The Role of Unawareness, Volition and Neural Hyperconnectivity in Alcohol Use Disorder

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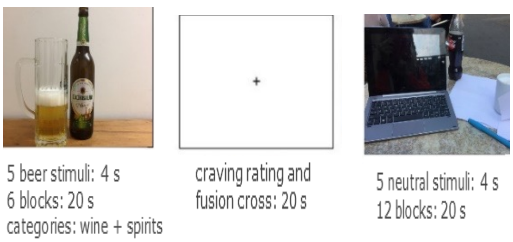
BACKGROUND

Automated alcohol craving and habitual alcohol consumption characterize the later stages of alcohol use disorder (AUD). This study re-analyzes previously collected functional neuroimaging data in combination with the Craving Automated Scale for Alcohol (CAS-A) questionnaire, a retrospective measure of automated alcohol craving over the last drinking period. The CAS-A aims to differentially assess individual components of habitual alcohol craving and consumption, including five factors along two general axes: 'unaware' and 'nonvolitional'. Here, we investigate the neural correlates and brain networks underlying automated craving and habitual consumption of alcohol using this assessment tool.

METHODS AND STUDY DESIGN

- 49 abstinent male AUD patients and 36 male healthy controls (HC) during a functional magnetic resonance imaging (fMRI)-based alcohol cue-reactivity task.
- Whole-brain analyses examining the associations between CAS-A and other clinical variables and neural activation patterns in the alcohol versus neutral contrast.
- Psychophysiological-interaction (PPI) analyses to assess the functional connectivity between predefined seed regions and other brain areas.

Figure 1. Cue-induced alcohol craving task



CAS-A Questionnaire

5 Factors:

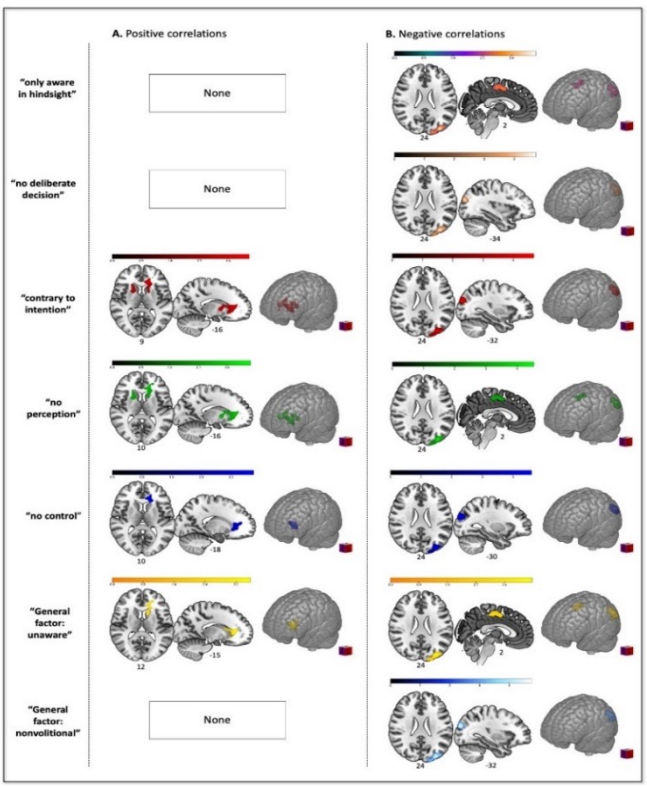
1. ***only aware in hindsight*** (Fac1)
2. ***no deliberate decision*** (Fac2)
3. ***contrary to intention*** (Fac3)
4. ***no perception*** (Fac4)
5. ***no control*** (Fac5)

2 General Factors:

1. ***unaware*** (g-Factor 1): Fac1, Fac4, Fac5
2. ***nonvolitional*** (g-Factor 2): Fac2, Fac3

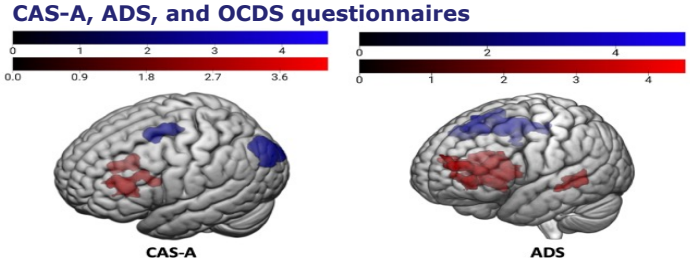
RESULTS

Figure 2. Correlating CAS-A scores with neural activity in an alcohol cue-reactivity task



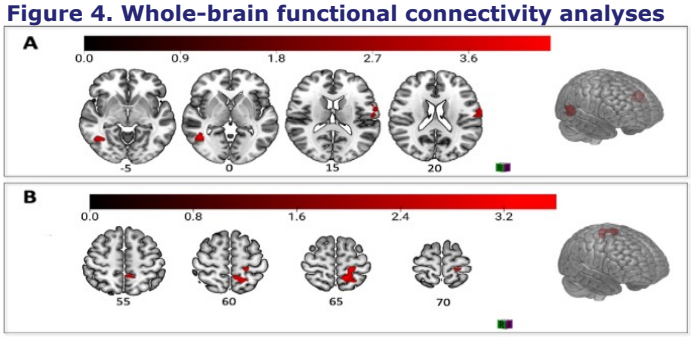
Multiple regression, contrast 'alcohol>neutral', covariate age, voxel-wise threshold, p < 0.005 and cluster-extent threshold, k >= 354 voxel, pFWE < 0.05 in AUD (n = 41)

Figure 3. Comparing brain activation correlated with the CAS-A, ADS, and OCDS questionnaires



Multiple regression, contrast 'alcohol > neutral', covariate age; voxel-wise threshold, p < 0.005 and cluster-extent threshold, k >= 354 voxel, pFWE < 0.05 for CAS-A and OCDS (n = 41), k >= 352 voxel, pFWE < 0.05 for ADS (n = 40). No significant correlations were found with OCDS.

Figure 4. Whole-brain functional connectivity analyses



Brain areas with increased task-related coupling in AUD subjects (n = 49) and controls (n = 36) with the regions of interest **A.** inferior frontal gyrus (voxel-wise threshold, p < 0.005 and cluster-extent threshold, k >= 308 voxel, with pFWE < 0.05), and **B.** angular gyrus (p < 0.005, k >= 320 voxel, pFWE < 0.05)

DISCUSSION

- To the best of our knowledge, this fMRI study is the first to examine associations between CAS-A scores and neural correlates underlying automated craving and habitual alcohol consumption.
- The results revealed specific brain areas directly associated with unawareness and nonvolition factors. Association between activation in dorsal striatal and pallidal areas with 'unaware' and 'nonvolitional' scores suggests that, with increased automated craving, alcohol-cue processing becomes similar to habit processing.
- Alcohol-use disorder individuals, who are not aware of their drinking, might have deficits in motor control, as indicated by the association between lower activation in motor control regions and high CAS-A unawareness factors.
- Attentional biases also appear to play a role in compulsive drinking, suggested by the negative associations between the middle and superior occipital gyrus activation and all of the unawareness- and nonvolition-related CAS-A factors.
- Higher neural functional connectivity in abstinent AUD participants compared with healthy controls suggests that abstainers employ prefrontal-driven compensatory mechanisms to increased alcohol-induced craving.
- Based on these results, we suggest that AUD individuals might benefit from individualized treatment strategies targeting different aspects of alcohol addiction, such as unconscious craving and loss of control over drinking.

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