



Default mode network resting-state functional connectivity in individuals with bipolar disorder and co-occurring alcohol dependence: Results from a 2x2 Factorial Design

Jade de Araújo, B.S., William Mellick, PhD, Helena Brenner, B.S., Sara Hix, B.S., and James J.

Prisciandaro, PhD

Background: Abnormal default mode network (DMN) resting-state functional connectivity (rsFC) has been reported in individuals with bipolar disorder (BD) and alcohol dependence (AD), particularly between the medial prefrontal cortex (mPFC) and the posterior cingulate cortex (PCC). The present study represents the first known investigation of DMN rsFC in individuals with co-occurring BD and AD (BD+AD). **Methods:** One-hundred and four participants who met DSM-IV-TR diagnostic criteria for BD+AD (n=23), BD alone (n=28), AD alone (n=25), or no diagnosis (n=25) completed a baseline assessment and returned for rs-fMRI scanning after demonstrating ≥ 1 week of abstinence from alcohol/drugs via blood serum and urine biomarkers. Two-by-two general linear univariate models of Fisher's z-scores were tested to examine rsFC between-group differences for each pair of DMN regions (mPFC, PCC, and bilateral angular gyri). Bivariate Pearson correlations between z-scores and symptom measures were explored within groups. **Results:** Main effects of BD and AD and the BD x AD interaction terms were non-significant in two-by-two models. Connectivity across bilateral angular gyri and the PCC positively correlated with depressive symptoms in BD+AD group (r 's ≥ 0.44 , p-values ≤ 0.034). The directionality of PCC-mPFC connectivity and alcohol craving correlations varied between AD ($r = -0.54$, $p = 0.005$) and BD+AD groups ($r = 0.52$, $p = 0.011$). **Conclusions:** Reducing angular gyrus functional connectivity may improve depressive symptoms in individuals with BD+AD as it has in prior treatment studies of major depressive disorder. Given associations with both depressive symptoms and alcohol craving, PCC functional connectivity may represent a putative treatment target for concurrent symptom reduction in BD+AD.