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How Can Genetically-Informed Research Help Inform the Next Generation of Interparental and Parenting Interventions?

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Abstract

There is robust evidence that the interparental relationship and parenting behaviors each have a significant influence on children's risk for internalizing and externalizing problems. Indeed, interventions targeting the interparental relationship and parenting processes show significant intervention-related reductions in child internalizing and externalizing problems. However, most evidence-based parenting- and couple-focused interventions result in small to medium effects on children's emotional and behavior problems. We believe there is room to improve upon these interventions through incorporation of knowledge from quantitative genetic research. We provide three recommendations for practitioners engaging in intervention work with children and families. These recommendations are contextualized relative to what quantitative genetic studies can tell us about the role of the interparental relationship and parenting behaviors on child outcomes.

How Can Genetically-Informed Research Help Inform the Next Generation of Interparental and Parenting Interventions?

The quality of the interparental relationship has been consistently shown to influence rates of child psychopathology (Rhoades, 2008). Similarly, parenting processes have well-documented influences on child externalizing and internalizing problems (Tully & Hunt, 2015; Yap & Jorm, 2015). Dozens of parenting-focused interventions have been tested using randomized controlled trials and are now included on evidence-based practice lists as being effective in reducing child externalizing and internalizing problems (<http://www.blueprintsprograms.com/>). Although less common, several evidence-based interventions also target the couple relationship (e.g., Cookston et al., 2007; Schulz, Cowan, & Cowan, 2006). Despite the overall preponderance of parenting- and couple-based interventions deemed to be effective, the vast majority of these programs have small to medium effect sizes (<http://www.blueprintsprograms.com/>). Further, the rates of child externalizing and internalizing problems worldwide are not decreasing (e.g., Bor et al., 2014). This suggests that we can, and should, seek ways to maximize the well-being of children and families at risk for behavioral and emotional problems by improving the effectiveness of interparental and parenting-focused interventions. The field of developmental science has formulated intervention strategies that work; our next challenge is to investigate strategies for refining them in order to create substantive increases in child well-being at the population level.

In this paper, we propose that the field of quantitative genetics can provide important clues about malleable family processes that developmental scientists can leverage to improve the effectiveness of evidence-based parenting and interparental interventions. We divide our paper into three sections. First, we provide a brief description of the discipline of quantitative genetics and include examples that illustrate how quantitative genetic findings on associations between

the interparental relationship, parenting, and child behavior problems can be useful in thinking about intervention strategies. Second, we discuss the limits of genetic research for intervention science. Third, based on the information in these two sections of the paper, we conclude with three core recommendations for practitioners working with children and families.

Part I: The Relevance of Quantitative Genetic Findings on Interparental Conflict, Parenting, and Child Behavior Problems for Intervention and Prevention Science

Multiple studies show that parents embroiled in a hostile and distressed couple relationship are typically more hostile and aggressive toward their children and less sensitive and emotionally responsive to their children's needs (Erel & Burman, 1995; Harold, Elam, Lewis & Thapar, 2012). The substantive theory underlying this research is that the effects of conflict between parents occur indirectly through a "spillover" of emotion from the couple relationship to the parent-child relationship; heightened levels of interparental conflict lead to more acrimonious parent-child relations, which in turn increase children's internalizing and externalizing problems. Three fundamental challenges to the spillover theory are that (1) linkages between the couple relationship, negative parenting practices, and child outcomes may be partially explained by common genetic factors shared between parents and children rather than solely through environmental effects; (2) children may evoke negative parenting and/or interparental conflict because of their own genetic propensities; and (3) inherited aspects of child behavior may interact with the environment such that the effects of negative parenting and interparental conflict on child behavior problems are not the same for all children. These three specific challenges, characterized by gene-environment interplay, have significant implications for intervention development. Specifically, because successful interventions have a clear theory of change that identifies and targets malleable precursors of problem behavior (Gottfredson et al., 2015), understanding the role of genetic factors in behavior development and change

processes is essential. Quantitative genetic designs are particularly useful in this regard because they can partition and/or disentangle genetic from environmental etiological factors, and also allow examination of their interplay. We provide a brief overview of the different types of quantitative genetic designs next, to help contextualize the findings emanating from this body of research.

Types of Quantitative Genetic Studies. A number of different research designs exist in the field of quantitative genetics (see Figure 1 for an overview of the most common quantitative genetic research designs). In *twin studies* it is assumed that monozygotic (from the same fertilized ovum) and dizygotic (from two separately fertilized ova) twin pairs share environments (e.g., parenting practices) to the same extent, so a greater degree of concordance in monozygotic pairs compared to dizygotic pairs is attributed to genetic factors, relative to environmental influences. *Extended family studies* provide the opportunity to study the association between particular environmental exposures and behavior problems in children, with adjustment for familial factors and genetic relatedness among family members (D’Onofrio, Lahey, Turkheimer, & Lichtenstein, 2013). For example, full siblings share half of their genes and some intrauterine exposures; half-siblings share a quarter of their genes and some intrauterine exposures only if both are genetically related to the mother. If correlations between sibling sets are stronger among siblings who are full siblings (vs. half or unrelated siblings), then genetic factors are assumed to be involved. One extension of this design is the Children of Twins (CoT) design. The CoT design makes use of adult twin pairs and their children, because when identical twins have children, those children are just as genetically related to their parents’ twin brother or sister as they are to their own parent. This unique feature of the CoT design offers an opportunity to distinguish whether transmission within families is because of genes, the environment, or both (see D’Onofrio et al., 2007). *Adoption studies* examine the resemblance between biologically

related and unrelated relatives. Similarities between adopted children and their biological parents are assumed to be due to shared genes, whereas similarities between adopted children and their rearing parents are assumed to result from environmental influences unconfounded by shared genetic factors. The *in-vitro fertilization* (IVF) design is similar to an adoption design in concept (Harold et al., 2012). Specifically, children are genetically related or genetically unrelated to one or both of their rearing parents on the basis of the “adoption” of gametes (sperm, eggs, embryos), which enables comparison of genetically unconfounded associations linking rearing experiences and outcomes. By comparing the association between two variables (e.g., hostile parenting and child externalizing problems) across parents and children who are genetically related and genetically unrelated, it is possible to ascertain whether the magnitude of association between parent and child is primarily genetically mediated, environmentally mediated, or a combination of the two.

Table 1 lists studies that have used quantitative genetic research designs to examine associations between the interparental relationship, parenting, and child behavior problems. The studies provided in Table 1 were derived from a search of the PubMed database and Google Scholar in May 2015, with the following key search terms: (adoption OR twin OR IVF OR genetically sensitive OR environment) AND (marital conflict OR parent disagreement), with the requirement that the study include a measure of parenting. We describe findings from several of these studies to illustrate how this body of evidence addresses three challenges to studies that do not employ genetically sensitive research designs, and provide new clues about the nature of the associations between the interparental relationship, parenting, and child behavior problems that are relevant to intervention and prevention program development.

The Confound of Passive Gene-Environment Correlation. Extant research has shown the direct and indirect effects of the interparental relationship on children’s externalizing and

internalizing problems (e.g., Grych & Fincham, 1990; Harold & Conger, 1997). However, when this work is conducted with biologically related parents and children, it is not possible to ascertain whether associations between aspects of the interparental relationship and child behavior problems represent direct environmental effects, or whether they are the result of shared genetic influences common to parent and child. For example, associations between interparental conflict and child externalizing problems may result from shared genetic factors that simultaneously influence both parental conflict and child aggression. As such, the association between interparental conflict and child behavior problems might simply be an artefact of shared genetic factors underlying this association, thereby remediating the role of the “environment” as a direct influence of child development, and by implication, shifting the focus of interventions. This process is referred to as *passive gene–environment correlation* (rGE ; Jaffee & Price, 2007).

Some quantitative genetic studies directly address the confound caused by passive rGE by using samples of parents and children who are *not* genetically related. This methodology allows stronger conclusions to be drawn about the direct environmental role of the interparental relationship and parenting on child behavior problems, and therefore can provide important information for a theory of change model and subsequent intervention development. As an example, Rhoades et al. (2011) used an adoption study to examine the spillover effect of interparental hostility on toddler anger through harsh parental discipline. Because the adoptive parents were genetically unrelated to the child, associations between interparental hostility, harsh parenting, and child anger were free from the confound of shared genetic factors, and thus represent more “pure” environmental influences on child behavior. The results of the Rhoades et al. study indicated an indirect effect from interparental hostility to subsequent toddler anger via parental harsh discipline. This study thus confirms that interparental hostility and warmth have environmental impacts on child behavior problems that operate via parenting practices, and that

these effects cannot be accounted for by the confound of common genetic factors (offering support to past studies conducted in this area). This knowledge advances theory of change models that are foundational to intervention development.

The Relevance of Evocative Gene-Environment Correlation. Research extending back more than 30 years has identified the potentially important role of child-on-parent effects (versus parent-on-child effects; Bell & Chapman, 1986). Genes may not only affect behavior directly, but they may also affect the rearing environments that children experience (e.g., the couple relationship, harsh parenting practices). Such genetically influenced child-on-parent effects are commonly termed *evocative gene-environment correlation* (r_{GE}), and refer to child characteristics that evoke patterned responses, such as negativity, from a parent (Ge et al., 1996). This area of research offers significant promise for the field of intervention research because domains of “at-risk” environmental processes (e.g., abusive or neglectful parenting behaviors) may be identified, supported, and made “resilient” to child-driven influences (Luthar & Brown, 2007). Within the family of quantitative genetic studies, the adoption design offers a unique research strategy in which evocative processes may be examined.

Ge et al. (1996) provided the first example of evocative r_{GE} processes in the field of developmental science. Using a relatively small adoption sample, these authors showed that biological mothers’ psychopathology was associated with negative adoptive mother hostility through disrupted child behavior characteristics. Building on this research, recent adoption studies that employ larger samples have found that genetically-influenced child characteristics evoke negative maternal and paternal parenting practices, which in turn are associated with subsequent peer and behavioral problems in the child (Elam et al., 2014; Harold et al., 2013). Twin studies have also evidenced evocative process (e.g., Neiderhiser et al., 2013).

The child evocative effects identified by quantitative genetic studies provide a new

potential pathway for intervention that is not otherwise discernable from non-genetically informed studies: If we can coach/train parents to identify and respond effectively to the potential for child evocative influences, we might be able to disrupt the negative cascade from a heritable child trait, to a harsh parenting response, to an increase in child behavior problems. This approach goes beyond the traditional one-size-fits-all parent training approach and can be individualized depending upon the specific heritable behaviors in a given child that set in motion adverse responses from caregivers. The specific child behavior–parent response pattern may vary from family to family on the basis of the inherited profile of each child. Notably, within the context of the intervention, it is not necessary to determine whether, or to what extent, a specific child behavior is or is not “genetic”; the quantitative genetic studies tackle that problem and provide the foundational basic science evidence. Rather, with that knowledge in hand, we can begin to apply the concepts underlying child-evoked effects to our interventions. We can teach parents about biologically-originating processes that may be specific to their family dynamics, with the goal of disrupting the potential for a negative cascade to develop within a family. Simply sharing the knowledge that children can be born with specific traits and behavioral tendencies that can present challenges to the interparental and parenting systems can be a useful tool to talk with parents about, and ultimately help them better manage their own responses to challenging child behavior and recognize the child’s inherited strengths.

The Role of Gene-Environment Interaction. A third challenge to non-genetically informed studies is *gene-environment interaction* (GxE). For example, the quantitative genetic literature suggests that the effects of the interparental relationship and parenting on children’s behavior problems may be strongest among children at high genetic risk (e.g., Rhoades et al., 2011; Rice, Harold, Shelton, & Thapar, 2006; Schermerhorn et al., 2012), and that children are differentially susceptible to certain types of family environments (interparental, parenting) as a

function of their own genetic make-up (Hyde et al., 2016; Leve et al., 2009). Among children living with their biological parents, this distinction is not discernable because children at the highest inherited risk are likely the same children as those who are at highest environmental risk (genetic and environmental effects are confounded because of passive rGE). However, an increasing proportion of today's generation of children are likely to live with genetically unrelated parents because of adoption, step-parenthood, or IVF reproductive technologies. As such, inherited risk and protective factors can be separated from environmental ones; inherited risks may be present *in the absence* of environmental risks, and inherited protective factors may be present in adverse environmental contexts. This has important implications for the development of interventions that are designed to promote resilience in the face of adversity (Luthar & Brown, 2007).

As an example of this process, Leve et al. (2009; 2010) examined associations between inherited risk for maladjustment (anxiety, depression, antisociality, and drug use measured via birth parent assessments), toddler behavior problems, and two aspects of parenting hypothesized to protect against child problems (i.e., maternal structured guidance and maternal positive reinforcement). The analyses indicated a significant interaction between birth mother maladjustment and adoptive mother observed structured guidance on toddler behavior problems: structured guidance provided a buffering effect on the behavior problems of toddlers at high inherited risk. However, for children at low inherited risk, structured guidance did not help to prevent child problems; and in some cases, it actually facilitated behavior 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 benefits of maternal structured guidance only extended to children at high inherited risk, whereas positive reinforcement benefited all children. Consistent

with a precision medicine approach (Collins, 2015), this type of finding allows for more precise targeting of personalized interventions that are matched with an individual's inherited characteristics and liabilities. It suggests that, when possible, clinicians should collect detailed information about the family history of biological relatives and use intervention strategies that are matched to the child's inherited risk and protective factors.

Part II: The Limits of Applying Genetic Research to Intervention Development

As described in the preceding sections, quantitative genetic research addresses three key challenges not discernable in non-genetically informed studies (passive rGE , evocative rGE , and $G \times E$). The identification and specification of these G-E interplay processes can help provide more accurate theories of change that inform basic science, and can subsequently lead to more precise intervention approaches that can be individualized based on a child's inherited characteristics. These strengths notwithstanding, there are limits to the transferability of findings from genetic research to intervention development.

Sample Characteristics. Interventions can be classified as universal (addressing an entire population, such as a whole school, with programs aimed at preventing problem behaviors from developing), selective (targeting a subset of the population based on membership in a specific at-risk group, for example, low income families, with the goal of preventing the development of serious problems), or indicated (aimed at individuals who exhibit signs of problems, such as youth in the juvenile justice system, with the aim of implementing programs to prevent further onset of difficulties), and different intervention strategies are recommended as a function of the type of intervention and population served (universal, selective, indicated). One challenge in translating findings from quantitative genetic research to intervention research is that the majority of genetically-informed studies have been conducted with normative, low-risk samples. Although such samples are useful in examining $G \times E$ interaction and rGE in normative

populations, genetic and environmental influences on behavior vary as a function of risk level (Rutter, 2006). Thus, practitioners need to carefully attend to sample characteristics in translational efforts in order to preserve the prevention implications of the original genetic findings. Further, the majority of quantitative genetic studies have relied on samples that are primarily Caucasian. Although there is no evidence to suggest that the gene-environment interplay processes described in this article vary by ethnicity, the developmental literature has evidence that parenting processes may have differential impacts as a function of ethnicity (Lansford et al., 2004). (Note: evidence from genetic studies in this area is limited, however in genetic studies where ethnicity is controlled, i.e., population stratification methodology, effects do not vary from those described here; Freedman et al., 2004).

Molecular Genetic Approaches. We have focused this commentary on quantitative genetic studies, however, there is a growing body of molecular genetic studies that have examined whether behavioral interventions are more or less effective for individuals with or without a hypothesized genetic marker of susceptibility. At least 22 GxE analyses have been conducted with intervention samples (Bakermans-Kranenburg & Van IJzendoorn 2015). Results suggest promise in using genetic information to tailor prevention strategies. However, in the majority of these studies, the GxE findings related to the intervention were hypothesized post-hoc, after the intervention had been completed. In addition, eight different candidate genes were identified as being involved in G x Intervention interactions, and the outcomes included a wide range of behaviors such as alcohol use, anxiety, externalizing behavior, literacy, IQ, and depression. Thus, although early molecular genetic research related to personalized intervention opportunities are innovative and hold promise, there is significant work to be done to connect a priori theories and genetic mechanisms to specific outcomes of interest. Further, molecular genetic discovery studies typically require sample sizes in the multiple thousands in order to

provide adequate statistical power, limiting the ability to collect observational data that would lend itself to understanding processes and mechanisms. Finally, effects sizes in molecular genetic studies of common alleles tend to be quite small (Thapar & Harold, 2014). One recent molecular genetic strategy that holds promise is the creation of ‘polygenic risk scores’, in which a composite genetic risk score is created based upon the average number of ‘risk’ alleles an individual carries (Dudbridge, 2013). Such polygenic scores leverage association evidence and effect size estimates from existing large genome-wide association studies, rather than depending on the specific sample for these, thus removing the requirement for large sample sizes. Nonetheless, such strategies still account for very limited variance in behavior (often less than 1%), whereas quantitative genetic approaches allow for the inclusion of the aggregate, anonymous effects of the whole genome.

Feasibility of Obtaining Genetic Information from Families. Another challenge to applying knowledge from genetic research to intervention development is that practitioners need to have access to a child’s genetic information. In translating findings from molecular genetic studies, this means that the provider would need access to the same aspects of the client’s DNA that were the focus of the original molecular genetic studies, in order to individualize the intervention based on the genetic make-up of the individual. Having access to genetic data is not commonplace among mental health service providers, particularly those serving high-risk populations in community health settings. Thus, significant groundwork needs to be laid for mental health service providers to collect and/or have access to the appropriate genetic data needed in order to implement a personalized intervention. Similarly, to translate knowledge from quantitative genetic studies, practitioners need access to family history information. This challenge is further discussed in Part III of this paper.

Heritability ≠ NonMalleability. We have emphasized the benefits of conducting quantitative genetic studies in order to develop more accurate theories of change, by better capturing the ways in which parenting and interparental environments are correlated with and interact with genetic influences. This knowledge could then be used to refine environmental intervention targets as a function of the child's genetic propensities. However, it is important to note that just because a behavior is identified as heritable does not mean that it is not malleable. For example, although weight is highly heritable, it can be influenced by prenatal exposures, diet, nutrition, and activity. The assumption that behaviors that are genetic are *not malleable* is a common misperception in applying genetic research to intervention development. In fact, the approach suggested in this review is that environmental interventions (those targeting parenting and/or interparental behaviors) can help suppress the expression of inherited risks and maximize the expression of genetic strengths. Such modifications of genetic expression are consistent with epigenetic processes, whereby environmental factors that switch genes on and off (via DNA methylation processes) affect how cells express genes (Weaver et al., 2004). Thus, although we focus on the translation of genetic research to refine family environmental intervention targets, such intervention efforts are hypothesized to operate by modifying the expression of inherited propensities.

Mean Level Shifts in Behavior. A final limitation in translating genetic findings to intervention development is that quantitative genetic methods typically use a *correlational approach* to examine associations between individuals and draw conclusions as to the relative genetic and environmental contributions to a behavior. Conversely, intervention studies typically focus on *mean level* improvements in behavior as a function of the intervention. The differences in the statistical approaches used by the two disciplines (mean level differences between groups

vs. correlations between variables within and between groups) has hampered the translation of findings from one field to the other. For example, it is not uncommon to hear professionals in the field confused over how a behavior can be highly heritable, and yet psychosocial intervention studies can target and improve this same behavior. For example, executive functioning is known to be heritable (Engelhardt et al., 2015), but it is also clear that it can be improved via environmental interventions (e.g., Tang et al., 2012). The root cause of the perceived discrepancy between the heritability of a behavior and its malleability is the use of different analytical approaches; quantitative genetic studies examine correlations between family members who are related to one another in varying degrees (e.g., identical twins, fraternal twins, cousins; or adoptees and their adoptive and biological parents) and infer the proportion of variance in a behavior that is due to shared environmental or heritable sources as a result of between group differences in the correlations. In contrast, intervention studies typically compare mean level changes in behavior between two or more groups of participants. This substantive issue can limit the translation from genetic studies to intervention development, and requires further clarification and explanation in interpreting research findings relevant to intervention science.

Part III: Recommendations for Practitioners

On balance, despite the limits of genetic research to the design and implementation of family-based interventions, there is significant potential for an increase in translational efforts between the disciplines of quantitative genetics and prevention. We offer three recommendations for practitioners to increase such efforts.

Collect a thorough family history of psychological symptoms of your clients. The potential for genetic research to benefit intervention efforts cannot be realized without some information on the genetic propensities of an individual. Recognizing the challenges for practitioners in collecting, analyzing, and using DNA samples to gain this information, we

suggest that practitioners obtain a detailed family history of their clients to capture “genome-wide” heritable influences on development. This approach is consistent with the quantitative genetic approach described in this commentary, and may provide practitioners with the necessary clues to a child’s inherited propensities to begin to tailor intervention services accordingly.

Stay abreast of the rapidly-evolving conclusions drawn from genetic studies and child development studies. Once information about a child’s genetic background is obtained, practitioners need a basic understanding of the current findings from genetic research and child development in order to develop personalized interventions. This is no easy feat, since the genetic research findings are spread across a range of academic journals and are not easily accessible to practitioners. Further, the field of genetics has rapidly evolved over the past two decades, with new methods and approaches coming online regularly and/or becoming more cost-effective. As discussed in our third recommendation (next), part of the burden of this translation falls to genetic and developmental researchers to increase the accessibility of their findings. Nonetheless, to the extent possible, reading summaries in journals such as *Child Development Perspectives* and reading blogs or other policy-oriented briefings written by developmental and genetic experts can help practitioners increase their understanding of how a child’s inherited characteristics can influence the types of parenting and interparental relationship qualities that optimally influence development, which can then provide clues as to how intervention strategies should be modified as a function of a specific child’s family history.

Encourage, contribute to, and seek out engagement with biosocial experts to promote efforts to better integrate the disciplines. Finally, as noted above, the translational process between genetically-informed research and intervention development needs bi-lateral engagement from biosocial experts and clinicians. To the extent that practitioners can reach out to local and national experts in developmental genetics, stronger bridges may start to be built to

facilitate translation across disciplines. Clearly, significant efforts are needed from leaders in multiple disciplines in this regard, and encouragement of efforts and engagement in public forums are a first step toward a more synergistic integration of the disciplines.

In summary, the three recommendations provided here are aimed at helping practitioners draw more definitive conclusions about how specific parenting and interparental environments might be tailored as a function of a child's inherited propensities. Intervention strategies that work well for one child may not be helpful for a child with a different genetic background, or might be equally effective irrespective of genetic propensity. We do not propose dramatic shifts in thinking or radically new intervention methods; rather, this commentary is intended to highlight ways in which applying a genetically-informed intervention approach might help improve effect sizes in intervention studies, and help a greater number of children and families show improved outcomes.

Figure 1: A summary of traditional behavioral genetic research designs.
Note. IVF = in vitro fertilization; MZ = monozygotic; DZ = dizygotic; CoT = Children of Twins

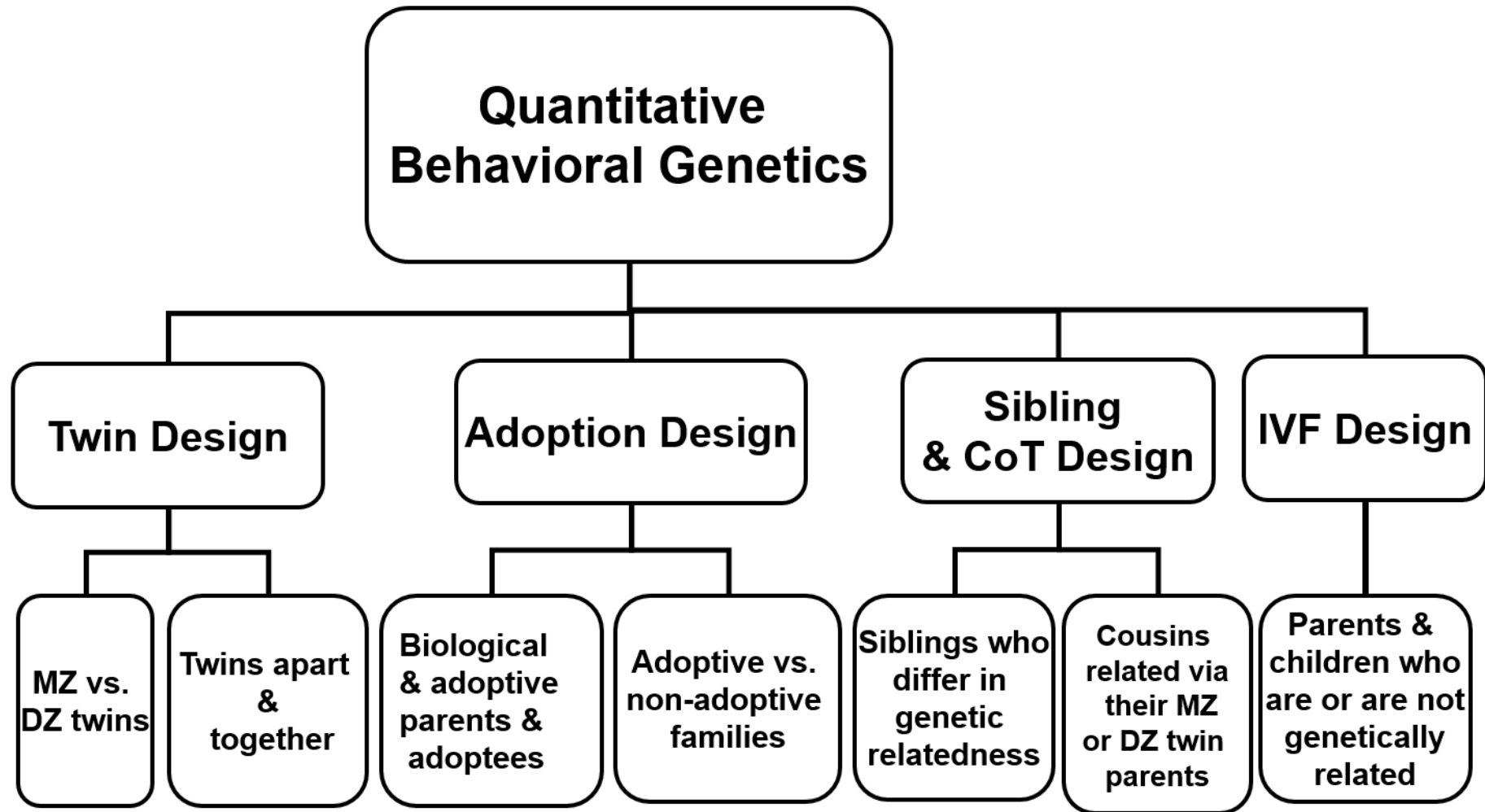


Table 1: Sampling of Quantitative Genetic Studies that have Examined the interparental Relationship, Parenting, and Child Behavior Problems.

Twin studies				
Authors (year)	Sample size	Constructs	Child age	Summary of findings
Bornovalova et al. (2013)	N = 1255	Parenting; interparental discord, parent ASB Outcome: child DBD (ADHD, ODD, CD)	Cross-sectional 11 years	Maladaptive parenting (parent report), interparental conflict, and divorce associated with child DBD. Associations remained after adjusting for coparent parenting and parental ASB. Mother's parenting had higher impact on child DBDs than father's parenting behaviors.
Neiderhiser et al. (2013)	NEAD N = 720	Interparental conflict, parent monitoring, sibling relationship, peer delinquency Outcome: drug use	Longitudinal 10–18 years, then 20–35 years	4 factors explain initiation of illegal drug use: 2 shaped by genetic influences, 2 shaped by environments shared by siblings. The 2 genetically shaped factors may have distinct mechanisms: (a) child-initiated coercive process in the family, (b) parent and peer processes shaped by child's disclosure. Environmentally influenced factors seemed affected by poor parental monitoring and effects of siblings on each other's deviancy.
Ulbricht et al. (2013)	NEAD N = 720 families	Interparental conflict, parent and child reports parenting Outcome: parenting	Cross-sectional (Wave1) 10–18 years	As interparental conflict declines, evocative child effects on parenting increase, while role of shared family experiences declines. Impact of interparental conflict on child-based genetic and child-specific nonshared environmental contributions to parenting differ for mothers and fathers.
Feinberg et al. (2005)	NEAD N = 720 families	Depression, ASB, interparental conflict, sibling negativity Outcome: child ASB	9–18 years	Results support theory that heightened levels of parental and sibling negativity and conflict are associated with siblings' similarity of ASB. However, Interparental conflict may lead to greater divergence of siblings' maladjustment.
Children of twin studies (CoT)				
Authors (year)	Sample size	Constructs	Child age	Summary of findings
Schermerhorn et al. (2011)	TOSS N = 867 twin pairs	Family conflict, interparental quality, agreement about parenting Outcome: offspring adjustment	Twins, 32–60 and spouses, 25–65 years. adolescent children, 11–22 years	Associations between exposure to family conflict and child adjustment were independent of genetic factors and other environmental factors. But when family conflict was assessed using only children's reports, results indicated that genetic factors also influenced these associations. Exposure to low interparental quality and agreement about parenting associated with children's internalizing and externalizing problems. Genetic factors also contributed to associations of interparental quality and agreement about parenting with offspring externalizing problems.
Adoption studies				
Authors (year)	Sample size	Constructs	Child age	Summary of findings
Fearon et al., (2015)	EGDS N = 561	Birth mother psychopathology, adoptive parent negativity, marital problems Outcome: parenting	Longitudinal 9 – 27 months	Genetic factors associated with birth mother externalizing psychopathology evoked negative reactions in adoptive mothers (evocative rGE), but only when the adoptive family environment was characterized by marital problems. Maternal negativity mediated the effects of genetic risk on child adjustment at 27 months.
Bornovalova et al. (2014)	N = 402 adoptive families, 204	Maternal and paternal parenting, ASB, interparental conflict, divorce	2 children between 11 and 21 years, no more than 5	Main effect of maternal and paternal parenting and interparental discord on child DBD (environmental effect). No direct environmental effect of maternal or paternal ASB, but maternal and paternal ASB had stronger associations with child DBD in

	biological families	Outcome: child DBD	years apart	biological families than in adoptive families (passive <i>rGE</i> .)
Hajal et al. (2015)	EGDS <i>N</i> = 503	Birth and adoptive parent temperament, interparental relationship Outcome: interparental relationship & parenting	Cross-sectional (3–6 months Birth parent) (9 months adoptive parent)	Adoptive fathers' harsh parenting inversely related to birth mother positive temperament (indicating evocative <i>rGE</i>) and to interparental relationship quality. Adoptive parents' negative temperamental characteristics related to hostile parenting for both fathers and mothers.
Rhoades et al. (2012)	EGDS <i>N</i> = 361	Interparental hostility, hostile parenting Outcome: sleep problems	Longitudinal 9 months–4.5 years	Mothers' interparental hostility at 9 months associated with child sleep problems at 4.5 years. Fathers' interparental hostility at 9 months evidenced indirect effect on child sleep problems at 4.5 years via fathers' hostile parenting at 27 months.
Stover et al. (2012)	EGDS <i>N</i> = 308	Interparental conflict, hostile parenting Outcome: child externalizing problems	Longitudinal 3–27 months	Hostile interparental relationship associated with hostile parenting in fathers and mothers, which was associated with aggressive behavior in toddlers. Subjective financial strain uniquely associated with interparental hostility and child aggression. Antisocial personality traits related to a more hostile interparental relationship and to hostile parenting.
Rhoades et al. (2011)	EGDS <i>N</i> = 361	Interparental hostility, harsh parenting, parental depressive symptoms Outcome: child anger	Longitudinal 9–18 months	Indirect effect from interparental hostility to toddler anger/frustration via parental harsh discipline, moderated by birth mother anger/frustration.
Leve et al. (2001)	<i>N</i> = 99	Temperament, interparental happiness Outcome: pleasure in parenting	5 months	Mothers and fathers who rated adoptive child as showing more distress to limitations reported less pleasure in routine parenting activities; this effect mediated by interparental happiness for fathers. Mothers reported less pleasure in parenting, with infants perceived to be more temperamentally fearful.
IVF studies				
Authors (year)	Sample size	Constructs	Child age	Summary of findings
Harold et al. (2013)	C-IVF <i>N</i> = 694 EGDS <i>N</i> = 218	Interparental conflict and hostile parenting, Outcome: Child externalizing problems (CBCL/SDQ)	Cross-sectional C-IVF = 5–8 years EGDS = 6 years	Indirect associations from interparental conflict to child externalizing problems through mother-to-child and father-to-child hostility for genetically related and unrelated groups. Associations between interparental conflict and parent-to-child hostility across genetically related and genetically unrelated parent–child groupings were significantly stronger for fathers compared to mothers.
Harold et al. (2012)	C-IVF <i>N</i> = 664	Interparental conflict, parent ASB, parent anxiety, hostile parenting Outcome: child ASB	Cross-sectional 4–10 years	Genetically related mothers: interparental conflict and maternal ASB indirectly influenced child ASB through mother-to-child hostility. Genetically unrelated mothers: effects only for maternal ASB on child ASB through mother-to-child hostility. Both genetically related and genetically unrelated fathers and children: interparental conflict and paternal ASB influenced child ASB through father-to-child hostility. Effects of parental anxiety symptoms on child ASB only for genetically related mothers and children.

Note. Measures/constructs: DBD: disruptive behavior disorder; ADHD: attention deficit hyperactivity disorder; ODD: oppositional defiant disorder; CD: conduct disorder; ASB: antisocial behavior; CBCL: Child Behavior Checklist; SDQ: Strengths & Difficulties Questionnaire;
Studies: NEAD: Nonshared Environment in Adolescent Development; TOSS Twin and Offspring Study in Sweden; EGDS: Early Growth & Development Study; C-IVF: Cardiff IVF study.

References

- Bakermans-Kranenburg, M. J., & Van IJzendoorn, M. H. (2015). The hidden efficacy of interventions: Gene× environment experiments from a differential susceptibility perspective. *Annual Review of Psychology*, *66*, 381–409.
- Bell, R. Q., & Chapman, M. (1986). Child effects in studies using experimental or brief longitudinal approaches to socialization. *Developmental Psychology*, *22*(5), 595–603.
- Bor, W., Dean, A. J., Najman, J., & Hayatbakhsh, R. (2014). Are child and adolescent mental health problems increasing in the 21st century? A systematic review. *Australian and New Zealand Journal of Psychiatry*, *48*, 606–616. doi: 10.1177/0004867414533834
- Bornovalova, M. A., Blazei, R., Malone, S. H., McGue, M., & Iacono, W. G. (2013). Disentangling the relative contribution of parental antisociality and family discord to child disruptive disorders. *Personality Disorders: Theory, Research, and Treatment*, *4*, 239–242. doi: 10.1037/a0028607
- Bornovalova, M. A., Cummings, J. R., Hunt, E., Blazei, R., Malone, S., & Iacono, W. G. (2014). Understanding the relative contributions of direct environmental effects and passive genotype-environment correlations in the association between familial risk factors and child disruptive behavior disorders. *Psychological Medicine*, *44*, 831–844.
- Collins, F. S., & Varmus, H. (2015). A new initiative on precision medicine. *New England Journal of Medicine*, *372*(9), 793–795. doi: 10.1056/NEJMp1500523
- Cookston, J. T., Braver, S. L., Griffin, W. A., De, L., Stephanie, R., & Miles, J. C. (2007). Effects of the Dads for Life intervention on interparental conflict and coparenting in the two years after divorce. *Family Process*, *46*(1), 123–137.
- D’Onofrio, B. M., Lahey, B. B., Turkheimer, E., & Lichtenstein, P. (2013). Critical need for family-based, quasi-experimental research in integrating genetic and social science research. *American Journal of Public Health*, *103*, S46–S55.
- D’Onofrio, B. M., Turkheimer, E., Emery, R. E., Maes, H. H., Silberg, J., & Eaves, L. J. (2007). A children of twins study of parental divorce and offspring psychopathology. *Journal of Child Psychology and Psychiatry*, *48*, 667–675.
- Dudbridge, F. (2013). Power and predictive accuracy of polygenic risk scores. *PLoS Genetics*, *9*, e1003348.
- Elam, K. K., Harold, G. T., Neiderhiser, J. M., Reiss, D., Shaw, D. S., Natsuaki, M. N., . . . Leve, Leslie D. (2014). Adoptive parent hostility and children’s peer behavior problems: Examining the role of genetically informed child attributes on adoptive parent behavior. *Developmental Psychology*, *50*(5), 1543–1552.
- Engelhardt, L. E., Briley, D. A., Mann, F. D., Harden, K. P., Tucket-Drob, E. M. (2015). Genes unite executive functions in children. *Psychological Science*, *26*, 1151–1163.
- Erel, O., & Burman, B. (1995). Interrelatedness of marital relations and parent–child relations: A meta-analytic review. *Psychological Bulletin*, *118*, 108–132.
- Fearon, P. R. M., Reiss, D., Leve, L., Shaw, D. S., Scaramella, L. V., Ganiban, J. M., Neiderhiser, J. M. (2015). Child-evoked maternal negativity from 9 to 27 months: Evidence of gene-environment correlation and its moderation by marital distress. *Development and Psychopathology*, *27*, 1251–1265.
- Feinberg, M. E., Reiss, D., Neiderhiser, J. M., & Hetherington, E. M. (2005). Differential association of family subsystem negativity on siblings’ maladjustment: Using behavior genetic methods to test process theory. *Journal of Family Psychology*, *19*, 601–610. doi: 10.1037/0893-3200.19.4.601
- Freedman, M. L., Reich, D., Penney, K. L., McDonald, G. J., Mignault, A. A., Patterson, N., . . . & Pato, M. T. (2004). Assessing the impact of population stratification on genetic association studies. *Nature Genetics*, *36*(4), 388–393. doi: 10.1038/ng1333
- Ge, X., Conger, R. D., Cadoret, R. J., Neiderhiser, J. M., Yates, W., Troughton, E., &

- Stewart, M. A. (1996). The developmental interface between nature and nurture: A mutual influence model of child antisocial behavior and parent behaviors. *Developmental Psychology, 32*, 574–589. doi: 10.1037/0012-1649.32.4.574
- Gottfredson, D. C., Cook, T. D., Gardner, F. E., Gorman-Smith, D., Howe, G. W., Sandler, I. N., & Zafft, K. M. (2015). Standards of evidence for efficacy, effectiveness, and scale-up research in prevention science: Next generation. *Prevention Science, 16*(7), 893–926. doi: 10.1007/s11121-015-0555-x.
- Grych, J. H., & Fincham, F. D. (1990). Marital conflict and children's adjustment: A cognitive-contextual framework. *Psychological Bulletin, 108*, 267–290.
- Hajal, N., Neiderhiser, J., Moore, G., Leve, L., Shaw, D., Harold, G.,... & Reiss, D. (2015). Angry responses to infant challenges: Parent, marital, and child genetic factors associated with harsh parenting. *Child Development, 86*, 80–93.
- Harold, G. T., & Conger, R. D. (1997). Marital conflict and adolescent distress: The role of adolescent awareness. *Child Development, 68*, 333–350.
- Harold, G. T., Elam, K. K., Lewis, G., Rice, F., & Thapar, A. (2012). Interparental conflict, parent psychopathology, hostile parenting, and child antisocial behavior: Examining the role of maternal versus paternal influences using a novel genetically sensitive research design. *Development and Psychopathology, 24*, 1283–1295.
- Harold, G. T., Leve, L. D., Elam, K. K., Thapar, A., Neiderhiser, J. M., Natsuaki, M. N., . . . Reiss, D. (2013). The nature of nurture: Disentangling passive genotype–environment correlation from family relationship influences on children's externalizing problems. *Journal of Family Psychology, 27*(1), 12–21. doi: 10.1037/a0031190
- Hyde, L., Waller, R., Trentacosta, C., Shaw, D., Neiderhiser, J., Ganiban, J., Reiss, D., & Leve, L. D. (2016). Heritable and non-heritable pathways to early callous unemotional behaviors. *American Journal of Psychiatry*. Epub ahead of print.
- Jaffee, S. R., & Price, T. S. (2007). Gene–environment correlations: A review of the evidence and implications for prevention of mental illness. *Molecular Psychiatry, 12*, 432–442.
- Lansford, J. E., Deater-Deckard, K., Dodge, K. A., Bates, J. E., & Pettit, G. S. (2004). Ethnic differences in the link between physical discipline and later adolescent externalizing behaviors. *Journal of Child Psychology and Psychiatry, 45*(4), 801–812.
- Leve, L. D., Harold, G. T., Ge, X., Neiderhiser, J. M., & Patterson, G. (2010). Refining intervention targets in family-based research: Lessons from quantitative behavioral genetics. *Perspectives on Psychological Science, 5*, 516–526.
- Leve, L. D., Harold, G. T., Ge, X., Neiderhiser, J. M., Shaw, D., Scaramella, L. V., & Reiss, D. (2009). Structured parenting of toddlers at high versus low genetic risk: Two pathways to child problems. *Journal of the American Academy of Child and Adolescent Psychiatry, 48*, 1102–1109. doi: 10.1097/CHI.0b013e3181b8bfc0
- Leve, L. D., Scaramella, L. V., & Fagot, B. I. (2001). Infant temperament, pleasure in parenting, and marital happiness in adoptive families. *Infant Mental Health, 22*(5), 545–558. doi: 10.1002/imhj.1017
- Luthar, S. S., & Brown, P. J. (2007). Maximizing resilience through diverse levels of inquiry: Prevailing paradigms, possibilities, and priorities for the future. *Development and Psychopathology, 19*, 931–955. doi: 10.1017/S0954579407000454
- Neiderhiser, J. M., Marceau, K., & Reiss, D. (2013). Four factors for the initiation of substance use by young adulthood: A 10-year follow-up twin and sibling study of marital conflict, monitoring, siblings, and peers. *Development and Psychopathology, 25*, 133–149. doi: 10.1017/S0954579412000958
- Rhoades, K. A. (2008). Children's responses to interparental conflict: A meta-analysis of their associations with child adjustment. *Child Development, 79*, 1942–1956.
- Rhoades, K. A., Leve, L. D., Harold, G. T., Mannering, A. M., Neiderhiser, J. M., Shaw, D.

- S., . . . Reiss, D. (2012). Marital hostility and child sleep problems: Direct and indirect associations via hostile parenting. *Journal of Family Psychology, 26*, 488–498.
- Rhoades, K. A., Leve, L. D., Harold, G. T., Neiderhiser, J. M., Shaw, D. S., & Reiss, D. (2011). Longitudinal pathways from marital hostility to child anger during toddlerhood: Genetic susceptibility and indirect effects via harsh parenting. *Journal of Family Psychology, 25*, 282–291. doi: 10.1037/a0022886
- Rice, F., Harold, G. T., Shelton, K. H., & Thapar, A. (2006). Family conflict interacts with genetic liability in predicting childhood and adolescent depression. *American Journal of Psychiatry, 163*, 841–848. doi: 10.1097/01.chi.0000219834.08602.44
- Rutter, M. (2006). *Genes and behavior: Nature–nurture interplay explained*. Malden, MA: Blackwell.
- Schermerhorn, A. C., D’Onofrio, B. M., Sluske, W. S., Emery, R. E., Turkheimer, E., Harden, K. P., . . . Martin, N. G. (2012). Offspring ADHD as a risk factor for parental marital problems: Controls for genetic and environmental confounds. *Twin Research and Human Genetics, 15*, 700–713. doi: 10.1017/thg.2012.55
- Schermerhorn, A. C., D’Onofrio, B. M., Turkheimer, E., Ganiban, J. M., Spotts, E. L., Lichtenstein, P., Reiss, D., & Neiderhiser, J. M. (2011). A Genetically Informed Study of Associations between Family Functioning and Child Psychosocial Adjustment. *Developmental Psychology, 47*(3), 707 - 725. doi: 10.1037/a0021362
- Schulz, M. S., Cowan, C. P., & Cowan, P. A. (2006). Promoting healthy beginnings: A randomized controlled trial of a preventive intervention to preserve marital quality during the transition to parenthood. *Journal of Consulting and Clinical Psychology, 74*, 20–31. doi: 10.1037/0022-006X.74.1.20
- Stover, C. S., Connell, C. M., Leve, L. D., Neiderhiser, J. M., Shaw, D. S., Scaramella, L. V., . . . Reiss, D. (2012). Fathering and mothering in the family system: Linking marital hostility and aggression in adopted toddlers. *Journal of Child Psychology and Psychiatry, 53*, 401–409. doi: 10.1111/j.1469-7610.2011.02510.x
- Tang, Y., Yang, L., Leve, L. D., Harold, G. T. (2012). Improving Executive Function and Its Neurobiological Mechanisms Through a Mindfulness-Based Intervention: Advances Within the Field of Developmental Neuroscience. *Child Development Perspectives, 6*(4), 361-366. doi: 10.1111/j.1750-8606.2012.00250.x
- Thapar, A., & Harold, G. (2014). Editorial Perspective: Why is there such a mismatch between traditional heritability estimates and molecular genetic findings for behavioural traits? *Journal of Child Psychology and Psychiatry, 55*, 1088-1091.
- Tully, L. A., & Hunt, C. (2015). Brief parenting interventions for children at risk of externalizing behavior problems: A systematic review. *Journal of Child and Family Studies, 24*, 1–15. doi: 10.1007/s10826-015-0284-6
- Ulbricht, J. A., Ganiban, J. M., Button, T. M. M., Feinberg, M., Reiss, D., & Neiderhiser, J. M. (2013). Marital adjustment as a moderator for genetic and environmental influences on parenting. *Journal of Family Psychology, 27*, 42–52.
- Weaver, I. C., Cervoni, N., Champagne, F. A., D’Alessio, A. C., Sharma, S., Seckl, J. R., . . . & Meaney, M. J. (2004). Epigenetic programming by maternal behavior. *Nature Neuroscience, 7*(8), 847-854. doi: 10.1038/nn1276
- Yap, M. B. H., & Jorm, A. F. (2015). Parental factors associated with childhood anxiety, depression, and internalizing problems: A systematic review and meta-analysis. *Journal of Affective Disorders, 175*, 424-440.