Decoding Bidirectional Interactions Between Alcohol and Pain

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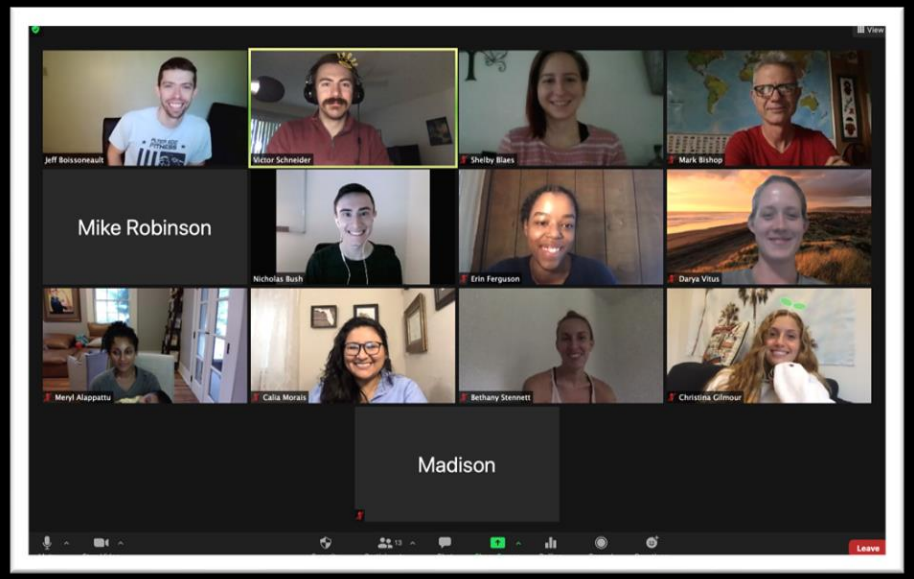


National Institute on Alcohol Abuse and Alcoholism

Center *for* Pain Research and Behavioral Health
DEPARTMENT *of* CLINICAL & HEALTH PSYCHOLOGY, COLLEGE *of* PHHP

Center *for* Addiction Research & Education

Overview

1. Introduction
2. Pain as an antecedent for alcohol use
3. Acute analgesic effects of alcohol
4. Discussion and future directions

Introduction

Pain Prevalence and Costs

- 20.4% of US adults have chronic pain (Dahlhamer et al., 2018)
- 8.0% have high-impact chronic pain, limiting activities on most days
- Prevalence elevated among older adults, women, veterans, and those living in poverty
- Overall costs to US economy > $600B USD/year (Institute of Medicine, 2011)
- Front line treatments have poor efficacy and significant side effects (e.g., Reinecke et al., 2015)

Dahlhamer, J., Lucas, J., Zelaya, C., Nahin, R., Mackey, S., DeBar, L., ... & Helmick, C. (2018). Prevalence of chronic pain and high-impact chronic pain among adults—United States, 2016. *Morbidity and Mortality Weekly Report*, *67*(36), 1001.
Institute of Medicine. (2011). Relieving Pain in America: A Blueprint for Transforming Prevention, Care, Education, and Research. Washington, DC: National Academies Press.
Reinecke, H., Weber, C., Lange, K., Simon, M., Stein, C., & Sorgatz, H. (2015). Analgesic efficacy of opioids in chronic pain: recent meta-analyses. *British journal of pharmacology*, *172*(2), 324-333.

Pain Self-Management with Alcohol

- Riley and King (2009) surveyed 4321 individuals with tooth, jaw, or arthritis pain
- Across conditions, ~25% of individuals endorsed the use of alcohol to manage pain
- Risk factors:
  - Male
  - Young adults
  - Greater pain severity
  - Higher SES
  - White racial identity
  - Depression
  - Longer pain duration
  - Use of prescription analgesics (e.g., opioids)

Riley, JL & King, C (2009). Self-report of alcohol use for pain in a multi-ethnic community sample. *Journal of Pain* 10(9):944-52. PMID: 19712901.

Risks of Pain Self-management with Alcohol

1. Interactions between alcohol and pain medications may have severe health consequences
   - Approximately 77% of the 100 most prescribed drugs in the US have potentially harmful interactions with alcohol
   - Includes drugs used for pain treatment:
     - All opioid analgesics
     - Antidepressants, including SSRIs and SNRIs (e.g., fluoxetine, duloxetine)
     - Non-steroidal anti-inflammatory drugs (e.g., ibuprofen, aspirin, naproxen)
     - Acetaminophen
     - Gabapentin
   - **Note: 36.8% of US adults over 65 take more than 5 medications**
     - Pain medications, benzodiazepines, muscle relaxants among most common

Smith RG (2009) An appraisal of potential drug interactions in cigarette smokers and alcohol drinkers. J Am Podiatr Med Assoc 99:81-88.
Young, E. H., Pan, S., Yap, A. G., Reveles, K. R., & Bhakta, K. (2021). Polypharmacy prevalence in older adults seen in United States physician offices from 2009 to 2016. *Plos one*, *16*(8), e0255642.

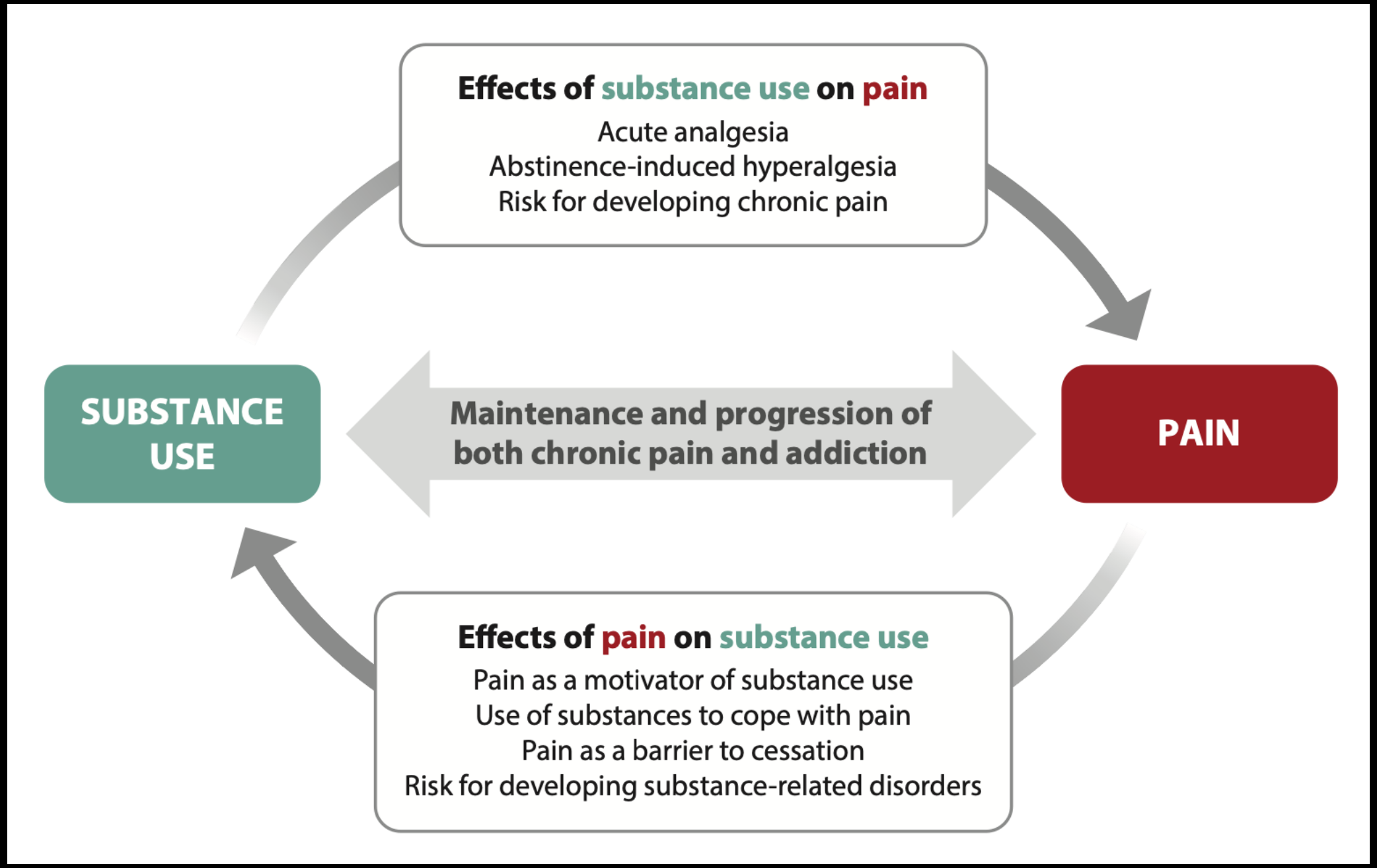
Risks of Pain Self-management with Alcohol

2. Self-medication of pain with alcohol likely results in hazardous drinking
   - Risk of developing painful alcohol-related neuropathy (25-60% of people with AUD)
   - Relief of pain provides additional negative reinforcement for alcohol use, increasing risk of developing AUD or return to use for those in recovery

3. Alcohol withdrawal increases pain severity and sensitivity

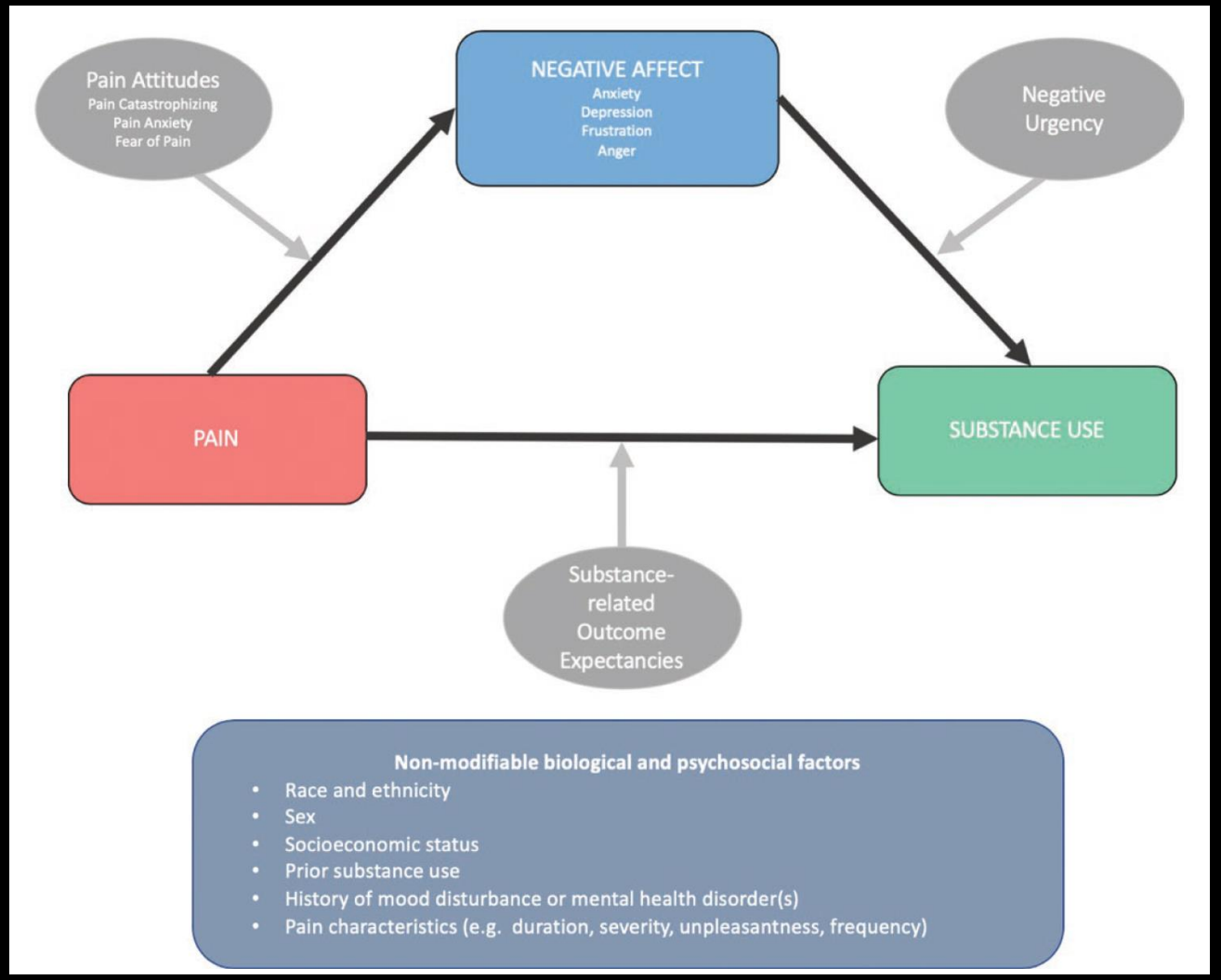
4. Alcohol use/misuse itself results in costs > $200B USD/year

National Institute on Alcohol Abuse and Alcoholism. (2013). Using Alcohol to Relieve Your Pain: What are the Risks? Bethesda, MD: U.S. Dept. of Health and Human Services, Public Health Service, National Institutes of Health, National Institute on Alcohol Abuse and Alcoholism.

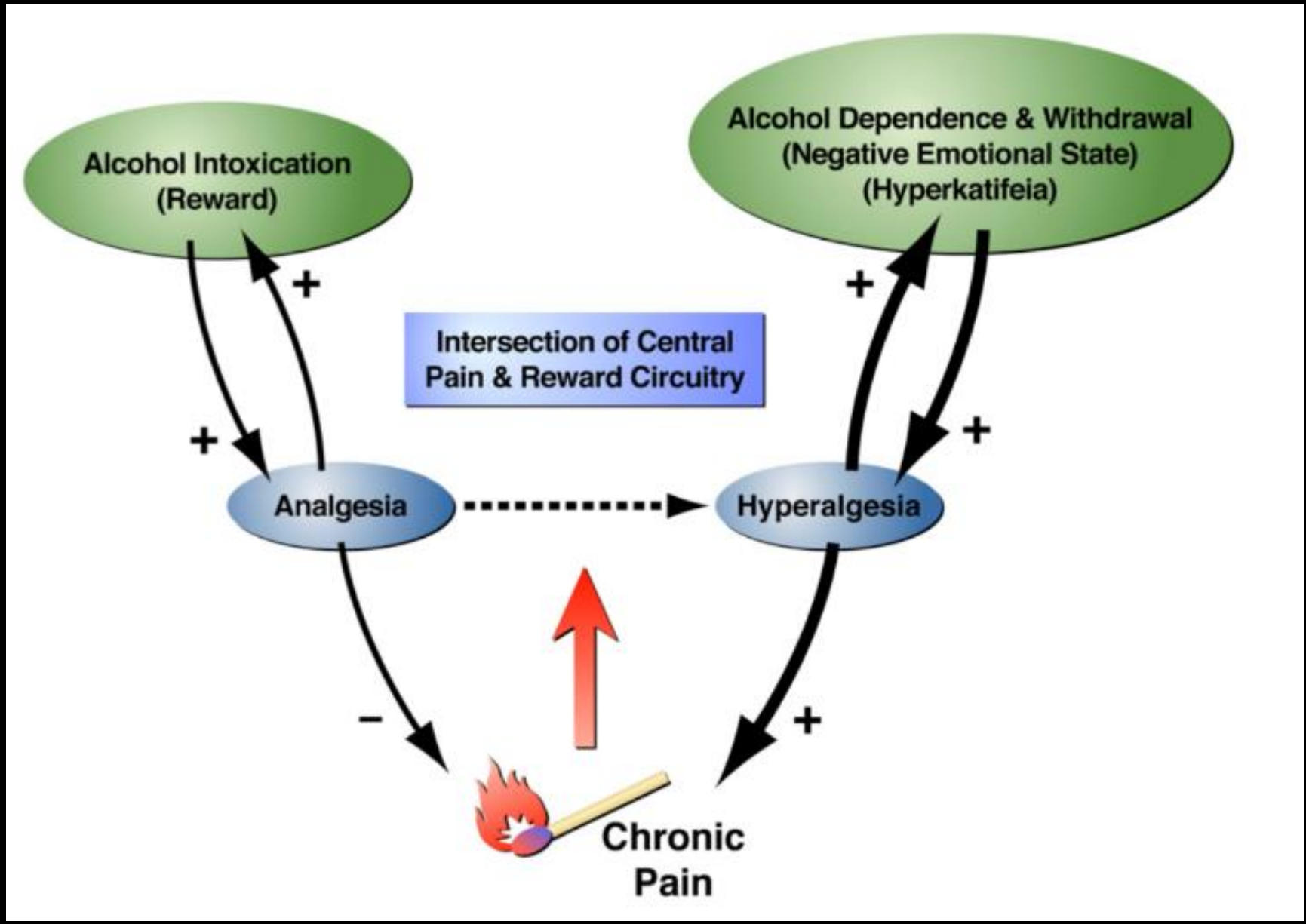


Ditre, J. W., Zale, E. L., & LaRowe, L. R. (2019). A reciprocal model of pain and substance use: Transdiagnostic considerations, clinical implications, and future directions. *Annual review of clinical psychology*, *15*, 503-528.

CANUE Model



Ferguson, E., Zale, E., Ditre, J., Wesolowicz, D., Stennett, B., Robinson, M., & Boissoneault, J. (2021). CANUE: A theoretical model of pain as an antecedent for substance use. *Annals of behavioral medicine*, *55*(5), 489-502.



Apkarian, A. V., Neugebauer, V., Koob, G., Edwards, S., Levine, J. D., Ferrari, L., ... & Regunathan, S. (2013). Neural mechanisms of pain and alcohol dependence. *Pharmacology Biochemistry and Behavior*, *112*, 34-41.

Pain as an Antecedent for Alcohol Use

Background

- Substantial evidence that pain is a potent predisposing factor for heavy drinking and alcohol-related consequences (e.g., Bush et al., 2022)
- Greater pain severity has been associated with greater odds of return to drinking both during and after treatment (Witkiewitz et al., 2015)
- Reductions in pain severity of the course of residential treatment predicted increased abstinence self-efficacy and quality of life, and reduced craving (Ferguson et al., 2022)
- Experimentally-induced pain increases urge and intention to drink in healthy young adults (Moskal et al., 2018)

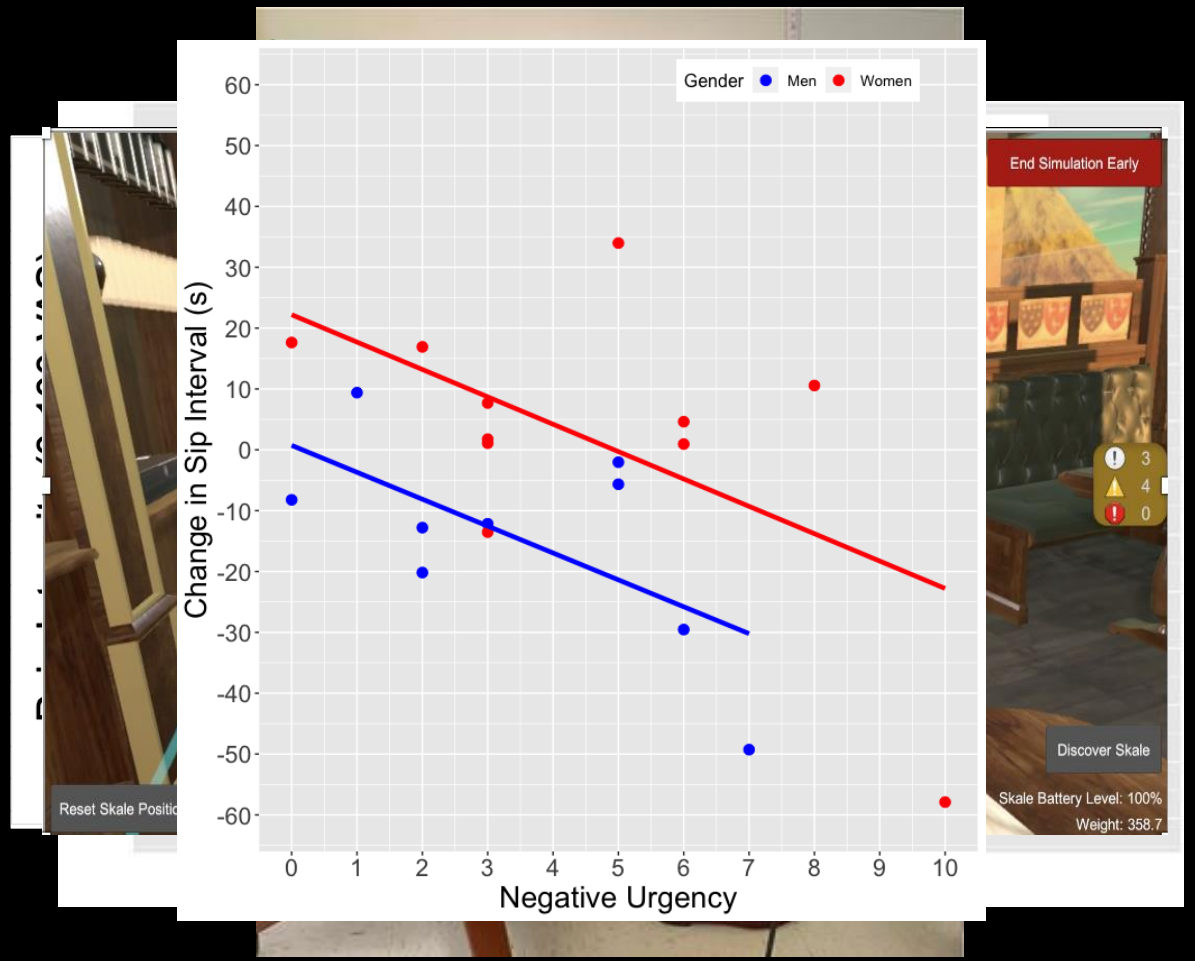
Bush, N. J., Schick, M. R., Spillane, N. S., & Boissoneault, J. (2022). Stress mediates the association between pain and alcohol use in college students. *Journal of pain research*, 757-766.
Ferguson, E., Lewis, B., Teitelbaum, S., Reisfield, G., Robinson, M., & Boissoneault, J. (2022). Longitudinal associations between pain and substance use disorder treatment outcomes. *Journal of Substance Use and Addiction Treatment*, *143*, 108892.
Moskal, D., Maisto, S. A., De Vita, M., & Ditre, J. W. (2018). Effects of experimental pain induction on alcohol urge, intention to consume alcohol, and alcohol demand. *Experimental and Clinical Psychopharmacology*, *26*(1), 65.
Witkiewitz, K., Vowles, KE, McCallion, E., Frohe, T., Kirouac, M, & Maisto, SA (2015). Pain as a predictor of heavy drinking and any drinking lapses in the COMBINE study and the UK Alcohol Treatment Trial. *Addiction* 110(8): 1262-71.

Effect of Musculoskeletal Pain on Reinforcing Efficacy of Alcohol

- Strength Training and Alcohol Consumption (STAC) Study
- N=53 (30 women) randomized to vigorous eccentric (DOMS) or low-intensity concentric bicep exercise (Sham DOMS)
- Demand assessed using Alcohol Purchase Task before and 48 hours after exercise
  - Intensity, breakpoint, Omax, Pmax, essential value

Stennett, B., Anderson, M. B., Vitus, D., Ferguson, E., Dallery, J., Alappattu, M., ... & Boissoneault, J. (2021). Sex moderates the effects of experimentally induced musculoskeletal pain on alcohol demand in healthy drinkers. *Drug and alcohol dependence*, *219*, 108475.

Effect of Pain on Drinking Topography



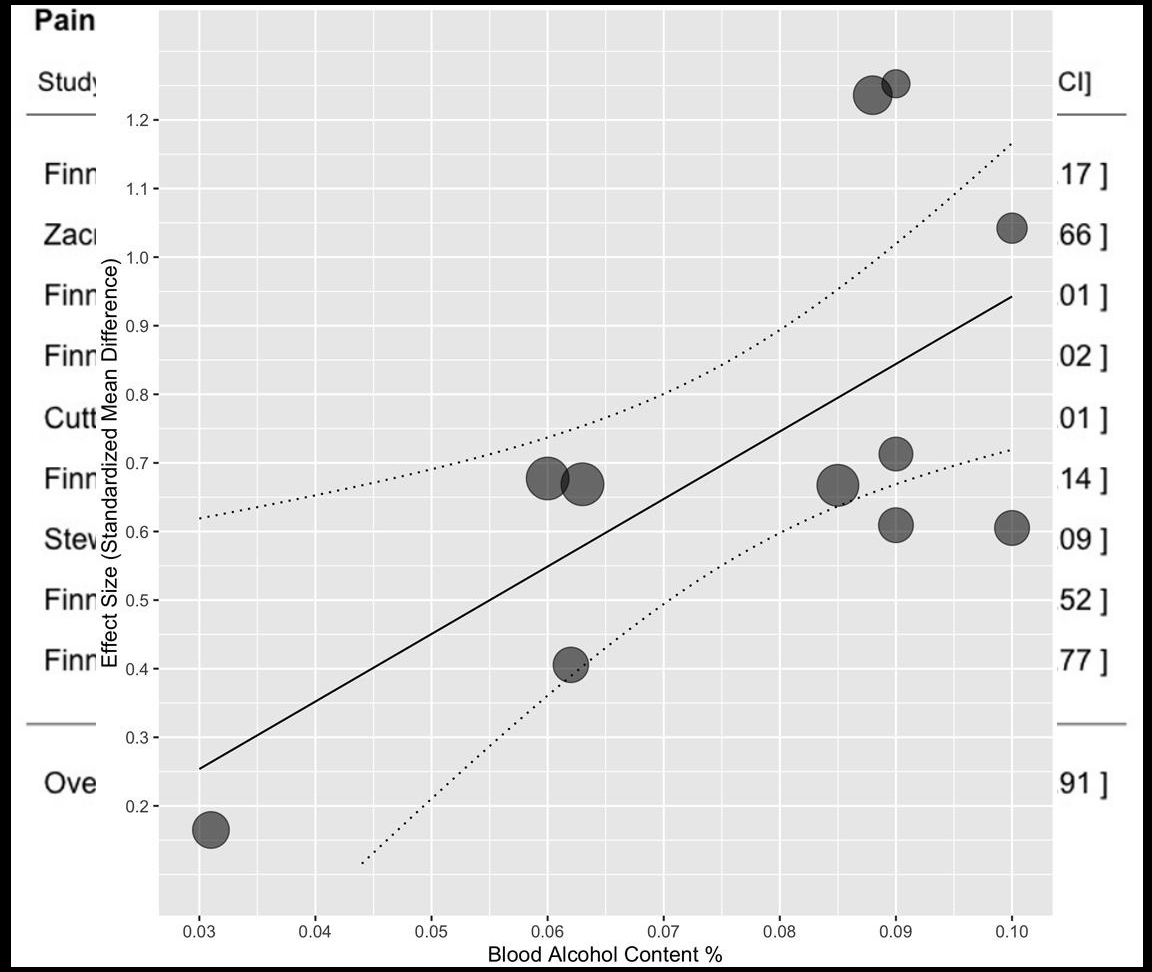
- Pain and Alcohol in Virtual Reality (PAVR) Study
- N=20 (11 women) completed two alcohol self-administration sessions in VR
  - Heat pain (44°C)
  - Non-noxious warmth (38°C)
- Drinking topography compared between sessions using multilevel modeling

Gilmour, C., Blaes, S., Bush, N. J., Vitus, D., Carpenter, R. W., Robinson, M., & Boissoneault, J. (2023). Pain and alcohol consumption in virtual reality. *Experimental and Clinical Psychopharmacology* 31(2):433-442.

Acute Analgesic Effects of Alcohol

Background

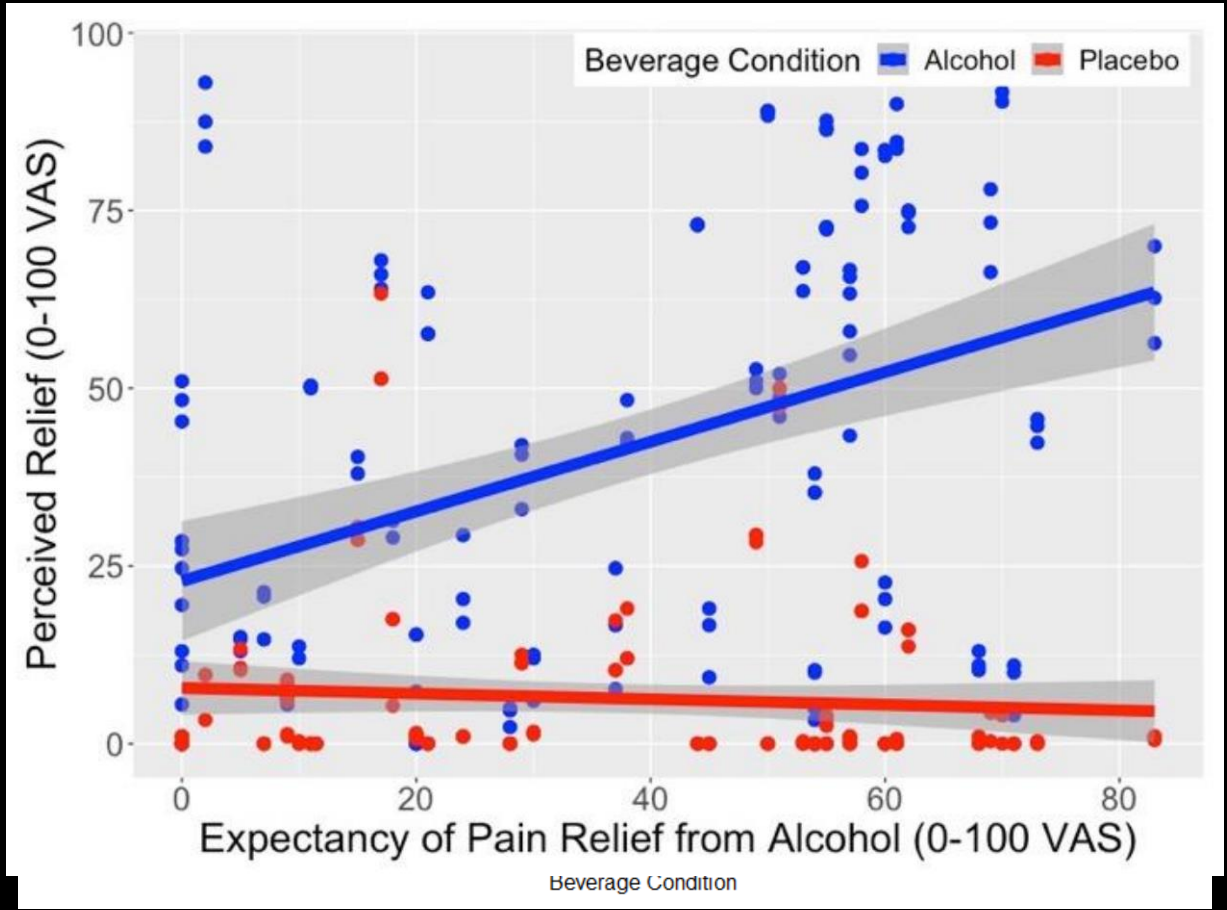
- Anecdotal and clinical reports of alcohol's analgesic effects date back as far as 1513 (Dundee et al., 1969)
- Consistent laboratory evidence that alcohol increases pain threshold and decreases pain intensity in healthy individuals (Thompson et al., 2017)
- However, studies often limited to men and people without chronic pain



Dundee, J. W., Isaac, M., & Clarke, R. S. (1969). Use of alcohol in anesthesia. *Anesthesia & Analgesia*, *48*(4), 665-669.

Thompson, T., Oram, C., Correll, C. U., Tsermentseli, S., & Stubbs, B. (2017). Analgesic effects of alcohol: a systematic review and meta-analysis of controlled experimental studies in healthy participants. *The Journal of Pain*, *18*(5), 499-510.

Analgesic Effects of Alcohol in Chronic Jaw Pain

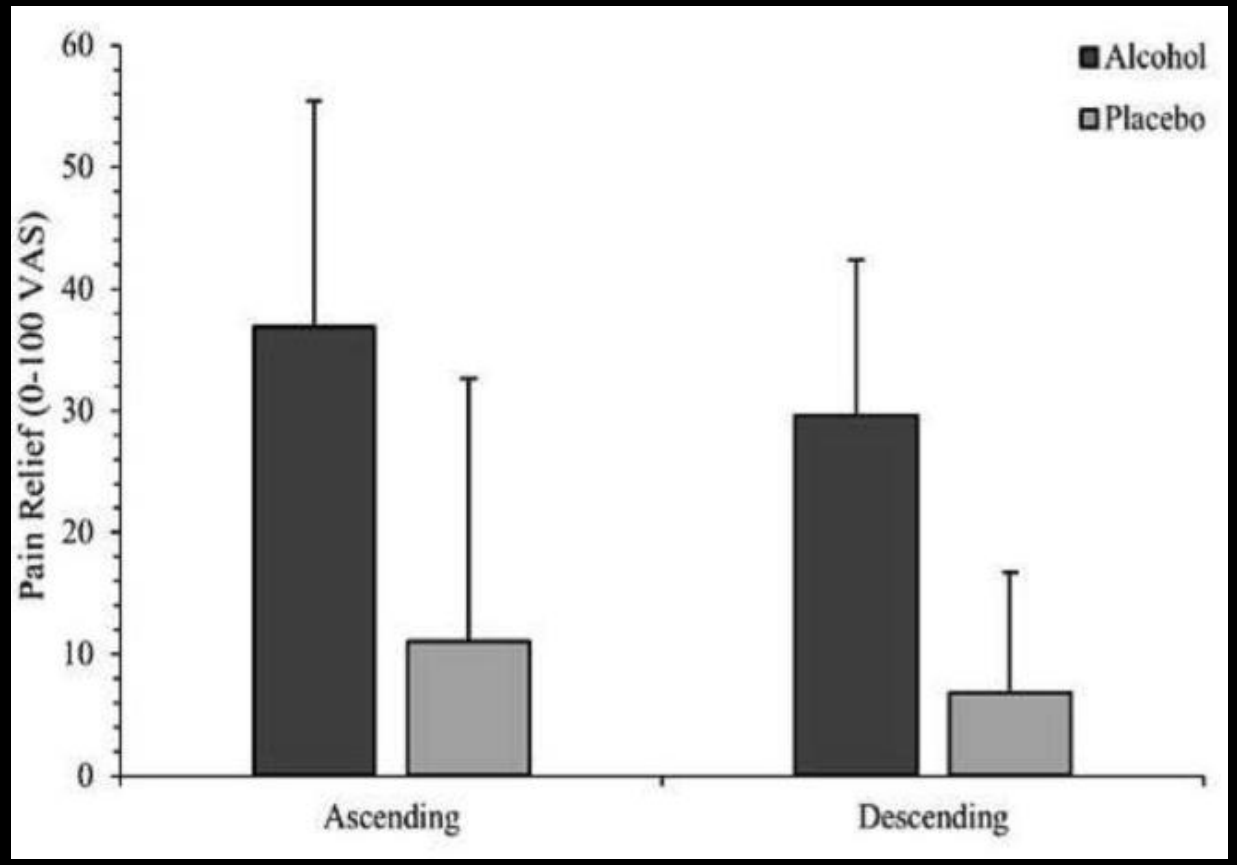


- NIAAA-funded R21
- N=48 (36 women; 19 chronic pain) completed two double-blind testing sessions
  - Alcohol (.08 g/dL target BrAC)
  - Placebo (0 g/dL target BrAC)
- Pressure algometry performed at masseter insertion
- Pain threshold, pain intensity, and perceived pain relief assessed using VASs

Vitus, D., Williams, M. K., Rizk, M., Neubert, J. K., Robinson, M., & Boissoneault, J. (2022). Analgesic effects of alcohol in adults with chronic jaw pain. *Alcohol: Clinical and Experimental Research*, *46*(8), 1515-1524.
Alexander, C., Bush, N. J., Neubert, J. K., Robinson, M., & Boissoneault, J. (in press). Expectancy of Alcohol Analgesia Moderates Perception of Pain Relief Following Acute Alcohol Intake. *Experimental and Clinical Psychopharmacology.*

Acute Tolerance and Functional Neural Correlates of Alcohol Analgesia

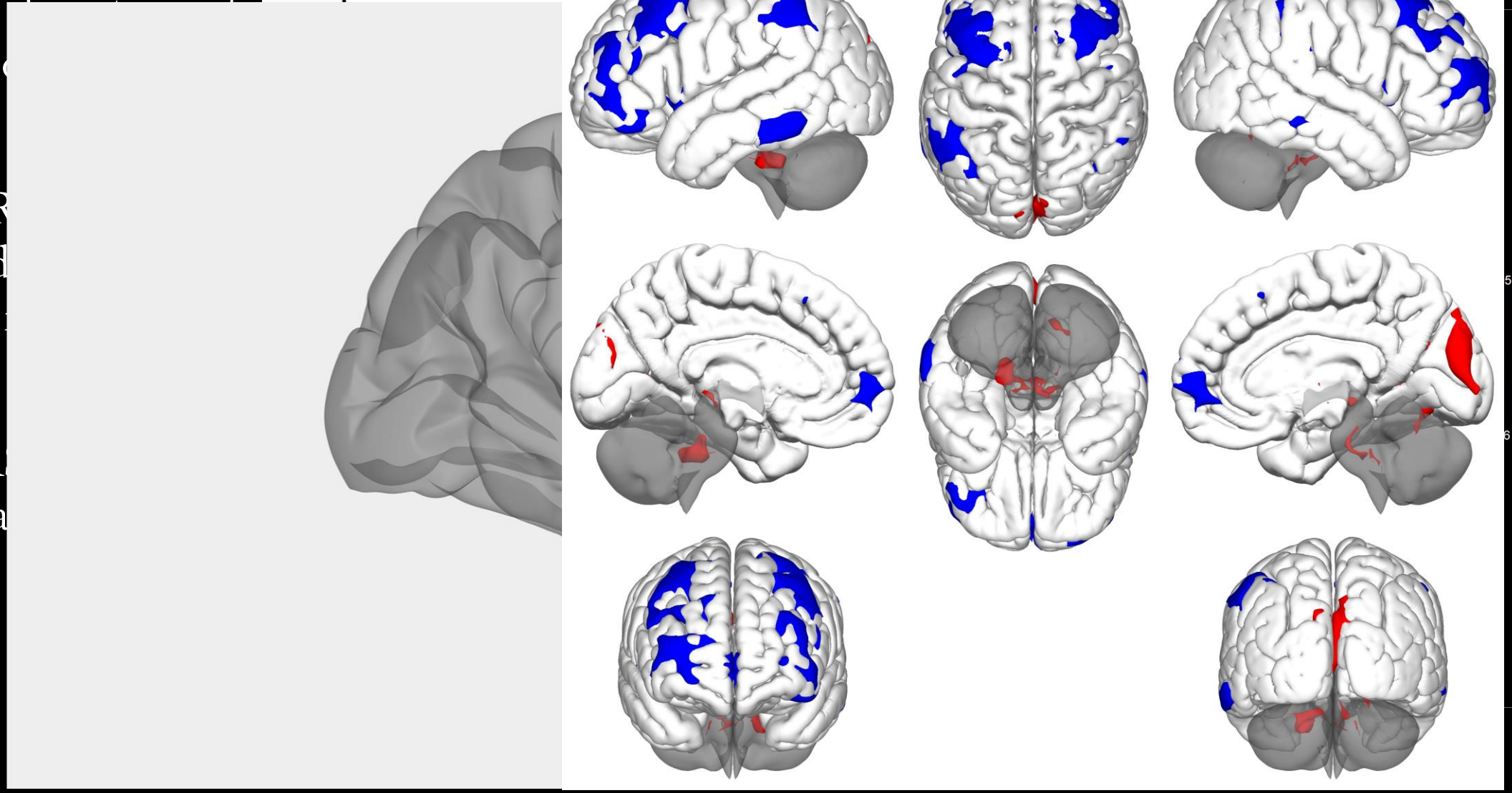
- NIAAA-funded R01
- N=110 (63 women; 45 family history positive) without chronic pain completed two double blind testing sessions
  - Alcohol (.08 g/dL target BrAC)
  - Placebo (0 g/dL target BrAC)
- Heat-based quantitative sensory used to characterize effects of alcohol on pain threshold, pain intensity, and perceived pain relief
- Resting state and task-based fMRI data collected at peak BrAC



Williams, M. K., Vitus, D., Ferguson, E., Stennett, B., Robinson, M., & Boissoneault, J. (2021). Acute tolerance to the analgesic effects of alcohol. *Journal of Studies on Alcohol and Drugs*, *82*(3), 422-430.

RSV Regional Connectivity

- Standard
  intensity
- Greater R
  improved
  and pain
- Higher R
  functiona
  region



Boissoneault, J., Stennett, B., & Robinson, M. E. (2020). Acute alcohol intake alters resting state functional connectivity of nucleus accumbens with pain-related corticolimbic structures. *Drug and alcohol dependence*, *207*, 107811.
Sevel, L., Stennett, B., Schneider, V., Bush, N., Nixon, S. J., Robinson, M., & Boissoneault, J. (2020). Acute alcohol intake produces widespread decreases in cortical resting signal variability in healthy social drinkers. *Alcohol: Clinical and Experimental Research*, *44*(7), 1410-1419.

Discussion and Future Directions

Overall Summary

- Results provide further evidence that pain increases the motivation to use alcohol, the reinforcing efficacy of alcohol, and alters drinking topography
- These effects appear to be especially strong among men and individuals with higher negative urgency
- Alcohol acutely increases pain threshold and perceived pain relief, and decreases pain intensity, but...
  - Effects on pain relief ratings are greater than pain threshold or intensity
  - Changes in pain relief ratings do not appear to be correlated with QST measures
  - Pain relief ratings are greater on the ascending than descending limb

Future Directions

- Need to more fully characterize:
  - Pain as an antecedent for alcohol use and/or return to use as a function of putative risk factors
    - Systematic inclusion of individuals at higher risk for alcohol-related consequences, including older adults, historically excluded and marginalized groups, individuals with chronic pain, people in AUD recovery
    - Adequately powered sample to test predictions of CANUE model
  - Impact of sex and family history on analgesic effects of alcohol and functional neural correlates
  - Mechanisms underlying negative reinforcing effects of alcohol intake in the context of pain
    - I.e., how do individuals determine that alcohol has produced pain relief?
  - Interventions to reduce risk of alcohol-related consequences in people with pain, and vice versa

Questions?

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