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Current Opinion in Psychology

Parenting intervention effects on children's externalizing behavior: the moderating role of genotype and temperament

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Recent research suggests that children's heightened susceptibility to parenting may have a (poly)genetic basis, and may be grounded in children's temperament. However, much current evidence is of a preliminary—correlational—nature. Because in correlational designs alternative explanations for gene–environment (G × E) or temperament–environment (T × E) interactions cannot be discounted, it is pivotal to conduct experimental studies in which parenting is actively manipulated. Based on data from a recently conducted randomized trial (n = 387) of the Incredible Years parenting intervention, experimental evidence is provided for G × E and T × E interactions in an at-risk population of children aged 4–8 years. The discussion centers around the use of polygenetic data and microtrial designs, and provides suggestions for how to integrate endophenotypes in tests of G × E and T × E.

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Current Opinion in Psychology 2017, **15**:143–148

This review comes from a themed issue on **Parenting**

Edited by **Marinus H van IJzendoorn** and **Marian J Bakermans-Kranenburg**

http://dx.doi.org/10.1016/j.copsyc.2017.02.025

Children's externalizing behavior is characterized by disobedience, defiance of authority, an angry or irritable mood state, and verbal or physical aggression toward others. A childhood-onset of externalizing behavior marks a heightened risk for a clinical diagnosis of externalizing disorders in young adulthood [1] and increases the likelihood of health problems, substance abuse, financial hardship and delinquency in adulthood [2]. Especially dysfunctional parenting and impaired family functioning have been identified as crucial factors in the development of children's externalizing behavior [3,4]. These findings imply that parenting interventions might yield significant reductions in children's externalizing behavior. Although meta-analyses indeed show that parenting interventions are effective [5] with sustained effects until months or even several years later [6,7•], these effects are generally of a limited size.

One possible explanation for the lower effect sizes for many parenting interventions is that children may differ in the extent to which they benefit from enriched parenting. Unfortunately, most intervention studies do not examine any differentiation in intervention response trajectories, and thus cannot speak to the issue of which children benefit most from improved, more positive parenting. Based on a differential susceptibility hypothesis, however, we would expect this. Specifically, the differential susceptibility hypothesis [8–11] implies that children most vulnerable to adverse parenting would also benefit most from positive parenting. Importantly, children's differential susceptibility may be grounded in children's genotype or temperament.

Indeed, different meta-analyses suggest that genetic polymorphisms related to the regulation of dopamine (*DAT1*, *DRD2*, *DRD4*) [12], serotonin (*5HTTLPR*) [13], and the degradation of specific enzymes (*MAOA*) [14], can modulate the effects of both adverse and enriched environments on children's pathological and prosocial development. There is also meta-analytical evidence that shows that children's susceptibility to parenting has a temperamental basis [15••]. Children with a difficult temperament, specifically, appear more vulnerable to negative parenting but also appear to profit more from positive parenting. The Slagt *et al.* [15••] meta-analysis showed that these inter-individual differences in susceptibility could be indexed across different outcome measures, such as children's externalizing and internalizing problems and children's levels of social and cognitive competence.

The meta-analyses reviewed above should be interpreted with caution, however, because they might to some extent be distorted by publication bias [16]. In addition, most studies meta-analyzed until now have relied on correlational research designs. Although such correlational studies provide much insight, they do come with several important limitations [see also 17•]. First, they are unable to rule out alternative explanations for gene or temperament-by-environment interactions (G × E and T × E, respectively). More specifically, they do not control for confounding effects of the linkages between children's genotype or temperament and—in this case—the child's parenting context. For instance, children with a difficult temperament perhaps evoke more

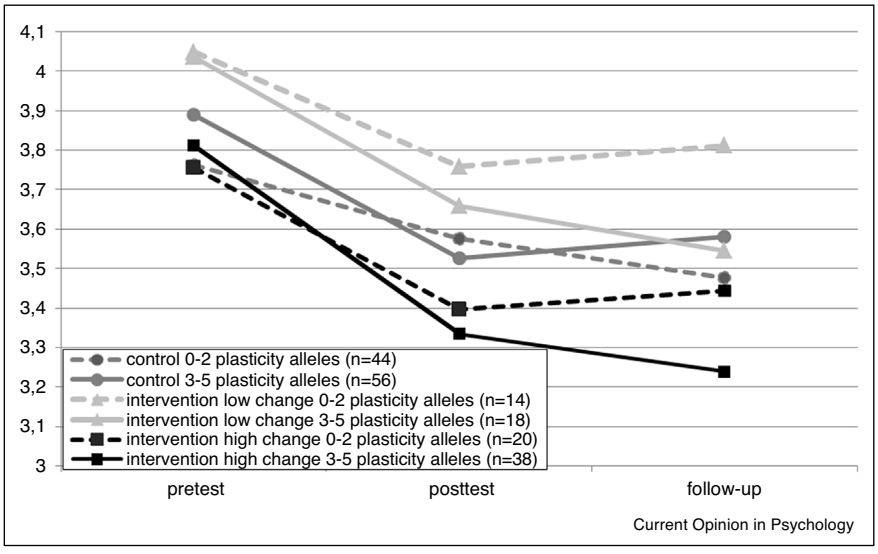
controlling and harsh parenting, and this effect may confound any identified person–environment interaction in a correlational design. Second, most previous correlational studies on G × E or T × E have been underpowered because of limited variance in the pathological outcome and environmental risk measure and in the G × E or T × E interaction terms [see 18].

These issues of low statistical power and uncontrolled confounder mechanisms can be effectively resolved in experiments in which parenting is actively manipulated. This is increasingly recognized in the field, and lead us to develop project ORCHIDS [19]. Project ORCHIDS features a randomized controlled trial of the Incredible Years (IY) parenting intervention in an at-risk sample of 387 families of children 4–8 years, who were screened for elevated levels of disruptive behavior (*i.e.*, 75th percentile on the Eyberg Child Behavior Inventory). Eligible families were randomly allocated to a control group or to an intervention group that received 15 two-hour IY sessions. In these IY sessions, parents engaged in parent group discussions, did role-plays, and examined and discussed video-vignettes. The IY intervention is aimed at empowering parents and at guiding parents toward using more positive, reward-based parenting strategies (*e.g.*, child-led play and using praise and incentive schemes) and toward using sensitive, consequent disciplining practices (*e.g.*, limit setting, ignoring unwanted behavior) [20].

Our randomized trial of IY showed that it significantly increased parent-reported positive parenting and successfully reduced parent-reported negative parenting and externalizing behavior in children [21]. Evidence for G × E emerged, showing that the IY intervention effects were much more pronounced in boys—not girls—with a high score on a dopamine-based polygenic index that comprised *DAT1*, *DRD2*, *DRD4*, *MAOA*, and *COMT* polymorphisms [22••]. The analyses also showed that, as expected, this effect was explained by improvements in positive parenting (Figure 1). Boys high on the polygenic plasticity index, and whose parents increased most in positive parenting, showed the greatest decline in parent-reported externalizing behavior from pretest to follow-up. Notably, the genetic moderation of the IY intervention effect was only present for parent-report data; when we analyzed observational data from parent–child interactions no significant G × E emerged. Perhaps this can be explained by the relatively limited variance in the observational measure of child externalizing behavior [21] in this study.

The ORCHIDS data also showed that the IY intervention effects were moderated by children's temperament, with a significant T × E emerging for children's effortful control—but not children's negative reactivity. This interaction effect demonstrated that children higher on effortful control retained the beneficial behavior effect of IY at follow-up, whereas children low on effortful control bounced back to pre-intervention levels of disruptive behavior at follow-up (G Overbeek *et al.*, unpublished; Table 1). Although this appeared to support the notion of temperament-based differential susceptibility in children, our analyses also demonstrated that children's temperament and externalizing behavior developed in

Figure 1



Incredible Years parenting intervention effects for boys (from: Chhangur *et al*. [22••]).
Note: 'Low change' and 'high change' categories refer to boys with, respectively, low or high levels of improvement in parent-reported positive parenting.