The Effects of Prenatal Maternal Stress on Early Temperament: The 2011 Queensland Flood Study

Gabrielle Simcock, PhD,*† Guillaume Elgbeili, Masters,‡ David P. Laplante, PhD,‡ Sue Kildea, PhD,*§ Vanessa Cobham, PhD,*† Helen Stapleton, PhD,*§ Marie-Paule Austin, PhD,‖ Alain Brunet, PhD,¶ Suzanne King, PhD‡¶

ABSTRACT: ***Objective:*** **This study examined the effects of disaster-related prenatal maternal stress on infant temperament and whether the sex of the infant or the timing of the stressor in pregnancy would moderate the effects.** ***Methods:*** **Mothers' objective experiences of a sudden-onset flood in Queensland, Australia, their subjective emotional reactions, and cognitive appraisal of the event were assessed. At 6 months postpartum, 121 mothers reported their infant's temperament on the 5 dimensions of the Short Temperament Scale for Infants.** ***Results:*** **When controlling for postnatal maternal factors, subjective prenatal maternal stress and cognitive appraisal of the disaster were associated with easier aspects of infant temperament. However, several interesting interactions emerged showing negative effects of the flood. With higher levels of objective hardship in pregnancy, boys (but not girls) received more irritable temperament ratings. When the flood occurred early in pregnancy, higher levels of objective hardship predicted more arrhythmic infant temperament. Finally, mothers whose emotional response to the flood exceeded the hardship they endured reported significantly more active-reactive infants.** ***Conclusion:*** **Prenatal maternal stress from a natural disaster predicted more difficult temperament ratings that were moderated by infant sex, timing of the flood in gestation, and mother's emotional response to the disaster.**

*(J Dev Behav Pediatr 0:*1–12, 2017) **Index terms:** QF2011, prenatal maternal stress, temperament, infant development, disaster.

Temperament is typically thought of as individual differences in reactivity, approach, adaptability, and self-regulation.[1] Temperament qualities are considered relatively stable across situations and time[2] and are associated with later outcomes in a number of developmental domains. For example, difficult or negative temperament characteristics early in life are predictive of poor mental health[3] and childhood behavior problems.[4,5] Thus, it is important to identify early risk factors that may contribute to difficult and/or negative temperaments to optimize mental health outcomes.

The intrauterine environment is one of the earliest influences on infant temperament,[6] although the interplay between genes and the environment on infant temperament is also recognized.[7] Research shows that mothers who self-reported experiencing pregnancy-specific anxiety,[8] general anxiety,[9] or depression[10–12] in pregnancy are more likely to describe their infants as fussier, slower to adapt to novelty, and more difficult than infants whose mothers did not experience depression or anxiety in pregnancy. Moreover, observational studies of infant behavior confirm findings from the maternal report studies, showing that infants of women who were depressed or anxious during pregnancy,[13] or who experienced a high number of stressful life events,[14] exhibit increased reactivity or fearfulness compared with infants of women who did not experience stress during pregnancy.

Both timing of the stressor in pregnancy and infant sex may moderate the effects of prenatal maternal mood on temperament. The negative effects of maternal anxiety or depression on infant temperament seem to be more pronounced during the first half of pregnancy[8,11,15] and affect female fetuses to a greater extent than male fetuses.[15]

In prenatal "stress" studies in which the pregnancy stressor is psychological distress or adverse life events or hassles, it is difficult to disentangle the extent to which any negative effects on aspects of infant temperament are due to the genetic inheritance of difficult personality traits from parents, versus the direct effects of intrauterine influences, versus the postnatal environment. Research that uses an independent stressor, such as a natural disaster, to study the effects of prenatal maternal stress (PNMS) on development mitigates these potential confounds.[16,17] In these cases, the stressor affects

From the *Mater Research Institute-The University of Queensland (UQ), Brisbane, Queensland, Australia; †School of Psychology, The University of Queensland, Brisbane, Queensland, Australia; ‡Schizophrenia and Neurodevelopmental Disorders Research, Douglas Mental Health Research Institute, Verdun, QC, Canada; §School of Nursing, Midwifery and Social Work, The University of Queensland, Brisbane, Queensland, Australia; ‖School of Psychiatry, University of New South Wales and St John of God Health Care, Sydney, Australia; ¶Department of Psychiatry, McGill University, Montreal, QC, Canada.

Received September 2016; accepted March 2017.

Funding was provided by the Canadian Institutes of Health Research (CHIR grant # MOP-1150067).

Disclosure: The authors declare no conflict of interest.

Address for reprints: Suzanne King, PhD, McGill University, Douglas Mental Health University Institute, Verdun, Québec H4H 1R3, Canada; e-mail: suzanne.king@mcgill.ca.

a large number of pregnant women independently of their own and their partners' mental health profile or personality. Furthermore, this kind of stressor affects pregnant women at all stages of gestation, and tends to be of sudden onset, allowing precise timing of in utero exposure. Furthermore, it enables researchers to understand more about how various aspects of the maternal stress response to a disaster—objective hardship, subjective emotional reactions, and/or cognitive evaluation of the event—can affect infant behavior.

One study has demonstrated that natural disaster–related objective (e.g., hardship experienced) and subjective (e.g., emotional distress) PNMS can affect infant temperament status in different ways.[18] When an ice storm occurred early in pregnancy, high levels of maternal subjective distress predicted more difficult, fussy temperaments in 6-month-old infants. Moreover, the pregnant women's objective degree of hardship from the disaster predicted more difficult infant temperament but only when combined with maternal illness or infection in the first trimester. However, the unadaptable dimension of temperament was not significantly affected by either aspect of PNMS. This study highlights how using natural disasters as a stressor enables researchers to study multiple facets of pregnant women's stress response.

This study also uses a natural disaster to assess various aspects of PNMS on early temperament status. A sudden-onset flood occurred in January 2011 in Queensland, Australia, providing another opportunity to study the impact of pregnancy stress from a natural disaster on infant development. The Queensland Flood Study (QF2011) was established shortly after floods severely affected 70% of Queensland, Australia, completely inundating 15,000 homes, partially inundating a further 18,000, and costing in excess of AU$2 billion in insurance and cleanup.[19] With QF2011, we extend previous PNMS disaster research by including more detailed assessments of the maternal stress response (i.e., the women's levels of objective hardship and her emotional and cognitive reactions to the flood) and examined how these aspects of PNMS influenced infant temperament at 6 months of age. We also examined potential moderating effects of timing of the flood in pregnancy and infant sex on temperament.

Based on previous research, we hypothesized that pregnant women's flood-related objective and subjective stress reactions[18] and a negative cognitive appraisal of the event[20] would have negative effects on infant temperament. We also hypothesized that girls' temperament would be more vulnerable to the adverse effects of PNMS than that of boys,[15] and that higher levels of flood-related stress in early pregnancy, but not late pregnancy, would have negative effects on infant temperament.[18]

METHOD

Participants and Procedures

The sample included 126 mother-infant dyads enrolled in the QF2011 longitudinal study for whom maternal flood exposure and infant temperament data were available. Eligibility for enrollment included English-speaking women older than 18 years who were pregnant with a singleton during the 2011 Queensland floods. Most recruitment occurred during antenatal visits at a public tertiary hospital in the flood-affected region, and some women responded to ads placed in local media. Recruitment commenced once ethical approval was received (April 2011) and continued until January 2012. For the current sample, at the time of recruitment, 38 women were pregnant and 88 had already given birth. The recruitment questionnaire was completed an average of 7 months after the flood (range = 3–10 months), which is similar to the timing of completion of the prenatal maternal stress (PNMS) questionnaires in Project Ice Storm 5 to 6 months after the disaster.[21] At recruitment and 12 months after the flood, mothers completed surveys regarding their demographics and flood-related PNMS experiences and reactions. At 6 months, postpartum mothers also completed surveys on their own mental health and on their infants' development. Full eligibility, recruitment, and procedural details are published elsewhere.[19]

Data were excluded from one participant because of preterm birth (<36 weeks gestation) or because the temperament surveys were completed beyond one month from the infant's 6 months birthday (n = 4). The final sample included 121 women who rated their infant's temperament at 6 months of age. The demographics for the final sample are shown in Table 1.

The study had ethic's approval from the study site ethical review board (#1844M) and the affiliated university ethics committee (#2013001236), and all participants provided written informed consent.

Outcome Variable

Infant Temperament Scales

The Short Temperament Scale for Infants (STSI)[22] was administered when the infants were 6 months old. The STSI is a 30-item questionnaire normed for Australian infants aged from 4 to 8 months. Mothers rated the occurrence of common infant behaviors on a 6-point Likert scale ranging from 1 (almost never) to 6 (almost always). The items comprise 5 dimensions of infant temperament, with 6 questions per dimension, measuring: approach (e.g., "The baby accepts straight away any change in place or position of feeding, or person giving the feed."), rhythmicity ("The baby wants daytime naps at differing times [over 1 hour difference] from day to day."), cooperation-manageability (The baby is content [smiles, coos] during interruptions of milk or solid feeds."), activity-reactivity ("The baby moves a lot [squirms, bounces, kicks] while lying awake in a cot."), and irritability ("The baby continues to cry in spite of several minutes of soothing."). Normed factor scores can be calculated from the raw scores for each dimension (range = 0–6). The scoring algorithms are such that infants scoring +1 *SD* above the standardized mean on

Table 1. Descriptive Statistics for the Factor Scores of the Dimensions of the Short Temperament Scale for Infants, the Predictor Variables, and the Covariates

	N (%)	Mean (*SD*)	Range
Outcome Variable			
Approach	121	2.00 (0.81)	1.00 to 5.14
Rhythmicity	121	2.53 (0.83)	1.00 to 5.17
Cooperation-manageability	113	3.07 (0.50)	2.00 to 4.50
Activity-reactivity	115	4.39 (0.84)	2.33 to 6.00
Irritability	119	2.83 (0.89)	1.00 to 5.00
Predictor variables			
Objective hardship (QFOSS)	121	21.15 (16.79)	3 to 74
Posttraumatic stress (IES-R)	121	7.61 (12.61)	0 to 66
Peritraumatic distress (PDI)	121	12.51 (9.09)	0 to 42
Peritraumatic dissociation (PDEQ)	121	6.42 (8.03)	0 to 32
Composite subjective stress (COSMOSS)	121	0.10 (1.12)	−1.08 to 4.65
Timing of exposure, days	121	116.31 (75.70)	−2.02 to 264.00
Cognitive appraisal: negative	48 (40)		
Very negative: n = 6			
Negative: n = 42			
Cognitive appraisal: neutral/positive	72 (60)		
Neutral: n = 54			
Positive: n = 18			
Very positive: n = 0			
Infant sex: boys	57 (47)		
Infant sex: girls	64 (53)		
Covariates			
Maternal yrs of schooling	97	14.70 (1.68)	10 to 16
Socioeconomic index (SEIFA)	121	1050.27 (57.77)	856 to 1150
Maternal depression (EPDS)	121	5.91 (4.30)	0 to 21
Maternal anxiety (STAI)	121	34.27 (10.18)	20 to 73
Parent-child dysfunction (PSIDI)	121	16.69 (5.64)	12 to 44
Gestational age at birth, wk	121	39.38 (1.17)	36 to 41
Age at assessment, mo	121	6.35 (0.42)	5.50 to 7.92

Untransformed scores are used for the PNMS measures. COSMOSS, composite score for mothers' subjective stress; EPDS, Edinburgh Postnatal Depression Scale; IES-R, Impact of Event Scale-Revised; PDEQ, Peritraumatic Dissociative Experiences Questionnaire; PDI, Peritraumatic Distress Inventory; PSIDI, Parent-Child Dysfunctional Interaction; QFOSS, Queensland Flood Objective Stress Score; SEIFA, Socio-Economic Index For Area; STAI, State-Trait Anxiety Inventory.

each dimension are classified as having difficult temperamental qualities, and infants scoring −1 *SD* below the mean on each dimension are classified as having easy temperamental qualities.

Predictor Variables

Objective Hardship

Women's objective hardship was assessed using a questionnaire similar to that used in previous disaster-related PNMS research[18,23] that was tailored specifically for the Queensland flood. Items assessed 4 key dimensions of food exposure: threat (e.g., "Were you injured?"), loss (e.g., "Did you experience loss of personal income?"), scope (e.g., How may days were you without electricity?"), and change (e.g., "Did you spend any time in a temporary shelter?"). Points were attributed to each item according to group consensus about severity, such that the scores on each dimension ranged from 0 (no impact) to 50 (extreme impact) giving a total possible Queensland Flood Objective Stress Score (QFOSS) of 200. Higher scores indicated higher levels of flood-related hardship.

Subjective Stress

The women's emotional reactions to the Queensland flood were assessed using 3 questionnaires. Two self-report questionnaires captured the women's immediate peritraumatic reactions to the event as recalled at a later time point. The severity of their initial emotional distress (e.g., "I thought I might die") and physical panic-like reactions (e.g., "I thought I might pass out") to the flood were assessed using the 13-item Peritraumatic Distress Inventory (PDI[24]) which has items rated on

a 0 (not true) to 4 (extremely true) rating scale. This scale has high internal consistency (coefficient alpha = .76) and stability. The women's dissociative-like experiences (e.g., "What was happening seemed unreal to me, like I was in a dream, or watching a movie or play") at the time of the flood were assessed using the 10-item Peritraumatic Dissociative Experiences Questionnaire (PDEQ[25]) with items rated on a 1 (not true) to 5 (extremely true) rating scale. This scale has high internal consistency (Cronbach's alpha = .85).

The Impact of Event Scale-Revised (IES-R[26]) is a commonly used self-report questionnaire assessing posttraumatic stress-like responses to stressful or traumatic events yielding a total score of 0 to 88, and with subscales of intrusion (e.g., "I had dreams about it"), hyperarousal (e.g., "I had trouble staying asleep"), and avoidance (e.g., "I tried to remove it from my memory"). The women rated the severity of each of the 22 symptoms during the preceding 7 days in relation to the Queensland flood on a 0 (not true) to 4 (extremely true) Likert scale. This scale has high internal consistency (alpha coefficients range = 0.79–0.94) and good retest reliability (correlation coefficients from 0.51 to 0.94).[27]

Composite Subjective Stress

The composite score for mothers' subjective stress (COSMOSS) was computed using Principal Component Analysis (PCA) on IES-R, PDI, and PDEQ total scores from all 230 participants who provided PNMS data at recruitment. The resulting loadings were 0.82, 0.91, and 0.89 for IES-R, PDI, and PDEQ, respectively. The PCA-derived algorithm was as follows: COSMOSS = (0.36 × IESR) + (0.40 × PDI) + (0.39 × PDEQ). The PCA resulted in one factor explaining 76.27% of the overall subjective stress variance. The COSMOSS variable is standardized with a mean of 0, such that positive and negative scores represent levels of subjective stress that are higher or lower than the mean, respectively.

Cognitive Appraisal

The women's cognitive appraisal of the flood was assessed according to their responses to the following question: "If you think about all of the consequences of the 2011 Queensland flood on you and your household, would you say that the flood has been": −2 (very negative) to 0 (neutral) to +2 (very positive) on a 5-point Likert scale. Because our interest was in prenatal "stress," that is, in the negative aspects of the experience, and because few women responded either "very negative" or "very positive" (Table 1), we dichotomized this variable into negative (n = 48) versus neutral/positive (n = 72). In the QF2011 cohort, responses on this item predict other aspects of infant development.[20] The reliability and validity of single-item measures in comparison with more comprehensive questionnaires has been demonstrated in other areas of health research.[28]

Timing of Stress in Pregnancy

The number of days between the flood peak date (January 10, 2011) and each woman's expected due date was calculated to indicate the timing of the flood exposure in pregnancy; the larger the value, the later in pregnancy the flood occurred.

Covariates

To control for potentially confounding variables that also influence infant temperament or may bias maternal reports of their infants' temperament, we assessed maternal mental health and functioning 6 months postnatally. We assessed maternal postnatal state anxiety using the State-Trait Anxiety Inventory (STAI[29]). The state scale of the STAI is a self-report tool commonly used to assess anxiety levels at the time of completion by rating 20 statements on a 1 (not at all) to 4 (very much so) Likert Scale. Postnatal depression was assessed using the Edinburgh Postnatal Depression Scale (EPDS[30]), a self-report tool in which 10 items regarding emotional stress over the last 7 days are rated. We also used the Parent-Child Dysfunctional Interaction subscale from the short form of the Parenting Stress Index (PSI).[31] The 36-item self-report PSI assesses the quality of the parent-child relationship.

Another potential maternal confounder controlled for included maternal education level (years schooling). We also included an estimate of household socioeconomic status using the Socio-Economic Index For Area scores based on Australian postcode and census data (M = 1000, SD = 100); higher numbers indicate well-resourced areas socially and economically compared with lower numbers. We also controlled for gestational age of the infant at birth and infant age at the time of assessment.

Statistical Analyses

As the objective hardship (QFOSS) and subjective measures (IES-R, PDEQ, PDI) of maternal stress were significantly skewed, these measures were log-transformed for all analyses. The composite subjective stress measure (COSMOSS) was not log-transformed.

We performed descriptive analyses on the 6 maternal stress variables, covariates, and infant temperament (Table 1). Next, we conducted Pearson Product-Moment correlations to examine the associations between the 5 STSI scale outcome variables and the 6 maternal stress variables and the covariates (Table 2).

Hierarchical liner regression analyses determined the effect of PNMS (objective hardship, COSMOSS, cognitive appraisal) on the STSI dimensions of infant temperament at 6 months of age. To reduce the amount of predictors in the model, the composite score for mothers subjective stress (COSMOSS) was used in the regressions analyses instead of the posttraumatic stress, peritraumatic distress, and peritraumatic dissociation scores. The models for the regression analyses for each of the 5 temperament dimensions were as follows: First, objective hardship was entered into the model, followed by composite subjective stress in Step 2, and then cognitive appraisal

Table 2. Intercorrelations Between the Dimensions of the Short Temperament Scale for Infants and Correlations Between the STSI Dimensions and the Predictors and Covariates

	Dimensions of the Short Temperament Scale for Infants (STSI)				
	Approach	**Rhythmicity**	**Cooperation-Manageability**	**Activity-Reactivity**	**Irritability**
STSI dimensions					
Approach	1	.28*	.13	−.10	.43*
Rhythmicity	.28*	1	.12	.04	.33*
Cooperation-manageability	.13	.12	1	−.07	.16
Activity-reactivity	−.10	.04	−.08	1	−.09
Irritability	.43*	.33*	.16	−.09	1
Predictor variables					
Objective hardship	−.06	.11	−.05	.04	.10
Posttraumatic stress (IES-R)	.05	.08	−.14	.09	.27*
Peritraumatic distress (PDI)	−.02	−.05	−.06	.21**	.10
Peritraumatic dissociation (PDEQ)	−.03	−.05	−.10	.11	.06
Composite subjective stress	.07	.04	−.16***	.10	.20**
Cognitive appraisal	−.01	−.13	−.06	−.10	.06
Timing of exposure	.04	.03	−.12	−.00	.16***
Infant sex (boy = 0)	−.12	−.01	−.04	.04	−.13
Covariates					
School level, yrs	−.02	.06	.05	−.28*	−.02
Socioeconomic status	−.14	.09	.02	.01	−.04
Depression (EPDS)	.16***	.25*	.07	−.05	.39*
Anxiety (STAI)	.37*	.33*	.16***	−.07	.45*
Parent-child dysfunction (PSIDI)	.38*	.22**	.22**	−.19**	.53*
Infant age (at assessment)	.23**	.22**	.17***	−.04	.30*
Gestational age at birth	.18***	.06	.07	.08	.10

*$p < .01$. **$p < .05$. ***$p < .1$. EPDS, Edinburgh Postnatal Depression Scale; IES-R, Impact of Event Scale-Revised; PDEQ, Peritraumatic Dissociative Experiences Questionnaire; PDI, Peritraumatic Distress Inventory; PSIDI, Parent-Child Dysfunctional Interaction; STAI, State-Trait Anxiety Inventory; STSI, Short Temperament Scale for Infants.

in Step 3. In Step 4, infant sex was entered into the model, followed by timing of the flood in gestation in Step 5. If there was a significant correlation with maternal factors and infant temperament, the next step included anxiety, depression, or parent-child interaction. Next, infant age at assessment was entered into the model, if it was significantly correlated with infant temperament. The last step included all possible interaction terms between the 3 PNMS variables and either timing or sex, as well as between objective hardship and composite subjective stress to test the effect of maternal reactions. Because of the relatively small sample size, all models were then trimmed of nonsignificant variables, except for objective hardship or variables included in an interaction effect, and the analyses were rerun. The p values of the interaction terms were corrected using the Benjamini-Hochberg procedure for false discovery rate correction.[32] Significant or marginal interactions were probed to determine the significance of their conditional effects using a pick-a-point approach implemented in Hayes' PROCESS macro.[33] Analyses were conducted using SPSS v22 (IBM Corp). All statistical tests used an alpha of .05 (2-sided test) unless otherwise specified.

RESULTS

Analyses revealed no differences in the demographic and psychological characteristics, or prenatal maternal stress (PNMS) scores, between the mothers who participated in this study and those who did not provide any infant data. However, the women who provided infant data were flood-affected earlier in pregnancy (M = 107.35 days, SD = 69.53) than those who did not provide data (M = 142.79 days, SD = 80.43): t (89.73) = 3.02, $p < .005$.

Temperament Dimension Scores

Infants' temperament factor scores for the 5 Short Temperament Scale for Infants (STSI) dimensions are shown in Table 1. For each temperament dimension, most of the QF2011 cohort scored within the expected range based on the standardized norms (i.e., within 1 *SD* from the mean). A certain percentage scored outside

the ±1 *SD* range: 17% (N = 20/121) of infants were classified as withdrawing and 15% (N = 18) as approaching; 13% (N = 16/121) of infants classified as arrhythmic and 18% (N = 22) as rhythmic; 14% (N = 16/113) classified as uncooperative-unmanageable and 13% (N = 15) as cooperative-manageable; 30% (N = 35/115) as active-reactive and 11% (N = 13) as inactive-unreactive; and 14% (N = 17/119) as irritable and 15% (N = 18) as less irritable. Furthermore, independent *t* tests showed no differences between girls and boys scores on any of the 5 temperament dimensions.

Correlations

The PNMS variables were somewhat intercorrelated. For example, although the negative cognitive appraisal group had significantly greater objective and subjective PNMS scores than the neutral/positive group (data not shown), the correlations between the 4-level cognitive appraisal score and objective hardship ($r = -.368$) and subjective stress (composite score for mothers' subjective stress [COSMOSS]; $r = -.315$) suggest that these aspects of the stress experience are relatively independent of each other. Similarly, objective hardship and COSMOSS correlated at 0.523, which, although statistically significant, indicates that the degree of objective hardship experienced explains only 27% of the variance in subjective distress.

As shown in Table 2, intercorrelations among the STSI dimensions showed significant relationships between approach, rhythmicity, and irritability; yet cooperation-manageability and activity-reactivity were unrelated to each other or the other temperament dimensions.

Table 3. Summary of the Final Models of the Hierarchical Regression Analyses for the Dimensions of the Short Temperament Scale for Infants

		Values in Final Model			Values After Entry of Each Variable			
Predictor Variables	**β**	***B***	***SE***	***R***	R^2	ΔR^2	***F***	ΔF
Approach								
Objective hardship	−.12	−.87	.69	.06	.00	.00	.39	.39
Composite subjective stress	.10	.49	.53	.13	.02	.01	1.03	1.67
Anxiety	.52*	.29*	.08	.39	.15	.13	6.84*	18.15*
Depression	−.38*	−.49*	.19	.44	.19	.04	6.87*	6.07**
Parent-child dysfunction	.265*	.27*	.09	.50	.24	.05	7.42*	7.95*
Rhythmicity								
Objective hardship	.47*	3.03*	1.10	.11	.01	.01	1.33	1.33
Composite subjective stress	−.15	−.66	.46	.11	.01	.00	.68	0.44
Timing	.86**	.06**	.02	.11	.01	.00	.48	.086
Anxiety	.34*	.17*	.05	.36	.13	.12	4.24*	15.33*
Infant age	.19**	2.21**	1.06	.39	.15	.02	4.08*	3.13***
Objective hardship × timing of exposure	−.96**	−.02**	.01	.44	.19	.04	4.53*	5.89**
Cooperation-manageability								
Objective hardship	.06	.24	.414	.047	.002	.002	.25	.25
Composite subjective stress	−.25**	−.68**	.291	.163	.027	.024	1.51	2.77***
Parent-child dysfunction	.28*	.15*	.051	.315	.099	.072	3.99*	8.75*
Activity-reactivity								
Objective hardship	−.08	−.49	.70	.04	.00	.00	.16	.16
Composite subjective stress	1.49	9.73	2.19	.11	.01	.01	.62	1.09
Parent-child dysfunction	−.23**	−.20**	.08	.24	.06	.05	2.24***	5.41**
Objective hardship × composite subjective stress	−1.32*	−1.82*	.65	.35	.12	.06	3.76*	7.90*
Irritability								
Objective hardship	.30*	1.74*	.65	.13	.02	.02	1.95	1.95
Composite subjective stress	.13	.53	.35	.25	.06	.04	3.73**	5.43**
Cognitive appraisal	.21**	1.87**	.74	.30	.09	.03	3.88**	3.99**
Infant sex	.72*	6.28*	2.36	.33	.11	.02	3.47*	2.13
Anxiety	.25*	.11*	.04	.54	.29	.18	9.14*	28.47*
Parent-child dysfunction	.42*	.32*	.06	.65	.42	.12	13.28*	24.38*
Objective hardship × infant sex	−.76*	−2.19*	.81	.67	.45	.04	13.05*	7.24*

*$p < .01$. **$p < .05$. ***$p < .1$. Sex: 0 = boy; 1 = girl.

As shown in Table 2, there were significant correlations between infant irritability scores and maternal posttraumatic-like symptoms (Impact of Event Scale-Revised) and composite subjective stress, suggesting higher subjective PNMS predicted more irritable infant behavior. More severe Peritraumatic Distress Inventory responses also predicted more difficult temperament in the Activity-Reactivity dimension. There were no other significant correlations between infant temperament scores and the PNMS measures, although several marginal associations were noted. As shown in Table 2, there were a number of significant correlations between the 5 temperament dimensions and maternal and infant covariates; of special note is the strong correlation between the Parent-Child Dysfunctional Interaction subscale of the Parenting Stress Index (PSI) and infant irritability (r = .528).

Hierarchical Linear Regression Analyses

The results of the final step of the trimmed regression models for the 5 temperament dimensions are shown in Table 3.

Approach

Maternal postnatal anxiety, depression, and parent-child dysfunction all accounted for significant variance on this scale (13.2%, 4.2%, and 5.2%, respectively). However, none of the PNMS variables were significantly associated with approach at 6 months.

Rhythmicity

Maternal anxiety and infant age at the assessment were significantly associated with rhythmicity at 6 months, accounting for 11.5% and 2.3% of variance, respectively. There were no direct effects of PNMS on infant rhythmicity; however, an interaction between objective hardship and timing of the flood in pregnancy emerged, accounting for 4.2% of variance. As illustrated in Figure 1, Panel A, infants exposed to the flood in early pregnancy were differentially susceptible to the effects of objective hardship on their rhythmicity: at low levels of objective hardship they had, on average, the most favorable rhythmicity scores, whereas at high levels of objective hardship, they had among the most arrhythmic scores. For infants exposed in late pregnancy, the trend was reversed but not significant. The effect of objective hardship on rhythmicity was significant for infants exposed to the flood before 12.51 weeks in pregnancy.

Cooperation-Manageability

Parent-child dysfunction at 6 months accounted for significant variance (7.2%) on this dimension. In relation to the PNMS variables, high levels of composite subjective stress predicted more cooperative-manageable infant behavior, accounting for 2.4% of variance. There were no significant main effects or interactions involving infant sex or timing of the flood in pregnancy with this scale, and no interactions among the PNMS variables.

Activity-Reactivity

Parent-child dysfunction rated at 6 months accounted for significant variance (4.6%) on this dimension. However, there were no significant main effects of the PNMS variables, and no interactions involving timing of the flood in pregnancy or infant sex with activity-reactivity. However, the interaction term of objective hardship by composite subjective stress accounted for 6.3% of variance in infant activity scores. As shown in Figure 1 Panel B, at high levels of objective hardship, there was no effect of maternal subjective distress: scores hovered close to the normed mean. However, the greater the "mismatch" between objective and subjective stress the more difficult the infants' activity levels such that the most difficult, active infants were those of mothers who reacted with high subjective stress to the lowest levels of objective hardship, so-called "over-reactors." The effect of subjective stress on infant activity level was significant when objective hardship levels were of 3.16 (log-scaled) or lower.

Irritability

Maternal anxiety and dysfunctional parenting stress were significantly associated with infant irritability,

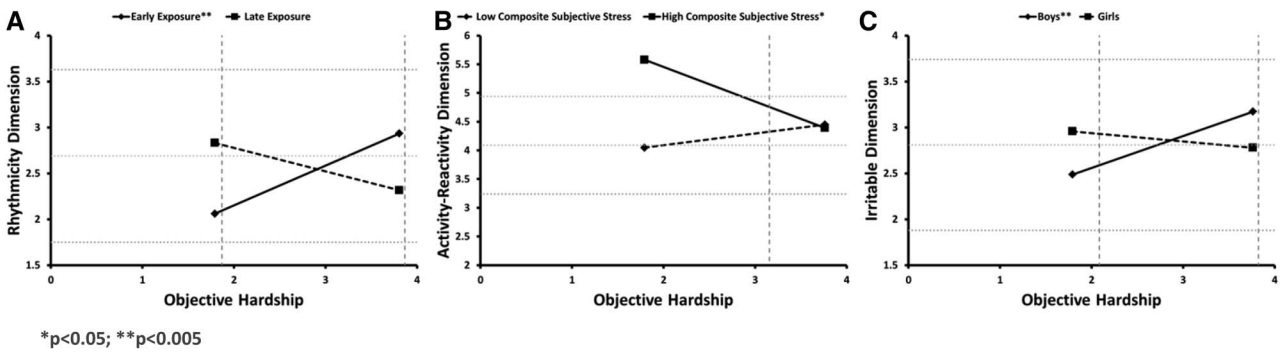

Figure 1. Moderation of the effects of objective hardship (log-transformed) on infant rhythmicity by timing of the flood in pregnancy (Panel A), on activity-reactivity by subjective stress (Panel B), and on irritability by sex of the infant (Panel C), with regions of significance (p = .05 at dashed line). For Panel A, the vertical dashed line indicates the level of objective hardship above or below which a significant effect of early or late pregnancy exposure is found. For Panel B, the vertical dashed line indicates the level of objective hardship below which a significant effect of maternal subjective distress is found. For Panel C, the vertical dashed lines indicate the objective hardship scores above (or below) which there is a significant difference in girls' and boys' rhythmicity. In all panels, the middle horizontal dashed line indicates the standardized mean and the upper and lower horizontal dashed lines indicate normed factor scores +1 *SD* and −1 *SD* from the mean, respectively.

accounting for 18.1%, and 12.8% of variance, respectively. In relation to the PNMS variables, maternal cognitive appraisal accounted for 3.2% of variance, with a neutral or positive appraisal style significantly associated with a more irritable temperament. Furthermore, there was an objective hardship by infant sex interaction, accounting for 3.6% of variance in this scale. As shown in Figure 1, Panel C, boys appeared to be differentially susceptible to their mothers' objective hardship such that when objective PNMS was low (2.08 or lower, log-scaled), boys were significantly less irritable than girls, but when objective PNMS was high (3.82 or higher, log-scaled), they were significantly more irritable than girls. For girls, however, their irritability ratings were near the normed mean irrespective of their mothers' stress levels.

DISCUSSION

The results of this study showed that flood-related prenatal maternal stress (PNMS) was directly associated with several aspects of infant temperament at 6 months of age. The study design, which used a sudden-onset flood, enabled comparison of the effects of objective hardship versus subjective distress on infant temperament, and also allowed for investigation of possible moderators of the effects of PNMS that may be obscured when only investigating PNMS main effects. Supporting the hypotheses, there were significant PNMS interactions involving infant sex, timing of the stressor in pregnancy, and mother's subjective reaction to the flood on dimensions of infant temperament, that endured even when controlling for concurrent maternal factors and adjusting significance for multiple testing. Furthermore, different types of flood-related PNMS (objective hardship, subjective distress, and maternal cognitive appraisal of the floods) were involved in these main effects and interactions.

Main Effects

The results from this study indicated that higher levels of maternal anxiety, depression, and parent-child dysfunctional interactions were predictive of negative infant temperament characteristics and together explained significant amounts of variance in all temperament scales: 23% for approach, 11.5% for rhythmicity, 7% for cooperation, 4.6% for activity, and explained 31% of the variance in irritability. These associations between maternal postnatal factors and infant temperament and behavior are documented elsewhere.[34,35] It was important to control for maternal factors in this study to isolate the unique effects of PNMS from the flood for 2 reasons: first, because maternal mood and parenting stress when completing the Short Temperament Scale for Infants (STSI) temperament scale could bias their perception and reporting of their infant's temperament, and second, because infant temperament and maternal mood could be associated because of shared genetics and postnatal environment.

Controlling for these effects of maternal mood and dysfunctional interactions, we detected few significant main effects of PNMS: although there was a small number of significant bivariate correlations showing that greater PNMS predicted more difficult temperament, in the multivariable regressions greater subjective stress predicted better cooperation-manageability, and a negative cognitive appraisal of the disaster was associated with decreased infant irritability. These latter results differ from previous findings showing that increased levels of disaster-related PNMS are associated with more negative temperaments in early development[17,18] and with our results and those from other research studying prenatal maternal anxiety and stressful life events in pregnancy.[10,13,36] Although PNMS generally has negative effects on development, a small number of studies have reported that stress in pregnancy can have positive influences on infant development.[37] Even within the QF2011 cohort, we have found that higher subjective stress has predicted better fine motor development at 2 months of age[20] and improved problem solving among boys at 6 months of age.[38]

Moderation of Objective Hardship by Infant Sex

The main findings from our study, however, are the significant interactions involving PNMS, all of which implicate the mothers' degree of objective hardship. This is the first study to report that infant sex moderates the effects of disaster-related PNMS on infant temperament. After controlling for maternal and infant factors, we found that the higher the mother's objective hardship, the higher her infant son's irritability, whereas objective hardship was unrelated to this dimension in daughters. Thus, in this study, boys demonstrated differential susceptibility[39] in response to their level of in utero exposure to maternal objective hardship: under conditions of low objective hardship, boys were rated as less irritable than girls, whereas under conditions of high levels of objective hardship, boys were rated as being more irritable than girls. This finding contrasts with our hypothesis that girls would be more susceptible than boys, which was based on research by Sandman and colleagues who showed that another dimension of infant temperament, fearfulness, is significantly associated with higher levels of maternal depressive symptoms and stress hormones in pregnancy for girls, but not for boys.[15] It is, however, quite possible that male fetuses are most sensitive to the objective hardship experienced by their mothers and that this sensitivity emerges as irritability, whereas girls are more sensitive to maternal stress hormones (which we did not test) and which emerges as greater fearfulness.

A number of studies also show that infant sex moderates the negative effects of psychological distress or life hassles in pregnancy on behavioral functioning in childhood, such as internalizing or externalizing disorders.[40,41] However, the literature is mixed with regard to whether girls or boys are more vulnerable to the

negative effects of psychosocial PNMS. Some research suggests boys are more vulnerable,[16] whereas other research shows girls are more at risk.[15,23] Perhaps these contradictory findings stem from the variety of ways that PNMS is operationalized: maternal psychological distress, stressful life events or hassles, or objective or subjective stress. Further discrepancy could arise from different aspects of development being measured, as girls tend to be more at risk of some behavior problems (e.g., internalizing), whereas boys are more at risk for others (e.g., externalizing); or even different ways of measuring the same domain of development (e.g., maternal report vs direct observation).

Moderation of Objective Hardship by Timing in Pregnancy

Similar discrepancies exist in the literature with regard to timing effects of stress in pregnancy on infant outcomes: different domains of development appear to be vulnerable to the effects of PNMS at different times in gestation. For example, motor function appears to be susceptible to late-pregnancy stress,[20,23] whereas temperament appears to be more sensitive to early-gestation or mid-gestation stress.[8,11,15,18] Consistent with this timing effect, when flood exposure occurred early in gestation, the higher the level of objective hardship, the more arrhythmic the infant temperament; when the flood occurred in the second or third trimester, however, there was no longer a significant effect of objective hardship on this dimension of temperament. Thus, it appears that, even when controlling for concurrent maternal factors, in utero exposure to high disaster-related objective hardship in early pregnancy can negatively affect how regular the infant's daily cycle will be.

Moderation of Objective Hardship by Subjective Stress

In this study, the mother's emotional reaction to the flood moderated how her degree of objective hardship affected her infant's activity-reactivity. When objective hardship was high, there were negligible additional effects of maternal subjective distress: activity levels were generally slightly above average. Infants of mothers who exhibited high emotional distress in response to the flood, while experiencing low objective hardship, however, showed the highest activity-reactivity scores that were well above the 1 *SD* mark. Similar interactions between maternal subjective distress and objective hardship, implicating maternal overreacting, were also found in the Project Ice Storm cohort with respect to infant birth outcomes[42] and childhood motor development.[23] Taken together, these findings suggest that optimal developmental outcomes are more likely when mothers' emotional reactions to a disaster are consistent with the severity of their exposure to it and that "over-reacting" can have negative effects on offspring development, including active-reactive temperaments.

Types of Maternal Stress

The results discussed above suggest that different types of maternal stress have differential effects on different dimensions of infant temperament, despite being somewhat correlated with each other (r = .41–.69); the degree of objective hardship was implicated in rhythmicity, activity, and irritability; cognitive appraisal had a significant effect on irritability, and subjective stress was implicated in cooperation and activity. The effects of the severity of the mothers' objective degree of hardship from the flood always depended on other moderating factors including the mothers' subjective distress, fetal sex, and the timing of the event in utero. Some of our results are consistent with those from Project Ice Storm in which objective, cognitive, and subjective stress are not highly correlated ($r < .35$) and which showed that high levels of subjective stress in pregnancy predicted difficult, fussy infant temperament, whereas objective hardship in early pregnancy also predicted fussy temperament, but only in conjunction with maternal illness or infection.[18] Similarly, in this study, objective hardship, subjective stress, and cognitive appraisal all influenced dimensions of infant temperament but in different combinations with each other and with other variables, including infant sex and timing of the flood in pregnancy. Controlling for maternal factors, flood-related stress explained the greatest amount of unique variance (12%) in infant irritability for which our model explained a total of 45% of variance.

The differential effects of disaster-related prenatal maternal objective hardship and subjective stress on infant outcomes have also been reported in other domains of development, including motor functioning[20,23] and cognitive and language development.[21] The role of cognitive appraisal in PNMS has been documented recently, where the way in which women evaluated the overall impact of the flood moderated negative effects of PNMS on infant motor functioning.[20] By contrast, however, the current results show that a neutral or positive maternal appraisal is related to increased infant irritability. This new measure of the maternal stress response highlights the complexities of PNMS and demonstrates that as well as objective and subjective PNMS, the way a pregnant woman cognitively appraises the overall impact of a stressful event plays an important role in predicting offspring behavior.

Mechanisms of PNMS

The effects of PNMS on offspring outcomes, such as those seen in this study, are generally explained by the fetal programming hypothesis.[43] This hypothesis suggests that stress in pregnancy increases maternal glucocorticoid levels that are then transmitted to the fetus through the placenta.[44] These stress hormones can have profound effects on fetal neurodevelopment at sensitive periods in gestation, with long-term consequences for behavioral development.[45] This could account for the

current early gestation timing effect on rhythmicity because the hippocampus, associated with behavioral regulation, develops in early gestation.[46,47] In addition, fetal sex is thought to play a regulating role in fetal programming with evidence that male and female fetuses respond differently to intrauterine stress,[48] which could account for the current finding that with higher levels of objective PNMS, boys were more vulnerable than girls on the irritability dimension.

Dimensions of Infant Temperament

We found that PNMS exerted inconsistent main effects and interactions on the different temperament dimensions of the STSI. Other PNMS research assessing multiple domains of infant temperament also finds varying effects of stress in pregnancy (e.g., anxiety or life events) on the different dimensions.[8,9] In this study, not all the dimensions of temperament were intercorrelated, which indicates that, to some extent, the temperament dimensions measure distinct aspects of infant behavior. This is further supported by differences in the correlations between the temperament dimensions and maternal mood, accounting for the different covariates entered into the regression models for each dimension. Research also shows that not all dimensions of temperament predict the same outcomes later in development, showing that they measure distinct behaviors. For example, the specific dimension of "approach-withdraw" is a risk factors for later internalizing problems,[3] whereas dimensions measuring "rhythmicity" and "manageability-cooperation" are not.

This also helps explain why different aspects of PNMS had inconsistent direct effects with the 5 dimensions of temperament and why different interactions emerged: although there is some relation between some of the dimensions, they are not all measuring the same aspects of infant behavior. The effect of pregnancy stress on fetal neurodevelopment can also explain why PNMS exerted different direct effects and interactions with the 5 dimensions of infant temperament in this study. Similar inconsistencies of PNMS on dimensions of temperament were found in Project Ice Storm[18] and with research using maternal mood and psychosocial stressors.[8,9] These inconsistencies are most likely because of how PNMS affects the different, but interrelated, brain structures underlying various domains of temperament.[47] For example, research shows that the hippocampus is implicated in behavioral regulation and anxiety, the amygdala is associated with fear and response to novelty, the orbitofrontal cortex is related to impulsivity, and the right dorsolateral prefrontal cortex with withdrawal behavior.[47]

Study Limitations and Strengths

There are some limitations to this study. First, we used a relatively small, homogenous, and socioeconomically advantaged community sample, which may have made detecting significant effects of PNMS difficult and may limit the generalizability of the findings. Furthermore, there is an inherent design confound as mothers reported on both their own flood-related experiences and their infant's temperament; these reports could have been influenced by recall or reporter biases, respectively. We attempted to reduce any such bias by always controlling for maternal self-reported anxiety, depression, and parenting stress assessed at the time of the temperament ratings.

These limitations, however, are offset by strengths of the study. First, this is only the second prospective study to examine the effects of disaster-related PNMS on infant temperament, and it is the first to find that infant sex, maternal reactions, and timing in pregnancy moderate objective PNMS effects. Unlike most prenatal stress studies, QF2011 includes a deep-level assessment of the objective hardship experienced by women going through an independent stressor. This study also included new assessments of the maternal stress reaction to the flood: cognitive appraisal and peritraumatic responses. Next, the STSI temperament scale was normed on Australian infants so it was culturally appropriate for use with the QF2011 cohort.[22] Furthermore, compared with observational studies of infant temperament, there are several advantages to maternal report: questionnaires can capture multiple dimensions of infant temperament, whereas observational studies usually only rate a single dimension of temperament, and infants may react differently in observational settings than they do on a day-to-day basis with their mothers.[49] Finally, the sudden-onset nature of the flood assured the internal validity of our results on the timing of stress in pregnancy.

Conclusion

These results suggest that disaster-related objective and subjective prenatal maternal stress, and women's cognitive appraisal, play significant roles in programming infant temperament, and that timing of the flood in pregnancy and sex of the infant can moderate these effects. These results indicate that infants with the most difficult temperaments may be those whose mothers have neutral or positive cognitive appraisals of a disaster in pregnancy (irritability), experience a high degree of objective hardship in early pregnancy (rhythmicity), experience more subjective distress (cooperation-manageability), experience high distress in the context of mild hardship (activity), and boys whose mothers experience a high degree of hardship (irritability). Given that these dimensions of difficult infant temperament predict risk for poor mental health outcomes in later life,[3,5] pregnant women affected by a natural disaster should be targeted for interventions that reduce hardship and distress to optimize their infants' long-term development.

ACKNOWLEDGMENTS

Many thanks to the QF2011 families who participated in this research. The authors would also like to thank Laura Shoo and Donna Amaraddio for input into participant recruitment and data management. The QF2011 Queensland Flood Study is primarily

funded by a grant from the Canadian Institutes of Health Research (CIHR; S. King, S. Kildea and M.-P.A., coprincipal investigators; MOP-1150067) and funding from the Mater Foundation, Mater Health, and Mater Research.

REFERENCES

1. Rothbart MK, Bates JE. Temperament. In: Damon, Eisenberg, eds. *Handbook of Child Psychology: Social, Emotional and Personality Development*. New York, NY: Wiley and Sons; 1998: 105–176.
2. Riese ML. Temperament in full-term and preterm infants: stability over ages 6 to 24 months. *J Dev Behav Pediatr.* 1988;9:6–11.
3. Rettew DC, McKee L. Temperament and its role in developmental psychopathology. *Harv Rev Psychiatry.* 2005;13:14–27.
4. Schwartz CE, Snidman N, Kagan J. Adolescent social anxiety as an outcome of inhibited temperament in childhood. *J Am Acad Child Adolesc Psychiatry.* 1999;38:1008–1015.
5. Rettew DC, Copeland W, Stanger C, et al. Associations between temperament and DSM-IV externalizing disorders in children and adolescents. *J Dev Behav Pediatr.* 2004;25:383–391.
6. Robinson M, Oddy WH, Whitehouse AJO, et al. Hypertensive diseases of pregnancy predict parent-reported difficult temperament in infancy. *J Dev Behav Pediatr.* 2013;34:174–180.
7. Ivorra JL, Suanjuan J, Jover M, et al. Gene-environment interaction of child temperament. *J Dev Behav Pediatr.* 2010;31:545–554.
8. Buitelaar JK, Huizink AC, Mulder EJ, et al. Prenatal stress and cognitive development and temperament in infants. *Neurobiol Aging.* 2003;24(suppl 1):S53–S60.
9. Henrichs J, Schenk JJ, Schmidt HG, et al. Maternal pre- and postnatal anxiety and infant temperament. The generation R study. *Infant Child Dev.* 2009;18:556–572.
10. Austin M-P, Hadzi-Pavlovic D, Leader L, et al. Maternal trait anxiety, depression and life event stress in pregnancy: relationships with infant temperament. *Early Hum Dev.* 2005;81:183–190.
11. Blair MM, Glynn LM, Sandman C, et al. Prenatal maternal anxiety and early childhood temperament. *Stress.* 2011;14:644–651.
12. Davis EP, Glynn LM, Schetter CD, et al. Prenatal exposure to maternal depression and cortisol influences infant temperament. *J Am Acad Child Adolesc Psychiatry.* 2007;46:737–746.
13. Davis EP, Snidman N, Wadhwa PD, et al. Prenatal maternal anxiety and depression predict negative behavioral reactivity in infancy. *Infancy.* 2004;6:319–331.
14. Bergman K, Sarkar P, O'Connor TG, et al. Maternal stress during pregnancy predicts cognitive ability and fearfulness in infancy. *J Am Acad Child Adolesc Psychiatry.* 2007;46:1454–1463.
15. Sandman CA, Glynn LM, Davis EP. Is there a viability-vulnerability tradeoff? Sex differences in fetal programming. *J Psychosom Res.* 2013;75:327–335.
16. Kinney DK, Miller AM, Crowley DJ, et al. Autism prevalence following prenatal exposure to hurricanes and tropical storms in Louisiana. *J Autism Dev Disord.* 2008;38:481–488.
17. Tees MT, Harville EW, Xiong X, et al. Hurricane Katrina-related maternal stress, maternal mental health, and early infant temperament. *Matern Child Health J.* 2010;14:511–518.
18. Laplante DP, Brunet A, King S. The effects of maternal stress and illness during pregnancy on infant temperament: project ice storm. *Pediatr Res.* 2016;79:107–113.
19. King S, Kildea S, Austin MP, et al. QF2011: a protocol to study the effects of the Queensland flood on pregnant women, their pregnancies, and their children's early development. *BMC Pregnancy Childbirth.* 2015;15:109.
20. Simcock G, Kildea S, Elgbeili G, et al. Age-related changes in the effects of stress in pregnancy on infant motor development by maternal report: the Queensland flood study. *Dev Psychobiol.* 2016;58:640–659.
21. Laplante DP, Brunet A, Schmitz N, et al. Project ice storm: prenatal maternal stress affects cognitive and linguistic functioning in 5½-year-old children. *J Am Acad Child Adolesc Psychiatry.* 2008;47:1063–1072.
22. Sanson A, Prior M, Garino E, et al. The structure of infant temperament: factor analysis of the revised infant temperament questionnaire. *Infant Behav Dev.* 1987;10:97–104.
23. Cao X, Laplante DP, Brunet A, et al. Prenatal maternal stress affects motor function in 5(1/2)-year-old children: project ice storm. *Dev Psychobiology.* 2014;56:117–125.
24. Brunet A, Weiss DS, Metzler TJ, et al. The peritraumatic distress inventory: a proposed measure of PTSD criterion A2. *Am J Psychiatry.* 2001;158:1480–1485.
25. Marmar CR, Weiss DS, Metzler TJ. The peritraumatic dissociative experiences questionnaire. In: Wilson JP, Keane TM, eds. *Assessing Psychological Trauma and PTSD*. New York, NY: Guilford Press; 1997:412–428.
26. Weiss DS, Marmar CR. *The Impact of Event Scale—Revised*. New York, NY: Guilford; 1997.
27. Creamer M, Bell R, Failla S. Psychometric properties of the impact of event scale—revised. *Behav Res Ther.* 2003;41:1489–1496.
28. Yohannes AM, Dodd M, Morris J, et al. Reliability and validity of a single item measure of quality of life scale for adult patients with cystic fibrosis. *Health Qual Life Outcomes.* 2011;9:105.
29. Spielberger CD, Gorsuch RL, Lushene PR, et al. *Manual for the State-trait Anxiety Inventory (Form Y)*. Palo Alto, CA: Consulting Psychologists Press, Inc; 1983.
30. Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression: development of the 10-item Edinburgh postnatal depression scale. *Br J Psychiatry.* 1987;150:782–786.
31. Abidin RR. *Parenting Stress Index: Professional Manual*. 3rd ed. Odessa, FL: Psychological Assessment Resources, Inc; 1995.
32. Benjamini Y, Hochberg Y. Controlling the false discovery rate: a practical and powerful approach to multiple testing. *J R Stat Soc Series B Methodol.* 1995;57:289–300.
33. Hayes AF. *Introduction to Mediation, Moderation, and Conditional Process Analysis*. New York, NY: The Guilford Press; 2013.
34. Nilsen W, Gustavson K, Roysamb E, et al. Pathways from maternal distress and child problem behavior to adolescent depressive symptoms: a prospective examination from early childhood to adolescence. *J Dev Behav Pediatr.* 2013;34:303–313.
35. Spence SH, Najman JM, Bor W, et al. Maternal anxiety and depression, poverty and marital relationship factors during early childhood as predictors of anxiety and depressive symptoms in adolescence. *J Child Psychol Psychiatry.* 2002;43:457–469.
36. Gutteling BM, de Weerth C, Willemsen-Swinkels SH, et al. The effects of prenatal stress on temperament and problem behavior of 27-month-old toddlers. *Eur Child Adolesc Psychiatry.* 2005;14: 41–51.
37. DiPietro JA, Novak MF, Costigan KA, et al. Maternal psychological distress during pregnancy in relation to child development at age two. *Child Dev.* 2006;77:573–587.
38. Simcock G, Laplante DP, Guillaume E, et al. Infant neurodevelopment is affected by prenatal maternal stress: the QF2011 flood study. *Infancy.* 2017;22:282–302.
39. Pluess M, Belsky J. Prenatal programming of postnatal plasticity? *Dev Psychopathol.* 2011;23:29–38.
40. O'Connor TG, Heron J, Golding J, et al. Maternal antenatal anxiety and behavioural/emotional problems in children: a test of a programming hypothesis. *J Child Psychol Psychiatry.* 2003;44: 1025–1036.
41. de Bruijn ATCE, van Bakel HJA, van Baar AL. Sex differences in the relation between prenatal maternal emotional complaints and child outcome. *Early Hum Development.* 2009;85:319–324.
42. Dancause KN, Laplante D, Oremus C, et al. Disaster-related prenatal maternal stress influences birth outcomes: project ice storm. *Early Hum Dev.* 2011;87:813–820.
43. Barker DJ. Developmental origins of adult health and disease. *J Epidemiol Community Health.* 2004;58:114–115.

44. Field T, Diego M. Cortisol: the culprit prenatal stress variable. *Int J Neurosci.* 2008;118:1181–1205.
45. Weinstock M. The long-term behavioural consequences of prenatal stress. *Neurosci Biobehav Rev.* 2008;32:1073–1086.
46. Humphrey T. The development of the human amygdala during embryonic life. *J Comp Neurol.* 1968;132:135–165.
47. Whittle S, Allen NB, Lubman DI, et al. The neurobiological basis of temperament: towards a better understanding of psychopathology. *Neurosci Biobehav Rev.* 2006;30:511–525.
48. Clifton VL. Review: sex and the human placenta: mediating differential strategies of fetal growth and survival. *Placenta.* 2010; 31:S33–S39.
49. Squires J, Bricker D, Potter L. Revision of a parent-completed developmental screening tool: ages and stages questionnaires. *J Pediatr Psychol.* 1997;22:313–328.