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Nature, Nurture, and the Development and Prevention of Antisocial Behavior Problems in Children

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Drs. Jonson-Reid, Constantino, and colleagues' article adds to a growing body of literature on the importance of both nature *and* nurture in the development of antisocial behavior problems across the lifecycle.¹ In the introduction they highlight Widom's classic paper published in 1989 addressing the question "Does Violence Beget Violence?"² That paper was criticized by DiLalla and Gottesman for focusing on social factors (e.g., maltreatment), and failing to review evidence supporting genetic and physiological bases of violent behavior.³ Two decades later there is at last consensus in the field that both nature and nurture matter, but understandings about how genes and environment interact to promote the development of aggression, sociopathy, and other stress-related psychiatric disorders continues to be elusive and the subject of considerable debate.

A highly publicized meta-analysis of studies examining genetic and environmental (GxE) predictors of depression was recently published in *JAMA* calling into question the utility of GxE candidate gene (e.g., serotonin transporter gene) studies in psychiatry.⁴ The results of the *JAMA* paper were reported in the New York Times,⁵ as well as many other popular press venues. The authors of the *JAMA* article concluded prior GxE candidate gene study results were consistent with chance findings, and did not withstand the test of meta-analysis.

We have published a correspondence which delineates our concerns with this conclusion, as there was a bias in sampling strategy used in the meta-analysis.⁶ The meta-analysis reported in the *JAMA* paper was conducted with data from half of the 26 studies that met inclusion criteria for the meta-analysis,⁴ with a trend for negative studies to be over represented. Of the 26 studies meeting the inclusion criteria for the meta-analysis, 78% (7/9) of the negative studies and only 35% (6/17) of the positive studies were included in the analysis (Fisher's Exact Test: $p < .10$). A comprehensive meta-analysis that includes the majority of available studies and takes into account variation in research quality and design is needed to resolve concerns about the utility of GxE candidate gene approaches in psychiatry.

Drs. Jonson-Reid, Constantino, and colleagues utilized other research strategies to examine genetic and environmental influences in their study.¹ They report data on two well characterized samples – the epidemiological Missouri Twin Registry (MOTWIN) cohort,

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and a clinically-ascertained sample of children from families affected by alcohol dependence participating in the Collaborative Study on the Genetics of Alcoholism (COGA). In the MOTWIN cohort, genetic liability was determined by the presence of clinically significant externalizing problems in the co-twin, and was considered to be highest in monozygotic twins with an affected twin, next highest in dizygotic twins with an affected twin, lower in dizygotic twins without an affected twin, and lowest in monozygotic twins without an affected twin. In the COGA study genetic liability to develop antisocial problems was operationalized by family loading for antisocial personality disorder, alcohol dependence, and substance dependence.

The MOTWIN and COGA data sets were then cross-referenced with child abuse registries in Missouri to simultaneously examine the contributions of maltreatment and inherited factors on the development of antisocial behavior problems. Maltreatment is one of the most potent predictors of violence and sociopathy, but few studies have utilized genetically informed research designs to disentangle genetic and environmental influences on the development of these problems. In both the MOTWIN and COGA studies, child maltreatment was found to be a potent predictor of externalizing problems after controlling for genetic liability, which also potentially predicted the presence of these problems in children.

Drs. Jonson-Reid, Constantino, and colleagues highlight the importance of future studies to delineate the mechanisms by which maltreatment promotes the development of antisocial behavior, including research on the effects of adverse early experience on the modulation of gene expression and neurodevelopment, with the hope that these approaches will lead to new insights for novel intervention strategies to prevent the long-term sequelae of maltreatment after it occurs. They also highlight the importance of efforts to prevent maltreatment⁷ — especially among children at elevated familial risk for antisocial behavior problems. I'd add to that a call to improve the child welfare system that serves maltreated children and their families, where extended stays in out-of-home care, multiple changes in foster care placements, separation from siblings and other important supports are common place, and further exacerbate risk for deleterious outcomes.^{8,9}

Can we prevent the development of antisocial behavior in all cases? Probably not. Is there more we need to learn about the molecular mechanisms by which genetic liability and experiences of maltreatment confer risk for antisocial behavior problems? Absolutely yes. Is there anything we can do in the interim? Yes again, with this latter belief being an essential point made by Drs. Jonson-Reid, Constantino, and colleagues. Child maltreatment is a preventable risk factor for the development of antisocial behavior and effective preventive intervention strategies exist.⁷ There is something we can do.

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