Biological Psychiatry

Treating Conduct Problems by Linking Nurture and Neurobiological Change

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Conduct problems (CPs) consist of aggressive, rulebreaking, destructive, and deceitful behaviors. For some children, CPs begin during preschool or early school years and increase the likelihood of academic underachievement, family dysfunction, legal system involvement, substance misuse, emotional distress, suicidality, teen pregnancy, and a host of health problems (1). Consequently, CPs are associated with high individual, family, and societal burden.

An extensive body of research identifies risk factors related to CPs that span biological and environmental factors. Neurobiological research of CPs in children and young people has emphasized the role of corticolimbic, corticostriatal, and prefrontal control circuits (2,3). Though these circuits have roles in reactivity to threat and emotion, processing rewards and learning, and response inhibition, respectively, their roles and functioning overlap substantially. There also is research identifying environmental exposures that increase risk for the development and maintenance of CPs in children and young people (1). One of the most heavily studied environmental risks for CPs is parenting. Parenting that is harsh and inconsistent has been linked robustly to the development of CPs (1,2,4). Harsh parenting is thought to model behaviors for children and undermine children's ability to develop emotion regulation skills. Inconsistency in parenting is thought to lead to reward contingencies that make aggressive, rulebreaking, destructive, and/or deceitful behaviors useful in some contexts. Building upon this work, increasingly, researchers are directly examining the link between neurobiological and environmental factors. For example, Gard *et al.* (5) showed that harsh parenting in early childhood predicted altered threat-related amygdala reactivity in early adulthood, which in turn predicted behaviors consistent with aggression, rulebreaking, and deceit.

Given the evidence supporting these neurobiological and environmental risk factors, interventions that target disrupted neural processing and problematic parenting practices appear to be the most promising for addressing CPs. In fact, parenting-based programs, especially those incorporating parent management training, often alongside cognitive behavioral therapy, effectively reduce CPs (6). Broadly speaking, these interventions help parents set boundaries, reinforce positive behaviors, and engage in regulated emotional expression. If we consider why these interventions are effective, we can see that theoretically, they address the key risk factors for CPs that relate to parenting styles and the neural bases of affect response and regulation, as well as learning. However, not all young people respond equally to treatment. There are important structural and environmental factors (e.g., poverty, access to treatment) that reduce the effectiveness for some people (6,7); however, it also is likely that there are intrinsic within-person differences that impact treatment effectiveness. Understanding who is likely to respond to treatment and why remains a pressing concern for promoting behavior change. Integrating research on neurobiological and environmental risk factors for CPs has potential to clarify the ways in which interventions exert their effects and for whom they are most effective. In the current issue of *Biological Psychiatry*, Sethi *et al.* (8) explore the neurobiological and learning factors associated with CPs in boys and examine how changes in parenting relate to neural activity and learning.

Sethi *et al.* (8) examined the effects of a parenting intervention on reward learning (measured via functional magnetic resonance imaging and Bayesian hierarchical modeling of learning during a passive avoidance go/no-go task) in 78 boys (5–10 years of age) with CPs compared with 35 typically developing (TD) boys. The parenting intervention (either Incredible Years or Triple-P) had parents complete facilitated, weekly group sessions, over 10 to 12 weeks, and homework between meetings focused on enhancing parenting skills, managing challenging behaviors, and strengthening the parent–child relationship through techniques such as explicit praise, limit setting, and emotion coaching. Boys and their parents were assessed at the beginning of the program and then approximately 18 weeks after the initial assessment. Boys in this study who displayed CPs were divided into 2 groups: those who showed persistent CPs postintervention (n = 39) and those who showed improvement postintervention (n = 39).

Overall, Sethi *et al.* (8) showed that improvements in behavior were associated with specific, positive changes in both brain activity and computational learning parameters, which were not observed in boys with persistent CPs or in TD control children. More specifically, boys in the improving group displayed increased neural activity in the direction of TD children in regions associated with reward processing and decision making (e.g., in the ventromedial prefrontal cortex, insula, posterior cingulate cortex, hippocampus, and midbrain) during the anticipation of reward. The boys in the persistent group and control group saw little change in neural activity in any of these regions. Further, analysis of task behavior using computational modeling showed that the boys in the improving group exhibited distinct changes in learning parameters. Specifically, boys in the improving group showed a decreased learning rate over time, suggesting a shift after intervention to a more controlled and sustained evaluation of

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whether future choices will lead to reward or punishment. These boys also showed a reduced bias toward action, which may reflect a reduction in impulsive decision making post-intervention. Finally, the boys in the improving group displayed increased reward/punishment sensitivity, suggesting a better ability to estimate severity of potential outcomes after intervention. These changes in learning were not observed in the persistent group. Together, these results suggest that for boys showing improvement in CPs after intervention, their improvement was due in part to changes in flexible decision making, impulse control, and reward/punishment sensitivity as reflected in neural and behavioral measures.

Sethi *et al.* (8) also examined the relationship between changes in parenting behavior and the child's brain changes. Across both CP groups, improvement in parent involvement, improvement in positive parenting, and reduced corporal punishment were correlated with changes in insula activity. In addition, in both CP groups, reduction in corporal punishment was associated with increased reward/punishment sensitivity. These results suggest that positive improvements in parenting behavior may act specifically on reward-related factors. This is the first evidence of a direct effect of parenting behavior changes on these measurable neural and behavioral markers in children with CPs.

The research covered by Sethi *et al.* (8) provides a compelling demonstration of one way to advance our understanding of behavior change, even for young people who might be considered difficult to treat. Specifically, we must leverage decades of rich research on risk factors for CPs and integrate multiple methods (e.g., neuroimaging, computational modeling) to test whether those factors serve as mechanisms of change. As an example, the present study took our current theoretical and empirical understanding of reward and learning difficulties in children with CPs, as well as our understanding of parenting behaviors as contributors to CPs, and tested whether the neurobiological risk factors were mechanisms of change in parenting intervention. And, in fact, changes in reward processing and learning were keys to successful treatment response in some boys with CPs. This work helps us understand why gold-standard parenting interventions work and for whom they are effective. Continuing to link existing treatments with biopsychological factors will help us understand whether the interventions designed to address specific behaviors do so directly or indirectly through key mechanistic targets.

However, it also was clear from the present study that not all children responded to the parenting intervention or showed corresponding changes in brain and learning factors. This highlights the heterogeneity within the CP population and underscores the need for matching treatment to the individual. While mapping intervention effects to neural and learning mechanisms is key to understanding why young people respond, we must also ensure that we are selecting interventions designed to target the appropriate mechanisms for each individual. This requires a clear understanding of the child's risk factors and selecting an intervention specifically designed to address them. We would argue that the persistent CPs group reflects a need for better conceptualization of risk factors and the design of tailored treatments. There is no clear evidence that these young people are untreatable, only that they have not yet received the correct treatment.

Overall, the work by Sethi *et al.* (8) importantly continues to dismantle the public pessimism about the treatability of young people with CPs (9). These behaviors are changeable, and several gold-standard interventions, on average, are effective in addressing the behaviors expressed by children with CPs (6). However, like any intervention, not all individuals will respond in the same way or for the same reasons. Taking an interdisciplinary scientific approach to identify which treatments work for which youth and why is the core promise of the science of behavior change. Systematically connecting intervention and biopsychological factors will allow researchers to identify gaps in both our mechanistic understanding and intervention science, thereby spurring the development of new treatments that target specific individual mechanisms.

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