

Differences in Neural Networks in Young Adult Males with Family History of Alcohol Use Disorder

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Introduction: Alcohol use disorder (AUD) is known to have a hereditary component, and several neural networks have been implicated in AUD, including the default mode (DMN), salience (SN) and dorsal attention networks (DAN). However, little is known about the potential differences in neural networks in healthy young adults with predisposition to AUD. We examined differences in inter- and intranetwork functional connectivity in individuals with and without family history of AUD to assess whether there are heritable differences which could contribute to AUD.

Methods: The study included young adults (ages 18-22) either with (FHP) or without (FHN) a family history of AUD. Groups were further subdivided based on biological sex, for a total of four groups: family history negative male (FHN_M, N=26), family history negative female (FHN_F, N=18), family history positive male (FHP_M, N=9), and family history positive female (FHP_F, N=24). 10 minutes of fMRI resting state data were collected. ROI-to-ROI analysis was conducted using the CONN toolbox. Three networks were selected (DAN, SN, DMN) and ROIs for each were taken from the CONN network atlas. Bivariate correlation was run and between group differences were analyzed. p-FDR was calculated for each test, and p-FDR < 0.05 was considered significant.

Results: When evaluating all FHN vs all FHP participants, there were no statistically significant differences in functional connectivity. However, when compared to the FHP_M group, the FHP_F group showed significantly increased negative connectivity between the precuneus cortex (PCC) of the DMN and the anterior cingulate cortex (ACC) of the SN (uncorrected $p < 0.001$, p-FDR = 0.008). When compared to the FHP_M group, the FHN_M group also showed significant negative connectivity between the PCC of the DMN and the ACC of the SN (uncorrected $p = 0.005$, p-FDR = 0.04). Additionally, the FHN_M group showed significantly increased positive connectivity between the PCC of the DMN and the right frontal eye fields of the dorsal attention network (uncorrected $p = 0.004$, p-FDR = 0.04). There were no significant differences in connectivity between the FHN_F and FHP_F groups.

Conclusions: Compared to FHN males and FHP females, FHP males seem to have significantly decreased connectivity between the DMN and SN, as evidenced by decreased functional connectivity between the anterior and precuneus cortex. It is possible that this difference represents a neural biomarker of predisposition to AUD that is specific to males.