Exploring differences in **brain response** to emotionally negative images among **veterans** with **Alcohol Use Disorder**: Implications for **relapse**

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Introduction

- **Alcohol Use Disorder** (AUD) is a chronic disorder, characterized by a relapse-remit cycle, with grave health effects. AUD is also particularly common among US military veterans with more than 40% lifetime prevalence[1]
- Previous studies have implicated the **role of neural response to emotionally salient stimuli** as a potential factor in the development and maintenance of AUD[2]
- **Study aim:** to investigate whether archival fMRI data revealed differences between relapsers, abstainers, and controls in brain response to emotionally negative facial images

Methods

Data Source

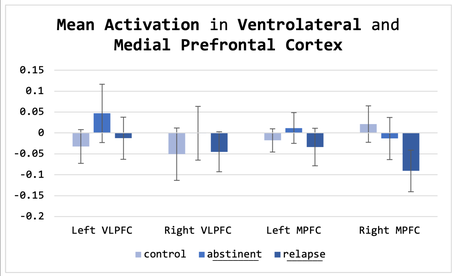
- Archival **fMRI and survey response data** from Dr. Padula's Brain Research on AUD and Veterans' Emotions (BRAVE) study

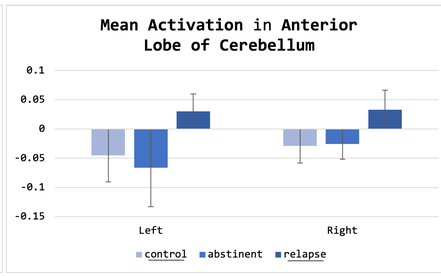
Subject Details

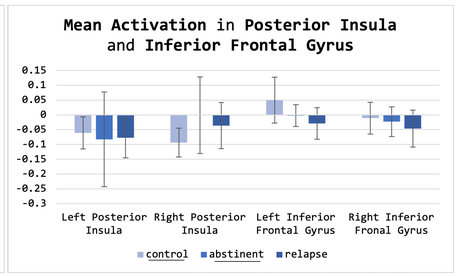
- We **age and sex matched** 10 control subjects with 10 subjects who relapsed within 6 months of treatment and 10 subjects who abstained throughout the 6 months following treatment. Matching was done with an optimization algorithm that minimized age differences across subject matches
- All subjects were US military **veterans**, and only the relapse and abstinent groups met criteria for AUD at the time of the study
- All subjects completed an **fMRI** scan while viewing the **Faces task**, which shows a variety of emotionally salient faces (fear, anger, disgust, sadness, and neutral). Example of fear shown on right

Analysis

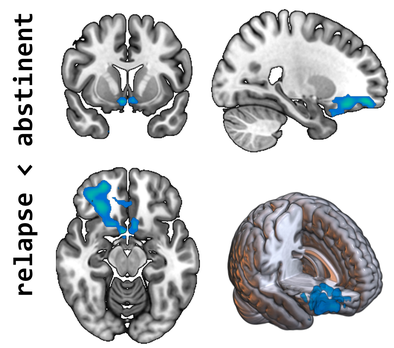
- Standard processing procedures for fMRI data were done in both **SPM and AFNI.** Statistical analyses were conducted in SPM to compare the **negative-emotion stimulus aggregation** (sadness, anger, disgust, fear) contrasted with **neutral facial stimulus** across the control, abstain and relapse groups
- For group comparison, we implemented a one-way **ANOVA** in SPM, followed by pairwise group comparisons

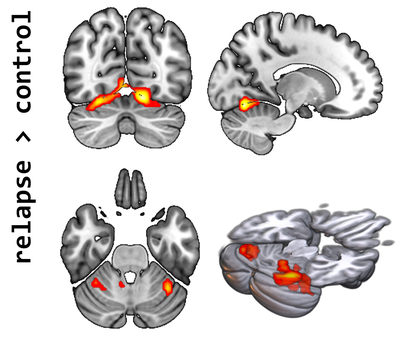


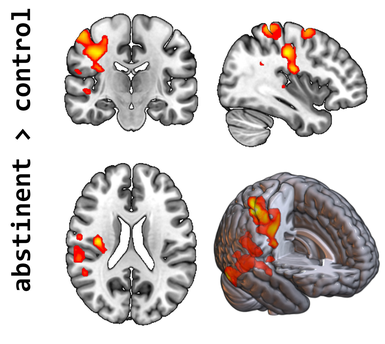


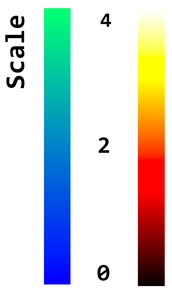


Underscores denote groups whose contrast is significant



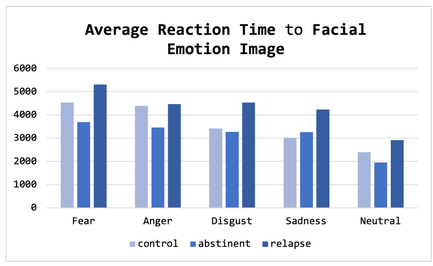






Results

In Short: among other findings, relapsers had more activation in the anterior lobe of **cerebellum** than controls, which may implicate cerebellar processing in both **affective** and **addictive systems**



Summary of Findings

- Our analysis focused on inter-group comparison for **values of contrast between negative-emotion** and **neutral stimuli**
- We found that: **(a)** the relapse group had less activation than the abstinent group in the **medial** and **ventrolateral prefrontal cortex**; **(b)** the relapse group had greater activation than the control group in the **anterior lobe** of the **cerebellum**; and **(c)** the abstinent group had greater activation than the control group in the **inferior frontal gyrus** and **posterior insula**
- All contrasts (a-c) had uncorrected p-values less than 0.05; other contrasts had uncorrected p-values above 0.05
- We also found the relapse group to have longer reaction times to emotionally negative facial images in a separate task (see chart to left)

Demographics

	Controls	Relapsers	Abstainers
n	10	10	10
Age ± SD	61.4 ± 13.3	60.1 ± 12.3	58.6 ± 10.7
Sex	9M 1F	9M 1F	9M 1F
Race	4 Black, 2 Asian, 2 White, 1 White/Native-American, 1 Other	7 White, 2 Mexican, 1 Other	3 Black, 5 White, 1 White/Native-American, 1 Pacific Islander
Ethnicity	1 Hispanic, 9 Non-Hispanic	4 Hispanic, 6 Non-Hispanic	1 Hispanic, 9 Non-Hispanic
DSM 5 Alcohol ± SD	0.8 ± 2.5	9.4 ± 2.2	10.4 ± 0.8

Discussion

- Group differences in cerebellar activity may provide evidence for an **interrelationship between sensorimotor, affective, and cognitive processing** which stands in line with notions[3] of a **Universal Cerebellar Transform** (UTC). The pronounced difference in cerebellar activity for relapse vs control/abstinent groups in combination with longer reaction times to negative emotions for the relapse group support the UTC-based interpretation that subjects who went on to relapse may have had cerebellar abnormalities which contribute to both emotional processing deficiencies as well as relapse outcomes
- Lower activation levels for relapsers in the **ventrolateral** and **medial prefrontal cortex** may provide evidence for further emotional processing deficiencies consistent with literature[4] on the role of the MPFC
- The **posterior insula** has been implicated in **self-awareness of emotion in the body**[5]. It may be the case that abstainers show greater activation in the posterior insula as a proxy for enhanced emotional awareness which contributes to their ability to **effectively manage negative emotion** and thereby abstain from alcohol

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