Disentangling Genetic and Environmental Influences on Children’s Development: Introducing A Novel Methodology

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Abstract: The present study describes a novel methodology to examine the interplay between genetic and environmental influences on children’s development. Families of children aged 4 – 10 years born by one of five methods of assisted reproductive technologies, specifically homologous in vitro fertilization (IVF), sperm donation, egg donation, embryo donation, and gestational surrogacy, were contacted through fertility clinics and mailed a set of questionnaires focusing on the quality of family interaction, parenting, marital satisfaction, parent and child psychological health, economic conditions and family demographics. Analyses are described that highlight the novelty of this research design to disentangle genetic, intrauterine and early social environmental influences on children’s development. First, results are described whereby comparisons were made between children born through assisted reproductive technologies and children conceived naturally in relation to patterns of association between levels of interparental conflict, parent-to-child hostility and children’s symptoms of depression. Second, results are described where comparisons were made between patterns of association between parent depressive symptoms, family relationship quality (interparental and parent-child relations) and children’s symptoms of depression. Finally, a strategy that allows examination of relative genetic and intrauterine environmental influences on children’s health and mental health outcomes is described. Results are discussed in relation to implications for development of future intervention and prevention programmes.

Keywords: assisted reproductive technologies; family relationships; gene × environment interaction

Understanding the aetiology of psychopathology in childhood and adolescence is an area that is receiving increasing international attention. While a large volume of research exists highlighting the types of problems regarded as common among children and adolescents (Ford, 2008), an impressive volume of research is now available suggesting specific mechanisms that may underlie individual differences in children’s normal and abnormal psychological development (see Rutter, 2006).

Two schools of thought have historically laid claim to explaining variation in children’s development. First, aberrant psychological functioning can be explained by genetic factors passed down from parents to children (Plomin, 1990). Second, disrupted psychological functioning is influenced by children’s exposure to hostile family environments and stressful life experiences (Collins, Maccoby, Steinberg, Hetherington & Bornstein, 2000). While evidence exists to support each of these perspectives, an increasing body of research suggests that genetic and environmental factors work together to explain individual differences in health and mental health related outcomes across the life-course (Rutter, 2006).

It is recognised that examining the interplay between genetic vulnerability and environmental risk likely provides a more complete explanation of individual differences in human development. Historically, assessment of ‘environmental risk’ has focused on the impact of social environmental influences, such as negative parenting, on children’s psychological development (Collins et al., 2000). The intrauterine environment, however, has also found to
be an important source of influence on individual differences in children’s development across the lifespan (Barker, 1998). To date, however, it has been difficult to identify the relative effects of genetic, intrauterine, and social environmental influences, particularly their interactions, on development using research designs other than those that involve animals. As a result, surprisingly little is known about how genetic vulnerability and pre- and post-natal environmental risk factors work together to influence children’s normal and abnormal psychological development. This article introduces a novel methodology that allows the relative effects of genetic, intrauterine and early social environmental influences on children’s development to be disentangled, using a sample of children born through assisted reproductive technologies (ART).

Genetics and Child Development

It is well established that genes play an important role in human development. Molecular and quantitative behaviour genetic research has identified genetic contributions to children’s susceptibility to depression, aggression, conduct problems, ADHD, substance abuse and related health problems (e.g., Langley, Rice, van den Bree & Thapar, 2005; Thapar et al., 2007; Rice, Harold, Shelton & Thapar, 2006). Indeed, major international efforts have been directed towards identifying susceptibility genes for a number of complex traits and disorders (ADHD, conduct problems, depression; Kraft, 2007). Because it will be some years, however, before most genetic variants accounting for common diseases and traits are identified, there remains a need for studies that employ other novel genetic epidemiological designs. Traditional twin and adoption studies are useful approaches within this genre of research but have important limitations in allowing the relative contribution of genes and specific environmental factors on development to be determined. Twin studies assume that monozygotic (from the same fertilised ovum) and dizygotic (from two separately fertilised ova) twin pairs share their environment to the same extent (equal environmental assumption), so a greater degree of concordance in any particular index of psychopathology (phenotype) in monozygotic as compared to dizygotic twin pairs is attributed principally to similarity in genetic factors. 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 (when intrauterine effects are taken into account) whereas similarities between adopted children and their non-biological rearing parents are assumed to be due to shared environment. Each of these designs has their own strengths and weaknesses (see Rutter, 2006).

While convincing evidence has been provided for the role of genes in the aetiology of childhood psychopathology in past research, it is equally indisputable that environmental factors also contribute to most common disorders and traits such that recent rising prevalence rates (see Ford, 2008) cannot be simply attributed to changes in gene pools.

Environmental Influences and Child Development

There are many types of potential ‘environmental’ influence on the developing child. Among these, parenting style and life stress have received the most frequent attention in genetic epidemiological studies. Children who are exposed to harsh, punitive parenting or negative life events (parent loss; school change) were found to be at greater risk for psychological disorder than children exposed to more positive family environments and who experience fewer negative life events (Plomin, 1990). Romanian adoptees exposed to severe environmental deprivation prior to adoption in the UK, for example, manifested long-term deficits in both cognitive functioning (e.g., IQ; Rutter et al., 1998) and rates of psychological disorder (e.g., conduct problems; Gunnar, Morison, Chisholm, & Schuder, 2001). Long-term influences of maternal postnatal depression and early poor nutrition have been found on subsequent rates of psychopathology in childhood (Murray, 1992).

While social environmental influences are identified as significant in explaining differences in children’s normal and abnormal development, intrauterine environment also plays a significant role in the aetiology of psychopathology in childhood. Prospective longitudinal studies have demonstrated links between a variety of antenatal insults and later anti-social behaviour (Raine, 2002). For example, the association between smoking in pregnancy and the disruptive behaviour disorders has been well established (Linnet et al., Langley et al, 2005;
Maughan, Taylor, Caspi, & Moffit, 2004). Mothers’ mental health problems during pregnancy are also associated with later behaviour problems (O’Connor et al., 2002). Understanding how the constellation of both antenatal and postnatal environmental risk factors work together with underlying genetic factors in accounting for individual differences in development constitutes an area of distinct research importance.

Gene–Environment Interplay and Child Development

It is increasingly clear that genetic and environmental research traditions offer complementary rather than competing possibilities in accounting for individual differences in normal and abnormal human development (see Rutter, 2006). Interest has therefore turned to exploring mechanisms, i.e., how and why these influences operate together to explain the origins of mental disorders across the life course, including childhood and adolescence. While conceptually promising, trying to capture the likely interactive nature of this relationship poses significant problems for traditional research designs. For example, research has shown that there is substantial genetic risk for many environmental factors such as parenting (see Collins et al., 2000), life events (Plomin, 1990), and peer group affiliation (Harris, 1995), such that genetically influenced attributes of the child (e.g., temperament and personality) or the parent (e.g. parent personality) can influence the parenting the child receives, the life events the child experiences, and the friends that the child makes (Plomin, 2008). This is known as gene-environment correlation (rGE). When genetic and environmental risk factors are correlated, the ability to disentangle the relative role of genes and environment using twin designs is compromised. For example, there is evidence that maternal intrauterine effects contribute to twin IQ similarity and that failing to take this ‘environmental’ influence into account may inflate heritability estimates (Prescott, Johnson & McArdle, 1999). Also, monochorionic MZ twins are more similar for cognitive abilities than dichorionic MZ twins (Henrichsen, Skinhøj & Andersen, 1986), further suggesting a role for intrauterine influences. The intrauterine environment also has implications for interpreting findings from studies that employ an adoption design. A major confound using this methodology is that children who have been adopted will not only share genes with their biological parents, but will have spent nine months in the intrauterine environment provided by the biological mother. Thus, any similarity between the biological mother and the adopted away offspring is not necessarily attributable to shared genes alone. Isolating the respective effects of genetic, intrauterine and early social environmental risk factors such that unique and combined (rather than correlated) effects can be identified will provide more fruitful insight into how genetic vulnerability and environmental risks work together. We offer a novel methodology that attains this objective.

Assisted Reproductive Technology and Child Development: A Novel Research Methodology

Assisted reproductive technologies (ART) are becoming increasingly important as a means of conception. Current estimates suggest 1.3% - 3.6% of European births are now due to in vitro fertilisation (IVF) technologies (Anderson, Gianaroli, Felberbaum, de Mouzon & Nygren, 2006). Children conceived via these methods may be genetically related to both parents (homologous IVF), the mother only (sperm donation), the father only (egg donation), or to neither parent (embryo donation). A further category exists where both parents are genetically related to the child but the intrauterine environment is provided by a genetically unrelated surrogate (gestational surrogacy). The differing degrees of genetic relatedness between parents and offspring in these families provide a unique opportunity to disentangle genetic, antenatal and postnatal environmental influences on children’s development. In this paper, we present some examples of research findings using a sample of children born through ART that (1) examines family relationship patterns and children’s psychological adjustment among naturally conceived children and children born through ART, and (2) examines patterns of association between levels of parent psychopathology, family relationship quality and children’s psychological adjustment among children and parents who are genetically related and genetically unrelated. Lastly, and most importantly, we describe how this research strategy may be employed to disentangle genetic and intrauterine influences on children’s health and mental health outcomes.
The Study Sample

**ART sample.** Families who had a live birth between 1994 and 2002 (children aged 4 to 10 years), following successful artificial reproductive treatment from any of the 5 conception groups described were recruited from 18 UK clinics and 1 USA clinic (Thapar et al., 2007). We required that gamete donors and surrogates were un-related to either parent. The study received approval from the Multi Centre Research Ethics Committee for Wales, UK. All data were collected by postal questionnaires, sent to families with children in the appropriate age range as identified by participating clinics. Nineteen of the 22 clinics contacted about the study agreed to participate and recruited families, representing a response rate of 86%. To date, clinic staff members have recruited approximately 900 families who provided questionnaire data (609 fathers & 885 mothers; 594 both parents in each family).

Findings presented in this report used a sample of 522 families who had complete information across the study variables of interest. Parents reported for an approximately even proportion of males (46.9%) and females (52.7%) who were aged between 4-10 years (mean= 6.23 years, \(SD = 1.23\)). Parent age at the birth of the child ranged from 21-54 years for mothers (mean = 35.21 years, \(SD = 4.77\)) and from 23-71 years for fathers (mean= 38.13 years, \(SD = 6.22\)). The number of families in each conception group was: 262 homologous IVF (50.2% parents own gametes used), 129 IVF with sperm donation (24.7%), 100 IVF with egg donation (19.2%), 19 IVF with embryo donation (3.6%), and 12 IVF with gestational surrogacy where the commissioning parents were the genetic parents but an un-related surrogate experienced the pregnancy (2.3%). Approximately 22% of the children were a multiple birth (21.8%; \(N = 114\); 101 twins & 13 triplets), a proportion comparable with UK national norms and, for a sub-sample of multiple births, to an age matched twin sample (see Shelton et al., in press). No differences were found between the conception groups except that fathers from the egg donation group rated children higher in conduct problems compared to other ART groups. No effects were observed by ART treatment type (ICSI vs. IVF, GIFT and IUI). There was some evidence of lower conduct problems and higher prosocial behaviour among children conceived through homologous IVF compared to national norms. Taken together, however, there were no appreciable differences between the sub-groups and in comparison to naturally conceived children for mother- or father-rated adjustment problems. Children conceived with ART, regardless of whether they are genetically related or unrelated to their parents or born by gestational surrogacy, did not differ in their levels of psychological adjustment. Nor did they appear to be at greater risk of psychological adjustment problems in middle childhood compared to naturally conceived children.

Sample representativeness: Comparisons were made between the different conception groups to UK national norms and, for a sub-sample of multiple births, to an age matched twin sample (see Shelton et al., in press). No differences were found between the conception groups except that fathers from the egg donation group rated children higher in conduct problems compared to other ART groups. No effects were observed by ART treatment type (ICSI vs. IVF, GIFT and IUI). There was some evidence of lower conduct problems and higher prosocial behaviour among children conceived through homologous IVF compared to national norms. Taken together, however, there were no appreciable differences between the sub-groups and in comparison to naturally conceived children for mother- or father-rated adjustment problems. Children conceived with ART, regardless of whether they are genetically related or unrelated to their parents or born by gestational surrogacy, did not differ in their levels of psychological adjustment. Nor did they appear to be at greater risk of psychological adjustment problems in middle childhood compared to naturally conceived children.

Natural conception sample: In order to compare family relationship patterns and children’s symptoms of psychological adjustment between children born through ART and those conceived naturally, we employed a comparison sample of parents with a naturally-conceived child derived from a three-year longitudinal study of 387 schoolchildren, parents and teachers living in the United Kingdom. The data for this comparison sample were collected for a study focusing on children’s experiences of family life and their socio-emotional development (age 11–13 years; Time 1, mean=11.69 years, \(SD=0.47\)). Because of the nature of the questions investigated in these analyses, children from all family types other than biologically related two-parent families were excluded from the present study. 289 parents (mothers & fathers) provided complete information in 1999 for the measures of interest and comprise the natural conception comparison sample.

Thirty eight percent of mothers and 34.7% of fathers completed secondary or high-school education only, 32.6% of mothers and 28.9% of fathers completed technical or vocational level training, and 29.8% of mothers and 36.4% of fathers completed university education. Ninety-eight percent of the children in the study were of White-European origin,
1.5% were of Indian, Sri-Lankan, or Pakistani origin, with the remaining 0.6% being of non-British origin (e.g., East African, Jamaican).

Examining Family Relationship Patterns and Children’s Psychological Adjustment among Naturally Conceived Children and Children Born Through ART

A family environment marked by hostile interparental and parent-child relationships has been shown to be detrimental to children’s psychological well being (see Harold & Murch, 2005), with recent studies suggesting that interparental conflict serves as a precursor to children’s psychopathology by affecting (1) the emotions, cognitions and representations of family relationships engendered in children who are exposed to hostile exchanges between their parents (Davies & Cummings, 2002; Harold, Aitken & Shelton, 2007; Harold, Shelton, Goeke-Morey & Cummings, 2004) and (2) the quality of relations children experience with their parents (Erel & Burman, 1995). Evidence supporting the latter of these hypotheses suggests that parents embroiled in a hostile and distressed marital relationship are typically more hostile and aggressive toward their children and less sensitive and emotionally responsive to their children’s needs (Harold, Fincham, Osborne & Conger, 1997). The effects of interparental conflict on children, therefore, are deemed to occur indirectly through a ‘spillover’ of emotion from the couple relationship to the parent-child relationship. In support of this proposal, there is a robust association between emotion expressed in the marital relationship and emotion expressed in the parent-child relationship (Erel & Burman, 1995).

While past research has examined differences in symptoms of psychological adjustment among children born through ART and naturally conceived children (see Shelton et al., in press), few studies have examined differences in family process variables such as interparental and parent-child relationship quality and associated patterns of adjustment among parents and children living in naturally conceived households and ART households. Some research suggests that relationship quality among parents and children living in ART families is higher (Golombok, 1995), whereas other studies suggest that the quality of family relationships is lower (Gibson et al., 2000), with other studies reporting no differences in relationship quality across both household types (Weaver et al., 1993; Colpin et al., 1997). Using the present research design, we examined this question further.

It is also unclear whether a presence or absence of genetic ties with their rearing parents would have any implications for children. We are aware of only one study that suggested greater psychological well-being among mothers and fathers in families where there was no genetic link between the mother and the child (Golombok, Murray, Brinsden, Abdalla, 1999). We examined this conceptually important question among ART subgroups as to the pattern of family relationships and associated symptoms in children where both parents are genetically related to the child (homologous), where only the mother is genetically related to the child (sperm donation), and where only the father is genetically related to the child (egg donation). A synopsis of both sets of results (see Harold et al., 2008) is presented in this report.

Summary of results: In relation to the first set of analyses conducted pertaining to possible differences in the pattern of relations between levels of interparental conflict (spouse hostility), parent-child relations (parent to child hostility) and children’s psychological symptoms (depression) across ART families and natural conception households, results suggested that parents whose children had been conceived naturally reported lower mean levels of interparental conflict compared to the three ART subgroups considered (homologous, sperm donation, egg donation). Significant correlations were apparent for each conception group across each measure of family relationship quality and children’s symptoms of psychological distress (r ranged from .13 to .52, p<.05 to .01). Differences between the pattern of correlations between parents and children living in naturally conceived households and the ART homologous subgroup were examined. Both groups shared one common factor in that children living in these households were born from their parents own gametes. Any difference in the pattern of associations noted might therefore suggest substantive differences between these groups in levels of family relationship quality and children’s associated symptoms based on conception method. No such differences were apparent. For all further analyses, the ART homologous group was therefore regarded as the ‘control’ group relative to other ART subgroups.

In terms of the second set of analyses conducted relating to possible differences in the pattern of
correlations between family measures and children’s symptoms between ART subgroups (homologous, sperm donation, egg donation), a number of interesting differences emerged. Specifically, significant differences were apparent between the sperm donation group and the homologous group in levels of association between husband-to-wife hostility and both mother-child and father-child hostility and between mother-child hostility and mother and father rated symptoms of child depression. No other differences were apparent across all other conception group comparisons. These results suggest however that where differences exist in the magnitude of association between family measures and children’s symptoms, greater disruption is apparent when fathers are not genetically related to their children.

Parent Psychopathology, Family Relationship Quality and Children’s Psychological Adjustment: Disentangling Genetic and Environmental Influences

Parent depression has been identified as a factor relevant to both children’s own psychological well being and to the quality of relations children and parents experience within the context of family life (McCauley, Pavlidis & Kendall, 2001). Parent depression has been associated with heightened levels of inter-parental conflict (Shelton & Harold, in press), parent-child rejection (Cummings & Davies, 1994) and children’s own symptoms of psychopathology (Downey & Coyne, 1990). Genetic and longitudinal epidemiological studies suggest intergenerational transmission of parent depression to child depression (Rice, Harold & Thapar, 2000; Downey & Coyne, 1990), with other studies suggesting environmental mediation of effects on development, specifically through the parent-child relationship (see Gelfand & Teti, 1990). Other studies still provide evidence that it is the interaction between genetic and environmental factors that is critical in the development of more severe forms of depression among the offspring of depressed parents (Rende, Plomin, Reiss & Hetherington, 1993). Given that genetic factors underlying parent psychopathology likely influence both depression in their offspring and the family environments provided by parents; disentangling genetic from environmental influences on child symptoms is critical. Using the present research design it is possible to assess patterns of association between parents’ symptoms of psychopathology (depression), each of the family measures described (interparental and parent-child relations) and children's psychological symptoms (depression) among children genetically related to their parents (mothers: homologous, sperm donation, gestational surrogacy; fathers: homologous, egg donation, gestational surrogacy) and those not genetically related to their parents (mothers: egg donation, embryo donation; fathers: sperm donation, embryo donation). We used this approach to examine patterns of association between parent symptoms, family measures and children’s symptoms as described (see Harold et al., 2008).

Summary of results: Comparing mean levels of parent depression, interparental and parent-child hostility and child depression indicated a significant difference in mother-reported symptoms of child depression among mothers who were genetically related to their child compared to mothers who were not genetically related to their child, with the former reporting higher symptoms in children compared to the latter. In relation to the pattern of correlations observed across groups, a number of significant differences were apparent. While associations were significant between parent and child symptoms, parent symptoms and each of the family measures, and between family measures and child symptoms across genetically related and unrelated groups (r ranged from .24 to .33, p<.05 to .01), significant differences were found for families of genetically related fathers compared to genetically unrelated fathers in relation to the magnitude of association between mother depression and mother-rated child depression, and between mother-child hostility and both mother and father-rated child depression, with coefficients stronger for fathers not genetically related to their child. These results again suggest greater disruption in the pattern of family relationships and children’s symptoms among families where fathers are not genetically related to their children. Understanding the processes that explain these differences requires further examination in future research.

Disentangling Genetic and Intrauterine Influences on Development

On of the most attractive features of the present research design is the possibility to disentangle genetic and intrauterine effects on development.
Using the same constellation of genetically related and genetically unrelated ART subgroups as outlined in the previous section; it is possible to isolate the effects of the intrauterine environment relative to genetic effects in examining individual differences in offspring development. Previously, this possibility has only been available in animal studies (see Francis et al., 2003). The present research design can be used to examine both the contribution of genetic and environmental influences on children’s phenotypic characteristics, such as depression, and to separate maternally provided genetic and environmental influences on children’s health and mental health related outcomes. In examining patterns of association between a maternally provided intrauterine risk effect (e.g. prenatal stress) and an index of childhood psychological distress (e.g. anxiety), it is possible to disambiguate the magnitude of association between these factors across genetically related and unrelated groups based on relative genetic and intrauterine contributions. For example, where an association between a maternally provided intrauterine risk factor and outcome is environmentally, but not genetically, mediated, association would be observed in families where the woman undergoes pregnancy and offspring are genetically related (homologous IVF, sperm donation), and also found to be significant in the offspring who are genetically unrelated to the woman who undergoes the pregnancy (egg donation, embryo donation, surrogacy). Where an association between the risk factor and outcome is entirely genetically mediated, we would expect to observe an association in families where the woman undergoes pregnancy and offspring are genetically related but not in those who are unrelated. Where genetic and environmental mediation both contribute, association will be observed be observed in genetically related and unrelated pairs. For example, if prenatal stress effects on offspring depressive symptoms were entirely genetically mediated, we would expect association between those variables in the homologous IVF and sperm donation groups but not in the other groups. The present research design will be used to examine differences in the pattern of association between specific intrauterine risk effects and children’s health and mental health related outcomes in future research (see Thapar et al., 2007)

Discussion

This report introduces a new study design involving families with children conceived through assisted reproductive technologies (ART). Through the use of this novel methodology it is now possible to not only disentangle genetic from early social environmental influences on development, but to disentangle intrauterine environmental effects from genetic effects in accounting for individual differences in development (see Thapar et al., 2007). Combined with developments in the area of molecular genetics and environmental assessment, this methodology offers a unique complement to the study of gene – environment interplay applicable to the areas of developmental psychology, psychiatric genetics and other areas of medicine, as well as for the area of prevention science. Using this novel research design, we have presented a synopsis of findings related to two primary research objectives: first, to examine whether there were differences in family relationship quality (interparental and parent-child relationship quality) and children’s symptoms of psychological distress among children living in ART households and those living in naturally-conceived households; second, to contrast a group of families where the parent was genetically related to the child with a group where the parent was not genetically related to the child to examine links between parent depressive symptoms, family relationship quality and child depressive symptoms. In addition, we outline how this research design may be used to disentangle intrauterine and genetic effects on children’s health and mental health related outcomes.

quality of relationships that children experience in ART compared to naturally conceived households. Most studies suggest no differences in general levels of couple satisfaction and the quality of the parent-child relationship (Weaver et al., 1993; Colpin et al., 1997) in ART households, some suggest lower levels of spouse satisfaction, particularly for husbands (Gibson et al., 2000b), others suggest higher relationship quality among ART couples (Golombok et al., 1995), with the same pattern of results observed for the parent-child relationship (Golombok et al., 1995, 2001). Results presented in this report suggest no differences in children’s symptoms of depression as reported by parents across ART households, with the same pattern observed for parent-reported levels of parent-child conflict across both groups. Interestingly, a significant difference was found for couple-reported levels of marital hostility between ART and natural conception households, with the latter group reporting lower levels of expressed hostility toward their partner. This is inconsistent with the view that relationship quality between couples in ART households is higher compared to natural conception households. Past research in this area has typically focused on the quality of relations between couples before, during and immediately following the period of pregnancy (Gibson et al., 2000b; Golombok 1995). Results from this study are among the very first to consider the quality of family relationships among an older group of children (4-10 years of age) born through ART and compared couple relationship quality between ART and natural conception households.

A number of differences were noted between ART subgroups. Specifically, the association between mother depression and mothers’ ratings of child depression was stronger in the homologous group compared to the sperm donation group. Significant differences were found between the sperm donation group and the IVF homologous group for the association between family relationship measures and children’s symptoms of psychological distress, suggesting a greater effect of disruption in family relationship on children’s symptoms when fathers are not genetically related to their children. No such differences were noted between the egg donation group and the homologous or sperm donation groups.

One of the distinct advantages of the present research design is the flexibility with which comparisons can be made in relation to child symptoms, family relationship quality and parent symptoms of psychopathology across groups of parents and children who are genetically related and genetically unrelated. While this possibility is present in animal studies (albeit to a limited degree) and adoption designs, the present study offers the unique opportunity to explore questions of gene-environment interplay using a constellation of genetically related and unrelated groupings in exploring the pattern of association between parent symptoms of depression, family relationship quality and children’s symptoms of psychological distress. Results from the present study suggest that mothers who are genetically related to their offspring report higher levels of child depression when compared to mothers who are not genetically related to their children. This poses an interesting question. Is this difference borne out of genetic effects linking mother and child depression, thereby facilitating a stronger magnitude of association in this group than mothers and children who are not genetically related; or is it a product of under-reporting of symptoms by mothers not genetically related to their children? This is a conceptually and methodologically important question and deserves further examination. Additional differences were apparent in the pattern of correlations linking family relationship factors with children’s symptoms across genetically related and genetically unrelated groups. Once again, effects were unique to fathers who were not genetically related to their children. In this group, the magnitude of association between mother depression and mother reports of child depression was significantly stronger than those where fathers were genetically related to their children. In addition, associations between mother-to-child hostility and both mother- and father-rated symptoms of child depression were stronger when fathers were not genetically related to their children than when fathers were genetically related to their children. This pattern of results again suggests susceptibility for children through disrupted family relationships when fathers, but not mothers, are not genetically related to their children. Overall, no other differences were apparent between genetically related and genetically unrelated groups.

Despite the novelty of findings presented in the present study, several limitations should be noted. First, the study design, while introducing a novel
methodology, remains at this stage a cross-sectional research design. Caution should therefore be exercised when inferring causality or hypothesised direction of effects linking parent psychopathology, family relationships and children’s symptoms. It is of course possible that children’s symptoms may operate to reduce family relationship quality, which in turn may further exacerbate children’s symptoms of psychological distress (see Bell, 1979). This possibility notwithstanding, a large volume of experimental and longitudinal research supports the direction of effects proposed in the present report (see Shelton & Harold, in press). Of course, longitudinal data would significantly improve confidence in the constellation of processes hypothesised in the present report. Second, all measures employed in the studies reviewed derive from parent reports across common measures of family relationships, parent symptoms and child symptoms. Because of the age of the children in the present study, it was necessary to rely on parent only reports. Method variance however may be a problem. Employing other informant or observational approaches to the assessment of family relationship quality and child and parent psychopathology in future studies of this type would significantly improve the confidence in relation to the interpretation of the pattern of associations derived.

One particularly noteworthy advantage of the present study design is the potential to disentangle intrauterine environmental influences from genetic effects in accounting for variation in children’s symptoms of psychological distress. Research over the past few decades has shown that many health-related and psychological conditions have their origins in early foetal experience (Rutter, Pickles, Murray, Eaves, 2001). This hypothesis has been examined directly in recent animal studies, where it is possible to randomly assign animals to conditions that allow exploration of intrauterine influences on development (Francis, Szegda, Campbell, Martin, Insel, 2003). Random allocation to differing intrauterine environments in human studies has, of course, not been possible; until now. The present study design directly provides a unique opportunity for exploring intrauterine influences on development, and most importantly, the opportunity to disentangle genetic from intrauterine effects in accounting for individual differences in development.

By effectively ‘unpacking’ genetic, intrauterine and early social environmental influences in studies of human development, significant opportunity will be accorded to the area of prevention science in allowing effective intervention and prevention programmes to be developed that target underlying mechanisms relating to individual differences in children’s normal and abnormal psychological development. The present study design significantly advances this objective.

References


**分离遗传与环境对儿童发展的影响：介绍一个新颖的研究方法**

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**摘 要**：本文介绍一个可以用于研究遗传与环境互动的新颖方法。此研究收集了上千个4~10岁儿童的数据。这些儿童的出生都借助于不同的辅助受孕技术(Assisted Reproductive Technologies)，包括试管婴儿、精子捐赠、卵子捐赠、胚胎捐赠及代孕技术。本项目通过妇科(助孕)医院收集被试的行为数据，包括家庭互动、养育方式、父母婚姻质量、家庭成员的心理健康及经济状况等。本文选择性地介绍一些分析的结果，以彰显这种设计在分离遗传和产前产后环境对儿童发展的贡献。首先，我们比较了“助孕”儿童与“自然孕”儿童在父母冲突、父母对子女敌意以及儿童抑郁症状之间关系的异同。其次，我们比较了这两组儿童在父母抑郁症状、家庭关系质量以及儿童抑郁症状之间关系的异同。再次，本文介绍了这一可分离遗传与环境因素的研究设计。最后，我们讨论了这一设计对发展心理病干预及预防的意义。

**关键词**：辅助受孕技术；家庭关系；遗传与环境互动

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