Interactive Effects of Naturalistic Drinking Context and Alcohol Sensitivity on Neural Alcohol Cue-Reactivity Responses

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- Alcohol sensitivity has been proposed as a research domain criterion related to AUD (e.g., Bujarski, Hutchison, Prause, & Ray, 2015; Kwako, Momenan, Litten, Koob, & Goldman, 2016; Litten et al., 2015; Ray, Bujarski, & Roche, 2016)

Mechanisms linking LS to heavy drinking and AUD

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  - LS individuals need relatively large amounts of alcohol to attain desired subjective effects (Schuckit, 1994; Schuckit & Smith, 2001; Trela, Piasecki, Bartholow, Heath, & Sher, 2016)

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  - LS individuals associate with heavy-drinking peers (Schuckit et al., 2005; Schuckit et al., 2016)
  - LS drinkers form positive alcohol outcome expectancies (e.g., Schuckit et al., 2005),
  - LS drinkers drinking to cope with stress (Schuckit et al., 2005; Schuckit et al., 2009)

Alternative mechanism linking LS to heavy drinking

- Enhanced reactivity to alcohol-related cues among LS individuals, relative to their higher-sensitivity (HS) peers:
  - Selective attention (Shin et al., 2010)
  - Approach motivational behavior (Fleming & Bartholow, 2014)
  - Feelings of craving (Fleming & Bartholow, 2019)
  - Interference with ongoing task-relevant goals (Baily & Bartholow, 2016; Fleming & Bartholow, 2014)
  - Real-world feelings of craving (Trela et al., 2018)

Incentive-Sensitization Theory of Addiction

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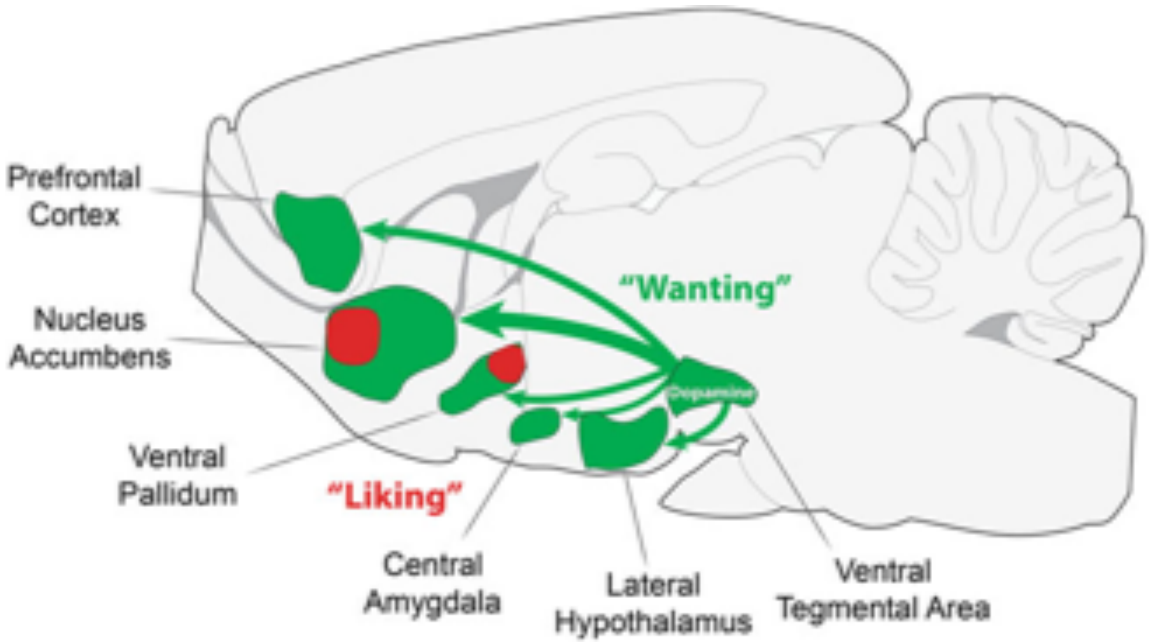

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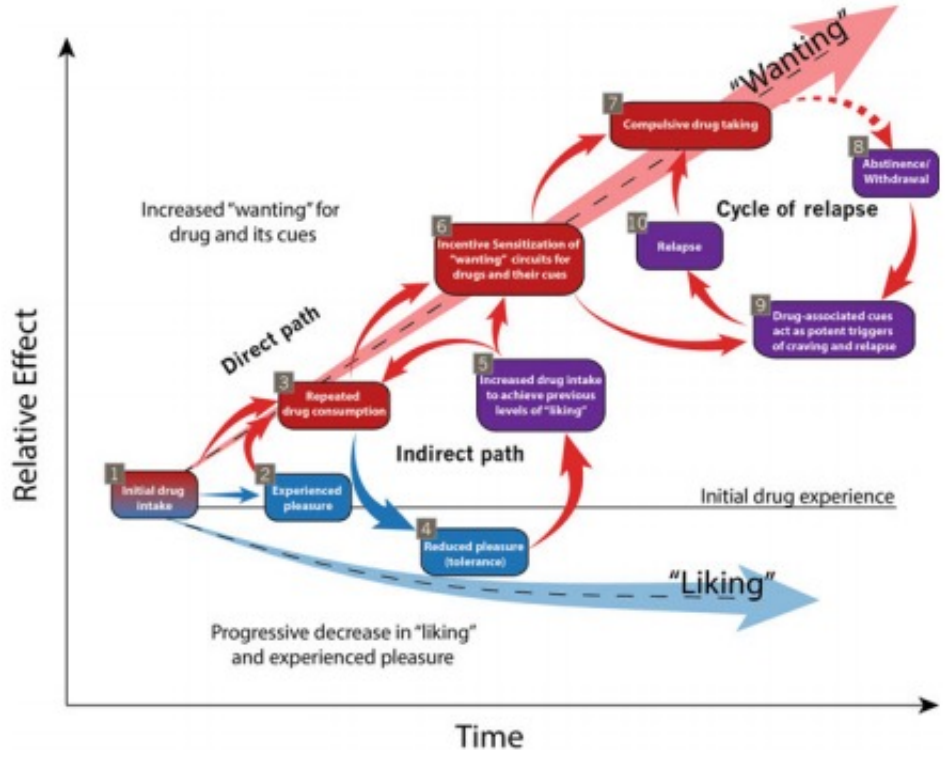

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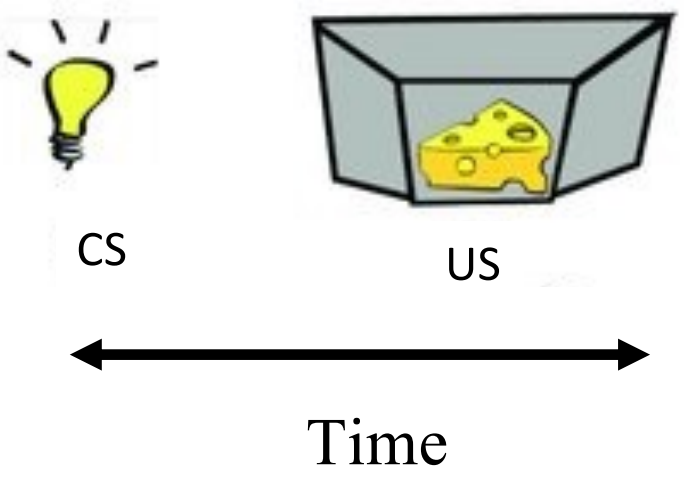
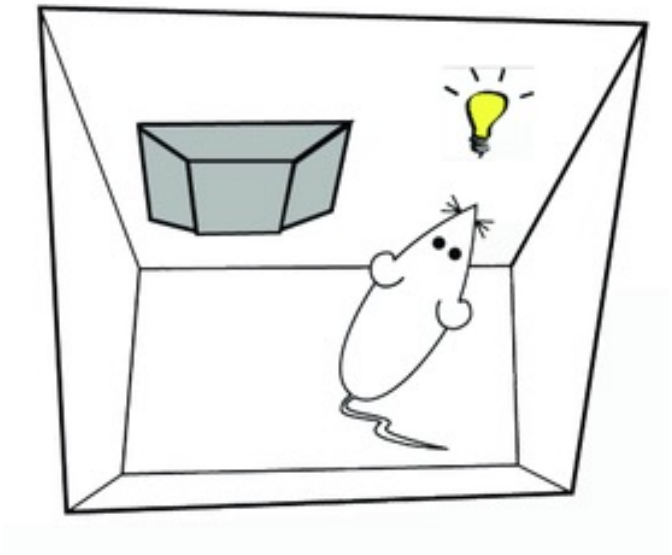
Individual Differences in Incentive Sensitization

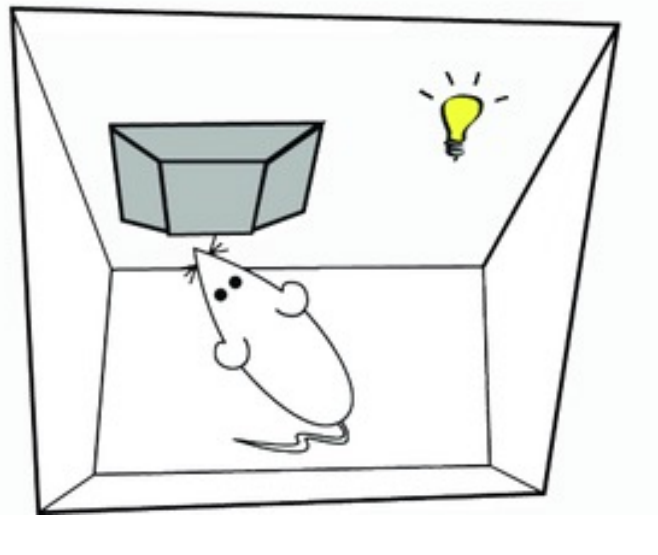


Individual Differences: Sign-Tracking versus Goal-Tracking

Sign-Tracking



Goal-Tracking



Sign-tracking phenotype – conditioned approach and appetitive responses to reward-predictive cues (e.g., Flagel & Robinson, 2017; Flagel, Watson, Robinson, & Akil, 2007; Flagel, Watson, Akil, & Robinson, 2008; Robinson et al., 2014)

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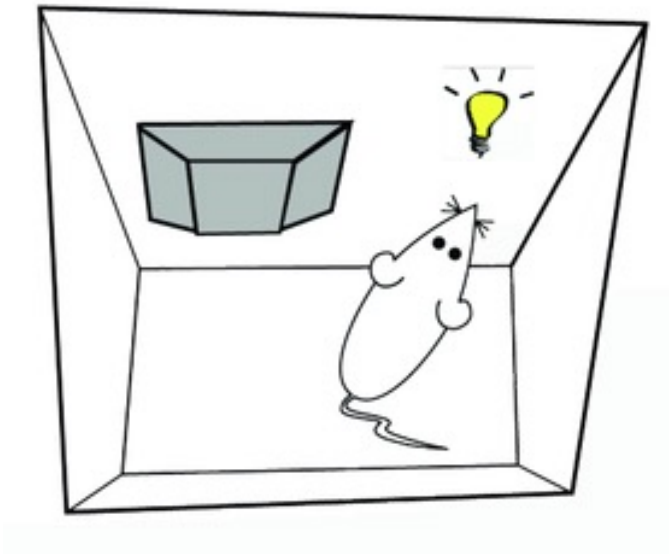
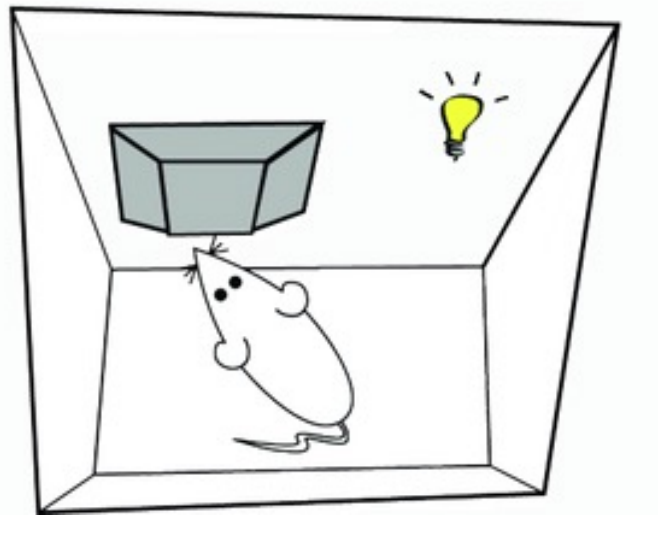


Goal-Tracking

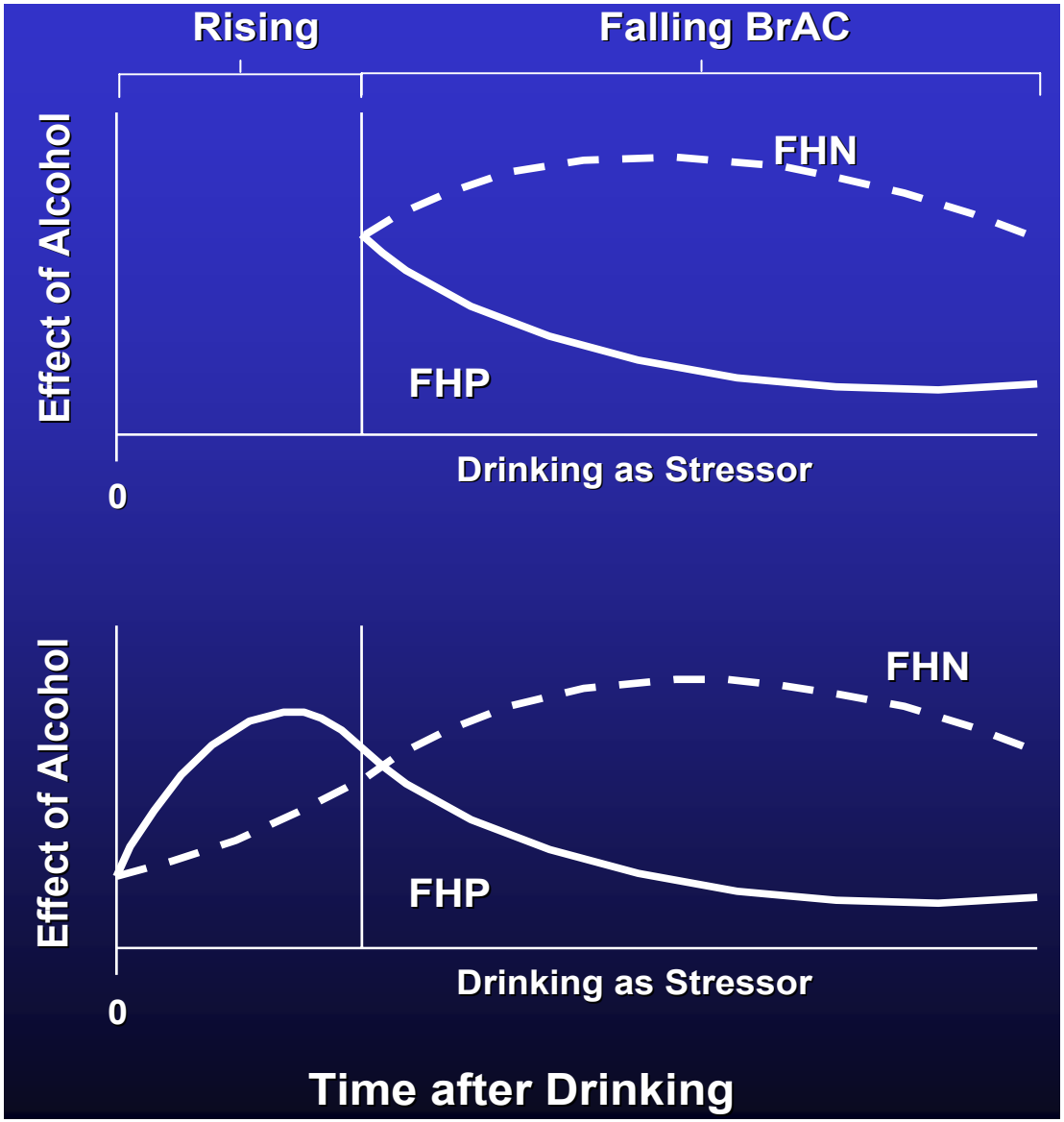


Goal-tracking phenotype – conditioned approach and appetitive responses to reward delivery (e.g., Flagel, Akil, & Robinson, 2009 ; Robinson & Flagel, 2009; Robinson et al., 2014)

Human Parallel Phenotype: Sign-Tracking

Among LS drinkers, alcohol cues appear to elicit conditioned appetitive motivational responses **reminiscent of sign-tracking**.

Limitations of Previous Research



Low Level of Response Model (Schuckit et al., Schuckit, 1980; 2009)

Differentiator Model (Newlin & Thompson, 1990; also see King et al., 2011, 2014, 2016)

Limitations of Previous Research

- No previous research has examined whether the increased alcohol cue reactivity profiles observed among low-sensitivity drinkers are associated with reduced sensitivity to alcohol's sedating-like effects, enhanced sensitivity to alcohol's stimulating-like effects, or both.

Limitations of Previous Research

- Cues are almost never presented in meaningful drinking contexts (e.g., Fey et al., 2017; Pronk et al., 2015; Pulido et al., 2010; Stauffer et al., 2017).

Limitations of Previous Research

- Affiliation with heavy-drinking peers (Schuckit et al., 2005; Schuckit et al., 2016)
  - It could be that alcohol cues presented in a social context are particularly likely to exacerbate ACR among LS individuals.

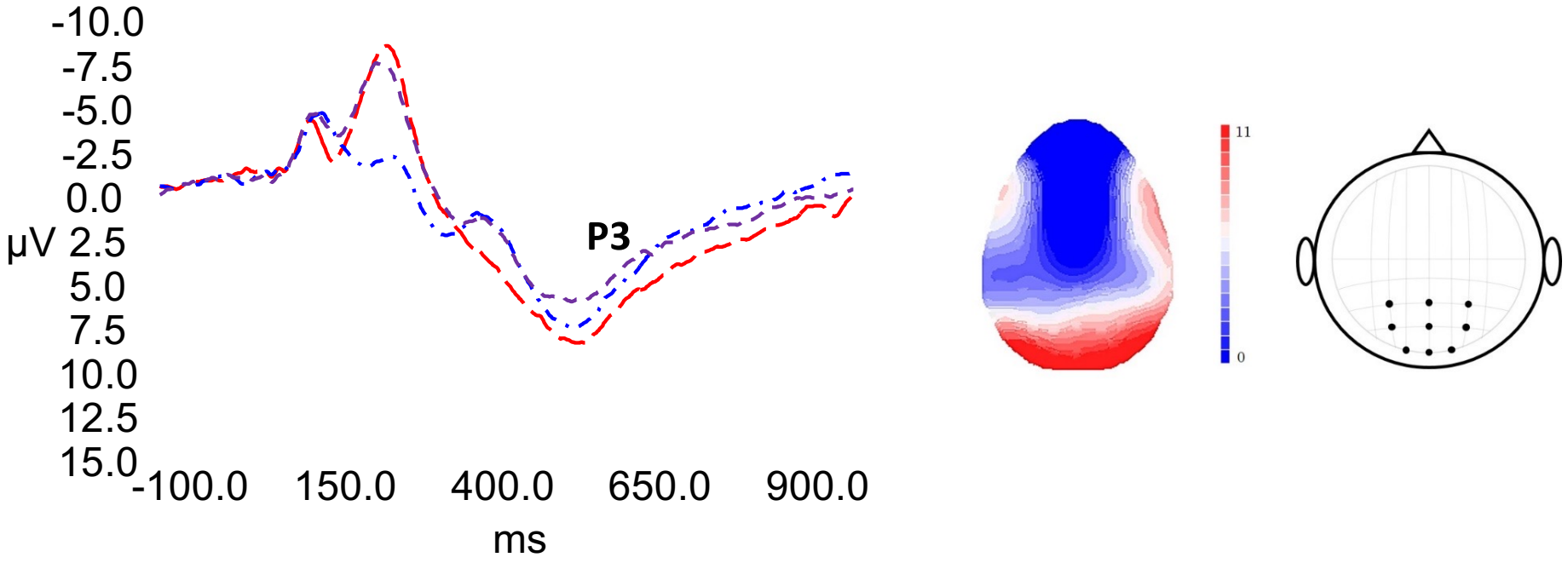
OVERVIEW OF THE PRESENT STUDY AND HYPOTHESES

Overview

- The current study examined the extent to which variability in two alcohol response phenotypes (i.e., enhanced sensitivity to lower-dose or stimulating effects and blunted sensitivity to higher-dose or sedating effects) is associated with enhanced alcohol cue-reactivity, as well as whether this reactivity varies according to contexts in which cues are presented.

Overview

- Individual differences in alcohol cue-reactivity



- Neurophysiological marker of the motivational significance of a stimulus

  (e.g., Begleiter, Porjesz, Chou, & Aunon, 1983; Franken, Van Strien, Bocanegra & Huijding, 2011; Nieuwenhuis et al., 2005)

Hypotheses

- Alcohol sensitivity scores reflecting enhanced sensitivity to lower-dose/stimulating effects and/or blunted sensitivity to higher-dose/sedating effects would be associated with the greatest alcohol cue P3 reactivity

- Alcohol cue P3 reactivity would be most pronounced, particularly among individuals with a differential alcohol response profile, in response to alcohol-related images including people drinking in naturalistic drinking contexts, especially those including multiple people.

METHODS

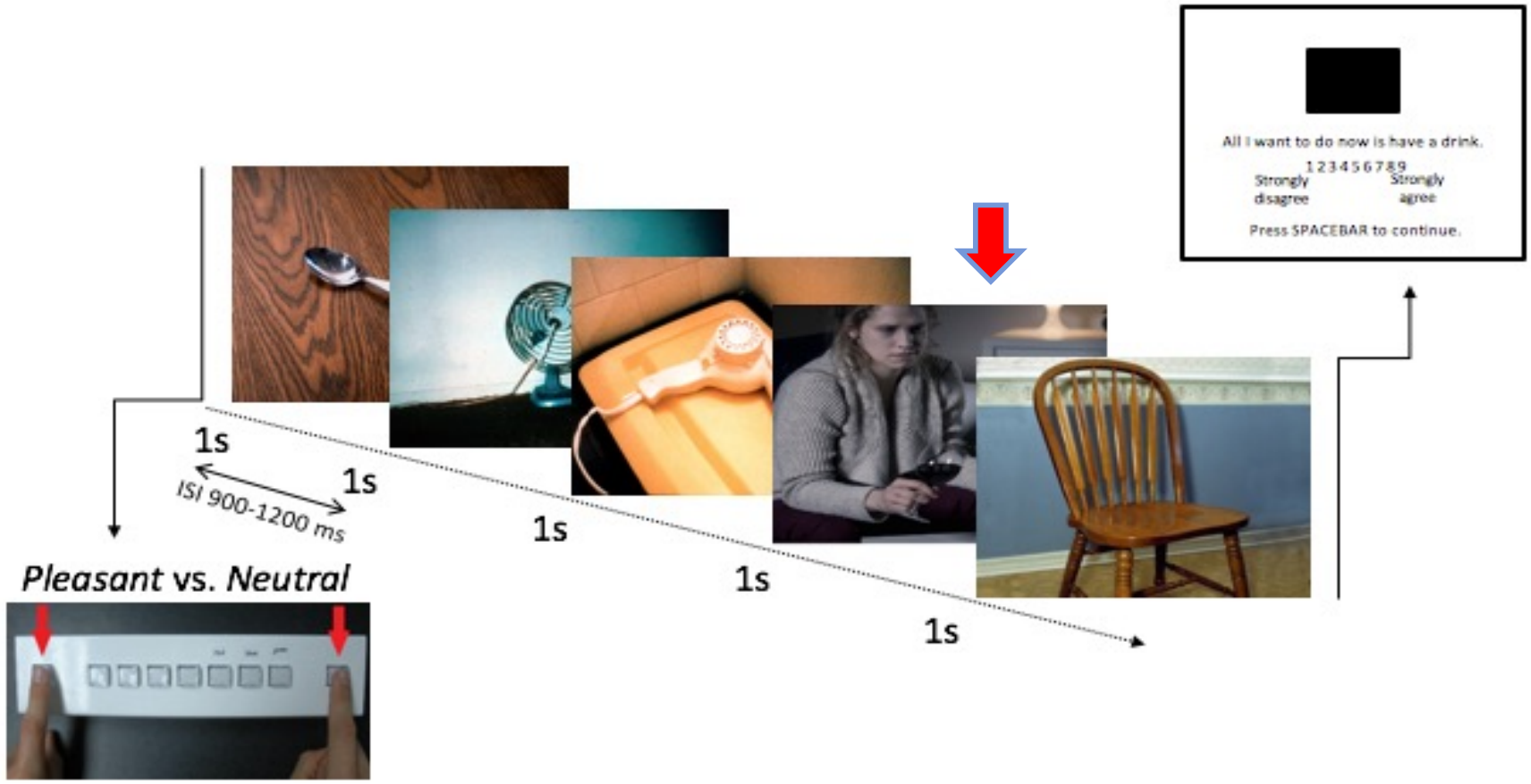
Participants

- 80 undergraduate students – Introductory Psychology
  - 47 female
  - 18 to 33 years-old
  - 90% Whites
- Exclusion criteria:
  - Younger than 18 years-old
  - History of head injury or neurologic disease
  - Hair styles that would make EEG data recording unusually difficult
- Compensated with course credit

Materials and Measures

- Picture-viewing oddball task
- Self-assessment manikin – SAM (Bradley & Lang, 1990)
- Online survey (programmed using Qualtrics)
  - Background and basic demographic information
  - Drinking Motives Questionnaire-Revised (Cooper, 1994)
  - Alcohol Sensitivity Questionnaire (Fleming et al., 2016)
  - Emotion Regulation Questionnaire (Gross & John, 2003)
  - Affect Balance Scale (Bradburn, 1969)
  - BIS/BAS scales (Craver & White, 1994)
  - Dampening of Positive Emotions Scale

Picture-Viewing Oddball Task



Materials and Measures

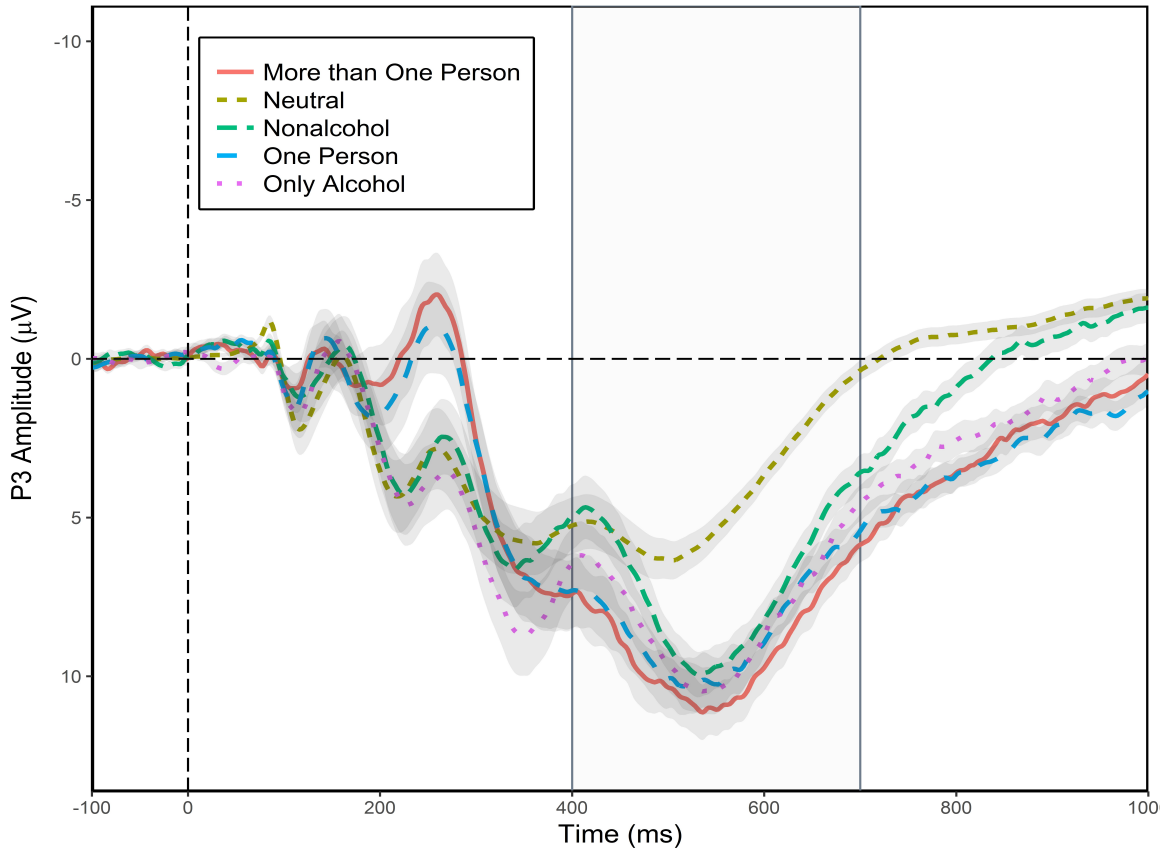
– Picture-viewing oddball task

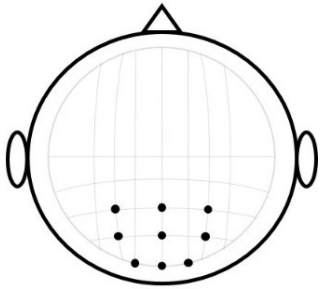
Materials and Measures

- Alcohol Sensitivity Questionnaire (ASQ)
  - 9 items – effects of alcohol often associated with *lighter drinking* and *stimulation* (**ASQ-L**)
    - "Do you ever become *more talkative* after drinking alcohol?"
    - "If yes, what is the minimum number of drinks you could consume before becoming more talkative?"
  - 6 items – effects most often associated with *heavier drinking* and *sedation* (**ASQ-H**)
    - "Do you ever pass out after drinking alcohol?"
    - "If yes, what is the maximum number of drinks you could consume without passing out?"
  - **Higher ASQ scores indicate lower alcohol sensitivity**

RESULTS

Waveforms

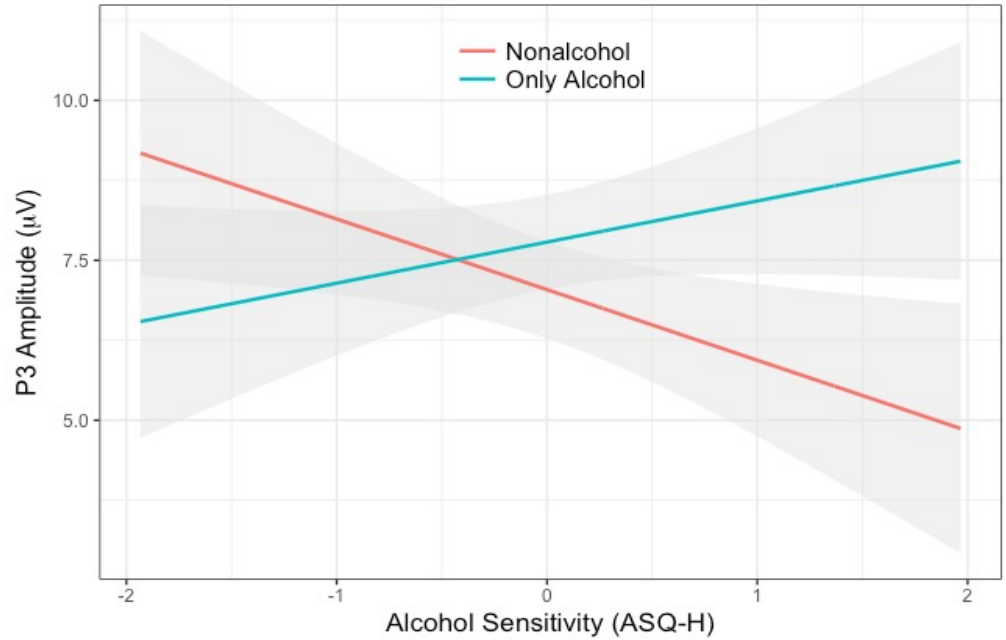


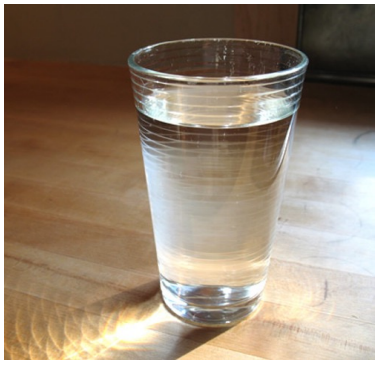


Averaged waveforms across electrodes P3, Pz, P4, PO3, POz, PO4, O1, Oz, and O2.

Alcohol P3 Reactivity and Alcohol Sensitivity

- To test the hypothesis whether ASQ-L and ASQ-H scores would be associated with enhanced alcohol P3 reactivity but not P3 reactivity to nonalcohol cues, controlling for sex, age, and AlcQF.





ASQ-H X Image Type (Only Alcohol vs. Nonalcohol) $F(1, 73.774) = 5.14$, $p = .026$

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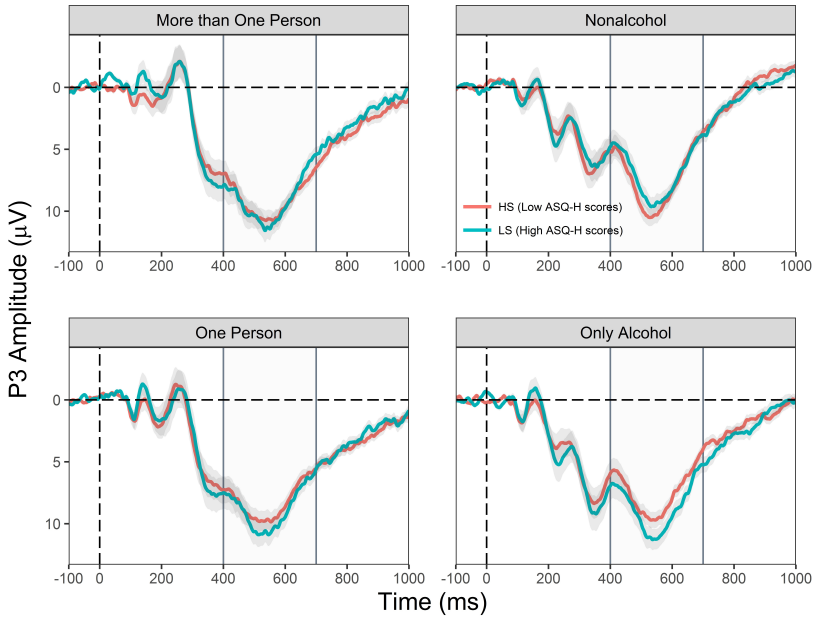

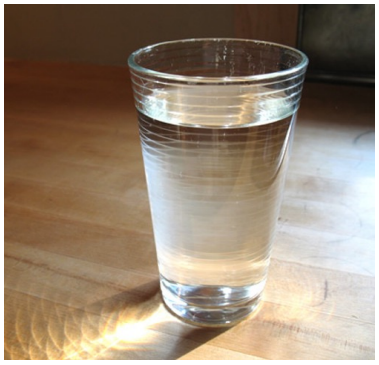

ASQ-H X Image Type (Only Alcohol vs. Nonalcohol) $F(1, 73.774) = 5.14$, $p = .026$

Alcohol P3 Reactivity, Alcohol Sensitivity, and People Drinking

- To test the hypothesis whether associations between alcohol sensitivity and alcohol P3 reactivity are potentiated when alcohol cues are shown in naturalistic drinking contexts, controlling for sex, age, and AlcQF.
  - *Image Type, F(1, 73.838) = 6.42, p = .013 --> People > Only Alcohol*
  - *ASQ-H X Image Type (People vs. Only Alcohol), F(1, 73.692) = 3.22, p = .077 --> People (b = -.42, SE = .83, t[73.086] = -.51, p = .612) vs. Only Alcohol (b = .64, SE = .86, t[73.096] =.75, p = .459, 95% CI [-1.08, 2.36])*



Alcohol P3 Reactivity, Alcohol Sensitivity, and Social Context vs. Privat Context

- To test whether ASQ-L and ASQ-H scores were differentially associated with P3 responses to images of multiple people drinking in social settings vs. people drinking alone in more private settings, controlling for sex, age, and AlcQF.
  - We failed to find that ASQ scores were differently related to P3 elicited by images differing in social (more than one person) vs. private settings (one person).

Conclusions

Conclusions

- Results indicated that ASQ scores reflecting sensitivity to higher-dose or sedating-like effects were differentially associated with P3 to alcohol cues and P3 reactivity elicited by nonalcohol cues in opposing directions.

- This finding extends earlier research by suggesting that previous evidence linking overall LS with enhanced incentive salience for alcohol-related cues is driven primarily by blunted sensitivity to higher-dose or sedating-like effects of alcohol.

Conclusions

- That is, individuals with blunted sensitivity to higher-dose or sedating-like effects might be particularly susceptible to incentive salience sensitization and enhanced attribution of incentive of alcohol-related cues. **Why?**

1. LS individuals --> The reinforcing and rewarding effects outweigh the negative and unpleasant effects of drinking
   a) Research on hangover symptoms (Piasecki et al., 2012)
   b) Research on alcohol consequences – regretted sex (Hone et al., 2017)

2. LS individuals --> Less intoxicated and impaired --> failure of signal to stop

Conclusions

- That is, individuals with blunted sensitivity to higher-dose or sedating-like effects might be particularly susceptible to *incentive salience sensitization* and *enhanced attribution of incentive of alcohol-related cues*. **Implications?**

1. Practical implications both for prevention and treatment

   a) Individuals with blunted sensitivity to higher-dose/sedation-like alcohol's effects may benefit more from certain types of interventions or treatment than others

   LS --> enhanced reactivity to alcohol cues --> craving

   Effective treatments: naltrexone and disulfiram

Conclusions

- Contrary to this prediction, pictures representing people drinking, whether alone or in groups, did not potentiate the effects of the two alcohol sensitivity phenotypes on ACR-P3.
  - Marginally significant interaction
    - Positive association between ASQ-H – P3 elicited by Only Alcohol
    - Negative association between ASQ-H – P3 elicited by People
  - Consistent with previous studies (Forestell et al., 2012; Miller & Fillmore, 2010)
  - Explanation: Dissociation between natural reinforcers (such as social interaction) and alcohol-related reinforcers (Goldstein & Volkow, 2011; MacKillop et al., 2010a, 2010b; Murphy & MacKillop, 2006)

Limitations

- Differing numbers of images across the image categories
  - 20-30 usable trials to maintain acceptable signal-to-noise ratio
- Absence of images of alcohol cues completely devoid of any naturalistic context
  - We cannot draw any conclusions concerning the effects of the physical setting on ACR-P3 amplitude
- Absence of depicting people drinking nonalcoholic beverages
  - We could not separate effects of social context from effects of beverage contents on P3 amplitude

Advantages

- The current study was the first to separately estimate associations between two theoretically distinct subjective response profiles and P3 amplitude
- Modeling both ASQ subscales --> to test specific and unique associations with P3 amplitudes
- Controlling for alcohol involvement --> to avoid the confounding of different levels of drinking
- The inclusion of stimuli representing naturalistic drinking contexts to enhance the ecological validity of the findings

Take Home Message

- The relationship between alcohol sensitivity and ACR-P3 is primarily driven by blunted sensitivity to the higher-dose/sedation-like effects.
- This association emerges for alcohol cues presented without people, but not when the cues depict people drinking
- The findings are consistent with the idea that individuals with blunted sensitivity to higher-dose/sedation-like effects might be particularly susceptible to incentive salience sensitization.
- The possibility that individuals at increased AUD risk due to blunted alcohol sensitivity show reduced reactivity to natural reinforcers, such as social interactions

Thank you!