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Original Research Article

A Developmental Cascade from Prenatal Stress to Child Internalizing and Externalizing Problems

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Abstract

Objective: This study utilized a developmental cascade approach to test alternative theories about the underlying mechanisms behind the association of maternal prenatal stress and child psychopathology. The fetal programming hypothesis suggests that prenatal stress affects fetal structural and physiological systems responsible for individual differences in child temperament, which further increases risk for internalizing and externalizing problems. Interpersonal models of stress transmission suggest that maternal stress influences child mental health via early parenting behaviors. We also examined a continuation of stress hypothesis, in which prenatal stress predicts child mental health via the continuation of maternal stress in the postpartum period. **Methods:** Participants were 1,992 mother–child pairs drawn from a prospective pregnancy cohort. Mothers reported on their perceived stress, anxiety, and depression during pregnancy and at 4-month postpartum. Birthweight was assessed via medical records of birthweight. At 4-month postpartum, hostile-reactive parenting behaviors were assessed. Child temperamental negative affect was measured at age 3. Child internalizing and externalizing problems were assessed at age 5. **Results:** Prenatal stress was associated with both internalizing and externalizing problems via postnatal stress and child temperament. Prenatal stress was also associated with externalizing behaviors via increased hostile-reactive parenting. After accounting for postnatal factors, prenatal stress continued to have a direct effect on child internalizing, but not externalizing, symptoms. **Conclusion:** Results provide support for the fetal programming, interpersonal stress transmission, and continuation of stress models. Findings highlight the need for prenatal preventative programs that continue into the early postnatal period, targeting maternal stress and parenting behaviors.

Key words: developmental psychopathology; fetal programming; mental health; prenatal stress.

Introduction

A robust literature within developmental science suggests that the early social environment plays a critical role in promoting children's health and well-being. However, recent advancements in research have suggested that the developmental origins of health and

disease (DOHaD) can be traced back to events that occur even before birth (Gillman, 2005). For example, when rodents are exposed to stressors (e.g., electric shocks, forced swim tests) during pregnancy, their offspring exhibit maladjusted behaviors, including anxiety and depressive behaviors, heightened emotional and physiological stress reactivity, and aggression (Abe et al., 2007; Eaton, Edmonds, Henry, Snellgrove, & Sloman, 2015). These findings have been replicated in observational research with humans. For example, maternal perceived stress, anxiety, and depression during the prenatal period have been associated with increased risk of attention-deficit hyperactivity disorder (ADHD), depression, and behavior problems (Madigan et al., 2018; Rodriguez & Bohlin, 2005), with some indications that prenatal stress might even increase the risk for more severe psychotic disorders, such as schizophrenia (Van Os & Selten, 1998).

A Search for Intermediary Factors: Two Proposed Models

A critical next step is to move beyond cataloguing these associations and toward identifying intermediary mechanisms that explain why and how prenatal stress influences later child mental health. In examining the underlying mechanisms, researchers often cite the fetal programming hypothesis, which postulates that exposure to events or stressors during gestation (e.g., heightened maternal anxiety) "programmes persisting changes in a range of metabolic, physiological, and structural parameters," which impact fetal neural development and regulatory capabilities (Barker, 1995, p. 171; O'Donnell, O'Connor, & Glover, 2009). One such "structural parameter" is fetal growth and size. Accordingly, prenatal stress has been associated with a higher risk of prematurity and low birthweight (Bussières et al., 2015; Grote et al., 2010). In addition, research has suggested that prenatal stress alters the physiological structure of the growing fetus, thereby increases the likelihood of infants and toddlers showing greater temperamental negative emotional reactivity (Davis et al., 2004; Madigan et al., 2018), defined as early emerging, biologically based individual differences in negative affect, such as anger, fear, and sadness (Rothbart, 2011). Notably, low birthweight has been tied to increased risk of both temperamental negative affect (Baibazarova et al., 2013) and the two broadband dimensions of psychopathology, namely internalizing and externalizing behaviors (Aarnoudse-Moens, Weisglas-Kuperus, van Goudoever, & Oosterlaan, 2009).

While much of the recent research on prenatal stress has operated from the perspective of the fetal programming hypothesis, interpersonal models of stress transmission offer the alternative hypothesis that maternal stress and depression impact child development through its spillover onto early parent–infant interactions and relations (Hammen, Shih, & Brennan, 2004). For example, Hammen et al. (2004) found that the association between maternal depression and child depression at age 15 years was entirely mediated by family and interpersonal stress effects (e.g., parenting). However, much of this research has been conducted with mothers experiencing postnatal depression or anxiety, thus it's unclear whether the same mechanisms underlie the link between prenatal stress and child mental health. To our knowledge, only two studies have examined how prenatal stress and maternal mental health impact postnatal parenting, with mixed results. Belsky, Ruttle, Boyce, Armstrong, & Essex (2015) found that prenatal maternal stress, defined as a composite of depression, marital conflict, and financial stress, did not predict negative parenting during infancy, whereas Lereya and Wolke (2013) found that prenatal anxiety and depression predicted higher maternal hostile and punitive parenting during preschool. Parents who are unable to control their own negative emotional reactions are further proposed to engender child problems in regulating their own behaviors (i.e., externalizing problems) and emotions (i.e., internalizing problems; Grusec & Davidov, 2010).

A notable limitation of the current body of research is that most studies tend to examine the association between prenatal stress on *either* neonatal physiology and health outcomes (e.g., birth weight), *or* child temperament, *or* child mental health outcomes. Accordingly, there is a significant lack of longitudinal research that examines how these complementary processes unfold over time. Through a developmental cascade approach, the primary aim of this article is to examine the potential downstream consequences of prenatal stress on child mental health through a longitudinal series of proposed underlying mechanisms. An advantage of a developmental cascade model is that it allows for the examination of how early predictors cumulatively influence a developmental outcome (e.g., child mental health) over time through multiple processes and systems (Masten & Cicchetti, 2010). Not only is this a more holistic approach to examining the developmental evolution of a child exposed to prenatal stress, but it also allows for the identification of multiple developmentally salient targets for intervention. Here, we simultaneously modeled proposed fetal programming (i.e., birthweight, child temperament) and interpersonal transmission effects (i.e., hostile parenting). To our knowledge, these alternative hypotheses have not been examined in conjunction.

Cascades of Stress

In addition, while recent studies often control for postpartum stress (e.g., Neuenschwander et al., 2018), few

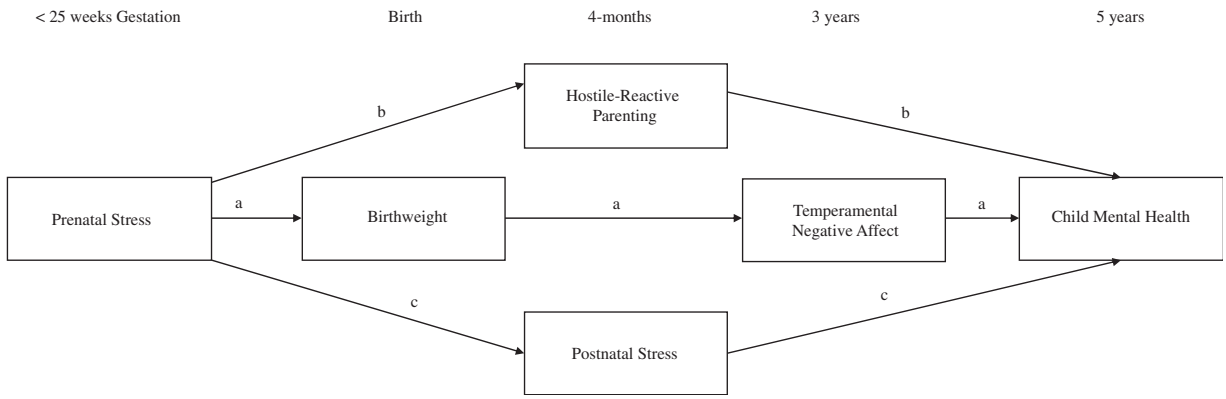

Figure 1. Conceptual model of developmental cascade from prenatal stress to child mental health. Pathway (a) denotes proposed fetal programming processes; Pathway (b) represents the hypothesized processes from the perspective of interpersonal models of stress transmission; and Pathway (c) denotes the effect of the continuation of stress into the postpartum period.

studies assess the impact of the continuation of maternal stress or mental health concerns into the postpartum period on child socioemotional development and mental health (Madigan et al., 2018). When studies include postpartum stress, they generally do so as a statistical covariate or by examining the relative predictive roles of prenatal and postnatal stress, independent of each other (e.g., Neuenschwander et al., 2018; O'Connor, Heron, Golding, Glover, & ALSPAC Study Team, 2003). Further, researchers focusing on postnatal stress are rarely able to control for prenatal stress. Thus, it is unclear whether the effects of postnatal stress can be accounted for by the continuation of stress from the prenatal period. As a notable exception, Barker, Jaffee, Uher, & Maughan(2011) examined the direct and indirect effects of prenatal depression and anxiety on child internalizing and externalizing through its association with postpartum maternal anxiety and depression, finding that both developmental periods were important for subsequent child mental health. However, this study did not include other potential postnatal mediating mechanisms, such as parenting and child negative affect. Simultaneously modeling prenatal stress and postnatal stress in a developmental cascade model will allow for greater understanding of the timing of effects between maternal stress and child mental health, which is critical when developing targeted preventive interventions.

The Current Study

The current study examines the intermediary processes proposed by different theoretical perspectives in one developmental cascade model (Figure 1), using an epidemiological pregnancy cohort that spans from the prenatal period to age five. Specifically, we hypothesized that prenatal maternal stress would predict child mental health (i.e., internalizing and externalizing) through three unique pathways. First, we predicted that prenatal stress would predict poorer child mental health through a set of biologically informed processes, including lower birth weight and toddler temperamental negative affect. Next, we hypothesized that prenatal stress would predict poorer mental health through its association with higher hostile-reactive parenting during infancy. Finally, we hypothesized that prenatal stress would be associated with later child mental health problems through the continuation of maternal stress during the postpartum period. Given recent research suggesting that prenatal stress might operate differently across sexes (Braithwaite et al., 2017; Plamondon et al., 2015), we also examined whether the developmental cascade model differed as a function of child sex.

Methods

Sample

Participants were drawn from an epidemiological prospective pregnancy cohort in a large city in western Canada. Pregnant women were recruited through community advertising and at local primary healthcare offices and the local laboratory services. Inclusion criteria included being at least 18 years of age, ability to communicate in English, a current gestational age of less than 25 weeks, and receiving prenatal care. Women with known multiple pregnancies were excluded. Between August 2008 and July 2011, 3,387 women were enrolled in the study. The original study was meant to end after 4-month postpartum, but subsequent funding allowed for additional follow-up assessments. Due to delays in funding acquisition, some participants had aged out of eligibility at these follow-up timepoints, resulting in smaller sample sizes (see Figure 2 for a flow chart of participant retention). Only participants with data available at age five ($N = 1992$) were included in the current study.

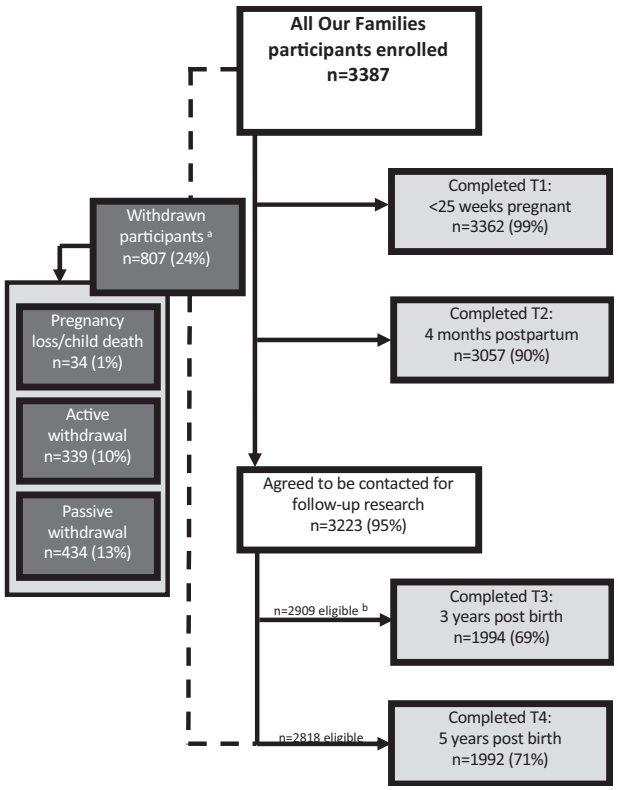

Figure 2. Participant flowchart from recruitment through age five of follow-up. [a]Participants who completed at least one prenatal questionnaire but did not complete any follow-up surveys, up to 5 years. [b]Sample size at follow-up time points decreased due to timing of questionnaire development and implementation, ethics approval, funding constraints, and attrition. Only participants who were still eligible, based on their child's age, were mailed follow-up questionnaires. Adapted and reprinted with permission from Tough et al. (2017).

About 24% ($n = 807$) of women were considered withdrawn from the study, defined as not completing any assessments after the pregnancy period. Approximately 13% of participants had passively withdrawn from the study, due to geographical moves, lost to follow-up, or unknown reasons. Common reasons for active withdrawal (10%) included loss of interest, lack of time, and lack of partner support. A small proportion of women (1%) withdrew due to pregnancy loss or child death. Participants who were retained at age five were more likely to have lower parental stress symptoms, have higher educational attainment and family incomes, be older, have fewer antepartum medical risks, and have infants with lower birthweights. However, differences tended to be small in magnitude (see Supplementary Table S1 for mean comparisons).

At the first wave of data collection, the average age of mothers was 30.87 ($SD = 4.36$) years. Mothers were predominantly white (81.9%), with smaller percentages of women identifying as Asian (10.7%), Latin American (1.6%), black (1.2%), indigenous (0.5%), or mixed/other (4.1%). Participants were generally from middle- to high-socioeconomic backgrounds, with 79.6% of participants having a university, college, or trade school degree and 80.8% with an annual family income level of $70,000 Canadian dollars or more per year (Tough et al., 2017). All procedures were approved by the University of Calgary Research Ethics Board.

Measures

Maternal Stress

During pregnancy and at 4-month postpartum, mothers completed the Perceived Stress Scale (PSS; Cohen, Kamarck, & Mermelstein, 1983), Edinburgh Postnatal Depression Scale (EDPS; Cox, Holden & Sagovsky, 1987), and the Spielberger State Anxiety Inventory (SAI; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1970). Internal reliabilities were all satisfactory (αs range from .80 to .93). Consistent with previous literature conceptualizing perceived stress, anxiety, and depression as indices of prenatal stress (e.g., Belsky et al., 2015; Madigan et al., 2018; Maxwell et al., 2018), these three scales were used as indicators of latent variables of maternal stress during the prenatal and early postnatal periods.

Birthweight

Maternal pregnancy medical records were available for 1,760 of the 1,992 participants and provided information regarding infant birthweight ($M = 3353.33$, $SD = 516.49$, range: 595–5071 g) at the time of delivery.

Hostile-Reactive Parenting

At the 4-month postpartum assessment period, mothers responded to two items ("I have been angry with my baby when he/she was particularly fussy" and "I have raised my voice with or shouted at my baby when he/she was particularly fussy") from the Parental Cognitions and Conduct Toward the Infant Scale (PACOTIS; Boivin et al., 2005) hostile-reactive subscale. Item responses were on a scale from 0 (*not at all what I did*) to 10 (*exactly what I did*). The two items ($r = .77$) were averaged together to create a variable of hostile-reactive parenting.

Child Negative Affect

When children were three years old, mothers completed the 12-item Negative Affect subscale of the Child Behavior Questionnaire-Very Short Form (CBQ-VSF; Putnam & Rothbart, 2006). This scale assesses the degree to which the child shows high temperamental negative affect, including anger, fear, sadness, and general upset. Item responses were on a scale from 0 (*extremely untrue*) to 7 (*extremely true*). Internal consistency was adequate ($\alpha = .69$).

Child Mental Health

When children were five years old, mothers completed the Behavior Assessment System for Children-Second Edition (BASC-2), a widely used assessment of child psychological problems with established reliability and validity (Kamphaus & Reynolds, 2007). The current study focused on the Externalizing ($\alpha = .86$) and Internalizing ($\alpha = .88$) scales of the BASC. All analyses were conducted using the combined-sex norm-referenced T scores.

Covariates

We controlled for child sex (male= 1; female = 2), maternal education, and family income in all analyses. Maternal education was reported on a scale of 1 (did not complete high school) to 6 (completed graduate school), while income was reported in increments of $10,000 (1 = ≤$10,000; 11 = ≥$100,000). We also controlled for antepartum health risk with the inclusion of an Antepartum Risk Score (APRS; Alberta Perinatal Health Program, 2009) from the pregnancy medical records. In Alberta, the APRS is completed at every birth by the physician or midwife caring for the mother at the time of delivery. The APRS assigns risk scores to mothers based on a number of pre-existing risk factors (e.g., obesity, maternal age <18 or ≥35 years), past pregnancy history (e.g., stillbirths), current pregnancy complications (e.g., gestational diabetes or hypertension), and other risk factors (e.g., substance use). A weighted value is assigned to each condition based on the severity of the condition, and all values are then summed to create a total risk score. Based on prior validation (Parboosingh, 1986), scores of 0 to 2 are considered low risk, scores of 3–6 indicate moderate risk, and scores of 7 or more reflect high risk.

Analytic Plan

To examine the direct and indirect associations between prenatal stress and child internalizing and externalizing problems at age five through the set of hypothesized mediating mechanisms, we conducted a structural equation model (SEM) in MPlus 8.0 (Muthén & Muthén, 1998–2017). Specifically, we examined the longitudinal relations between: (a) prenatal maternal stress at <25 weeks gestation; (b) birthweight; (c) maternal postnatal stress and hostile-reactive parenting at 4 months; (d) child negative affect at 3 years; and (e) child internalizing and externalizing symptoms at age five. All possible predictive pathways between exogenous and endogenous variables were estimated, as were covariances between predictors assessed at the same time point (e.g., internalizing and externalizing at 5 years).

Missing Data

To evaluate whether data were missing completely at random (MCAR), we conducted Little's MCAR test (Little, 1988). Results of Little's MCAR test suggested that data were not MCAR, χ^2 (967) = 1,181.39, $p <$ .001. Unlike MCAR, there is no way to rigorously test whether the data are missing at random (MAR) or not missing at random (NMAR). However, including covariates thought to be related to missingness or values on the outcomes (e.g., maternal education, family income, maternal stress/depression) can make the MAR assumption more likely, thus limiting the potential bias occurring if the data were NMAR (Collins, Schafer, & Kam, 2001; Graham, 2009). Therefore, missing data were estimated using full information maximum likelihood (FIML), which is robust to conditions of MAR (Enders & Bandalos, 2001). FIML procedures do not impute scores for missing data but rather utilize the raw data to establish parameter estimates (Enders & Bandalos, 2001). The model was estimated in MPlus using the maximum likelihood with robust standard errors estimator (MLR).

Results

Descriptive statistics for all study variables are included in Table I. Results of the developmental cascade model are shown in Figure 3. Only significant pathways are shown. Note that previously described covariates were included as predictors of all longitudinal pathways but are not shown for clarity of presentation. Consistent with best practices, covariances were also estimated between identical measurements across time but are not shown in the figure (Marsh, Morin, Parker, & Kaur, 2014). Fit indices suggested that the model provided a good representation of the data (χ^2 [47, N = 1,933] = 117.23, root mean square of error of approximation (RMSEA) = .03, comparative fit index (CFI) = 0.99, Tucker-Lewis Index (TLI) = 0.98).

Direct Effects

As shown in Figure 3, prenatal maternal stress had a direct effect on child internalizing at age five, $\beta = .16$, $p < .001$, but not externalizing symptoms, $\beta = .05$, $p = .15$. In addition, prenatal stress negatively predicted birthweight, $\beta = -.07$, $p = .008$, and positively predicted both postpartum stress, $\beta = .60$, $p < .001$, and hostile-reactive parenting at four months, $\beta = .26$, $p < .001$, and child negative affect at three years, $\beta = .11$, $p = .002$. Hostile-reactive parenting, in turn, predicted higher child externalizing problems at age five, $\beta = .12$, $p = .001$. Postnatal stress positively predicted child negative affect at three years, $\beta = .14$, $p = .001$, and both child internalizing $\beta = .09$, $p = .01$, and externalizing, $\beta = .11$, $p = .001$, symptoms at age five. Birthweight did not predict subsequent parent (i.e., parenting, stress) or child functioning (i.e., temperament, internalizing, externalizing). Finally, higher

Table I. *Means, Standard Deviations, and Correlations Among the Variables in the Primary Analyses of the Study*

	M	*SD*	Range	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Child sex			1–2														
2. APRS	1.94	2.04	0–14	−.02													
3. Maternal education	4.00	1.04	1–6	.02	−.03												
4. Family income	9.39	2.36	1–11	.00	−.03	.30*											
5. T1 PSS	13.12	6.13	0–36	.01	.08*	−.08*	−.18*										
6. T1 EPDS	4.90	4.22	0–24	.02	.09*	−.06*	−.18*	.74*									
7. T1 SAI	30.35	8.36	20–73	.01	.12*	−.06*	−.14*	.69*	.71*								
8. Birthweight (g)	3353	516	595–5071	−.09*	−.17*	.02	.04	−.06*	−.08*	−.10*							
9. T2 PSS	11.49	6.44	0–40	−.02	.09*	−.03	−.16*	.53*	.48*	.47*	−.04						
10. T2 EPDS	4.03	4.09	0–30	.00	.05*	−.02	−.12*	.44*	.48*	.43*	−.03	.77*					
11. T2 SAI	29.70	8.81	20 − 78	.00	.11*	−.01	−.13*	.45*	.43*	.52*	−.05*	.74*	.77*				
12. T2 hostile-reactive parenting	1.39	1.97	0–10	−.05	−.01	.04	−.08*	.23*	.18*	.23*	−.05	.34*	.32*	.27*			
13. T3 negative affect	3.62	.79	1–7	.06*	.01	−.05*	−.12*	.22*	.21*	.18*	.02	.22*	.20*	.18*	.10*		
14. T4 externalizing	49.21	8.24	33–93	−.19*	.01	−.07*	−.06*	.15*	.16*	.15*	.04	.21*	.20*	.19*	.19*	.28*	
15. T4 internalizing	50.46	9.55	28–98	.03	−.01	−.02	−.05*	.23*	.24*	.20*	.01	.20*	.24*	.11*	.11*	.39*	.51*

Note. Range values reflect observed range, not all possible values. Child sex: 1 = male; 2 = female. APRS = Antepartum Risk Score; PSS = Perceived Stress Scale (possible range: 0–40); EDPS = Edinburgh Postnatal Depression Scale (possible range: 0–30); SAI = Spielberger State Anxiety Inventory (possible range: 20–80); T1 = < 25 weeks gestation; T2 = 4 months postpartum; T3 = 3 years; T4 = 5 years.

*$p < .05$.

temperamental negative affect at age three predicted both higher internalizing, $\beta = .32$, $p < .001$, and externalizing, $\beta = .24$, $p < .001$, symptoms at age five.

Indirect Effects

Next, we examined the indirect effects of prenatal stress on child internalizing and externalizing symptoms through its association with birthweight, parenting, postpartum stress, and child negative affect. Indirect effects were estimated using the bootstrapping procedure in MPlus 8.0. Birthweight did not predict subsequent child or parental functioning and were therefore not included in the indirect effect estimates.

Results for all standardized estimated indirect effects are presented in Table II. There were four significant indirect effects from prenatal maternal stress to child externalizing symptoms. First, there were indirect effects from prenatal stress to child externalizing through hostile-reactive parenting, $\beta = .03$, $p = .002$, postnatal maternal stress, $\beta = .07$, $p = .001$, and child temperamental negative affect, $\beta = .03$, $p = .003$. In addition, the indirect pathway between prenatal stress, postnatal stress, child negative affect, and child externalizing symptoms was also significant, $\beta = .02$, $p = .001$. There were three significant indirect effects between prenatal stress and child internalizing symptoms at age five. Specifically, there were indirect effects through postnatal maternal stress, $\beta = .05$, $p = .01$, and child negative affect at age three, $\beta = .03$, $p = .002$. The indirect pathway between prenatal stress, postnatal stress, child negative affect, and child internalizing symptoms was also significant, $\beta = .03$, $p < .001$.

Sex Differences

We conducted multigroup comparison analyses to explore whether the effects of prenatal stress differed according to child sex. First, we ran the SEM simultaneously for males and females, specifying a fully constrained model in which the coefficient of every structural path was set to be equal across males and females. We then compared the relative fit of this model to a nested model in which all the structural paths were free to vary between males and females. The free-to-vary model did not evidence significantly better fit than the constrained model ($\Delta\chi^2 = 25.98$, $\Delta df = 19$, $p = .13$, ΔRMSEA = .004), showing that the results of the model were comparable across male and female children in the sample.

Follow-Up Sensitivity Analyses

To ensure that results were not biased by only including participants who had data available at age five, we also reran the model using the full sample of 3,387 participants, using FIML to estimate missing data. The pattern of results was the same, with

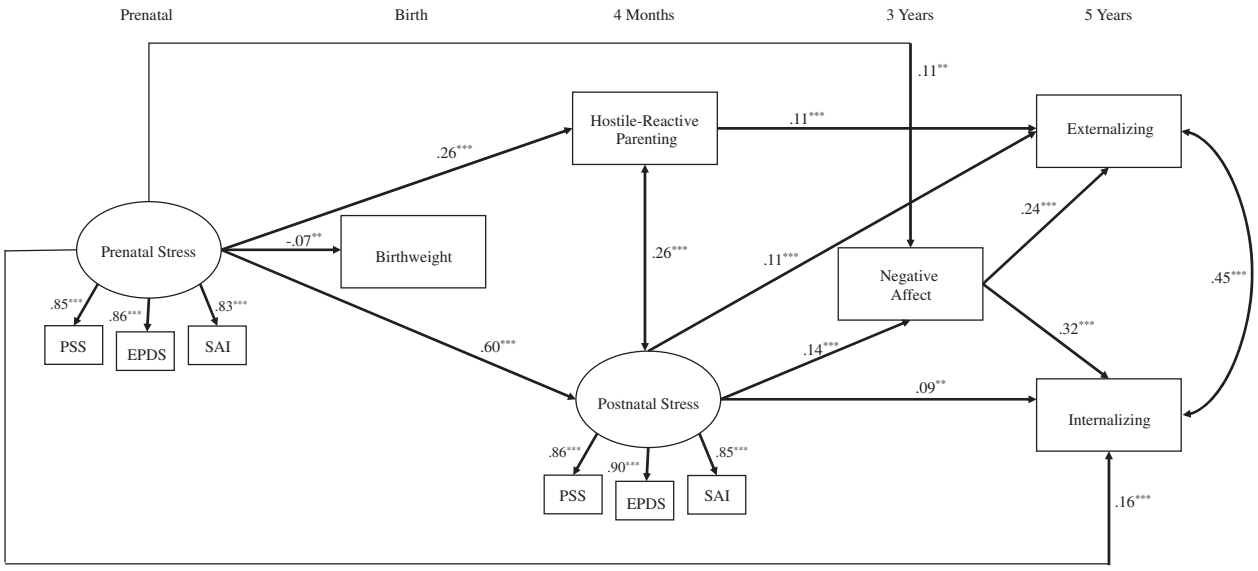

Figure 3. Standardized path coefficients in developmental cascade from maternal prenatal stress to child internalizing and externalizing symptoms at age five. Only significant pathways are shown. EDPS = Edinburgh Postnatal Depression Scale; PSS = Perceived Stress Scale; SAI = Spielberger State Anxiety Inventory. $^{**}p \leq .01$; $^{***}p \leq .001$.

Table II . *Indirect Effects of Prenatal Stress to Child Externalizing and Internalizing Problems*

	β	95% CI
To externalizing		
Direct effect	.05	[−.02, .11]
Specific indirect effects		
Hostile-reactive parenting	**.03**	[.01, .05]
Postnatal stress	**.07**	[.03, .10]
Negative affect	**.03**	[.01, .04]
Hostile-reactive parenting → negative affect	.00	[−.004, .004]
Postnatal stress → negative affect	**.02**	[.01, .03]
Total indirect effect	**.14**	[.10, .18]
Total effect	**.18**	[.13, .23]
To internalizing		
Direct effect	**.16**	[.10, .22]
Specific indirect effects		
Hostile-reactive parenting	.00	[−.01, .02]
Postnatal stress	**.05**	[.01, .09]
Negative affect	**.03**	[.01, .06]
Hostile-reactive parenting → negative affect	.00	[−.01, .01]
Postnatal stress → negative affect	**.03**	[.01, .04]
Total indirect effect	**.11**	[.08, .15]
Total effect	**.27**	[.22, .33]

Note. Bolded values represent significant effects.

some minor differences in standardized effect sizes, ranging from .00 to .03 (see Supplementary Figure S1).

Discussion

Using a developmental cascade model capturing stage-salient processes at five timepoints, this study provided support for both the fetal programming and interpersonal models of stress transmission. Specifically, prenatal stress predicted both externalizing and internalizing problems through child negative affect, supporting the fetal programming hypothesis. Prenatal stress also predicted externalizing problems at age five through its effect on hostile-reactive parenting during infancy, supporting interpersonal transmission models. We did not find evidence of sex differences. While some evidence suggests that prenatal stress might have different effects on males and females (Braithwaite et al., 2017), our finding is consistent with a recent meta-analysis on prenatal stress and child socioemotional outcomes, which failed to find gender differences (Madigan et al., 2018).

According to fetal programming hypotheses, exposure to stressors *in utero* may alter the growing physiological systems responsible for aspects of temperament, such as the hypothalamus–adrenal–pituitary (HPA) axis (Gartstein & Skinner, 2018). However, few studies have simultaneously modeled the effects of prenatal stress and of postnatal stress on child temperament. Thus, it is notable that the current study found a significant effect of both prenatal stress and postnatal stress on child negative affect. As temperament is thought to be at least partially genetically determined (Rothbart, 2011), these results might underscore an underlying genetic component that gives rise to heightened maternal stress, anxiety, and depression in both the pre- and postnatal periods as well as child temperamental negative affect. Higher toddler negative affect, in turn, increased the risk for both internalizing and externalizing problems at age five.

Providing partial support for the interpersonal transmission of stress models, we found that prenatal stress was associated with increased hostile-reactive

parenting at four months. Hostile-reactive parenting during infancy, meanwhile, predicted greater externalizing, but not internalizing, problems at age five. This is also in line with coercive process models, which posit that early hostile and over-reactive parenting engenders increased noncompliance and difficultness from the child, which further increases hostile parenting (Patterson, 2002). Over time, this cyclical and escalating process results in the development of externalizing problems characterized by greater aggression, impulsivity, and/or inattention. To our knowledge, this is the first study to show that prenatal stress is associated with externalizing problems five years later via hostile parenting in early infancy.

Taken together, these results highlight concepts within the developmental psychopathology perspective, which posits that there are a multitude of pathways and processes that contribute to the development of adaptive or maladaptive behaviors (Cicchetti & Rogosch, 1996). For example, the principle of multifinality suggests that a single starting point (i.e., prenatal stress) can diverge into multiple pathways and child outcomes (e.g., externalizing and internalizing), while the principle of equifinality suggests that a single outcome can be reached through a multitude of pathways or processes (e.g., externalizing problems predicted by pathways involving prenatal maternal stress, postpartum stress, hostile parenting, and child negative affect). By using a developmental cascade model, the current study showcases both concepts, underscoring the complex psychobiological processes that occur between prenatal maternal stress and later child mental health problems.

In line with previous research (Bussières et al., 2015; Grote et al., 2010), prenatal stress was also associated with poorer fetal growth in the form of lower birthweight. Contrary to our expectations, birthweight did not predict later negative affect at age three or mental health problems at age five. Although research has suggested that low birthweight infants have more difficult temperament characteristics (e.g., Baibazarova et al., 2013), these studies have almost exclusively measured temperament during infancy, when temperament is more labile and subject to change compared with toddlerhood (Durbin, Hayden, Klein, & Olino, 2007). Thus, it is possible that low birthweight predisposes infants to higher negative emotional reactivity, but that this effect is not long-lasting and may not represent stable temperamental characteristics. Indeed, one study found that irritability (a form of temperamental negative affect) was moderately stable from three to seven months among full-term infants but evidenced no stability among preterm, low birthweight infants (Garcia Coll, Halpern, Vohr, Seifer, & Oh, 1992).

It is also noteworthy that our study did not find long-lasting implications of birthweight on child mental health problems. While previous research has suggested that low birthweight infants are at risk for greater internalizing and externalizing problems at school age, much of this research has focused on very preterm infants born prior to 32 weeks old and with birthweights less than 1,500 g (see Bhutta, Cleves, Casey, Cradock, & Anand, 2002 for a meta-analysis). Samples characterized by extreme values (e.g., <1,500 g) can result in higher correlations between variables, increasing the potential for inflated or biased effect sizes (MacCallum, Zhang, Preacher, & Rucker, 2002). Thus, while extremely low birthweight infants might be at risk for psychological problems, our results suggest that birthweight measured along a continuous scale in an epidemiological sample does not impart greater risk of mental health problems at age five. However, it is possible that there is an indirect effect of low birthweight on child psychopathology through other intermediary variables not assessed in this study (e.g., neurocognitive development). Future research should explore this possibility.

Implications

Increasing evidence and awareness about the effects of prenatal stress and depression on the developing child has led to calls to develop effective intervention and prevention programs for pregnant women specifically aimed at curbing prenatal stress (Nolvi et al., 2016; Zhang, Cui, Zhou, & Li, 2019). However, interventions are generally constrained to the pregnancy period, and few intervention studies have included follow-up assessments into the postpartum period, particularly in regard to child socioemotional outcomes. Meanwhile, interventions aimed at reducing postpartum depression in high-risk samples generally start after birth or in late pregnancy (Sangsawang, Wacharasin, & Sangsawang, 2019). As the current study underscores, however, maternal stress, anxiety, and depression are relatively stable and are thus likely to occur during both pregnancy and the postnatal period as well. While prenatal stress had a direct effect on child internalizing problems at age five in the current study, prenatal stress was only indirectly associated with child externalizing problems via postnatal processes (e.g., postnatal stress, early parenting). Results highlight the complex, dynamic processes that occur between prenatal stress and increased risk for child mental health problems. While the fetal programming and interpersonal stress transmission models are often discussed and examined separately, results from the current study suggest that they occur simultaneously in a mutually informative manner. Therefore, intervention and prevention programs may be more effective if they continue into the postpartum period for high-risk women and also include psychoeducational components and parenting supports that foster positive parent–child relationships. Future

research should also attempt to capture other theoretical models of stress transmission, including niche selection, which proposes that biological (e.g., fetal programming), environmental (e.g., parenting), and individual (e.g., temperament) characteristics mutually influence an individual to self-select into specific niches or situations (e.g., problematic peer groups) that operate to maintain continuity of stress over time (Ellman, Murphy, & Maxwell, 2018; Wachs, 1996).

Limitations

Several limitations of the current study also merit discussion. First, the current sample was a relatively low-risk community sample that evidenced high incomes and maternal educational status, so our results may not generalize to more at-risk or specialized samples (e.g., adolescent mothers). Second, although we included medical reports of child birthweight and maternal medical risk, the majority of our constructs were measured by maternal report. Therefore, we cannot rule out the possibility of reporter bias. For example, perceptions of child temperamental negative affect could be influenced by the mother's own psychopathology and negative affect (i.e., depression, anxiety). Thus, future research should attempt to utilize multi-informant and multimethod constructs of maternal stress, parenting, temperament, and child mental health symptoms. Third, while our assessment of prenatal stress is consistent with prior literature, distinct sources of maternal stress (e.g., depression, anxiety, negative life events) may operate differently on child outcomes and should be explored further in future research. Fourth, only hostile-reactive parenting was measured in the sample at 4 months. Our construct is consistent with other prior studies, which have assessed the association between prenatal stress and harsh or hostile parenting behaviors (e.g., Belsky et al., 2015; Lereya & Wolke, 2013). However, it is possible that other domains of parenting (e.g., sensitivity) could also be involved in the developmental cascade between prenatal stress and child mental health problems. In addition, temperament was only measured once at 36 months, which precludes our ability to examine the effect of infant temperament on hostile-reactive parenting behaviors. Finally, although previous studies have argued that links between prenatal stress and both birthweight and child temperament support the fetal programming hypothesis, physiological indices of neonatal functioning may be more robust indicators of programming effects and should be explored in future developmental cascade approaches.

Conclusions

The current study provides support for multiple mechanisms of risk in explaining the links between prenatal stress and child mental health problems. Prenatal stress continued to exert a direct effect on internalizing problems at age five, even after controlling for postnatal stress, birthweight, hostile-reactive parenting, and child negative affect. However, prenatal stress was only indirectly related to child behavior problems at age five, through multiple pathways, including postnatal stress, hostile parenting, and child negative affect. Study results highlight the potential benefit of preventative mental health programs that start during the prenatal period and continue into the early infancy period.

Supplementary Data

Supplementary data can be found at: https://academic.oup.com/jpepsy.

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