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Utilising Genetically-Informed Research Designs to Better Understand Family Processes and Child Development: Implications for Adoption and Foster-Care Focused Interventions

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Abstract

Understanding the interplay between genetic factors and family environmental processes (e.g., inter-parental relationship quality, positive versus negative parenting practices) and children's mental health (e.g., anxiety, depression, conduct problems, ADHD) in the contexts of adoption and foster-care research and practice is critical for effective prevention and intervention programme development. Whilst evidence highlights the importance of family environmental processes for the mental health and well-being of children in adoption and foster care, there is relatively limited evidence of effective interventions specifically for these families. Additionally, family-based interventions not specific to the context of adoption and foster-care typically show small to medium effects, and even where interventions are efficacious, not all children benefit. One explanation for why interventions may not work well for some is that responses to intervention may be influenced by an individual's genetic make-up. This paper summarises how genetically-informed research designs can help disentangle genetic from environmental processes underlying psychopathology outcomes for children, and how this evidence can provide improved insights into the development of more effective preventative intervention targets for adoption and foster-care families. We discuss current difficulties in translating behavioural genetics research to prevention science, and provide recommendations to bridge the gap between behavioural genetics research and prevention science, with lessons for adoption and foster-care research and practice.

Key words: quantitative genetics, genetically-informed research designs, family, child, mental health, intervention, adoption, foster-care, prevention science

Introduction

Children and young people in adoption and foster care constitute a group who are at elevated risk of developing multiple poor outcomes, including internalising (e.g., depression, anxiety) and externalising (e.g., conduct problems, aggression) problems, substance misuse, cognitive impairments (e.g., poor language development), negative peer relationships, and reduced academic attainment (Fisher, 2015). Understanding the processes that impact poor child outcomes is crucial for developing and providing efficacious intervention and prevention services aimed at improving outcomes for children and young people. Evidence highlights the relevance of positive rearing environments (e.g., positive inter-parental and parent-child relationships) for the well-being of children in adoption and foster care (Harold et al., 2017; Hyde et al., 2016). However, fundamental questions remain as to the efficacy of ‘environmental’ interventions (i.e., those that target family relationship processes, such as parenting practices) aimed at children in the contexts of adoption and foster care. In particular, the relative role of genetic factors passed on from birth parents to children, and how these biologically sourced factors influence (and are influenced by) the rearing environments experienced by adopted children and children in foster care remain poorly understood by academics, practitioners, policy makers, and parents/carers working to improve outcomes for children and families. This paper aims to clarify evidence relating to the interplay between genetic and environmental (adoptive parent/carer caregiving) factors and psychopathology outcomes for children, presented with a specific UK practice and policy focus.

Adoption and Fostering: The Current UK context

The UK has recently experienced two major challenges with regards to looked after children, with substantive implications for children in a foster-care and adoption context: (1) the increase in the number of children placed in care, and (2) the breakdown of adoption and

foster care placements, meaning more children are placed in long-term care. Recent legislative recommendations stating that adoption orders should only be placed against the wishes of the birth parent as a last resort (2013: <https://www.supremecourt.uk/cases/docs/uksc-2013-0022-judgment.pdf>), have been linked to a reduction in the number of children placed for adoption through the social care system in the UK (Simmonds, 2016). This has resulted in an increase in the number of children remaining in care relative to children being placed for adoption; in 2016, there were 70,440 looked after children in England alone, rising 13% from 2012, with 51,850 of these children in foster care (DfE 2016: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/556331/SFR41_2016_Text.pdf). Conversely, only 2,490 (4%) looked after children were placed for adoption in 2016, falling 18% from 2015-2016 (DfE, 2016), demonstrating the decrease in adoption placements as a result of the change in legal ruling. In addition, it is estimated that approximately 4% of children adopted in the UK are returned to care after an Adoption Order is granted (Triseliotis, 2002). However, estimates range from 10% to 50% when additional factors (including age of the child at placement, specific learning or developmental difficulties, specific challenging behaviours) are considered (see also Selwyn et al., 2013; Selwyn, Wijedasa & Meakings, 2014). Furthermore, it is estimated that only 68% of looked after children remained in the same placement for one year, whilst 32% of children had two or more placements (e.g. moving between foster placements) within one year (DfE, 2016), demonstrating instability of placements for children in care. Thus, more children are remaining in care, highlighting the need for support for these vulnerable children.

Whilst the number of adoption orders is decreasing (UK focus), it is important to have effective interventions for families in the context of adoption and foster care to reduce placement breakdown (thus preventing the number of children in care further increasing), and

to improve outcomes for children. However, there is relatively limited evidence of effective interventions specifically for adoptive families or foster-care families, specifically with a UK focus. It is therefore necessary to develop more robust evidence-led interventions (or to modify and apply existing interventions) specifically targeting adoptive and foster-care families, with the goal of reducing placement breakdown and improving child outcomes. Broadly speaking, we know that family-based interventions (not specific to looked after children) can reduce rates of child psychopathology (Tolan & Dodge, 2005; Weisz et al., 2005; Chamberlain et al., 2008; Leve et al., 2012). Such interventions have primarily focused on the parent-child relationship, with an emphasis on promoting positive parenting practices as a key family process mechanism leading to improvements in child outcomes (e.g., Conduct Problems Prevention Research Group, 2002; Eddy & Chamberlain, 2000; Martinez & Forgatch, 2001; Webster-Stratton & Herman, 2008). However, these parent and family-based interventions typically show small to medium effects in terms of improving parenting and/or child outcomes. Further, not all children benefit or show sustained effects (i.e. not all children demonstrate long-term improved outcomes as a result of intervention). One explanation for why interventions may not work for some children is that underlying genetic predispositions may affect children's responses to the environment (e.g., genetic predispositions leading to children responding more negatively to a certain parenting behaviour), and therefore influence their responses to interventions targeting these environments (e.g., responding negatively to interventions that target this parenting behaviour; Reiss & Leve, 2007; Reiss, Neiderhiser, Hetherington, & Plomin, 2000; Van Ijzendoorn & Bakermans-Kranenburg, 2015). Quantitative behavioural genetics research can be used to disentangle genetic and environmental (e.g., parenting) influences on child outcomes, and to examine how genetic predispositions and the rearing environment can interact to influence child outcomes. Therefore, findings from such research designs can be informative for intervention and

prevention strategies (i.e., by highlighting aspects of the rearing environment that are important intervention targets, and when interventions may or may not be appropriate), and thus help improve the efficacy of interventions for at-risk children and families.

This paper will outline how genetically-informed research designs can improve understanding of the interplay between genetic and environmental processes that impact child and adolescent psychopathology (e.g., depression, anxiety, aggression, conduct problems, ADHD), and in turn, how this evidence can provide improved insights into the development of effective preventative intervention targets, with a specific focus on adoption and foster-care families. We discuss current difficulties in translating behavioural genetics research to prevention efforts, and provide recommendations to bridge the gap between traditional behavioural genetics research and adoption and foster care focused prevention and intervention research and practice.

Understanding the interplay between genetic factors, family environmental processes and child psychopathology

Family environmental processes, such as the quality of the inter-parental relationship or the consistency of positive versus negative parent-child interaction quality, are recognised as significant influences on children's emotional and behavioural development (Harold et al., 2017). However, despite advances in understanding the interplay between family level processes (e.g., parenting) and child mental health (e.g., conduct problems), one of the limitations of past research is that the vast majority of research has predominantly relied on studies involving biologically related parents/carers and children; therefore it is not possible to unambiguously separate environmental (e.g., parenting) from shared genetic effects (i.e., genes passed on from genetically related/birth parents to their children/offspring). Although molecular genetics research has provided evidence linking specific genetic processes to child psychopathology (see Thapar & Harold, 2015), research suggests that genetic factors are

unlikely to fully explain variation in child developmental outcomes, rather such variation is more likely explained as a result of specific interplay between genetic factors and family environmental experiences (Henry, Boivin, & Tarabulsky, 2015; Caspi et al., 2003; Kim-Cohen et al., 2006). It is therefore important to use genetically informed research designs that provide the opportunity to examine associations between family-level processes (e.g., the interparental relationship, parenting) and child outcomes (e.g., depression, conduct problems) with a focus on gene-environment interplay (i.e., relative genetic and environmental contributions and their interaction in explaining child outcomes). Further, without the careful implementation of genetically informed research designs, it is impossible to contend with a fundamental challenge to interpreting any association between an index of rearing environmental experience (e.g. negative parenting practices) and child psychopathology (e.g. conduct disorder) in that associations derived from biologically related parents and children may be confounded by common genes passed on from parents to children that influence both the rearing environmental factor and the outcomes observed in children (see Harold & Sellers, 2018).

There are three primary ways in which genetic factors passed on from biologically related parents to children/offspring can influence associations between parental behaviour and child outcomes (examples of which are presented in Table 1). First, in standard research designs (i.e., where parents and children are genetically related), the examination of associations between postnatal environmental factors (e.g., parenting practices) and child outcomes (e.g., conduct problems) may be confounded by shared genes passed on from birth parents to their children, affecting the strength of associations between parenting behaviours and child behaviours (referred to as *passive gene-environment correlation*, or *rGE*; Jaffee & Price, 2007). An adoption-at-birth design (see below), allows the examination of associations between parenting behaviours and child behaviours where the confound of passive *rGE* is

removed (when children are placed with a non-relative adoptive family). Second, it is recognized that parenting responses to a child may be a response to genetically influenced attributes in the child (i.e., child-on-parent effects, known as *evocative gene–environment correlation*, or *rGE*; Ge et al., 1996). The adoption design (see below) provides unique insight into genetic versus environmental contributions to child psychopathology, as it allows the effects of genetically influenced attributes in the child (measured directly or through birth parent information) to be assessed relative to genetically unrelated caregiver (adoptive parent) responses to child behaviour (Ge et al., 1996). Research examining evocative *rGE* therefore allows examination of child effects on parenting, and the influence of child evoked parenting on subsequent child developmental outcomes (see Harold et al., 2013). Third, gene-environment interaction (GxE) refers to the interaction between genes and the environment in influencing child outcomes; specifically, how environmental influences (e.g., parenting) may moderate (change the direction or magnitude of) genetic effects on child outcomes and vice-versa (i.e., a child’s genes may moderate the effect of the rearing environment on child outcomes; Reiss et al., 2013; Leve et al., 2017). There are two forms of gene-environment interactions that are important for intervention and prevention science. The first is the ‘diathesis-stress’ model of GxE, where psychopathology results from inherited risk (diathesis) that occurs under particular environmental risks (stressors). Examples of ‘diathesis-stress’ GxE is evident from twin studies (e.g. Kendler et al., 1995) and adoption studies (e.g., Cadoret et al., 1995; Leve et al; 2010). The second form of GxE that has been more recently specified is ‘differential susceptibility’, whereby an individual is differentially sensitive/susceptible to high levels of both positive and negative rearing environments: inherited risks increase susceptibility to the environment, resulting in more positive developmental outcomes in more positive environments (e.g., warm, nurturing parenting), and more negative developmental outcomes from more negative environments (e.g., poor

parent monitoring; Brody et al., 2013; Dick et al., 2011). Studies examining GxE therefore illustrate how specific environments may have positive or negative effects for some individuals depending on their genetic susceptibility (see Leve et al., 2013). This provides evidence for targeted interventions that are informed by biological risk, and demonstrates that environments such as parenting (i.e., intervention target) can interact with heritable traits to improve child outcomes. Indeed, based on a meta-analysis of 22 randomised controlled trials, Van Ijzendoorn and Bakermans-Kranenburg (2015) reported that the combined effect sizes for interventions targeted at those at genetic risk were significant and large (i.e., effect size $r = .33$), whereas those who were not at genetic risk did not show significant improvements after interventions (i.e., effect size $r = .06$). This supports the hypothesis of differential susceptibility and suggests that even in the absence of overall efficacy, interventions may have a large impact on a subgroup of genetically susceptible individuals (Van Ijzendoorn & Bakermans-Kranenburg, 2015).

Understanding gene-environment interplay (GxE, passive and evocative rGE) therefore has important implications for the development of interventions and the evaluation of their efficacy, highlighting where parents' responses to child behaviour may be altered through intervention, and how targeting specific rearing environments (e.g., parenting behaviours) may or may not improve child outcomes depending on the child's genetic make-up. It is also necessary to employ research designs that can identify environmental risks that are independent of common genetic influences if we are to better understand what malleable environmental factors may be targeted to reduce poor outcomes for children (see Harold, Leve, & Sellers, 2017). Understanding relative genetic and environmental contributions to child outcomes is of particular relevance for the development of efficacious interventions specific to families in which parents and children are genetically unrelated (i.e., specific to an adoption and foster-care context). For example, understanding how the rearing environment

can impact child outcomes among genetically unrelated parents and children can translate to a potential intervention target for genetically unrelated parents and children in an adoption and foster care context. Whilst relatively limited interventions specifically target adoptive and foster families, we provide examples of the evaluation of two interventions specific to adoption and foster care later in this paper, the findings of which demonstrate that adapting the rearing environment can improve outcomes for children among these genetically unrelated parent/carer – child groupings.

Quantitative behavioural genetics research designs: A practice focused primer

Quantitative behavioural genetic research designs identify genetic and environmental contributions to behaviour by examining the variation in genetic relatedness between family members (see Figure 1). The most commonly used design is the twin study which examines similarities between monozygotic (MZ) twins who share 100% of their genes, with dizygotic twins (DZ) who share, on average, 50% of their genes. Greater similarity between MZ compared to DZ twins indicates genetic influences. Where MZ and DZ twin pairs share a trait to an equal extent within the twin pair, this is indicative of environmental factors (Thapar, Harold, Rice, Langley, O'Donovan, 2006).

The extended family design examines associations between siblings who differ in their genetic relatedness (D'Onofrio, Lahey, Turkheimer, & Lichtenstein, 2013): full siblings (sharing, on average, 50% of their genes), half siblings (sharing, on average, 25% of their genes) and step siblings (sharing no genes). If associations for a particular trait are stronger between full sibling pairs than half or step sibling pairs, this would be indicative of genetic influence. Conversely, where associations are similar between the different sibling pair types, this would suggest environmental factors as influences on children's outcomes.

The Children of Twins (CoT) design is an extension of the 'extended family' design and takes advantage of the fact that children of MZ twins are equally genetically related to

their parents as they are to the twin's sibling (i.e., their uncle/aunt), but they do not typically share an environment with the parent's twin sibling (D'Onofrio et al., 2007). In MZ twin families, if the correlation between parent-child is greater than the MZ uncle/aunt-child correlation (avuncular correlation), this is indicative of environmental influences. If the parent-child correlation is similar to the MZ uncle/aunt-child (avuncular) correlation, this suggests genetic influences. The comparison between avuncular correlations (uncle/aunt-child) between MZ and DZ families provides insights into the nature of familial effects: if MZ avuncular correlations are larger than DZ avuncular correlations, then genetic factors are implied.

Studies of siblings reared apart can also examine the relative roles of genes and the environment for child development (Rutter et al., 2001; Bouchard et al., 1990; Pederson et al., 1991; Leve et al., 2017; Mednick et al., 1984). Siblings reared apart do not share a rearing environment, but as part of the study design, genetic similarities are controlled for, therefore any differences between siblings are ascribed to (different) rearing environments. Studies of siblings reared apart can include MZ twins who are reared apart: as MZ twins share 100% of their genes, any differences between siblings are ascribed to differences in rearing environment. Studies of siblings reared apart can also compare adopted children (who are reared by biologically unrelated parents) with their biological siblings who remain with their birth parent(s) (e.g., Sorensen et al., 1989; Kendler et al., 2016). This method provides insights into how different environmental influences can affect child outcomes where children share genes, and can be used to infer what the outcomes for children may have been had they not been adopted (Harold et al., 2017).

The adoption design can also be used to examine environmental influences on children. Adopted children who are placed in non-relative placements are genetically unrelated to their rearing parents (removing the confound of passive r_{GE}), therefore

associations between adoptive parents and the adopted child are attributed to environmental processes (e.g., Leve et al., 2013; Rhea et al., 2013). A full adoption design also includes birth parents, providing the opportunity to examine genetic influences: where children are adopted at birth, associations between birth parents and adopted children can only be attributed to genetic factors, (and specific to the birth mother: intrauterine influences). In addition, where a full adoption design is longitudinal, evocative effects (i.e., genetically influenced attributes in the child that ‘evoke’ specific rearing environment responses; evocative *rGE*, Ge et al., 1996) can also be examined. Therefore, in addition to allowing the examination of rearing environmental influences on child development, the full adoption design also provides insight into how child behaviour (which is in part attributable to genetic influences) can influence/evoke specific parenting behaviours in genetically unrelated (adoptive) parents.

Artificial Reproductive Technologies (ART) provide the opportunity to examine associations between parents and children who are genetically related or genetically unrelated to either or both of their rearing parents (‘adoption at conception’; Harold et al., 2012). Through in-vitro fertilization (IVF), children can be genetically related to: both rearing parents (homologous IVF); the rearing mother but not father (sperm donation); the rearing father but not mother (egg donation); neither parent (embryo donation). In an additional group (gestational surrogacy) children are genetically related to both parents, but the prenatal environment is provided by a surrogate, thus allowing the examination of prenatal influences separate from genetic influences. Associations between genetically related parent-child dyads but not between genetically unrelated parent-child dyads indicate genetic influences. Associations between genetically unrelated parent-child dyads indicate environmental influences (see Harold et al., 2014; Thapar et al., 2009).

Unlike the above study designs, which examine associations between parents/carers and children who differ in their degree of genetic relatedness, molecular genetic studies focus on specific measured genes assayed from DNA samples. Whilst there is increasing evidence of interactions between measured genetic factors and environmental exposures (GxE) for child outcomes (Belsky, Palm-Suppli, Israel, 2014; Caspi & Rutter, 2005), more research is required to better understand how specific genetic susceptibilities work with specific environmental exposures (Thapar & Harold, 2014). In addition, molecular genetic studies typically require very large sample sizes (to provide adequate statistical power), which may limit the ability to acquire environmental process information (psychometrically robust measures of the environment) that would allow effective examination of gene-environment interplay (Leve, Harold, Sellers, 2016). Furthermore, effect sizes in molecular genetic studies tend to be quite small (Thapar & Harold, 2014). Therefore, we focus primarily on the importance of quantitative behavioural genetic research for prevention science in this article.

Converting findings from quantitative behaviour genetics research to front-line practice: An update on the evidence

As summarised, it is well-established that both genetic and environmental factors contribute to child development. Adoption and twin studies have demonstrated genetic influences on multiple outcomes, including cognitive ability, language development, depression, anxiety, ADHD, school achievement and other outcomes (Leve et al., 2013; Haworth et al., 2010; Thapar et al., 2006). There is also evidence of genetic factors contributing to long-term outcomes including the intergenerational transmission of poor mental health outcomes: some twin and adoption studies provide evidence of strong genetic influences on antisocial behaviours (Bornovalova et al., 2014; Arseneault et al., 2003), with a recent sibling study suggesting that intergenerational transmission of anxiety may be accounted for by genetic confounding (Bekkhuis et al., 2017). However, environmental

influences are also recognised as important for child development, with meta-analyses of twin and adoption studies finding evidence of both genetic and environmental contributions to child psychopathology, including depression, anxiety, conduct disorder and broader internalizing and externalizing symptoms (Burt, 2009). A recent study of siblings reared apart provides evidence of environmental influences of risk for child substance abuse, with children living with their biological parents being at increased risk compared to their adopted siblings (Kendler et al., 2016). Children of twins (CoT) studies examining intergenerational transmission find that the transmission of anxiety and depression is primarily attributed to environmental influences (Eley et al., 2015; Natsuaki et al., 2014; Silberg et al., 2010). However, findings are complex with evidence highlighting that associations may differ depending on outcomes: associations between parental depression and child depression are accounted for by environmental factors, whereas associations between parental depression and child conduct problems are accounted for by both genetic and environmental factors (Silberg et al., 2010; Singh et al., 2011). Building on this evidence, a fundamental problem for intervention programme development using traditional and some quantitative behavioural genetic research designs (e.g., twin designs) is the inability to unambiguously disentangle genetic influences underlying the associations between environmental processes and child outcomes (passive and evocative *rGE*, implications for testing *GxE*).

Removing the confound of passive rGE: Some quantitative genetic research designs are able to directly address the confound of passive *rGE* by employing samples of parents and children who are not biologically related: adoption studies and studies of children conceived via IVF. Evidence from such study designs demonstrates the importance of a range of specific family processes as environmental factors that impact on child outcomes. Specifically, inter-parental conflict and poor parenting practices have been identified as important risks for child outcomes, with inter-parental conflict predicting child ADHD

symptoms (Harold et al., 2013a), child disruptive behaviours (Bornovalova et al., 2014), child sleep problems (Mannering et al., 2011), and adolescent delinquency (Burt et al., 2007) via disrupted parenting practices (see Harold et al., 2017). Evidence further highlights that the interplay between inter-parental conflict and poor parenting practices may extend beyond a traditional focus on the mother-child relationship, with very recent evidence highlighting the importance of both mother and father parenting practices in the context of interparental conflict and child outcomes (Rhoades et al., 2012; Stover et al., 2012; Harold et al., 2013b).

Examining the relevance of evocative rGE: As noted earlier, evocative *rGE* examines how genetically influenced child characteristics may evoke specific patterns of response, such as parental hostility (Ge et al., 1996). This is of interest to intervention research as particular environmental processes can be identified and supported to reduce the impact of child-driven effects (Luthar & Brown, 2007). A relatively small adoption sample provided the first example of evocative *rGE* in the field of developmental science (Ge et al., 1996), finding that birth mother psychopathology was associated with disrupted child behaviour, which in turn was associated with adoptive mother hostility. More recently, larger adoption studies have advanced understanding of evocative *rGE*, identifying genetically influenced child characteristics that evoke negative maternal and paternal parenting practices (Elam et al., 2014; Harold et al., 2013; Hajal et al., 2015; Fearon et al., 2015). Furthermore, adoption studies have also demonstrated how child evoked negative parenting behaviours can in turn increase children's negative behaviours (Elam et al., 2014; Harold et al., 2013), highlighting child evoked negative parenting as a mechanism for continuity (and increase) in negative child behaviours over time. Twin studies have also demonstrated evocative processes, evidencing the effect of children's genetically-influenced characteristics on parenting behaviour (Klahr & Burt, 2014), and negative family relationships (Feinberg et al., 2005; Neiderhiser et al., 2013; Reiss et al., 2000). These illustrative examples show how

quantitative behavioural genetics studies can be used to demonstrate child-on-parent effects, and how child evoked parenting can influence long-term child development. Furthermore, this research provides information for potential intervention pathways that would not be evident from studies that are not genetically-informed. Findings suggest that sensitively informing parents that children can inherit specific behaviours, and helping parents to become 'resilient' to potential child evoked effects may interrupt the processes through which heritable traits and harsh parenting responses may increase long-term child behaviour problems.

Exploring gene-environment (GxE) interaction: Evidence from quantitative behavioural genetics studies suggests that the impact of specific family processes (including inter-parental conflict; negative parenting/hostility; maltreatment) on child behaviour problems may differ as a function of children at high versus low genetic risk (e.g., Rhoades et al., 2011; Rice, Harold, Shelton, & Thapar, 2006; Schermerhorn et al., 2012; Jaffee et al., 2005; Cadoret et al., 1995; Rhoades et al., 2011). Rather than being vulnerable to specific risk environments, children may be differentially susceptible to certain types of family environments as a function of their own genetic makeup (Hyde et al., 2016; Leve et al., 2009). According to a recent study, positive parenting buffered the impact of genetic risk, reducing early callous-unemotional behaviours in children at high genetic risk (Hyde et al., 2016). Furthermore, a study using an adoption design (Leve et al., 2009) found that specific parenting strategies differentially impacted on child behaviour problems depending on child genetic risk: structured parenting (providing clear instructions and structure for child activities) decreased child behaviour problems in children at high genetic risk, but was associated with increased child behaviour problems where children were at low genetic risk. Conversely, positive reinforcement benefited children regardless of genetic risk. These results indicate that the interventions that promote structured parenting may only be beneficial for

children at high genetic risk but that alternative parenting techniques may be more beneficial for children at low genetic risk. Furthermore, evidence from quantitative behavioural genetics studies also suggests that specific family processes can also be differentially impacted by child genetic risk. In an adoption study, birth mother externalising problems (a marker of child genetic risk) predicted adoptive mother negativity but only in the context of adoptive parent inter-parental hostility (Fearon et al., 2015). This provides evidence of evocative *rGE* interacting with specific features of the rearing environment (inter-parental relationship hostility) and associated impacts on parenting.

Overall, genetically informed studies highlight the importance of the family environmental processes (e.g., inter-parental conflict, maternal and paternal parenting) for child outcomes whether parents are biologically related to their children or not (e.g., in the contexts of adoption and foster care). This underscores the importance of the rearing environment for intervention targets. Findings from gene-environment interaction focused research have important implications for the development of interventions (Collins & Varmus, 2015); findings suggest more precise targeting of interventions should be matched to a child's specific characteristics, thereby potentially promoting more positive child outcomes. Evidence of evocative gene-environment correlations are also informative for interventions: findings can inform areas where parents may be affected by genetically-influenced child behaviours (i.e., increasing awareness of child effects on parenting); targeting such processes to support parents to become resilient to these child effects could promote more resilient/adaptive rearing environments and ultimately improve outcomes for children. As an illustrative example to this hypothesis, we provide a brief synopsis of two interventions focusing on primary family process/environmental factors reviewed in this article (parenting practices) specific to foster-care and adoption contexts.

Examples of interventions in the context of adoption and foster care

Treatment Foster Care Oregon (TFCO)

TFCO (formerly known as Multidimensional Treatment Foster Care, MTFC) is a US-based intervention designed for foster carers of children and adolescents who had experienced maltreatment and are at risk for delinquency (Chamberlain, 2003; Fisher & Stoolmiller, 2008). In TFCO, foster parents are provided with intense parent skills training (e.g., providing support, mentoring, supervision and consistent limit setting). TFCO has been shown to improve outcomes (e.g. depression, delinquency, psychosis, teenage pregnancies) for both children and adolescents in the US and Sweden (Poulton et al., 2014; Harold et al., 2013; Leve et al., 2012; Westermarck et al., 2011). One study has evaluated the effectiveness of this intervention in the UK, finding that improvements in adjustment were only evident for those with antisocial behaviour (Green et al., 2014), although limitations due to sample constraints reduced the statistical power of this study to detect overall group differences (Harold & DeGarmo, 2014).

AdOpt Parenting Programme

A recently implemented programme in the UK aimed at adoptive parents and children is the AdOpt parenting programme (National Implementation Service, NIS; <http://www.evidencebasedinterventions.org.uk/about/national-implementation-service>), adapted from a US intervention (KEEP; Keeping Foster & Kinship Carers Supported; Price, Chamberlain, Landsverk & Reid, 2009) for adoptive parents post-legal Order with children age 3-8 years. The programme is designed as a preventative programme to help parents understand the often complex needs of their adopted children and to support positive parenting techniques, with the aim of enhancing positive behaviours in children. This parenting programme has been evaluated in the UK, and demonstrated improvements in parenting behaviours, in addition to reductions in child total problems and conduct problems

(Harold et al., 2017). The programme did not demonstrate improvements in child emotional, hyperactivity, or peer problems, nor did it improve prosocial behaviours. The evaluation of the AdOpt parenting programme suggests that the programme is suitable as a universal intervention for the specified population (adoptive families, post legal-order), impacting on parenting behaviours, child total problems and conduct problems. However, evidence derived from quantitative behavioural genetics studies may help illuminate the mechanisms and processes that impact on other mental health difficulties that were not evidenced to be impacted by the intervention (e.g., emotional problems, peer problems, hyperactivity problems), to develop an understanding of intervention targets specific to these difficulties in the context of genetic risk.

Challenges in translating research from quantitative behavioural genetics to prevention science

Quantitative behavioural genetics research has identified the role of specific family environmental factors relative to underlying genetic susceptibility in explaining variation in multiple child developmental outcomes. These research designs help address limitations of research that is not genetically informed by examining gene-environment interplay, specifically passive *rGE*, evocative *rGE*, and *GxE*. This evidence can inform prevention science, by providing an evidence base for more precise intervention targets (what to target and for whom) based on genetically influenced child characteristics. However, there are a number of existing challenges to translating quantitative behavioural genetics to prevention science.

(1) Environments are multifaceted and dynamic

Many family-based intervention studies focus on a specific collection of ‘environmental’ targets. For example, the AdOpt parenting programme targets a range of parenting behaviours including parental support, sensitivity and warmth, as well as

monitoring and limit setting (Harold et al., 2017). In contrast, quantitative genetics research often focuses on unidimensional constructs of parenting, rather than on multiple measures of parenting (as one index of family environmental influence). This has limited translation of behavioural genetics research to prevention science. More recently, quantitative behavioural genetics research has begun to examine how multiple aspects of the family environment can influence child behaviour (Leve et al., 2017). This more closely aligns with intervention studies that target multiple environmental processes (see Harold & Sellers, 2018).

In addition, employing a longitudinal research design is advantageous. Longitudinal research provides the opportunity to examine modifiable, mediating mechanisms - a central component of preventive interventions. Studies that remove the confound of passive *rGE* and examine evocative *rGE* may be more readily translated to prevention studies (Ge et al., 1996; O'Connor et al., 1998). Specifically, examination of *rGE* provides the opportunity for two targets for prevention science: (1) examining evocative *rGE* can identify genetically influenced child behaviours that can evoke negative responses from parents, enabling interventions to target environmental responses to genetically influenced traits, for example promoting resilient parenting for specific child evoked characteristics; (2) removing the confound of passive *rGE* allows the identification of specific environmental influences on children's development, enabling interventions to promote individual strengths to reduce adverse responses to specific environmental risks, for example, promoting child resilience to adverse environments. Furthermore, examining GxE can identify aspects of the environment that can be targeted by intervention to offset genetic risk, allowing interventions to be tailored to individuals depending on their genetic susceptibility (Van Ijzendoorn & Bakermans-Kranenburg, 2015). However, only a small number of studies have examined GxE or *rGE* (passive and evocative) on child outcomes longitudinally (see Harold et al., 2017). It is therefore important for future research to examine how aspects of the environment affect

child outcomes at a later time point and how this relationship may vary as a function of genetic risk.

(2) Promoting positive rearing environments in intervention studies as compared to measuring negative rearing environments in research studies

Preventative interventions focus on enhancing positive rearing environments (e.g., building parenting skills and promoting positive environmental change) to prevent negative child outcomes: for example, the AdOpt parenting programme focuses on promoting positive parenting strategies (Harold et al., 2017). In contrast, many genetically-informed studies focus on environmental risks (e.g., hostile parent-child relationships, harsh parenting practices), and how genetic risks interact with environmental risk to impact on child outcomes (e.g., Harold et al., 2013a; Rhoades et al., 2011; Leve et al., 2009). This makes it challenging to translate findings from behavioural genetic research to prevention and intervention contexts. Studies that examine GxE and rGE that examine positive, strength-based environments (e.g., parent-child warmth, inter-parental satisfaction, etc.) and that evidence how these positive environments can offset genetic risk (or promote child strengths) would more closely align to prevention science efforts (e.g., Ganiban et al., 2007; Neiderhiser, Reiss, Lichtenstein, Spotts, & Ganiban, 2007; Leve et al., 2009).

(3) The importance of employing accurate statistical approaches to examining questions and interpreting findings

Another limitation of translating quantitative behavioural genetics research to intervention development and prevention science is that different statistical approaches are typically used by the two disciplines: quantitative behavioural genetics studies typically employ correlational approaches (to examine associations between variables or groups). Conversely, intervention studies tend to compare mean/variance scores between groups (i.e. comparing mean scores between a group who has received an intervention and a group who has not received an intervention). These different statistical approaches typically employed

by these respective disciplines (i.e. mean level differences between groups vs correlations between variables) has hindered the translation of findings to practice contexts. For example, a common misconception in applying genetic research to intervention development is that heritable behaviours are not modifiable (and would therefore be unsuitable intervention targets). Quantitative genetic studies examine correlations between family members who differ in their degree of genetic relatedness (e.g., MZ or DZ twins) to calculate heritability (the proportion of variance in behaviours attributable to genetic factors). However, this heritability is not equivalent to non-malleability (i.e. impenetrable to change). Indeed, the misconception that heritability equates to non-malleability remains in research and practice circles, despite multiple quantitative genetic studies (e.g. Leve et al., 2009) demonstrating that positive rearing environments can interact with heritable behaviours to offset genetic risk and improve outcomes for children (thus providing evidence to suggest that heritable behaviours *are* malleable via environmental processes; see also Leve et al., 2010). This underlines the need for better clarification and interpretation of findings from quantitative behavioural genetics studies, to more effectively increase translation from research to intervention/prevention practice.

(4) The relevance of sample characteristics to the interpretation of substantive findings

Another challenge to translating research from quantitative genetics to prevention studies is that intervention research is typically conducted with high-risk samples. This is in contrast to the majority of quantitative genetics research that has been conducted with low-risk samples. Existing GxE research demonstrates that genetic and environmental influences on behaviour vary as a function of risk (Rutter, 2006). Therefore, sample characteristics need to be considered in translation efforts to ensure intervention implications map on to research findings. In addition, examining GxE and rGE processes in risk-based samples would also

improve translation efforts (e.g. Jaffee et al., 2005). Further, interpretation of the ‘environment’ relative to prevention science targets needs to be responsive to the complexities of family, community and wider environmental impacts on outcomes.

(5) Bridging the gap between genetically-informed research and preventative interventions

Despite the limitations and challenges (outlined above) of translating genetically-informed research to prevention science, and the implementation of family-based interventions in the context of adoption and foster care, there is significant potential for translation between disciplines. Leve et al. (2017) outline how translational efforts can be made from genetically informed research to preventative intervention development. Specifically, they outline steps for both quantitative genetics research and for preventative intervention research. Quantitative behavioural genetics researchers should conduct studies that: (1) specify a theory of change; (2) examine the role of genetic and environmental influences on outcomes by employing robust measures that map onto preventative intervention targets; and (3) are replicable and demonstrate robust effects. Alongside such practical steps, prevention science should (1) identify an intervention that maps onto a theory of change specified in quantitative genetics studies; (2) ensure that the intervention targets the specified environmental mechanism, and that there is overlap with quantitative genetic studies regarding the measurement of this mechanism; (3) employ designs and samples that identify individuals and conditions under which the intervention is most effective (Leve et al., 2017). These steps will allow quantitative genetics studies to map onto an intervention mechanism of change, thus intervention can be appropriately modified, taking into account inherited characteristics to provide more precise mechanisms of change.

Summary and Recommendations

It is well-established that family environmental processes are important for child outcomes, whether parents/carers and children are genetically related or not. Developing effective interventions is crucial, particularly in at-risk groups such as adoption and foster care where children are at elevated risk of psychopathology and other related outcomes (e.g. reduced academic attainment, adverse intergenerational transmission processes). The evidence base from quantitative behavioural genetics research can substantively inform intervention and prevention studies. These research designs can generate insights into the role of specific mechanisms underlying specified child outcomes, and can inform why specific environments may be moderated by inherited child characteristics. Where genetically informed studies are longitudinal, they can also generate knowledge of dynamic processes that may illuminate how adaptation may vary during specific developmental periods (e.g. infancy, childhood, adolescence). This knowledge can then be integrated into prevention science strategies aimed at increasing the efficacy of family-based interventions targeting improved child outcomes. Additionally, quantitative behaviour genetic research designs can provide insights into how a child's inherited propensities may affect the efficacy of interventions – what works well for one child may not work for another. These insights can allow interventions to be tailored to specific risks, and therefore improve specified child outcomes. In some countries (e.g. specific states in the US), the administrative processes leading to adoption and foster care placement decisions are highly visible and lend themselves to an offer of intervention by social (state) or health agencies at or even before the time of placement (see Leve et al., 2012). This creates real opportunities to offer evidenced-based interventions to families at high risk of intergenerational challenge, particularly at the time of placement. However there are also risks to the ever-delicate balance between the needs of parental care-givers and children. The language of scientific research and associated

literatures can potentially be experienced as stigmatising and critical of a group of parents and even would-be parental caregivers who are already far more heavily scrutinised than most biological parents. Interventions in this field need to be carefully pre-piloted and scrutinized for potential unwanted effects, both on the families recruited and also on readiness to offer adoption and foster-care placement. Given the emerging importance of evocative *rGE* effects, primary care health professionals will often be the first in line to recognise family stressors and related mechanisms in such families. Interventions to help health professionals be more aware that parental and child distress may be best addressed through family-based interventions is likely to require considerable adjustment of referral routes in order to improve programme alignment and targeted child outcomes.

Notwithstanding these important caveats, opportunity is at hand to integrate and translate quantitative behavioural genetics research into prevention science efforts to provide a robust evidence-base for practice, and to promote efficacious and individually-targeted supports to help children and their families.

References

- Arseneault, L., Moffitt, T. E., Caspi, A., Taylor, A., Rijdsdijk, F. V., Jaffee, S. R., ... & Measelle, J. R. (2003). Strong genetic effects on cross-situational antisocial behaviour among 5-year-old children according to mothers, teachers, examiner-observers, and twins' self-reports. *Journal of Child Psychology and Psychiatry*, *44*(6), 832-848.
- Bekkhus, M., Lee, Y., Nordhagen, R., Magnus, P., Samuelsen, S. O., & Borge, A. I. (2017). Re-examining the link between prenatal maternal anxiety and child emotional difficulties, using a sibling design. *International Journal of Epidemiology*.
- Belsky, D. W., Suppli, N. P., & Israel, S. (2014). Gene-environment interaction research in psychiatric epidemiology: a framework and implications for study design. *Social psychiatry and psychiatric epidemiology*, *49*(10), 1525-1529.
- 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*(4), 831-844.
- Bouchard, T. J., Lykken, D. T., McGue, M., Segal, N. L., & Tellegen, A. (1990). Sources of human psychological differences: The Minnesota study of twins reared apart. *Science*, *250*, 223–228.
- Brody, G. H., Yu, T., Chen, Y. F., Kogan, S. M., Evans, G. W., Windle, M., ... & Philibert, R. A. (2013). Supportive family environments, genes that confer sensitivity, and allostatic load among rural African American emerging adults: A prospective analysis. *Journal of Family Psychology*, *27*, 22–29.
- Burt, S. A. (2009). Rethinking environmental contributions to child and adolescent psychopathology: A meta-analysis of shared environmental influences. *Psychological Bulletin*, *135*, 608-637.
- Burt, S. A., McGue, M., Krueger, R. F., & Iacono, W. G. (2007). Environmental contributions to adolescent delinquency: A fresh look at the shared environment. *Journal of Abnormal Child Psychology*, *35*(5), 787-800.
- Cadoret, R. J., Yates, W. R., Woodworth, G., & Stewart, M. A. (1995). Genetic-environmental interaction in the genesis of aggressivity and conduct disorders. *Archives of General Psychiatry*, *52*(11), 916-924.
- Caspi, A., McClay, J., Moffitt, T.E., Mill, J., Martin, J., Craig, I.W., et al. (2002). Role of genotype in the cycle of violence in maltreated children. *Science*, *297*, 851–854.
- Caspi, A., Sugden, K., Moffitt, T. E., Taylor, A., Craig, I. W., Harrington, H., . . . Braithwaite, A. (2003). Influence of life stress on depression: moderation by a polymorphism in the 5-HTT gene. *Science*, *301*(5631), 386-389.

- Chamberlain, P. (2003). *Treating chronic juvenile offenders: Advances made through the Oregon Multidimensional Treatment Foster Care model*. Washington, DC: American Psychological Association.
- Chamberlain, P., Price, J., Leve, L.D., Laurent, H., Landsverk, J.A., & Reid, J.B. (2008). Prevention of behavior problems for children in foster care: Outcomes and mediation effects. *Prevention Science, 9*, 17–27
- Collins, F. S., & Varmus, H. (2015). A new initiative on precision medicine. *New England Journal of Medicine, 372*(9), 793-795.
- Conduct Problems Prevention Research Group. (2002). Evaluation of the first 3 years of the Fast Track prevention trial with children at high risk for adolescent conduct problems. *Journal of Abnormal Child Psychology, 30*, 19–35.
- D'onofrio, B. M., Lahey, B. B., Turkheimer, E., & Lichtenstein, P. (2013). Critical need for family-based, quasi-experimental designs in integrating genetic and social science research. *American Journal of Public Health, 103*(S1), S46-S55.
- D'Onofrio, B. M., Slutske, W. S., Turkheimer, E., Emery, R. E., Harden, K. P., Heath, A. C., ... & Martin, N. G. (2007). Intergenerational transmission of childhood conduct problems: a Children of Twins Study. *Archives of General Psychiatry, 64*(7), 820-829.
- DfE. (2016b). Children looked after in England (including adoption) year ending 31 March 2016.
- Dick, D. M., Meyers, J. L., Latendresse, S. J., Creemers, H. E., Lansford, J. E., Pettit, G. S., ... & Buitelaar, J. K. (2011). CHR2, Parental monitoring, and adolescent externalizing behavior evidence for gene-environment interaction. *Psychological Science, 22*, 481–489.
- Eddy, J.M., & Chamberlain, P. (2000). Family management and deviant peer association as mediators of the impact of treatment condition on youth antisocial behavior. *Journal of Consulting and Clinical Psychology, 68*, 857–863.
- Elam, K. K., Harold, G. T., Neiderhiser, J. M., Reiss, D., Shaw, D. S., Natsuaki, M. N., . . . Leve, L. 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.
- Eley, T. C., McAdams, T. A., Rijdsdijk, F. V., Lichtenstein, P., Narusyte, J., Reiss, D., . . . Neiderhiser, J. M. (2015). The intergenerational transmission of anxiety: a children-of-twins study. *American Journal of Psychiatry, 172*(7), 630-637.
- Fearon, R. P., Reiss, D., Leve, L. D., 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(401), 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(4), 601-610.
- Fincham, F. D., Beach, F. D., Harold, G. T., & Osborne, L. N. (1997). Marital satisfaction and depression: Different causal relationships for men and women. *Psychological Science*, 8(5), 351-357.
- Fisher, P. A. (2015). Review: Adoption, fostering, and the needs of looked-after and adopted children. *Child and Adolescent Mental Health*, 20(1), 5-12.
- Fisher, P. A., & Stoolmiller, M. (2008). Intervention effects on foster parent stress: Associations with children's cortisol levels. *Development and Psychopathology*, 20(3), 1003-1021.
- Ganiban, J.M., Spotts, E.L., Lichtenstein, P., Khera, G.S., Reiss, D., & Neiderhiser, J.M. (2007). Can genetic factors explain the spillover of warmth and negativity across family relationships? *Twin Research and Human Genetics*, 10, 299–313.
- Ge, X., Conger, R.D., Cadoret, R.J., Neiderhiser, J.M., Yates, W., Troughton, E., et al. (1996). The developmental interface between nature and nurture: A mutual influence model of child antisocial behavior and parent behaviors. *Developmental Psychology*, 32, 574–589.
- Green, J., Biehal, N., Roberts, C., Dixon, J., Kay, C., Parry, E., . . . Scott, S. (2014). Multidimensional Treatment Foster Care for Adolescents in English care: randomised trial and observational cohort evaluation. *The British Journal of Psychiatry*, 204(3), 214-221.
- 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(1), 80-93.
- Harold, G. T., & DeGarmo, D. S. (2014). Concerns regarding an evaluation of MTFC-A for adolescents in English care. *The British Journal of Psychiatry*, 205(6), 498-498.
- Harold, G. T., Hampden-Thompson, G., Rodic, M., & Sellers, R. (2017). An evaluation of the AdOpt parenting programme.
- Harold, G., Leve, L. D., Barrett, D., Elam, K., Neiderhiser, J. M., Natsuaki, M. N., . . . Thapar, A. (2013a). Biological and rearing mother influences on child ADHD symptoms: revisiting the developmental interface between nature and nurture. *Journal of Child Psychology and Psychiatry*, 54(10), 1038-1046.

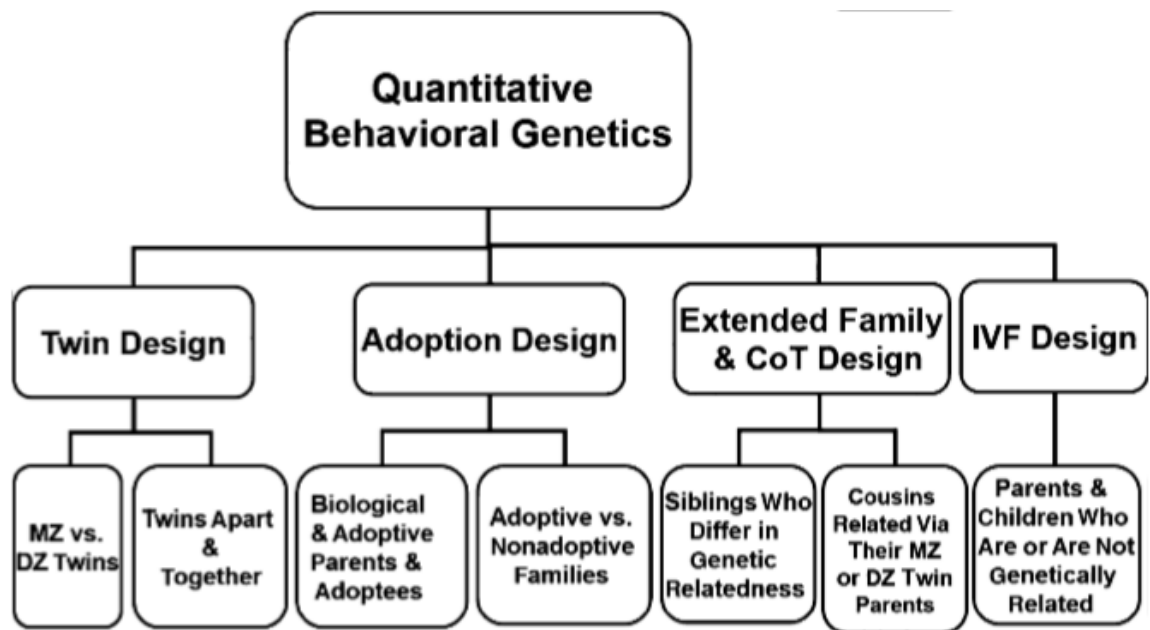
- Harold, G., Leve, L. D., Elam, K. K., Thapar, A., Neiderhiser, J. M., Natsuaki, M. N., . . . Reiss, D. (2013b). The nature of nurture: Disentangling passive genotype–environment correlation from family relationship influences on children's externalizing problems. *Journal of Family Psychology, 27*(1), 12-21.
- Harold, G. T., Leve, L. D., & Sellers, R. (2017). How Can Genetically Informed Research Help Inform the Next Generation of Interparental and Parenting Interventions?. *Child Development, 88*(2), 446-458.
- Harold, G., Rice, F., Hay, D. F., Boivin, J., Van Den Bree, M., & Thapar, A. (2011). Familial transmission of depression and antisocial behavior symptoms: disentangling the contribution of inherited and environmental factors and testing the mediating role of parenting. *Psychological Medicine, 41*(06), 1175-1185.
- Haworth, C. M., Wright, M. J., Luciano, M., Martin, N. G., De Geus, E. J. C., Van Beijsterveldt, C. E. M., ... & Kovas, Y. (2010). The heritability of general cognitive ability increases linearly from childhood to young adulthood. *Molecular Psychiatry, 15*(11), 1112.
- Henry, J., Boivin, M., & Tarabulsy, G. (2015). Gene-environment interplay in parenting young children. In *Gene-Environment Interplay in Interpersonal Relationships across the Lifespan* (pp. 13-55). Springer, New York, NY.
- Hyde, L. W., Waller, R., Trentacosta, C. J., Shaw, D. S., Neiderhiser, J. M., Ganiban, J. M., . . . Leve, L. D. (2016). Heritable and nonheritable pathways to early callous-unemotional behaviors. *American Journal of Psychiatry, 173*(9), 903-910.
- 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*(5), 432.
- Jaffee, S. R., Caspi, A., Moffitt, T. E., Dodge, K. A., Rutter, M., Taylor, A., & Tully, L. A. (2005). Nature× nurture: Genetic vulnerabilities interact with physical maltreatment to promote conduct problems. *Development and Psychopathology, 17*(01), 67-84.
- Kendler, K. S., Ohlsson, H., Sundquist, J., & Sundquist, K. (2016). The rearing environment and risk for drug abuse: A Swedish national high-risk adopted and not adopted co-sibling control study. *Psychological Medicine, 46*, 1359–1366.
- Kendler, K. S., Walters, E. E., Neale, M. C., Kessler, R. C., Heath, A. C., & Eaves, L. J. (1995). The structure of the genetic and environmental risk factors for six major psychiatric disorders in women: Phobia, generalized anxiety disorder, panic disorder, bulimia, major depression, and alcoholism. *Archives of General Psychiatry, 52*(5), 374-383.
- Kim-Cohen, J., Caspi, A., Taylor, A., Williams, B., Newcombe, R., Craig, I. W., & Moffitt, T. E. (2006). MAOA, maltreatment, and gene–environment interaction predicting

- children's mental health: new evidence and a meta-analysis. *Molecular Psychiatry*, *11*(10), 903-913.
- Klahr, A. M., & Burt, S. A. (2014). Elucidating the etiology of individual differences in parenting: A meta-analysis of behavioral genetic research. *Psychological Bulletin*, *140*(2), 544-586.
- Leve, L. D., Harold, G. T., Chamberlain, P., Landsverk, J. A., Fisher, P. A., & Vostanis, P. (2012). Practitioner review: children in foster care—vulnerabilities and evidence-based interventions that promote resilience processes. *Journal of Child Psychology and Psychiatry*, *53*(12), 1197-1211.
- 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*(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 & Adolescent Psychiatry*, *48*(11), 1102-1109.
- Leve, L. D., Neiderhiser, J. M., Harold, G. T., Natsuaki, M. N., Bohannon, B. J., & Cresko, W. A. (2017). Naturalistic experimental designs as tools for understanding the role of genes and the environment in prevention research. *Prevention Science*, 1-11.
- Leve, L. D., Neiderhiser, J. M., Shaw, D. S., Ganiban, J., Natsuaki, M. N., & Reiss, D. (2013). The early growth and development study: A prospective adoption study of child behavior from birth through middle childhood. *Twin Research and Human Genetics*, *16*, 412-423.
- 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*(3), 931-955.
- Mannering, A. M., Harold, G. T., Leve, L. D., Shelton, K. H., Shaw, D. S., Conger, R. D., . . . Reiss, D. (2011). Longitudinal associations between marital instability and child sleep problems across infancy and toddlerhood in adoptive families. *Child Development*, *82*(4), 1252-1266.
- Martinez, C.R., Jr., & Forgatch, M.S. (2001). Preventing problems with boys' noncompliance: Effects of a parent training intervention for divorcing mothers. *Journal of Consulting and Clinical Psychology*, *69*, 416-428.
- Mednick, S. A., Gabrielli, W. F., & Hutchings, B. (1984). Genetic influences in criminal convictions: Evidence from an adoption cohort. *Science*, *224*, 891-894.

- Moffitt, T.E., Caspi, A., & Rutter, M. (2005). Strategy for investigating interactions between measured genes and measured environments. *Archives of General Psychiatry*, *62*, 473–481.
- Natsuaki, M. N., Shaw, D. S., Neiderhiser, J. M., Ganiban, J. M., Harold, G. T., Reiss, D., & Leve, L. D. (2014). Raised by depressed parents: is it an environmental risk? *Clinical Child and Family Psychology Review*, *17*(4), 357-367.
- 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*(01), 133-149.;
- Neiderhiser, J. M., Reiss, D., Lichtenstein, P., Spotts, E. L., & Ganiban, J. (2007). Father-adolescent relationships and the role of genotype-environment correlation. *Journal of Family Psychology*, *21*(4), 560-571.
- O'Connor, T. G., Deater-Deckard, K., Fulker, D., Rutter, M., & Plomin, R. (1998). Genotype–environment correlations in late childhood and early adolescence: Antisocial behavioral problems and coercive parenting. *Developmental Psychology*, *34*(5), 970-981.
- Pedersen, N. L., McClearn, G. E., Plomin, R., Nesselroade, J. R., Berg, S., & DeFaire, U. (1991). The Swedish adoption twin study of aging: An update. *Acta Geneticae Medicae et Gemellologiae: Twin Research*, *40*, 7–20.
- Pedersen, N. L., Plomin, R., & McClearn, G. E. (1994). Is there G beyond g? (Is there genetic influence on specific cognitive abilities independent of genetic influence on general cognitive ability?). *Intelligence*, *18*(2), 133-143.
- Plomin, R., & Petrill, S. A. (1997). Genetics and intelligence: What's new? *Intelligence*, *24*(1), 53-77.
- Poulton, R., Van Ryzin, M.J., Harold, G.T., Chamberlain, P., Fowler, D., Cannon, M., Arseneault, L., Leve, L.D. (2014). Effects of multidimensional treatment foster care on psychotic symptoms in girls. *Journal of the American Academy of Child and Adolescent Psychiatry*, *53* (12), 1279-1287.
- Price, J. M., Chamberlain, P., Landsverk, J., & Reid, J. (2009). KEEP foster-parent training intervention: Model description and effectiveness. *Child & Family Social Work*, *14*(2), 233-242.
- Reiss, D., & Leve, L.D. (2007). Genetic expression outside the skin: Clues to mechanisms of Genotype Environment interaction. *Development and Psychopathology*, *19*, 1005–1027.
- Reiss, D., Leve, L. D., & Neiderhiser, J. M. (2013). How genes and the social environment moderate each other. *American Journal of Public Health*, *103*(S1), S111-S121.

- Reiss, D., Neiderhiser, J., Hetherington, E.M., & Plomin, R. (2000). *The relationship code: Deciphering genetic and social patterns in adolescent development*. Cambridge, MA: Harvard University Press.
- Rhea, S. A., Bricker, J. B., Corley, R. P., DeFries, J. C., & Wadsworth, S. J. (2013). Design, utility, and history of the Colorado Adoption Project: Examples involving adjustment interactions. *Adoption Quarterly*, *16*(1), 17-39.
- 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*(4), 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*(2), 282-291.
- Rice, F., Harold, G. T., Shelton, K. H., & Thapar, A. (2006). Family conflict interacts with genetic liability in predicting childhood and adolescent depression. *Journal of the American Academy of Child & Adolescent Psychiatry*, *45*(7), 841-848.
- Rutter, M. (2006). *Genes and behavior: Nature–nurture interplay explained*. Malden, MA: Blackwell.
- Rutter, M., Pickles, A., Murray, R., & Eaves, L. (2001). Testing hypotheses on specific environmental causal effects on behavior. *Psychological Bulletin*, *127*, 291–324.
- Schermerhorn, A. C., D'onofrio, B. M., Turkheimer, E., Ganiban, J. M., Spotts, E. L., Lichtenstein, P., . . . Neiderhiser, J. M. (2011). A genetically informed study of associations between family functioning and child psychosocial adjustment. *Developmental Psychology*, *47*(3), 707-725.
- Selwyn, J., Wijedasa, D., Meakings, S. (2014). *Beyond the Adoption Order: challenges, interventions and adoption disruption*. Department for Education, Ref: ISBN 978-1-78105-307-2, DFE-RR336.
- Shelton, K. H., & Harold, G. T. (2008). Interparental conflict, negative parenting, and children's adjustment: Bridging links between parents' depression and children's psychological distress. *Journal of Family Psychology*, *22*(5), 712-724.
- Silberg, J. L., Maes, H., & Eaves, L. J. (2010). Genetic and environmental influences on the transmission of parental depression to children's depression and conduct disturbance: an extended Children of Twins study. *Journal of Child Psychology and Psychiatry*, *51*(6), 734-744.
- Simmonds, J. (2016) Family placement: continuity and discontinuity over time. In Barratt., S & Lobatto., W. *Surviving and thriving in care and beyond: Personal and professional perspectives* (pp. 3-20). London, Karnac Books Ltd.

- Singh, A.L., D'onofrio, B.M., Slutske, W.S., Turkheimer, E., Emery, R.E., Harden, K.P., Heath, A.C., Madden, P.A.F., Statham, D.J. and Martin, N.G., 2011. Parental depression and offspring psychopathology: a Children of Twins study. *Psychological Medicine*, 41(7), pp.1385-1395.
- Sorensen, T. I., Price, R. A., Stunkard, A. J., & Schulsinger, F. (1989). Genetics of obesity in adult adoptees and their biological siblings. *British Medical Journal*, 298, 87–90.
- 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(4), 401-409.
- Thapar, A., Harold, G. T., Rice, F. J., Langley, K., & O'Donovan, M. (2007). The contribution of gene-environment interaction to psychopathology. *Development and Psychopathology*, 19(4), 989-1004.
- Thapar, A., Rice, F., Hay, D., Boivin, J., Langley, K., Van Den Bree, M., . . . Harold, G. (2009). Prenatal smoking might not cause attention-deficit/hyperactivity disorder: evidence from a novel design. *Biological Psychiatry*, 66(8), 722-727.
- Tolan, P.H., & Dodge, K.A. (2005). Children's mental health as a primary care and concern: A system for comprehensive support and service. *American Psychologist*, 60, 601–614.
- Triseliotis, J. (2002). Long-term foster care or adoption? The evidence examined. *Child & Family Social Work*, 7(1), 23-33.
- Van Ijzendoorn, M.H. & Bakermans-Kranenburg, M.J. (2015). Genetic differential susceptibility on trial: Meta-analytic support from randomised controlled experiments. *Development & Psychopathology*, 27, 151-162.
- Webster-Stratton, C. & Herman, K.C. (2008). The impact of parent behavior-management training on child depressive symptoms. *Journal of Counseling Psychology*, 55, 473–484.
- Weisz, J.R., Sandler, I.N., Durlak, J.A., & Anton, S.A. (2005). Promoting and protecting youth mental health through evidence based prevention and treatment. *American Psychologist*, 60, 628–648.
- Westermarck, P. K., Hansson, K., & Olsson, M. (2011). Multidimensional treatment foster care (MTFC): results from an independent replication. *Journal of Family Therapy*, 33(1), 20-41.



MZ = monozygotic; DZ = dizygotic; CoT = children of twins; IVF = in vitro fertilisation

Figure 1: A summary of traditional behavioural genetic research designs (Harold, Leve, Sellers, 2017).

Table 1. Description and examples of how heritable characteristics provide insight into the relationship between parenting and child adjustment

Heritable characteristic	Definition	Example
Passive rGE	Associations between parents and children may be attributable to environment or shared genes	The association between hostile parenting and child disruptive behaviour may be due to hostile parenting acting as an environmental influence on child behaviour (i.e. children may act in a disruptive manner in direct response to hostile parenting, for example by modelling hostile behaviours), or associations may be due to the same genes underlying both hostile parenting and disruptive child behaviour. Passive rGE refers to the concept that the association between hostile parenting and child conduct problems may be better explained by shared genes between parents and children (although research suggests that this is not the case; Harold et al., 2011).
Evocative rGE	Children's genetically influenced behaviour can evoke negative responses from parents	In the context of an adoption-at-birth design, genetically risk for child impulsivity (indicated by birth parent psychopathology) predicts child impulsivity which in turn predicts subsequent hostile parenting in adoptive parents (e.g. Harold et al., 2013a)
GxE	Children's genes interact with their environment to influence behaviour (child responses to environment differ depending on genetic risk and vice-versa)	Structured parenting can reduce behaviour problems in children with high genetic risk (indicated by birth parent psychopathology e.g. alcohol/drug use, antisociality), but can increase behaviour problems in children with low genetic risk (e.g. Leve et al., 2009).

rGE = gene-environment correlation, GxE = gene-environment interaction