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Insights into the multivariate genetic architecture of externalizing spectrum behaviors and disorders: Preliminary results from the Externalizing Consortium

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The *externalizing spectrum* is a constellation of behaviors, traits, and disorders that are characterized by under-controlled or impulsive action. It encompasses multiple clinical diagnoses across development, including attention deficit hyperactivity disorder, conduct disorder, oppositional defiant disorder, antisocial personality disorder, alcohol use disorders, and substance use disorders. Notably, twin and family studies have found that genetic influences on these phenotypes tend to be broadly shared across the externalizing spectrum. However, while these studies have broadly characterized genetic influence, they have done little to elucidate the specific genetic architecture of the externalizing spectrum. To address this, we have launched a new consortium that will conduct and leverage genome-wide association studies (GWASs) to (i) estimate the genetic factors that underlie the externalizing spectrum, (ii) identify genes that are involved in shared liability to externalizing behavior versus genes that are unique to specific constituent phenotypes, and (iii) boost statistical power for GWASs of specific externalizing phenotypes that have only been conducted in small samples. Here, we capitalize on the known genetic overlap between externalizing phenotypes, and conduct a multivariate GWAS of the externalizing spectrum in a Genomic SEM framework. This multivariate framework incorporates results from both new and existing GWASs of substance use phenotypes, including addictive behavior, alcohol use, cannabis use, illicit drug use, impulsivity, risk preferences, and more. We present results from these initial analyses, as well as our plans for future directions. Finally, we provide details about the Externalizing Consortium, and invite interested groups to join in the next wave of analyses.