Understanding the co-emergence of PTSD and alcohol use: exploring time since trauma and the role of the vmPFC

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BACKGROUND

- Excessive alcohol use and posttraumatic stress disorder (PTSD) often co-occur.
- Two hypotheses to explain the potential underlying mechanisms of the relationship between these two variables are the susceptibility and self-medication hypotheses.
- Using a multi-site longitudinal study design, we explored the relative fit of each of these two theoretical models.
- Furthermore, neuroimaging data in response to a modified monetary reward task was used to determined whether neural correlates of reward explained the relationship between alcohol consumption and PTSD symptoms.

METHODS

- A cross-lagged panel model for alcohol consumption (PhenX Toolkit; quantity*frequency) and PCL-5 (PTSD Checklist for DSM-5) scores over five time points was conducted using Lavaan (v0.6-9) in RStudio (v1.4.1717) to determine the temporal association between these two variables.
- Reward-related neural activation was assessed at 2 weeks using functional magnetic resonance imaging (fMRI) during a modified monetary reward task and analyzed in *fMRIprep* and *SPM12.* Two group-level analyses were conducted:
  - Whole-brain voxelwise correlations
  - Connectivity analyses using CONN Toolbox (v21.a)

Table 1. Demographic and Clinical Characteristics n=286	
Variable	**Count (%)/Mean (SD)**
Sex (M/F)	107(37.4%)/179(62.6%)
Age (Years)	33.75 (12.61)
Race/ethnicity*	
Hispanic/Latin American	45 (15.8%)
White-American	102 (35.9%)
Black-American	123 (43.3%)
"Other" American	14 (5%)
Week 8 Alcohol Consumption	17.99 (51.07)
Month 3 PCL-5 Total Scores	23.31 (17.51)

Table 1. Breakdown of demographic and clinical characteristics of our participant sample. *n = 284

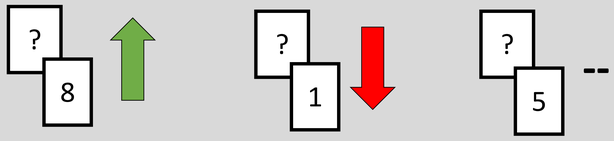

Fig. 1. Overview of the modified monetary reward task from Delgado et al., 2000

RESULTS

Changes in Alcohol Consumption and PCL-5 Total Scores Across Time

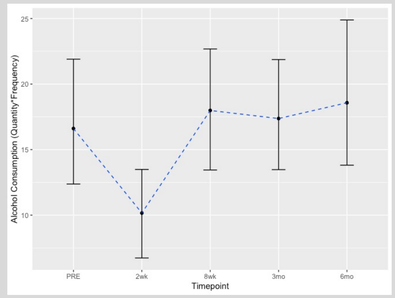

Fig. 2. Mean alcohol consumption (quantity*frequency) for each of the five time points.

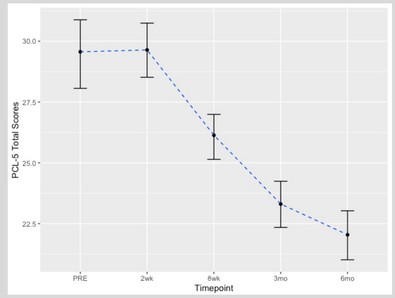

Fig. 3. Mean PCL-5 total scores for each of the five time points.

Cross-lagged Panel Model

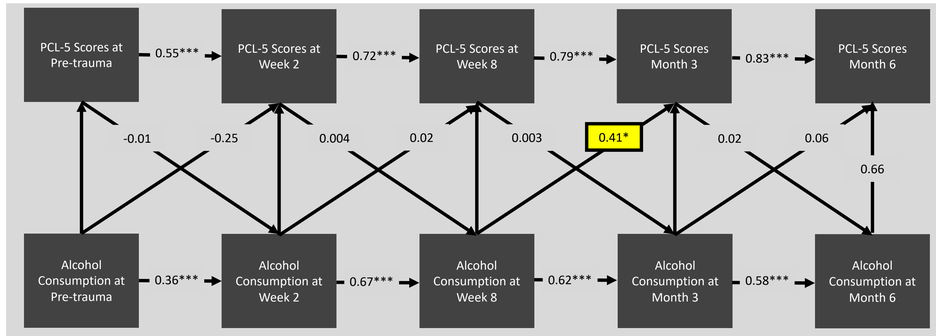

Fig. 4. Cross-lagged panel model. Testing whether alcohol consumption is the cause of PCL-5 total scores or PCL-5 total scores are the cause of alcohol consumption or whether alcohol consumption and PCL-5 total scores are simply correlated for reasons outside the model and if they tend to persist over time.
Alcohol consumption at week 8 significantly predicted PCL-5 total scores at month 3, B = .41, SE = .19, p = .03.

mPFC Activation is Correlated with Alcohol Consumption and PCL-5 Total Scores

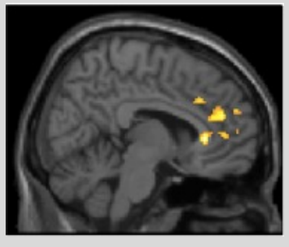

Fig. 5. Whole-brain voxelwise correlation between alcohol consumption at week 8 and brain activation during the gain versus loss contrast.

A significant positive correlation between alcohol consumption at week 8 and the medial prefrontal cortex (mPFC; [8, 30, 4], t = 3.48, z = 3.44, p < .001, K_E = 3) was found when examining the gain versus loss contrast.

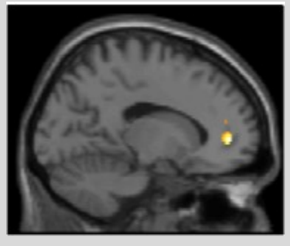

Fig. 6. Whole-brain voxelwise correlation between PCL-5 total scores at month 3 and brain activation during the gain versus loss contrast.

A significant negative correlation between PCL-5 total scores at month 3 and the mPFC (-14, 48, 2; t = 4.05, z = 3.99, p < .001, K_E = 10) was found when examining the gain versus loss contrast.

mPFC is Functionally Connected to Reward Neurocircuitry

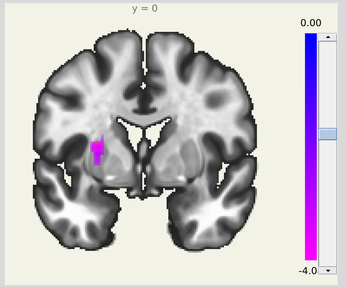

Fig. 7. Exploring the effect of alcohol consumption at week 8 on seed-based connectivity.
Given the similar overlap within the mPFC, we chose a bilateral BA32 structural ROI as our seed region and found significantly lesser functional connectivity between this seed and the left putamen.

(-26, 0, 12) K_E = 128
Voxel threshold: p < 0.005, p-unc = 0.0026
Cluster threshold: p < 0.05, p-unc < 0.001

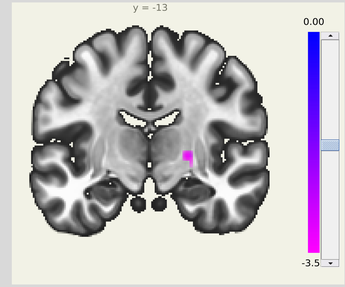

Fig. 8. Exploring the effect of PCL-5 total scores at month 3 on seed-based connectivity.
Similarly, using the same bilateral BA32 structural ROI as our seed, we found significantly lesser functional connectivity between this region and the right pallidum.

(24, -12, 0) K_E = 51
Voxel threshold: p < 0.005, p-unc = 0.04
Cluster threshold: p < 0.05, p-unc < 0.001

DISCUSSION

- This data provides a better understanding of the temporal relationship between the emergence of alcohol consumption and PTSD symptoms and provides evidence for the susceptibility hypothesis.
- We also discovered the potential importance of the mPFC and its functional connectivity with regions important in the reward neurocircuitry.
- Our findings suggest that there is lesser connectivity between the primary inhibitory region (mPFC) to brain regions responsible in mediating reward, perhaps contributing to the high comorbidity of these disorders.

FUTURE DIRECTIONS

- Our future work will seek to further explore the role of the vmPFC and reward neurocircuitry in the development and maintenance of these often-co-occurring diagnoses.

FUNDING

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