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Refining Intervention Targets in Family-Based Research: Lessons From Quantitative Behavioral Genetics

Leslie D. Leve, PhD,
Oregon Social Learning Center, Eugene, OR

Gordon T. Harold, PhD,
Centre for Research on Children and Families and Department of Psychology, University of Otago, Dunedin, New Zealand

Xiaojia Ge, PhD,
Institute of Child Development, University of Minnesota, Minneapolis, MN

Jenae M. Neiderhiser, PhD, and
The Pennsylvania State University, University Park, PA

Gerald Patterson, PhD
Oregon Social Learning Center, Eugene, OR

Abstract

The results from a large body of family-based research studies indicate that modifying the environment (specifically dimensions of the social environment) through intervention is an effective mechanism for achieving positive outcomes. Parallel to this work is a growing body of evidence from genetically informed studies indicating that social environmental factors are central to enhancing or offsetting genetic influences. Increased precision in the understanding of the role of the social environment in offsetting genetic risk might provide new information about environmental mechanisms that could be applied to prevention science. However, at present, the multifaceted conceptualization of the environment in prevention science is mismatched with the more limited measurement of the environment in many genetically informed studies. A framework for translating quantitative behavioral genetic research to inform the development of preventive interventions is presented in this article. The measurement of environmental indices amenable to modification is discussed within the context of quantitative behavioral genetic studies. In particular, emphasis is placed on the necessary elements that lead to benefits in prevention science, specifically the development of evidence-based interventions. An example from an ongoing prospective adoption study is provided to illustrate the potential of this translational process to inform the selection of preventive intervention targets.

Keywords

quantitative genetics; prevention; family; child

Researchers increasingly employ randomized controlled trial designs to evaluate the efficacy of preventive intervention programs, and a number of programs have been shown to produce enduring effects on child, adolescent, and adult well-being (Botvin, Mihalic, & Grotpeter, 1998; Forgatch, Patterson, DeGarmo, & Beldavs, 2009; Greenberg, Kusche, & Mihalic,

Correspondence regarding this article should be sent to Dr. Leslie D. Leve, Oregon Social Learning Center, 10 Shelton McMurphey Boulevard, Eugene, OR 97401. Phone: (541) 485-2711. Fax: (541) 485-7087. lesliel@oslc.org.

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1998; Olds, 2002; Vinokur, Van Ryn, Gramlich, & Price, 1991; Webster-Stratton, Reid, & Hammond, 2001). Several family-based interventions have been shown to reduce the incidence of future disorders among children (Tolan & Dodge, 2005; Weisz, Sandler, Durlak, & Anton, 2005); others have been shown to effectively improve parenting practices and reduce child problem behaviors under real-world conditions (Chamberlain et al., 2008). A key theme of many efficacious intervention programs is the mediating role of parenting in accounting for intervention effects on child outcomes (Conduct Problems Prevention Research Group, 2002; Eddy & Chamberlain, 2000; Martinez & Forgatch, 2001; Webster-Stratton & Herman, 2008). However, even within the context of highly efficacious prevention programs, many youths fail to benefit from intervention. Further, some youths experience immediate improvements that are not maintained. Thus, even well-supported, cost-effective interventions can be improved upon.

One reason that standard prevention programs might not work for some individuals is that underlying, genetically influenced predispositions might affect the impact of specific environmental inputs (Reiss & Leve, 2007; Reiss, Neiderhiser, Hetherington, & Plomin, 2000). This would suggest an important role for genetic research within the context of prevention science. However, genetically informed research has historically been contained to theory-development and knowledge-generating perspectives, without direct or immediate benefits for individuals and families. Recently, prevention scientists and quantitative behavioral genetic researchers have highlighted the potential value of integrating their fields to improve individual outcomes (Brody et al., 2009; Jaffee & Price, 2007; Moffitt, 2005; Reiss & Leve, 2007; Rice, Harold, Shelton, & Thapar, 2006; Rutter, 2005). Despite previous endeavors to integrate the quantitative behavioral genetic and prevention science fields, only theoretical rather than operational (i.e., actual) benefits have been highlighted.

In this article, we aim to encourage a theory-guided integration of genetically informed research with prevention science through an evidence-based, prevention science oriented model. We focus on family-based research with children, although the model and steps postulated here could be applied across the lifespan. First, we describe the importance of the social environment in prevention science and identify six fundamental design aspects as they pertain to measurement of the environment in prevention science research, highlighting examples from quantitative behavioral genetics that are consistent with these prevention science themes. Second, we propose a set of sequential steps to serve as a framework for determining when there is adequate knowledge to move forward with the systematic translation from quantitative behavioral genetic research to inform prevention science research. Third, we provide an example from a prospective adoption study to illustrate how the findings from genetically informed research can provide insight into the development of preventive intervention targets, in accordance with the steps and environmental measurement issues outlined in the first and second sections of the manuscript.

Key Concepts and Definitions

Before turning to the main foci of this manuscript, we define several concepts used throughout this manuscript.

Prevention science

The development of systematic prevention programs began early in the 20th century with the mental hygiene movement, social reforms in youth services, and the first child guidance clinics (Weisz et al., 2005). Early prevention programs were not systematically built on a solid research base, but the scientific rigor of prevention science has increased dramatically (Coie et al., 1993; Kellam & Langevin, 2003; Nitzkin & Smith, 2004; Reid, 1993). As of

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2002, over 1000 outcome evaluation studies on mental health promotion and substance abuse prevention interventions had been published (Weisz et al., 2005).

Prevention science assumes a public health view to address the needs of all individuals. As such, prevention science studies fall into three categories. The first category, universal intervention, includes systematic interventions designed to improve outcomes for everyone in a population. All of the individuals in a given setting participate in universal interventions and are assumed to benefit regardless of risk status. The second category, selective intervention, targets individuals who have been identified as having one or more risk factors but are not symptomatic. The third category, indicated intervention, targets individuals at higher levels of risk (e.g., those exposed to chronic adversity) who still do not yet qualify for a diagnosable disorder. Through independent analyses of hundreds of trials, federal agencies and public health organizations have published lists of rigorously tested preventive interventions that have been shown to be efficacious (e.g., Blueprints for Violence Prevention, SAMHSA Model Programs, and Helping America's Youth), several of which are referenced in the following sections.

A factor common to these programs and relevant to the underlying theme of this article is that efficacious programs for reducing maladaptive child behavior are typically based on malleable facets of the social environment. However, accumulating evidence has suggested that children's exposure to specific parenting environments, for example, might be correlated with genetic factors (genotype–environment correlation [*r*GE]) and that genetic factors might magnify or reduce the impact of the parenting environment (Genotype x Environment [GxE] interaction). Thus, considering genetically informed research is imperative for efforts to improve the efficacy of preventive intervention programs.

GxE interaction and rGE

Two key concepts from quantitative behavioral genetic research reoccur throughout this manuscript: *r*GE and GxE interaction. In the past two decades, researchers have illustrated how genetically influenced characteristics correlate with or evoke specific responses from the social environment. This *r*GE process has been described in detail elsewhere (Neiderhiser et al., 2004; Plomin, DeFries, & Loehlin, 1977; Scarr & McCartney, 1983). In short, these researchers suggest that heritable child characteristics influence parental behavior towards children in three ways: (a) in passive *r*GE, the parents' genes are correlated with their parenting practices such that parents who contribute "risky" genes to their child tend to provide negative rearing environments; (b) in evocative *r*GE, the child's genetically influenced characteristics evoke specific responses from individuals in their rearing environment; and (c) in active *r*GE, the child's genetically influenced behavior affects the environmental experiences that s/he will actively seek out (Rutter, 2006). The results from this body of work highlight *r*GE processes in explaining the associations between parenting behavior and child outcomes.

In GxE interaction, an individual's inherited propensity to be more sensitive to certain environmental events allows environmental influences to moderate genetic effects on development. The results from GxE interaction studies provide additional evidence for the interplay between genes and the environment, potentially illustrating how genetic predispositions render some individuals more susceptible to the negative or positive effects of certain environments and how environmental conditions enhance or reduce genetic risk (Cadoret, Yates, Troughton, Woodworth, & Stewart, 1995; Caspi et al., 2002, 2003; Jaffee & Price, 2007; Moffitt, Caspi, & Rutter, 2005).

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Quantitative behavioral genetics

In quantitative behavioral genetics, naturally occurring variation in the genetic relatedness of family members is used to identify genetic and environmental contributions to behavior. The most commonly used design is the twin design, in which similarities and differences in identical (monozygotic) and fraternal (dizygotic) twins are compared to estimate genetic and environmental influences. The adoption design is another quantitative behavioral genetic approach that is particularly useful for identifying environmental influences that make family members similar to one another (shared environment). Adopted children who are placed with nonrelatives at birth are genetically unrelated to their rearing parents yet share the family environment and the larger social context. In the absence of selective placement, similarities between an adopted child and his/her adoptive parents are best explained by shared environmental influences. A full adoption design includes birth parents to enable the estimation of genetic influences.

By comparison, molecular genetic studies focus on measured genes assessed through the collection of DNA. There is an increasing body of research demonstrating interactions between specific measured genes and specific measured environments (Caspi et al., 2003; Kim-Cohen et al., 2006). In this article, we focus primarily on systematic translation from quantitative behavioral genetic research to prevention science, although many of the examples and intervention extensions described here are also applicable to molecular genetic research.

Translation from Quantitative Behavioral Genetics to Prevention Science: Measurement of the Social Environment

Optimizing the measurement of the environment is a critical step in the pursuit of knowledge about how genes interact with the environment to affect adjustment (Moffitt et al., 2005). Moffitt et al. identified several features of environmental measurement that have been consistently underspecified in prior molecular genetic research (e.g., proximal risk factors, age-specific environmental risk factors, cumulative environmental risk factors, and well-validated measurement techniques for examining retrospective recall) and suggested that molecular genetic studies of gene-environment interplay would benefit from more specified environmental features.

Although the criteria defined by Moffitt et al. (2005) are exemplary in highlighting the importance of carefully measuring the environment in GxE interaction research, additional definitional considerations come into play when extending genetic research to inform prevention science. Without comparable measurement of the social environment across prevention science and quantitative behavioral genetics, it is difficult to synthesize findings to inform future prevention research. In this section, we identify six features of the social environment that are fundamental to prevention science research: (a) environment as a multifaceted context, (b) process orientation, (c) focus on health promotion, (d) use of longitudinal designs, (e) environmental mediation of intervention effects, and (f) use of risk-based samples. We provide examples from quantitative behavioral genetics that have defined the social environment consistent with these criteria to illustrate how quantitative genetics can inform prevention science through a common measurement paradigm.

Environment as a multifaceted context

The majority of family-based preventive intervention studies focus on a specified constellation of environmental intervention targets associated with a specified outcome. For example, the Nurse-Family Partnership intervention, an evidence-based community health program for vulnerable mothers pregnant with their first children, includes a set of services

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targeting multiple aspects of the environment (e.g., prenatal care, diet, education, work, and cigarette, alcohol, and illegal substance use; Olds, 2002). In contrast, until fairly recently, environmental influences in quantitative behavioral genetic studies have been estimated based on statistical inference (e.g., the twin method) or measured as unidimensional constructs (often collected via retrospective report). The translation from quantitative behavioral genetics to prevention science has therefore been hindered by this narrow operationalization of the environment, typically focused unidimensional measurement of a single construct rather than multifaceted measurement focused on an array of normative, daily experiences. Quantitative behavioral genetic research that examines how multiple aspects of the environment affect the expression of genetic influences on behavior can be more readily translated to prevention research. For example, quantitative behavioral genetic studies that consider parental warmth and parental negativity (Feinberg, Button, Neiderhiser, Reiss, & Hetherington, 2007) map more closely onto preventive intervention targets than do studies that include a single dimension of parenting or those that infer environmental influences via twin correlations.

Process orientation

Rather than focusing on stagnant aspects of the environment or specific characteristics of an individual, prevention science researchers recognize the targets within this process-oriented approach as participants in dyadic relationships (e.g., parent–child or husband–wife). For example, interventions where dyadic-based processes are highlighted to each member of the couple result in more enduring and pervasive effects at the couple and family levels, resulting in improved coparenting skills (Cowan & Cowan, 2002). In comparison, it is rare to find genetically informed studies that measure process-oriented aspects of the environment similar to those targeted in prevention science. More commonly, self-perceptions of how one is treated by others or how one behaves toward others (e.g., self-report of the parenting relationship) are generally measured in genetically informed studies. Because family-based prevention science researchers typically observe dyadic interactions and subsequently target process-oriented aspects of relationships, quantitative behavioral genetic studies that solely assess participants' self-reports of relationship processes might fail to capture aspects of relationship processes that are amenable to change in preventive intervention research. In contrast, genetically informed observational studies that capture process-oriented interactions between family members are more compatible with prevention science studies that target dyadic-level interaction processes (Leve, Winebarger, Fagot, Reid, & Goldsmith, 1998; O'Connor, Hetherington, Reiss, & Plomin, 1995).

Focus on health promotion

A defining feature of prevention science is the focus on averting negative outcomes and enhancing positive ones. Accordingly, prevention scientists endeavor to enhance the positive functioning of individuals via the construction of positive, supportive social environmental contexts. For example, the Providing Alternative THinking Strategies program is designed to promote social competence in children through the development of self-control, emotional awareness, and interpersonal problem-solving skills (Greenberg et al., 1998). In contrast, many GxE interaction and *r*GE studies are focused on negative environmental experiences (e.g., maltreatment and harsh parenting) and on poor outcomes that occur when adverse environmental conditions combine with genetic risk (Rice et al., 2006). Because prevention science programs typically focus on building skills and cultivating positive environmental change, it can be difficult to directly translate information from genetically informed research to prevention science. For example, in addition to knowing that maltreatment is more strongly associated with antisocial behavior in individuals with certain genetic predispositions (Caspi et al., 2002), prevention scientists would benefit from understanding how consistent, warm parenting practices differentially affect the expression

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of adaptive behavior as a function of inherited characteristics. GxE interaction and *r*GE studies that are focused on positive, strength-building characteristics of the environment (e.g., warm parenting, marital cohesion, and social support mechanisms) and on how such environments can offset genetic risk will be more closely linked to prevention science applications (e.g., Ganiban et al., 2007; Neiderhiser, Reiss, Lichtenstein, Spotts, & Ganiban, 2007).

Use of longitudinal research designs

A fundamental requirement of any intervention study is the use of a longitudinal research design. Rigorous prevention science research is comprised of at least three time points: baseline, intervention, and follow-up. This design permits statistical inferences about whether, in a randomized controlled trial, the intervention had the hypothesized effect on the outcome, controlling for any baseline group differences. Specifically, such trials can test whether environmental manipulations at one time point affect outcomes at a later time point. Although genetic factors have been identified regarding individual differences in a child's adaptation to specific social environments (i.e., the likely efficacy of any associated intervention program), only a small handful of studies have examined the effects of GxE interaction or *r*GE on children's social outcomes longitudinally (Burt, McGue, Krueger, & Iacono, 2005; Forget-Dubois et al., 2007; O'Connor, Neiderhiser, Reiss, Hetherington, & Plomin, 1998; Reiss et al., 2000). GxE interaction and *r*GE studies that are cross-sectional in nature are less useful to the understanding of how environmental change alters child outcomes. More pertinent to prevention science research are GxE interaction and *r*GE studies that examine how measured aspects of the environment at one time point impact an individual at a later time point as a function of genotype, controlling for initial levels of behavior.

Environmental mediation of intervention effects

A related feature of prevention science research is the use of longitudinal designs to examine how the environment mediates intervention effects. For example, in Multidimensional Treatment Foster Care (Chamberlain, 2003), initially developed as a means of preventing subsequent delinquency in juvenile justice populations, researchers have shown that the targeted areas of the intervention mediate the effects of assignment to treatment and control conditions on delinquency (Eddy & Chamberlain, 2000). As such, the role of the environment as a modifiable, mediating mechanism is central in prevention science. Accordingly, genetically informed studies that focus on *r*GE (as compared to GxE interaction) might be more readily translated to prevention science. As is described above, a significant *r*GE might indicate environmental mediation of genetic influences on child outcomes (Ge et al., 1996; O'Connor et al., 1998), thereby providing a conceptual parallel to the approach that prevention researchers take when targeting environmental effects. As is shown in Figure 1, genetically informed studies that focus on *r*GE facilitate two potential intervention sites. First, prevention scientists could target environmental responses to a genetically influenced characteristic, thereby mediating adverse effects on outcomes that might arise from the genetically influenced characteristic. Second, prevention scientists could focus on enhancing an individual's strengths, thereby modifying that individual's response to the adverse environmental experience to promote resiliency. Thus, although there has been a recent surge in GxE interaction research, a focus on *r*GE might ultimately provide highly relevant evidence for the translation to prevention science (Neiderhiser et al., 2004, 2007).

Use of risk-based samples

The inclusion of risk-based (i.e., indicated or selected) samples is a central feature of prevention science research. For example, in the Linking the Interests of Families and

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Teachers program (Stoolmiller, Eddy, & Reid, 2000), each family was selected based on the child's attendance at a school with a high level of free and reduced lunch program eligibility. The larger population was deemed at risk for behavioral and school problems (though not all children would develop such problems). In contrast, nearly all genetically informed studies rely on convenience or epidemiological samples. Although such samples are useful in determining GxE interaction and *r*GE in normative populations, genetic and environmental influences on behavior vary as a function of risk level (Rutter, 2006). Thus, the translation to prevention science would be facilitated by an examination of GxE interaction and *r*GE in risk-based samples, as put into practice in the E-Risk Study (e.g., Jaffee et al., 2005).

Programmatic Steps for Integrating Quantitative Behavioral Genetic and Prevention Science Research

As is described above, identifying parallels between quantitative behavioral genetic research and prevention science in the conceptualization and measurement of the social environment could facilitate the cross-application of work. Once studies that are parallel in measurement have been identified, a roadmap outlining the strategic steps for applying evidence from quantitative behavioral genetic research to preventive intervention development could help to guide subsequent work. In this section, we propose seven programmatic steps (see Figure 2) that will facilitate hypothesis-driven translational efforts leading to genetically informed preventive intervention development by suggesting new targets for intervention, providing new information about the effective timing of interventions, and explaining individual differences in the successes or failures of an intervention. In outlining these steps, we provide examples from coercion theory (Patterson, 1982;Patterson, Reid, & Dishion, 1992;Reid, Patterson, & Snyder, 2002) to illustrate one area in which the translation from quantitative behavioral genetics to prevention science is already well underway.

Step 1: Developmental theory

Prevention science and quantitative behavioral genetic research share a focus on understanding the effects of environmental processes. Given this common principle, the first criterion for maximizing the benefits of translational research is to have a developmental theory that explicates discrete environmental processes hypothesized to affect outcomes. For example, in the coercion theory model, a cascading set of interactions beginning in the home between parent and child and extending to the peer realm lead to a youth's engagement in antisocial behavior. The process begins with a parent's lack of resources, support, and skills to effectively manage common child behaviors. These circumstances set the stage for the child to engage in negative, coercive behaviors (e.g., crying, whining, and temper tantrums) to elicit a response from the parent, who then responds with harsh and inconsistent parenting, thereby reinforcing the child's negative behavior and leading to an escalation of child externalizing problems. This, in turn, is hypothesized to further disrupt parenting. After extensive practice with this interaction style at home, the child enters the peer realm having learned a host of coercive behaviors and negative reinforcement processes and having failed to learn prosocial behaviors. This constellation of behaviors is hypothesized to attract antisocial peers, which leads to engagement in group-based antisocial activity such as drug use and engagement in criminal behavior. Thus, following coercion theory, harsh parenting and deviant peer affiliations are hypothesized as environmental mechanisms that have potentiating effects on antisocial behavior. As such, the developmental theory (coercion theory, in this example) sets the framework for the remaining six steps.

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Step 2: Genetic and environmental influences

Within any given developmental theory, quantitative behavioral genetic studies can provide information about the etiology of an outcome by assessing its genetic and environmental influences. In regard to coercion theory, genetic studies can provide information about how the child's genotype might affect the parenting and peer reinforcement mechanisms, thereby providing additional information about the underlying etiology of delinquent behavior and potential information about intervention targets. For example, if the results from a quantitative behavioral genetic study measuring the family environment indicated that the shared environment accounted for a significant portion of the variance in delinquency, the specific family process measured might be an optimal intervention target in prevention science. Conversely, if such a study found nonshared environmental effects to be prominent, a more successful intervention target might be the unique processes children are exposed to, as measured in the specific study (e.g., school, classroom, or peer influences). As such, the common measurement strategy described in the first section of this manuscript is key for translating the findings in Step 2.

Step 3: Longitudinal environmental mediation

Step 3 involves examining longitudinal evidence for the predictive relationship between the environmental variable and the outcome hypothesized in the developmental theory (Step 1). In coercion theory research, longitudinal studies have provided evidence of the association between harsh parenting and antisocial behavior and of the mediating role of effective parenting in offsetting risk (Patterson et al., 1992; Reid et al., 2002). As Cowan and Cowan (2002) discussed, family-based research should utilize theory to focus on specific targets within the family (e.g., emotion regulation in marital and parent-child relationships) and on the inclusion of measures to test whether change in the hypothesized mediator accounts for variation in outcome. According to Cowan and Cowan, this strategy will contribute to a more differentiated understanding of how family factors affect youth development and will help to guide clinicians in the design of more effective preventive and therapeutic interventions. Without support for environmentally mediated effects on child outcomes, it would be premature to consider a randomized trial targeting such environmental processes; longitudinal data can uniquely provide support for the hypothesized causal relationship between a specified aspect of the environment and a specified outcome that could be modified via intervention.

Step 4: Longitudinal variation in impact

Researchers can uniquely leverage longitudinal quantitative behavioral genetic studies to learn when in development a specific environmental variable has its most salient effects on an outcome. Through repeated assessments of the same environmental and outcome measures over time, quantitative behavioral genetic analyses can be used to identify developmental periods when a specific environmental effect is most strongly associated with an outcome or when genetic effects primarily account for individual differences in an outcome. Using this information, prevention scientists can determine the optimal developmental period(s) for preventive interventions.

Step 5: Causal environmental mediation

Step 5 involves examining evidence from randomized controlled trials regarding the mediating effects of specific environmental variables on specific outcomes (i.e., an experimental test of the Step 1 developmental theory). Randomized clinical trials can build upon the knowledge generated in Steps 2-4 to provide more conclusive evidence for a hypothesized environmental mediator as an agent of change on a specified outcome, thereby

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demonstrating a causal and malleable relationship between the two (e.g., the mediating role of harsh parenting on child antisocial behavior).

Step 6: GxE interaction and/or rGE

Quantitative behavioral genetic studies offer unique information about how specific environmental variables covary or interact with genetic influences on specific outcomes, thereby providing insight into individual differences in outcomes and unique targets for intervention. For example, in light of the finding that harsh discipline mediates risk for externalizing problems (Steps 3 and 5), *r*GE research has been used to show that genetically influenced child behaviors can *evoke* harsh parenting practices (Ge et al., 1996; O'Connor et al., 1998). The cumulative findings from developmental, intervention, and quantitative behavioral genetic studies can thus be used to indicate bidirectional associations between specific environmental mediators and specific outcomes. Based on the examples given here, an optimal focus for prevention science might be to enhance a traditional parenting management training intervention with a component specifically targeting the evocative effects identified in the quantitative behavioral genetic research. For example, a component could be added to inform parents how to recognize the effect of the child's maladaptive behavior on their parenting and to teach alternative techniques for responding to such behavior, thus preventing the reinforcement of a preexisting, genetically influenced negative tendency in the child. Similarly, GxE interaction research can be used to provide information about the mechanisms underlying individual differences in intervention outcomes. For example, GxE interaction research could be used to determine whether the effects of a harsh family environment are more detrimental for individuals who also have certain genetic predispositions.

Step 7: Intervention successes and failures

Because interventions vary in effectiveness, Step 7 includes conducting statistical analyses to determine the implementation fidelity and the effect size of the completed interventions reviewed in Step 5. The results from these analyses can help to determine the ubiquity of the intervention effects on the participants and the extent to which enhancements informed by quantitative behavioral genetics are needed. Almost invariably, some children and families respond more favorably than others to specific treatments, and some interventions are delivered with greater fidelity than are others (Forgatch, Patterson, & DeGarmo, 2005). For example, an intervention with a large effect size could be highly successful for many participants but result in many others being no better off than the participants in the control condition. Conversely, an intervention with a small effect size could result in very modest but practically significant improvements in functioning for the majority of the participants. Understanding the differential implementation of a given intervention and the differential responsiveness of its participants can facilitate a more robust understanding of whether the intervention could be improved by modifying it for a specific subpopulation, should be generally enhanced because of low effect sizes, or is highly effective and has few systematic differences in treatment effectiveness. The results from these analyses ultimately enable the knowledge gained from quantitative behavioral genetic research to be selectively applied to the interventions and/or individuals that could most benefit from such enhancements.

The knowledge base for each of the seven steps should include replicated findings, using varied samples and methods rather than resting on a single study or sample. In a similar vein, the steps are intended to be iterative and cycle back to Step 1 to revise or refine the developmental theory after new knowledge is garnered from later steps in the process. When ample evidence has been generated for a given environment outcome pairing through each of the above steps, prevention scientists will be well poised to utilize quantitative behavioral genetic knowledge to enhance interventions and consider the effect of a child's genetic

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makeup on behavior and the environment (and vice versa). Prevention scientists will have new information about the optimal timing of an environmental intervention, about potential intervention targets, and about individual differences in intervention successes to inform the development of subsequent trials.

Extending Quantitative Behavioral Genetic Research to Inform the Selection of Prevention Targets: An Illustrative Example

In this section, we provide an example from the Early Growth and Development Study (EGDS; Leve et al., 2007) to illustrate how the seven steps (outlined above and in Figure 2) can guide the selection of preventive intervention targets by utilizing studies that contain comparable measurement of the environment. The EGDS is an ongoing longitudinal, prospective adoption study of 361 linked triads (i.e., adopted child, his/her adoptive parents, and his/her birth parent[s]). The children were placed in nonrelative adoptive families within the first 3 months of life (*M* age = 3 days) and were studied across early childhood beginning at 9-months of age. As is noted previously, the adoption design uniquely allows for the identification of specific environmental influences on behavior, while simultaneously permitting the examination of genetic influences and the interplay between genes and the environment. With an overarching goal of informing prevention science, the assessment protocols and measures in the EGDS were designed to closely mirror the multifaceted, process-oriented risk and protective factors targeted in prevention research (as highlighted in the first section of this manuscript).

Step 1

In Step 1, we focused on understanding genetic and environmental influences on the pathways for externalizing behavior during early childhood and therefore grounded this work within the coercion theory framework. This led us to focus on assessing mother–child interactions in a noncompliance task (clean-up task) during a challenging development period (toddlerhood), measuring toddler externalizing behavior as the outcome of interest.

Step 2

In Step 2, we examined twin and adoption studies that assessed parenting and toddler externalizing behavior to better understand how externalizing behavior and parenting during early childhood are influenced by genetic and environmental factors. In their review of the literature, Saudino, Carter, Purper-Ouakil, and Gorwood (2008) found that toddler externalizing problems were moderately heritable, although considerable effects of the family environment were also present. In addition, other quantitative behavior genetic studies have found that infants with more difficult temperaments evoked more hostile styles of parenting (Boivin et al., 2005; Forget-Dubois et al., 2007). Together, this evidence provided support for the development of hypotheses targeting the effects of the family environment on toddler externalizing problems while simultaneously considering genetic effects on child temperament and on parenting.

Step 3

In Step 3, we examined longitudinal studies that focused on parenting as a mediator of externalizing problems during early childhood. The results from numerous developmental studies supported the role of parenting (effective maternal guidance in particular) on externalizing problems during early childhood (e.g., Smeekens, Riksen-Walraven, & van Bakel, 2007). Therefore, we focused on two domains of parenting: maternal structured guidance and maternal positive reinforcement.

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Step 4

In Step 4, we examined quantitative behavioral genetic studies across childhood to assess how environmental influences on externalizing problems increase or decrease during specific developmental periods. The evidence from meta-analyses indicated that family environmental effects on externalizing problems tend to decrease over time (Bergen, Gardner, & Kendler, 2007; Rhee & Waldman, 2002), highlighting the centrality of toddlerhood as a developmental period for identifying family environmental factors associated with child externalizing problems that might be amenable to intervention.

Step 5

In Step 5, we examined randomized trials targeting parenting as a mediator of intervention effects on early childhood externalizing problems. Although the evidence from such randomized trials is fairly sparse, several efficacious programs that each included a parenting component have been shown to prevent problems during early childhood (Olds, 2002; Webster-Stratton et al., 2001). This evidence suggested that specific parenting processes could be effective intervention targets during toddlerhood.

Step 6

In Step 6, based on the evidence from Steps 1–5, we conducted a new set of analyses on the EGDS dataset to examine GxE interaction processes in the prediction of toddler externalizing problems. Specifically, we examined associations between genetic risk for maladjustment (measured via birth parent assessments), toddler externalizing problems, and two aspects of parenting hypothesized to protect against child externalizing problems (i.e., maternal structured guidance and maternal positive reinforcement). The analyses, which controlled for prior temperament, indicated a significant interaction between birth mother maladjustment and adoptive mother observed structured guidance on toddler externalizing problems; structured guidance provided a buffering effect on the externalizing problems of toddlers at high genetic risk. However, for children at low genetic risk, structured guidance did not help to prevent child externalizing problems; in some cases, it actually facilitated child externalizing problems. Conversely, although main effects of maternal positive reinforcement were present, no interaction effects were found. These results indicate a unique level of specificity that could inform subsequent intervention development. The effects of maternal structured guidance on toddler externalizing problems were moderated by the child's inherited characteristics such that only toddlers at high genetic risk benefited. Further, the positive effects of maternal positive reinforcement were not subject to differential impact based on the child's genetic risk (portions of these analyses are presented in Leve et al., 2009). Such findings could inform early childhood preventive interventions by suggesting that only toddlers at high risk for externalizing problems might benefit from parenting interventions that focus on enhancing maternal structured guidance.

Step 7

In Step 7 (underway), we are examining the differential effectiveness of existing preventive intervention programs targeting parenting behavior and the prevention of early childhood externalizing problems (cf., Olds, 2002; Webster-Stratton et al., 2001). Specifically, we aim to learn whether there are subgroups of individuals for whom the original intervention was not successful and for whom exposure to an enhanced, genetically informed intervention module might be warranted. Once Step 7 is complete, the next step will be to reexamine the developmental theory (Step 1) to make modifications based on the knowledge gained in Steps 2-6, and continue the iterative seven-step process.

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Although the example here focused on early childhood, this seven-step process and the importance of matching the measurement of the environment in quantitative behavioral genetic research with the measurement of the environment in prevention science is applicable across the lifespan. For example, interventions aimed at preventing physical health problems in the elderly can be informed by longitudinal studies of the predictors of physical health. However, these interventions can be further informed by quantitative behavioral genetic studies on the association between physical health problems and social activity; such studies can provide novel information about genetic and environmental influences underlying the bidirectional associations between the physical health problems and social activity (McGue & Christensen, 2007).

Limitations and Future Directions

Although we argue for the timely and rigorous translation of quantitative behavioral genetics to prevention science, two caveats must be noted. First, the methods suggested here imply that preventive interventions are optimally structured around the environmentally mediated aspects of behavior (as opposed to more genetically influenced aspects of behavior). However, ample evidence indicates that environmental modifications can ameliorate genetically influenced behaviors. For example, the effects of phenylketonuria (PKU), a genetically based disease resulting in mental retardation and neurological problems, can be averted through a purely environmental intervention consisting of a strict diet that eliminates all high protein foods in the first few weeks after birth. The success of this environmental intervention is so effective that every state in the United States screens for PKU in newborns so that dietary interventions can begin in a timely, preventative manner. Thus, despite the focus on interventions that target variation in behavior due to environmental influences, environmental interventions can alter the expression of genetic risk and decrease the rates of undesirable outcomes regarding highly genetically influenced behaviors.

Second, we focused on linking prevention science to findings from quantitative behavioral genetics despite the emerging body of molecular genetic research demonstrating that environments can offset or enhance propensities inherited through specified genetic polymorphisms (Caspi et al., 2003; Kim-Cohen et al., 2006). Although molecular genetic studies provide information about environmental processes that might moderate the expression of a measured gene, we chose to emphasize the translation from quantitative behavioral genetic research for two reasons: (a) it has more developed history and greater accumulation of evidence specific to psychosocial characteristics and (b) we were interested in understanding the effects of the whole genome on behavior rather than the effects a small number of recognized gene variants (e.g., 5-HTTLPR, COMT, and MAOA). Nonetheless, molecular genetic studies have and will continue to complement this body of work by advancing our understanding of the biological underpinnings of social behavior (Caspi & Moffitt, 2006; Moffitt, et al., 2005; Moffitt, Caspi, & Rutter, 2006; Rutter, 2006) and our understanding of GxE interaction processes within the context of interventions (Brody et al., 2009).

In conclusion, systematically highlighting the evidence base from quantitative behavioral genetic research to inform prevention science could generate new insight into the role of specific mechanisms underlying individual differences in how children adapt to specific environmental influences and how adaptation might vary during specific developmental periods; this, in turn, will increase the efficacy of family-based interventions and improve child outcomes. Given the solid foundation of knowledge that has accumulated in prevention science and quantitative behavioral genetics, this is an opportune time to apply the cumulative knowledge to move forward with an integrative translational research model designed to measurably improve outcomes for children and families across the lifespan.

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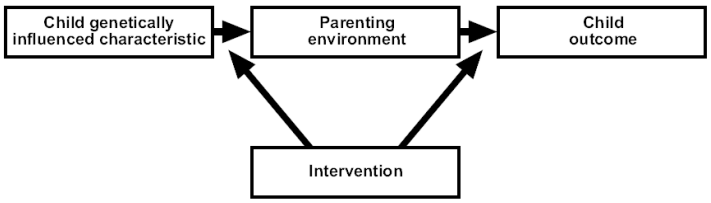

Figure 1.
Mediated model illustrating *r*GE and potential intervention sites within a genetically informed design.

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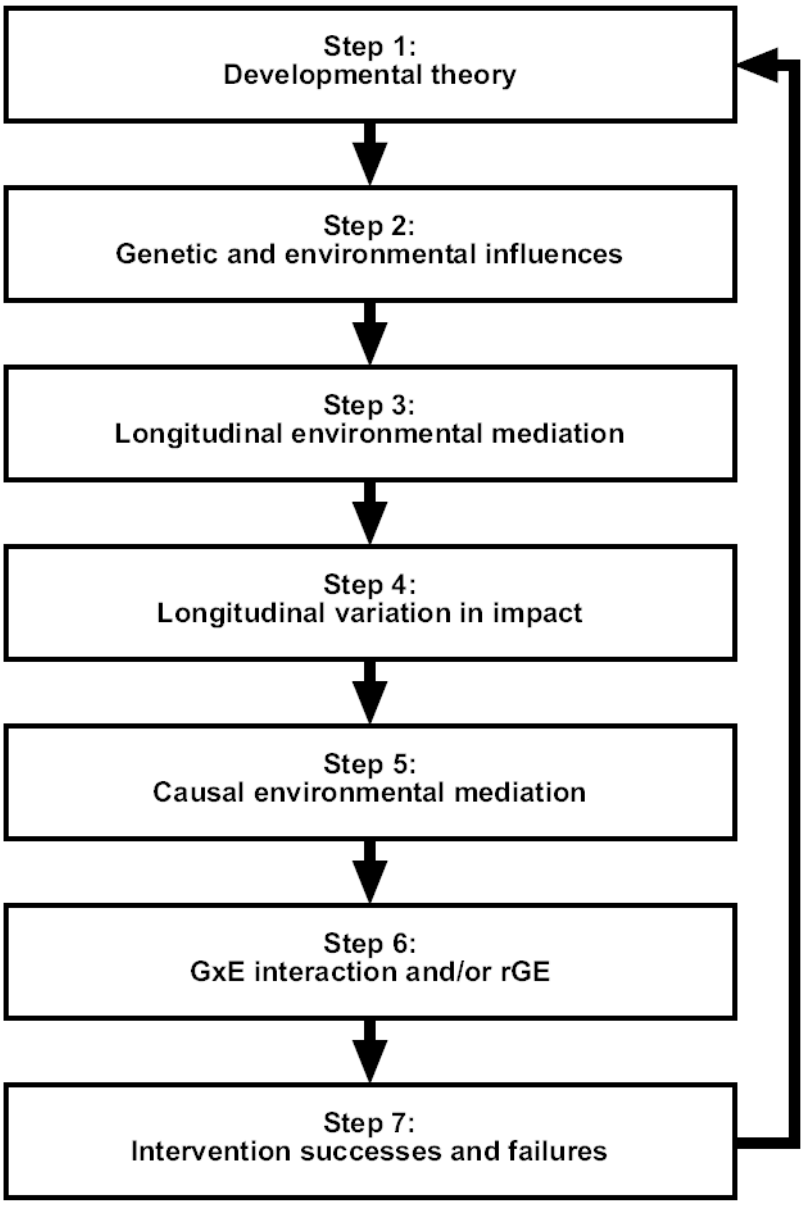

Figure 2.
Seven programmatic steps for integrating quantitative behavioral genetic and prevention science research.