Sex Differences in Neural Responding to Alcohol and Conflict Cues Among Individuals with Alcohol Use Disorder and Couples Conflict

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Background and Introduction

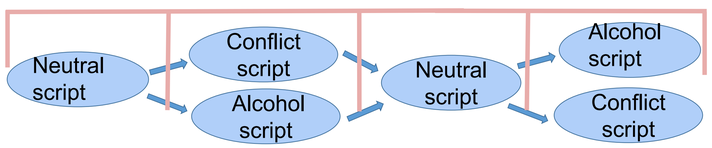
- Stress is a major contributor to AUD and promotes relapse in abstinent individuals. Therefore, stress must be considered in the context of AUD treatment.[1]
- Relationship conflict, similarly, hinders effective treatment for AUD, while adaptive relationship functioning improves AUD treatment outcomes.[2]
- There is little work that directly compares treatment outcomes by gender for Alcohol Use Disorder (AUD).
- Understanding sex differences in AUD and couple conflict is necessary for tailoring effective and personalized interventions.
- The Anterior Cingulate Gyrus is linked to cognitive conflict resolution[3]; the amygdala promotes the stress response, is involved in alcohol dependence, and its functions may be sexually dimorphic.[4]

Objectives and Hypothesis

- This study investigated the neuronal differences between men and women with AUD in response to auditory alcohol and conflict cues.
- The objective was to understand treatment targets by sex for Alcohol Behavioral Couples Therapy (ABCT).
- Hypothesis: Compared to males, females with AUD will exhibit greater amygdala-anterior cingulate functional connectivity while listening to conflict cues since females tend to demonstrate a greater amygdala response to negative material.

Methods

- Participants (N=34) with AUD were part of a larger clinical trial examining effects of oxytocin vs. placebo administered alongside ABCT.
- Patients were diagnosed with AUD using the MINI[5] or SCID-V[6].
- Individuals listened to 2-minute personalized auditory scripts that recounted an experience when one or both partners disagreed (conflict cue), an experience when alcohol was consumed (alcohol cue), and an experience that was relaxing/non-stressful (neutral cue).
- Each auditory cue was followed by visual analog ratings of feelings of stress and alcohol craving.
- Standard fMRI preprocessing was followed by (a) general linear modeling of BOLD activation for each cue condition and (b) psychophysiological interaction (PPI) modeling to examine amygdala connectivity modulated by each cue.
- fMRI voxel-wise group analysis examined difference between females and males, with cluster correction (Z > 3.1, p = .05).
- Exclusion criteria: Participants with head motion > 0.99 mm.
- Analyses reflect pre-treatment data only.

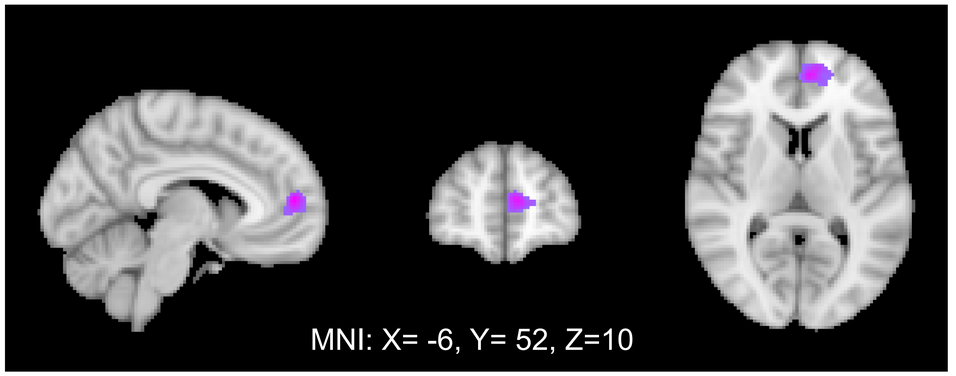


RESULTS

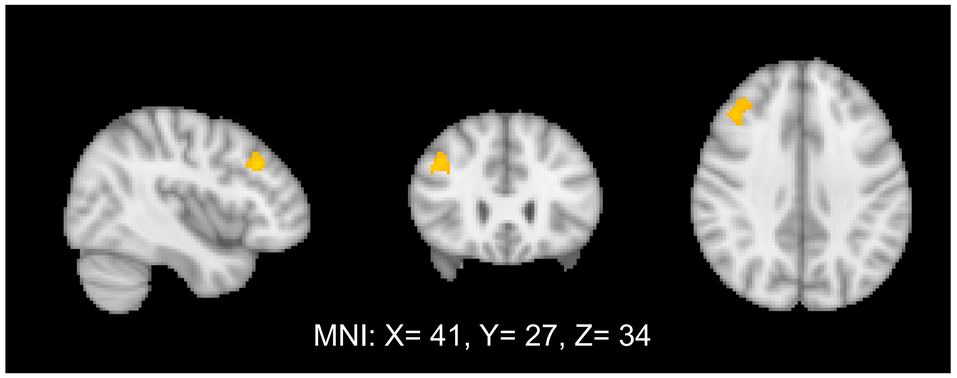
Diagnosis was not statistically significant by sex (*U*=94.5, *p*=.09102)

	Male (N/M(SD))	Female (N/M(SD))
Total	16	18
Race (Caucasian)	14	18
Age	39.56 (13.63)	38.77 (15.05)
Mild AUD	3	8
Moderate AUD	4	5
Severe AUD	9	5

Males show greater recruitment of the left paracingulate gyrus in response to conflict cues compared to females.



Females show left amygdala-to-right middle frontal gyrus connectivity for conflict > alcohol cues, but males do not



Conclusion and Discussion

- Males exhibited greater activation in the paracingulate gyrus compared to females in response to conflict cues.
- This paracingulate region overlaps with the dorsal anterior cingulate which is involved in the processing of emotional conflict.[7]
- Females showed connectivity of the left amygdala with the right middle frontal gyrus, whereas males did not.
- The middle frontal gyrus is associated with numerous higher level cognitive functions such as causal reasoning, behavioral inhibition, working memory and emotion regulation.[7]
- Males and females show different neural profiles of reflective cognitive processing while listening to conflict cues.
- Females show connectivity between the amygdala, which is heavily involved in automatic stress responding, and right middle frontal gyrus, a region involved in numerous reflective and regulatory processes.[7]
- Males, in contrast, recruit a region focused on conflict detection.
- Diagnosis was not statistically significant by sex. Therefore, results may be attributed to sex rather than difference in severity of AUD.

Future Directions

- This is the first ABCT or dyadic alcohol treatment study that has had an imaging element to examine the neurobiological underpinnings of couple conflict and AUD.
- Intimate Partner Violence and relationship stress at baseline is a consideration for future analyses.
- Linking these imaging data to baseline clinical characteristics is needed to understand behavioral relevance.
- Linking these imaging data at baseline to post-treatment clinical indices is also needed to establish prognostic indicators of treatment.

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