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Estimating the Roles of Genetic Risk, Perinatal Risk, and Marital Hostility on Early Childhood Adjustment: Medical Records and Self-Reports

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Abstract

A wide variety of perinatal risk factors have been linked to later developmental outcomes in children. Much of this work has relied on either birth/medical records or mothers' self-reports collected after delivery, and there has been an ongoing debate about which strategy provides the most accurate and reliable data. This report uses a parent-offspring adoption design ($N = 561$ families) to (1) examine the correspondence between medical record data and self-report data, (2) examine how perinatal risk factors may influence child internalizing and externalizing behavior at age 4.5 years, and (3) explore interactions among genetic, perinatal risk, and rearing environment on child internalizing and externalizing behavior during early childhood.

The agreement of self-reports and medical records data was relatively high (51–100%), although there was some variation based on the construct. There were few main effects of perinatal risk on

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child outcomes; however, there were several 2- and 3-way interactions suggesting that the combined influences of genetic, perinatal, and rearing environmental risks are important, particularly for predicting whether children exhibit internalizing versus externalizing symptoms at age 4.5 years.

Keywords

Genetic; perinatal; marital hostility; behavior problems; adoption; self-report; medical records

There is a sizable literature linking a wide variety of prenatal and perinatal risk factors to later developmental outcomes in children including problematic behavioral and emotional outcomes (e.g., Pechtel & Pizzagalli, 2011). These early risk factors include substance use during pregnancy, infections during pregnancy, pre-eclampsia, pre-term birth, and low birth weight (e.g., Robinson et al., 2008). In this report, we refer to these prenatal and early life (delivery and neonatal) risks as perinatal risks for simplicity. When genetically informed samples have been used, the direct effects seen in other reports are frequently explained by other factors, including genetic influences (Class et al., 2014). There are also many studies that have found that the effects of perinatal risks on child behavioral outcomes are reduced when risks due to the rearing environment, like marital conflict, are included in the model (e.g., Fergusson & Woodward, 1999). Much of this work has relied on either birth/medical records or maternal self-reports collected after delivery. Currently, there is much debate about which strategy provides the most accurate and reliable data for predicting child outcomes. This report has three objectives. First, we provide a comparison of perinatal risks obtained from medical records and mother self-reports. Next, we examine the interrelationships among perinatal risks and genetic and rearing environmental factors in influencing child internalizing and externalizing behaviors in 4.5-year-old children using a longitudinal parent-offspring adoption design. Finally, we consider possible interactions among genetic, perinatal risk, and rearing environment on child internalizing and externalizing behavior during early childhood.

The Importance of Measurement of Perinatal Environment

One challenge for studies that seek to assess perinatal risk is measurement. Depending on the type of study, it may be difficult or impossible to assess pregnant women to collect the data prospectively. As a result, a variety of strategies have been used. Many studies rely on official records such as birth records, medical records, or registry information (e.g., Behnke & Eyler, 1993; Olson, Shu, Ross, Pendergrass, & Robison, 1997; Pollard, 2000). Although these data are often collected concurrently, which can be a methodological strength, they may be limited in other ways. For example, state birth records often record prenatal smoking but, as noted in another paper in this volume (Knopik et al., this issue), those reports are not always reliable. Similarly, there is wide variation in the quality of medical records and some indication that reports of substance use in the records are often inaccurate when compared to self-reports (Tomeo et al., 1999). Another strategy often used is to assess prenatal risk many years after the pregnancy. This approach is necessary when a sample is recruited at an older age and medical or other records data are not available. Several studies have compared the

accuracy of self-report data recalled over various time spans and have found that recall accuracy depends upon the specific construct (Coolman et al., 2010). For example, women were able to accurately recall the child's length and birthweight, and her own pre-pregnancy weight and smoking during pregnancy over 30 or more years (Tomeo et al., 1999). However, in another study maternal reports of preeclampsia were less accurate: 50% of mothers falsely reported preeclampsia at just 2 months postpartum (Coolman et al., 2010). Similarly, a study of maternal recall 8 to 10 years after pregnancy found high agreement between maternal self-report and medical records for most variables. Yet, the recall for specific medical problems during pregnancy, neonatal intensive care, and post-delivery complications were recalled with low accuracy (Liu, Tuvblad, Li, Raine, & Baker, 2013). Similar patterns of findings were reported in two studies examining self-reports and birth records at 4 months postpartum (Dietz et al., 2014), with better recall for women with a college degree (Bat-Erdene, Metcalfe, McDonald, & Tough, 2013). Therefore, based on the literature, medical records can provide useful, albeit imperfect, information about pregnancy events and risks. Maternal self-reports, even when collected many years postpartum, may be considered useful supplements, and in some cases proxies, for prospectively collected data.

Perinatal Risk and Child Behavioral Outcomes

Maternal substance use during pregnancy is one of the most established domains of perinatal risk that has been linked to later child functioning, particularly child behavioral outcomes (Olson & O'Connor, 2001). Maternal smoking is the most well studied prenatal substance exposure. Many developmental studies have reported that maternal smoking during pregnancy increased child risk for a wide range of problematic outcomes, including externalizing behavior problems, ADHD, and nicotine dependence (e.g., Fergusson, 1999; Wakschlag & Hans, 2002; Weissman, Warner, Wickramaratne, & Kandel, 1999). Moderate levels of maternal alcohol use during pregnancy have also been associated with a variety of child behavioral outcomes, including deficits in memory and learning (Alati et al., 2013; Richardson, Ryan, Willford, Day, & Goldschmidt, 2002). Maternal use of other substances during pregnancy, most commonly marijuana or cocaine, has been negatively associated with learning and memory and positively associated with impulsivity, delinquency and attention problems, and to adolescent substance use (Bada et al., 2011; Day, Leech, & Goldschmidt, 2011; Delaney-Black et al., 2011; Mayes, 2002; Richardson, 1998; Richardson et al., 2002). These findings suggest that there is a teratogenic effect via biological mechanisms that directly impacts development as a result of exposure to substances during pregnancy, which is a mechanism of effect that has been reported in animal studies (e.g., Slotkin, 2004). In sum, maternal substance use during pregnancy has been associated with a wide range of negative child outcomes, especially those in the externalizing spectrum.

A number of other perinatal risk factors, especially those indicating fetal growth restriction, such as low birth weight (less than 2,500 grams) or small for gestational age (weight below the 10th percentile for the gestational age), have been linked with child behavioral outcomes. For example, children who are small for gestational age or who have a low birth weight may have experienced medically relevant pregnancy complications, including maternal gestational hypertension and preeclampsia. Specifically, children who are small for

gestational age have been found to be at risk for behavior problems during childhood (Robinson et al., 2009; Schlotz & Phillips, 2009), for adult psychological distress (Wiles, Peters, Leon, & Lewis, 2005), and for lower cognitive functioning or ability during adulthood (Lohaugen et al., 2013; Schlotz & Phillips, 2009; Stromme, Stromme, Bjertness, & Lien, 2014).

It is often not possible to accurately compute small for gestational age, so low birth weight has commonly been used as a proxy. A recent meta-analysis of 18 studies found only weak associations between low birth weight and later psychological distress (Wojcik, Lee, Colman, Hard, & Hotopf, 2013). However, additional studies have found that low birth weight is linked to child behavior problems and ADHD (e.g., Hultman et al., 2007; Wagner, Schmidt, Lemery-Chalfant, Leavitt, & Goldsmith, 2009), and emotional problems (Breslau et al., 1996; Hultman et al., 2007; Indredavik, Vik, Heyerdahl, Kulseng, & Brubakk, 2005; McCormick, Workman-Daniels, & Brooks-Gunn, 1996; Mick, Biederman, Faraone, Sayer, & Kleinman, 2002; van Os et al., 2001).

There have been few systematic studies of other perinatal risks in relation to child or adult behavioral outcomes. One review of pregnancy complications associated with increased risk for development of internalizing problems found that the two categories of perinatal risk most commonly found to be risk factors are birth weight/gestational age and intrapartum hypoxia, with the latter indicated by a variety of obstetric variables such as low Apgar score, fetal distress, and cesarean delivery (Gardener, Spiegelman & Buka, 2011; Smith et al., 2016 this issue). A different study examined child behavioral outcomes of perinatal risks associated with obstetric complications (i.e., preterm labor, asphyxia, neonatal complications) and family risk factors (i.e., low parental education, parent psychiatric disorder, marital discord). The authors found that the two were independently linked with behavior problems (Kolevzon, Gross, & Reichenberg, 2007). Taken as a whole, small for gestational age and low birth weight have been linked with a variety of adverse behavioral outcomes along the internalizing and externalizing spectrum in children and adults. It is notable, however, that the majority of studies reviewed did not consider possible interactions between these risk factors and family risk in predicting children's long term outcomes.

There is a relatively clear pattern of findings for small for gestational age and low birth weight. What is less clear is what perinatal events contribute to these birth outcomes and whether there may be different patterns of adverse outcomes for different types of perinatal events. In other words, two perinatal events (preeclampsia and maternal smoking during pregnancy) have been found to increase the risk of low birth weight (e.g., Lohaugen et al., 2013; Vogler & Kozlowski, 2002), yet each event has been linked with a different pattern of adverse outcomes in children. For example, Laucht et al, (2000) reported some variation in the patterns of associations with outcomes for maternal smoking during pregnancy, maternal prenatal alcohol use, nutrition, infections, and stress. However, these differences were subtle and often indicated by just a few studies (Laucht et al., 2000). In another report, common but serious complications during pregnancy (i.e., heavy bleeding, hypertension) were uniquely associated with anxiety in children, but the total number of pregnancy problems experienced, independent of severity, also predicted risk of anxiety in children (Schlotz & Phillips, 2009). Many of the studies that have assessed multiple categories of perinatal

complications and risks have yielded similar findings across categories or have collapsed the categories into a single risk index (Hirshfeld-Becker et al., 2004). Therefore, although there may be differential prediction of outcomes based on specific types of risk, most studies have found that aggregating the sum of perinatal risk factors across domains demonstrates comparable or superior predictive validity (e.g., Calhoun et al., 2010; Korhonen, Vahaeskel, Sillanpaa, & Kero, 1993; Wagner et al., 2009).

Disentangling Genetic, Perinatal Risks, and Postnatal Environment

There are two important shortcomings of much of the previous work in this area. First, in typical family-based studies it is impossible to disentangle the effects of prenatal risk from the effects of genes shared between the mother and the child in relation to the child's behavioral outcome. This is particularly problematic because the types of child behavioral outcomes that have been linked with prenatal risks have also been shown to be heritable. Therefore, the links between prenatal exposures and risks and child behavioral outcomes may be due to children inheriting these behaviors rather than to the exposures or risks that they experienced prenatally. There are several detailed discussions of these issues in regard to prenatal substance use specifically (e.g., Rutter, 1971; Sameroff, 1998) and for perinatal risks more generally (Knopik, 2009, 2010; Repetti, Taylor & Seeman, 2002). A second limitation of the typical developmental work in this area is that the same parent who provided the risky prenatal environment also parents the child. In the case of prenatal substance use, the mother who used substances during her pregnancy is likely to continue use after her pregnancy, thus impairing her parenting and confounding the prenatal and postnatal environments that the child experiences. The strategies used to control for genetic confounds of prenatal risks can also help to control for the effects of the rearing environment, although in some of these designs it is difficult to clearly distinguish between genetic and rearing environmental effects. Many developmental studies have attempted to address these shortcomings by including parent psychopathology and parenting practices in the model as control variables, often finding evidence for effects of prenatal risks above and beyond the effects of the controls (e.g., Wakschlag et al., 1997).

The majority of the genetically informed research has focused on maternal substance use during pregnancy, most often on maternal smoking during pregnancy. Generally, studies have found that after accounting for genetic influences, maternal smoking during pregnancy does not have a direct environmental impact on child's risk for problematic behavioral outcomes (e.g., D'Onofrio et al., 2012; Lindblad & Hjern, 2010; Silberg et al., 2003). There are, however, a handful of studies that have found that the effects of maternal smoking during pregnancy remain significant, although are substantially reduced, even after genetic influences are taken into account (e.g., Knopik et al., 2016; Thapar et al., 2003). There is also at least one study that has found that maternal smoking during pregnancy has an effect on early child behavior, even after disentangling the contributions of prenatal and rearing environments through the use of adoption and IVF designs (Gaysina et al., 2013), although this study did not control for possible genetic effects. A few genetically informed studies have also examined the effects of prenatal exposure to alcohol with more mixed findings than for maternal smoking during pregnancy. Specifically, there is some evidence for independent effects of both genetic and direct prenatal environmental exposure (e.g.,

Knopik, Bucholz, Madden, & Heath, 2005). To date, however, there have been no genetically informed designs examining the direct effects of prenatal exposure to drugs other than alcohol or smoking on child outcomes. It is not clear if these effects are also due, at least in part, to genetic influences rather than direct environmental influences.

A handful of studies have used genetically informed designs in an effort to distinguish effects due to genetic factors from risks due to fetal growth restriction. Generally, these studies have found that low birth weight is associated with later behavioral problems independent of genetic factors (Hultman et al., 2007; van Os et al., 2001). Other perinatal risks examined within genetically informed designs include preterm birth (D'Onofrio et al., 2013), pre-pregnancy body mass index (Chen et al., 2014), prenatal stress (Class et al., 2014; Class, Khashan, Lichtenstein, Langstrom, & D'Onofrio, 2013), and fetal growth (Class et al., 2014). A previous study using the same sample as this report found evidence that perinatal risks both attenuated genetic risk and served as mediators of that risk on toddler problem behaviors (Marceau et al., 2013). One explanation for the relatively few studies of perinatal risks beyond substance use and birthweight, both in the phenotypic and genetic literature, is that although most births may experience one or more risks, the majority of risks are minor. This complexity makes it challenging to examine the impact of specific perinatal risks with adequate variation, even when using large samples.

The Current Report

The current report has three aims. First, we seek to clarify where self-reports and medical records agree and differ and to create a score that best represents perinatal risk. We expect that overall the agreement between self-report and medical records will be high. For those perinatal risks that are more medically relevant and for substance use during pregnancy, we expect to see less agreement. Specifically, birth mothers are unlikely to accurately recall specific medical events, as reported elsewhere and may be less likely to accurately report to care providers about their substance use during pregnancy (Liu, Tuvblad, Li, Raine, & Baker, 2013; Pickett et al., 2009). In the second aim, we use a parent-offspring adoption design to extend the existing work focused on disentangling genetic, perinatal environmental, and postnatal environmental influences on child externalizing and internalizing problems at age 4.5 years. The parent-offspring adoption design, which includes birth parents, adoptive families, and the adopted child, is especially well suited for clarifying the effects of the rearing environment independent of genetic and perinatal environmental effects. Although the genetic and perinatal environmental effects can also be clarified to some extent when only birth mothers are used, the inclusion of birth fathers, as in the current report, allows for all three influences to be distinguished more clearly. Based on prior literature and reports using this sample, we expected direct effects of the rearing environment on child behavioral outcomes, and to a lesser extent with fewer significant associations, direct effects of genetic risk and perinatal risk on child outcomes. Finally in the third aim we consider the effects of interactions among genetic, perinatal risk, and rearing environment on child internalizing and externalizing behavior during early childhood. This last aim is exploratory, however, because there are few studies that have examined these interactions to date.

Method

Participants and Procedures

Participants were 561 linked sets of adoptive parents (APs), birth parents (BPs), and adopted children (ACs) recruited in two cohorts as a part of the Early Growth and Development Study (EGDS), a multi-site prospective longitudinal adoption study (Leve et al., 2013). Participants were eligible for participation if (1) the adoption was domestic, (2) the child was placed with a non-relative adoptive family, (3) adoption occurred prior to 3 months of age ($M = 7.11$ days postpartum, $SD = 13.28$), (4) the child had no known major medical conditions, and (5) the birth mother and adoptive parents could read or understand English at least at an eighth-grade level. Fifty-seven percent of the children were male. The sample has been well characterized elsewhere (Leve et al., 2013). This study used data from interviews (usually in their homes) of birth mothers and birth fathers (birth parents: BPs) (561 birth mothers, 193 birth fathers) at approximately 4 and 18 months postpartum and from adoptive families ($N = 407$) when the child was 4.5 years old. Including data from birth fathers helped to distinguish between genetic and prenatal environmental influences as the birth father does not contribute to the prenatal environment. During the first in-person visit birth mothers were also asked to release their prenatal care and delivery records to the study by signing a medical record release form.

We first examined whether there were differences between birth mothers for whom we were able to obtain birth records vs. those for whom we were not able using Wilcoxon-Mann-Whitney tests on demographic (race/ethnicity, income, education, age) and study variables (substance use, internalizing psychopathology, and externalizing psychopathology). Only one of the seven contrasts was significant: birth mother race/ethnicity, $\chi^2 = 4.15$, $p < .05$. The proportion of white mothers was higher among those from whom we obtained records (74%) than for those we could not obtain records from (60%) and a lower proportion of African American mothers among those from whom we could obtain records (10%) than those we could not (22%). There were no other differences in birth mothers for whom we could vs. could not obtain medical records data, χ^2 's < 3.53 , p 's $> .05$.

We then tested for differences between the sample ($N = 407$ with outcome data) and the sample recruited into the study but without outcome data ($N = 154$) on demographic and study variables. Only three of 22 contrasts were significant. For families who completed the wave 4.5 year assessment there were more birth mother internalizing symptoms during pregnancy than for those who did not, $\chi^2 = 6.22$, $p < .05$. Similarly, for families who completed the wave 4.5 year assessment there were more total obstetric complications during pregnancy than for those who did not, $\chi^2 = 3.93$, $p < .05$. Finally, families who completed the wave 4.5 year assessment had lower education among the second adoptive parent (usually the father) than those who did not, $\chi^2 = 9.48$, $p < .05$. The families who completed and did not complete the 4.5 year assessment did not vary on birth mother race/ethnicity, education, income, age at child birth, whether the adoptive mother or father was considered the first adoptive parent, race/ethnicity, and income, the first adoptive parents' education, the other prenatal risk scores (neonatal complications, substance use, exposure to toxins, pregnancy complications, and labor/delivery complications), openness of the

adoption, marital hostility at the first assessment, and birth parent internalizing, externalizing, and substance use scores (see below), χ^2 's < 3.54, p 's > .05. Thus, on the whole there were few differences (below chance levels) for families for whom we were vs. were not able to collect birth/medical records, and who did vs. did not complete the 4.5-year-old assessments.

Measures

Genetic Influences—Adopted children's genetic risk for behavior problems was assessed by creating composite "genetic risk" scores using data from both birth mothers and birth fathers. These scores were comprised of: (a) number of BP's psychopathology symptoms, (b) number of BP diagnoses, and (c) the earliest age of onset of BP disorders from the Composite International Diagnostic Interview (CIDI; Kessler & Üstün, 2004) collected at the 18-month assessment (for the purposes of this scale these data were coded as missing if the BP never received a diagnosis); and (d) the proportion of first degree relatives experiencing problems with psychopathology (reported at the 4-month assessment) from the Family History-Research Diagnostic Criteria (Endicott, Andreasen, & Spitzer, 1977). Three genetic risk scores were created: internalizing ($\alpha = .64$), externalizing ($\alpha = .65$), and substance use ($\alpha = .74$). Specifically, we took the z -score of each of the indicators for birth mothers and fathers, and then averaged the z -scores (after reverse coding the age of onset so that higher scores reflected higher risk). These genetic risk scores are proxies for actual genetic risks inherited by the child to the extent that they are correlated with child internalizing and externalizing independent of perinatal risks.

Perinatal Risk—We collected information on perinatal risk using BM self-reports and medical record data. Additional details on the measures can be found in Marceau et al. (2013) for self-report data only, and Marceau et al. (2016) for self-report and medical record data and in the Appendix.

Self-report—To optimize the quality of the self-report data, we used a modified Life History Calendar method (Caspi et al., 1996; Freedman, Thornton, Camburn, Alwin, & Young-DeMarco, 1988) specific to the prenatal period to assess prenatal substance use (alcohol, cigarettes, and illicit drugs) and symptoms of depression and anxiety. Depression and anxiety symptoms were assessed with seven items from the Beck Depression Inventory (BDI; Beck, Steer, & Brown, 1996) and five items from the Beck Anxiety Inventory (BAI; Beck & Steer, 1993). BMs also completed a pregnancy screener that asked about medical aspects of the pregnancy (i.e., when and how the BM realized she was pregnant, weight change, blood pressure, vitamin use, medications, laboratory tests, due and birth dates, timing and frequency of doctor visits, and symptoms of illnesses such as the flu, sexually transmitted infections, pre-eclampsia).

Medical Records—We developed a coding form to extract relevant information from the prenatal care and delivery records (see Marceau et al., 2016 for additional detail) assessing both close-ended and open-ended questions assessing a wide array of maternal and fetal complications as well as medical record quality. In addition, basic information on demographics and birth outcomes were also extracted. Thirty-nine records were not coded

because they were illegible or of very low copy quality; medical records data were available for 389 birth mothers. All remaining medical records were triple-coded to ensure all information was collected and recorded accurately. Sixteen coders were trained until they reached 100% agreement when coding close-ended questions and 90% agreement when coding open-ended questions on practice records, and each coder's reliability was checked every 10 records.

“Best” scores—In cases when both self-report and medical record data assessed the same type of risk, we computed the rates of agreement. After evaluating the agreement across medical record data and self-report, we created “best” scores that incorporate the most reliable and comprehensive score for each construct. Information regarding many perinatal risks was only reported within medical records. After consulting with an Obstetrician, medical records were judged as the most reliable source for medically relevant risks (e.g., prematurity, postmaturity, gestational age, low birth weight, infections, high blood pressure, pre-eclampsia). For weight gain and weight loss during pregnancy, we used self-reported data if the birth mother had not seen a doctor before the 12th week of her pregnancy. At 12 weeks weight begins to show pregnancy-related changes and the medical records would not provide an accurate record of her pre-pregnancy weight. However, if the BM began prenatal care prior to 12 weeks, the medical record was used. For maternal age at birth, we used self-report based on maternal and child dates of birth. Finally, for exposures to toxins, we used whichever response reported exposure, as neither reporter was judged to be likely to be more reliable than the other. In other words, the best score for exposures to toxins may be from self-report, medical record, or some combination of the two. On the other hand, information regarding drug use was more complete within the parent reports. Medical records' reports of the quantity/frequency of substance use was often of poor quality (not reported, or reported with inadequate detail to code severity), self-report was judged to be the more reliable source.

Perinatal Risk Index—To code for the severity of various perinatal risks, we relied heavily on the McNeil- Sjöström obstetric complications scale (McNeil, Cantor-Graae, & Sjöström, 1994; McNeil & Sjöström, 1995). This scale assigns a level of risk to the fetus for each perinatal risk/experience based on McNeil's general obstetric and pediatric experiences, previous studies of pregnancy risk factors, and use of consultants. We also used other resources to assign risk levels falling within the M-S scale coding scheme, including prenatal care visits (Kotelchuck, 1994), exposures to toxins (Williams & Ross, 2007), and internalizing symptoms (Van den Bergh, Mulder, Mennes, & Glover, 2005). These decisions were formalized into a measure: the *Perinatal Risk Index*. This index catalogs and aggregates the various risks experienced during pregnancy into a series of summary scores. The *Perinatal Risk Index* is presented in detail elsewhere (Marceau et al., 2013 for self-report only; Marceau et al., under review for combined self-report and medical record data). For each specific risk, a score of one to six was given categorizing the severity of risk to the fetus:

1. = Not harmful or relevant
2. = Not likely harmful or relevant

3. = Potentially but not clearly harmful or relevant
4. = Potentially clearly harmful or relevant
5. = Potentially clearly greatly harmful/relevant
6. = Very great harm to or deviation in offspring

Seven indexes of pregnancy risk were created: one total score comprised of five subscales, and one independent subscale. Each index was comprised of sums of specific items and/or subtotals of item sets with representative items listed here: (1) Pregnancy Complications (e.g., prenatal care, intrauterine growth retardation, fetal anemia, pre-eclampsia, obesity, maternal infections); (2) Neonatal Complications (e.g., prematurity, post-term, low birth weight, bilirubin, pneumonia, low body temperature); (3) Substance Use (e.g., cigarettes, secondhand cigarette smoke (if not also smoking), alcohol, marijuana, cocaine, hallucinogens, amphetamines, heroine, prescription painkillers (used illegally), inhalants, sedatives, tranquilizers); (4) Exposure to Toxins (e.g., exposure to radiation, X-rays, lead, chemical toxins); (5) Labor and Delivery (e.g., rupture of placental membranes, induced labor, abnormal presentation, operative delivery or intervention, intrapartum fetal asphyxia conditions, cord complications during delivery, analgesics/anesthetics/pharmacology); (6) Internalizing Problems (anxiety and depressive symptoms); (7) Obstetric Complications is a total score across the six specific categories of perinatal risk excluding Internalizing Problems as this was not a construct included in the M-S.

To capture the severity of risk, we created weighted risk totals (McNeil & Sjöström, 1995). Here, we were only interested in capturing the severity of risk factors that would meet criteria for sufficient severity to potentially affect the developing child. Thus, the weighted risk total scores were computed as the sum of each risk score when risk was greater than or equal to “3” (i.e., potentially, but not clearly harmful or relevant), but was equal to zero if the risk score was less than or equal to “2” (i.e., not harmful or likely harmful or relevant).

The prevalence for each of these perinatal risks is reported in detail in Marceau et al. (2016). In general, most mothers (75.0%) experienced one to three pregnancy complications ranging from sexually transmitted infections other than HIV, high blood pressure, and other infections. Neonatal complications were less common with most mothers experiencing no neonatal complications (61.7%) or only one (30.9%). Similarly, labor/delivery complications were experienced by only 16.7% of mothers. Prenatal substance use was relatively common in this sample with 28.5% of women using one and 26.4% using two or three substances during pregnancy (40% used no substances during pregnancy). The intercorrelations among the seven perinatal risk indices are reported in Table 1. As can be seen in Table 1 only obstetric complications, which was a sum of the other perinatal risks excluding internalizing symptoms, was consistently correlated with the other perinatal risks with a modest-to-large effect size. With a few exceptions, the other perinatal risks correlations were small and nonsignificant.

Rearing Environment Risk—To create an index of rearing environment risk, marital hostility at child age 4.5 years was used. Each spouse reported on his/her behavior towards his/her spouse, (13 items, $\alpha > .88$) and the spouse’s behavior towards him/her (7 items, $\alpha > .$

91) on a 7-point scale ranging from 1 (*never*) to 7 (*always*). Items were summed to create scores indexing marital conflict/hostility toward each respondent and partner for each reporter. The average of these four scores was used as a global measure of marital conflict (r 's = .46–.75, α = .85).

Child Behavioral Outcomes—Adoptive parent reports on child internalizing and externalizing behavior on the Child Behavior Checklist at age 4.5 were used as the child behavioral outcomes. First, the average of both adoptive parents' report on internalizing and externalizing symptoms was computed (α 's > .86; correlations between mother and father reports are .49 for internalizing and .52 for externalizing). Next, to include both internalizing and externalizing symptoms in the same model without issues of multicollinearity, severity and directionality scores were created (e.g., Essex, Klein, Cho, & Kraemer, 2003) using a principal components analysis approach. Internalizing and externalizing scores were entered into the principal components analysis and two orthogonal factors were extracted and saved. The first factor represents what the two scores have in common (symptom severity, regardless of whether the symptoms fall on the internalizing vs. externalizing spectrum); internalizing and externalizing symptoms load equally and strongly onto this factor (factor loadings = .90). The second factor represents what differentiates the two scores (directionality), and indicates whether the psychopathology symptoms reflect a preponderance of internalizing versus externalizing symptoms when youth exhibited differing levels of each symptom type (e.g., having equal levels of internalizing and externalizing symptoms at high, average, or low levels would each result in a directionality score of 0). The factor loadings for the directionality factor are equal in weight but opposite in direction for internalizing (.44) and externalizing (–.44) ratings. High positive directionality scores indicate more internalizing symptoms and high negative directionality scores indicate more externalizing scores. Thus, symptom severity and directionality are independent, orthogonal scores that can be included simultaneously in analyses without multicollinearity problems (in contrast to internalizing and externalizing scores), and together provide a clear picture of the psychopathology symptoms of each child. Together severity and directionality will account for 100% of the variance in symptoms. In this analysis, the first factor, the severity score, explained 81% of the variance, suggesting that most children are showing elevated levels of both types of symptoms if they are showing elevated levels of either (corroborated by the correlation of .62 between internalizing and externalizing symptoms). This high co-occurrence of internalizing and externalizing symptoms highlights the usefulness of the severity and directionality approach used here.

Covariates—Openness of the adoption and knowledge of the other (birth/adoptive) parent could potentially increase associations between birth and adoptive parents, especially for parent reports of child behavior (see Ge et al., 2008 for more detail). Therefore, openness/contact in the adoption was included as a covariate. Openness of the adoption was assessed via BM and adoptive parent report on the extent to which they perceived that the adoption was open on a 7-point scale ranging from 1 (*very closed*) to 7 (*very open*). The average BM ratings at 4 months and adoptive parent ratings at 9 months were used to control for openness of the adoption with generally high agreement across reporters (correlations ranged from .75 to .85).

Analytic Strategy

Aim 1—We examined cross-tabulation tables to assess the percent agreement across self-report and medical record data for each specific risk factor assessed by both types of data. Missing data on specific variables were deleted list-wise. The analytic N for each comparison is listed in Table 2.

Aims 2 and 3—The second and third aims were examined with a series of regression analyses in Mplus (Muthen & Muthen, 2004), including all available data and using full information maximum likelihood to handle missing data. Symptom severity and directionality were simultaneously entered as outcomes. Separate models were constructed for each perinatal risk score described in the measures section: obstetric complications, neonatal complications, exposure to toxins, pregnancy complications, labor/delivery complications, substance use, and psychiatric symptoms during pregnancy. Main effects of genetic risk (for internalizing, externalizing, and substance use), the index of perinatal risk, marital hostility, all two-way interactions across risk types, and three-way interactions were all added as predictors. Finally, openness of the adoption, knowledge of the birth/adoptive parent, child sex, and birth mothers' age were entered as covariates. Interaction tests were probed using model-based significance regions (Hayes & Matthes, 2009; Johnson & Neyman, 1936). The simple slopes from the model-based probes at ± 1 *SD* from the sample mean of the moderator are presented in Figures 1 through 5.

Results

Aim 1: Agreement Across Raters

Table 2 includes a list (column 1) of perinatal risk variables assessed via both self-report and medical record report. For the absence/presence of each risk, the % agreement and chi-square values noting significant agreement across raters are presented. Because of the number of tests, patterns of findings, rather than specific findings for each variable, are presented in text. For half of the medically relevant risks (e.g., abnormal fetal heartbeat, fetal heart rate deviations, pre-eclampsia, weight loss, diabetes, maternal infections, long labor, presentation at birth, C-section delivery, cord prolapse, low birth weight), there was substantial agreement in whether the risk was absent or present ($> 90\%$). However, for the other half of medically relevant risks (e.g., bright red vaginal bleeding, high blood pressure, weight gain, maternal disorders, lead exposure, induced labor, epidural, prematurity, deviations in maturation at birth, Apgar score, maternal age), there was lower agreement on the absence/presence of risks (19–89%). Taken as a whole, agreement for the presence/absence of risk and the severity of risks were comparable for medically relevant risks, and generally on measures where a risk was either present or absent (e.g. cesarean section). However, there were several noteworthy instances where the severity of risks had substantially lower agreement than the absence/presence (e.g., weight gain, maternal disorders, maternal infections, lead exposure, Apgar, maternal age).

For substance use variables, the agreement regarding the absence/presence of use was relatively high ($> 80\%$), although the more prevalent substances had lower agreement (cigarette use, alcohol use, marijuana use; 81–89%). However, the agreement on severity of

risk was quite low, and substantially lower than the agreement on absence/presence of use of the various substances (< 80% except hallucinogens and heroin which had very low prevalence in the sample). This was particularly true for the more commonly used substances (19–70% agreement on severity of risk for cigarette exposure, secondhand smoke exposure, alcohol use, and marijuana).

Aims 2 and 3: Genetic, Perinatal, and Postnatal Environmental Interactions and Child Psychopathology Symptoms

Correlations between genetic and perinatal risks are presented in Table 1. Due to the number of findings, we focus only on systematic main effects and interaction effects of the regression analyses. Standardized parameter estimates are presented in Tables 3 (medically relevant perinatal risks) and 4 (substance use and psychiatric perinatal risks). Across the seven models tested, marital hostility was consistently associated with higher levels of symptom severity. Child gender was a significant predictor of symptom directionality: Being female was generally associated with a preponderance of internalizing symptoms (as opposed to a preponderance of externalizing symptoms or highly comorbid, average, or low levels of both symptoms) in the children, although this effect only reached significance in some models (and trend-level in others). Perinatal risk was generally not independently associated with symptom severity or directionality, except for exposure to toxins, which was associated with lower symptom severity.

There were five significant interactions related to child symptom directionality. First, marital hostility moderated the effects of obstetric complications such that at extremely low levels of marital hostility, experiencing obstetric complications was associated with child externalizing symptoms (as opposed to a preponderance of internalizing symptoms or highly comorbid, average, or low levels of both symptom types), whereas at average and high levels of marital hostility, obstetric complications were unrelated to symptom directionality (not observable at ± 1 SD of the sample mean for marital hostility; Figure 1). Second, there was an interaction of obstetric complications and genetic risk for substance use. At extremely low levels of genetic risk for substance use, experiencing more obstetric complications was associated with more externalizing symptoms than internalizing symptoms or highly comorbid, average, or low levels of both symptom types, whereas at higher levels of genetic risk for substance use, obstetric complications were not associated with symptom directionality (Figure 2).

Within the context of lower levels of genetic risk for substance use (significant at -1 SD of the sample mean for genetic risk for substance use), experiencing more pregnancy complications was associated with exhibiting more externalizing symptoms than internalizing symptoms or highly comorbid, average, or low levels of both symptom types. At very high levels of genetic risk for substance use, however, experiencing more pregnancy complications was associated with exhibiting internalizing symptoms than externalizing symptoms or highly comorbid, average, or low levels of both symptom types (Figure 3).

In regard to rearing environment $\times$ perinatal risk interactions, there was an interaction of marital hostility and labor/delivery complications such that at lower levels of marital hostility, labor/delivery complications were associated with exhibiting more externalizing

symptoms than internalizing symptoms or highly comorbid, average, or low levels of both symptom types, whereas at higher levels of marital hostility, labor/delivery complications were associated with exhibiting more internalizing symptoms than externalizing symptoms or highly comorbid, average, or low levels of both symptom types (Figure 4). Finally, there was a 3-way interaction of pregnancy complications, genetic risk for externalizing problems, and marital hostility (Figure 5). At lower than average levels of marital hostility, there was no effect of pregnancy complications on directionality at any level of genetic risk. However, for higher than average levels of marital hostility, at higher levels of genetic risk for externalizing problems, experiencing pregnancy complications was associated with exhibiting more externalizing symptoms than internalizing symptoms or highly comorbid, average, or low levels of both symptom types. In contrast, at lower levels of genetic risk for externalizing problems, experiencing pregnancy complications was associated with exhibiting more internalizing symptoms than externalizing symptoms or highly comorbid, average, or low levels of both symptom types. In other words, the combination of high marital hostility and more genetic risk was associated with externalizing symptoms in 4.5-year-old children when pregnancy complications were present ($G \times \text{postnatal } E \times \text{perinatal } E$). On the other hand, when genetic risk was low, pregnancy complications were associated with internalizing symptoms in 4.5-year-old children at any level of marital hostility ($G \times \text{perinatal } E$). There were no significant interactions predicting symptom severity.

Discussion

Our findings indicate that self-report data and medical records can be used together to assess perinatal risks. Specifically, self-report appears to provide more information on frequency of substance use while medical records provide more information on pregnancy and delivery complications. Overall, however, there is high agreement between self-report and medical records supporting the use of either as an index of perinatal risks. The second and third aims of our study, to examine how genetic, perinatal, and rearing environmental risks worked together to influence child behavioral outcome, revealed two key patterns of findings. First, there were no systematic main effects of perinatal risks on symptom severity or directionality in children at age 4.5 years, consistent with other reports. Second, within the exploratory analyses, both genetic risk and marital hostility moderated the effects of perinatal risk on child symptom directionality. The most interesting finding was the interaction among genetic risk $\times$ perinatal environment $\times$ rearing environment, which highlights the importance of considering these three potential sources of risk simultaneously. These findings and their implications are discussed in more depth below.

Although a number of studies have reported links between perinatal risks and behavioral outcomes in children and adults (e.g., Lukkari et al., 2012; Marceau et al., 2013; Robinson et al., 2008), it is rare for perinatal risks to be systematically included in developmental studies. This study attempts to highlight the importance of including perinatal risks while also providing a strategy for compiling perinatal risks into a form that is relatively easy to use. We demonstrate that there is a relatively high level of agreement for self-reports and medical records on most constructs, which is consistent with previous reports (e.g., Liu et al., 2013; Olson et al., 1997), although perinatal events more medical in nature typically show lower agreement with medical records (e.g., Coolman et al., 2010). This report also demonstrates

the usefulness of collapsing across multiple specific perinatal risks to create more general indices that represent categories of risk. Because many specific perinatal risks are relatively low-frequency events, although some perinatal risks experienced by many, combining across risks allows for normative or population-based samples to include these constructs in a meaningful way.

Our findings highlight the importance of considering multiple sources of influence when attempting to understand child behavioral outcomes. When examining the direct effects of genetic and perinatal risks, we found one significant effect – exposure to toxins prenatally was associated with lower severity of both internalizing and externalizing symptoms in children. In contrast, marital hostility was significantly associated with both severity and directionality, with more marital hostility linked to more severe symptoms of externalizing behavior, a finding consistent with other phenotypic work in this area (e.g., Beck & Shaw, 2005). Considering these genetic, perinatal, and rearing environment risks together, however, provides a more nuanced picture of how these different components of risk work together, with evidence of perinatal environment $\times$ rearing environment, genetic $\times$ perinatal environment, and genetic $\times$ perinatal environment $\times$ rearing environment interactions emerging, albeit not always in the anticipated direction. Specifically, we found that pregnancy complications were associated with more externalizing symptoms when both genetic risk for externalizing was high and marital hostility was high. In other words, there was no association if marital hostility was low and there was no association with internalizing, with highly comorbid externalizing and internalizing symptoms, or with average, or low levels of both symptom types. In contrast, when genetic risk for externalizing was low and marital hostility was high, pregnancy complications were associated with higher levels of child internalizing symptoms than with externalizing symptoms or highly comorbid, average, or low levels of both symptom types. These findings suggest that the effects of pregnancy complications vary depending on genetic risk, while the effects of marital hostility appear more general, such that more marital hostility increases the negative effects of pregnancy complications with no meaningful impact on directionality. If we had not included perinatal risk in the model, we would not have seen any effects of genetic risk, thus missing a significant influence on child behavioral outcomes.

Limitations and Future Directions

There are a number of limitations to this report. First, we do not have prospective assessment of perinatal risks throughout the pregnancy. Although collecting data prospectively would have been ideal, especially for understanding patterns of substance use and for conducting comparisons such as those reported here, we wanted to avoid any possibility of influencing the decision of birth parents to place or parent their child. We did, however, begin recruitment of birth parents shortly after the adoption was finalized, one month post-placement in most states, and birth mother assessments occurred at 4 months post-partum, on average. Although we used the life history calendar method to assess substance use and internalizing symptoms during pregnancy, we did not use this strategy to collect other pregnancy-related information and events. This may have had an adverse impact on the birth mother's ability to accurately recall those events, leading to lower levels of agreement with medical records. Because our sample is located throughout the United States, we did not

have medical records from a single health-care system or provider. This resulted in a wide variability in the quality of the records, variability that was also affected by when the birth mother began prenatal care and by the regularity of her prenatal care visits. Although we did not use records scored as poor quality in this report, it is possible that the overall variability has reduced the similarity in medical records and self-reports of perinatal risks. Our measures of genetic risk were limited by the design. Although we strove to include birth mothers and birth fathers, birth father data were unavailable for the majority of the sample (60%), thus genetic risk represented only half of the genetic risk for that proportion sample. However, there were no mean differences in genetic risk for when there was versus was not birth father data available and this sample of birth fathers is one of the largest included in a longitudinal domestic adoption study to date. It is possible that using a more comprehensive total genetic risk score would provide a better index of genetic risk, although the specificity of the findings in this report would then be lost. Similarly, examining measured genes, rather than relying on birth parent characteristics, may provide a more specific and direct index of genetic risk. Nonetheless, birth parent characteristics have been shown to be directly linked to child behavioral outcomes and to moderate rearing environmental influences on child behavioral outcomes, making this a reasonable approach for this report (e.g., Fearon et al., 2014; Ge et al., 1996). We chose to use marital hostility as a more general index of rearing environment risk, consistent with the “Risky Families” model proposed by Repetti, Taylor, & Seeman (2002). It is possible that measures of rearing environment focused on the family in general or on factors beyond interpersonal relationships would provide a better index of rearing environment risk. Nonetheless, marital hostility appears to be a particularly important component of rearing environment with direct links to child symptom severity and directionality as well as a key moderator of both genetic and perinatal environment risks. Finally, our analyses were exploratory in nature, leading to a larger number of statistical tests but few predictions. Because there is little literature available from which to build hypotheses about genetic $\times$ perinatal $\times$ postnatal environmental influences on child behavior, we strove to include all of our data and interpret specific effects with caution in an attempt to begin to build this important literature.

There are a number of important directions for future work in this area. First, examination of other aspects of rearing environment, both risk and protective, should be examined. It is possible that different patterns of findings will emerge in relation to parenting, for example. Second, the effects of genetic, perinatal risk, and rearing environment should be explored for behavioral outcomes in older children and on trajectories of behavioral outcomes as these may show different patterns of findings. Finally, future reports should consider more specific perinatal risk factors and more specific child outcomes. As demonstrated in Marceau et al. (2013), different perinatal risks show different patterns of associations with child outcomes with some mediating or attenuating genetic risk and others showing an independent direct effect on child outcomes.

In conclusion, this report provides preliminary evidence of interactions among genetic, perinatal risk, and rearing environment risk in a sample of children adopted at birth. The confounds of shared genes between rearing parents and children is eliminated, thus effects of rearing environment are not due to passive gene-environment correlations. Similarly, because birth fathers are included in the model, there is some control for genetic effects

independent of prenatal environment. Thus, the associations reported here suggest that the effects of genetic risk, perinatal risk, and rearing environment risk are interrelated and warrant additional examination. We also provide support for use of composite perinatal risk indices and for using the best data available to tap these risks, with both self-report and medical records showing high agreement.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Figure 1. Marital hostility moderates the association of obstetric complications with symptom directionality at age 4.5 years

Lines represent ± 1 SD of the sample mean for genetic risk for substance use. Obstetric complications risk is associated with externalizing symptoms at very low levels of marital hostility (effect not seen at -1 SD).

Figure 2. Genetic risk for substance use moderates the association of obstetric complications with symptom directionality at age 4.5 years

Lines represent ± 1 SD of the sample mean for genetic risk for substance use. Obstetric complications risk is associated with externalizing symptoms at very low levels of genetic risk for substance use (effect not seen at -1 SD).

Figure 3. Genetic risk for substance use moderates the association of pregnancy complications with symptom directionality at age 4.5 years

Lines represent ± 1 SD of the sample mean for genetic risk for substance use. * $p < .05$.

Figure 4. Marital hostility moderates the association of labor/delivery complications with symptom directionality at age 4.5 years

Lines represent ± 1 SD of the sample mean for marital hostility. * $p < .05$.

Figure 5. Genetic risk for externalizing and marital hostility moderate the association of pregnancy complications with symptom directionality at age 4.5 years
 Lines represent +/- 1SD of the sample mean for genetic risk for externalizing. Low and high marital hostility was categorized with a mean split. * $p < .05$.

Table 1
Correlations Among Genetic Risk, Perinatal Risk, and Between Genetic Risk and Perinatal Risk

	Genetic Risk			Perinatal Risk					
	1	2	3	4	5	6	7	8	9
	Genetic Risk								
1. Internalizing									
2. Externalizing	.36 *								
3. Substance Use	.46 *	.63 *							
	Perinatal Risk								
4. Obstetric Complications	.12 *	.10 *	.13 *						
5. Pregnancy Complications	.09 *	.04	.03	.68 *					
6. Neonatal Complications	-.04	-.05	-.02	.44 *	.02				
7. Exposure to Toxins	.05	.04	.09 *	.28 *	.08 *	.04			
8. Labor and Delivery	-.03	-.01	.00	.61 *	.07	.08	-.02		
9. Substance Use	.21 *	.21 *	.30 *	.46 *	.06	.01	.19 *	.08	
10. Internalizing Problems	.27 *	.17 *	.16 *	.19 *	.08 *	.06	.10 *	.09	.26 *

Note.

* $p < .05$.

Table 2

Percent Agreement Across Self-Report and Medical Record Reported Data for the Severity of Risk and Absence/Presence of Various Perinatal Risks

Variable	Severity		Absence/Presence	
	% agreement	% agreement	χ^2	N Frequency Endorsed ^a
Medically Relevant Perinatal Risks				
Diabetes (CII)	89%	98%	18.70 *	200 5
Pre-eclampsia (CII)	96%	96%	0.1	200 4
Long labor (CII)	96%	96%	12.93 [†]	200 2
Delivery (C-section) (CII)	97%	96%	156.37 *	200 37
Cord prolapse (CII)	95%	96%	0.04	200 1
Abnormal fetal heartbeat (CII)	95%	95%	0.15	200 4
Fetal heart rate deviations (CII)	95%	95%	0.15	200 6
Low birthweight	95%	95%	168.36 *	561 15
Presentation at birth (CII)	94%	94%	25.95 *	200 13
Weight loss	91%	91%	0.44	561 7
Maternal infections	67%	91%	0.95	561 81
Bright red vaginal bleeding (CI)	88%	90%	17.69 *	361 4
Deviations in maturation at birth	86%	89%	121.55 *	561 74
Apgar (CII)	63%	89%	0.12	200 21
Maternal Age	19%	87%	230.91 *	561 144
Premature	81%	83%	45.29 *	561 66
Weight gain	43%	80%	3.41 [†]	561 13
Lead	43%	69%	0.44	561 172
Induced labor (CII)	69%	69%	23.80 *	200 57
Epidural (CII)	58%	66%	30.56 *	200 92
High blood pressure	62%	65%	2.50 [†]	361 124
Maternal Disorders subtotal	41%	65%	17.34 *	561 231
Substance Use Perinatal Risks				

Variable	Severity		Absence/Presence		
	% agreement	% agreement	χ^2	N	Frequency Endorsed ^a
Heroin	83%	99%	136.22 *	561	12
Hallucinogens	98%	99%	0.003	561	3
Cocaine	80%	95%	18.83 *	561	34
Amphetamines	69%	94%	143.91 *	561	48
Prescription Pain Killers	75%	94%	11.03 *	561	35
Sedatives	67%	94%	0.47	561	35
Secondhand smoke exposure	59%	92%	0.02	561	48
Alcohol use	37%	89%	2.84	561	67
Marijuana	70%	89%	45.42 *	561	81
Cigarette use	19%	81%	122.05 *	561	184

Note. If there are less than 5 people per cell then the fisher exact *p*-value was used instead of the chi-square *p*-value. There were several other risks assessed by both reporters that were not included here because the risk could not meet a risk cutoff (e.g., possible risk values were 2 or less; nausea, X-rays, decreased fetal movement, obesity, edema) or there were no cases present according to one or both reporters (HIV/AIDS, STDs, chemical toxin exposure, inhalant use, absent fetal heart rate, post-term birth, methadone use).

^aFrequency endorsed represents the frequency of the risk being present for the “best” score.

CI refers to measure available for Cohort I only, CII refers to measure available for Cohort II only.

* $p < .05$.

Table 3

FIML Regression Results for Medically Relevant Perinatal Risks

	Obstetric Complications			Pregnancy Complications			Neonatal Complications			Exposure to Toxins			Labor/Delivery Complications		
	SEV ^a	DIR	SEV	DIR	SEV	DIR	SEV	DIR	SEV	DIR	SEV	DIR	SEV	DIR	SEV
Control variables															
Openness	.01 (.06)	.00 (.06)	.00 (.06)	.00 (.06)	.01 (.06)	-.01 (.06)	.00 (.06)	-.01 (.06)	.00 (.06)	.00 (.06)	.00 (.06)	-.01 (.06)	.00 (.06)	-.01 (.06)	.00 (.06)
Knowledge	-.11 (.06)	.06 (.06)	-.11 (.06)	.07 (.06)	-.10 (.06)	.06 (.06)	-.10 (.06)	.06 (.06)	-.10 (.06)	.05 (.06)	-.09 (.06)	.05 (.06)	-.09 (.06)	.06 (.06)	-.09 (.06)
Child Sex	-.02 (.05)	.10* (.05)	-.02 (.05)	.09 (.05)	-.02 (.05)	.08 (.05)	-.02 (.05)	.08 (.05)	-.02 (.05)	.10 (.05)	-.03 (.05)	.10 (.05)	-.03 (.05)	.09 (.05)	-.03 (.05)
BM age	.07 (.05)	.05 (.06)	.06 (.06)	.06 (.06)	.06 (.06)	.03 (.06)	.06 (.06)	.03 (.06)	.09 (.05)	.05 (.06)	.10 (.05)	.05 (.06)	.10 (.05)	.04 (.06)	.10 (.05)
Genetic risk															
BP Internalizing (INT)	-.02 (.05)	.06 (.06)	-.02 (.06)	.05 (.06)	-.06 (.06)	.07 (.06)	-.06 (.06)	.07 (.06)	-.05 (.06)	.08 (.06)	-.06 (.06)	.08 (.06)	-.06 (.06)	.07 (.06)	-.06 (.06)
BP Externalizing (EXT)	.02 (.07)	-.02 (.07)	.02 (.07)	.00 (.07)	.06 (.07)	.01 (.07)	.06 (.07)	.01 (.07)	.06 (.07)	.00 (.07)	.06 (.07)	.00 (.07)	.06 (.07)	-.02 (.07)	.06 (.07)
BP Substance Use (SU)	.04 (.07)	-.07 (.07)	.04 (.07)	-.10 (.07)	.04 (.07)	-.13 (.08)	.04 (.07)	-.13 (.08)	.03 (.07)	-.12 (.07)	.00 (.07)	-.12 (.07)	.00 (.07)	-.10 (.07)	.00 (.07)
Environment risk															
Marital Hostility (MH)	.15* (.05)	.11* (.05)	.16* (.05)	.09 (.05)	.16* (.05)	.09 (.05)	.16* (.05)	.09 (.05)	.16* (.05)	.09 (.05)	.15* (.05)	.09 (.05)	.15* (.05)	.08 (.05)	.15* (.05)
G × E															
BP INT × MH	-.06 (.07)	.02 (.07)	-.06 (.07)	-.01 (.06)	-.03 (.07)	.01 (.07)	-.03 (.07)	.01 (.07)	-.05 (.06)	.02 (.06)	-.08 (.06)	.02 (.06)	-.08 (.06)	.05 (.07)	-.08 (.06)
BP EXT × MH	.07 (.07)	.01 (.07)	.07 (.07)	.05 (.07)	.07 (.07)	.05 (.07)	.07 (.07)	.05 (.07)	.06 (.07)	.03 (.07)	.05 (.07)	.03 (.07)	.05 (.07)	.02 (.07)	.05 (.07)
BP SU × MH	.06 (.07)	.00 (.05)	.04 (.07)	.01 (.07)	.03 (.07)	-.02 (.07)	.03 (.07)	-.02 (.07)	.03 (.06)	-.02 (.07)	.02 (.07)	-.02 (.07)	.02 (.07)	-.01 (.06)	.02 (.07)
Perinatal Risk ^b	-.05 (.05)	-.01 (.06)	-.03 (.05)	-.04 (.05)	.03 (.07)	.10 (.07)	.03 (.07)	.10 (.07)	-.10* (.05)	.01 (.05)	.01 (.07)	.01 (.05)	.01 (.07)	.01 (.07)	.01 (.07)
G × Perinatal Risk															
BP INT × Perinatal Risk	.10 (.06)	-.04 (.06)	.08 (.07)	-.03 (.07)	-.03 (.08)	-.09 (.07)	-.03 (.08)	-.09 (.07)	.08 (.06)	.03 (.06)	.03 (.08)	.03 (.06)	.03 (.08)	-.02 (.07)	.03 (.08)
BP EXT × Perinatal Risk	-.01 (.07)	-.09 (.07)	-.05 (.07)	-.11 (.07)	.05 (.09)	-.01 (.08)	.05 (.09)	-.01 (.08)	-.10 (.07)	-.03 (.07)	.13 (.08)	-.03 (.07)	.13 (.08)	-.08 (.08)	.13 (.08)
BP SU × Perinatal Risk	.05 (.07)	.16* (.07)	.00 (.07)	.14* (.07)	-.11 (.10)	.06 (.08)	-.11 (.10)	.06 (.08)	-.03 (.07)	.00 (.07)	.00 (.08)	.00 (.07)	.00 (.08)	.07 (.08)	.00 (.08)
E × Perinatal Risk															
MH × Perinatal Risk	.06 (.05)	.11* (.05)	-.08 (.05)	.02 (.05)	-.09 (.07)	.08 (.07)	-.09 (.07)	.08 (.07)	.02 (.05)	-.02 (.05)	.00 (.07)	-.02 (.05)	.00 (.07)	.17* (.06)	.00 (.07)
G × E × Perinatal Risk (PR)															
BP INT × MH × PR	.05 (.07)	.04 (.07)	-.08 (.06)	.10 (.06)	.14 (.09)	.04 (.09)	.14 (.09)	.04 (.09)	.06 (.06)	.01 (.06)	-.08 (.09)	.01 (.06)	-.08 (.09)	-.01 (.08)	-.08 (.09)
BP EXT × MH × PR	-.01 (.07)	-.13 (.07)	.00 (.06)	-.15* (.06)	-.05 (.10)	-.10 (.10)	-.05 (.10)	-.10 (.10)	-.04 (.07)	.01 (.07)	.16 (.08)	.01 (.07)	.16 (.08)	-.03 (.08)	.16 (.08)

	Perinatal Risk						Labor/Delivery Complications					
	Obstetric Complications		Pregnancy Complications		Neonatal Complications		Exposure to Toxins		DIR		SEV	
	SEV ^a	DIR	SEV	DIR	SEV	DIR	SEV	DIR	SEV	DIR	SEV	DIR
BP SU × MH × PR	.09 (.07)	.01 (.07)	.05 (.07)	.01 (.07)	-.05 (.09)	-.02 (.08)	-.06 (.07)	-.02 (.07)	.11 (.09)			.02 (.09)

Note. Standardized path estimates are presented, with standard errors below in parentheses.

^aSEV = symptom severity; DIR = symptom directionality. Severity and directionality were entered into the models simultaneously.

^bPerinatal risk scales were entered in separate models. Each scale is labeled across the top, therefore the findings indicated by Perinatal Risk are referring to the scale listed in the first row.

BP=birth parent; INT=internalizing; EXT=externalizing; SU=substance use, MH=marital hostility; PR=perinatal risk; G=parent genetic risk score; E=rearing environment risk (marital hostility)

*
p < .05.

Table 4

FIML Regression Results for Substance Use and Psychiatric Perinatal Risks

	Perinatal Risk			
	Substance Use		Internalizing symptoms	
	SEV	DIR	SEV	DIR
Control variables				
Openness	.02 (.06)	-.01 (.06)	.00 (.06)	-.01 (.06)
Knowledge	-.11 (.06)	.06 (.06)	-.11 (.06)	.06 (.06)
Child Sex	-.02 (.05)	.10* (.05)	-.03 (.05)	.11* (.05)
BM age	.07 (.06)	.07 (.06)	.07 (.06)	.05 (.06)
Genetic risk				
BP Internalizing (INT)	-.06 (.06)	.08 (.06)	-.04 (.06)	.07 (.06)
BP Externalizing (EXT)	.04 (.07)	.00 (.07)	.03 (.07)	.00 (.07)
BP Substance Use (SU)	.04 (.07)	-.10 (.07)	.02 (.07)	-.12 (.07)
Environment risk				
Marital Hostility (MH)	.15* (.06)	.08 (.06)	.16* (.05)	.08 (.05)
G × E				
BP INT × MH	-.05 (.06)	.02 (.06)	-.04 (.07)	.03 (.06)
BP EXT × MH	.03 (.07)	.05 (.07)	.06 (.07)	.02 (.07)
BP SU × MH	.02 (.07)	-.03 (.07)	.04 (.07)	-.03 (.07)
Perinatal Risk ^b	.03 (.06)	-.05 (.06)	.03 (.06)	.05 (.06)
G × Perinatal Risk				
BP INT × Perinatal Risk	.00 (.06)	-.02 (.06)	-.10 (.07)	-.08 (.07)
BP EXT × Perinatal Risk	.00 (.08)	.05 (.08)	.00 (.08)	.06 (.08)
BP SU × Perinatal Risk	-.14 (.08)	.06 (.09)	.00 (.08)	.04 (.08)
E × Perinatal Risk				
MH × Perinatal Risk	.07 (.06)	.00 (.06)	-.05 (.05)	-.06 (.05)
G × E × Perinatal Risk (PR)				
BP INT × MH × PR	-.08 (.07)	-.06 (.07)	.00 (.07)	-.04 (.07)
BP EXT × MH × PR	-.15 (.09)	.11 (.09)	.01 (.08)	-.04 (.08)
BP SU × MH × PR	.18 (.10)	-.02 (.10)	.06 (.07)	.02 (.07)