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Analysis of copy number variation in conduct disorder

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Objective: Conduct disorder (CD) is a disorder of childhood that is characterized by aggression, rule-breaking, and disregard for the wellbeing of others. Copy number variation (CNV) is an important risk factor for several neurodevelopmental disorders; however, the role of this form of genetic variation in CD is poorly understood. Methods: CNVs were defined from genotyped individuals within the Vanderbilt BioVU biobank using PennCNV. We identified individuals of European ancestry meeting criteria for CD based on higher-order phenotypic annotation of linked electronic health records (known as "phecodes"). Controls were defined based on the absence of CD and closely related phecodes. Results: CD cases demonstrated a higher overall CNV burden (both number of CNVs and total length), an effect which was more pronounced in females than in males. Genome wide association identified four regions meeting significance criteria following correction for multiple comparisons, including regions implicated in brain development and dysfunction. Phenome wide association within the case-control cohort revealed significant associations between CD and substance use disorders in adults. Conclusions: These preliminary results identify novel genetic associations with CD. Such vulnerabilities could inform early therapeutic intervention and improve predictive models related to the progression of externalizing pathology and development of substance use disorders.