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Characterizing Addiction Risk Across Development in Large Epidemiological and Population-Based Samples

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It is widely recognized that large samples are needed to identify genes involved in substance use disorders and other complex traits. However, post-gene-discovery, large datasets are also necessary to map genetic risk across development, in order to use genomic information for prevention and early intervention. In the current study, we used polygenic scores (PGS), derived from a multivariate GWAS identifying genes that impact addiction outcomes via selfregulation (Karlsson Linnér et al., 2021), to estimate associations of genetic risk with relevant behavioral phenotypes within and across developmental periods, ranging from toddlerhood to early adulthood. We used data from five population-based and epidemiological datasets spanning three countries, and found significant associations between the PGS and a variety of phenotypes from toddlerhood to early adulthood. In toddlerhood and early childhood, children with higher PGS were rated as more active, more social, and less shy. Higher PGS was consistently associated with measures of impulsivity from early adolescence to early adulthood. Individuals with higher PGS were more likely to experience symptoms of conduct disorder, oppositional defiant disorder, and attention deficit hyperactivity disorder, as well as greater alcohol use and problems, and nicotine, cannabis, and other drug use starting in early adolescence. Overall, findings show wide ranging manifestations of genetic risk for self-regulation deficits across a variety of developmental periods, with implications for how we can use genetic information to target early intervention to prevent substance use problems before they start.