Scripps Research Alcohol Center Neuroscience Course

Alcohol use disorder

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Science Changing Life

Today's Topics

- Alcohol use disorder (AUD)
- Underage drinking
- Example of an animal model of AUD

https://www.nytimes.com/2020/01/31/sunday-review/alcohol-drinking-problem.html

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Alcohol Use Disorder (AUD)

- A medical condition characterized by an impaired ability to stop or control alcohol use despite negative social, occupational, or health consequences.
- It encompasses the conditions that some people refer to as alcohol abuse, alcohol dependence, and alcohol addiction.
- Considered a brain disorder, AUD can be mild, moderate, or severe.
- Lasting changes in the brain caused by alcohol misuse increase risk of developing an AUD, perpetuate an AUD and make individuals vulnerable to relapse.
- The good news is that no matter how severe the problem may seem, evidence-based treatment with behavioral therapies, mutual-support groups, and/or medications can help people with AUD achieve and maintain recovery.

https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/understanding-alcohol-use-disorder

Alcohol Use Disorder (AUD) characteristics

Impaired Control	Social Problems	Risky Use	Physical/Emotional Dependence
Drinking more than you meant to	Neglecting responsibilities and relationships	Drinking in risky settings	Needing to drink more to get same effect (tolerance)
Wanting to cut down or stop drinking, but not able to	Giving up activities because of drinking	Continued drinking despite known problems	Having withdrawal symptoms when not using (trouble sleeping, shakiness, restlessness, nausea, sweating, a racing heart, feeling crappy or sick)
	Inability to complete tasks at home, school or work		Feeling anxious, depressed, hyperkatifeia (negative emotional state) when not using

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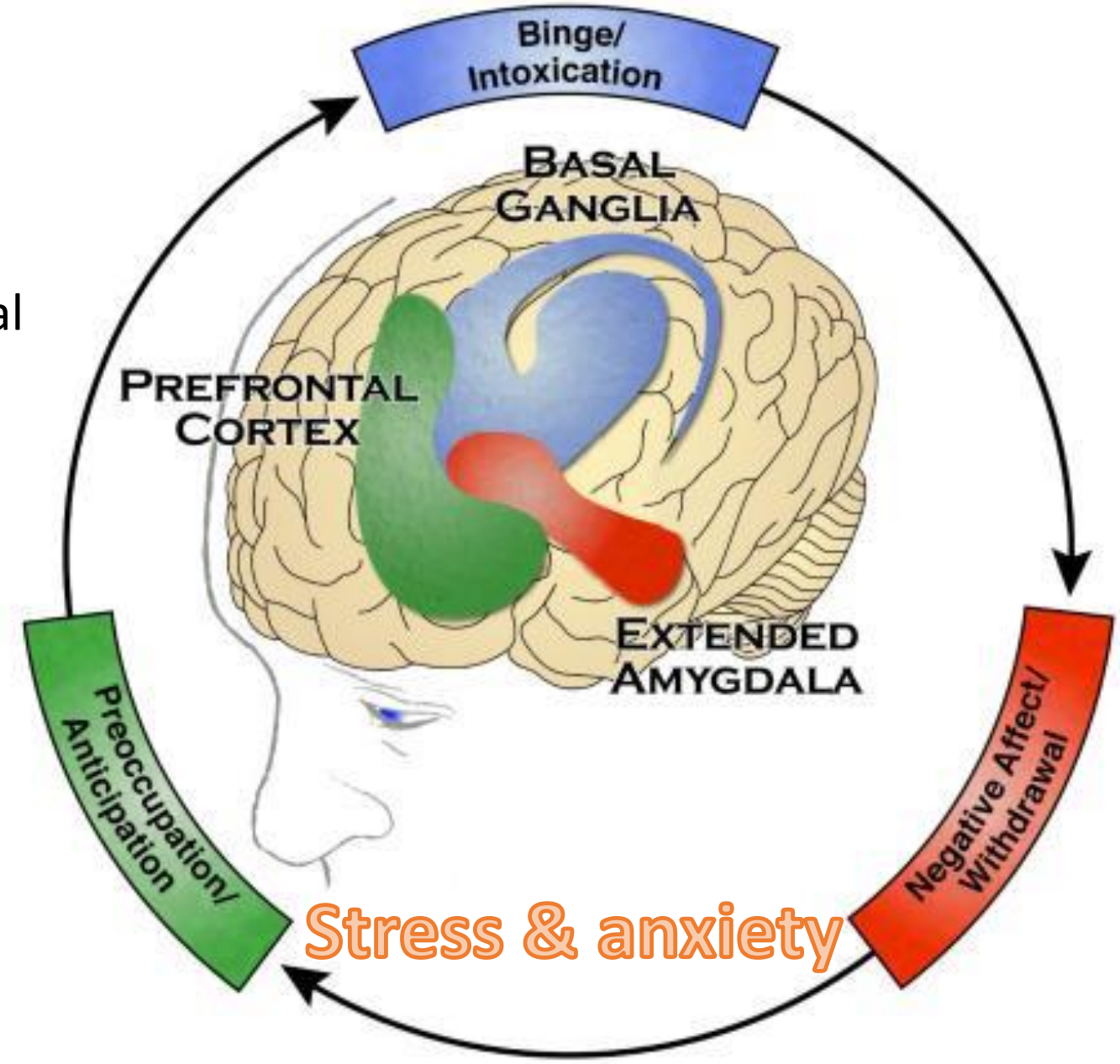
2-3 symptoms: Mild

4-5 symptoms: Moderate

6+ symptoms: Severe

Addiction cycle

- Binge/intoxication
  - Drinking to feel euphoric, more social
  - Drinking to cope with stress, social anxiety, bad mood
- Negative affect withdrawal
  - Feeling bad (emotionally and/or physically) when not drinking
- Preoccupation/anticipation
  - Thinking about the next drink
  - Craving
  - Feeling out of control



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How concerned should we be about people drinking to deal with the stress of the COVID-19 pandemic?

George F. Koob, Ph.D., director of the National Institute on Alcohol Abuse and Alcoholism. Photo courtesy of NIAAA.

GEORGE F. KOOB, PH.D.: Drinking because of a big crisis is not unusual. For example, we saw spikes in alcohol use in response to the 1993 bombing of the World Trade Center. Alcohol consumption by Black and African Americans in New Orleans almost tripled when their communities were devastated by Hurricane Katrina in August 2005. Many people drank more after the 9/11 attacks.

The COVID-19 pandemic was similar to other major catastrophes as it caused widespread illness and loss of life. But there was another factor that really affected people: isolation from their fellow human beings. People had to maintain social distancing to slow the spread of COVID-19. For many, stress from the pandemic, including from social isolation, resulted in an increase in drinking.

It was really no surprise that during the first year of the pandemic, alcohol sales jumped by nearly 3%, the largest increase in more than 50 years. Multiple small studies suggest that during the pandemic, about 25% of people drank more than usual, often to cope with stress. Sales of hard liquor, or spirits, accounted for most of the increase.

With other disasters, we've seen that these spikes in drinking last 5 or 6 years and then alcohol consumption slowly returns to usual levels. We hope that the high rates of alcohol use and negative health effects will decline over time as we return to more typical interactions with each other.

Underage alcohol drinking

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MONITORING THE FUTURE

- Each year, a total of approximately 50,000 8th, 10th and 12th grade students are surveyed
- Students from 420 public and private high schools and middle schools across the U.S. are surveyed
- The study has been conducted by the University of Michigan under a series of research grants from the National Institute on Drug Abuse, a part of the National Institutes of Health
- The results of the study are used by policymakers at all levels of government to monitor progress toward national health goals and to monitor trends in substance use and abuse among adolescents and young adults

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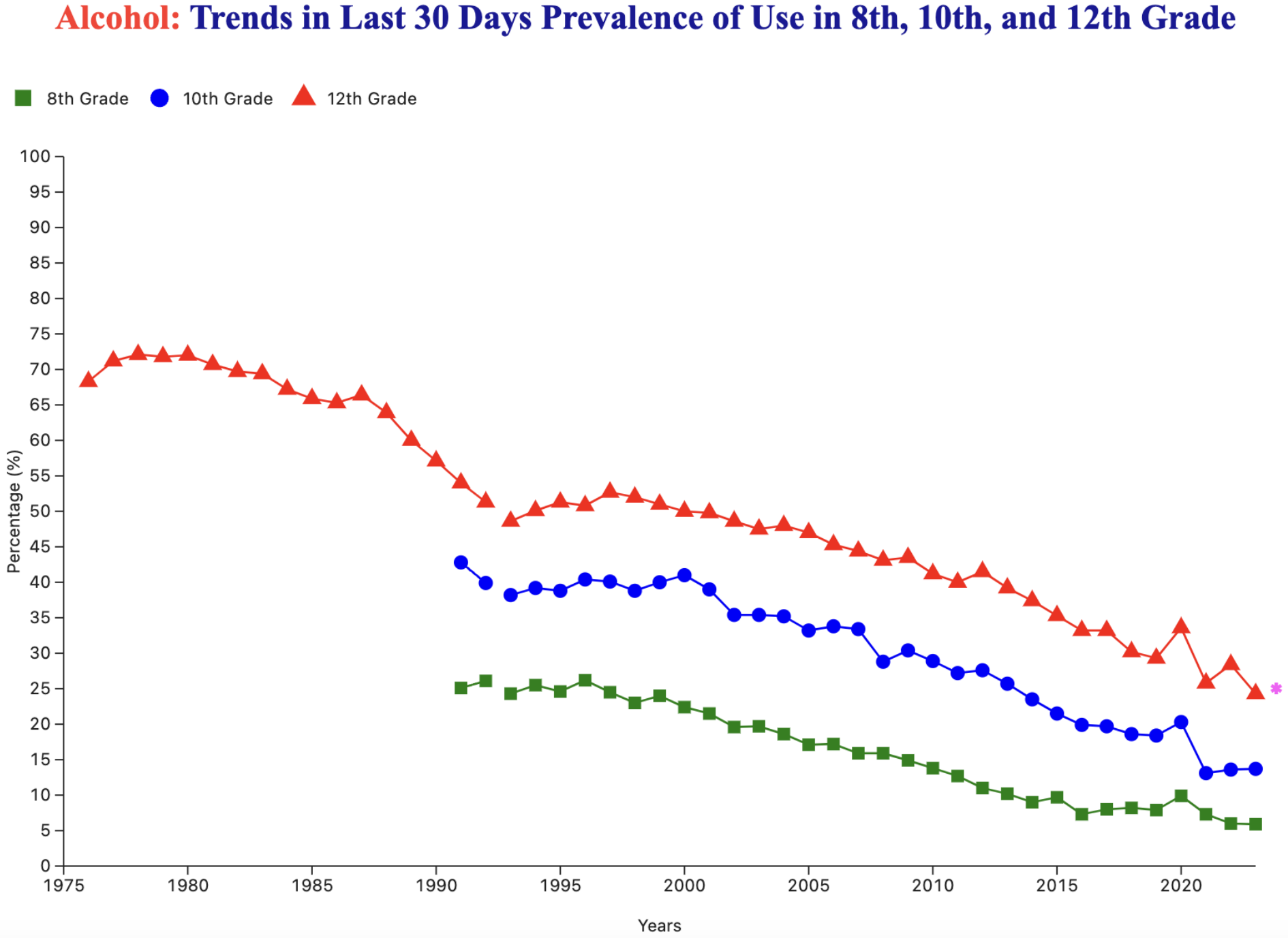
https://monitoringthefuture.org/about/

Underage alcohol drinking



https://monitoringthefuture.org/

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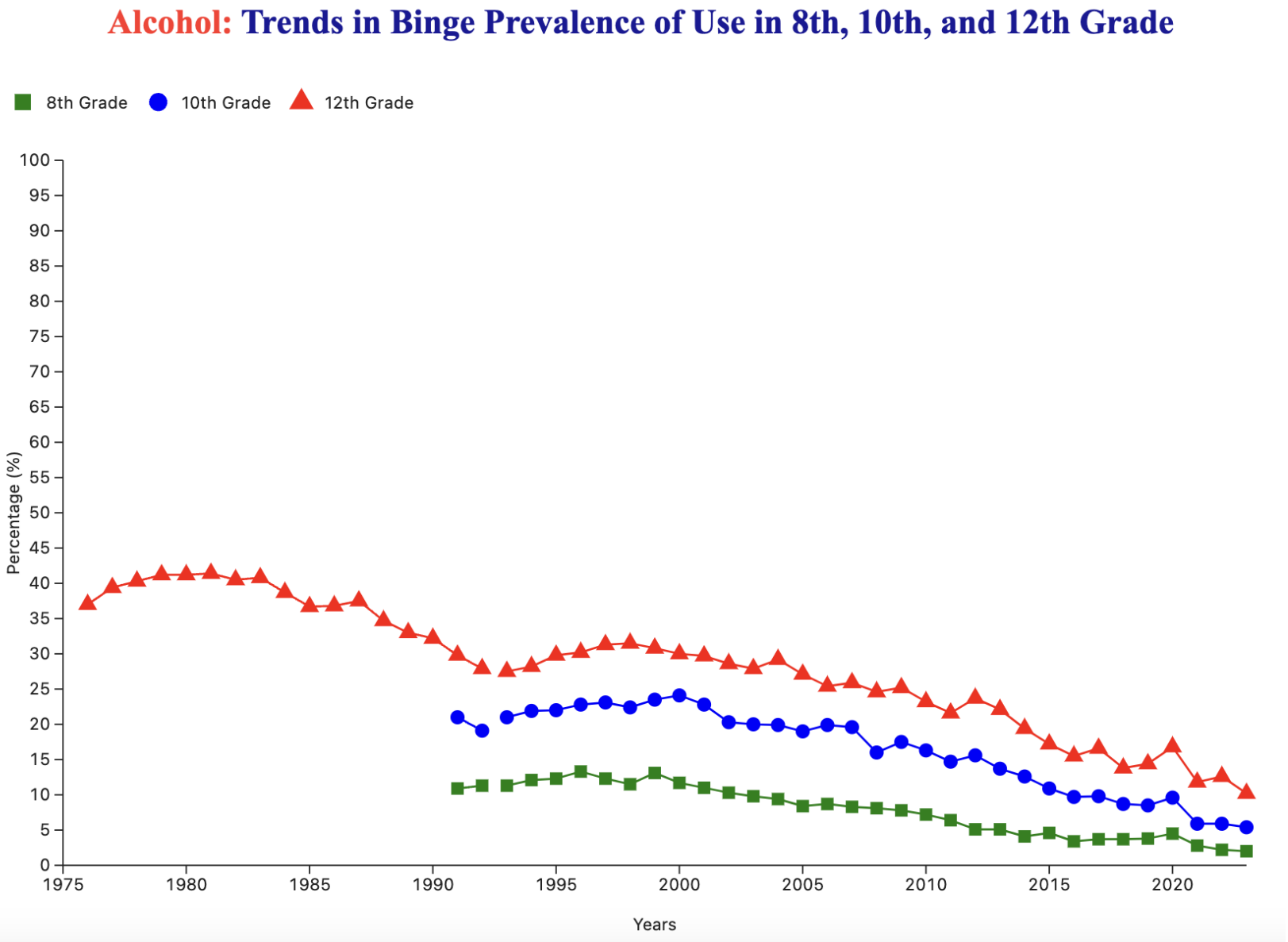
Underage alcohol drinking: Binge drinking



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Underage Drinking: Age 8-20

- While drinking in adolescents has been decreasing, it isn't decreasing as much in girls
- Interferes with normal adolescent brain development
- Increases the risk of developing alcohol use disorder
- contributes to a range of short-term consequences, such as injuries, sexual assaults, alcohol overdoses, and deaths—including those from motor vehicle crashes

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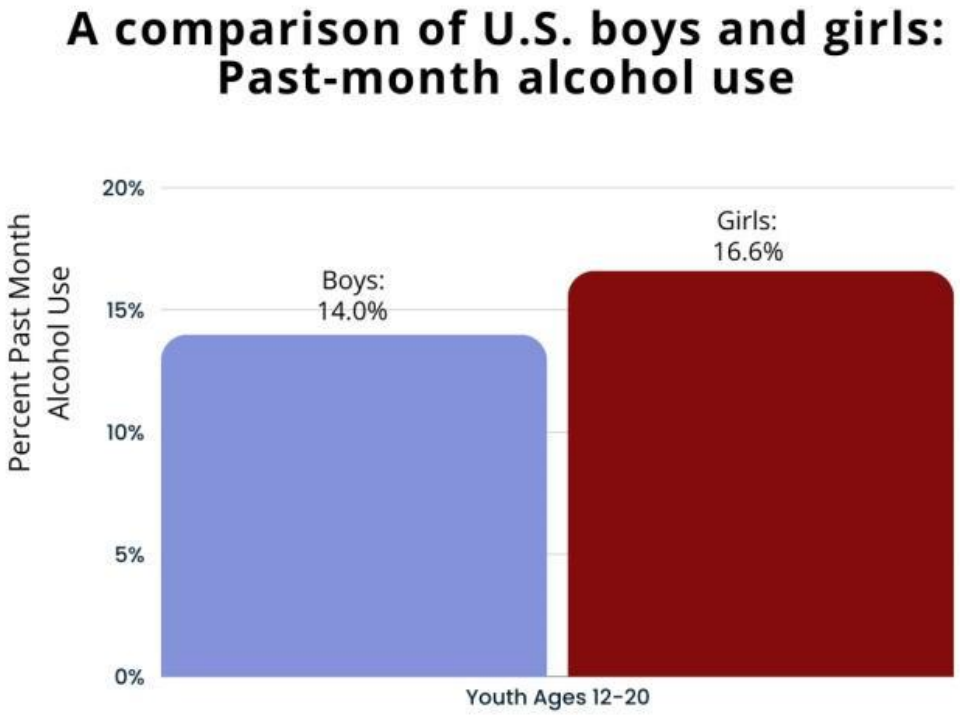
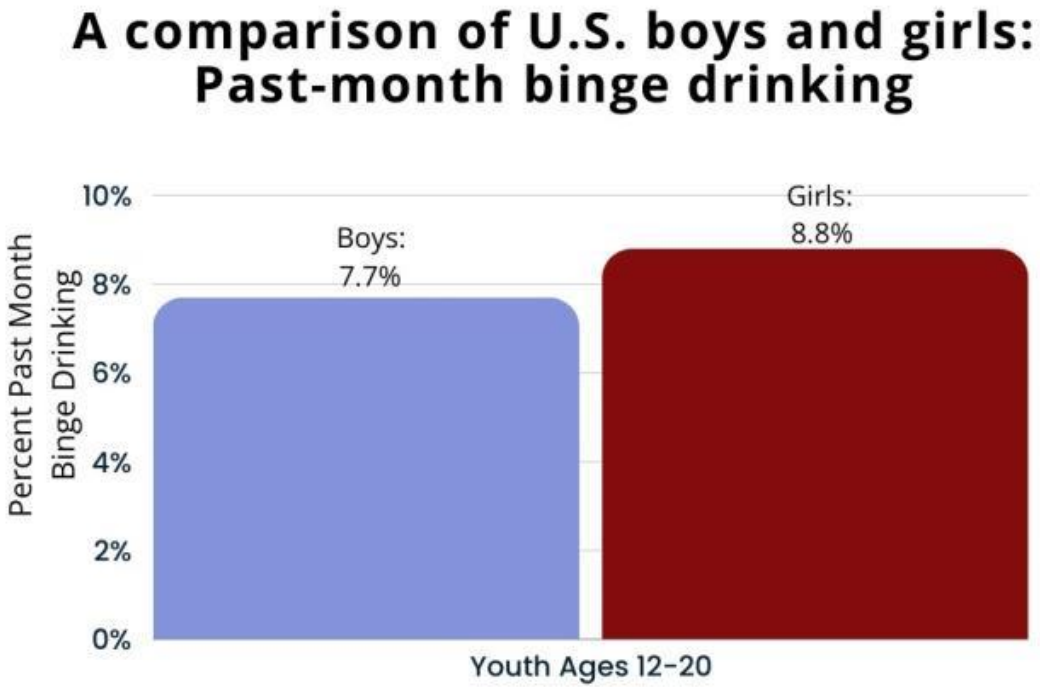
https://www.niaaa.nih.gov/alcohols-effects-health/alcohol-topics/alcohol-facts-and-statistics

Troubling statistics concerning sex differences





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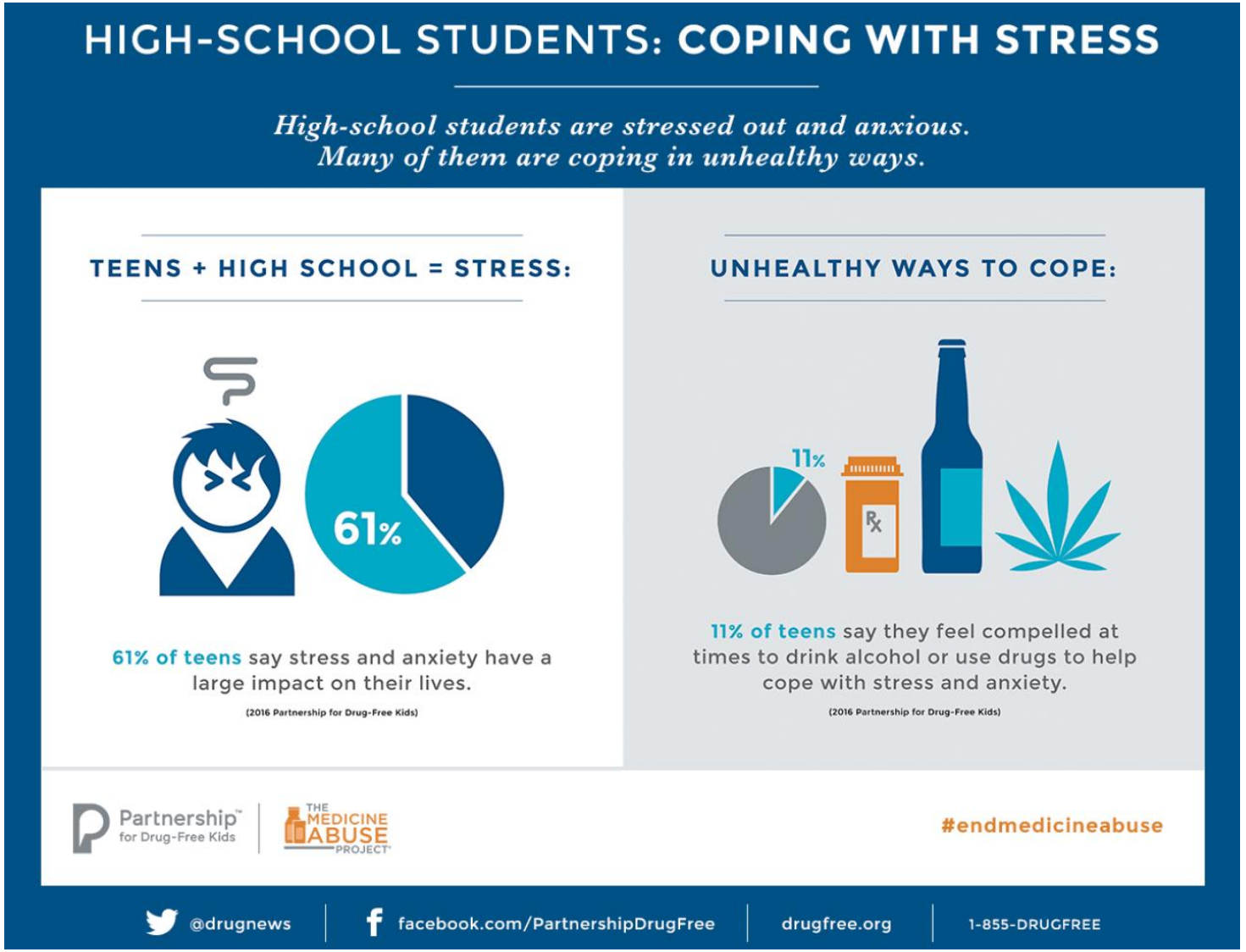
https://www.niaaa.nih.gov/publications/brochures-and-fact-sheets/underage-drinking

Why do kids drink?

- Peer pressure
- Increased independence
- Stress



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https://www.poehealth.org/op-ed-drinking-to-cope-poor-stress-coping-skills-fueling-adolescent-binge-drinking/

What increases risk for AUD?

Drinking at an early age

- Drinking before age 15 associated with 5x increased risk of AUD

Genetics & family history of alcohol problems

- Genes, environment and the interaction

Mental health conditions and a history of trauma

- Depression, ADHD, anxiety disorders, PTSD
- Childhood trauma

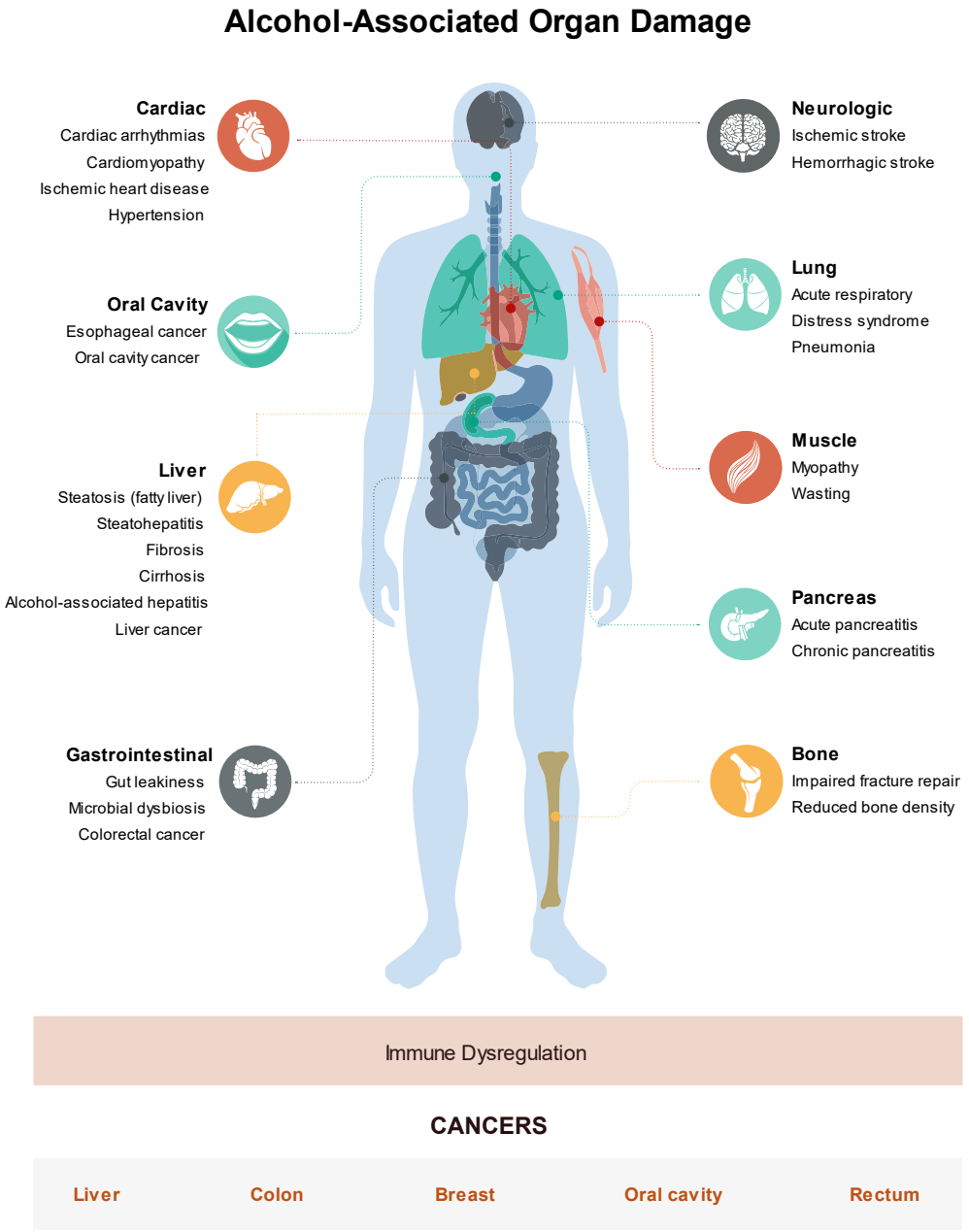
AUD treatment

- Medications
  - Naltrexone, acamprosate, disulfiram
  - Might need to medicate during withdrawal
- Behavioral treatments
  - Talk therapy, coping strategies, mindfulness-based
- Support groups
  - Alcoholics Anonymous most famous, but others

Acamprosate is thought to ease the negative effects related to quitting drinking by dampening glutamate activity and reducing some of the brain's hyperexcitability associated with alcohol withdrawal.

Naltrexone blocks opioid receptors involved in the pleasant sensations associated with drinking and can reduce alcohol craving.

Alcohol Effects on the Body



Brain:

- Changes mood and behavior
- Makes it harder to think clearly
- Makes it harder to move with coordination
- Increases risk for AUD and substance use disorders (SUD)
- In adolescents: may affect brain development!!!

https://www.niaaa.nih.gov/alcohols-effects-health/alcohols-effects-body

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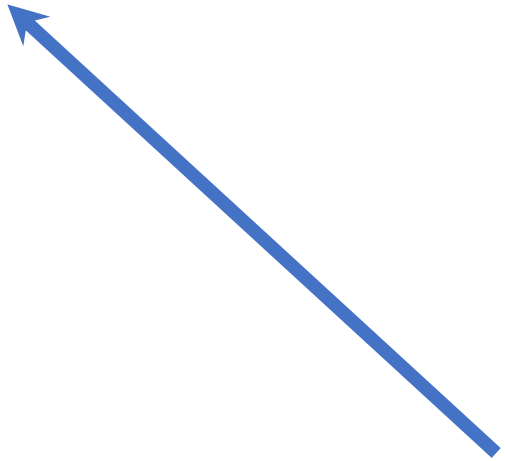
NUCLEUS ACCUMBENS
- This area of the brain responds to things that help you survive and thrive—like delicious food.
- Alcohol and other drugs "trick" this part of the brain, making alcohol seem even

Alcohol Use Disorder (AUD) Research

National Institute on Alcohol Abuse & Alcoholism

A subdivision of the National Institutes on Health focused on AUD

A portion of the government's budget (which comes from the taxes we pay) is assigned to NIAAA and funds biomedical and clinical alcohol research



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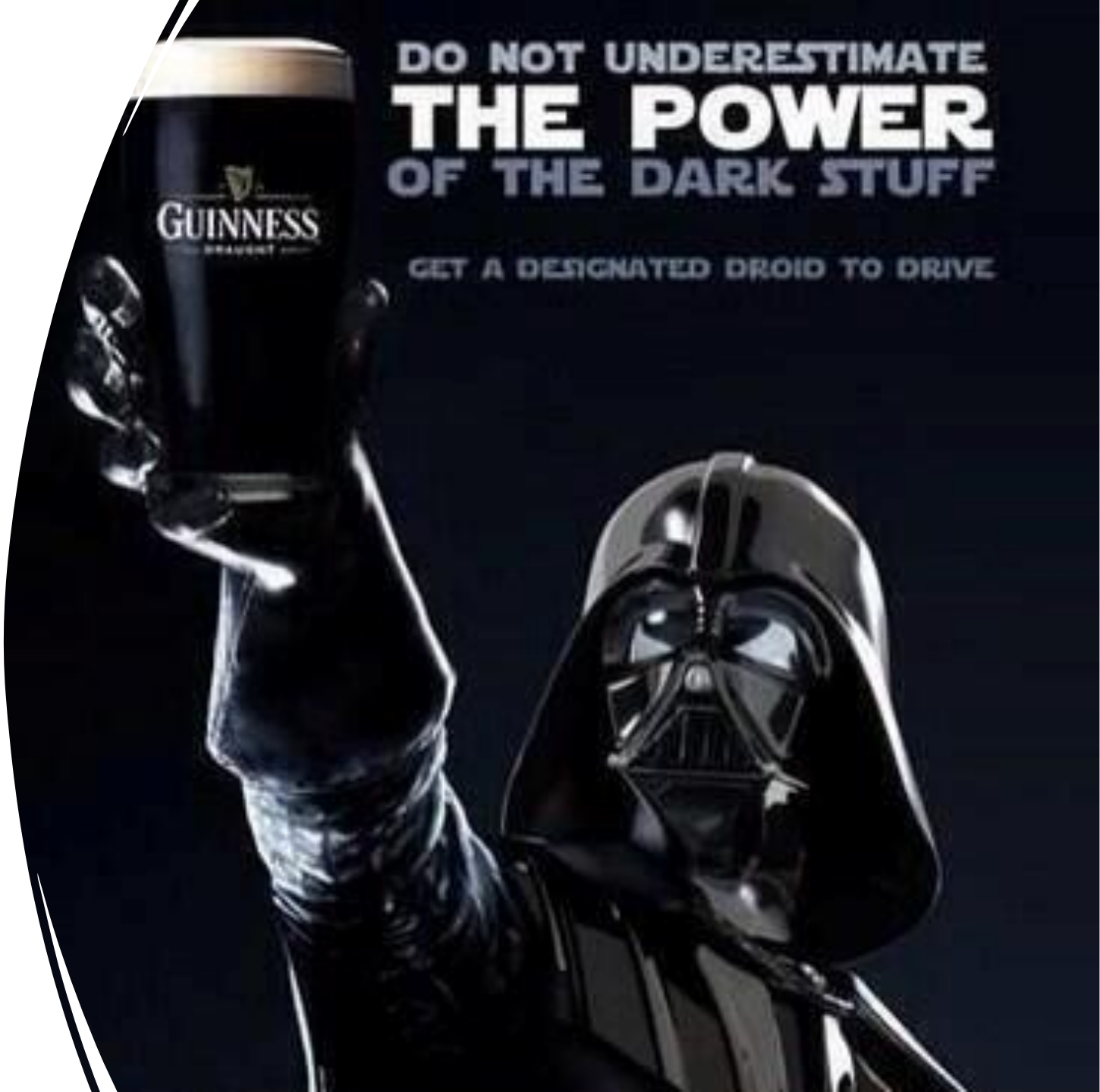
The Scripps Research Institute's Alcohol Research Center (TSRI-ARC)

- Exploring the "**DARK SIDE**" of alcohol use disorder
  - The "LIGHT SIDE" – using alcohol to increase good feelings – euphoria, relaxation, taste
  - The "DARK SIDE" – using alcohol to to decrease negative feelings – stress, anxiety, depressed mood, sleep problems



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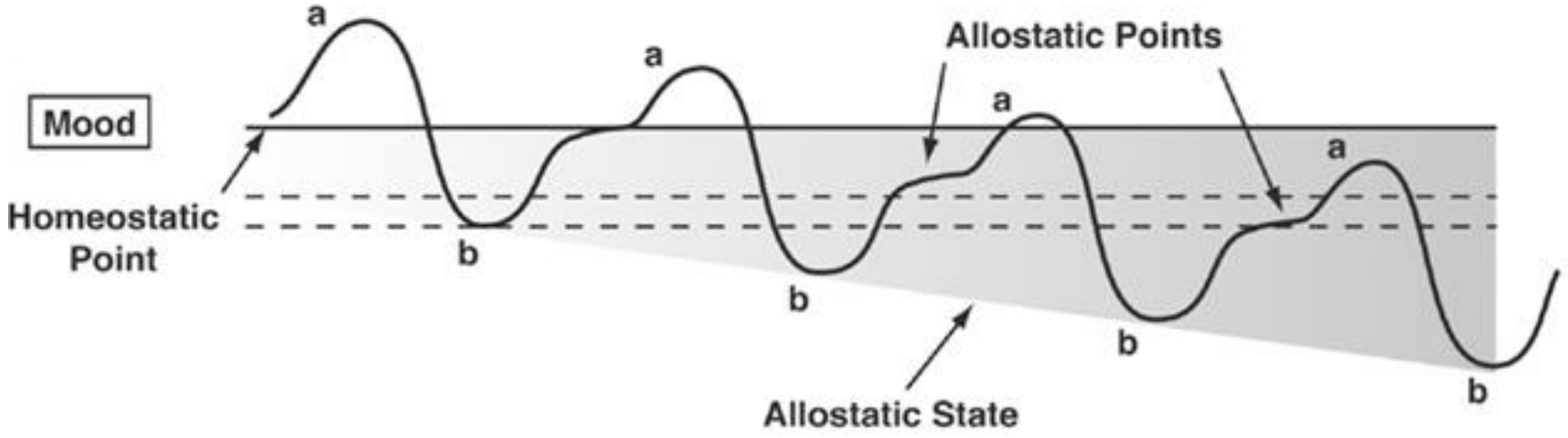
Addressing the dark side of alcohol use disorder (AUD)



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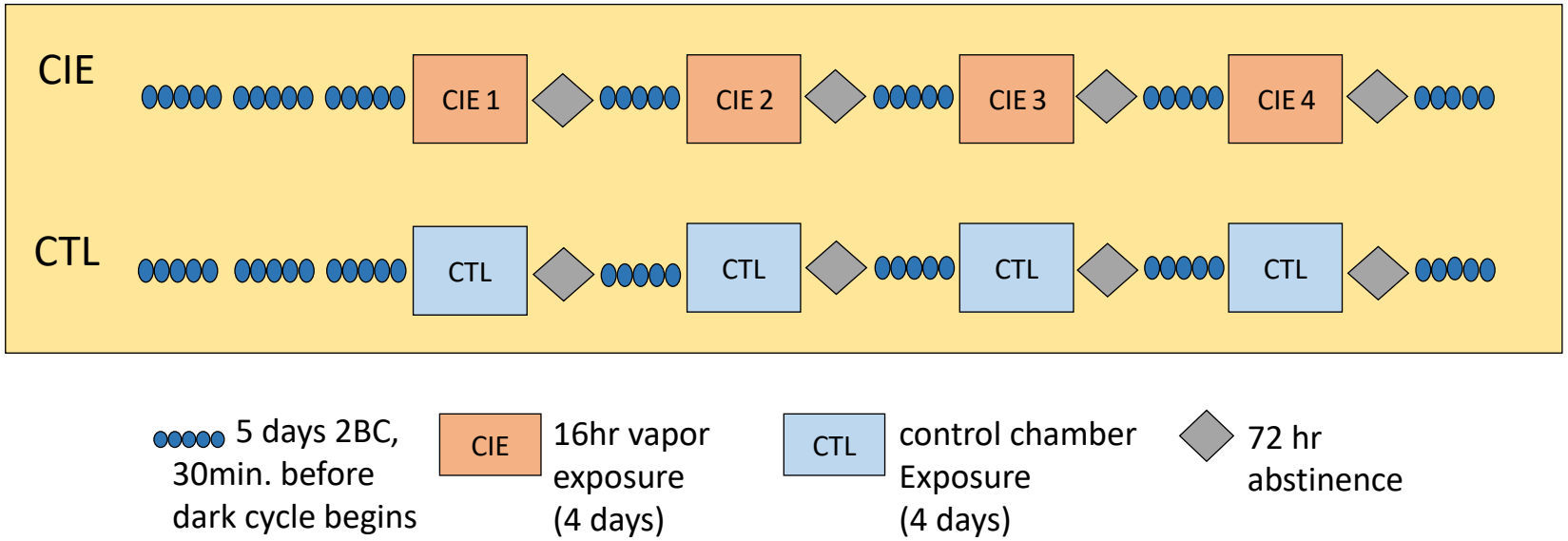
Animal Models of AUD

- Escalation in drinking
- Negative affect (anxiety, irritability) in abstinence
- Increased susceptibility to relapse (craving)

A mouse model of AUD

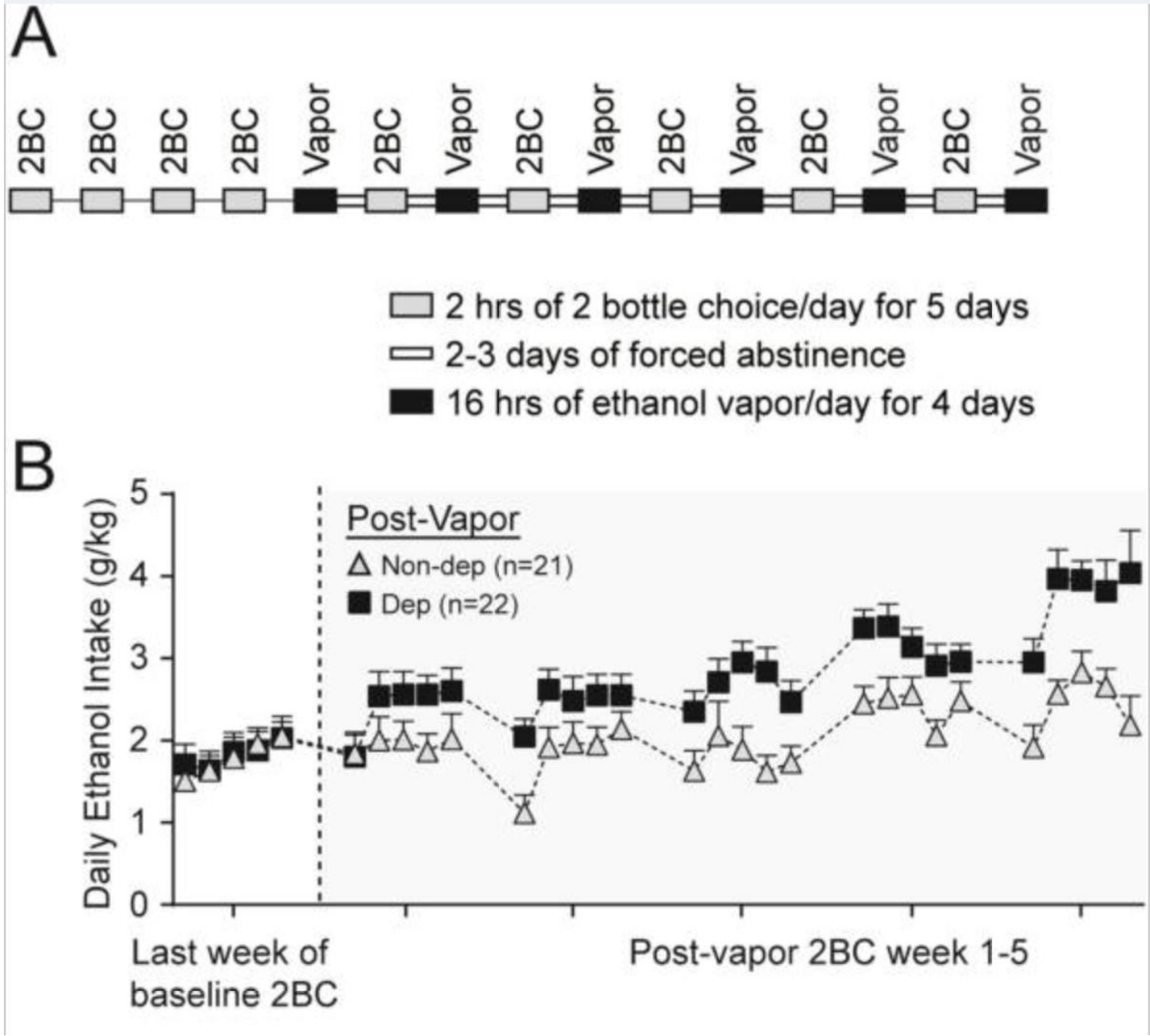


- 2BC = Two bottle choice. Mice get one bottle of water and one bottle of 15% alcohol (ethanol) for 2 hours Monday – Friday
- CIE = Chronic intermittent ethanol exposure in vapor chambers

The two bottle choice set-up

Alcohol vapor chambers: for chronic intermittent ethanol (CIE) exposure

Example data



Athanason AC, Nadav T, Cates-Gatto C, Roberts AJ, Roberto M, Varodayan FP. Chronic ethanol alters adrenergic receptor gene expression and produces cognitive deficits in male mice. Neurobiol Stress. 2023 Apr 27;24:100542. doi: 10.1016/j.ynstr.2023.100542. PMID: 37197395; PMCID: PMC10184141.

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