

Preempting the Development of Antisocial Behavior and Psychopathic Traits

Alexandra Junewicz, MD, and Stephen Bates Billick, MD

Antisocial behavior and psychopathic traits are subject to complex patterns of inheritance, gene-environment interactive effects, and powerful environmental influences. Yet genetic factors are important in the etiology of antisocial behavior and psychopathic traits, and identifying youth with an elevated genetic risk may lead to improved interventions and preventive efforts. Additionally, research revealing the importance of gene-environment interactions in the development of antisocial behavior and psychopathic traits should be harnessed to promote more rehabilitative, developmentally appropriate policies to benefit youth in the juvenile justice and social welfare systems.

J Am Acad Psychiatry Law 49:66–76, 2021. DOI:10.29158/JAAPL.200060-20

Key words: conduct disorder; callous-unemotional traits; antisocial personality disorder; psychopathy; gene-environment interactions

Society has long looked to genetics to explain deviant human behaviors. More recently, legal systems have sought to use genetic research to account for violent and antisocial acts.¹ Many have raised concerns that research into the genetic roots of antisocial behavior and psychopathic traits could be misinterpreted and misconstrued, possibly reducing individuals to their genetic profiles, oversimplifying complex pathologies, and fueling beliefs in “genetic determinism.”^{1–6} The risk of overstating genetic findings might lead individuals to be labeled inaccurately and inappropriately, possibly subjecting them to unfounded fear, stigma, and bias.^{7–8} Due in part to such concerns, the concept that genetic factors underlie antisocial behaviors and psychopathic traits has been controversial.⁶

An extensive body of research has established that genetic influences are important in the etiology of antisocial behavior and psychopathic traits,

but studies have yet to identify the specific genes and biological mechanisms involved.^{9–12} While there have been a few exceptions, research on genetic factors generally has been limited by small sample sizes and difficulties defining the study populations.^{9–11,13,14} Moreover, environmental influences and gene-environment interactions play a powerful role in the development of antisocial behavior and psychopathic traits.

There may be a benefit in identifying individuals with an elevated genetic risk for antisocial behavior and psychopathic traits with the goal of using this information to guide interventions and preventive efforts. An expanded understanding of the impact of environmental factors on the expression and behavioral manifestations of genes may lead to improved interventions to curtail the development of antisocial behavior and psychopathic traits. Further, research revealing the importance of gene-environment interactions in the development of antisocial behavior and psychopathic traits may encourage expanded supports and more rehabilitative policies for youth in the juvenile justice and social welfare systems.

Diagnoses and Constructs

In adults, antisocial behavior is most often associated with antisocial personality disorder and psycho-

Published online January 6, 2021.

Dr. Junewicz is Clinical Assistant Professor, Department of Child and Adolescent Psychiatry, New York University School of Medicine, New York, NY and Clinical Psychiatrist, Bellevue Hospital Center, New York, NY. Dr. Billick is Clinical Professor, Department of Psychiatry and Department of Child and Adolescent Psychiatry, New York University School of Medicine, New York, NY. Address correspondence to: Alexandra Junewicz, MD. E-mail: alexandra.junewicz@nyulangone.org.

Disclosures of financial or other potential conflicts of interest: None.

pathy. Antisocial behaviors are those that disregard and violate the basic rights of others.¹⁵ Antisocial personality disorder is a pervasive pattern of such behavior and is marked by deceitfulness, impulsivity, irritability, aggression, consistent irresponsibility, lack of remorse, a reckless disregard for the safety of oneself or others, and a failure to conform to social norms with regard to lawful behaviors.¹⁵ While antisocial behavior and antisocial personality disorder are defined by observable characteristics, psychopathic traits consist of affective and interpersonal qualities. Psychopathic traits include a lack of empathy, shallow emotions, lack of remorse, grandiosity, glibness, and conning, deceptive behaviors.¹⁶ Psychopathy is distinguished by the presence of such traits and is observed in a subset of adults with antisocial personality disorder.¹⁷ Unlike antisocial personality disorder, psychopathy is not a DSM-5 diagnosis; rather, it is a construct deriving from the conceptualization set forth by Cleckley in *The Mask of Sanity*.¹⁸ The presence of psychopathy is most often established on the basis of an assessment of psychopathic traits with the Hare Psychopathy Checklist.^{17,19}

In youth, antisocial behaviors are part of the diagnostic criteria for conduct disorder, which is characterized by a constellation of repetitive and persistent behaviors involving aggression toward people or animals, destruction of property, deceitfulness or theft, and serious violation of rules.¹⁵ Conduct disorder has been conceptualized as a neurodevelopmental disorder, and some believe that its manifestations represent one step in a developmental progression of antisocial behavior.^{20–22} For example, it is believed that oppositional defiant disorder may represent a developmental precursor to conduct disorder, and that conduct disorder may represent a developmental precursor to antisocial personality disorder.^{10,23,24} Indeed, evidence of conduct disorder prior to the age of 15 years is required to diagnose antisocial personality disorder in adults, consistent with theories that these conditions reflect patterns of antisocial behavior that evolve throughout development and across the lifespan. There is evidence that the point at which antisocial behavior emerges during development may predict its persistence and severity. Moffitt²² proposed a developmental taxonomy of antisocial behavior, which classified conduct disorder as either “childhood-onset” or “adolescent-onset,” and as either “life-course persistent” or “adolescence-limited.” Youth with conduct disorder that begins in

childhood and persists throughout life exhibit more severe symptomatology, as well as a greater risk for various antisocial behaviors and mental health problems in adulthood, including psychopathic traits, mental illness, substance dependence, violent crimes, and violence against women and children.^{6,25}

Approximately 50 percent of youth with conduct disorder are further characterized by “limited prosocial emotions,” also known as callous-unemotional traits. Youth with conduct disorder and callous-unemotional traits are considered by some to have the childhood equivalent of psychopathy.^{10,11,15,23,24} Authors have argued that the identification of callous-unemotional traits and the possible emergence of psychopathy in children present an opportunity for early intervention and prevention.^{23–24} Others have raised concerns about the application of the psychopathy construct to youth, however, noting that certain “psychopathic traits” are common at certain developmental points, such as adolescence.^{6,26,27}

Antisocial behaviors and psychopathic traits during childhood do not always persist into adulthood. It is estimated that antisocial personality disorder develops in only half of youth with childhood-onset conduct disorder.^{6,10,11} Similarly, studies have indicated that callous-unemotional traits have stability coefficients of 0.5 to 0.7 over four to nine years.¹¹ Psychopathy may be even less likely to persist throughout the lifespan. A study by Lynam *et al.* revealed that psychopathy at age 13 accounted for only 10 percent of the variance in psychopathy at age 24.²⁸ The fact that 90 percent of the variance was unexplained by history of psychopathy at age 13 indicates that other factors contribute to the development of psychopathy in adulthood.

Exploring Genetic Roots

Antisocial behaviors and psychopathic traits may reflect genetic factors that are subject to complex mechanisms and pathways.^{9,29} Genetic factors may lead to antisocial behaviors and psychopathic traits via their effects on biological systems, such as brain structure, neural function, and the physiologic stress response. For example, there is evidence that a genetic polymorphism that affects oxytocin functioning is associated with increased right amygdala reactivity and antisocial behavior.³⁰ Studies have also reported smaller posterior and right dorsal anterior cingulate gyrus volumes in individuals with psychopathic traits, a difference that has been found to be

moderately heritable.^{29,31} Genetic variants affecting serotonergic and enzyme function have been associated with increased amygdala threat responses and increased aggressive behavior, and it has been suggested that other genetic variants might lead to decreased amygdala threat responses and psychopathic traits.¹¹ Such evidence indicates that one's genetic profile may have biological sequelae that shape the individual's developmental trajectory.

Candidate gene studies and genome-wide association studies have sought to identify specific genes that underlie antisocial behavior and psychopathic traits. While candidate gene studies investigate individual genes hypothesized to be associated with a given trait, genome-wide association studies search the whole genome to identify genetic polymorphisms more common across a group with a given trait. To explore the genetic roots of antisocial behavior and psychopathic traits, these methods have examined several genes that affect the functioning of serotonin and dopamine.^{10,13,32,33}

While there is some dispute, several studies have implicated the monoamine oxidase A enzyme (MAO-A), the catechol-O-methyltransferase enzyme (COMT), and the sodium-dependent serotonin and dopamine transporter genes in antisocial behavior.^{10,13,32-35} In a meta-analysis by Ficks and Waldman,³² polymorphisms of the MAO-A and serotonin transporter gene were each associated with aggressive or antisocial behavior in youth. Various genes that affect dopamine neurotransmission and availability have been associated with externalizing behaviors, including the dopamine receptor 4 and 5 genes (*DRD4* and *DRD5*), the dopamine transporter 1 gene (*DAT1*), and the *COMT* gene.³⁶⁻³⁸ Several other genes have been associated with aggressive and externalizing behaviors in youth, including genes involved in gamma-aminobutyric acid (GABA) neurotransmission and hormones that drive social behaviors, such as oxytocin and vasopressin.^{13,21,34,38,39}

Despite some conflict among results, studies of youth with callous-unemotional traits and adults with psychopathic traits have implicated genes involved in the serotonin and dopamine systems, including polymorphisms of the genes for COMT, MAO-A, and the serotonin transporter.^{9,10,29,34,35} For example, several studies have reported that individuals homozygous for the long allele of the serotonin transporter gene exhibit psychopathic features, including reduced response to threat in the

amygdala, impaired fear conditioning, reduced cortisol reactivity, increased risk-taking behavior, and an impaired ability to make decisions based on reward and punishment.²⁹ Other genes implicated in psychopathy are involved in amygdala responsivity to threat and stress, learning and reward activity, and cannabinoid functioning.²⁹ Additionally, there is evidence for genes and single nucleotide variants involved in the oxytocin system, which influences amygdala activity and is associated with social bonding and recognition of social cues.^{9,29}

Ascertaining the Impact of Genes

Studies have attempted to ascertain the impact of genetic influences on antisocial behavior and psychopathic traits. Twin studies attempt to parse out the relative contributions of genetic and environmental factors to a given trait by comparing identical and non-identical twins in similar and dissimilar environments.^{2,29} Genetic factors may be additive, meaning that they have a cumulative effect in contributing to a trait. Shared environmental factors refer to those that are shared between both twins, such as socioeconomic status and parental discipline. On the other hand, nonshared environmental factors refer to those that are unique to each twin, such as peer group. While twin studies are subject to limitations, the power of the twin study approach lies in its ability to distinguish the relative contributions of additive genetic factors versus shared and nonshared environmental factors.

Heritability is a measure of the variation that may be attributed to genetic factors in a given environment. Heritability estimates can be misleading and are easily misinterpreted. Heritability is often misunderstood as a purely genetic construct. Yet even when heritability is high, environmental factors still shape phenotype, as the heritability of a trait depends on its environmental variance.² Moreover, high heritability implies neither genetic determinism nor that an individual's phenotype will be known once the genotype is known.² Certain traits may be more heritable in more favorable environments, or at certain ages and developmental stages.² For example, in a population with universal good parenting practices, positive peer group influences, and no meaningful environmental risk factors for antisocial behavior, the heritability of antisocial behavior would likely be high.

While there is some dispute, most studies indicate that callous-unemotional traits in youth have higher heritability than conduct disorder alone.^{6,10,13,20,40,41}

According to a comprehensive review of 50 years of twin studies by Polderman *et al.*,⁴² approximately 40 to 50 percent of the variance in liability to conduct disorder is due to genetic influences. According to a recent systematic review of 24 twin studies by Moore *et al.*,⁹ the heritability of callous-unemotional traits is likely between 36 and 67 percent. While Viding *et al.*⁴³ found a 67 percent heritability of callous-unemotional traits in a twin study of seven-year-old children, this high figure likely stems from the use of a selected sample with extreme callous-unemotional traits.⁹ Heritability estimates of conduct disorder symptoms increase over time from childhood to adolescence.^{10,13} While this may reflect difficulties in detecting early conduct problems, this also indicates that genetic influences on conduct disorder change with developmental stage and age. Salvatore and Dick suggest that this may be due to “new genes coming ‘online,’” or the emergence of new genetic influences during development (Ref. 13. p 93).

Likewise, in adults, psychopathy appears to have higher heritability than antisocial personality disorder alone. According to a meta-analysis of 51 twin and adoption studies by Rhee and Waldman,¹² additive genetic influences contribute 32 percent and nonadditive genetic influences contribute nine percent to the heritability of antisocial behavior. Heritability estimates for psychopathy are slightly higher, ranging from 40 to 60 percent.^{12,16,29} There is evidence that additive genetic factors contribute 49 percent to the heritability of psychopathy.⁴⁴ Other studies have looked at individual psychopathic traits.²⁹ For example, studies have estimated the heritability of “fearless dominance” to be 45 to 51 percent, and the heritability of “impulsive antisociality” to be 32 to 49 percent.^{45,46}

Genetics, Complexities, and Unknowns

While genes are important in the development of antisocial behavior and psychopathic traits, studies have not yet localized individual genes or determined the mechanisms by which they might affect biology and development. The associations that have emerged account for only a small fraction of the variance in antisocial behavior and psychopathic traits.¹⁰ This may in part be related to research limitations, such as small sample sizes and difficulty defining

study populations. As samples with tens to hundreds of thousands of individuals are needed to identify genetic variants, the small sample sizes of several studies have limited their ability to answer the scientific questions at hand.¹⁰ Consequently, studies have been plagued by relatively small effect sizes and a lack of sufficient power.^{6,9,13,16,21} Moreover, efforts to define study populations have been limited by the use of individual self-report rather than diagnoses, as well as by the inherent heterogeneity of the conditions associated with antisocial behaviors and psychopathic traits.^{9,10} For example, it has been estimated that 32,000 different symptom profiles can qualify for a conduct disorder diagnosis.¹⁰

Genetic influences represent only one factor within a complex etiology and often vary in their connection to behavior. Given the polygenic nature of psychiatric disorders, the contribution of any single gene may be small. Indeed, specific individual genes are believed to play a very minor role in conduct disorder, callous-unemotional traits, antisocial personality disorder, and psychopathy, as an array of genes shape a single trait.^{9,10,29–31,47}

The Power of the Environment

Despite the importance of genetic factors in the development of antisocial behavior and psychopathic traits, environmental factors play a powerful role.^{10,21,38,48} Approximately 50 percent of the variance in antisocial behaviors and psychopathic traits in children and adults stems from prenatal, perinatal, familial, neighborhood, and other environmental factors.^{9,10} In their review of twin studies, Polderman *et al.*⁴² reported that approximately 14 to 30 percent of the variance in conduct disorder is due to shared environmental factors. Moreover, many studies establish that nonshared environmental factors, such as peer relationships, play a critical role in the etiology of callous-unemotional traits in youth, and in antisocial personality disorder and psychopathy in adults.^{9,16,29,43,49} Indeed, these findings highlight that antisocial behavior and psychopathic traits do not result from genes and biology alone.

Environmental factors can operate to increase a youth’s risk for conduct disorder and callous-unemotional traits at several points across the lifespan. Evidence suggests that maternal smoking, alcohol use, drug use, stress, and anxiety during pregnancy can increase the risk that a child will develop conduct problems in later years.^{10,50} After birth, obstetric

complications, malnutrition, exposure to heavy metals, parental psychopathology, deviant peer groups, poverty, low socioeconomic status, and exposure to community violence confer an increased risk for antisocial behavior and callous-unemotional traits among youth.^{10,50} Parent-child conflict and negative parent-child interactions, such as maltreatment, maladaptive parenting, and harsh, inconsistent, coercive discipline have been particularly strongly associated with youth conduct problems.^{10,50}

The mechanisms by which environmental factors alter a youth's development, predisposing to antisocial behavior and psychopathic traits, are complex. Environmental factors can lead to lasting neurodevelopmental effects by affecting neurocognitive functions.⁵⁰ For example, maternal smoking and stress during pregnancy affect the development of the amygdala, ventromedial prefrontal cortex, and other neural structures.⁵⁰ The impact of environmental factors may also vary based on a child's individual traits.⁵⁰ For example, a child's level of stress reactivity may determine the response to harsh, inconsistent, or coercive parenting.⁵⁰

Genes and the Environment, Intertwined

The interplay between genetic and environmental factors can be difficult to ascertain. Genetic and environmental influences often correlate with each other, given that the biological parents often determine both the child's genes and environment.¹³ For example, children of parents with antisocial personality disorder may be more likely to be subject to harsh discipline, maltreatment, inconsistent supervision, or lack of warmth and affection, all of which can lead to an increased risk of conduct disorder in childhood and antisocial personality disorder in adulthood.⁴⁷ Furthermore, genetically influenced predispositions can lead individuals to seek out certain environments, and genetically influenced behaviors can promote certain environmental responses.¹³ For example, Kendler *et al.*⁵¹ describe the manner in which genetic factors may drive youth to socialize with deviant peers, leading them to develop antisocial behaviors that subsequently become reinforced by social influences.

Genetic and environmental factors can interact to moderate or amplify each other's effects. Several studies have suggested that the impact of genetic influences on conduct disorder varies based on environmental factors, such as urban versus rural residency, greater versus less parental monitoring, and

higher peer deviance.¹³ A study by Caspi *et al.*⁵² provides a quintessential example of this effect. They found that maltreated children with low levels of MAO-A expression were far more likely to develop antisocial behavior, and that this gene-environment interaction between low levels of MAO-A expression and maltreatment accounted for 65 percent of the variability in the development of antisocial behavior.⁵² Despite some inconsistency in efforts to replicate the findings of Caspi *et al.*,⁵² particularly in certain subgroups, the interaction between MAO-A expression and maltreatment has been one of the few findings to hold up relatively consistently in meta-analyses.^{6,10,53-55} In other examples, variations in the *5-HTTLPR* genotype interact with environmental adversity and childhood maltreatment to moderate the risk of antisocial personality disorder, and variations in MAO-A and *5-HTTLPR* interact with the subtype, age of onset, and chronicity of maltreatment to predict antisocial behavior.^{9,56-58} Further, it has been suggested that environmental factors may have more powerful genetic interactions during certain developmental stages, such as harsh parenting during early childhood or deviant peer groups during adolescence.⁵⁹

Epigenetics serves as a potential mechanism for these gene-environment interactive effects, as it enables environmental influences to make chemical changes to DNA and thereby alter the expression of genes, the functioning of neurons, and the behavior of individuals. Evidence suggests that epigenetics allows factors such as poor nutrition, neurotoxins, and maternal care to elicit DNA modifications that affect an individual's stress response and dopamine functioning, possibly leading to externalizing disorders.^{13,21} Epigenetics is a new area of investigation, with few studies thus far, yet relationships between DNA methylation patterns and conduct disorder-related symptoms and behaviors have emerged.^{10,13,21} Adolescent callous-unemotional traits have been associated with oxytocin and serotonin receptor gene methylation, which in turn has been associated with maternal psychopathology and prenatal risk factors.^{9,60,61} Further, epigenetic regulation of genes involved in serotonergic and neuroendocrine functioning has been associated with aggression.^{62,63} Epigenetics thus provides a biological mechanism whereby environmental and genetic influences can shape each other and thereby shape developmental trajectories and outcomes.

Research suggests that genetics may predict the impact of environmental factors, and thus may have a role in predicting outcomes and responsivity to interventions. Belsky *et al.*⁶⁴ propose a “differential susceptibility” framework wherein genetic factors afford developmental plasticity that render an individual more prone to poor outcomes in adverse environments and more prone to optimal outcomes in supportive environments. Further, Pluess and Belsky⁶⁵ propose a “vantage sensitivity” framework wherein genetic factors render an individual uniquely able to benefit from positive experiences. Consistent with these theories, studies have found that the presence of a particular variant of the dopamine receptor gene (*DRD4-7R*) may predict which children will benefit more from computer programs designed to improve literacy.^{66,67} Additionally, the presence of a particular variant of the serotonin transporter gene (*5-HTTLPR*) may predict which children will exhibit more problems with externalizing behaviors in institutional settings versus alternative settings, such as high-quality foster care.⁶⁸

Not only might genetics predict treatment outcomes, but environmental interventions might counteract an elevated risk conferred by genes. Environmental interventions can profoundly alter the trajectories of psychiatric conditions with complex patterns of inheritance. For example, cognitive-behavioral interventions that promote stress resilience, cognitive functioning, and social integration may prevent the development of psychosis among individuals at risk for schizophrenia.⁶⁹ Further, family psychoeducation, individual resilience-focused psychotherapy, and supportive employment have been associated with improved quality of life and lower depression after first psychotic episodes.⁷⁰ As another example, attention-deficit/hyperactivity disorder (ADHD) may be effectively managed with behavioral therapies that actively involve the child, parents, and teachers.⁷¹ Taken together, the critical importance of gene–environment interactions, the predictive potential of genetics, and the power of environmental interventions to counteract genetic risk provide compelling evidence that findings from genetic research can be harnessed to guide interventions and facilitate improved outcomes for antisocial behavior and psychopathic traits.

Improving Interventions

Whereas antisocial personality disorder and psychopathy in adults are generally considered untreat-

able with poor prognoses, there are several effective, evidence-based interventions for youth with conduct disorder and callous-unemotional traits. Psychosocial interventions targeting various aspects of a youth’s family, home, and social environment are the mainstay of treatment.¹⁰ Behavioral parent-training programs, such as the Incredible Years Program, guide parents in fostering warm parent–child interactions and in using positive reinforcement to promote desirable behaviors in their children.^{10,72} Cognitive-behavioral skills training teaches youth social problem-solving and self-regulation skills.¹⁰ Adolescents often benefit from interventions that also target peer relationships and the broader social environment, such as Multisystemic Therapy and Functional Family Therapy.¹⁰ While pharmacological interventions may at times be helpful, particularly in youth with co-morbid externalizing conditions like ADHD, such programs supplement psychosocial interventions, which remain key to effecting lasting change.^{10,11}

Interventions may prevent the progression of conduct problems, thereby changing a youth’s developmental trajectory.^{10,11,23,73} For example, the Perry Preschool Project decreased future risk of criminal behavior and offending by providing preschool-age children with educational activities to foster their decision-making and problem-solving skills, and by providing their parents with support in reinforcing the curriculum at home.⁷⁴ While youth with callous-unemotional traits tend to exhibit poorer treatment responses, interventions may be enhanced for such youth by incorporating components that promote emotion-processing skills.¹⁰ Indeed, treatment interventions that are individually tailored to a child’s specific needs are most likely to be successful.²³

In the future, findings from genetic and gene–environment studies might be used to improve interventions. Given that antisocial behaviors and psychopathic traits have complex patterns of inheritance and are subject to gene–environment interactions, environmental interventions might profoundly influence their emergence and progression. The importance of genetic factors and gene–environment interactions in the etiology and development of these problems suggests that genetic evidence might be harnessed to design better interventions. In a broad sense, genetic information might help predict which youth will develop antisocial behavior and psychopathic traits, and which interventions might best ameliorate the impact of life adversity.

Identifying the best way to utilize findings from genetic and gene–environment studies to improve interventions is a complicated matter. Given the complexity of the genetic influences on antisocial behavior and psychopathic traits, authors have suggested pooling single gene findings together to create polygenic risk scores (PRS).¹⁰ PRS scores attempt to quantify an individual’s total “burden” of genetic risk for a particular disorder.⁷⁵ Researchers are hopeful that, in the future, PRS scores might provide legitimate biomarkers for psychiatric conditions and permit a personalized medicine approach to their management by aiding diagnosis, targeting preventive interventions, and predicting treatment response.^{8,75}

There is evidence that PRS scores predict the development of antisocial behavior and psychopathic traits. In a recent study by Tielbeek *et al.*,¹⁴ PRS scores predicted antisocial phenotypes in an adult forensic sample. Other studies have indicated that PRS scores predict conduct problems and “uncaring” traits in youth.^{76,77} PRS scores might also predict antisocial trajectories throughout the life course. In a recent study by Wertz *et al.*,⁷⁸ PRS scores for lower cognitive abilities, impaired self-control, truancy, and academic difficulties during primary school were associated with criminal records in midlife. Further, PRS scores might predict detrimental gene–environment interactive effects. There is evidence that PRS scores can predict the extent to which an adverse life event will increase the likelihood a child will develop antisocial behavior or psychopathic traits.⁷⁷ In a recent study by Musci *et al.*,⁷⁹ youth with low PRS scores for conduct problems who witnessed violence during middle school were more likely to develop aggressive, impulsive behavior than youth with low PRS scores for conduct problems who did not witness violence during middle school. In the future, PRS scores may help elucidate the manner in which antisocial behavior and psychopathic traits develop across the life span, and the manner in which genes potentially lead to criminal offending.⁷⁸

While PRS scores for antisocial behavior and psychopathic traits are currently used only in research settings, they may prove useful in clinical settings in the future.⁸ PRS scores have recently shown promise for clinical use in several medical conditions, including screening, therapeutic interventions, and life planning for breast cancer, heart disease, prostate cancer, Alzheimer disease, and diabetes.^{75,80} Indeed,

polygenic testing will likely be implemented in specialized familial breast cancer clinics.⁸¹ If polygenic testing for antisocial behavior and psychopathic traits were to prove similarly useful in clinical practice, such testing might help identify children with an elevated biological risk. Polygenic risk scores above a certain threshold might be considered high, and this information might then be incorporated into algorithms that include other risk factors.^{8,82} Such approaches might enable clinicians to use information about a child’s genes to guide prevention or early intervention. For example, a child determined to carry a high genetic burden for antisocial behavior or psychopathic traits might benefit from early parent-training programs, community organizations that promote prosocial peer relationships, and increased availability of mental health resources at critical times, such as during the transition to adolescence. Additionally, effectively communicating polygenic testing results to a child’s parents and other social supports might encourage their engagement in preventive or early intervention services.⁸ While sharing this information with family, the clinician might highlight evidence that environmental interventions, such as specific parenting practices with increased positive reinforcement, can counteract the elevated genetic risk for antisocial behavior and psychopathic traits.⁹

It is possible that before they have clinical use in the care of individual patients, PRS scores might facilitate public health efforts to prevent antisocial behavior and psychopathic traits. In psychiatric research studies, PRS scores are able to differentiate groups of individuals on a population level.^{8,75} Currently, PRS scores are able to stratify levels of risk for medical conditions, such as breast cancer.⁸¹ In a similar fashion, it might become possible to use PRS scores to stratify populations of youth into groups with different risk levels for antisocial behaviors and psychopathic traits, which might assist with allocating resources and preventive interventions.⁸ For example, public health policies and programs might expand access to mental health services, parenting resources, and other supports for groups determined to have high risk for antisocial behavior and psychopathic traits.

Realistically, however, the availability of polygenic testing to predict antisocial behavior or psychopathic traits in individual youths or in populations of youth remains far away. PRS scores are currently unable to

ascertain any given individual's risk for a psychiatric condition.^{8,75} Despite promising research, the predictive ability of PRS scores remains limited. In studies of psychiatric conditions, PRS scores have accounted for less than 15 percent of variation.⁸ Additionally, PRS scores have been derived from relatively small samples with limited ethnic diversity, and there is significant overlap among PRS scores for various traits and psychiatric diagnoses.^{75,82} Further research into the utility of PRS scores for antisocial behavior and psychopathic traits is needed.^{8,75}

Informing Policy Changes

While research into the potential clinical and public health applications of polygenic testing for antisocial behavior and psychopathic traits continues to advance and evolve, existing research highlighting the importance of gene–environment interactions should be used to advocate for expanded supports and more rehabilitative policies for all youth. It is well known that certain environments generally have detrimental effects on youth and adults. For example, incarceration leads to higher rates of psychiatric disorders, substance use, and suicide, as well as increased criminal behavior among youth.¹⁰ Additionally, environmental interventions remain effective even when an individual's level of genetic risk remains unknown. Further, psychosocial interventions to prevent antisocial behavior and psychopathic traits in certain youth might have indirect benefits for other youth within a community. Widespread preventive interventions might have cumulative effects within communities, fostering an optimal environment that benefits all youth. For example, given that prosocial peer group influences are associated with a lower risk for developing antisocial behavior, an intervention that promotes prosocial behavior in one child might indirectly benefit the child's peers, and as more and more youth engage in prosocial behaviors, rates of juvenile crime, youth trauma, and other environmental risk factors for antisocial behavior and psychopathic traits might decline. Given the significant influence of social factors on antisocial behavior and psychopathic traits, the cumulative effects of preventive interventions within communities could be profound.

Moreover, the influence of gene–environment interactions suggests that expanding environmental interventions to benefit all youth would greatly enhance their ability to counteract genetic risk and

prevent the emergence of antisocial behavior and psychopathic traits. When environmental interventions reach greater numbers of youth, their beneficial impact within communities may be amplified. These amplified benefits may then operate through gene–environment interactions to counteract the influence of biological factors in youth with elevated genetic risk for antisocial behavior and psychopathic traits. In this way, the collective impact of environmental influences and gene–environment interactions might preempt the development of antisocial behavior and psychopathic traits.

Therefore, evidence of the importance of gene–environment interactive effects should be harnessed to advocate for expanded resources, public education programs, and policies that support healthy child development for all youth. Indeed, Musci *et al.*⁷⁹ note that their research revealing the interaction between genes and violence exposure in the development of antisocial, impulsive behavior underscores the importance of policies and multifaceted, community-wide prevention efforts to reduce violence. They recommend societal changes and resources to benefit all youth, such as expanding and promoting mentoring programs, organizations that help youth establish prosocial relationships, and opportunities for disadvantaged families to move to safer neighborhoods.⁷⁹

Evidence of the power of gene–environment interactive effects should be used to advocate for more rehabilitative, developmentally appropriate policies for justice-involved youth. In its position paper on reducing youth incarceration, the Society for Adolescent Health and Medicine argues that youth justice policies should be scientifically based and focus on fostering healthy youth development by providing community-based supports and building healthy social environments for youth and their families.⁸³ The timing may be ripe to harness research revealing the importance of gene–environment interactions to bolster their argument. In recent years, neuroscience research revealing biological differences in the adolescent brain have been successfully used to benefit justice-involved youth by supporting arguments to ban the death penalty, limit the use of life without parole, and raise the age of adult criminal responsibility.^{84–86} Research revealing the importance of gene–environment interactions in the development of antisocial behavior and psychopathic traits would add to the body of science benefiting justice-involved youth by highlighting the rehabili-

tative potential of youth and the potential for the environment to alter a youth's trajectory.

Conclusion

Antisocial behavior and psychopathic traits are subject to complex patterns of inheritance and gene–environment interactive effects and are profoundly influenced by environmental interventions. Identifying youth with an elevated genetic risk for antisocial behavior and psychopathic traits should lead to improved interventions and preventive efforts. Moreover, research revealing the importance of gene–environment interactions in the development of antisocial behavior and psychopathic traits can and should be harnessed to promote more rehabilitative, developmentally appropriate policies to benefit youth, particularly those involved in our juvenile justice and social welfare systems. Indeed, an expanded understanding and awareness of underlying genetic factors and gene–environment interactions would facilitate a larger goal of preempting the development of antisocial behavior and psychopathic traits.

References

- Sabatello M, Appelbaum PS: Behavioral genetics in criminal and civil courts. *Harv Rev Psychiatry* 25:289–301, 2017
- Visscher PM, Hill WG, Wray NR: Heritability in the genomics era—concepts and misconceptions. *Nat Rev Genet* 9:255–66, 2008
- Dinwiddie SH: Psychiatric genetics and forensic psychiatry: a review. *Bull Am Acad Psychiatry Law* 22:327–42, 1994
- Sabatello M, Appelbaum S: Psychiatric genetics in child custody proceedings: ethical, legal, and social issues. *Curr Genet Med Rep* 4:98–106, 2016
- Treadway MT, Buckholtz JW: On the use and misuse of genomic and neuroimaging science in forensic psychiatry: current roles and future directions. *Child Adolesc Psychiatr Clin N Am* 20:533–46, 2011
- Moffitt TE, Arseneault L, Jaffee SR, *et al*: Research review: DSM-V conduct disorder: research needs for an evidence base. *J Child Psychol Psychiatry* 49:3–33, 2008
- Appelbaum PS, Scurich N: Impact of behavioral genetic evidence on the adjudication of criminal behavior. *J Am Acad Psychiatry Law* 42:91–100, 2014
- Palk AC, Dalvie S, de Vries J, *et al*: Potential use of clinical polygenic risk scores in psychiatry - ethical implications and communicating high polygenic risk. *Philos Ethics Humanit Med* 14:4, 2019
- Moore AA, Blair RJ, Hettrema JM, Roberson-Nay R: The genetic underpinnings of callous-unemotional traits: a systematic research review. *Neurosci Biobehav Rev* 100:85–97, 2019
- Fairchild F, Hawes DJ, Frick PJ, *et al*: Conduct disorder. *Nat Rev Dis Primers* 5:43, 2019
- Blair RJ, Leibenluft E, Pine PS: Conduct disorder and callous-unemotional traits in youth. *N Engl J Med* 371:2207–16, 2014
- Rhee SH, Waldman ID: Genetic and environmental influences on antisocial behavior: a meta-analysis of twin and adoption studies. *Psychol Bull* 128:490–529, 2002
- Salvatore JE, Dick DM: Genetic influences on conduct disorder. *Neurosci Biobehav Rev* 91:91–101, 2018
- Tielbeek JJ, Johansson A, Polderman TJC, *et al*: Genome-wide association studies of a broad spectrum of antisocial behavior. *JAMA Psychiatry* 74:1242–50, 2017
- American Psychiatric Association: *Diagnostic and Statistical Manual of Mental Disorders, Fifth Edition*. Arlington, VA: American Psychiatric Association, 2013
- Werner KB, Few LR, Bucholz KK: Epidemiology, comorbidity, and behavioral genetics of antisocial personality disorder and psychopathy. *Psychiatr Ann* 45:195–9, 2015
- Maden A, Newman S: Antisocial personality disorder and psychopathy, in *Principles and Practice of Forensic Psychiatry, 3rd Edition*. Edited by Rosner R, Scott CL, Boca Raton FL: Taylor and Francis Group, 2017, pp 613–622
- Cleckley HM. *The Mask of Sanity: An Attempt to Reinterpret the So-Called Psychopathic Personality*. St. Louis: The C.V. Mosby Company, 1941
- Hare RD, Neumann CS, Moknos A: The PCL-R assessment of psychopathy, in *Handbook of Psychopathy, 2nd Edition*. Edited by Patrick CJ. New York: The Guilford Press, 2018, pp 39–79
- Gao Y, Glenn AL, Schug RA, *et al*: The neurobiology of psychopathy: a neurodevelopmental perspective. *Can J Psychiatry* 54:813–23, 2009
- McDonough-Caplan HM, Beauchaine TP: Conduct disorder: a neurodevelopmental perspective, in *Developmental Pathways to Disruptive, Impulse-Control, and Conduct Disorders*. Edited by Martel M. London: Academic Press, 2018, pp 53–89
- Moffitt TE: Adolescence-limited and life-course-persistent antisocial behavior: a developmental taxonomy. *Psychol Rev* 100:674–701, 1993
- Frick PJ: Extending the construct of psychopathy to youth: implications for understanding, diagnosing, and treating antisocial children and adolescents. *Can J Psychiatry* 54:803–12, 2009
- Frick PJ, White SF: Research review: the importance of callous-unemotional traits for developmental models of aggressive and antisocial behavior. *J Child Psychol Psychiatry* 49:359–75, 2008
- Moffitt TE, Caspi A, Harrington H, *et al*: Males on the life-course-persistent and adolescence-limited antisocial pathways: follow-up at age 26 years. *Dev Psychopathol* 14:179–207, 2002
- Seagrave D, Grisso T: Adolescent development and the measurement of juvenile psychopathy. *Law & Hum Behav* 26:219–39, 2002
- Hart SD, Watt KA, Vincent GM: Commentary on Seagrave and Grisso: impressions of the state of the art. *Law & Hum Behav* 26:241–5, 2002
- Lynam DR, Caspi A, Moffitt TE, *et al*: Longitudinal evidence that psychopathy scores in early adolescence predict adult psychopathy. *J Abnorm Psychol* 116:155–65, 2007
- Glenn AL, Raine A: *Psychopathy: An Introduction to Biological Findings and Their Implications*. New York: New York University Press, 2014
- Waller R, Corral-Frías NS, Vannucci B, *et al*: An oxytocin receptor polymorphism predicts amygdala reactivity and behavior in men. *Soc Cogn Affect Neurosci* 11:1218–26, 2016
- Rijsdijk FV, Viding E, De Brito S, *et al*: Heritable variations in gray matter concentration as a potential endophenotype for psychopathic traits. *Arch Gen Psychiatry* 67:406–13, 2010

32. Ficks CA, Waldman ID: Candidate genes for aggression and antisocial behavior: a meta-analysis of association studies of the 5HTTLPR and MAOA-uVNTR. *Behav Genet* 44:427–44, 2014
33. Van Goozen SHM, Fairchild G: How can the study of biological processes help design new interventions for children with severe antisocial behavior? *Dev Psychopathol* 20:941–73, 2008
34. Viding E, Price TS, Jaffee SR, *et al*: Genetics of callous-unemotional behavior in children. *PLoS One* 8:e65789, 2013
35. Viding E, Hanscombe KB, Curtis CJ, *et al*: In search of genes associated with risk for psychopathic tendencies in children: a two-stage genome-wide association study of pooled DNA. *J Child Psychol Psychiatry* 51:780–8, 2010
36. Ehlers CL, Gilder DA, Slutske WS, *et al*: Externalizing disorders in American Indians: comorbidity and a genome wide linkage analysis. *Am J Med Genet B Neuropsychiatr Genet* 147B:690–8, 2008
37. Gizer IR, Ficks C, Waldman ID: Candidate gene studies of ADHD: a meta-analytic review. *Hum Genet* 126:51–90, 2009
38. Veroude K, Zhang-James Y, Fernández-Castillo N, *et al*: Genetics of aggressive behavior: an overview. *Am J Med Genet B Neuropsychiatr Genet* 171B:3–43, 2016
39. Dick DM, Bierut L, Hinrichs A, *et al*: The role of GABRA2 in risk for conduct disorder and alcohol and drug dependence across developmental stages. *Behav Genet* 36:577–90, 2006
40. Dhamija D, Tuvblad C, Baker L: Behavioral genetics of the externalizing spectrum, in *The Oxford Handbook of Externalizing Spectrum Disorders*. Edited by Beauchaine TP, Hinshaw SP. Oxford, UK: Oxford University Press, 2016
41. Baker LA, Jacobson KC, Raine A, *et al*: Genetic and environmental bases of childhood antisocial behavior: a multi-informant twin study. *J Abnorm Psychol* 116: 219–35, 2007
42. Polderman TJ, Benyamin B, de Leeuw CA, *et al*: Meta-analysis of the heritability of human traits based on fifty years of twin studies. *Nat Genet* 47:702–9, 2015
43. Viding E, Blair RJ, Moffitt TE, *et al*: Evidence for substantial genetic risk for psychopathy in 7-year-olds. *J Child Psychol Psychiatry* 46:592–7, 2005
44. Gunter TD, Vaughn MG, Philibert RA: Behavioral genetics in antisocial spectrum disorders and psychopathy: a review of the recent literature. *Behav Sci & L* 28:148–73, 2010
45. Blonigen DM, Hicks BM, Krueger RF, *et al*: Psychopathic personality traits: heritability and genetic overlap with internalizing and externalizing psychopathology. *Psychol Med* 35:637–48, 2005
46. Brook M, Panizzon MS, Kosson DS, *et al*: Psychopathic personality traits in middle-aged male twins: a behavior genetic investigation. *J Pers Disord* 24:473–86, 2010
47. Glenn AL, Johnson AK, Raine A: Antisocial personality disorder: a current review. *Curr Psychiatry Rep* 15:427, 2013
48. Moffitt TE: The new look of behavioral genetics in developmental psychopathology: gene-environment interplay in antisocial behaviors. *Psychol Bull* 131:533–54, 2005
49. Larsson H, Andershed H, Lichtenstein P: A genetic factor explains most of the variation in the psychopathic personality. *J Abnorm Psychol* 115:221–30, 2006
50. Blair RJ: The neurobiology of psychopathic traits in youths. *Nat Rev Neurosci* 14:786–99, 2013
51. Kendler KS, Jacobson K, Myers JM, *et al*: A genetically informative developmental study of the relationship between conduct disorder and peer deviance in males. *Psychol Med* 38:1001–11, 2008
52. Caspi A, McClay J, Moffitt TE, *et al*: Role of genotype in the cycle of violence in maltreated children. *Science* 297:851–4, 2002
53. Widom CS, Brzustowicz LM: MAOA and the cycle of violence: childhood abuse and neglect, MAOA genotype, and risk for violent and antisocial behavior. *Biol Psychiatry* 60:684–9, 2006
54. Huizinga D, Haberstick BC, Smolen A, *et al*: Childhood maltreatment, subsequent antisocial behavior, and the role of monoamine oxidase A genotype. *Biol Psychiatry* 60:677–83, 2006
55. Foley DL, Eaves LJ, Wormley B, *et al*: Childhood adversity, monoamine oxidase A genotype, and risk for conduct disorder. *Arch Gen Psychiatry* 61:738–44, 2004
56. Tielbeek JJ, Karlsson Linnér R, Beers K, *et al*: Meta-analysis of the serotonin transporter promoter variant (5-HTTLPR) in relation to adverse environment and antisocial behavior. *Am J Med Genet B Neuropsychiatr Genet* 171:748–60, 2016
57. Douglas K, Chan G, Gelernter J, *et al*: 5-HTTLPR as a potential moderator of the effects of adverse childhood experiences on risk of antisocial personality disorder. *Psychiatr Genet* 21:240–8, 2010
58. Cicchetti D, Rogosch FA, Thibodeau EL: The effects of child maltreatment on early signs of antisocial behavior: genetic moderation by tryptophan hydroxylase, serotonin transporter, and monoamine oxidase A genes. *Dev Psychopathol* 24:907–28, 2012
59. Hyde LW: Developmental psychopathology in an era of molecular genetics and neuroimaging: a developmental neurogenetics approach. *Dev Psychopathol* 27:587–613, 2015
60. Dadds MR, Moul C, Cauchi A, *et al*: Methylation of the oxytocin receptor gene and oxytocin blood levels in the development of psychopathy. *Dev Psychopathol* 26:33–40, 2014
61. Cecil CA, Lysenko LJ, Jaffee SR, *et al*: Environmental risk, oxytocin receptor gene (OXTR) methylation and youth callous-unemotional traits: a 13-year longitudinal study. *Mol Psychiatry* 19:1071–7, 2014
62. Provençal N, Suderman MJ, Caramaschi D, *et al*: Differential DNA methylation regions in cytokine and transcription factor genomic loci associate with childhood physical aggression. *PLoS One* 8:e71691, 2013
63. Palumbo S, Mariotti V, Iofrida C, *et al*: Genes and aggressive behavior: epigenetic mechanisms underlying individual susceptibility to aversive environments. *Front Behav Neurosci* 12:117, 2018
64. Belsky J, Jonassaint C, Pluess M, *et al*: Vulnerability genes or plasticity genes? *Mol Psychiatry* 14:746–54, 2009
65. Pluess M, Belsky J: Vantage sensitivity: individual differences in response to positive experiences. *Psychol Bull* 139:901–16, 2013
66. Plak RD, Kegel CA, Bus AG: Genetic differential susceptibility in literacy-delayed children: a randomized controlled trial on emergent literacy in kindergarten. *Dev Psychopathol* 27:69–79, 2015
67. Kegel CAT, Bus AG, van IJzendoorn MH: Differential susceptibility in early literacy instruction through computer games: The role of the dopamine D4 receptor gene (DRD4). *Mind Brain Educ* 5:71–8, 2011
68. Brett ZH, Humphreys KL, Smyke AT: Serotonin transporter linked polymorphic region (5-HTTLPR) genotype moderates the longitudinal impact of early caregiving on externalizing behavior. *Dev Psychopathol* 27:7–18, 2015
69. Millan MJ, Andrieux A, Bartzokis G: Altering the course of schizophrenia: progress and perspectives. *Nat Rev Drug Discov* 15:485–515, 2016
70. Lieberman JA, Small SA, Girgis RR: Early detection and preventive intervention in schizophrenia: from fantasy to reality. *Am J Psychiatry* 176:794–810, 2019
71. Catalá-López F, Hutton B, Núñez-Beltrán A, *et al*: The pharmacological and non-pharmacological treatment of attention deficit hyperactivity disorder in children and adolescents: a systematic review with network meta-analyses of randomised trials. *PLoS One* 12:e0180355, 2017
72. Leijten P, Gardner F, Landau S, *et al*: Research review: harnessing the power of individual participant data in a meta-analysis of the

Preempting Development of Antisocial Behavior and Psychopathic Traits

- benefits and harms of the Incredible Years parenting program. *J Child Psychol Psychiatry* 59:99–109, 2018
73. Bakker MJ, Greven CU, Buitelaar JK, *et al*: Practitioner review: psychological treatments for children and adolescents with conduct disorder problems: a systematic review and meta-analysis. *J Child Psychol Psychiatry* 58:4–18, 2017
 74. Social Programs That Work. Evidence summary for the Perry Preschool Project. Social Programs that Work Review, updated November 2017. Available at: <https://evidencebasedprograms.org/document/perry-preschool-project-evidence-summary>. Accessed June 16, 2020
 75. Fullerton JM, Nurnberger JI: Polygenic risk scores in psychiatry: Will they be useful for clinicians? *F1000Res* 8:1293, 2019
 76. Shaw DS, Galán CA, Lemery-Chalfant K, *et al*: Trajectories and predictors of children's early-starting conduct problems: child, family, genetic, and intervention effects. *Dev Psychopathol* 31:1911–21, 2019
 77. Ruisch IH, Dietrich A, Klein M, *et al*: Aggression based genome-wide, glutamatergic, dopaminergic and neuroendocrine polygenic risk scores predict callous-unemotional traits. *Neuropsychopharmacology* 45:761–9, 2020
 78. Wertz J, Caspi A, Belsky DW, *et al*: Genetics and crime: integrating new genomic discoveries into psychological research about antisocial behavior. *Psychol Sci* 29:791–803, 2018
 79. Musci RJ, Bettencourt AF, Sisto D, *et al*: Violence exposure in an urban city: a GxE interaction with aggressive and impulsive behaviors. *J Child Psychol Psychiatry* 60:72–81, 2019
 80. Torkamani A, Wineinger NE, Topol EJ: The personal and clinical utility of polygenic risk scores. *Nat Rev Genet* 19:581–90, 2018
 81. Yanes T, Young MA, Meiser B, *et al*: Clinical applications of polygenic breast cancer risk: a critical review and perspectives of an emerging field. *Breast Cancer Res* 22:21, 2020
 82. Kahn RS, Sommer IE, Murray RM, *et al*: Schizophrenia. *Nat Rev Dis Primers* 1:15067, 2015
 83. Society for Adolescent Health and Medicine: International youth justice systems: promoting youth development and alternative approaches: a position paper of the society for adolescent health and medicine. *J Adolesc Health* 59:482–6, 2016
 84. *Roper v. Simmons*, 543 U.S. 551 (2005)
 85. *Graham v. Florida*, 560 U.S. 48 (2010)
 86. *Miller v. Alabama*, 567 U.S. 460 (2012)