DRD4 Variants Moderate the Impact of Parental Characteristics on Child Attention-Deficit Hyperactivity Disorder: Exploratory Evidence from a Multiplex Family Design.

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Abstract

Parental ADHD symptomatology and related impairments have been robustly associated with youth ADHD across decades of work. Notably, these factors may impede the typical development of child self-regulation capabilities through both neurobiological and interpersonal processes. High heritability of estimates for the disorder further suggests that these effects are likely genetically-mediated, at least in part. Variation within the dopamine D4 receptor gene (DRD4) has been shown to moderate parental influences on youth ADHD. Use of a multiplex family design (i.e., samples of families that included multiple affected members) may facilitate identification of additional gene variants of interest and advance understanding of gene-environment interplay in regard to parenting. Thirty multiplex families consisting of 114 individuals (66 youth, 48 parents) completed a multi-stage, multi-informant diagnostic and neurocognitive assessment, measures of parenting, and provided saliva samples for DNA analyses. Sanger sequencing of the DRD4 gene yielded 16 rare variants; a polygenic risk score was computed for both parents and youth. Generalised estimating equations (GEE) examined the predictive effects of parental ADHD symptoms, parental neurocognitive functioning, and poor parenting dimensions on youth ADHD as well as moderation of these effects by parental and youth DRD4 variants. Findings indicated that parental DRD4 variants moderated the impact of parental ADHD and neurocognitive functioning on youth ADHD symptoms. Youth DRD4 variants moderated the impact of parental inconsistent discipline on child ADHD. In all cases, stronger associations were observed for those individuals with more risk variants. These exploratory findings highlight the potential utility of a multiplex family design for examining the interplay between parent and child characteristics in predicting youth outcomes.