

Chapter 2

Influences of Gene–Environment Interaction and Correlation on Disruptive Behavior in the Family Context

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Introduction

There are diverse developmental pathways to and among disruptive behavior disorders. As evidenced by this volume, our understanding of the development of disruptive behavior disorders has been greatly advanced through developmental strategies examining genetic, prenatal, neuroendocrine, neuroanatomical, and social influences. The current chapter focuses on advances in our understanding of the development of disruptive behavior problems that have been gained through using behavioral genetic methods, and proposes a strategy for integrating across multiple areas in order to gain a more complete understanding of the development of disruptive behaviors in children. We begin by placing the behavioral genetic work we will discuss in a larger developmental framework.

Three comprehensive, broad developmental approaches have been described for the development of disruptive behavior disorder in children: additive, interactionist, and transactional (e.g., Dodge & Petit, 2003; Kimonis & Frick, 2010). In additive models, different developmental influences work together in an aggregate way, each producing independent effects to influence trajectories of development. In interactionist models, different developmental influences produce a joint effect on development of the phenotype¹ through moderation, modifying or amplifying the influence of other developmental influences. In transactional models, different developmental factors influence each other and the phenotype of interest across development. Additive and interactionist models are combinatory, emphasizing the joint effect of previously measured “risk” or “protective” factors on an outcome.

¹Phenotype is defined here as a measured variable of interest, for example, a measure of disruptive behavior.

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In transactional models, however, the joint effects of “risk” or “protective” factors are hypothesized to develop and change over time. Thus, in transactional models it is possible that the interrelations of different influences on behavior may change over time, or have different meaning over the course of development. Conceptually, gene–environment interplay (e.g., gene–environment correlation and interaction) best fits into the transactional approach.

Gene–environment interplay is defined here as genetic and environmental influences acting together on the development of behavior, encompassing gene–environment correlation and interaction over time. Gene–environment interplay occurs on multiple organizational levels. Environmental influences may moderate the functional roles of genes on behavior throughout development as well as at specific times, and gene variants may impact susceptibility to certain environmental influences. Even on a cellular level, gene expression may act to change internal environmental factors (i.e., hormone or neurotransmitter levels, e.g., Joffe & Cohen, 1998) which then can moderate the expression of other genes (e.g., through epigenetic mechanisms, see Meaney, 2010). On a broader scale, genes and environments work together through gene–environment correlation and interaction processes across development, and gene–environment correlation and interaction themselves may also moderate the effect of environmental influences on the development of later, more severe disruptive behaviors, particularly conduct disorder and substance abuse. On each of these organizational levels, genes and environments have transactional influences on each other and on phenotypic outcomes over the course of development. Thus, findings from behavioral genetic studies examining the role of gene–environment correlation and interaction in the developmental course of disruptive behavior problems can be considered within a transactional developmental framework.

Although an individual’s genes may influence his/her behavior, the family helps to control how and when genetic influences operate. Thus, it is important to consider the role of genetic and environmental influences on the development of disruptive behavior problems within the family context. Because biological parents pass on genes (each parent shares exactly 50 % of their genes with each of their children) and provide the rearing environment for the developing child, genetic and/or environmental influences can explain parental influences on child behavior. Thus, we consider the role of genes and environments on the development of disruptive behavior problems as a family issue. Specifically, using different types of family-based designs we may begin to understand how genes and environments work together through mechanisms of gene–environment interplay including gene–environment correlation and interaction (described below). While there are limitations to each of the family-based study designs reviewed below, converging evidence from multiple study designs provides a much more nuanced picture of the development of disruptive (and other) behaviors. By considering the findings across various designs, we can be confident that the different forms of gene–environment interplay involved in the development of disruptive behavior are not mechanisms of development limited to one type of family composition, or an artifact of the particular statistics used in each type of family study. Considering behavioral

genetics as a family-based approach allows developmental behavioral geneticists to disentangle the multiple ways in which parents and children can influence each other and to consider the bidirectional effects of parent–child relationships and children’s disruptive behavior problems over time.

In this chapter we will provide a brief review of the behavioral genetic approach including the current theory and methods used to investigate gene–environment interplay. We will review relevant findings from quantitative and molecular genetic research illustrating gene–environment correlation and interaction influences on the development of disruptive behavior, focusing on the role of the family environment. Finally, we offer suggestions for how findings from other models of the development of disruptive behavior can inform future research on gene–environment correlation and interaction influences on the development of disruptive behavior, and better integrate and test transactional conceptual models of the development of disruptive behavior disorders.

A Brief Overview of Behavioral Genetics

There are two broad avenues of research into how genetic and environmental influences operate to influence development: quantitative and molecular genetics. Quantitative genetic strategies take advantage of the natural quasi-experimental design of family members who vary in degree of genetic relatedness (e.g., twin, sibling, and adoption designs). Typically, quantitative genetic studies use latent modeling techniques from a broader, top down (i.e., theory to method) approach to estimate genetic and environmental influences on behavior based on quantitative genetic theory. Quantitative genetic models are built on theoretically derived assumptions, and genetic influences are operationalized as latent factors subsuming all genetic influences from structural differences in genotypes. Molecular genetic strategies use technological advances and a bottom up (i.e., method to theory) approach to examine how specific genes (or sets of genes) influence behavior. While some molecular genetic methods are hypothesis-driven, most are data-driven, as parts of or the entirety of the genome is scanned in attempt to find associations between individual genes and the phenotype of interest.

Quantitative genetics. Quantitative genetic research uses samples of families whose members share different proportions of their segregating genes. Quantitative genetic studies parse the variance in any given phenotype (e.g., disruptive behavior) into three variance components: genetic, shared, and nonshared environmental influences. First, genetic influences are derived based on quantitative genetic theory specifying the average proportion of segregating genes family members share. Using twins and siblings as an example, monozygotic (MZ) twins share 100 % of their segregating genes, dizygotic (DZ) twins and full siblings share on average 50 %, half siblings and cousin pairs whose parents are monozygotic twins share on average 25 %, and cousin pairs whose parents are dizygotic twins share on average 12.5 % of their segregating genes whereas adoptive or step siblings systematically

do not share any genes. By comparing the relative likeness of different types of siblings and/or family members for disruptive behaviors (correlations between sibling 1's disruptive behavior and sibling 2's disruptive behavior in each family, compared across sibling types), quantitative geneticists estimate the extent to which variation in genes contributes to disruptive behavior. Shared environmental influences are a latent construct representing all nongenetic influences contributing to likeness among family members. Shared environmental influences, then, are necessarily correlated 1 between siblings across all sibling types residing in the same household and 0 for related individuals not residing together (e.g., biological parents and the child they placed for adoption). Finally, nonshared environmental influences are a latent construct representing all nongenetic influences contributing to differences in family members, and are therefore uncorrelated between siblings. The estimate of nonshared environmental influences also includes error.

Together, these principles drawn from quantitative genetic theory about family similarity are used to infer genetic, shared, and nonshared environmental influences. For example, if monozygotic twins are 2 times more similar for their disruptive behaviors than dizygotic twins, genetic influences are operating, because we know that monozygotic twins share (on average) twice as many genes as dizygotic twins. However, the extent to which correlations between sibling 1 and sibling 2 disruptive behavior for monozygotic twins and dizygotic twins/full siblings are equal, or the extent to which genetically unrelated siblings are correlated for disruptive behavior suggests that shared environmental influences contribute to disruptive behaviors, but not genetic influences. The extent to which monozygotic twins are not perfectly correlated indicates the contribution of nonshared environmental influences on the phenotype.

There are several assumptions applicable to twin and sibling studies that can impact the estimates of genetic and environmental influences recovered in quantitative genetic analyses. First, quantitative genetic studies are built on the equal environments assumption: shared and nonshared environmental influences are equivalent for each sibling type. That is, monozygotic twins' environments are not more similar than genetically unrelated siblings' environments. Thus far, no systematic differences have been found negating the validity of the equal environments assumption (Loehlin & Nichols, 1976; Neiderhiser et al., 2004; Reiss, Neiderhiser, Hetherington, & Plomin, 2000).

Second, assortative mating can affect estimates of genetic and shared environmental influences. Assortative mating occurs when individuals choose their mates based on heritable characteristics for which they are alike. Thus, parents who have assortatively mated are more likely to pass on similar genetic influences to offspring. While assortative mating is generally modest for most psychological traits (e.g., Plomin, DeFries, & McClearn, 1990), there is evidence of moderate assortative mating for antisocial behavior (e.g., Du Fort, Boothroyd, Bland, Newman, & Kakuma, 2002), making this assumption less tenable in quantitative studies of disruptive behavior, at least for samples selected for high levels of disruptive behavior or focusing on extremes. It is possible, however, to test for such effects if related constructs are assessed in the parents.

The presence of assortative mating on traits involved in the intergenerational transmission of disruptive behavior disorders inflates shared environmental influences at the expense of genetic influences (because MZ and DZ twins will appear more similar, reducing the contrast in correlations that would suggest genetic influences on disruptive behavior). The inclusion of genetically unrelated siblings in quantitative genetic designs helps to attenuate this bias. Assortative mating on antisocial behavior also suggests that passive *rGE* is more likely contributing to the development of disruptive behavior disorders, thus highlighting the importance of studying gene–environment interplay especially for externalizing problems.

Molecular genetics. As noted above, molecular genetic studies examine genetic effects using a bottom up approach, starting with specific genes (either selected by a hypothesis-driven method, or using genome-wide association). Molecular genetic studies do not rely on specific sample types, but instead on the collection of DNA, and frequently require very large sample sizes. Molecular genetic studies originally sought to determine whether specific gene regions and allelic variations in genes were associated with disruptive behavior in order to determine which genes specifically contributed to latent heritability factors from quantitative genetic models. In general, several genes of the serotonin and dopamine systems have been implicated in disruptive behavior (see below), though no one particular gene has been found to explain a sizable proportion of variance on any disruptive behavior phenotypes. While some specific genes have been identified that account for variance in phenotypes of interest to the development of disruptive behavior disorders, specific genes rarely explain more than 2–3 % of the variance in any given behavioral phenotype.

Molecular genetic methods assume that the structure of DNA (i.e., which alleles are inherited) affects behavior. Developmental molecular genetic studies of humans thus far have not directly tested the role of epigenetics though there is evidence that changes in gene expression impact the development and intergenerational transmission of several phenotypes, and that gene expression can change throughout development (Meaney, 2010). Thus, in molecular genetic studies, it is assumed that individual differences in alleles carried incorporate the effects of gene expression, because the expression of different alleles would probabilistically contribute to, or eventually result in, different phenotypes. For example, the effect of methylation is essentially to “turn a gene off” or reduce the activity. If methylation varies systematically with allelic variants under study, then the effects of allelic variants are confounded with epigenetic effects. If all allele variants are systematically methylated, then no main effect of gene variant would be found (even if, when unmethylated, specific alleles were differentially correlated with behavior). Further, if methylation status also affects the phenotype, and is evenly distributed across people with each gene variant, the effect of gene variants could be washed out. In the future, studies may clarify findings from molecular genetic research by empirically disentangling effects of allele variants from epigenetic effects.

Genetic and Environmental Influences on Disruptive Behavior Problems

Univariate quantitative genetic studies consistently demonstrate that genetic influences are important for disruptive behavior problems in childhood and adolescence, though there is inconsistency in the proportion of variance explained by these genetic effects (Burt, 2009; Miles & Carey, 1997; Rhee & Waldman, 2002). Most studies indicate that the majority of variance can be explained by genetic influences with little contribution of shared environmental influences, although some reports indicate significant and sizable shared environmental influences. For example, Deater-Deckard and Plomin (1999) reported that in middle childhood, studies tend to show genetic influences account for 13–94 % of the variance in disruptive behavior problems, whereas shared environmental influences account for less than 62 % of the variance in disruptive behavior problems. This is a particularly wide range in variance estimates for both genetic and shared environmental influences, prompting developmental researchers to try to understand what causes the variability in estimates of genetic and environmental influences on disruptive behavior problems across childhood.

There are several explanations for observed differences in the relative influence of genetic and environmental contributions to disruptive behaviors across studies, including definition specificity, age, and error (see Burt, 2009; Marceau et al., 2012; Rhee & Waldman, 2002 for a discussion of these issues). The measurement of disruptive behavior problems offers yet another compelling possibility, as it is widely acknowledged that heritability estimates vary by informant (Burt, 2009). Finally, other sample-related differences (e.g., environmental adversity, Meyers & Dick, 2010) may drive differences in genetic and environmental influences on disruptive behavior problems, since estimates of genetic and environmental influences rely on variations in correlations across sibling types within a sample, and thus are particularly sample-specific.

Type of disruptive behaviors. Some systematic differences found in estimates of genetic and environmental influences across studies stem from differences in the specific disruptive behaviors assessed (i.e., aggression vs. delinquency; and conduct disorder vs. hyperactivity or oppositional defiant disorders) (e.g., Dick, Viken, Kaprio, Pulkkinen, & Rose, 2005; van der Valk, Verhulst, Neale, & Boomsma, 1998). When nonaggressive and aggressive antisocial behaviors were considered separately in a recent meta-analysis, genetic influences accounted for approximately half of the variance in nonaggressive antisocial behavior (48 %) with the remaining being split between shared and nonshared environmental influences (Burt, 2009). For aggression, however, additive genetic influences and nonshared environmental influences accounted for most of the variance (65 %), leaving little explained by shared environmental influences (5 %). Thus, shared environmental influences explained more of the etiology of nonaggressive disruptive behaviors than it did of aggressive disruptive behaviors (see also Rutter et al., 1990; van den Oord, Boomsma, & Verhulst, 1994).

There is evidence of an underlying genetic factor common to multiple externalizing problems including attention deficit hyperactivity, oppositional defiant, and conduct disorders in boys and girls in middle childhood and adolescence (e.g., Eaves et al., 2000; Tuvblad, Zheng, Raine, & Baker, 2009). This underlying genetic factor common to different externalizing disorders suggests a common genetic liability to different disruptive behavior disorders. This genetic liability to externalizing-type disorders is supported by adult literature showing that across psychiatric disorders, there appear to be two primary genetic liabilities across traits: one underlying internalizing-type disorders (i.e., anxiety, depression, and phobias) and a distinct genetic liability underlying externalizing-type disorders (i.e., substance use, antisocial, and conduct disorders; e.g., Kendler, Prescott, Myers, & Neale, 2003). It appears, based on the findings reviewed above, that the genetic liability common to externalizing-type disruptive behavior disorders is observable even in childhood. One study suggests that there is a common genetic liability underlying symptoms of both internalizing and externalizing disorders in children (Lahey, Van Hulle, Singh, Waldman, & Rathouz, 2011), though more studies are needed to confirm this finding and to understand the developmental progression of common and unique genetic liabilities to multiple types of problems. Further, these findings suggest that environmental influences are particularly important for differences in the presentation of disruptive behavior disorder (i.e., which specific disorder a child is diagnosed as having).

Age. A second source of systematic differences found in estimates of genetic and environmental influences across studies is age, or developmental change within the child. Overall, most studies have shown that genetic and nonshared environmental influences increase, whereas shared environmental influences decrease, from adolescence to adulthood (i.e., as individuals mature and widen social circles beyond the home; Miles & Carey, 1997). In contrast, Rhee and Waldman (2002) showed different patterns of estimates of genetic and environmental influences using age groupings. Comparing “childhood” vs. “adolescence” vs. “adulthood,” findings showed that both genetic and shared environmental influences decreased with age, whereas nonshared environmental influences increased. This inconsistency may be caused by the use of very wide age ranges in each group in Rhee and Waldman (2002) (i.e., “childhood” included samples with a mean age of 2 as well as samples with a mean age of 10).

A more recent meta-analysis clarified how age affects the relative genetic and environmental influences on externalizing problems by narrowing the age ranges of comparison groups and considering aggressive and nonaggressive externalizing behaviors separately. Burt’s (2009) meta-analysis grouped youth into three age groups: 1–5, 6–10, and 11–18. Results indicated that genetic and environmental influences on aggressive vs. nonaggressive behaviors did not differ in early and middle childhood, but were pronounced by adolescence (i.e., genetic influences were stronger for aggression, whereas shared environmental influences were stronger for rule-breaking). Moreover, genetic influences on aggression increased with age while shared environmental influences decreased, whereas genetic influences on rule-breaking decreased with age and shared environmental influences remained stable (Burt, 2009). Generally, findings suggest that there are age-related changes in

genetic and environmental influences on externalizing problems across childhood and adolescence. For aggressive externalizing behaviors, genetic influences can be expected to increase across adolescence, but when externalizing behaviors are primarily nonaggressive environmental influences may become more salient across adolescence.

Consistent with the cross-sectional work reviewed above, longitudinal studies of disruptive behavior have shown that genetic influences make an important contribution to the stability of disruptive behaviors but that environmental influences exert primarily age-specific influences on disruptive behaviors (e.g., Petittclerc, Boivin, Dionne, Perusse, & Tremblay, 2011). For example, from 20 to 54 months of age, genetic influences accounted for an underlying liability in disregard for rules across early childhood, while environmental influences on disregard for rules were largely age-specific. Further, genetic influences accounted for intercept levels of disregard for rules, and there were small trends for increases in nonshared environmental influences on disregard for rules over time (Petittclerc et al., 2011). However, across childhood (age 3–12 years) genetic and shared environmental influences both contributed to stability in aggressive behaviors (Van Beijsterveldt, Bartels, Hudziak, & Boomsma, 2003). Genetic and shared environmental influences both contributed to the stability in conduct disorder and oppositional defiant disorder symptoms (examined together) from age 11 to 14 (Burt, McGue, Krueger, & Iacono, 2005), whereas solely genetic influences accounted for stability in anti-social behavior from middle to late adolescence (Neiderhiser, Reiss, Hetherington, & Plomin, 1999). Together, these findings suggest that genetic influences play an important role in the stability of several different types of disruptive behaviors from early childhood through adolescence. However, during middle childhood and early adolescence, shared environmental influences also exert an influence on the stability of disruptive behaviors.

Middle childhood appears to be a particularly important age to examine genetic and environmental influences on disruptive behavior problems, because early-onset disorders are generally defined as having severe problems before the age of 10 (e.g., Zahn-Waxler, Shirtcliff, & Marceau, 2008). Further, the transition from middle childhood to adolescence appears to coincide with meaningful shifts in genetic and environmental influences. For example, shared environmental influences on observed externalizing behavior were greater in two samples of children in middle childhood, whereas genetic influences on observed externalizing behavior were greater in a sample of adolescents (Marceau et al., 2012). Further, Burt and Neiderhiser (2009) showed that age moderates the genetic and environmental influences on delinquent behaviors specifically, in that genetic influences increase dramatically from age 10 to 18, whereas shared environmental influences decreased.

In summary, there are genetic and environmental influences on disruptive behavior problems in childhood and adolescence. While the relative influences of genes and environments differ for distinct disruptive behavior disorders, there is evidence of an underlying genetic vulnerability common to multiple disruptive behavior problems and to multiple types of disruptive behavior problems over time. There is also evidence that the relative influences of genetic and environmental influences on

externalizing problems change across childhood and adolescence. Taken together, these findings suggest that it is essential to take a developmental perspective when studying disruptive behavior problems. Further, it is important to understand the mechanisms by which changing genetic and environmental influences impact the development of disruptive behavior problems.

Genes cannot act to change behavior without working through biological functions within the individual and the function of genes is often moderated by environmental influences. Thus, molecular genetic studies searching for main effects of specific gene variants fall short of testing for mechanisms of development. In quantitative genetic studies, while parsing variance into discrete categories made great impact on how researchers think about development (McGue, 2010) simply quantifying latent genetic and environmental influences hasn't satisfied developmental researchers. Considering theories of development that emphasize transactional influences among genetic, biological, and environmental influences, simply parsing the variance in phenotypes and the covariance across phenotypes, falls short of testing developmental mechanisms. Thus, studies using behavioral genetic approaches have moved beyond measures of genetic and environmental influences in the development of disruptive behavior (see Moffitt, 2005 for review). The remainder of this chapter focuses on this next generation of behavioral genetic studies seeking to understand how genetic and environmental influences work together in the development of disruptive behavior problems, rather than those that examine the relative influence of genes and environments.

Gene–Environment Interplay

An emerging body of research demonstrates how genes and family environmental factors work together to influence child and adolescent development (Horwitz, Marceau, & Neiderhiser, 2011). Broadly, the goals of research investigating gene–environment interplay are to understand how genetic influences of both parents and children operate through environmental mechanisms, and to understand how genetic factors may moderate the effects of frequently studied “environmental” influences. Harnessing the power of genetically informed, family-based designs, researchers have made great progress on understanding how genes and environments work together in the development of disruptive behavior.

Conceptualizing Gene–Environment Correlation and Interaction

The two most often examined forms of gene–environment interplay are genotype–environment correlation and genotype \times environment interaction. Genotype–environment correlation (rGE) refers to correlations between genes

and environments. Typically, three types of *rGE* are described: passive, active, and evocative (Plomin, DeFries, & Loehlin, 1977; Scarr & McCartney, 1983). Passive *rGE* occurs when parents pass on genes to their offspring and also provide an environment correlated with the heritable characteristics of the offspring. This type of *rGE* would be expected to occur more commonly during infancy and early childhood (i.e., before children can actively choose or influence their environment) although there is little support for this. For example, there was some evidence of passive *rGE* contributing to the association between maternal criticism and adolescent externalizing problems (Narusyte et al., 2011). Active *rGE* occurs when individuals seek out environments correlated with their heritable characteristics, whereas evocative *rGE* occurs when individuals evoke responses from the environment because of their heritable characteristics. These different forms of *rGE* are not mutually exclusive, and may simultaneously affect expression of a phenotype (e.g., Narusyte et al., 2011; Neiderhiser, Reiss, Lichtenstein, Spotts, & Ganiban, 2007; Neiderhiser et al., 2004).

The other commonly studied form of gene–environment interplay is genotype \times environment interaction ($G \times E$). $G \times E$ tests whether genetic factors moderate the influence of environmental factors, or whether environmental factors moderate the influence of genes on behavior. $G \times E$ and *rGE* are conceptually independent, but likely occur simultaneously in development. A number of different behavioral genetic designs have been used to examine the role of *rGE* and $G \times E$. *rGE* and $G \times E$ have been investigated using latent genetic and environmental constructs (e.g., Narusyte et al., 2008, 2011; Neiderhiser et al., 2004, 2007; Tuvblad, Grann, & Lichtenstein, 2006), or using specific, measured genetic and environmental influences (see review below).

It is important to note that the “E” in *rGE* and $G \times E$ is not a truly environmental factor—in fact it is highly unlikely that there are any truly environmental factors. Commonly studied “environmental” influences on behavior include childhood stressors like abuse, availability and access to drugs and alcohol, negative peer groups, religiosity, parental monitoring, and harsh parenting (Meyers & Dick, 2010). The confounding of genes in these environmental influences is especially problematic for family environmental influences like parenting. Especially considering behavioral genetics as a family-based approach, family environmental influences are of primary interest as a predictor of child behavior problems. An ongoing goal of behavioral geneticists should be (and for many, is) better and more nuanced measurement of environmental factors, like parenting. Poor measurement is a limitation common to behavioral genetic studies generally, because the number of participants needed for adequate power for behavioral genetic analyses is so high that the cost of research limits the feasibility of some measures. This limitation has likely contributed to the mixed findings found across behavioral genetic studies. Behavioral genetic studies can be used not only to identify *rGE* and $G \times E$ operating during development but also to clarify the phenotypes of interest (Moffitt, 2005).

Evidence of Gene–Environment Correlation and Interaction

Quantitative genetic studies. A wide body of quantitative genetic research using twin/sibling studies has shown that genetic influences account for a large proportion of the correlation between negative parenting and child or adolescent adjustment (Burt et al., 2005; Horwitz et al., 2011; Pike, McGuire, Hetherington, & Reiss, 1996; Reiss et al., 2000). Broadly, this suggests the influence of rGE between the environmental factor “negative parenting” and influences of the children’s genes on externalizing problems.

One study attempted to examine genetic influences on negative parenting and externalizing behavior longitudinally by also considering a child temperamental mediator of this association. Specifically, genetic influences on the association between parental criticism and adolescent antisocial behavior were partially explained by adolescent aggressive temperament 3 years earlier (Narusyte, Andershed, Neiderhiser, & Lichtenstein, 2007), suggesting that adolescents’ aggressive temperament evokes negative parenting, which, in turn, shapes adolescents’ development of antisocial behavior. Further, genetic influences accounted for the correlation between environmental risk (e.g., negative life events) and externalizing behavior, suggesting gene–environment correlation (Button, Lau, Maughan, & Eley, 2008).

Other longitudinal studies have found evidence for genetic influences on the associations between parenting and adolescent antisocial behavior over time. Specifically, findings from a cross-lagged longitudinal design suggested roughly equal genetic, shared environmental, and nonshared environmental influences explaining the association between parent–child conflict in early adolescence and youth externalizing behavior in mid-adolescence (Burt et al., 2005). An earlier study also found that parent–child negativity in middle adolescence contributed to change in antisocial behavior from middle to later adolescence and this association was explained by primarily genetic influences (Neiderhiser et al., 1999). These findings, taken together, suggest rGE , showing that the environmental risk (parent–child conflict) is associated with the phenotype (externalizing behavior) because of the adolescents’ genetic influences. Most likely, this rGE represents evocative rGE , as the power to detect evocative rGE lies in the influence of children’s genes. However, in twin and sibling only studies, rGE is inferred, not tested, and it is not possible to determine which type of rGE is driving the associations, or if passive and evocative rGE are occurring simultaneously.

Studies of twins who are parents can help to clarify the direction of effects and presence of rGE . For example, intergenerational transmission of conduct problems was attributable to direct environmental influence for boys, but parents’ genetic influences and environmental risk were confounded (suggesting passive rGE) in girls (D’Onofrio et al., 2007). However, the transmission of alcohol use disorder in twin parents to externalizing problems (risk for alcohol use disorder) in child and adolescent offspring was entirely mediated by genetic influences (Waldron, Martin, Heath, & Phil, 2009). Several studies of parents who are twins suggest that

parenting is influenced by parents' genotype and environmental influences (e.g., Kendler, 1996; Losoya, Callor, Rowe, & Goldsmith, 1997; Narusyte et al., 2008; Neiderhiser et al., 2004, 2007). This evidence supports earlier findings that parenting may impact offspring development via passive *rGE* while both evocative *rGE* and causal, environmental mechanisms may also be operating. Samples with parents who are twins are, however, limited in power to test for evocative *rGE* because of limited variability in genetic relatedness of offspring (genes are correlated on average 0.25 for children of MZ twins, 0.125 for children of DZ twins). Nonetheless, this strategy has permitted a careful examination of the role of passive *rGE* in influencing child and adolescent outcomes.

In response to the limitations of each type of twin study, and to enable passive and evocative *rGE* to be disentangled and the direct effects of environment to be estimated, the extended children-of-twins (ECOT) design (Narusyte et al., 2008, 2011) was developed. The ECOT design uses samples of twins who are children (classic twin design) and twins who are parents (children of twins design) to examine how genetic and environmental influences of the children and of the parents influence phenotypes of interest. These two designs are analyzed together in the same model. The ECOT design can distinguish between passive and evocative *rGE* operating within families as well as estimate direct environmental effects on child behavior. The power to detect evocative *rGE* lies in the child-based design, which takes advantage of sibling types of differing genetic relatedness, thus estimating the influence of children's own genes on their behavior and on their parents' behavior. Similarly, the power to detect passive *rGE* lies in the parent-based design, which tests the influence of parents' genes and environmental influences on their behavior and their children's behavior. By analyzing both sample types together, the ECOT model distinguishes between direct environmental influences, passive, and evocative *rGE* (see Fig. 2.1).

The ECOT design has shown that the association between adolescent externalizing problems and maternal criticism arises because of evocative *rGE*, and to a lesser extent passive *rGE*, but that paternal criticism has a direct environmental effect exacerbating adolescents' externalizing problems (Narusyte et al., 2011). Thus, while parental criticism is associated with adolescent's externalizing problems, these findings suggest that the nature of the associations differs for relationships with mothers vs. fathers. Paternal criticism appears to be an environmental risk factor for adolescent externalizing problems, so the direction of effects is such that fathering impacts child behavior. However, mothers respond to their children's externalizing problems with criticism, so the direction of effects is such that child behavior impacts mothering. In addition to child effects on mothering, there is a second mechanism for the association between maternal criticism and externalizing problems: mothers also pass on a critical parenting environment consistent with her genes—both of which increase the probability that her adolescent will engage in externalizing behaviors. However, another study suggested that the association between parental negativity and adolescent externalizing problems was explained entirely by evocative *rGE* for mothers and fathers (Marceau, Horwitz et al., *in press*). Therefore, findings from ECOT designs suggest that different types of parenting behaviors may be associated with adolescent externalizing problems through different mechanisms.

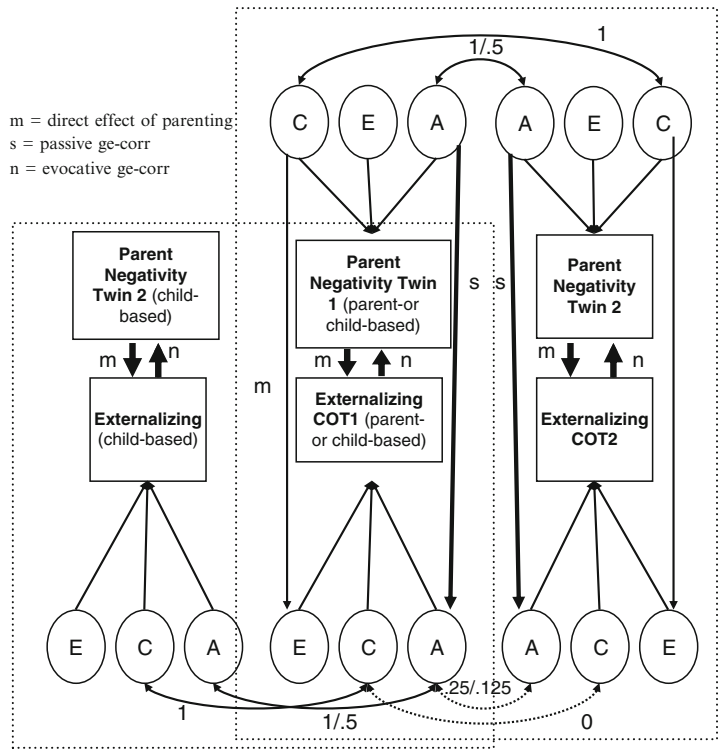


Fig. 2.1 Extended children of twins (ECOT) model. This is a representation of the ECOT model testing the association between parent negativity and child externalizing problems. The lower box on the *left* represents the classic twin sample, while the larger box on the *right* represents the children of twins sample. M is a measure of the direct effect of parenting, while s indicates passive rGE and n indicates evocative rGE . A are additive genetic effects (correlated 1 for MZ twins, 0.5 for DZ twins, etc., see text), C are shared environmental influences, and E are nonshared environmental influences

Converging evidence from family-based studies of twin children, twin parents, and a combination of both twin children and parents suggest that both evocative and passive rGE underlie the association between negative parenting behaviors and adolescent disruptive behaviors. In light of the studies using the ECOT design, and other studies suggesting differences in rGE mechanisms that underlie parenting behaviors (e.g., Neiderhiser et al., 2004, 2007), future quantitative genetic studies should also examine sex differences of both parents and children in the mechanisms underlying the association between parenting and externalizing behavior.

Because estimates of genetic and environmental influences are latent in twin and sibling studies, twin/sibling studies cannot test whether genetic predispositions moderate the influence of environmental factors (gene–environment interaction). However, these studies can test whether genetically and environmentally influenced constructs moderate the influence of genes on behavior. Both parental negativity

and warmth have been found to moderate genetic influences on aggressive and non-aggressive forms of adolescent antisocial behavior (Feinberg, Button, Neiderhiser, Reiss, & Hetherington, 2007) such that genetic influences were greater for adolescent antisocial behavior when parenting behaviors were more negative or less warm. Further, the magnitude of the influence of genetic risk on externalizing behavior was found to be contextually dependent, even after controlling for gene–environment correlation, suggesting $G \times E$ (Button et al., 2008). Generally, findings from twin studies testing moderation of genetic influences on externalizing behavior by putatively environmental influences suggest that genetic influences on externalizing spectrum disorders are greater in the presence of environmental adversity (see Meyers & Dick, 2010; Tuvblad et al., 2006).

Adoption designs also use genetic relatedness of family members to disentangle genetic from environmental influences on child and/or adolescent behavior. Adoption designs use the genetic (un)relatedness of family members by taking advantage of the natural break of the confound between genetic and environmental influences provided by parents to offspring. However, they differ from the quantitative genetic studies described above in the way that genetic risk is inferred—genetic influences are operationalized as birth parent characteristics that influence children's behavior when they are not reared by the birth parent. Adoption designs have also been extended to study differences between adoptive children and biological children raised together. Any similarity between adoptive and biological children must be due to shared environmental influences because they do not share genes, but do share the same rearing environment. The extent to which parents and their biological children are more similar on the phenotype than parents and their adoptive children are indicates genetic influences on the phenotype. Finally, the extent to which characteristics of the biological parent and adoptive parent are correlated indicates evocative rGE , because the genetic risk passed from biological parents to children is evoking negative responses from the parent.

Generally, findings from adoption studies suggest that evocative rGE explains associations between negative family environmental influences (e.g., parenting/parent–child conflict) and youths' disruptive behavior symptoms (e.g., Deater-Deckard & O'Connor, 2000; Ge et al., 1996; Narusyte et al., 2007; O'Connor, Deater-Deckard, Fulker, Rutter, & Plomin, 1998). For example, birth mothers' antisocial behavior (genetic risk) was associated with adoptive parents' negative control (environment) in middle childhood and early adolescence. Children at genetic risk for antisocial behavior consistently received more negative, controlling parenting behaviors, suggesting evocative rGE . Birth parents' antisocial behavior did not completely explain the association between adoptive parents' negative control and children's externalizing problems, however, suggesting that negative, controlling parenting may also be an independent environmental influence on children's externalizing problems (O'Connor et al., 1998).

Findings comparing adopted and biological children of the same parents also suggest that passive rGE operates in infancy, early and middle childhood, and adolescence (Braungart-Rieker, Rende, Plomin, DeFries, & Fulker, 1995; McGue, Sharma, & Benson, 1996). However, adoption studies comparing adolescent

antisocial behavior of biological and adopted children in the same families suggest that shared environmental influences contribute to stability of antisocial behavior (Burt, McGue, & Iacono, 2010), and that maternal depression represents a shared environmental risk for antisocial behavior (maternal depression had the same effect on biological and genetically unrelated offspring; Tully, Iacono, & McGue, 2008). Also in adolescence, parent–child conflict predicted conduct problems, but conduct problems did not predict later parent–child conflict in a sample of adoptive families, suggesting the role of shared environmental influences in the development of conduct disorder, rather than evocative *r*GE (Klahr, McGue, Iacono, & Burt, 2011).

Thus, like findings from twin and sibling studies, adoption studies confirm that there are multiple mechanisms explaining the association between negative parenting and disruptive behavior in childhood. In many family types (families where children are twins, or the children of twins, or adopted, or where adopted and biological offspring are reared in the same home by the same parents), evocative *r*GE plays a particularly prominent role in the development of disruptive behavior, and in the associations between parenting and disruptive behavior, though there has been some evidence that passive *r*GE also operates in the development of disruptive behavior problems. Further, in each of these family-based study designs, parenting—particularly fathering—has been shown to exert a purely environmental influence on disruptive behavior. More studies are required to understand whether there are gender differences in these associations, and whether there are differences in the associations between mothering vs. fathering in adoption studies.

G×E can also be tested using adoption designs. The classic example is that youth with biological parents who have psychopathology, and adoptive parents with psychopathology are much more likely to develop psychopathology than youth who have either biological or adoptive parents with psychopathology (Cadoret, Cain, & Crowe, 1983; see Reiss & Leve, 2007). Generally, adoption studies have shown that the confluence of both genetic (biological parent psychopathology) and environmental risk factors (harsh or negative parenting or family environments, adoptive parent or sibling psychopathology) confers an additional, interactive risk for developing disruptive behavior disorders in childhood and adolescence (Reiss & Leve, 2007).

There is evidence of G×E in the development of externalizing behavior even in infancy and toddlerhood. For example, birth parents' substance dependence and antisocial behavior predicted higher levels of novelty seeking during a frustration task (an early predictor of externalizing behavior) in 9-month-olds only when adoptive parents also had higher levels of depressive and anxiety symptoms (Leve et al., 2010). Among 18-month-olds, marital instability between adoptive parents earlier in infancy predicted elevated levels of toddlers' anger and frustration only among toddlers whose birth mothers reported high levels of anger and frustration (Rhoades et al., 2011). In summary, studies using quantitative genetic designs including twin and adoption designs suggest that positive and negative aspects of parenting and the development of disruptive behaviors are linked through passive and evocative *r*GE as well as through G×E.

Molecular genetic studies. Molecular genetic analyses can be applied to any type of study if DNA is collected. In molecular genetic studies, genetic influences are measured, not estimated. Molecular genetic studies have examined genes associated with behavior, as well as genes that interact with environmental influences on behavior. There are three overarching approaches to finding specific genes to use in measured rGE and $G \times E$ studies: candidate gene approach, linkage, and association studies (see Meyers & Dick, 2010; Plomin & Rutter, 1998 for review). The candidate gene approach is hypothesis-driven: specific genes are chosen for study because of hypothesized or known biologic functions influencing the development of the phenotype.

Linkage and association studies are data-driven. Using advances in technology, large portions of the genome are scanned and processed in order to identify regions of the genome that are associated with the phenotype of interest. Linkage studies use this technology by comparing frequencies of alleles across similarly affected family members. Linkage studies work well for identifying single regions or genes that impact a phenotype, but are not optimal for finding multiple genes implicated in a single phenotype. Because disruptive behavior problems, like most complex phenotypes, are hypothesized to be influenced by multiple genes, genome-wide association studies (GWAS) are thought to be better suited to identify specific genes influencing disruptive behavior. GWAS have the added benefit over linkage studies of scanning the entire genome, instead of distinct regions, and have more power to detect subtle effects of specific genes on the phenotype of interest. An association with a specific gene variant and the phenotype of interest indicates rGE , while an interaction between a specific gene variant and some measured environmental factor predicting disruptive behavior problems indicates $G \times E$. Generally, molecular genetic studies of disruptive behavior have focused on $G \times E$ effects.

Specific genes from several systems (e.g., serotonergic, dopaminergic, GABA) have been implicated in disruptive behavior. Here, we focus primarily on candidate genes of the serotonergic system. We note, however, that this is not the only systems implicated in $G \times E$ studies of the development of DBD. For example, studies have suggested that genes of the dopaminergic system (e.g., DRD2, DRD4, DAT1, COMT) interact with environmental influences (e.g., parenting, negative life events; Brennan et al., 2011; Creemers et al., 2011; Kahn, Khoury, Nichols, & Lanphear, 2003; Zai et al., 2011) in the development of disruptive behavior problems. GABRA2 (a receptor gene for GABA implicated originally in adult alcoholism) has also been associated with externalizing and alcohol use problems in adolescents (see Meyers & Dick, 2010). Further, parental monitoring may buffer the association between specific GABRA2 alleles and externalizing problems (Dick et al., 2007).

The serotonergic system, most often examined by considering a common polymorphism in the serotonin transporter receptor gene (5HTTLPR), is hypothesized to affect behavior through modulation of the stress response system (see Caspi, Hariri, Holmes, Uher, & Moffitt, 2010). Thus, specific alleles of 5HTTLPR may create a sensitivity to environmental influences in youth (though evidence is mixed as to which alleles may confer “risk”). If the child also experiences negative environmental influences, they are more likely to develop behavior problems. Though

5HTTLPR has received more attention in the development of depression, the same mechanism is thought to apply to the development of disruptive behavior problems. For example, youth had increased externalizing behaviors if they had the 5HTTLPR long allele variant (LL) and antisocial biological parents, or if they had one or more short alleles (SS/SL) and biological parents with alcoholism (Cadoret et al., 2003). 5HTTLPR alleles coding for high and low activity vs. intermediate serotonin transporter activity interacted with self-blame of interparental conflict to predict attention deficit hyperactivity disorder symptoms (Nikolas, Friderici, Waldman, Jernigan, & Nigg, 2010).

MAOA is a gene involved in the degradation of several neurotransmitters, including serotonin. Thus low-activity alleles of MAOA contribute to extra serotonin, and are thought to operate through a mechanism similar to variants of 5HTTLPR increasing the activity of serotonin receptors (both result in more serotonin, active for longer periods of time in the system). The interaction of specific alleles of MAOA and maternal disengagement has been shown to predict serious and violent delinquency (Beaver, DeLisi, Wright, & Vaughn, 2009). Further, low-activity alleles of MAOA interacted with sexual abuse and harsh parenting to predict externalizing disorders in young adulthood (Derringer, Krueger, Irons, & Iacono, 2010), and child maltreatment to predict childhood antisocial behavior (Caspi et al., 2002) especially in boys (Kim-Cohen et al., 2006). Thus, specific alleles of genes implicated in regulating the activity of several neurotransmitters have been implicated in the development of disruptive behavior problems.

Though less frequently reported, molecular genetic studies can also detect *r*GE. Applicable to the development of disruptive behavior in children, 5HTTLPR and OXTR (an oxytocin receptor gene) alleles in parents were associated with their observed parenting (Bakermans-Kranenburg & van IJzendoorn, 2008), evidencing passive *r*GE. However, most studies investigating reporting specific gene–environment correlations have assessed adults (see Jaffee & Price, 2007). While *r*GE and $G \times E$ are modeled separately, they are not necessarily independent. Including *r*GE in molecular genetic studies of $G \times E$ is particularly important because failing to do so biases results of $G \times E$ (Jaffee & Price, 2007). In summary, studies using a molecular genetic approach have identified several specific gene–environment interactions important in the development of disruptive behavior disorder. While the role of passive *r*GE has been demonstrated, more research is needed to understand how *r*GE operates at the level of specific genes in the development of disruptive behavior disorders.

Bridging Quantitative and Molecular Genetic Findings

A major criticism of behavioral genetics is the vast difference between top down (quantitative) and bottom up (molecular) approaches to understanding genetic influences on behavior. Many quantitative genetic studies have posited that finding increased genetic influences on a phenotype identifies that phenotype as appropriate

for molecular genetic studies. However, molecular genetics can also help inform/interpret quantitative genetic findings. An obvious limitation of twin studies is the “black box” argument: detecting genetic influence on a phenotype does not tell us which genes are influencing behavior, or how. Findings from molecular genetic studies can be used to inform what types of genes are likely subsumed in a latent genetic factor. The mismatch between the percent of variance explained by specific genes and attributable to a latent genetic factor also indicates that taking a specific, single gene approach does not come close to explaining how genetic influences impact behavior. We are still developing a framework for integrating these different conceptualizations and approaches to studying how genetic and environmental influences are interrelated and collectively affect behavioral development.

Very recently, advances in analytic methods for examining GWAS/molecular genetic data show promise for reconciling differences in genetic and environmental influences obtained through molecular and quantitative genetic methods. Using GWAS to compound the influence of all measured genes in a large sample, the total genetic influence on intelligence was estimated at 40–50 %, which is quite similar to the 60 % typically reported by quantitative genetic studies (Davies et al., 2011). This study suggests that examining poly-gene correlations and interactions is an important future direction for molecular genetic studies of individual’s characteristics, and should be applied to the development of disruptive behaviors in the future.

Even on a smaller scale, for investigators without access to GWAS data but who can collect DNA, investigating poly-gene correlations and interactions (e.g., Schmidt, Fox, & Hamer, 2007) and rGE and $G \times E$ together is a logical next step to bridging quantitative and molecular genetic findings. The idea of experience-expectant plasticity (see Lenroot & Giedd, 2011) and the concept of plasticity genes (Belsky et al., 2009) have gained traction recently. That is, certain clusters of genes may together exert influence on the individual’s sensitivity to environmental influences and context (i.e., creating a biological sensitivity to context; e.g., Ellis, Jackson, & Boyce, 2006, or differential susceptibility to the environment; Belsky, Bakermans-Kranenburg, & Van IJzendoorn, 2007). Generally, findings reviewed here do support these hypotheses. For example, both 5-HTT and MAOA have been implicated in resilience in addition to risk for disruptive behavior (see Kim-Cohen & Gold, 2009 for review). Thus, examining gene variants with similar effects that contribute to both risk and resiliency in the same model testing gene–gene and gene–environment interactions and correlations will advance our understanding of the role of genes in behavioral development. However, studies testing different forms of genetic influences on plasticity must also consider the timing of gene expression, resulting in sensitive periods of development for different types of internal and external environmental influences (e.g., Lenroot & Giedd, 2011).

What do behavioral genetic studies tell us about development? While linkage studies and GWAS are useful for detecting genes associated with outcomes, these studies do not help us to understand the process by which behavior develops. Likewise, non-longitudinal quantitative genetic studies also cannot speak to the relative influences of genetic and environmental influences across development.

In order to be of interest to developmentalists, genes must have a functional effect on a biological process that eventually reaches the brain to affect the behaviors and development of the individual. Indeed, a principle of developmental biology is that the only way genes may influence a phenotype is through interaction with the environment (e.g., Meaney, 2010).

Behavioral genetic approaches have more recently been applied by developmentalists to inform research on the mechanisms of behavioral development. Behavioral genetic designs are particularly useful for detecting environmental mechanisms (Moffitt, 2005). For example, using longitudinal quantitative genetic studies, researchers have discovered that genetic influences on a phenotype can change with age. While this may reflect measurement differences at different ages, it is unlikely that drastic changes in proportions of genetic and environmental influences on a phenotype over time are due only to measurement error (and this potential explanation can be tested within longitudinal quantitative genetic models). Instead, it is more likely that longitudinal quantitative genetic studies pick up on developmental changes in the importance of genes, operating through rGE and $G \times E$. Quantitative genetic studies are often assumed to be a purely structural measure of genetic influences. That is, genetic influences are estimated by comparing phenotypes in different groups with different average percentages of shared differentiating genes. If quantitative genetic studies were purely structural, then the unstandardized variance for the genetic influence would remain constant across development. Because unstandardized variance estimates do change across time within the same sample, findings from quantitative genetic studies must be driven by functional differences in the genes shared by twins and siblings. However, twin studies cannot tell us which genes twins and siblings do or do not share act to impact behavior.

From a molecular genetic perspective, the candidate gene approach has potential to inform developmental research because genes are selected using a hypothesized biologic mechanism. However, the candidate gene approach is limited by our understanding of how biological processes impact behavior. Thus far, with little collaboration between biologists and behavioral geneticists in psychology-related fields, the potential of the candidate gene approach is likely far from realized.

Susman and Pollak (Chap. 3) review neuroanatomical and neuroendocrine influences on the development of disruptive behavior disorders. These studies have helped to identify potential candidate genes for use in $G \times E$ studies (e.g., 5-HTT). Single gene and single gene by specific environmental interaction influences have predicted only small amounts of the variance in disruptive behaviors (e.g., Plomin & Rutter, 1998). However, applying the candidate gene approach based on findings from other biological research (i.e., neuroanatomical and neuroendocrine factors) will help us to identify other specific genes likely to be involved, albeit not necessarily in a direct “main effect” way. Building on the substantial advances in our understanding of the development of disruptive behavior in somewhat disparate fields exemplified in this volume, it is now time to work towards integrative approaches to examining the development of disruptive behavior problems.

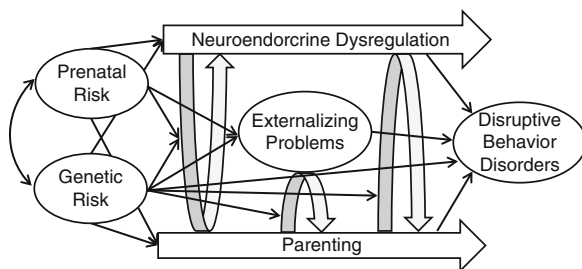


Fig. 2.2 An integrative transactional developmental model of the development of disruptive behavior disorders. This is a proposed transactional model in which genetic, prenatal, and neuroendocrine risks are considered in conjunction with parenting over time in the development of disruptive behavior disorders. *Thick arrows* represent the development of neuroendocrine dysregulation and parenting over time (across childhood and adolescence), and the transactional nature of this co-development. Genetic influences are not only present for each construct but also predict the nature of how transactions among other constructs occur and develop. This is an example of how multiple biological and environmental risk factors can be considered together in a transactional model, and tested using genetically informed study designs

As an example, in Fig. 2.2 we present a conceptual model of a comprehensive, transactional approach for the development of disruptive behavior problems. Genetic risk is an important component in the model, influencing prenatal risk, the development of neuroendocrine dysregulation and parenting over time, transactions between parenting and neuroendocrine dysregulation over time, early externalizing problems, transactions between parenting and earlier externalizing problems over time, and ultimately disruptive behavior disorders.

Existing evidence supports parts of this model, though to date important components remain untested. For example, there are genetic influences on externalizing behavior in childhood and adolescence (e.g., Burt, 2009; Rhee & Waldman, 2002), and both parents' and children's genes influence parenting (e.g., Neiderhiser et al., 2004, 2007). The studies reviewed above provide evidence for how genes and environments influence associations between parenting and externalizing behavior across adolescence (e.g., Burt et al., 2005; Narusyte et al., 2011; Neiderhiser et al., 1999). Poor emotional health in mothers prenatally is associated with disruptive behavior disorder and substance use during pregnancy is associated with offspring risk for substance use disorders (e.g., Allen, Lewinsohn, & Seeley, 1998), indicating the role of prenatal risk in the development of disruptive behavior problems. There is also some evidence that genetic influences are associated with prenatal risk for early externalizing problems (e.g., Marceau, Hajal et al., *in press*; Pemberton et al., 2010). A few studies have shown genetic influences on neuroendocrine dysregulation (e.g., Bartels, Van den Berg, Sluyter, Boomsma, & de Geus, 2003; Wüst, Federenko, Hellhammer, & Kirschbaum, 2000). Prenatal risk factors (maternal stress and mental health problems) predict offspring neuroendocrine dysregulation (e.g., Wadhwa et al., 2001). The role of

neuroendocrine regulation in the development of disruptive behavior problems is explicated in Chap. 3 of Susman and Pollak.

Evidence from studies investigating biological sensitivity to context suggests that both genetic influences and cortisol dysregulation may serve as biological risk factors for the development of disruptive behavior problems (e.g., Belsky et al., 2007; Ellis et al., 2006). However, these studies have not yet taken the next step to apply quantitative genetic methods to understanding how neuroanatomical and neuroendocrine processes are related to behavior. Thus, there is a call for more comprehensive models of the development of disruptive behavior that incorporates multiple biological factors and social/environmental factors to characterize and predict the development of disruptive behavior disorders.

By including measures of hormones in different genetically informed designs, this model could be tested using measured genetic risk, either using combinations of candidate genes coding for stress and sex hormones, parenting, and externalizing problems (i.e., molecular genetic studies), or inferred through birth parent characteristics of externalizing psychopathology and/or neuroendocrine dysregulation (i.e., adoption design) or both. This model could also be applied in longitudinal, multivariate quantitative genetic studies. Including two distinct, but related biologic mechanisms (in this example, genes and hormones) gives us information using measured genetic influences on multiple risk factors (e.g., genetic risk for neuroendocrine dysregulation and externalizing problems), or on how gene–environment correlation operates for associations found in the literature (e.g., the associations between harsh parenting and externalizing, or neuroendocrine dysregulation and externalizing). Further, candidate genes for each phenotype in the model can be tested separately and together to investigate gene–gene interaction, and poly-gene \times environment correlation and interaction.

In this example, behavior genetic and hormone studies are paired for a more comprehensive model of the development of disruptive behavior problems. Quantitative genetic studies have also been brought to bear to some extent on neuroanatomical correlates of disruptive behavior disorders (see Lenroot & Giedd, 2011 for review). A similar model could be developed incorporating neuroanatomical development. Thus, combining quantitative and molecular genetic approaches to understanding the joint influence of genetic and environmental influences on the development of disruptive behavior problems with other biological approaches (e.g., neuroanatomical, neuroendocrine) will help us to clarify studies of $G \times E$ and rGE , and why and how different risk factors impact disruptive behaviors across development and at specific developmental sensitive periods.

Future Directions

There are several directions researchers using a developmental behavioral genetic approach should take to continue to advance our understanding how genetic and environmental influences operate together in the development of disruptive

behavior disorders. First, from a molecular genetic perspective, it has become increasingly important to understand how multiple genes together impact development, and how groups of genes act in concert with environmental influences through gene–environment correlation and interaction processes. Investigating the role of plasticity genes, and the ways in which composites of genes believed to code for openness to the environment will help us to understand other proposed mechanisms of development including biological sensitivity to context theory, from a genetic perspective as described above.

Future studies should attempt to understand how reconcile genetic and environmental influences estimated from different genetically informed designs. The recent GWAS explaining a sizable proportion of the heritability estimates recovered in quantitative genetic studies by compounding measured allelic differences (Davies et al., 2011) provides an excellent example of one method for reconciling differences across approaches. As relevant data accumulate, this approach can be applied to the study of disruptive behavior disorders and also to samples of different ages to incorporate possible developmental differences. Additionally, twin/sibling studies can also use composites sets of genes believed to be related either conceptually or biologically within quantitative genetic frameworks to test the proportion of the additive genetic component estimated in quantitative genetic designs are accounted for by composites of multiple genes.

Further, considering behavioral genetics as a family issue highlights the importance of including both parents' and children's genes in molecular genetic studies. By including both parents' and children's genes in studies of the transmission of disruptive behaviors, it is then possible to begin to understand how the transmission of specific genes and parenting behaviors contributes to the association between parenting and child disruptive behaviors. In other words, obtaining a complete picture both from a genetic and environmental perspective is crucial for understanding how genes and environments work together to influence development.

Finally, developmental researchers must work with other scientists in other disciplines to integrate across fields. Studies investigating the confluence of genetic and endocrine or neuroanatomical influences, like our theoretically derived conceptual model for the development of disruptive behaviors, will advance our understanding of how genes, physiological, and family environmental influences exert transactional influences on the development of disruptive behavior problems over time. Genetic risk is an important component in the model, influencing prenatal risk, the development of neuroendocrine dysregulation and negative parenting over time, and both early childhood and adolescent externalizing problems, as per quantitative genetic theory. It is worth noting here that this cross-disciplinary approach is becoming much more commonplace in a variety of fields, including developmental behavioral genetics. Because behavioral genetic research involves the recruitment and assessment of difficult-to-obtain samples, there is often an effort to maximize data collection by collaborating with a wide variety of researchers. We are suggesting that this type of cross-disciplinary work be continued and

expanded to include endocrine and neuroanatomical processes as well as genetic and family influences to help provide a more complete picture of mechanisms of the development of disruptive behavior disorders.

Genetic influences are also hypothesized to moderate transactions between parenting and neuroendocrine dysregulation over time and transactions between parenting and early externalizing problems over time. These hypothesized transactions are in accordance with the theoretical frameworks, including gene–environment interplay and the biological sensitivity to context theory, described in this chapter and throughout the volume. The developmental transactions between genetic, hormonal, and family environmental influences over time play the most prominent role in the development of adolescent externalizing problems. Therefore, in the future, the strengths of developmental behavioral genetic approaches should be harnessed in combination with more advanced longitudinal data analytic approaches and hypothesized physiological mechanisms in order to match with current theoretical frameworks hypothesizing transactional influences of genetic, hormonal, and environmental influences on the development on disruptive behavior problems.

Conclusions. Developmental behavioral genetic approaches have facilitated important advances in understanding the associations between parents' and children's behaviors, and the role of the family in disruptive behavior disorders. We now understand not only that parents pass genes and environments consistent with those genes to their children which may result in a higher probability that the child develops disruptive behavior disorders but also that the genetically and environmentally influenced disruptive behaviors of the child in turn impact parenting behaviors. We also are now beginning to understand the multiple mechanisms by which genetic and environmental influences exert transactional influences on each other and on family members' behaviors, which may serve to exacerbate or attenuate disruptive behavior disorders.

While research in developmental behavioral genetics has provided substantial insight into family issues surrounding genetic and environmental influences on disruptive behavior disorders in children, there are many exciting possibilities for future research. As the strategies for data collection continue to advance, especially in regard to the techniques available (i.e., using cell phones to collect data on more occasions), developmental behavioral geneticists will be able to fine-tune models of gene–environment interplay and track the joint influences of genes and environments on other aspects of parenting and child behaviors—including how gene–environment interplay may shape daily interactions and variations in children's disruptive behavior problems on shorter-term time scales. Through creative extensions of data collection and analytic techniques, developmental behavioral genetics and collaboration across multiple disciplines developmental behavioral genetic approaches will continue to advance our understanding of the role of the family in the development of disruptive behaviors.

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