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Genomic structural equation modeling of impulsivity and risk-taking traits reveals three latent factors distinctly associated with brain structure and development

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Background
Impulsivity is a multifaceted trait that emerges in childhood and is linked to several psychiatric disorders, such as attention-deficit/hyperactivity disorder and substance use disorders. Recent genomic and neuroimaging studies have identified genetic loci and brain systems associated with impulsivity and risk-taking behaviors. However, how these genetic underpinnings overlap across different facets of impulsivity and risk-taking, and how they are associated with brain morphology during early development remain unknown.
Methods
We applied genomic structural equation modeling to 17 impulsivity and risk-taking GWAS datasets to explore the overlapping genetic architecture underlying these phenotypes. We then computed polygenic scores (PGSs) for each genetic latent factor in 4,142 participants from the Adolescent Brain Cognitive Development Study and examined how each factor was associated with the brain structure during early development. We further tested whether socioeconomic status modulated the association between the PGSs and brain structures.
Results
We identified three genetic latent factors, which we labeled as lack of self-control, reward drive, and sensation seeking. These showed distinct associations with brain structure in late childhood and early adolescence. Specifically, lack of self-control PGS was related to reduced cortical thickness and surface area, while reward drive PGS was associated with heightened cellularity in subcortical structures. Finally, sensation seeking PGS showed positive association with cortical surface area and higher white matter integrity. Interaction analysis revealed that the association between PGS of lack of self-control and white matter mean diffusivity was modulated by socioeconomic status.
Conclusions
Our findings revealed that genetic predisposition for impulsivity and risk-taking is associated with morphological brain differences as early as ages 9–10. We also highlighted the importance of capturing the multidimensional nature of these traits to better understand their neurodevelopmental basis.

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