> Behavioral Testing -> Biochemical test
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**

- Male
- Female
- Adult
- Adolescent
Irrespective of sex, adolescent binge-drinkers displayed an increase in anxiety-like behavior in late withdrawal.
Binge-drinking adolescent males exhibit anxiety-like behavior in early withdrawal?

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

High expression of Homer 2a/b=drug-seeking /anxiety-like behavior
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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References


