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Conduct Disorder Genomewide Association Study Extension to Affective Brain Function

Namrata Vakkalagadda
Washington University in St. Louis

Conduct Disorder Genomewide Association Study and Extension to Affective Brain Function

Namrata Vakkalagadda

Mentor: Ryan Bogdan

Conduct disorder (CD) is a moderately heritable childhood externalizing disorder associated with substantial personal and societal burden. The current study sought to examine its molecular genetic architecture and neural mechanisms that may underlie associations between genetic risk and disorder expression. The authors performed a genomewide association study (GWAS) of retrospectively reported CD among Australians of European ancestry who completed the Comorbidity and Trauma Study (ncases=680, ncontrols=995). They then tested genetic risk factors identified from the GWAS for association with self-reported psychopathy and regional differences in neural activity to an emotional face-matching task in an independent sample of 406 non-Hispanic U.S. undergraduate students of European ancestry. The authors find that the major A allele of the intergenic rs12536973 polymorphism was associated with increased risk for CD (OR=2.00, p=3.74E-08), and gene-based analyses revealed an association with GOLM1. The A allele of rs12536973, as well as genomewide polygenic risk scores (PRS) developed from the discovery GWAS, were associated with increased self-reported psychopathy in the independent college sample. CD PRS were negatively coupled with left anterior insula activity to emotional faces in whole-brain analyses. Post hoc conjunction analyses showed that both CD PRS and self-reported psychopathy were associated with reduced activation in overlapping clusters within the bilateral anterior insula and supramarginal gyri. Collectively, these results provide insight into the genetic architecture of CD risk and suggest that blunted neural responses to affective social stimuli in regions previously linked to empathy may represent a neural mechanism through which genomic risk may promote its expression.