Development and Psychopathology **25** (2013), 37–50

doi:10.1017/S0954579412000880

SPECIAL SECTION ARTICLE

Examining the role of passive gene–environment correlation in childhood depression using a novel genetically sensitive design

FRANCES RICE,[a] GEMMA LEWIS,[b] GORDON T. HAROLD,[c] AND ANITA THAPAR[b]
[a]*University College London;* [b]*Cardiff University; and* [c]*University of Leicester*

Abstract

Parental depression is associated with disruptions in the parent–child relationship, exposure to stressful family life events, and offspring depressive symptoms. Evidence suggests that intergenerational transmission of depression involves environmental and inherited contributions. We sought to evaluate the role of passive gene–environment correlation (*r*GE) in relation to depression, family life events that were due to parental behavior, and parental positivity in a sample where children varied in genetic relatedness to their rearing parents. Our study included 865 families with children born through assisted conception (444 related to both parents, 210 related to the mother only, 175 related to the father only, and 36 related to neither parent). Consistent with previous studies, the intergenerational transmission of depressive symptoms was largely due to environmental factors, although parent and child gender influenced results. Maternal and paternal depressive symptoms were associated with reduced positivity and increased parentally imposed life events regardless of parent–child relatedness. Results of path analysis were consistent with passive *r*GE for both maternal and paternal positivity in that positivity partially mediated the link between maternal/paternal depression and child depression only in genetically related parent–child pairs. Results also suggested passive *r*GE involving parentally imposed life events for mothers and fathers although passive *r*GE effects were smaller than for positivity.

It is well established that the offspring of clinically depressed parents are more likely to exhibit depressive symptoms and depressive disorder than healthy comparison groups (e.g., Rice, Harold, & Thapar, 2002; Weissman et al., 2006). Similar findings have been reported in community studies examining depressive symptoms in parents and children (e.g., Connell & Goodman, 2002; Kane & Garber, 2004). It is widely accepted that the etiology of depression in young people is multifactorial, involving both genes and environment. Specific mechanisms implicated in the intergenerational transmission of depression include compromised parenting behavior and exposure to a stressful family environment. Many studies have shown that depression in a parent is associated with disruptions in the parent–child relationship and increased levels of stress in the domains of social relationships, finances, and employment (Hammen, Brennan, & Shih, 2004; Lovejoy, Graczyk, O'Hare, & Neuman, 2000). For instance, depressed mothers report feelings of rejection and hostility toward their children, perceive themselves to be less effective parents, and show elevated levels of negative and disengaged parenting (Downey & Coyne, 1990; Hammen et al., 1987; Lovejoy et al., 2000). Difficulties in the parent–child relationship are associated with child depressive symptoms in both cross-sectional and longitudinal studies (Branje, Hale, Frijins, & Meuus, 2010; Hale, Van der Valke, Akse, & Meuus, 2008; Hipwell et al., 2008; Jacobvitz, Hazen, Curran, & Hitchens, 2004; Stice, Ragan, & Randall, 2004). There is also a consistent link between social adversity and depression whereby recent stressful life events have been implicated in the onset of depression in adults (Kendler & Gardner, 2010; Kendler, Gardner, & Prescott, 2002, 2006) and young people (Goodyer, Cooper, Vize, & Ashby, 1993; Monroe, Rohde, Seeley, & Lewinsohn, 1999; Repetti, Taylor, & Seeman, 2002). Moreover, families where a parent is depressed are often exposed to chronic stressors in the form of financial and employment stress as well as stress in the

This project has been funded by a Wellcome Trust Showcase Award and a Wellcome Trust Project grant. We thank Val Russell for administrative support and Allyson Lewis for collecting antenatal data. Thanks also to the late Xiaojia Ge for contributions to the study design. We are extremely grateful to our collaborators at the following fertility centers: Assisted Conception Unit, St. James Hospital, Leeds; Assisted Reproduction Unit, Aberdeen University; Boston IVF, Boston; Bourn Hall Clinic; Bridgewater Hospital, Manchester; Cardiff Assisted Reproduction Unit; CARE at Sheffield Fertility Centre; Centre for Reproductive Medicine, University of Bristol; Centre for Reproductive Medicine, Walsgrave Hospital, Coventry; Childlessness Overcome Through Surrogacy; Clarendon Wing, Leeds General Infirmary; Cromwell IVF and Fertility Centre, London; Edinburgh Royal Infirmary; the Hewitt Centre for Reproductive Medicine Unit, Liverpool Women's Hospital; London Fertility and Gynaecology Centre; London Women's Clinic; Midland Fertility Services; St. Mary's Hospital Regional IVF; and DI Unit, Manchester. Finally, we thank all of the families who generously participated in this study.

Address correspondence and reprint requests to: Frances Rice, Department of Clinical, Educational, and Health Psychology, University College London, 26 Bedford Way, London WC1H 0AP, UK; E-mail: f.rice@ucl.ac.uk.

marital and parent–child relationships. Thus, it is possible that the children of parents with depressive disorder or depressive symptoms may develop psychopathology in part because of the stressful context of their lives.

One difficulty with disentangling genetic and environmental pathways involved in the intergenerational transmission of psychopathology is gene–environment correlation (*r*GE), which simply refers to the fact that genetic and environmental influences on a trait are correlated. Three types of *r*GE have been differentiated (passive, active, and evocative), which are described in detail elsewhere (Eaves, Last, Martin, & Jinks, 1977; Plomin, DeFries, & Loehlin, 1977; Plomin, DeFries, McClearn, & McGuffin, 2008; Scarr & McCartney, 1983). The focus of this report is on passive *r*GE. In brief, however, active and evocative *r*GE arise because the child's genetically influenced characteristics and behavior correlate with the environment that they "create," evoke, or select while passive *r*GE arises because parental genes are correlated with the environments they provide for their child, and those parental genes and environments in turn influence the child's trait. In most circumstances, parents provide both genes and environment for their children (Jaffee & Price, 2008; Plomin et al., 2008), which means that the rearing environment is correlated with genetic characteristics in the parental generation; and because parents pass genes on to their offspring, this is also the case in the child generation. Studies have shown that many environmental factors that have important risk effects on psychopathology in children, such as parenting style, parent–child affiliation, and stressful life events, are influenced by parents' heritable characteristics (Jaffee & Price, 2008; Reiss, Neiderhiser, Hetherington, & Plomin, 2000). Passive *r*GE can therefore be said to refer to the possibility that, in the parental generation, a seemingly environmental risk factor (e.g., family stress or parenting style) is a marker of parental genetic predisposition (e.g., to psychopathology or personality style), and these same genes are then expressed in the parent's offspring. Identifying whether passive *r*GE is present is important because it gives insight into the nature of the relationship between individuals and their social environments. Passive *r*GE has implications for whether environmental risk factors are likely to have true causal effects on offspring outcomes or are markers of genetic risk (Jaffee & Price, 2008; Lahey, D'Onofrio, & Waldman, 2009; Rutter, 2007; Thapar & Rutter, 2009). Evidence suggests that passive *r*GE does contribute to the association between environmental variables and childhood psychopathology: For instance, the association between maternal smoking in pregnancy and offspring conduct problems and attention-deficit/hyperactivity disorder has been shown to be due to genes shared between mother and child in an in vitro fertilization (IVF) design and in discordant sibling designs (D'Onofrio et al., 2008; Rice et al., 2009; Thapar et al., 2009). Passive *r*GE is particularly important to detect when genetic factors completely account for the relationship between the putative environmental factor and the child outcome. However, passive *r*GE may make a contribution to environment–psychopathology associations while not fully accounting for observed effects. Although the role of passive *r*GE in child and adolescent depression has not been well examined, there is converging evidence that it is likely to be important.

First, observations that depression in a parent is related to family functioning (Downey & Coyne, 1990; Goodman & Gotlib, 1999; Lovejoy et al., 2000), which in turn affects child depressive symptoms (Goodyer et al., 1993; Hipwell et al., 2008; Jacobvitz et al., 2004; Repetti et al., 2002), are consistent with the possibility that passive *r*GE may be involved in the generational transmission of depression. Studies have examined the genetic and environmental etiology of a range of factors, including parenting style and negative life events, which are thought to be involved in the development of depression, and found that genetic factors contribute (Kendler & Baker, 2007).

For instance, many studies have demonstrated that aspects of parenting style (e.g., warmth, positivity, negativity, and control) are influenced by genetic factors (Feinberg, Neiderhiser, Howe, & Hetherington, 2001; Kendler & Baker, 2007; McGue, Elkins, Walden, & Iacano, 2005; Neiderhiser et al., 2004). This therefore raises the possibility that parental genotype affects the kind of parenting provided (passive *r*GE) or that children's own behavior somehow evokes particular behaviors from parents (evocative *r*GE). One study used a combination of a sample of child twins and a sample of twin mothers to disentangle the contribution of passive and nonpassive (active and evocative) *r*GE (Neiderhiser et al., 2004). As described by Neiderhiser and colleagues, passive *r*GE indicates that "a parent's genetically influenced characteristic influences the way he/she treats the child independent of the characteristics of the child." In contrast, nonpassive *r*GE (active or evocative) occurs when parental behavior is at least partly due to the parent responding to genetically influenced characteristics of the child. Thus, child-based twin designs examine the role of genetic factors in the elicitation of parental behavior, and parent-based designs examine how inherited factors contribute to the provision of parental care (Kendler & Baker, 2007). Evidence for passive *r*GE would be found if, in the a study of twin parents, the "environmental" factor was influenced by genetic factors, while in a child-based twin design, univariate analysis of the environmental factor instead emerged as due to shared environmental factors (because both monozygotic and dizygotic twins share 50% of their genes with their parents, meaning that exposure to the putative environmental risk factor is not contingent upon twin zygosity in the child generation). Neiderhiser and colleagues examined maternal parenting behavior and found evidence supporting passive *r*GE for maternal positivity and monitoring (genetic influences in the twin mother sample and shared environmental influences in the child twin sample), while there was evidence of nonpassive *r*GE for maternal negativity and control (genetic influences in the child twin sample and environmental influences in the twin mother sample). Bivariate twin studies of child and adolescent depression and dimensions of parenting have also shown evidence of

*r*GE (though they do not distinguish between passive or non-passive types) in that shared genetic influences significantly contribute to associations between these putative environmental measures and child depression symptoms (Neiderhiser, Reiss, Hetherington, & Plomin, 1999; Pike, McGuire, Hetherington, Reiss, & Plomin, 1996).

Twin studies of stressful life events have also illustrated genetic influences (Kendler & Baker, 2007; Rice, Harold, & Thapar, 2003; Thapar & McGuffin, 1996) and shown that there is *r*GE between negative life events and depression (Rice et al., 2003; Thapar, Harold, & McGuffin, 1998). In general, genetic influences on stressful life events are thought to involve either active or evocative *r*GE, given observations that genetic contributions are greater for events that are controllable and dependent (where dependent is defined as probably attributable to the respondent's own behavior) than for those that are uncontrollable and independent (where independent is defined as probably unrelated to the respondent's own behavior; Kendler & Baker, 2007). In adults, recent evidence using a discordant identical twin design and propensity-score matching methods suggests, however, that dependent life events have modest causal environmental risk effects on depression when genetic factors are taken into account (Kendler & Gardner, 2010). However, with the exception of the specific life event of divorce (McGue & Lykken, 1992; Middeldorp, Cath, Vink, & Boomsma, 2005), *r*GE for life events experienced by children that are at least partly the result of parental behavior has not previously been examined.

Second, another important source of evidence to support the possibility that passive *r*GE may be operating for child and adolescent depression is the observation that twin, adoption, and other genetically informative studies of child and adolescent depression report contrasting findings. Passive *r*GE is thought to be removed in adoption studies, whereas in a classic twin design, passive *r*GE will tend to be subsumed within the heritability estimate (Jaffee & Price, 2007). Thus, if adoption studies show no evidence of genetic transmission while twin studies do show evidence of genetic contributions, this could suggest the role of passive *r*GE (although additional factors may contribute; see the Discussion Section). Although precise heritability estimates vary across different twin studies, twin studies *within* generations (e.g., of adults or of adolescents) generally report evidence of moderate genetic influence (Glowinski, Madden, Bucholz, Lynskey, & Heath, 2003; Rice, Harold, & Thapar, 2002; Sullivan, Neale, & Kendler, 2000) with heritability estimates of approximately 30% for both adults and adolescents. In contrast, results from adoption studies of child and adolescent depression show little evidence of significant genetic contributions (Eley, Deater-Deckard, Fombonne, Fulker, & Plomin, 1998; Tully, Iacono, & McGue, 2008; van den Oord, Boomsma, & Verhulst, 1994). All three adoption studies of childhood/adolescent depression have found evidence for the importance of environmental factors in the etiology of depression with only one reporting evidence that genetic factors also contributed to intergenerational transmission (Tully et al., 2008).

Other types of parent–offspring research design have implicated the importance of environmental factors in the intergenerational transmission of depression. Two independent studies have used the children of twins design to examine this question. The rationale of the children of twins design is that the offspring of adult identical (monozygotic) twins will be social cousins but genetic half siblings. To take the example of depression, if parental depression involves a genetically mediated risk to offspring, the risk should apply as much to the offspring of the monozygotic cotwin as to the children reared by the monozygotic twin with depression. In contrast, this will not apply to the same extent to the offspring of fraternal (duzygotic) twins because they share only 50% of their genes on average, whereas monozygotic twins share 100% of their genes. Two studies have used this approach and found evidence consistent with environmental transmission of depression within families (Silberg, Maes, & Eaves, 2010; Singh et al., 2011), and one found evidence of passive *r*GE (Silberg et al., 2010).

One study used an IVF design to examine the transmission of maternal depression to child internalizing problems (Lewis, Rice, Harold, Collishaw, & Thapar, 2011). In this design, parents differ in genetic relatedness to their children as a result of assisted reproductive technologies. That study found support for environmental transmission of depression although there was evidence that child gender may contribute to the generational transmission of maternal depression. Using the same IVF design, Harold and colleagues (2011) examined the intergenerational transmission of depression and tested the mediating role of parenting. That study reported that findings differed for mothers and fathers and according to the particular aspect of parenting measured. Measures of warmth and hostility were examined as potential mediators of the generational transmission of depression. In related mother–child pairs, maternal–child hostility partly mediated the relationship between maternal depression and child depression. However, in unrelated mother–child pairs, this mediated pathway was not present, potentially suggesting passive *r*GE since the effect was only observed when mothers were genetically related to their children. This same pattern was not seen for fathers, suggesting that it is important to examine associations separately according to parent gender. The importance of examining generational associations separately for mothers and fathers is emphasized by reports of stronger deleterious effects of maternal depression in younger children compared to greater associations of paternal depression with adolescent psychopathology (Connell & Goodman, 2002). In addition, there is a relative paucity of research examining the effects of paternal depression (Ramchandani & Psychogiou, 2009) as well as reports that child outcomes are partly dependent on both parent and child gender (Davis & Windle, 1997; Ramchandani & Psycholgiou, 2009).

In this study, we use the same IVF research design mentioned previously, where mothers and fathers differ in genetic relatedness to their children as a result of assisted reproductive technologies, in order to examine passive *r*GE. We examine

passive *r*GE for two measured variables (stressful life events and parental positivity) thought to be important in the etiology of childhood and adolescent depression. We also distinguish between two types of stressful life events: life events dependent on parental behavior, where passive *r*GE might be expected to be present, and life events independent of parental behavior, where passive *r*GE should not be present. Here we aim to extend previous work by testing a number of specific predictions about the role of passive *r*GE in child depression. We examined intergenerational transmission of maternal and paternal depression separately. We also examined whether patterns of association differed by child gender, given previous suggestions that this may be important (Lewis et al., 2011). If passive *r*GE is present, we would expect to observe the following patterns of association:

1. Parental depression will be associated with measured aspects of the caregiving environment (parental positivity and parentally imposed life events) regardless of parent–child relatedness.
2. Associations between aspects of the caregiving environment (positivity and parentally imposed life events) and child depression will be stronger when parent and child are genetically related.
3. Measured aspects of the caregiving environment will mediate the association between parental and child depression only when parent and child are genetically related.

Method

Sample

Families who had a live birth between 1994 and 2002 after successful IVF treatment were recruited from 19 UK clinics and one US clinic. Children included in this report were conceived via one of four IVF methods: homologous IVF (genetically related to both parents), sperm donation (genetically related to mother only), egg donation (genetically related to father only), or embryo donation (genetically related to neither parent). All gamete donors were unrelated to parents. One child from each family participated. Parents were invited to report only on the index child for whom information on the method of conception was available. In the case of multiple births, parents were asked to report on the firstborn child only. Data were collected by postal questionnaires from mothers and fathers.

Responses were received from 852 families (852 mothers, 592 fathers). The numbers in each conception group were as follows: homologous IVF (436 mother reports, 307 father reports), sperm donation (208 mother reports, 148 father reports), egg donation (173 mother reports, 115 father reports), and embryo donation (35 mother reports, 22 father reports). Comparisons with UK national norms show that this sample does not differ from the general population in terms of psychological adjustment and that there are minimal differences between the conception groups (Rice et al., 2010; Shelton et al., 2009). Children were aged 4–10 years (mean = 6.7 years), mothers were aged 28–62 years (mean = 41.72 years), and fathers were aged 21–76 years (mean = 44.6 years). The majority of children (91%) resided with both parents.

Measures

Parent depressive symptoms

Mothers and fathers completed the seven-item depression subscale of the Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983). Internal consistency was good for both mother and father reports ($\alpha = 0.75$ for mothers, $\alpha = 0.76$ for fathers). Scores range from 0 to 21, with higher scores representing greater depressive symptoms, and clinical cut-points have been validated (Bjelland, Dahl, Haug, & Neckelmann, 2002).

Child depressive symptoms

Mothers and fathers completed the shortened version of the Mood and Feelings Questionnaire about their child's depressive symptoms (Angold et al., 1995). This is a 13-item questionnaire that assesses the presence and severity of *Diagnostic and Statistical Manual of Mental Disorders* (3rd edition, revised) symptoms with items rated on a 3-point scale. It is recommended as a screening questionnaire for depression in nonclinical populations (National Institute for Clinical Excellence, UK, 2005) and is well validated (Angold et al., 1995). Internal consistency was good ($\alpha = 0.78$ for mothers, $\alpha = 0.79$ for fathers).

Stressful life events

Mothers and fathers completed a 35-item checklist (Johnson & McCutcheon, 1980) about the occurrence of a range of significant family life events in the past 12 months. Maternal and paternal responses were combined such that if one parent endorsed a life event as having occurred it was deemed present. This approach has been used in previous research and has been found to result in more accurate estimates of exposure to adversity than single informant measures (Gest, Reed, & Masten, 1999). Two scores were calculated: 8 items reflected parentally imposed recent life events and 6 items reflected negative independent life events that were likely to have been outside either the parent or the child's control. Items included in the parentally imposed life events composite were (a) parents divorced or separated, (b) increased quarreling between parents, (c) father away from home more often, (d) mother away from home more often, (e) parent getting into trouble with the police, (f) mother going back to work or starting work for the first time, (g) mother losing job, and (h) father losing job. The maternally imposed life events composite score omitted items (a) and (c), which were clearly due to paternal behavior, and the paternally imposed life events

composite score omitted items (d), (f), and (g), which were clearly due to maternal behavior. Items included in the negative independent life events composite were of a more serious nature: (a) serious illness or injury to parent, brother, or sister; (b) death of parent, brother, or sister; (c) death of grandparent; (d) death of a close friend; (e) serious illness or injury in a close friend; and (f) death of pet.

Parental positivity

Mothers and fathers completed the Parental Affiliative Style Questionnaire (Davies et al., 2002; Rohner, 1984). This is a 12-item scale that measures the level and quality of parental engagement with the child and assesses three dimensions of parental positivity: verbal positivity (e.g., I say nice things to my child), positive engagement (e.g., I enjoy having my child around me), and parental warmth (e.g., I talk to my child in a warm and affectionate way). We use the term parental positivity throughout given that this measure indexes both positive parental affect and positive parental behaviors. Items are scored on a 4-point scale ranging from *almost always true* to *almost never true*, with low scores representing greater levels of warmth. Internal consistency of the scale was good (mothers $\alpha = 0.78$, fathers $\alpha = 0.86$).

Statistics and analytical approach

Path analysis was used for primary analyses. Correlation coefficients between parent and offspring depressive symptoms and between parent depressive symptoms and measures of the caregiving environment were first calculated separately in related and unrelated parent–child dyads. Potential mediation of the association between parent depression and child depression by the measured environmental factors was examined using the path analysis model outlined in Figure 1. The significance of indirect paths linking parental and child depressive symptoms via parental positivity (paths C and E) were tested while controlling for the effect of parental depression on parentally imposed life events and vice versa. The difference in the magnitude of paths via positivity and life events (Figure 1) in related and unrelated groups was evaluated using stacked modeling procedures. This involves comparison of the chi-square (χ^2) statistic derived from a model where a specific pathway is treated as equivalent across groups to that derived from a model where the path in each subgroup model (related or unrelated) is allowed to freely vary. The magnitude of difference per degree of freedom change in these χ^2 statistics provides an estimate of the significance of the difference between related and unrelated parent–child pairs. In order to address potentially inflated correlations due to shared method variance, cross rater associations were examined where mothers and fathers reported on their own depressive symptoms and the other parent reported on child symptoms. Therefore, only two-parent families were included in the analyses presented. Child depressive symptoms were adjusted for age and gender by regressing depressive symptoms on age and gender and analyzing the unstandardized residuals. Where analyses were carried out separately for boys and girls, age was adjusted for in the same way.

In the related group, association between parent and child variables can be due to both genetic and environmental factors. In the unrelated group, association can only be due to environmental factors. Therefore, if association is seen in *both* related and unrelated pairs, this suggests environmental factors underlie the association. In contrast, if association is seen *only* in the related group (and not in the unrelated group), this suggests that genetic factors account for the association. Where both genetic and environmental factors contribute, the association will be present in both groups but greater in the genetically related parent–child dyads. A significant difference in the magnitude of an association in related and unrelated groups would indicate that genes predominantly account for the association. For instance, a significant group difference in the association between parent depression and child depression via parental positivity would indicate that association was due predominantly to parental genotype. However, as discussed above, passive *r*GE can exist in cases where it fully accounts for an association and in cases where it only partly accounts for an association. Thus, a significant group difference in association for related and unrelated pairs is not necessary to show the presence of passive *r*GE but rather to show that passive *r*GE dominates the observed association.

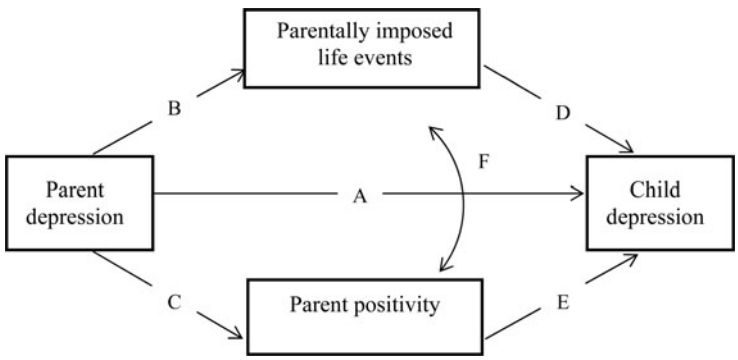

Figure 1. The path analysis model.

Results

Descriptives

Conception group differences for key study variables were examined through one-way analysis of variance with child gender and age included as covariates. There were no significant differences according to relatedness group for any of the variables examined (all Fs < 2.78, all ps $>.10$). Means and standard deviations are shown in Table 1.

Correlational analysis

Intergenerational similarity. Table 2 illustrates correlations between key study variables according to parent–child relatedness separately for mothers and fathers. Results of analyses suggest that the intergenerational similarity of depression is largely due to environmental factors, given that associations are similar when mothers and fathers are unrelated to their children as described previously (Harold et al., 2011; Lewis et al., 2011; related mother–child pairs $r = .177$, $p < .001$; unrelated mother–child pairs $r = .274$, $p < .001$; related father–child pairs $r = .188$, $p < .001$; unrelated father–child pairs $r = .147$, $p = .06$).

Partial correlations examining the association between parent–child depression, adjusting for the other parent's depressive symptoms, were calculated. In line with previous studies (Silberg et al., 2010), we assume that assortative mating for depression is based on the measured phenotype for the trait. These partial correlations also attempt to adjust for shared reporter variance (e.g., between maternal depression and mother-rated child depression). Adjusting for assortative mating did not alter results substantially for mothers (related partial $r = .117$, $p = .02$; unrelated partial $r = .206$, $p = .02$), but the association for unrelated fathers was attenuated and nonsignificant when maternal depression symptoms were adjusted for (related fathers partial $r = .139$, $p = .005$; unrelated fathers partial $r = .069$, $p = .381$).

Parent depression and the caregiving environment

Correlations in Table 2 show that maternal and paternal depressive symptoms were significantly associated with reduced positivity toward the child regardless of genetic relatedness (related mother–child pairs $r = –.371$, $p < .001$; unrelated mother–child pairs $r = –.187$, $p < .05$; related father–child pairs $r = –.333$, $p < .001$; unrelated father–child pairs $r = –.381$, $p < .001$). Maternal and paternal depressive symptoms were also correlated with parentally imposed life events in all groups with the exception of unrelated mother–child pairs (related mother–child pairs $r = .111$, $p < .05$; unrelated mother–child pairs $r = .061$, $p > .1$; related father–child pairs $r = .159$, $p < .001$; unrelated father–child pairs $r = .228$, $p < .01$). Negative independent life events reported to have been experienced by the child were not associated

Table 1. *Means (standard deviations) for genetically related and unrelated mother–child and father–child pairs*

	Parent Depression	Parentally Imposed Life Events	Independent Life Events	Parent Positivity	Child Depression (Adj. for Child Age and Gender, Oppos. Parent Report)
	Mean (*SD*)	Mean (*SD*)	Mean (*SD*)	Mean (*SD*)	Mean (*SD*)
Related mother–child pairs ($N = 435$)	4.21 (3.11)	0.32 (0.56)	0.48 (0.70)	46.89 (1.83)	0.08 (2.92)
Unrelated mother–child pairs ($N = 134$)	4.51 (3.01)	0.20 (0.53)	0.60 (0.78)	46.90 (1.79)	−0.27 (2.52)
Related father–child pairs ($N = 398$)	3.85 (3.13)	0.25 (0.55)	0.50 (0.73)	46.05 (2.82)	−0.19 (2.70)
Unrelated father–child pairs ($N = 163$)	3.85 (2.73)	0.33 (0.59)	0.51 (0.69)	46.26 (2.70)	−0.01 (3.17)
					Child Depression (Adj. for Child Age, Oppos. Parent Report)
					Mean (*SD*)
Related mother–daughter pairs	4.16 (2.94)	0.29 (0.56)	0.50 (0.69)	47.05 (1.63)	−0.06 (2.76)
Related mother–son pairs	4.26 (3.30)	0.36 (0.61)	0.46 (0.70)	46.71 (2.02)	0.11 (3.10)
Unrelated mother–daughter pairs	4.24 (3.02)	0.20 (0.55)	0.72 (0.82)	47.19 (1.46)	−0.07 (2.64)
Unrelated mother–son pairs	4.85 (3.00)	0.20 (0.51)	0.47 (0.70)	46.55 (2.09)	−0.50 (2.38)
Related father–daughter pairs	3.95 (3.28)	0.21 (0.48)	0.52 (0.72)	46.07 (2.82)	−0.32 (2.49)
Related father–son pairs	3.76 (2.97)	0.29 (0.61)	0.49 (0.74)	46.02 (2.81)	−0.05 (2.90)
Unrelated father–daughter pairs	3.67 (2.48)	0.32 (0.59)	0.58 (0.75)	46.38 (2.54)	−0.27 (3.08)
Unrelated father–son pairs	4.10 (3.05)	0.33 (0.59)	0.40 (0.58)	46.09 (2.94)	0.35 (3.28)

Table 2. *Correlations for genetically related and genetically unrelated mother–child and father–child pairs*

	Related					Unrelated				
	Mother–Child Pairs ($N = 435$)					Mother–Child Pairs ($N = 134$)				
	1	2	3	4	5	1	2	3	4	5
Mother depression	—					—				
Parentally imposed life events	.111*	—				.061	—			
Independent negative life events	.070	.147**	—			.136	.195*	—		
Mother positivity	−.371***	−.028	−.007	—		−.187*	−.035	−.050		
Child depression (adj. for child age and gender, oppos. parent report)	.177***	.115*	−.026	−.197***	—	.274***	.201*	.181*	−.147†	—
	Father–Child Pairs ($N = 398$)					Father–Child Pairs ($N = 163$)				
	1	2	3	4	5	1	2	3	4	5
Father depression	—					—				
Parentally imposed life events	.159***	—				.228**	—			
Independent negative life events	.151***	.226***	—			−.083	.153†	—		
Father positivity	−.333***	−.206***	−.099*	—		−.381***	−.244**	.035		
Child depression (adj. for child age and gender, oppos. parent report)	.188***	.194***	.126*	−.189***	—	.147†	.078	-.019	−.140†	—

†$p < .1$. *$p < .05$. **$p < .01$. ***$p < .001$.

with maternal or paternal depression, the exception being genetically related father–child pairs ($r = .151$, $p < .01$).

Associations between the caregiving environment and child depression

As an initial indication of passive *r*GE, correlations between the caregiving environment and child depression were examined in related and unrelated parent–child dyads. For both maternal and paternal positivity, there was some indication of passive *r*GE, given that the association with child depression was attenuated in unrelated parent–child pairs (related mothers $r = –.197$, $p < .001$; unrelated mothers $r = –.147$, $p < .1$; related fathers $r = –.189$, $p < .001$; unrelated fathers $r = –.140$, $p < .1$). For parentally imposed life events and child depression, there was no evidence of passive *r*GE for mothers, in that associations were present in related ($r = .115$, $p < .05$) and unrelated ($r = .201$, $p < .05$) mother–child pairs. For fathers the association was slightly greater in related ($r = .194$, $p < .001$) than unrelated ($r = .078$, $p > .1$) father–child pairs. For independent negative life events, as expected, there was no clear pattern of association contingent upon parent–child genetic relatedness.

Child gender

Correlations by parent and child gender are shown in Table 3 and Table 4. The contribution of genetic and environmental processes to the intergenerational transmission of depression differed by both parent and child gender. Mother–son transmission was only significant in related mothers and sons (related $r = .157$, $p < .05$; unrelated $r = .048$, $p > .1$). However, this pattern of results was not seen for father–son transmission with environmental factors contributing (related father–son pairs $r = .227$, $p < .001$; unrelated father–son pairs $r = .251$, $p < .05$). Mother–daughter transmission was present in both relatedness groups, implying environmental processes as previously reported (Lewis et al., 2011; related $r = .200$, $p < .01$; unrelated $r = .454$, $p < .001$). Father–daughter transmission was present only in related father–daughter pairs (related $r = .153$, $p < .05$; unrelated $r = .042$, $p > .1$). Thus, environmental factors appeared to contribute in same-sex parent–child pairs.

Path analysis

Table 5 presents results from path analysis (Figure 1) carried out separately in related and unrelated parent–child pairs. Standardized path coefficients are presented, which are interpreted in the same way as standardized regression coefficients (see Bollen, 1989).

Maternal positivity

For genetically related mother–child pairs, significant paths were found between maternal depression and maternal positivity (path C, $\beta = –0.37$, $p < .01$). Maternal positivity was also significantly associated with child depression (path E, $\beta = –0.15$, $p < .05$). The correlation between maternal positivity and parentally imposed life events was nonsignificant (path F, $\beta = 0.01$). There was also a significant direct path linking

Table 3. *Correlations for genetically related and genetically unrelated mother–daughter and mother–son pairs*

	Genetically Related					Genetically Unrelated				
	Mother–Daughter Pairs ($N = 227$)					Mother–Daughter Pairs ($N = 74$)				
	1	2	3	4	5	1	2	3	4	5
Mother depression	—					—				
Parentally imposed life events	.087	—				.069	—			
Independent negative life events	.003	.093	—			.350***	.252*	—		
Mother positivity	−.393***	−.064	−.080	—		−.241*	−.049	.080		
Child depression (adj. for child age, oppos. parent report)	.200**	.127†	−.037	−.302***	—	.454***	.396***	.389***	−.116	—
	Mother–Son Pairs ($N = 208$)					Mother–Son Pairs ($N = 60$)				
	1	2	3	4	5	1	2	3	4	5
Father depression	—					—				
Parentally imposed life events	.131†	—				.053	—			
Independent negative life events	.135†	.205**	—			−.127	.113	—		
Father positivity	−.355***	.011	.051	—		−.119	−.025	−.248†		
Child depression (adj. for child age, oppos. parent report)	.157†	.102	−.014	−.113	—	.048	−.084	−.174	−.214	—

†$p < .1$. *$p < .05$. **$p < .01$. ***$p < .001$.

Table 4. *Correlations for genetically related and genetically unrelated father–daughter and father–son pairs*

	Genetically Related					Genetically Unrelated				
	Father–Daughter Pairs ($N = 199$)					Father–Daughter Pairs ($N = 96$)				
	1	2	3	4	5	1	2	3	4	5
Father depression	—					—				
Parentally imposed life events	.142*	—				.147	—			
Independent negative life events	.179*	.191**	—			−.098	.117	—		
Father positivity	−.289***	−.180*	−.119†	—		−.449***	−.378***	.078	—	
Child depression (adj. for child age, oppos. parent report)	.153*	.132†	.029	−.163†	—	.042	.163	−.054	−.185†	—
	Father–Son Pairs ($N = 199$)					Father–Son Pairs ($N = 67$)				
	1	2	3	4	5	1	2	3	4	5
Father depression	—					—				
Parentally imposed life events	.182**	—				.328**	—			
Independent negative life events	.121†	.260***	—			−.041	.229†	—		
Father positivity	−.384***	−.229***	−.079	—		−.309*	−.079	−.048		
Child depression (adj. for child age, oppos. parent report)	.227***	.234***	.209**	−.212**	—	.251*	−.036	.070	−.081	—

†$p < .1$. *$p < .05$. **$p < .01$. ***$p < .001$.

maternal depression and child depression (path A, $\beta = 0.11$, $p < .05$). Thus direct and indirect paths through maternal positivity were observed for genetically related mother–child pairs.

In genetically unrelated mother–child pairs, a significant path was again found between maternal depression and maternal positivity (path C, $\beta = –0.19$, $p < .05$); however, there was no significant path between maternal positivity and child depression (path E, $\beta = –0.09$, $p > .10$). Thus, maternal positivity partially mediated the link between maternal depression and child depression only in genetically related mother–child

Table 5. *Results of path analysis for the model outlined in Figure 1*

	Genetically Related		Genetically Unrelated	
	Mothers	Fathers	Mothers	Fathers
	β	β	β	β
A: path from parent depression to child depression	0.11*	0.13*	0.25*	0.10
B: path from parent depression to life events	0.11*	0.16*	0.06	0.29*
C: path from parent depression to positivity	−0.37**	−0.33**	−0.19*	−0.38**
D: path from life events to child depression	0.10*	0.15*	0.18*	0.03
E: path from positivity to child depression	−0.15*	−0.12*	−0.09	−0.09
F: correlation between life events and positivity	−0.01	−0.15*	−0.02	−0.13
	Mother–Daughter	Father–Daughter	Mother–Daughter	Father–Daughter
	β	β	β	β
A: path from parent depression to child depression	0.09	0.15*	0.43**	−0.05
B: path from parent depression to life events	0.09	0.14	0.07	0.15
C: path from parent depression to positivity	−0.39**	−0.29**	−0.24*	−0.45**
D: path from life events to child depression	0.10	0.13	0.37*	0.11
E: path from positivity to child depression	−0.26**	−0.16	0.01	−0.17
F: correlation between life events and positivity	−0.03	−0.14*	−0.03	−0.31*
	Mother–Son	Father–Son	Mother–Son	Father–Son
	β	β	β	β
A: path from parent depression to child depression	0.12*	0.15*	0.04	0.28*
B: path from parent depression to life events	0.13*	0.18*	0.05	0.33*
C: path from parent depression to positivity	−0.35**	−0.38**	−0.12	−0.31*
D: path from life events to child depression	0.09	0.18*	−0.08	−0.09
E: path from positivity to child depression	−0.07	0.11	−0.21	0.00
F: correlation between life events and positivity	−0.06	−0.16*	−0.05	−0.02

*$p < .05$. **$p < .01$.

pairs, which is consistent with passive *r*GE. The significance of the indirect path linking maternal depression to child depression via positivity was assessed. This indirect path was significant for related ($\beta = 0.06$, $p < .01$) but not unrelated ($\beta = 0.02$, $p > .1$) mother–child pairs. Stacked modeling procedures also showed that the pathway between maternal depression and maternal positivity was significantly greater in related than unrelated mother–child pairs ($\Delta df = 1$, $\Delta\chi = 3.63$, $p < .05$), although the magnitude of other parameter estimates for pathways shown in Figure 1 did not differ significantly between related and unrelated mother–child pairs.

Paternal positivity

In genetically related fathers, paternal depression was associated with paternal positivity (path C, $\beta = –0.33$, $p < .01$). The correlation between life events and positivity was also significant (path F, $\beta = –0.15$, $p < .05$). Paternal positivity significantly influenced child depression (path E, $\beta = –0.12$, $p < .05$). Finally, the direct path between paternal and child depression was significant (path A, $\beta = 0.13$, $p < .05$). Thus, there was evidence that paternal positivity partly explained the link between father and child depression in the related group. In genetically unrelated father–child pairs, paternal depression was associated with paternal positivity (path C, $\beta = –0.38$, $p < .01$). However, paternal positivity did not influence child depression (path E, positivity $\beta = –0.09$). The correlation between parentally imposed life events and positivity was non significant (path F, $\beta = –0.13$), and there was no significant direct path between father and child depression (path A, $\beta = 0.10$). Consistent with this, the indirect path linking paternal depression and child depression via paternal positivity was significant only in the related group (related $\beta = 0.04$, $p < .05$; unrelated $\beta = 0.03$, $p > .1$).

However, stacked modeling procedures showed no significant differences in the magnitude of parameter estimates between related and unrelated father–child pairs.

Parentally imposed life events and maternal depression

For genetically related mother–child pairs, significant paths were found between maternal depression and parentally imposed life events (path B, $\beta = 0.11$, $p < .05$). Parentally imposed life events were also significantly associated with child depression (path D, $\beta = -0.10$, $p < .05$). However, the indirect effect via parentally imposed life events fell short of significance ($\beta = 0.01$, $p > .1$). In genetically unrelated mother–child pairs, maternal depression did not influence parentally imposed life events (path B, $\beta = 0.06$, $p > .10$), but parentally imposed life events did influence child depression (path D, $\beta = 0.18$, $p < .05$) and the indirect path was not significant ($\beta = 0.01$, $p > .1$). The correlation between parentally imposed life events and maternal positivity was nonsignificant in both related and unrelated mother–child pairs. Finally, there was a significant direct path linking maternal depression and child depression in unrelated mother–child pairs (path A, $\beta = 0.25$, $p < .05$). Thus, an indirect pathway from maternal depression to child depression via parentally imposed life events was observed only in the related mother–child pairs, consistent with passive *r*GE. However, the indirect path was small, and formal testing revealed it was not significant in related or unrelated mother–child pairs.

Parentally imposed life events and paternal depression

In genetically related fathers, paternal depression was associated with parentally imposed life events (path B, $\beta = 0.16$, $p < .05$). Life events in turn influenced child depression (path D, $\beta = 0.15$, $p < .05$). In genetically unrelated father–child pairs, paternal depression was associated with parentally imposed life events (path B, $\beta = 0.29$, $p < .05$) but did not influence child depression (path D, life events $\beta = 0.03$; path E, positivity $\beta = -0.09$). The indirect path via life events showed a trend toward significance for the related fathers ($\beta = 0.02$, $p < .1$) but no significant association in the unrelated fathers ($\beta = 0.01$, $p > .1$). To summarize, consistent with results for mothers, both paternal positivity and parentally imposed life events partially mediated the link between paternal depression and child depression only in genetically related father–child pairs, which is consistent with passive *r*GE. Paternally imposed life events were associated with a significant reduction in paternal positivity only in genetically related fathers.

Independent negative life events

As expected, there was no evidence that negative independent life events mediated the association between parental depression and child depression in either related or unrelated parent–child pairs (results available from first author).

Child gender. Path analysis was carried out separately by parent and child gender (Table 5). Correlations separated by parent and child gender are presented in Tables 3 and 4. In general, the pattern of correlations did not show large differences in the association between parent depression and parent positivity according to child gender, with similar results for boys and girls separately to that observed in the full sample (Tables 3 and 4). The pattern of association between parental positivity and child depression and between parentally imposed life events and child depression did not differ markedly by child gender. Results of path analyses showed evidence of greater passive *r*GE for same-sex parent–offspring pairs. For fathers, there was evidence of passive *r*GE via parentally imposed life events for father–son transmission only (related father–son pairs, path B, $\beta = 0.18$, $p < .05$; path D, $\beta = 0.18$, $p < .05$; related father–daughter pairs, path B, $\beta = 0.14$, $p > .1$; path D, $\beta = 0.13$, $p > .1$). Nevertheless, there was also a direct path between paternal depression and son depression in both related and unrelated father–son pairs, which indicates that passive *r*GE with life events did not fully account for intergenerational transmission. For mothers, there was evidence of passive *r*GE via maternal positivity for mother–daughter pairs only. For genetically related mother–daughter pairs, there was an indirect effect of maternal depression on child depression via maternal positivity (path C, $\beta = -0.39$, $p < .01$; path E, $\beta = -0.26$, $p < .01$), whereas this indirect effect was not observed in genetically related mother–son pairs (path C, $\beta = -0.35$, $p < .01$; path E, $\beta = 0.01$, $p > .1$). This indirect path was not present in unrelated mother–daughter or mother–son pairs. This result is therefore consistent with greater passive *r*GE for mother–daughter pairs than for mother–son pairs. There was no evidence of significant intergenerational transmission through the hypothesized pathways (Figure 1) in father–daughter or mother–son pairs.

Discussion

This study utilized a sample of children who differed in degree of genetic relatedness to their rearing parents as a result of assisted reproductive technologies in order to examine passive *r*GE for child depression. We examined the intergenerational transmission of depressive symptoms and tested for passive *r*GE with parentally imposed life events and parental positivity.

Intergenerational similarity

Intergenerational similarity of depressive symptoms was largely due to environmental factors, in that associations were present in both related and unrelated parent–child dyads. This finding is consistent with a previous study of this cohort that examined child internalizing symptoms as an outcome measure (Lewis et al., 2011) and with two previous studies that used a children of twins design (Silberg et al., 2010; Singh et al., 2011). The similarity of findings across studies with differing age ranges of participants and different mea-

surements of depression is noteworthy and affords greater confidence in results as they converge across study designs, measurements, and age groups.

We then examined whether environmental transmission differed according to child gender and found evidence for genetic contributions to mother–son transmission consistent with a previous analysis of this sample (Lewis et al., 2011). However, no genetically sensitive study to date has examined father to child transmission separately for boys and girls. Here, we found evidence to support a greater environmental contribution to father–son than father–daughter transmission. This finding of reduced environmental transmission for opposite-sex parent–child pairs seems likely due to either passive *r*GE or rater effects. There are at least two plausible biological explanations for gender differences in genetic transmission: (a) qualitative sex differences (i.e., different sets of genes influence the phenotype in males and females) or (b) quantitative sex differences (i.e., genes influence the phenotype to different extents in males and females). The first type of explanation would have the effect of increasing genetic influences in same-sex compared to opposite-sex parent–child dyads, which is opposite to the pattern we observed. The second explanation would have the effect of increasing genetic effects in, for instance, boys compared to girls. Although we do observe a greater genetic contribution for opposite-sex parent–child pairs, this is not consistently observed for a single child gender (e.g., boys). Given that girls and boys inherit an equal proportion of maternal and paternal genes, our observed pattern of results does not seem to be biologically plausible. Instead, it seems likely that this result is attributable to passive *r*GE, rater effects, or chance. Results of path analysis were not consistent with greater passive *r*GE via parental positivity and/or parentally imposed life events for opposite-sex parent–child pairs. Although we attempted to take shared method variance into account in our intergenerational similarity analysis by using the opposite parent to report on the child's symptoms, it is known that mother and father ratings of child psychopathology are influenced by different parent and offspring characteristics (Hay et al., 1999), and mother and father ratings of child psychopathology are not completely independent of each other. Thus, it is possible that some kind of rater effect may explain the pattern of greater environmental transmission observed for same-sex parent–offspring pairs. Finally, because separate analyses by child gender and by parent–offspring relatedness included small sample sizes, we cannot rule out the possibility that this is a chance finding and it merits attention in additional types of genetically sensitive designs. Additional work is needed to identify the specific environmental factors that contribute to the intergenerational transmission of depression.

Passive rGE

We expected to observe the following pattern of association if passive *r*GE was present. Parental depression would be associated with measured aspects of the caregiving environment regardless of the child's genetic characteristics, associations between aspects of the caregiving environment and child depression would be stronger when parent and child are genetically related, and measured aspects of the caregiving environment would mediate the association between parental and child depression only when parent and child are genetically related.

Parental positivity

Maternal positivity. Maternal depression was associated with reductions in maternal positivity to child regardless of parent–child relatedness. There was evidence of passive *r*GE from correlations and path analysis conducted separately in related and unrelated mother–child pairs. Correlations between maternal positivity and child depression were greater in related compared to unrelated mother–child pairs. Consistent with passive *r*GE, results of path analysis showed an indirect path linking maternal and child depression via maternal positivity that was present only in related mother–child pairs. Formal testing of the significance of the indirect path from maternal depression via reduced positivity to child depression showed that this was significant only in genetically related mother–child pairs. The path linking maternal depression and positivity was also significantly greater in related than unrelated mother–child pairs. There was also evidence that this passive *r*GE via maternal positivity was greater for mother–daughter pairs than for mother–son pairs.

Paternal positivity. Results were very similar to those observed for maternal positivity. Paternal depression was associated with reduced positivity regardless of the father's genetic relatedness to the child. Paternal positivity influenced child depression more strongly in related father–child pairs than in unrelated father–child pairs although there was a trend toward association in the unrelated pairs, which implies that this association is not entirely due to passive *r*GE. Results of path analysis indicated that paternal positivity partially mediated the link between paternal depression and child depression only in related father–child pairs, and this indirect path was significant only in related father–child pairs. Thus, there was evidence of a contribution of passive *r*GE for paternal positivity, although it did not fully account for the association between paternal and child depression (as there was still a significant direct path from parent to child depression, consistent with the results for mothers). The indirect path between paternal depression and child depression via paternal positivity was nonsignificant when analyses were run separately by child gender.

Parentally imposed life events

There was evidence that passive *r*GE made a contribution to the link between parent depression, parentally imposed life events, and child depression for both mothers and fathers with evidence of a stronger effect in father–child pairs. When analyses were run separately by child gender, this was only significant for father–son transmission. The correlation

between parentally imposed life events and positivity was significant only in fathers, so it is also possible that stressful life events may have a greater influence on expressed positivity to children in fathers than in mothers. Nevertheless, it is important to note that the contribution of passive *r*GE via life events was smaller than that observed for parental positivity (indirect effects of parent depression on child depression via parentally imposed life events fell short of statistical significance in related mother and related father–child pairs). This is consistent with evidence that stressful life events exert a modest causal effect on depression when genetic influences on life event exposure are taken into consideration (Kendler & Gardner, 2010).

The present study used a genetically sensitive design that made it possible to disentangle inherited and environmental contributions to the intergenerational transmission of depression. Very few types of study design are able to address questions of genetic and environmental contributions to intergenerational transmission processes. Nevertheless, there are a number of limitations and issues in this study that warrant discussion. In this study, we examined *r*GE and did not consider the possibility of gene–environment interaction. Children may differ in genetic susceptibility to the same environmental risk, and it should be recognized that *r*GE and gene–environment interaction may not be independent and may simultaneously influence risk for depression (Eaves, Silberg, & Erkanli, 2003).

One of the reasons we outlined for examining passive *r*GE for depression is the discrepancy between findings from twin and adoption studies. However, differences in the results of twin and adoption studies could also be attributable to factors other than passive *r*GE. In particular, twin studies compare siblings of exactly the same age whereas adoption studies do not, thus any developmental differences in the etiology and phenomenology of depression will be controlled for in twin but not adoption studies. Thus, if there were genetic heterogeneity between childhood and adult depression, this would affect the ability of a parent–offspring adoption design to detect significant genetic influences. Longitudinal twin studies do suggest that genetic influences on depression differ between childhood, adolescence, and adulthood (Kendler, Gardner, & Lichenstein, 2008; Lau & Eley, 2006; Scourfield et al., 2003). Thus, it is possible that genetic heterogeneity between generations could make it difficult to detect genetic transmission. A limitation of our study is that we focused on a restricted set of family variables that might not be capturing either those constructs that are mediating risk through environmental mechanisms or those that most strongly contribute to passive *r*GE. For example, alternative variables that might be tested in the future could include measures that assess modeling of parental depressive behaviors, negative cognitive style, or parental withdrawal.

We took the approach of utilizing parent self-reports of depressive symptoms and the opposite parent's report of child depressive symptoms in order to address potentially inflated correlations due to shared method variance. However, maternal and paternal reports of child psychopathology each provide unique information, and intercorrelations among different informants are often low (Cantwell, Lewinsohn, Rohde, & Seeley, 1997; Des Los Reyes & Kazdin, 2005; Hay et al., 1999), meaning that using the cross-informant approach could have influenced results (Rutter, Pickles, Murray, & Eaves, 2001). We also relied on questionnaire measures of parenting behavior, which differ from direct observations of behavior. Our measure of parentally imposed life events examined life events potentially due to both parents' behavior (e.g., quarreling) as well as behaviors primarily due to one parent's behavior (e.g., mother losing job). Thus, although when examining maternally imposed life events we dropped behaviors that were due to paternal behavior (and vice versa), we were unable to separately examine the effect of maternally and paternally imposed life events, which could have affected our results. Cell numbers were small for some comparisons especially when examining the influence of child gender in the unrelated parent–offspring groups, so the influence of child gender on intergenerational transmission processes requires examination in other genetically sensitive study designs. The sample includes fewer unrelated than related parent–child pairs. It is possible that the difference in sample size between related and unrelated groups may contribute to nonsignificant findings in the unrelated group when effect sizes are small. We examined the transmission of depressive symptoms, and results may differ for more severe symptomatology. Finally, although mean levels of warmth and positivity do not differ markedly between families with children conceived via a range of types of assisted reproductive technologies compared to naturally conceived children (Golombok & MacCallum, 2003; Golombok et al., 2006; Shelton et al., 2009), the effects of parent positivity in families of wanted children conceived through assisted reproductive technologies might be very different to higher risk families. This may therefore limit the generalizability of these findings to naturally conceived families.

Conclusion and Future Directions for Translating Research on *r*GE Into Intervention

It is essential to recognize the contribution of *r*GE, including passive *r*GE, where the goal is to identify causal environmental risk factors on child psychopathology. If prevention and early intervention strategies for child and adolescent depression are to be effective, they need to be targeted at risks that are likely to be causal. The use of different types of research design that include genetically informative studies, randomized controlled trials, and quasiexperimental studies can help elucidate likely causal factors (Rutter, 2007). The present study suggests that although improving parent positivity and reducing parent-related stressors might be helpful for some aspects of child adjustment and family life, they do not appear to be priority targets for reducing child depression symptoms. Further work needs to be undertaken to identify environmental contributors to the intergenerational transmission of depression.

References

Angold, A., Costello, E. J., Messer, S. C., Pickles, A., Winder, F., & Silver, D. (1995). The development of a short questionnaire for use in epidemiological studies in children and adolescents. *International Journal of Methods in Psychiatric Research*, *5*, 237–249.

Bjelland, I., Dahl, A. A., Haug, T. T., & Neckelmann, D. (2002). The validity of the Hospital Anxiety and Depression Scale: An updated literature review. *Journal of Psychosomatic Research*, *52*, 69–77.

Bollen, K. (1989). *Structural equations with latent variables*. New York: Wiley.

Branje, S. J. T., Hale, W. W., Frijins, T., & Meeus, W. H. J. (2010). Longitudinal associations between perceived parent–child relationship quality and depressive symptoms in adolescence. *Journal of Abnormal Child Psychology*, *38*, 751–763.

Cantwell, D., Lewinsohn, P., Rohde, P., & Seeley, J. (1997). Correspondence between adolescent report and parent report of psychiatric diagnostic data. *Journal of the American Academy of Child & Adolescent Psychiatry*, *36*, 610–619.

Connell, A. M., & Goodman, S. H. (2002). The association between psychopathology in fathers versus mothers and children's internalizing and externalizing behavior problems: A meta-analysis. *Psycholological Bulletin*, *128*, 746–773.

Davies, P. T., Harold, G. T., Goeke-Morey, M. C., Cummings, E. M., Shelton, K., Rasi, J. A., et al. (2002). Child emotional security and interparental conflict. *Monographs of the Society for Research in Child Development*, *67*, 1–127.

Davies, P.T., & Windle, M. (1997). Gender-specific pathways between maternal depressive symptoms, family discord, and adolescent adjustment. *Developmental Psychology*, *33*, 657–668.

De Los Reyes, A., & Kazdin, A. E. (2005). Informant discrepancies in the assessment of childhood psychopathology: A critical review, theoretical framework and recommendations for further study. *Psychological Bulletin*, *131*, 483–509.

D'Onofrio, B. M., Van Hulle, C. A., Waldman, I. D., Rodgers, J. L., Harden, K. P., Rathouz, P. J., et al. (2008). Smoking during pregnancy and offspring externalizing problems: An exploration of genetic and environmental confounds. *Development and Psychopathology*, *20*, 139–164.

Downey, G., & Coyne, J. C. (1990). Children of depressed parents: An integrative review. *Psychological Bulletin*, *108*, 50–76.

Eaves, L. J., Last, K., Martin, N. G., & Jinks, J. L. (1977). A progressive approach to non-additivity and genotype–environmental covariance in the analysis of human differences. *British Journal of Mathematical and Statistical Psychology*, *30*, 1–42.

Eaves, L. J., Silberg, J. L., & Erkanli, A. (2003). Resolving multiple epigenetic pathways to adolescent depression. *Journal of Child Psychology and Psychiatry*, *44*, 1006–1014.

Eley, T. C., Deater-Deckard, K., Fombonne, E., Fulker, D. W., & Plomin, R. (1998). An adoption study of depressive symptoms in middle childhood. *Journal of Child Psychology and Psychiatry*, *39*, 337–345.

Feinberg, M., Neiderhiser, J.M., Howe, G., & Hetherington, E. M. (2001). Adolescent, parent, and observer perceptions of parenting: Genetic and environmental influences on shared and distinct perceptions. *Child Development*, *72*, 1266–1284.

Gest, S. D., Reed, M. G. J., & Masten, A. S. (1999). Measuring developmental changes in exposure to adversity: A life chart and rating scale approach. *Development and Psychopathology*, *11*, 171–192.

Glowinski, A. L., Madden, P. A. F., Bucholz, K. K., Lynskey, M. T., & Heath, A. C. (2003). Genetic epidemiology of self-reported lifetime DSM-IV major depressive disorder in a population-based twin sample of female adolescents. *Journal of Child Psychology and Psychiatry*, *44*, 988–996.

Golombok, S., & MacCallum, F. (2003). Practitioner review: Outcomes for parents and children following nontraditional conception: What do clinicians need to know? *Journal of Child Psychology and Psychiatry*, *44*, 303–315.

Golombok, S., Murray, C., Jadva, V., Lycett, E., MacCallum, F., & Rust, J. (2006). Non-genetic and non-gestational parenthood: Consequences for parent–child relationships and the psychological well-being of mothers, fathers and children at age 3. *Human Reproduction*, *21*, 1918–1924.

Goodman, S. H., & Gotlib, I. H. (1999). Risk for psychopathology in the children of depressed mothers: A developmental model for understanding mechanisms of transmission. *Psychological Review*, *106*, 458–490.

Goodyer, I. M., Cooper, P. J., Vize, C. M., & Ashby, L. (1993). Depression in 11–16-year-old girls—The role of past parental psychopathology and exposure to recent life events. *Journal of Child Psychology and Psychiatry*, *34*, 1103–1115.

Hale, W. W., Van der Valk, I., Akse, J., & Meeus, W. (2008). The interplay of early adolescents' depressive symptoms, aggression and perceived parental rejection: A four-year community study. *Journal of Youth and Adolescence*, *37*, 928–940.

Hammen, C., Brennan, P. A., & Shih, J. H. (2004). Family discord and stress predictors of depression and others in adolescent children of depressed and nondepressed women. *Journal of the American Academy of Child & Adolescent Psychiatry*, *43*, 994–1002.

Hammen, C., Gordon, D., Burge, D., Adrian, C., Jaenicke, C., & Hiroto, D. (1987). Maternal affective disorders, illness and stress: Risk for children's psychopathology. *American Journal of Psychiatry*, *144*, 736–741.

Harold, G. T., Rice, F., Hay, D. F., Boivin, J., van den Bree, M., & Thapar, A. (2011). Familial transmission of depression and antisocial behaviour symptoms: Disentangling the contribution of inherited and environmental factors and testing the mediating role of parenting. *Psychological Medicine*, *41*, 1175–1185.

Hay, D. F., Pawlby, S., Sharp, D., Schmucker, G., Mills, A., Allen, H., et al. (1999). Parents' judgments about young children's problems: Why mothers and fathers might disagree yet still predict later outcomes. *Journal of Child Psychology and Psychiatry*, *40*, 1249–1258.

Hipwell, A., Keenan, K., Kasza, K., Loeber, R., Stouthamer-Loeber, M., & Bean, T. (2008). Reciprocal influences between girls' conduct problems and depression, and parental punishment and warmth: A six-year prospective analysis. *Journal of Abnormal Child Psychology*, *36*, 663–677.

Jacobvitz, D., Hazen, N., Curran, M., & Hitchens, K. (2004). Observations of early triadic family interactions: Boundary disturbances in the family predict symptoms of depression, anxiety, and attention-deficit/hyperactivity disorder in middle childhood. *Development and Psychopathology*, *16*, 577–592.

Jaffee, S. R., & Price, T. (2007). Gene–environment correlations: A review of the evidence and implications for prevention of mental illness. *Molecular Psychiatry*, *12*, 432–442.

Jaffee, S. R., & Price, T. (2008). Genotype–environment correlations: Implications for determining the relationship between environmental exposures and psychiatric illness. *Psychiatry*, *7*, 496–499.

Johnson, J. H., & McCutcheon, S. (1980). Assessing life stress in older children and adolescents: Preliminary findings with the life events checklist. In I. E. Sarason & C. D. Spielberger (Eds.), *Stress and anxiety* (pp. 111–125). New York: Hemisphere.

Kane, P., & Garber, J. (2004). The relations among depression in fathers, children's psychopathology and father–child conflict: A meta-analysis. *Clinical Psychology Review*, *24*, 339–360.

Kendler, K. S., & Baker, J. H. (2007). Genetic influences on measures of the environment: A systematic review. *Psychological Medicine*, *37*, 615–626.

Kendler, K. S., & Gardner, C. O. (2010). Dependent stressful life events and prior depressive episodes in the prediction of major depression: The problem of causal inferences in psychiatric epidemiology. *Archives of General Psychiatry*, *67*, 1120–1127.

Kendler, K. S., Gardner, C. O., & Lichtenstein, P. (2008). A developmental twin study of symptoms of anxiety and depression: Evidence for genetic innovation and attenuation. *Psychological Medicine*, *38*, 1567–1575.

Kendler, K. S., Gardner, C. O., & Prescott, C. A. (2002). Toward a comprehensive developmental model for major depression in women. *American Journal of Psychiatry*, *159*, 1133–1145.

Kendler, K. S., Gardner, C. O., & Prescott, C. A. (2006). Toward a comprehensive developmental model for major depression in men. *American Journal of Psychiatry*, *163*, 115–123.

Lahey, B. B., D'Onofrio, B. M., & Waldman, I. D. (2009). Using epidemiologic methods to test hypotheses regarding causal influences on child and adolescent mental disorders. *Journal of Child Psychology and Psychiatry*, *50*, 53–62.

Lau, J. Y., & Eley, T. C. (2006). Changes in genetic and environmental influences on depressive symptoms across adolescence and young adulthood. *British Journal of Psychiatry*, *189*, 422–427.

Lewis, G., Rice, F., Harold, G. T., Collishaw, S., & Thapar, A. (2011). Investigating environmental links between maternal depression and child anxiety/depression symptoms using a genetic design. *Journal of the American Academy of Child & Adolescent Psychiatry*, *50*, 451–459.

Lovejoy, M. C., Graczyk, P. A., O'Hare, E., & Neuman, G. (2000). Maternal depression and parenting behavior: A meta-analytic review. *Clinical Psychology Review*, *20*, 561–592.

McGue, M., Elkins, I., Walden, B., & Iacono, W. G. (2005). Perceptions of the parent–adolescent relationship: A longitudinal investigation. *Developmental Psychology*, *41*, 971–984.

McGue, M., & Lykken, D. T. (1992). Genetic influence on divorce. *Psychological Science*, *3*, 368–373.

Middeldorp, C. M., Cath, D. C., Vink, J. M., & Boomsma, D. I. (2005). Twin and genetic effects on life events. *Twin Research and Human Genetics*, *8*, 224–231.

Monroe, S. M., Rohde, P., Seeley, J. R., & Lewinsohn, P. M. (1999). Life events and depression in adolescence: Relationship loss as a prospective risk factor for first onset of major depressive disorder. *Journal of Abnormal Psychology*, *108*, 606–614.

National Institute for Clinical Excellence, UK. (2005). *Depression in children and young people: Identification and management in primary, community and secondary care* (National Clinical Practice Guideline Number 28). Unpublished manuscript.

Neiderhiser, J. M., Reiss, D., Hetherington, E. M., & Plomin, R. (1999). Relationships between parenting and adolescent adjustment over time: Genetic and environmental contributions. *Developmental Psychology*, *35*, 680–692.

Neiderhiser, J. M., Reiss, D., Pedersen, N. L., Lichtenstein, P., Spotts, E. L., Hansson, K., et al. (2004). Genetic and environmental influences on mothering of adolescents: A comparison of two samples. *Developmental Psychology*, *40*, 335–351.

Pike, A., McGuire, S., Hetherington, E. M., Reiss, D., & Plomin, R. (1996). Family environment and adolescent depressive symptoms and antisocial behavior: A multivariate genetic analysis. *Developmental Psychology*, *32*, 590–603.

Plomin, R., DeFries, J. C., & Loehlin, J. C. (1977). Genotype–environment interaction and correlation in the analysis of human behavior. *Psychological Bulletin*, *84*, 309–322.

Plomin, R., DeFries, J. C., McClearn, G. E., & McGuffin, P. (2008). *Behavioral genetics* (5th ed.). New York: Worth.

Ramchandani, P., & Psychogiou, L. (2009). Paternal psychiatric disorders and children's psychosocial development. *Lancet*, *374*, 646–653.

Reiss, D., Neiderhiser, J. M., Hetherington, E. M., & Plomin, R. (2000). *The relationship code: Deciphering genetic and social influences on adolescent development*. Cambridge, MA: Harvard University Press.

Repetti, R. L., Taylor, S. E., & Seeman, T. E. (2002). Risky families: Family social environments and the mental and physical health of offspring. *Psychological Bulletin*, *128*, 330–366.

Rice, F., Harold, G. T., Boivin, J., Hay, D., van den Bree, M. M. B., & Thapar, A. (2009). Disentangling prenatal and inherited influences in humans with an experimental design. *Proceedings of the National Academy of Sciences*, *106*, 2464–2467.

Rice, F., Harold, G. T., Boivin, J., Hay, D., van den Bree, M. M. B., & Thapar, A. (2010). The effects of gestational stress on offspring birth weight and psychopathology: Disentangling prenatal environmental and inherited influences. *Psychological Medicine*, *40*, 335–345.

Rice, F., Harold, G. T., & Thapar, A. (2002). The genetic aetiology of childhood depression: A review. *Journal of Child Psychology and Psychiatry*, *43*, 65–79.

Rice, F., Harold, G. T., & Thapar, A. (2003). Negative life events as an account of the age-related differences in the aetiology of depression in childhood and adolescence. *Journal of Child Psychology and Psychiatry*, *44*, 977–987.

Rohner, R. (1984). *Handbook for the study of parental acceptance and rejection*. Storrs, CT: University of Connecticut, Center for the Study of Parental Acceptance and Rejection.

Rutter, M. (2007). Proceeding from observed correlation to causal inference: The use of natural experiments. *Perspectives on Psychological Science*, *2*, 377–395.

Rutter, M., Pickles, A., Murray, R., & Eaves, L. (2001). Testing hypotheses on specific environmental causal effects on behavior. *Psychological Bulletin*, *127*, 291–324.

Scarr, S., & McCartney, K. (1983). How people make their own environments: A theory of genotype–environment effects. *Child Development*, *54*, 424–435.

Scourfield, J., Rice, F., Thapar, A., Harold, G. T., Martin, N., & McGuffin, P. (2003). Depressive symptoms in children and adolescents: Changing aetiological influences with development. *Journal of Child Psychology and Psychiatry*, *44*, 968–976.

Shelton, K. H., Boivin, J., Hay, D., Boivin, J., van den Bree, M. B. M., & Thapar, A. (2009). Examining differences in psychological adjustment problems among children conceived by assisted reproductive technologies. *International Journal of Behavioral Development*, *33*, 385–392.

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*, 734–744.

Singh, A. L., D'Onofrio, B. M., Slutske, W. S., Turkheimer, E., Emery, R. E., Harden, K. P., et al. (2011). Parental depression and offspring psychopathology: A children of twins study. *Psychological Medicine*, *41*, 1385–1395.

Stice, E., Ragan, J., & Randall, P. (2004). Prospective relations between social support and depression: Differential direction of effects for parent and peer support? *Journal of Abnormal Psychology*, *113*, 155–159.

Sullivan, P. F., Neale, M. C., & Kendler, K. S. (2000). Genetic epidemiology of major depression: Review and meta-analysis. *American Journal of Psychiatry*, *157*, 1552–1562.

Thapar, A., Harold, G. T., & McGuffin, P. (1998). Life events and depression symptoms in childhood—Shared genes or shared adversity? A research note. *Journal of Child Psychology and Psychiatry*, *39*, 1153–1158.

Thapar, A., & McGuffin, P. (1996). Genetic influences on life events in childhood. *Psychological Medicine*, *26*, 813–820.

Thapar, A., Rice, F., Hay, D., Boivin, J., Langley, K., van den Bree, M. M. B., et al. (2009). Prenatal smoking may not cause ADHD: Evidence from a novel design. *Biological Psychiatry*, *66*, 722–727.

Thapar, A., & Rutter, M. (2009). Do prenatal risk factors cause psychiatric disorder? Be wary of causal claims. *British Journal of Psychiatry*, *195*, 100–101.

Tully, E. C., Iacono, W. G., & McGue, M. (2008). An adoption study of parental depression as an environmental liability for adolescent depression and childhood disruptive disorders. *American Journal of Psychiatry*, *165*, 1148–1154.

van den Oord, E., Boomsma, D. I., & Verhulst, F. C. (1994). A study of problem behaviors in 10- to 15- year-old biologically related and unrelated international adoptees. *Behavior Genetics*, *24*, 193–205.

Weissman, M. M., Wickramaratne, P., Nomura, Y., Warner, V., Pilowsky, D., & Verdeli, H. (2006). Offspring of depressed parents: 20 years later. *American Journal of Psychiatry*, *163*, 1001–1008.

Zigmond, A. S., & Snaith, R. P. (1983). The hospital anxiety and depression scale. *Acta Psychiatrica Scandinavica*, *67*, 361–370.