DIFFERENTIAL BRAIN RESPONSES TO ALCOHOL-RELATED AND NATURAL REWARDS ARE ASSOCIATED WITH ALCOHOL USE AND PROBLEMS: EVIDENCE FOR REWARD DYSREGULATION

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SUSTANCE USE DISORDERS AND REWARD CUES

Individuals with SUDs and heavy users have *blunted* reactivity to non-drug-related rewards and *enhanced* reactivity to drug-related cues.

Natural Reinforcers

Drug-Related Cues

INFLUENCIAL THEORETICAL PERSPECTIVES OF ADDICTION

The incentive-sensitization theory of addiction (Berridge & Robinson, 1993) posits that cues signaling drug availability take on incentive value of the drugs themselves.

Reward-deficit models posit that risk for drug use is conferred by blunted incentive-motivational value of natural (i.e., nondrug) reinforcers.

- Reward-deficiency hypothesis (Blum et al., 1996, 2013)
- Allostatic model (Koob & Le Moal, 2001, 2008)

Behavioral economic and value-based decision-making models (Bickel et al., 2014; Field, 2020) assert that the ratio of drug-free and drug reward is critical to addiction.

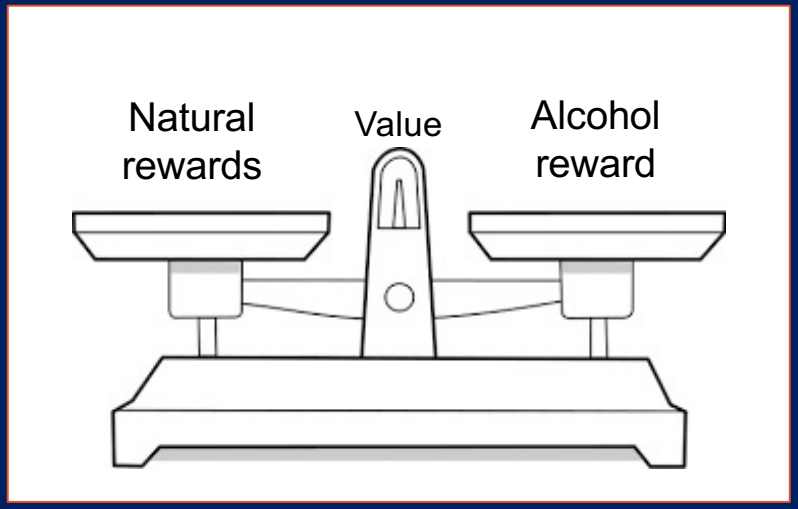
LIMITATIONS OF PREVIOUS RESEARCH

Even though previous research demonstrates that heavy drinkers and individuals with alcohol use disorder (AUD) typically show enhanced reactivity to alcohol-related cues and blunted reactivity to natural reinforcers (e.g., sex, food, money), these indices show low predictive power and inconsistent associations with measures of intensity of use, craving, and likelihood of relapse.

Witteman et al. (2015) *Psychopharmacology*
Rohsenow et al. (1994) *J Consult Clin Psychol.*
Field, Marhe & Franken (2014) *CNS Spectrums*

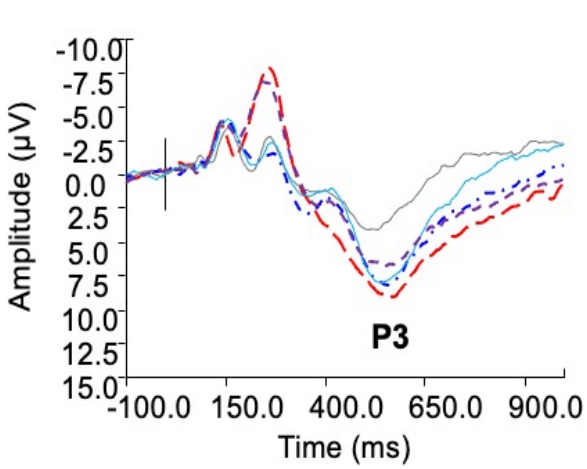
THE CURRENT STUDY

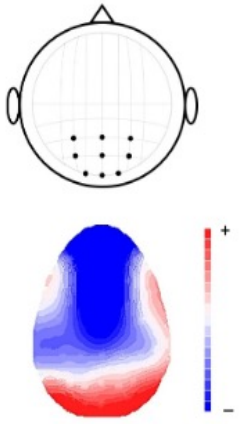
The current study examined reward dysregulation P3–a neurophysiological response representing differential reactivity to alcohol cues and reactivity to natural rewards–as a potential neurobiobehavioral marker of problematic drinking and AUD risk.



WHAT IS THE P3 (OR P300) OF THE ERP?

Individual differences in reactivity to stimuli: P3 amplitude of the ERPs





Source: http://www.hanix.net/En/Products/info/id/100.html

Neurophysiological marker of the incentive salience or motivational significance of a stimulus (e.g., Begleiter, Porjesz, Chou, & Aunon, 1983; Franken et al., 2011).

HYPOTHESES

H1: P3 amplitude elicited by alcohol cues (ACR-P3) would be positively associated with alcohol use and problems.

H2: P3 amplitude elicited by natural rewards (Reward-P3) would be negatively associated with alcohol use and problems.

H3: The *difference* in the ACR-P3 – Reward-P3 (i.e., *Reward dysregulation P3*) would be more strongly associated with alcohol use and problems.

H4: Reward dysregulation P3 would better differentiate at-risk individuals from low/moderate-risk drinkers than either of its constituent components.

METHODS

PARTICIPANTS

156 nondependent young adults – University of Missouri and surrounding community

- 18 to 30 years-old
- Mean age = 21.91 (*SD* = 2.97)
- 61% female
- 88% White

Eligibility criteria:

- Fluent in English
- Aged between 18 to 30 years old
- No current or past attempts to quit drinking
- No alcohol withdrawal symptoms
- No history of head trauma or neurological disorder

Compensated with $10 per hour

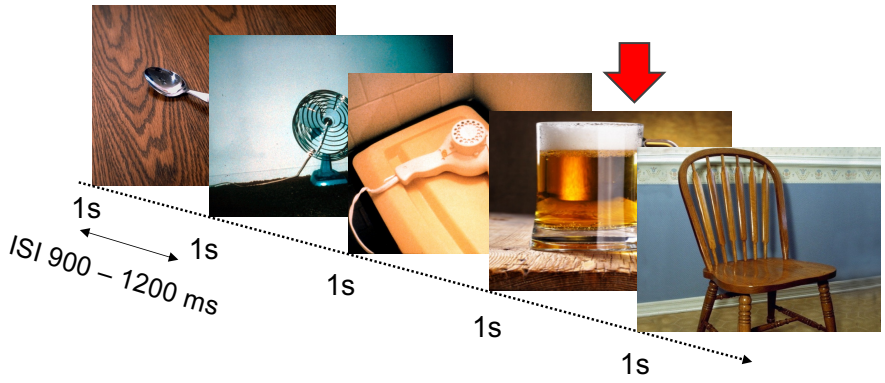
MATERIALS AND MEASURES

Picture-viewing 'oddball' task (e.g., Bartholow et al., 2010; Martins et al., 2019)

Alcohol-related self-report measures :

- Alcohol use (NIAAA, 2003):
  - Past 12 mo. drinking quantity and frequency
- Binge drinking (NIAAA, 2003):
  - Past 12 mo. binge-drinking frequency
- Heavy drinking (NIAAA, 2003):
  - Past 12. mo. max. drinks in 24 hours
- Alcohol problems (YAACQ; Kahler et al. 2005)
  - Young Adult Alcohol Consequences Questionnaire (Kahler et al., 2005)
  - Levels of risk for harmful and hazardous drinking (Read et al., 2016)
    - Low/moderate level of risk: $n = 77$ (YAACQ score ≤ 15)
    - High level of risk: $n = 26$ (YAACQ total score ≥ 16)

PICTURE-VIEWING ‘ODDBALL’ TASK

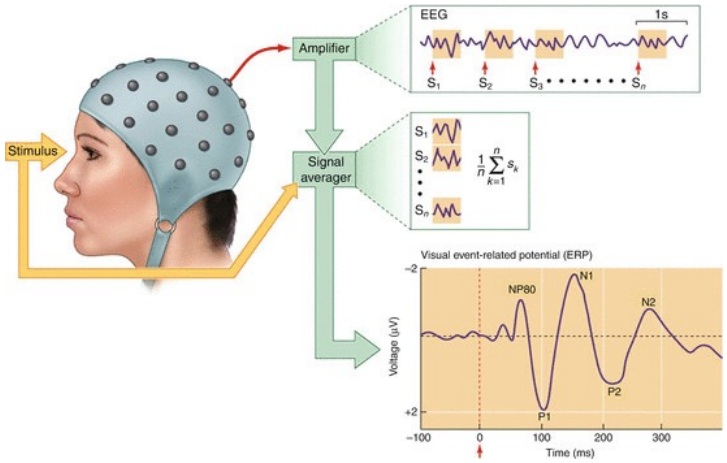


Pleasant vs. Neutral

Adventurous

Erotic

Alcohol



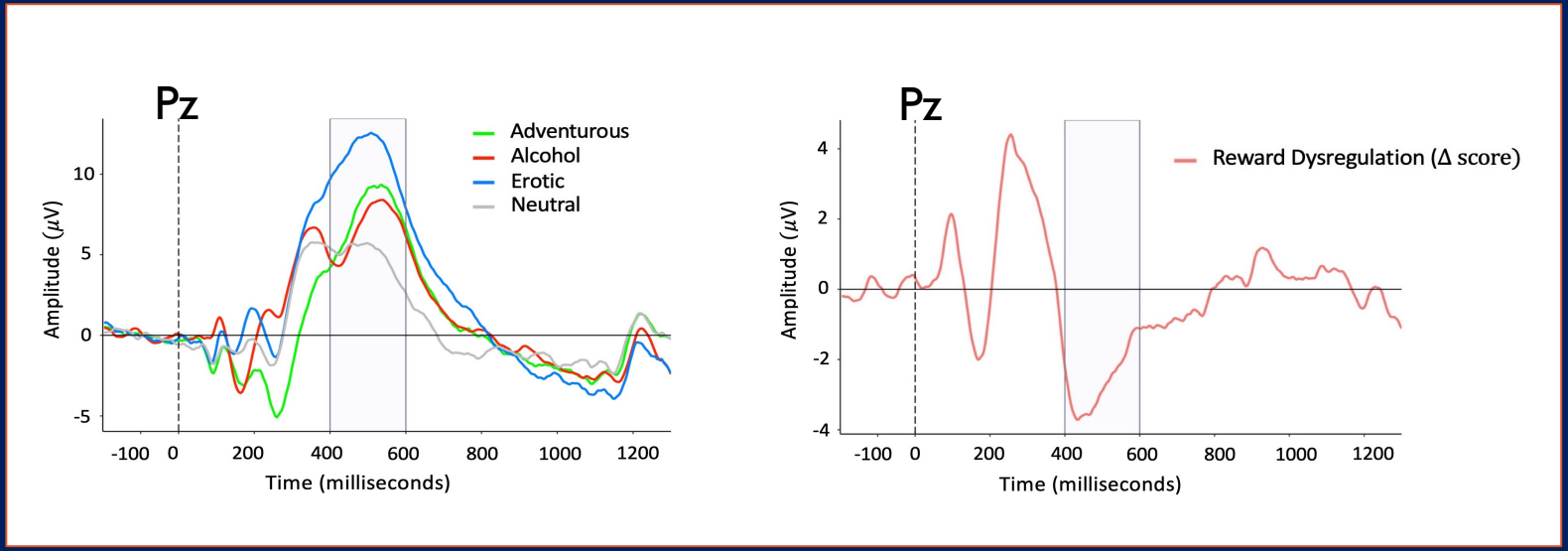
Source: https://sciencebeam.com/accessories-fnirs-bci-erp-sleep-mobo/

Bartholow et al. (2010) *Psychol Addict Behav.*

Martins et al. (2019) *Alcohol Clin Exp Res.*

ERP WAVEFORMS

Grand-averaged, stimulus-locked waveforms at channel Pz:



P3-ERP amplitude measures:

- P3 amplitude elicited by alcohol cues => ACR-P3
- P3 amplitude elicited by naturals rewards = erotic + adventurous => Reward-P3
- ACR-P3 – Reward-P3 => Reward dysregulation P3

RESULTS

REGRESSION MODELS PREDICTING DRINKING OUTCOMES

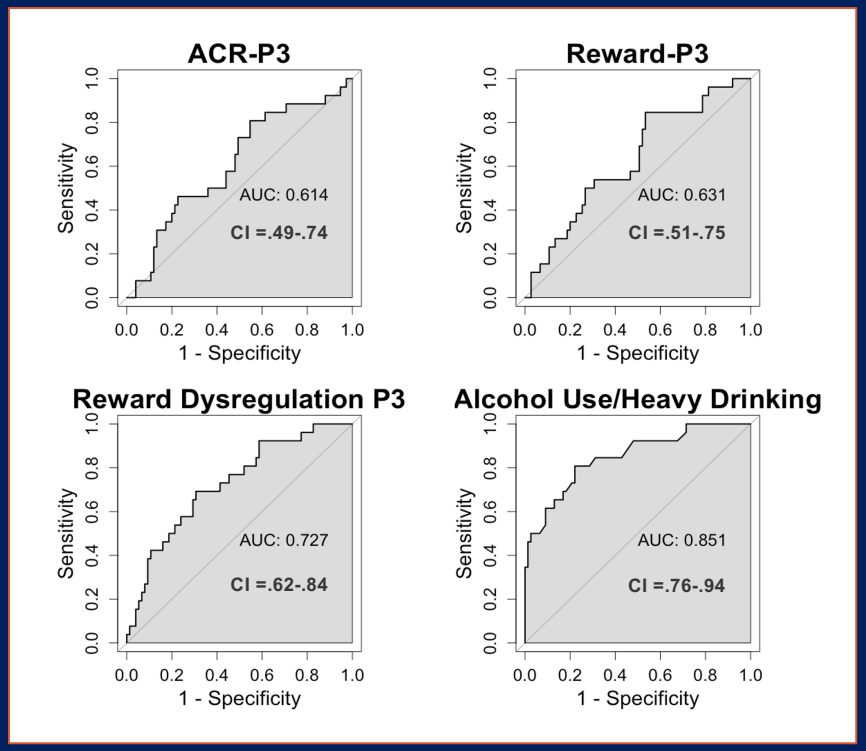
Regression models predicting drinking outcomes:

Model	Alcohol Use				Binge Drinking				Heavy Drinking				Alcohol Problems			
	Adj. R^2	*b*	*SE b*	*p*	Adj. R^2	*b*	*SE b*	*p*	Adj. R^2	*b*	*SE b*	*p*	Adj. pseudo-R^2	*b*	*SE b*	*p*
Model 1: ACR-P3	.11				.09				.07				.15			
ACR-P3		0.53	0.34	.115		**0.11**	**0.04**	**.004**		0.09	0.12	.422		**0.03**	**0.01**	**.014**
Model 2: Reward-P3	.09				.03				.09				.14			
Reward-P3		-1.71	2.01	.398		-0.12	0.24	.619		-1.33	0.68	.051		0.01	0.08	.855
Model 3: ACR-P3 + Reward-P3	.12				.12				.11				.16			
ACR-P3		**0.90**	**0.38**	**.021**		**0.16**	**0.04**	**<.001**		**0.27**	**0.13**	**.040**		**0.05**	**0.02**	**.004**
Reward-P3		-4.33	2.28	.059		**-0.59**	**0.26**	**.024**		**-2.12**	**0.77**	**<.001**		-0.13	0.09	.150
Model 4: Reward Dysregulation P3	.13				.11				.11				.15			
Reward Dysregulation P3		**4.15**	**1.68**	**.015**		**0.68**	**0.19**	**<.001**		**1.58**	**0.57**	**<.001**		**0.17**	**0.07**	**.018**

Note. All ordinary least squares (OLS) regression models were estimated controlling for age (in years), sex (female/male), and race/ethnicity, In addition, regression models predicting alcohol problems controlled for an alcohol use/heavy drinking composite (including alcohol use, binge drinking and heavy drinking).

ROC CURVES: CLASSIFICATION PERFORMANCE

ROC curves summarizing classification performance in discriminating high risk:



Reward dysregulation P3 responses successfully differentiated high-risk from low/moderate-risk drinkers (AUC = .73, 95% CI = .62-.84), and did so almost nearly as well as an alcohol use/heavy drinking composite (AUC = .85, 95% CI = .76-.94): AUCs = .73 vs. .85; *Z* statistic = -1.83, *p*-value = .067.

CONCLUSIONS

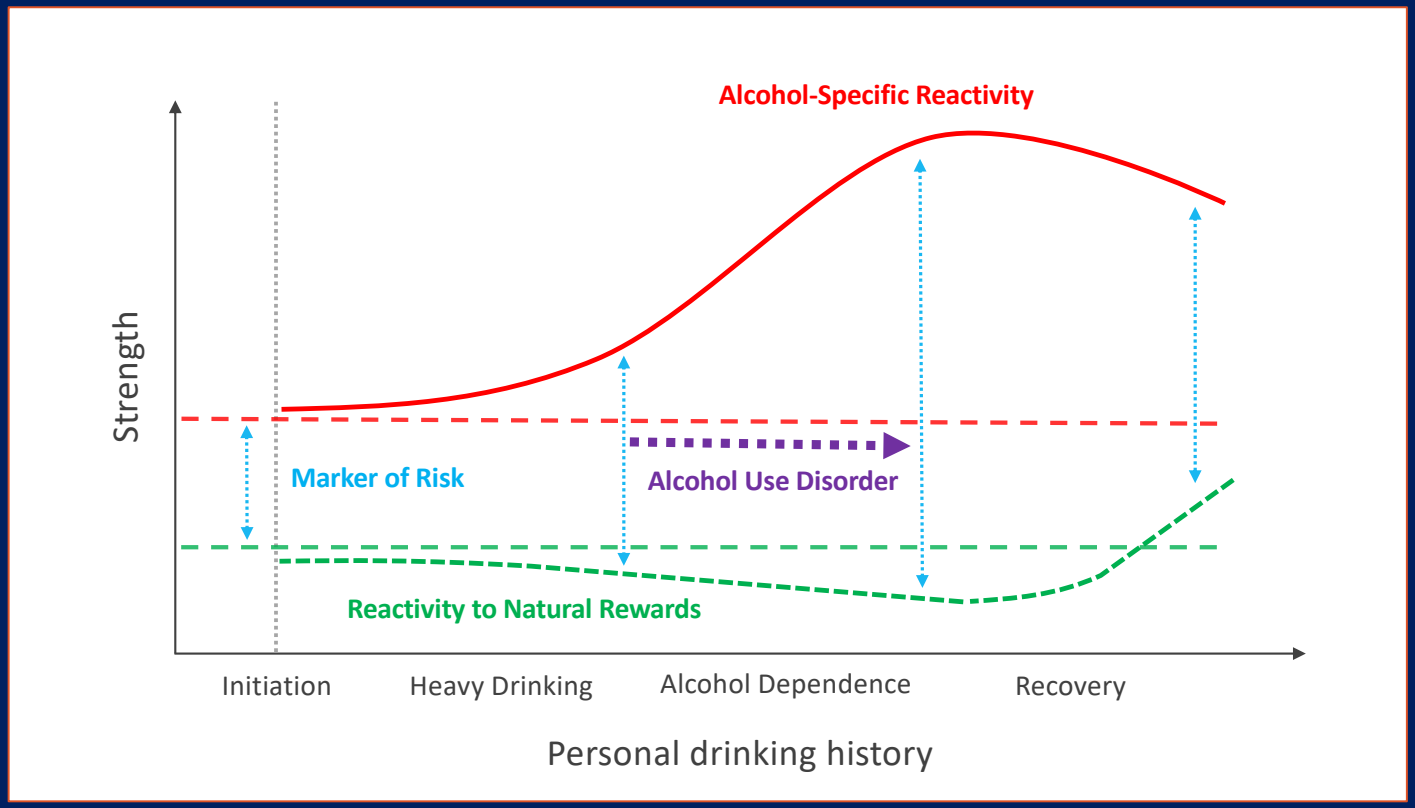
TAKE HOME MESSAGES

Consistent with its conceptualization as a neurobiobehavioral marker of risk for heavy and problematic drinking, the *reward dysregulation P3* was quite robustly and consistently associated with all drinking outcomes.

Reward dysregulation P3 showed some ability to discriminate individuals at risk for problematic drinking and did so with similar accuracy as an alcohol use/heavy drinking composite, a "gold standard" measure of risky drinking.

THEORETICAL IMPLICATIONS

Theoretical Model of Vulnerability for Alcohol Dependence:



CLINICAL SIGNIFICANCE

The utility of neurophysiological measures (i.e., reward dysregulation P3) for both clinical diagnosis and vulnerability assessment beyond that provided by self-report measures.

The current findings can contribute to the development of both prevention programs and intervention efforts aimed at reducing the burden of alcohol misuse and AUD.

LIMITATIONS

- The inability to resolve the etiology of the reward dysregulation P3.
- The extent to which the Reward-P3 and ACR-P3 share sources in the reward processing brain circuits is not clear.
- The sample homogeneity in terms of demographic characteristics.
- Limited number and content of stimuli used to elicit P3-ERP responses.

FUTURE DIRECTIONS

- To examine reward dysregulation P3 and its relation to drinking outcomes in more diverse populations and expand the types of reward-relevant cues used (e.g., money).
- To clarify the ontogeny of the reward dysregulation phenotype using longitudinal and/or genetically informed designs (e.g., twin studies).
- To evaluate the specificity vs. generality of its effects–in particular, whether reward dysregulation P3 indexes risk for problematic drinking specifically or is associated with broader, transdiagnostic traits (e.g., externalizing proneness).

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NIH National Institute on Alcohol Abuse and Alcoholism

POPH QUALIFICAR É CRESCER.

QREN QUADRO DE REFERÊNCIA ESTRATÉGICO NACIONAL PORTUGAL 2007-2013

GOVERNO DA REPÚBLICA PORTUGUESA

UNIÃO EUROPEIA Fundo Social Europeu

THANK YOU!