



An Introduction to the Special Issue: Developmental Behavior Genetics and Externalizing Psychopathology

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Externalizing behavior is a broad construct encompassing various forms of aggression, delinquency, behavioral disinhibition, and substance use. A wealth of research has demonstrated genetic influences on externalizing behaviors generally (e.g., Burt 2009; DiLalla 2002; Salvatore and Dick 2018). Understanding how genetics and gene–environment interplay contribute to externalizing behaviors over time can help to delineate underlying mechanisms within and across developmental periods. This special issue of *Behavior Genetics* provides a developmental examination of genetic influences on externalizing behaviors from multiple theoretical and methodological perspectives across several different indices of externalizing behavior.

The expression of externalizing behavior can vary across age, making it both difficult and interesting to examine developmentally. Externalizing behavior can manifest early in childhood as aggression and behavioral disinhibition and can continue throughout life as other behaviors arise, including delinquency and substance use in adolescence, which may develop into antisociality, criminality, and/or substance use problems in adulthood. Past research and theoretical perspectives have made great strides in examining genetic influences on externalizing behavior over time. Converging evidence indicates that there is largely shared genetic etiology underlying different facets of externalizing behavior (McGue et al. 2013; Vrieze et al. 2013). Yet the relative influence of genetics may vary over time based on a combination of the developmental period, measure of genetic predisposition, and type of externalizing behavior being examined. Twin research indicates that there are genetic influences for various aspects of externalizing behavior at

different developmental periods, but also variability in these genetic and environmental influences based on age (Hatoum et al. 2018; Hicks et al. 2007). These estimates capture direct genetic influences on externalizing behavior and also likely gene–environment interplay. Molecular genetic research has identified individual variants and polygenic indices predictive of externalizing behavior across development (Salvatore and Dick 2018). This is supported by longitudinal research on gene–environment interplay identifying gene by environment interaction ($G \times E$) and gene–environment correlation (rGE) effects underlying externalizing outcomes (e.g., Elam et al. 2020; Rabinowitz et al., 2018). This growing field has resulted in past special issues focused on the etiology of substance use (Prescott et al. 2006) and the interplay between genetic and social influences in adolescent development (Mullineaux and DiLalla 2015).

Especially important when considering externalizing behavior from a developmental perspective is accounting for the method of data collection. With young children, parents are often utilized as reporters of children’s behaviors. As children get older, parents still complete many questionnaires or surveys, but children themselves are also more involved in providing data. Teachers and peers also may be asked to provide information. By adulthood, the primary method is self-report, although public records, such as court records, can also provide meaningful assessments of externalizing behaviors. Various biases come into play for each of these methods, and they must be considered, especially when engaging in twin studies where co-twins are compared to each other. Parent rating assimilation and contrast biases for various child behaviors have been demonstrated for monozygotic (MZ) and dizygotic (DZ) pairs, respectively (Bartels et al. 2004; Saudino 2003). Self-reports also are prone to social report biases (Nikstat and Riemann 2020), as in all research. Court records may reflect social or cultural biases (Ahonen et al 2017; Stevens and Morash 2015). Importantly, behavior genetic studies appear to demonstrate that genetic influences on aggression are not simply

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a function of reporter bias (DiLalla 2002). Nonetheless, such biases should be considered as studies are interpreted.

The studies in this special issue address current gaps in the literature and provide evidence of genetic influences on externalizing behavior across the life span. These studies offer novel examinations of genetic and environmental mechanisms, novel use of innovative methodologies, and examination of effects in diverse samples. Collectively, this body of research contributes to and advances research on genetic influences on the development of externalizing behavior. We outline the articles in a developmental sequence below with the intention of examining genetic and environmental influences on externalizing behavior across much of the life span, from infancy through adulthood.

Childhood

Three studies examined the impact of GxE in relation to the family in predicting externalizing behavior in young children. Across these studies, family behaviors were examined when children were 2–5 years old and externalizing when children were between 5 and 14 years; all showed significant effects of parenting on externalizing behaviors in addition to interactions with other family or child measures. In the first study, using an adoption sample and different raters across measures, Ganiban et al. (2021) found that adoptive parent laxness at 27 months moderated the effects of heritable risk for poor effortful control (birth mother emotional dysregulation or low agreeableness) in predicting children's effortful control at 4.5 years of age, which in turn predicted parent-rated externalizing behavior at 7 years of age. In particular, parent laxness and child effortful control were positively associated when children had high heritable risk for poor effortful control but negatively associated at low heritable risk for effortful control.

DiLalla et al. (2021) created a novel genetic risk index for aggression based on twin similarity in observational coding of 4-year-old behavioral aggression and examined interactions with negative emotionality, family income, and birth complications in predicting externalizing at multiple ages. For children at low genetic risk, increased negative emotionality was associated with greater parent-rated externalizing; interactions also showed that children with many perinatal birth complications or from families with low income were at greater risk to exhibit externalizing behaviors, as were children rated high on negative emotionality and in low-income homes. Finally, Womack et al. (2021) demonstrated an interaction between a polygenic risk score for aggression and early childhood family instability in predicting parent and teacher ratings of externalizing from middle childhood to early adolescence. Children from less stable homes showed higher initial levels of aggression, but the interaction

showed that children with lower family instability and lower polygenic risk had a steeper decrease in aggression over time. Thus, across different designs, multiple reporters, and innovative methods, these studies provide evidence that very early genetic risk for externalizing is moderated by family factors.

Late Childhood and Adolescence

Five studies examined direct genetic effects and/or gene–environment interplay in accounting for externalizing behavior in late childhood and adolescence. Using a twin design in a novel way to determine whether temperamental moderation occurred across several different environmental effects, Markovitch et al. (2021) examined moderation of negative emotionality by individual, parent, peer, and school-level influences from ages 11 to 13 in an Israeli sample. Their findings were consistent with those from the younger sample in DiLalla et al. Genetic and environmental variance in externalizing was moderated by negative emotionality such that children with more negative emotionality were more sensitive to negative environments. That is, they showed greater externalizing in negative family environments (in this sample, low parental support), negative peer environments (increased bullying at school), and marginally in negative school climates. Genetic effects on externalizing varied across levels of negative emotionality within different environments. Extending the measurement of externalizing, Oro et al. (2021) examined predictors of externalizing and internalizing factors of psychopathology assessed from a clinical interview during adolescence (mean age 13), with a bifactor model best fitting the data. Externalizing and internalizing factors were heritable, with shared genetic influence, and both were influenced by the nonshared environment. In addition, paternal alcohol use disorder (AUD) predicted both externalizing and internalizing problems when these factors were correlated, showing that the risk from paternal AUD is general rather than specific to externalizing.

Investigations in adolescence facilitated examination of substance use as a measure of externalizing problems in three studies. Zheng et al. (2021) examined whether maternal supervision and harshness moderated genetic and environmental variance of latent classes of early-onset alcohol use, normative increasing alcohol use, and low alcohol use in adolescents aged 13–17 years old using growth mixture modelling. Greater maternal harshness increased shared environmental influence for the early-onset alcohol use trajectory and non-shared environmental influence for the low alcohol use trajectory. Maternal supervision increased non-shared environmental influence for the normative increasing alcohol use and early-onset alcohol use trajectories.

Kuo et al. (2021) created a polygenic score for externalizing, leveraging the largest GWAS to date on externalizing spectrum behavior. In European ancestry individuals, the polygenic score directly predicted externalizing behaviors over time (inclusive of substance use, conduct disorder, and oppositional defiant disorder), as well as via peer substance use. Marceau et al. (2021) examined maternal prenatal substance use and a polygenic score for pubertal development in predicting differentiation of internalizing vs. externalizing symptoms at age 13 and subsequent substance use at age 18. In boys, greater maternal prenatal substance use contributed to substance use via greater differentiation to externalizing vs. internalizing symptoms. In girls, direct associations between maternal prenatal substance use and adolescent substance use were detected. Collectively these studies demonstrate that individual, familial, and peer processes are involved in gene–environment interplay in externalizing in late childhood and adolescence.

Adulthood

Three studies examined genetic effects on externalizing behaviors spanning multiple developmental periods, extending investigations into adulthood. Carroll et al. (2021) examined stability and change in genetic and environmental influences on parent-reported antisocial behavior across a large age range, from 3 to 22 years old, using a twin design, providing one of the most longitudinal behavior genetic studies of externalizing behaviors. Early childhood genetic and non-shared environmental influences contributed to stability and change in antisocial behavior over time whereas emerging genetic and nonshared environmental influences contributed to change over time. van der Laan et al. (2021) examined polygenic predisposition for aggression in predicting self-reported aggression from late childhood to adulthood in samples from the Netherlands and Australia. The polygenic score predicted aggression from 12 to 41 years of age in the Netherlands sample whereas the polygenic effect peaked at age 40 in the Australian sample. Finally, Elam et al. (2021) created a functional polygenic score for aggression in predicting substance use disorder (SUD) diagnoses at age 27 via substance use offending at age 19, obtained from court records. Participants were from a randomized control trial of a family-based intervention in adolescence, the Family Check-Up, so gene-by-intervention effects were also examined. Greater polygenic risk for aggression was found to increase risk for substance use offending which in turn was associated with greater likelihood of being diagnosed with SUD at age 27. Further, individuals in the control group had greater risk for SUD diagnoses with increasing polygenic risk for aggression. Altogether, these studies provide

evidence of long-term genetic effects on different facets of externalizing behavior.

Summary and Future Directions

This collection of studies presents a novel examination of genetic effects on the broadly defined construct of externalizing behavior across multiple stages of development. This highlights the diverse but also interrelated character of externalizing behavior and its changing nature with age, particularly with the emergence of substance use later in life. These studies use a variety of innovative methods, samples, and analytic approaches that cover an impressive age range, from the prenatal period to 70 years of age. Over half of the studies used twin or adoption designs, emphasizing their ability to examine the whole genome as well as genetic interplay with the social environment. The polygenic studies leveraged large genome-wide findings, functional variants, and interplay with the social environment to study externalizing behavior. Across all studies, samples represented the United Kingdom, Netherlands, Australia, and Israel, as well as diverse populations from the United States. Collectively, these studies extend and advance the study of developmental genetic effects on externalizing behavior and inform future directions for this field.

As illustrated in the studies in this special issue, genetic influences on externalizing can emerge relative to specific behaviors that arise during different developmental periods. Conversely, the same genetic predisposition may relate to different behaviors dependent on when they emerge, such as aggression in childhood and substance use in adolescence and adulthood. This reflects the pleiotropic nature of externalizing behaviors and underlying shared polygenic architecture of individual behaviors. Future twin and adoption studies could extend this research by examining continuity and change in genetic effects across multiple indices of externalizing behavior. Polygenic studies should leverage GWAS that are developmentally aligned with replication samples and examine effects on elements of externalizing behavior that emerge over time in richly phenotyped samples.

Another key area for future directions is a continued emphasis on diversity and inclusion in behavior genetics research as the majority of samples were of European ancestry. Future studies should examine genetic influences on externalizing behavior in different racial/ethnic groups. This is especially important given that different genetic and social processes may underlie externalizing psychopathology which may be conflated with racism, discrimination, and broader social inequality. Two studies in this issue did demonstrate that although there were

some differences between Black and White individuals, the models predicting externalizing behaviors were mostly similar (Elam et al. 2021; Womack et al. 2021), although some differences did emerge (Elam et al. 2021), suggesting the need for further research on larger samples of ethnically diverse groups. Future behavior genetic studies that include more information about different social groups and sociocultural influences can help clarify ways in which genes and environments interact to affect externalizing problem behaviors. Such endeavors will help behavior genetic research to benefit diverse populations.

Finally, the advances captured in this special issue have important implications for externalizing psychopathology. Identifying developmental periods when genetic influences are more or less prominent and distinct social processes relative to these influences can help to inform preventive interventions. This is especially important given evidence from studies in this issue that externalizing behavior can persist across the lifespan and that psychosocial interventions can buffer genetic predispositions for externalizing behavior.

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Conflict of interest Kit K. Elam and Lisabeth Fisher DiLalla declare that they have no conflicts of interest.

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