Stress-induced IV Alcohol Self-Administration Behavior: A Human Experimental Model for Stress-cue Reactivity and Risk for Alcohol Use Disorder

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INTRODUCTION

The relationship between stress and alcohol use and problems has been well supported in dependent drinkers (Sinha et al., 2009; Sinha et al., 2011). However, the effects of stress on alcohol use and problems in non-dependent drinkers are less clear.

Computer-assisted self-infusion of ethanol (CASE) is method that measures alcohol self-administration behavior that is driven primarily by the pharmacological effects of alcohol (Zimmermann et al., 2012). CASE has been used to examine several determinants of alcohol intake behavior including family history of alcoholism, recent drinking history, gender and personality characteristics.

Methodological Question Being Addressed: To develop a model that measures stress-induced self-administration of ethanol using personalized guided imagery scripts. Specifically, do stress and alcohol-related cues increase self-administration behavior for alcohol in non-dependent drinkers?

Schematic of CASE Paradigm
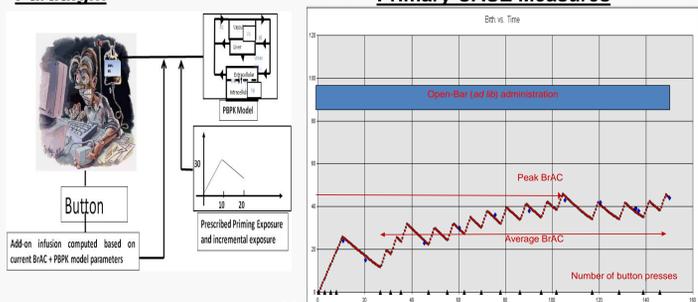
Typical CASE Session Data Output Showing Primary CASE Measures
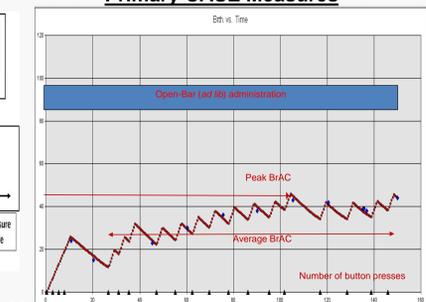
METHODS

- Data were obtained from 14 healthy, 21-45 year-old, non-dependent drinkers participating in NIAAA clinical studies.
- Participants were stratified into two groups: binge drinkers (N=7) and non-binge drinkers (N=7). Binge drinkers consumed 4+ drinks (for females) or 5+ drinks (for males) at least twice a month, as reported on the 90-day Time-Line Follow-Back during the screening evaluation.
- Participants were interviewed to create three 5-min audio recordings of personalized guided imagery scripts (Sinha, 2009) that were designed to induce acute stress, alcohol craving, and a neutral-relaxing state.
- Participants then returned for three separate CASE session visits.
- Each CASE session consisting of:
  - *Script (5 min):* Script-type was randomized across all sessions and were blinded to the researchers.
  - *Ad lib phase (125 min):* Subjects had free access to standardized IV alcohol infusions (maximum BrAC=100 mg%) immediately following the script.
- Serial measures of subjective response were taken throughout the session which included the Alcohol Urge Questionnaire (AUQ), Drug Effects Questionnaire (DEQ) and the Subjective Units of Distress Scale (SUDS).
- Serial blood draws were taken for cortisol (CORT) and adrenocorticotropic hormone (ACTH).
- Primary self-administration measures included total number of rewards, peak (PEAK) and average (AVG) breath alcohol concentration (BrAC) and total EtOH administered.
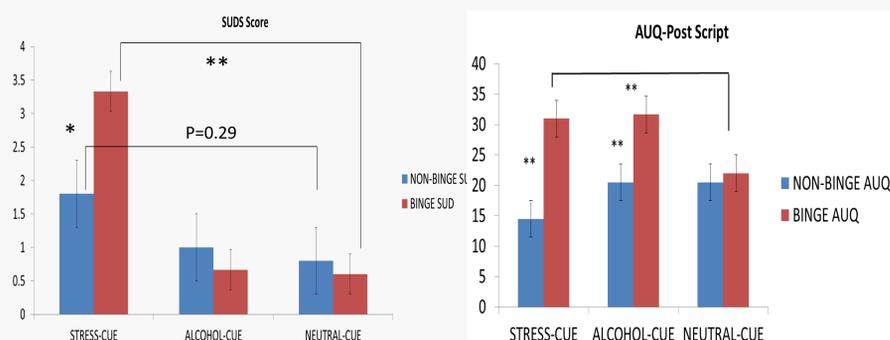
RESULTS

Subject Demographics (Mean ± SD)

|	Binge Drinkers (n=7)	Non-Binge Drinkers (n=7)	p
Age [years]	26.1 ± 5.2	27.0 ± 6.9	NS
AUDIT	5.9 ± 1.6	3.3 ± 1.1	<0.05
Total Drinks in 90 Days	107 ± 39	32 ± 23	<0.01
Total Drinking Days in 90 Days	31 ± 11	19 ± 14	<0.01
Drinks per Drinking Day in 90 Days	3.6 ± 1.4	1.7 ± 0.3	<0.01
Heavy Drinking Days in 90 Days[a]	9 ± 6.3	0.0 ± 0.0	<0.01

a: Heavy Drinking Day = 4 or more drinks for females and 5 or more drinks for males.

BINGE vs NON-BINGE DRINKERS

Scripts Effectively Induce Stress and Craving

IV Alcohol Self-Administration Measures

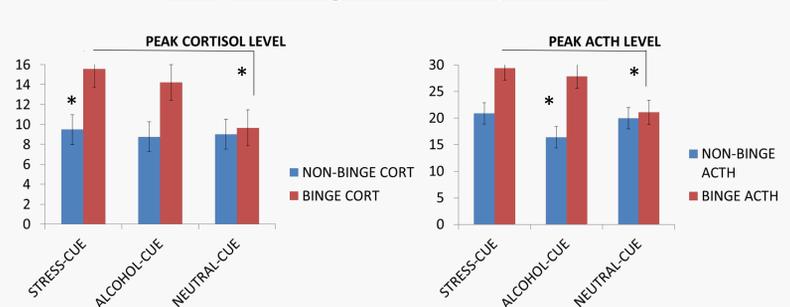### Subjective Response

Physiological Response
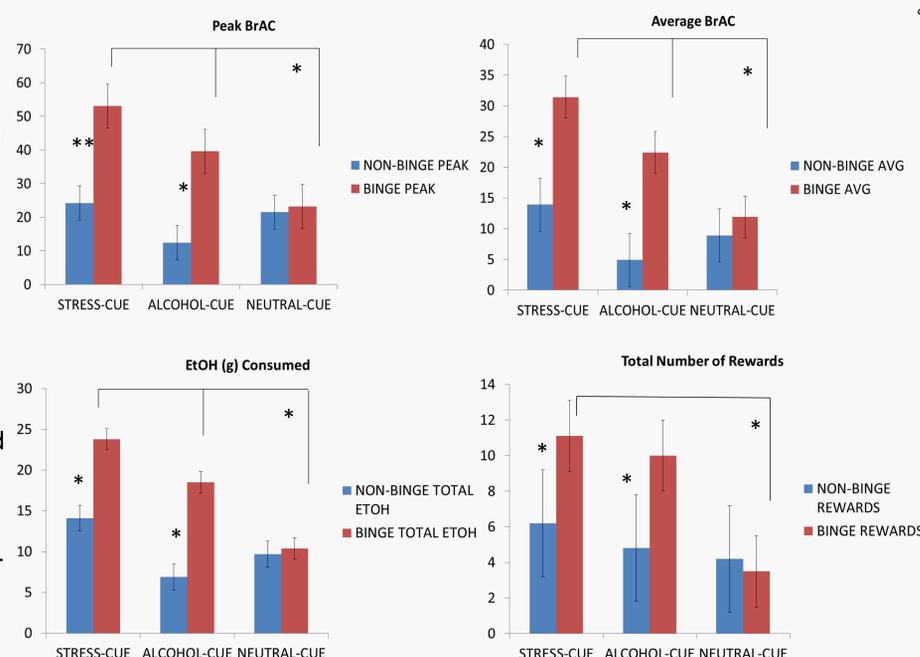
CONCLUSIONS

- These results are the first demonstration, to our knowledge, of stress-induced IV alcohol self-administration in non-dependent drinkers.
- The imagery scripts successfully induced reactivity following the stress-cue compared with the neutral-relaxing cue.
- Binge drinkers had greater measures of craving, ACTH, CORT, and IV-ASA compared to non-binge drinkers.
- These data may help explain the relationship between stress and alcohol-seeking behavior that may underlie risk for alcohol-related problems
- Comparisons between binge and non-binge drinkers may provide important information on potential triggers for excessive alcohol use in this sample of non-dependent drinkers.
- This method may complement pre-clinical models of alcoholism and serve as a translational tool to examine the effectiveness of novel pharmacological agents, including NK1 antagonists and CRH antagonists, on stress-induced IV-ASA and relapse, particularly in alcoholics with anxious traits.
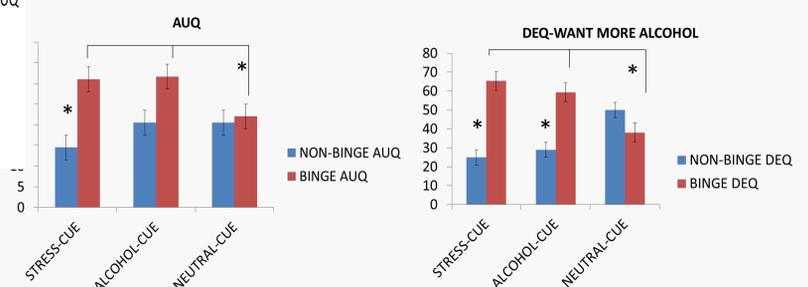
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