

Infant Neurodevelopment is Affected by Prenatal Maternal Stress: The QF2011 Queensland Flood Study

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Research shows that prenatal maternal stress (PNMS) negatively affects a range of infant outcomes; yet no single study has explored the effects of stress in pregnancy from a natural disaster on multiple aspects of infant neurodevelopment. This study examined the effects of flood-related stress in pregnancy on 6-month-olds' neurodevelopment and examined the moderating effects of timing of the stressor in gestation and infant sex on these outcomes. Women exposed to the 2011 Queensland (Australia) floods in pregnancy completed surveys on their flood-related objective and subjective experiences at recruitment and reported on their infants' neurodevelopment on the problem solving, communication, and personal-social scales of the Ages and Stages-III at 6 months postpartum ($N = 115$). Interaction results showed that subjective flood stress in pregnancy had significantly different effects in boys and girls, and that at high levels of stress girls had significantly lower problem solving scores than boys. Timing of the flood later in pregnancy predicted lower personal-social scores in the sample, and there was a trend ($p < .10$) for greater objective flood exposure to predict lower scores. PNMS had no effect on infants' communication skills. In conclusion, differential aspects of maternal flood-related stress in pregnancy influenced aspects of 6-month-olds' neurodevelopment.

It is well recognized that maternal medical complications and physical health which precede and endure throughout pregnancy can be risk factors for compromised infant development (Barker, Eriksson, Forsen, & Osmond, 2002; Linnert et al., 2003; Orlebeke, Knol, & Verhulst, 1999; Schlotz & Phillips, 2009). Improving pregnant women's health, which is known to optimize neonatal and developmental outcomes, has been a focus of major public health campaigns (Thangaratinam et al., 2012). In a similar vein, understanding more about how infant development is affected by other risk factors that occur in pregnancy, such as maternal stress, could enable the development of targeted interventions to protect this vulnerable population *in utero* (Glover, 2014).

Research shows that prenatal maternal stress (PNMS) poses a significant risk factor for compromised birth outcomes, childhood growth (Dancause et al., 2012; Lederman et al., 2004; Tegethoff, Greene, Olsen, Meyer, & Meinschmidt, 2010; Xiong et al., 2008) and health (Dancause et al., 2012; Veru, Laplante, Luheshi, & King, 2014). Stress in pregnancy can also negatively affect young children's neurodevelopment, including cognition, language skill and behavioral development (Graignic-Philippe, Dayan, Chokron, Jacquet, & Tordjman, 2014). The purpose of this study was to determine the extent to which variance in these developmental domains in 6-month-olds can be explained by flood-related objective and subjective PNMS and whether timing of the stressor *in utero* or sex of the infant moderates these effects.

We examined the effects of PNMS on neurodevelopment at 6 months as a number of important psychological changes begin to occur around this age. For example, infants exhibit new problem solving skills, such as coordinated reaching and grasping (Bhat, Heathcock, & Galloway, 2005), evidence of the foundations of global-level category discrimination (Mandler & McDonough, 1998), and they show an emerging understanding of causality (Leslie & Kebble, 1987). Infants at this age also demonstrate the first signs of verbal communication by recognizing spoken words for familiar objects or people (e.g., "mommy" and "daddy"), and they begin to produce early babbling sounds such as "ba" and "pa" (Tincoff & Jusczyk, 1999). From 6 months, infants start to exhibit new responses to others, such as looking at their caregivers to guide their behavior in unfamiliar situations (Rosen, Adamson, & Bakemos, 1992) and showing signs of distress when separated from their caregivers (Cohen & Campos, 1974).

A number of studies have shown that early cognitive functioning is often impaired by PNMS. For example, daily hassles or stressful events during pregnancy (Bergman, Sarkar, O'Connor, Modi, & Glover, 2007; Huizink, Robles de Medina, Mulder, Visser, & Buitelaar, 2003; Slykerman et al., 2005) and pregnancy-specific anxiety (Buitelaar, Huizink, Mulder, de Medina, & Visser, 2003; Davis & Sandman, 2010) predict lower levels of infant cognition. In contrast, however, one study found that mild levels of psychological distress in pregnancy predict higher levels of infant cognition (DiPietro, Novak, Costigan, Atella, & Reusing, 2006). High objective levels of prenatal hardship exposure to a severe ice storm compromised reasoning and problem solving in 2½- and 5-year-olds, but their cognition was not affected by mothers' traumatic stress responses to the storm (Laplante, Brunet, Schmitz, Ciampi, & King, 2008; Laplante et al., 2004). Two studies found increased negative effects of PNMS on infant cognition if the stressor occurred early in pregnancy (Davis & Sandman, 2010; Laplante et al., 2004).

Research from the Project Ice Storm cohort has also demonstrated that young children's language development is compromised by *in utero* maternal stress. Mothers who experienced high objective hardship from the ice storm reported lower vocabularies in their 2-year-olds than did mothers who had experienced less hardship; these effects were greater when maternal exposure to the ice storm occurred early in gestation (Laplante et al., 2004). However, there were no associations between infant language development and mothers' degree of traumatic distress during the ice storm. These negative effects of PNMS on vocabulary were still apparent in the ice storm cohort at 5½ and 11½ years of age (King & Laplante, 2015; Laplante et al., 2008). Although there were no sex differences in the effects of *in utero* ice storm exposure on language skill in early childhood, at 11½ years, higher levels of PNMS had a linearly positive effect on girls' vocabularies but a curvilinear, inverted-U effect on boys' vocabularies such that moderate levels of PNMS predicted higher levels of vocabulary than either lower or higher levels of PNMS (King & Laplante, 2015).

Results from the ice storm cohort also showed that infant temperament at 6 months was negatively affected by maternal illness in the first trimester, by the mothers' traumatic responses to the ice storm especially when exposure was early in pregnancy, and by their objective experiences of the disaster if it was coupled with maternal illness in the first trimester (Laplante, Brunet, & King, 2016). Other studies show that mothers who experienced anxiety, depression, or negative events or hassles in pregnancy were more likely to report their infant's behavior as difficult (Austin, Hadzi-Pavlovic, Leader, Saint, & Parker, 2005), negative (Blair, Glynn, Sandman, & Davis, 2011), inadapt-able (Buitelaar et al., 2003), reactive (Davis et al., 2004), or fearful (Bergman et al., 2007). Two further studies reported that early-pregnancy stress was predictive of difficult infant temperament (Blair et al., 2011; Buitelaar et al., 2003); and there is evidence that mid-gestation PNMS is related to increased fearfulness in infant girls but not boys (Sandman, Glynn, & Davis, 2013).

These effects of stress in pregnancy are generally attributed to the fetal programming hypothesis (Barker, 2004), the process by which prenatal insults can cause long-lasting changes to the developing fetus. The hypothalamic-pituitary-adrenal (HPA) axis is considered the primary mechanism responsible for transmitting maternal stress to the fetus (Davis, Waffarn, & Sandman, 2011; Gunnar, 1992). High levels of circulating maternal hormones (glucocorticoids or cortisol) are released in response to stress, and these hormones cross the placental barrier altering fetal neurodevelopment at critical time-points in gestation (Gitau, Fisk, Teixeira, Cameron, & Glover, 2001). The

fetal programming hypothesis may also account for the sex differences described above as one line of research suggests that male and female placentas differ in their responsiveness to maternal glucocorticoids, thereby potentially moderating how stress-related hormone levels affect prenatal development for each sex (Clifton, 2010).

As reviewed above, empirical studies that have reported that PNMS is related to children's outcomes have typically examined a single developmental domain. Further, this literature is unclear as to what extent the sex of the fetus and the timing of the stressor *in utero* affect developmental outcomes. The aim of this study was to examine the effects of PNMS on 6-month-olds' neurodevelopment in three domains: communication, problem solving, and personal-social skills, using one assessment tool: the Ages and Stages-III (Squires, Bricker, & Potter, 1997). Each of these three domains corresponds to the infant's emerging language skills, cognitive functioning and behavioral development, respectively. The Ages and Stages Questionnaire (ASQ) is the most widely used screening tool to assess for early developmental delay as it is easy and cost-effective to administer. Furthermore, parent report of their infant abilities overcomes the problem of an infant failing to exhibit a specific behavior in the course of a professional assessment, perhaps due to fatigue, hunger, illness or fussiness (Fallah, Islami, & Mosavian, 2011).

We also used a different, independently occurring, disaster (a flood) as the pregnancy stressor and undertook more comprehensive assessments of the mother's stress response, evaluating her objective hardship, subjective stress reactions (peritraumatic and post-traumatic reactions), and cognitive appraisal of the overall impact of the event. Utilizing a natural disaster overcomes the design confound inherent in PNMS studies that use daily hassles, life events, or mental health as the pregnancy stressor: as these types of stressors often co-occur, it is not possible to untangle the extent to which they are related to the parents' personality traits, which may account for offspring development rather than the effects of PNMS *per se* (King & Laplante, 2015).

Further, we control for postnatal maternal life events and perinatal (at recruitment into the study) and postnatal mental health (at 6 months postpartum) to isolate the effects of the stressful flood in pregnancy on infant development versus postnatal stressors that also negatively influence infant development (Grace, Evindar, & Stewart, 2003; Kingston, Tough, & Whitfield, 2012). Perinatal and postnatal maternal mood may affect the nature of mother-child interactions thereby influencing infant development (Nicol-Harper, Harvey, & Stein, 2007; Seymour, Giallo, Cooklin, & Dunning, 2015); as well, controlling for maternal mental health at the time of the ASQ adjusts for any maternal response bias. Using a sudden onset disaster also enabled us to investigate the moderating effect of timing of the stressor in pregnancy on infant development with great accuracy.

The women participating in the Queensland Flood study (QF2011) were all pregnant when they were exposed to the sudden-on-set floods that severely affected large areas of Queensland, Australia, peaking in the city of Brisbane on January 10, 2011. Over 70% of the State was declared a disaster zone, and the floods completely inundated 15,000 homes and partially inundated a further 18,000. Economic damage was in excess of \$2 billion, and there were 35 flood-related fatalities (Carbone & Hanson, 2012). We hypothesized that during pregnancy, higher levels of flood-related objective stress and/or subjective stress, or a negative appraisal of the event, would predict poorer infant problem solving, communication, and personal-social skills compared to outcomes for infants whose mothers experienced less objective and/or subjective stress,

or who had a positive or neutral appraisal of the event. Based on the literature, we also hypothesized that girls' development would be more vulnerable to the negative effects of PNMS than that of boys (Sandman et al., 2013), and that early- to mid-gestation exposure to the flood would have negative effects on neurodevelopment (Blair et al., 2011; Buitelaar et al., 2003; Davis & Sandman, 2010; Laplante et al., 2004).

METHOD

Participants and procedure

Women were recruited into the QF2011 study if they were English speaking, over 18-years old and pregnant with a singleton at the peak of the flood. Recruitment commenced on April 11, 2011, once ethical approval had been obtained, and continued until 12 months postflood, January 2012. Women who were already enrolled in an unrelated study at a major tertiary hospital in Brisbane (Midwives @ New Group practice Options, M@NGO) (Tracy et al., 2011) were invited to participate in the QF2011 study, and women were also invited to join the study by midwives during antenatal check-ups at the same hospital to increase sample size. Additional women also responded to recruitment information flyers that were placed in nearby hospitals or doctors' offices.

From these recruitment methods, 230 women completed a survey about their recollections of their flood experiences, demographic data, and mental health at recruitment into the study ($M = 5.25$ months postflood, $SD = 1.71$) and/or 12 months postflood ($M = 11.22$ months postflood, $SD = 0.51$). Data regarding the women's objective flood-related hardship were merged from the recruitment and postflood surveys if both were completed, using the postflood information to update objective stress scores (e.g., insurance payments). Women in this study who completed the recruitment and/or postflood surveys were flood-exposed at a similar time in pregnancy ($M = 16.79$ weeks, $SD = 10.93$ and $M = 15.70$ weeks, $SD = 10.53$, respectively). Approximately half of the women (58%) were pregnant when they completed the recruitment survey and all women had given birth by 12 months postflood. See King et al. (2015) for a detailed description of eligibility criteria and recruitment methods.

All women were invited to complete questionnaires about their infants' development and their own mental health status at 6 months postpartum. From this initial sample, 126 (54.78% response rate) women returned the 6-month questionnaire; 11 of these were excluded: three because of preterm birth (<36 weeks gestation) and eight because they had been completed outside the accepted infant age-range for the ASQ scales (5.0–7.0 months). Analyses revealed no differences in the demographic or psychological characteristics between the mothers who returned developmental questionnaires at 6 months and those who did not. Maternal demographic data and characteristics are shown in Table 1. The study had ethical approval from study site hospital Ethical Review Board (1709M) and affiliated university (#2013001236).

Infant outcome variables

Infant neurodevelopment was assessed using the Ages and Stages Questionnaire-III (Squires, Twombly, Bricker, & Potter, 2009), a parent-completed screening tool

TABLE 1
Descriptive Statistics for the Ages and Stages Questionnaire (ASQ) Outcomes, Predictor Variables, and Covariates. ASQ Standardized Means and Cutoff Scores ($-2 SD$) are Also Displayed

<i>Variables</i>	<i>N</i>	<i>Mean</i>	<i>SD</i>	<i>Range</i>
Outcome variables				
QF2011 communication	115	47.52	9.35	25 to 60
ASQ standardized mean		48.90	9.63	
ASQ cutoff score		29.65		
ASQ problem solving	115	50.38	10.07	20 to 60
ASQ standardized mean		50.41	11.35	
ASQ cutoff score		22.72		
ASQ personal-social	115	46.74	10.94	10 to 60
ASQ standardized mean		48.31	11.48	
ASQ cutoff score		25.34		
Maternal stress variables				
Objective stress (QFOSS)	115	20.88	16.82	3.00 to 74.00
Post-traumatic stress (IES-R)	115	6.76	11.25	0.00 to 55.00
Composite subjective stress (COSMOSS)	115	0.03	1.05	-1.08 to 3.44
Peritraumatic dissociation (PDEQ)	115	6.25	7.78	0.00 to 32.00
Peritraumatic distress (PDI)	115	11.95	8.76	0.00 to 35.00
Cognitive appraisal: negative	42			
Cognitive appraisal: neutral/positive	72			
Maternal covariates				
Years schoolings	92	14.67	4.71	10 to 16
Socio-economic status	115	1052	57.43	856 to 1150
Recruitment anxiety (STAI)	115	35.67	8.85	20 to 59
6-month anxiety (STAI)	115	33.50	9.27	20 to 60
6-month depression (EPDS)	115	5.72	4.10	0 to 20
Total life events	113	1.50	1.80	1 to 10
Marital status: married/ <i>de facto</i>	84			
Marital status: single/divorced	8			
Infant variables				
<i>In utero</i> flood exposed (days)	115	112.56	74.59	-2 to 267
Gestational age (weeks)	115	39.36	1.179	36 to 41
Birthweight (kgs)	115	35.50	4.54	2.71 to 5.05
Parity	110	0.73	0.91	0 to 4
Age at ASQ (months)	115	6.25	0.33	5.31 to 6.98
Sex: Girl	61			
Sex: Boy	54			

QFOSS, Queensland Flood Objective Stress Scale; IES-R, Impact of Event Scale—Revised; PDEQ, Peritraumatic Dissociative Experiences Questionnaire; PDI, Peritraumatic Distress Inventory; COSMOSS, Composite Score for Mothers' Subjective Stress (IES-R, PDI, PDEQ); STAI, State Trait Anxiety Inventory; EPDS, Edinburgh Postnatal Depression Scale.

administered at 6 months postpartum. The communication, problem solving, and personal-social scales are reported on here. The communication scale assesses vocalizing, hearing, and comprehension (e.g., "Does your baby make sounds like 'da,' 'ga,' 'ka,' and 'ba'?"); the problem solving scale assesses learning and toy play (e.g., "When a toy is in front of your baby, does she reach for it with both hands?"); and the personal-social scale assesses solitary social play and interactions with other's (e.g., "Does your baby act differently toward strangers than he does with you and other familiar people?"). Mothers rated whether their infant had achieved the six target

activities on each scale as: “yes,” “sometimes,” or “not yet.” If scores on any scale were two standard deviations below the mean (cutoff scores) specialist follow up was recommended.

Over 45 independent studies have replicated and validated the ASQ tool (Macy, 2012). The ASQ scales (Squires et al., 1997) have high concurrent validity (overall 83%) to similar practitioner-administered tools such as the Bayley Scales of Infant Development (Bayley, 1993) and the Battelle Developmental Inventory (BDI) (Newborg, Stock, Wnek, Guidubaldi, & Svinicki, 2005). The ASQ scales also have high test–retest reliability (overall agreement for classifications = 92%; correlation coefficients: 0.75–0.82) and good internal consistency (Cronbach alphas range: 0.51–0.87) (Squires et al., 2009). Studies show the ASQ has good predictive validity for detecting developmental delays with the BDI and the Denver-II (positive validity range = 0.40–0.97; negative validity range = 0.75–0.98) (Kapci, Kucuker, & Runa, 2010; Lindsay, Healy, Colditz, & Lingwood, 2008; Skellern, Rogers, & O’Callaghan, 2001).

Maternal stress predictor variables

Mothers’ objective stress experiences of the floods were assessed with an especially designed 55-item questionnaire that measured four key dimensions of objective hardship: Threat (e.g., “Were you injured?”), Loss (e.g., “Did you experience loss of personal income?”), Scope (e.g., “Was your primary residence flooded?”), and Change (e.g., “Did you spend any time in a temporary shelter?”). This questionnaire was adapted from one used in a previous study of flood-related PNMS (Brock et al., 2015; Yong Ping et al., 2015). The research team determined the weighting of each response for each item such that possible scores for each of the four scales ranged from 0 (no impact) to 50 (extreme impact). Scores on the four scales were summed, yielding a total Queensland Flood Objective Stress Score (QFOSS) between 0 and 200; higher scores indicated that higher objective hardship was experienced during the flood.

Mothers’ subjective stress reactions to the floods were assessed with three questionnaires. Post-traumatic stress reactions were assessed using the self-report Impact of Event Scale—Revised (IES-R; Weiss & Marmar, 1997), which assessed discrete aspects of post-traumatic stress symptomology: intrusive thoughts, avoidance/numbing, and hyperarousal. Women rated the 22-items on a 0 (not true) to 4 (extremely true) Likert scale in terms of their symptoms in response to the Queensland floods during the preceding 7 days. The IES-R has high internal consistency (alpha coefficients range: 0.79–0.94) and good test–retest reliability (correlation coefficients range: 0.51–0.94) (Creamer, Bell, & Failla, 2003; Weiss & Marmar, 1997). Peritraumatic stress reactions to the floods were assessed with the 13-item Peritraumatic Distress Inventory (PDI; Brunet et al., 2001) and the 10-item Peritraumatic Dissociative Experiences Questionnaire (PDEQ; Marmar, Weiss, & Metzler, 1997). The PDI assessed women’s recollection of emotional distress and panic-like reactions experienced at the time of the event. The PDEQ assessed the severity of dissociative-like experiences at the time of the event. Women rated the statements in each questionnaire on a 5-point rating scale (“not true” to “very true”).

A composite subjective stress score was calculated to reduce the number of predictor variables in the regression analyses. The Composite Score for Mothers’ Subjective

Stress (COSMOSS) was computed using principal component analysis (PCA) on the total scores of the three traumatic stress measures (IES-R, PDI, and PDEQ) for the 230 women who provided PNMS data. The PCA-derived algorithm was $\text{COSMOSS} = 0.358 \cdot \text{IESR} + 0.397 \cdot \text{PDI} + 0.387 \cdot \text{PDEQ}$. The PCA resulted in one factor explaining 76.27% of the overall subjective stress variance. The COSMOSS variable was standardized with a mean of 0, so that a positive score represents levels of subjective stress that is higher than the mean.

Mothers' cognitive appraisal of the overall impact of the floods was assessed by asking a single question: "If you think about all of the consequences of the 2011 Queensland flood on you and your household, would you say the flood has been...?" A 5-point Likert scale, from very negative (-2) to very positive (+2) rated their appraisal of the event. Due to the narrow range of responses on this scale, this variable was dichotomized into a "negative" impact of the flood versus a "neutral or positive" impact of the flood.

In utero timing of flood exposure was calculated as the number of days between estimated conception date and the peak of the flood. Estimated conception date was calculated by subtracting 280 days (40 weeks) from each woman's due date (based on infant gestational age and date at delivery).

Maternal and infant covariates

Mothers' mood, in the perinatal period, which could potentially influence early parenting style, and at the time of the assessment, which could potentially bias maternal ratings of their infant, was controlled for at recruitment and 6 months postpartum, respectively. At recruitment, the state anxiety scale of the State Trait Anxiety Inventory (SAI; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983) was administered, and at 6 months, both the state-STAI and the Edinburgh Postnatal Depression Scale (EPDS; Cox, Holden, & Sagovsky, 1987) were administered.

Other major life events that mothers may have experienced following childbirth were assessed when infants were aged 6 months using a modified version of the Life Experiences Survey (LES; Sarason, Sarason, Shearin, & Pierce, 1987), which describes 26 categories of life events (e.g., divorce, illness). Mothers reported whether they had experienced the event, the date of the event, and the impact which they rated on a 7-point Likert scale ranging from -3 (Extremely negative) to +3 (Extremely positive). The total number of major life events the mother experienced was included in this study.

Mothers' demographic data, including socio-economic status (SEIFA; Australian Socio-Economic Indexes For Area), marital status (married or *de Facto* versus single or divorced), and education level (number of years schooling), were also assessed. The SEIFA score is based on census data and indicates the socio-economic characteristics of Australian people and families by postal code in relation to their access to resources (material and social) and participation in society. The mean score is 1000 ($SD = 100$), and higher scores indicate that an area is relatively advantaged compared to areas with lower scores.

Infant birth data, including gestational age at birth, birthweight, and parity, were collected from routine hospital records and included as control variables if they significantly correlated with the outcome variables.

Statistical analyses

Descriptive analyses were performed on the outcome and predictor variables and covariates (see Table 1). The distributions of four of the measures of maternal stress (objective and subjective stress, and peritraumatic distress and dissociation) were significantly different from the normal distribution using the Kolmogorov–Smirnov test, based on their positive skewness (1.47, 2.65, 1.00, and 1.71, respectively) and their kurtosis (1.96, 7.65, 0.72, and 2.39, respectively). Thus, these measures were naturally log-transformed to normalize the data. The COSMOSS variable entered into the regressions was not log-transformed.

Pearson product–moment correlations were conducted to examine the associations between the ASQ subscale scores, predictor variables, and covariates (Table 2).

The data from the communication, problem solving, and personal–social scales were subjected to hierarchical regression analyses to examine possible relationships between prenatal maternal objective and subjective stress and infant outcomes. The model for the regressions was the same for each scale: Control variables were entered first; covariates were entered into the model if the correlation coefficients revealed any significant relationship with the ASQ outcomes. Next, objective stress was entered into the model, followed by the composite subjective stress score, then the cognitive appraisal score. The next step included entering the timing of exposure, followed in the next step by infant sex. The last step included the interaction term between one of the three PNMS variables entered in the model and either timing or sex. As the sample was relatively small, the equations were trimmed of any nonsignificant variables that were forced into the equation (unless they were included in a significant interaction) and rerun. Interactions ($p < .1$) were probed using the PROCESS macro (Hayes, 2013). All correlation and main effect analyses were significant for p -values $< .05$. However, to control for the number of moderation analyses, the interaction term significance levels were corrected using the Benjamini–Hochberg method for false discovery rate at the 5% level (Benjamini & Hochberg, 1995). Analyses were conducted using SPSS v22.

RESULTS

Descriptive statistics

Descriptive statistics for the outcome variables, predictor variables, and covariates for the sample are shown in Table 1. The maternal stress scores showed that the women were flood-affected to varying degrees, with some experiencing little flood-related hardship or low levels of subjective distress, while others were more severely impacted by the event. Mean scores on objective hardship (QFOSS: $M = 20.88$, $SD = 16.82$) or post-traumatic distress (IES-R: $M = 6.67$, $SD = 11.25$) scales were comparable to those in two prior disaster studies using similar tools (King & Laplante, 2015; Yong Ping et al., 2015). Eight women (7%) scored above the IES-R cutoff point of 22, and 16 women (14%) scored above the PDI cutoff point of 23, which indicate potential diagnosis of post-traumatic stress disorder.

The women in the sample were relatively high-functioning with mean state anxiety scores no different at recruitment ($t_{114} = .58$, $p = .57$), and marginally lower at 6 months (less anxious; $t_{114} = -1.96$, $p = .05$), than STAI state anxiety norms based on adult women ($M = 35.20$, $SD = 10.61$). In terms of depression, $N = 5$ women (4%)

TABLE 2
Intercorrelations Between Ages and Stages Questionnaire (ASQ) Outcomes, Predictor Variables, and Covariates

Variable	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	
1. Communication	—																			
2. Problem solving	.34**	—																		
3. Personal-social	.30**	.44**	—																	
4. Objective stress ^a	-.11	-.19*	-.17 [§]	—																
5. Post-traumatic stress ^b	-.06	-.23*	-.18*	.59**	—															
6. Peritraumatic Dissociation ^a	.05	-.00	-.05	.49**	.61**	—														
7. Peritraumatic distress ^a	.03	.05	-.11	.50**	.62**	.72**	—													
8. Composite subjective stress	.03	-.05	-.11	.59**	.81**	.88**	.88**	—												
9. Cognitive appraisal	-.04	.08	.06	-.48**	-.44**	-.28**	-.31**	-.38**	—											
10. Years schooling	.01	.08	-.02	.09	-.21*	-.08	-.11	-.18	.03	—										
11. Socio-economic status	.01	.01	-.04	.25*	.06	.06	.02	.05 [§]	-.31**	.51**	—									
12. Recruitment anxiety (STAI)	.03	-.12	-.05	.22*	.18*	.30**	.13	.24*	-.13	-.10	.07	—								
13. 6 Month anxiety (STAI)	-.04	-.07	.07	.17	.21*	.20*	.09	.20*	-.07	.09	.04	.57**	—							
14. 6 Month depression (EPDS)	-.03	-.06	.00	.22*	.33**	.31**	.27**	.36**	.07	.13	.00	.36**	.77**	—						
15. Life events	-.01	.01	.02	.16 [§]	-.02	-.01	.13	.03	.04	.11	.01	.07	.08	.16	—					
16. Parity	-.04	-.15	-.21*	-.07	.07	-.01	.05	.04	.01	-.04	-.02	.06	-.08	-.12	.17 [§]	—				
17. Gestational age	.15	.13	.20*	-.08	-.12	-.01	-.11	-.11	.03	.05	.07	.13	.21*	.05	.00	-.07	—			
18. Birthweight	.12	.28*	.14	-.04	.11	-.12	.10	.01	-.07	.18 [§]	.06	.12	.20*	.12	.06	.15	.44**	—		
19. <i>In utero</i> flood exposed	.09	-.04	-.15	-.03	-.02	-.10	-.05	-.07	.07	.19	.11	-.20*	-.06	-.09	.03	.08	.11	.19*	—	
20. Infant sex (0 = M, 1 = F)	.06	-.05	.10	-.02	-.03	.03	-.02	-.06	-.06	.03	.09	-.05	-.17 [§]	-.25**	.03	.12	.03	-.04	-.04	.08

[§] $p < .1$; * $p \leq .05$; ** $p < .01$; ^aLog-transformed scores.

scored over 12 on the EPDS at 6 months, above which the likelihood of depression diagnosis is high.

The percent of QF2011 infants who scored below the ASQ cutoff score levels on the communication (2%, $n = 2$), problem solving (4%, $n = 5$), and personal-social (5%, $n = 6$) scales was below the expected percentage of 16% of the sample. Furthermore, one-sampled *t*-tests showed that the QF2011 sample mean scores did not differ significantly from the ASQ standardized means for the communication ($p = .12$), problem-solving ($p = .98$), or personal-social ($p = .13$) scales which were all within 14% of two SD below the normed mean.

Correlations with infant development

Pearson's product-moment correlations showed no significant relationship between infants' communication skills and the mothers' PNMS measures, or the covariates. However, there were negative correlations between infants' problem solving abilities and both maternal objective hardship and post-traumatic stress scores (see Table 2), indicating that higher stress on these measures predicted poorer infant problem solving ability at 6 months of age. There was a significant negative correlation between infants' personal-social skills and mothers' post-traumatic stress, suggesting that higher stress on this measure was associated with poorer infant personal-social skills. There was a marginally significant negative relationship between infants' personal-social skill and mothers' objective stress experiences. There were no significant correlations between a mother's peritraumatic stress responses, the composite subjective stress measure, or her cognitive appraisal of the impact of the floods, and infant development on any of the three neurodevelopmental scales.

As for the covariates, there was a significant correlation between infant problem-solving and birthweight: Heavier infants at birth performed better on this scale. There were also significant correlations between infants' personal-social skills and gestational age and parity: Longer gestations and first born infants were rated as performing better on this scale than shorter gestations and latter borns.

Regression analyses

The hierarchical regression models showed there were no significant main effects or interactions from mothers' PNMS measures associated with infants' communication skills at 6 months of age (data not shown).

The results of the hierarchical regressions for the problem solving scale are presented in Table 3 (part a). In Step 1, infant birthweight explained 7.7% of variance ($p < .00$): The heavier the infants, the better the performance on the problem solving scale. In Step 2, mothers' objective stress explained a significant additional proportion (3.2%) of the variance in infants' problem solving skills ($p = .05$): Higher objective stress was related to lower problem solving skills at 6 months of age. In Steps 3 and 4, neither the main effects of mothers' composite subjective stress nor infant sex were significantly related to infants' problem solving skills after controlling for maternal objective stress. Additionally, in Step 5, the addition of the interaction term for mothers' composite subjective stress by infant sex to the model explained an additional 4.6% of unique variance in problem solving ($p = .049$). As shown in Figure 1, although the significant interaction indicates that the slope of the effect of COSMOSS on problem-

TABLE 3
 Summary of Hierarchical Regression Analyses for the Ages and Stages Questionnaire (ASQ) Problem Solving and Personal–Social Scales at 6 Months of Age

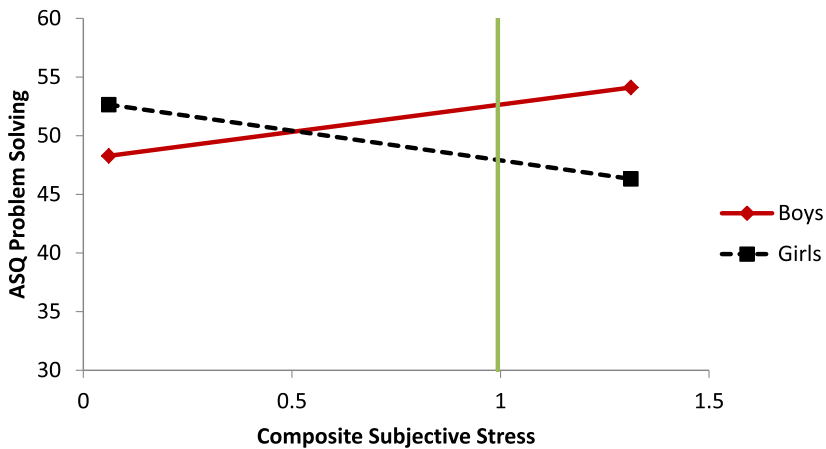
Predictor variables	β	<i>B</i>	<i>SE</i>	<i>R</i>	<i>R</i> ²	ΔR^2	<i>F</i>	ΔF
a) <i>Problem solving</i>								
Step 1								
Birthweight	0.277**	0.006	0.002	.277	.077	.077	9.397**	9.397**
Step 2								
Birthweight	0.270**	0.006	0.002	.330	.109	.032	6.648**	4.046*
Objective stress	-0.180*	-2.326	1.157					
Step 3								
Birthweight	0.265**	0.006	0.002	.332	.110	.001	4.576**	0.138
Objective stress	-0.202 [§]	-2.623	1.410					
Composite subjective stress	0.041	0.899	2.420					
Step 4								
Birthweight	0.264**	0.006	0.002	.334	.112	.002	3.464*	0.222
Objective stress	-0.203 [§]	-2.629	1.415					
Composite subjective stress	0.040	0.885	2.428					
Infant sex	-0.042	-0.850	1.806					
Step 5								
Birthweight	0.254**	0.006	0.002	.397	.158	.046	4.083**	5.94*
Objective stress	-0.159	-2.059	1.404					
Composite subjective stress	0.210	4.657	2.835					
Infant sex	0.247	4.961	2.968					
Composite subjective stress \times infant sex	-0.408*	-9.717	3.987					
b) <i>Personal–social</i>								
Step 1								
Parity	-0.206*	-2.485	1.136	.206	.042	.042	4.785*	4.785*
Step 2								
Parity	-2.079*	-2.349	1.130	.258	.067	.024	3.828*	2.792 [§]
Gestational age	1.671 [§]	1.480	0.885					
Step 3								
Parity	-0.206*	-2.485	1.122	.303	.092	.025	3.574*	2.927 [§]
Gestational age	0.151	1.428	0.878					
Objective stress	-0.159 [§]	1.322	1.322					
Step 4								
Parity	-0.190*	-2.294	1.109	.357	.127	.036	3.833*	4.278*
Gestational age	0.174 [§]	1.649	0.871					
Objective stress	-0.163 [§]	-2.320	1.302					
Timing <i>in utero</i>	-0.191*	-0.028	0.013					

Infant sex: boy = 0; girl = 1.

[§]*p* < .1; **p* < .05; ***p* < .01.

solving differed significantly by sex, neither of these slopes were significantly different from zero. However, when mothers had composite subjective stress scores of 0.99 or greater, boys had significantly better problem solving skills than girls; at high levels of flood-related maternal subjective stress from the flood, boys scored nearly 1 full standard deviation above girls on this scale. The final model explained 15.8% of the variance in problem solving at 6 months (*p* = .00).

The results of the hierarchical regression for infants' personal–social skills are presented in Table 3 (part b). In Step 1, parity was significantly related to the infants' personal–social skills, explaining 3.4% if the variance (*p* = .03): The greater the number of older siblings, the lower the score. In Step 2, gestational age was marginally



* $p < 0.05$

Figure 1 Significant moderation by infant sex of mothers' composite subjective stress score (COSMOSS) on 6-month-olds' problem solving skills. The slope was not significant for either boys or girls. The vertical green line indicates the region of significant difference ($p < 0.05$) in ASQ scores for boys and girls.

significantly associated with infants' personal–social abilities, explaining an additional 2.4% of the variance ($p = .10$): The longer the gestation, the better the score. In Step 3, there was a tendency for mothers' objective stress to be related to infants' personal–social skills, explaining an additional 2.5% of the variance in infants' personal–social abilities ($p = .09$): Higher objective stress levels were associated lower personal–social skills. In Step 4, timing of *in utero* exposure to the flood was entered into the model, explaining an additional 3.6% of unique variance in infants' personal–social abilities ($p = .05$): The later in pregnancy the mother was exposed to the flood, the lower the infants' personal–social skills. The final model explained 12.7% of the variance in personal–social skills at 6 months. Mothers' composite subjective stress levels or cognitive appraisal were not significant predictors of infants' personal–social skills when controlling for levels of maternal objective stress, and infant sex did not enter into any significant main effects or interactions.

DISCUSSION

To our knowledge, this is the first study to show that flood-related PNMS influences selected aspects of infant neurodevelopment at 6 months of age. Using a natural disaster as the pregnancy stressor enabled comparison of the effects of women's objective experience of the floods, their subjective responses to the disaster, and overall appraisal of the event, as well as investigation of the *in utero* timing on infant neurodevelopment in three areas: communication, problem solving, and personal–social skills.

None of our predictor variables had significant associations with infant communication skills. Results showed that objective aspects of flood exposure in pregnancy had negative effects on both problem solving and personal–social skills when controlling

for covariates. With regard to maternal composite subjective stress and infant development, infant sex moderated the effects on problem solving skill such that, when maternal subjective distress from the floods was high, boys scored better on problem solving than did girls. There was a significant main effect of *in utero* timing on infants' personal-social development when controlling for other factors, suggesting that late pregnancy is a vulnerable period for the development of these skills. Mothers' cognitive appraisals of the flood did not influence any aspect of infant neurodevelopment.

In contrast to prior research which demonstrated that language development at age 2 years was compromised by maternal exposure to a severe ice storm in pregnancy (Laplante et al., 2004, 2008), there was no evidence in the current study that early communicative skills, such as babbling and vocalizing, were affected. It is possible that more advanced language skills specific to children's receptive and productive vocabulary are more susceptible to the negative effects of PNMS; therefore, these effects may not be apparent until later in development, when children start talking. Alternatively, it may be that language or communication scales generally have lower validity when administered at 6 months of age than at 2 years when language skills are more established.

While research usually shows that fetal development may be negatively altered by stress in pregnancy (Bergman et al., 2007; Buitelaar et al., 2003; Laplante et al., 2004), the current results suggest that that under certain conditions PNMS can have no effect, or even beneficial effects, on fetal development; when maternal subjective distress from the floods was high, boys scored better on problem solving than did girls. A small number of other studies have found similar results with some evidence of curvilinear effects of PNMS, for example, moderate levels of ice storm-related stress in pregnancy being more beneficial than lower levels (Laplante et al., 2008). One study found mild levels of prenatal maternal psychological distress had positive effects on infant cognition (DiPietro et al., 2006) and another found that fetal exposure to high levels of maternal cortisol (but not maternal psychological distress) late in gestation predicted better cognitive skills in 12-month-olds (Davis & Sandman, 2010).

As hypothesized, in the current study, there was a negative correlation between mothers' post-traumatic stress responses (IES-R) and infants' problem solving and personal-social skills. Moreover, with the regressions, there was a trend for mothers' objective stress levels to be related to poorer infant personal-social skills, and a significant effect of timing on personal-social skills was also noted. While we believe this is the first study to measure the effects of PNMS on young infants' personal-social skills *per se*, our findings are consistent with studies showing negative effects of PNMS on infant temperament (Austin et al., 2005; Davis et al., 2004; Huizink et al., 2003) and childhood emotional-behavioral problems (O'Connor, Heron, Golding, & Glover, 2003; Van den Bergh & Marcoen, 2004).

Our current findings with the personal-social ASQ scale support the fetal programming hypothesis and prior research showing sex differences in response to intrauterine stress (Clifton, 2010) and prenatal cortisol levels (Glynn & Sandman, 2012). Past research has also found that infant sex can moderate PNMS effects, although there are inconsistencies with some studies reporting that girls are more vulnerable than boys, as we found here (Barrett, Redmon, Wang, Sparks, & Swan, 2014; Cao, Laplante, Brunet, Ciampi, & King, 2014; O'Connor et al., 2003), while other studies report that boys are more vulnerable than girls (Kinney, Miller, Crowley, Huang, & Gerber, 2008; Walder et al., 2014). However, other research has failed to find any evidence to

support the premise that infant sex moderates negative effects of PNMS on developmental outcomes (Buitelaar et al., 2003; Laplante et al., 2004).

In contrast to our hypothesis that *in utero* timing of the stressor would moderate the effects of PNMS on infant neurodevelopment, we found only a marginally significant effect of exposure timing on infants' personal-social skills: The later in pregnancy the exposure, the poorer their personal-social skills. This timing effect may be due to the effects of PNMS on the fetal cerebellum, which develops in the third trimester and has been implicated in problems involving social and interpersonal skills such as autism (Brambilla et al., 2003). This result is consistent with Project Ice Storm's finding of third trimester vulnerability for motor skills at age 5 years, and our own replication of this finding in QF2011 using the ASQ motor scales (Simcock et al., 2016) and the Bayley motor score (Moss et al., in revision) in infancy. The association between early motor skills and social behavior has been increasingly recognized in the literature (Campos et al., 2000).

There exists other literature, however, suggesting that early gestation is a vulnerable period for social behaviors. Consistent with studies on infant temperament (Blair et al., 2011; Buitelaar et al., 2003; Laplante et al., 2016), we had anticipated a sensitive developmental period for personal-social skills in early gestation, coinciding with the development of the amygdala and hippocampus (Humphrey, 1964, 1968). These brain structures are associated with emotional reactivity and affective disorders and are sensitive to high levels of cortisol in early fetal development (Buss et al., 2012). However, the current contradictory timing results may have occurred as dimensions of temperament (e.g., fearfulness, reactivity, negativity) and early behavioral problems (e.g., internalizing, externalizing) in other PNMS studies differ to the personal-social skills (e.g., responsiveness to caregiver, reactions to mirror image) assessed here with the ASQ-III, which may be less associated with the amygdala and hippocampus. Although the importance of timing of PNMS in gestation on other neurodevelopmental domains, including cognition (Davis & Sandman, 2010) and motor skill (Cao et al., 2014), has been previously demonstrated, there are inconsistencies in the literature, and other studies have failed to find that *in utero* timing moderates the effects of PNMS on developmental domains including language skill (Laplante et al., 2008).

As in other PNMS studies, we found that birth data significantly predicted later infant outcomes (Laplante et al., 2004; Schneider, 1992). In this study, higher birth-weight was associated with better problem solving skills, and lower parity and longer gestations were associated with better personal-social skills. These findings persisted even though we removed three preterm infants (36 weeks gestation, 2.91–3.13 kg birth-weight) from the sample. Thus, even within a full-term and healthy-weight sample such as this, aspects of infant neurodevelopment can be influenced by variations in birth outcomes which is consistent with past research using the ASQ with high-risk infants receiving neonatal care (Fallah et al., 2011).

However, there were no significant correlations between maternal demographic factors (SES, marital status, and level of schooling), maternal mood (perinatal anxiety at recruitment and postnatal anxiety or depression at 6 months), or major postnatal life events on infants' performance on the three developmental domains investigated here. Thus, the effects of PNMS on infant development in this study cannot be attributed to these variables that have been documented elsewhere to explain variance in infant and child development (Grace et al., 2003; Kingston et al., 2012; Tough, Siever, Benzies, Leew, & Johnston, 2010), even though we found significant associations between

maternal mental health and mothers' ratings of difficult infant temperament in the same QF2011 cohort (Simcock et al., under review). However, that was not the case here, perhaps due to the different domains of development assessed in the current study. Other research, using similar assessment tools, has also found that maternal reports of their children's outcomes are not always associated with their SES or education level (Johnson et al., 2004; Kim, O'Connor, McLean, Robson, & Chance, 1996). It is also possible that we did not find a relationship between the maternal covariates and infant development due to the homogenous characteristics of the sample (i.e., well-educated, middle- to upper-SES women) which restricted variance. Finally, it is also possible that the impact of the external stressor, the floods, "trumped" the usual associations seen between maternal demographics and infant ASQ neurodevelopmental outcomes.

Using a natural disaster (a flood) as the pregnancy stressor, we were in a unique position to explore how infant development can be affected by mothers' objective versus subjective stress experiences and their cognitive appraisals of the stressful event. Although we showed no effects of maternal cognitive appraisal on infant neurodevelopment at 6 months of age, our results showed that mothers' objective and subjective stress responses operated differentially on infants' problem solving and personal-social skills, and that none of the PNMS variables had an effect on infant communication skills at this age. Infant problem solving was negatively affected by maternal objective stress, but infant sex moderated the effect of composite subjective stress so that boys performed better with higher maternal composite stress than did girls. However, infants' personal-social skills were significantly associated with *in utero* timing of the floods, and only marginally related to their mother's objective stress response. These differential effects of objective versus subjective pregnancy-related stress on infant development are consistent with results from other disaster-related PNMS studies that have used similar methodologies to compare the effects of objective versus subjective PNMS on infant outcomes (Dancause et al., 2011; King & Laplante, 2015; King et al., 2009, 2015; Laplante, Zelazo, Brunet, & King, 2007; Laplante et al., 2008; Tees et al., 2010; Yong Ping et al., 2015).

The current findings are limited as they are based on a relatively small sample size ($N = 115$), so it is possible that some effects of PNMS were unable to be detected due to lack of power. Also, the sample was homogenous, so the generalizability of the results to populations other than high-functioning, well-educated, and relatively high SES families may be questionable. Furthermore, as the ASQ is based on maternal report, there may be biases in recollection or reporting. That said, the proven psychometric qualities of this tool have shown that mothers typically do report on their infants' development accurately (Squires et al., 2009), and our data failed to show any significant associations between maternal psychosocial characteristics and maternal ratings of their infants on the ASQ.

As natural disasters are an increasing phenomena worldwide (Leaning & Guha-Sapir, 2013), it is important to recognize that the stress pregnant women experience during such events can place their infants' development at risk. This knowledge may enable the development of interventions that reduce the worst effects of maternal stress arising from exposure to a natural disaster in pregnancy, and thereby optimize infant development. The results of our research generalize to stressors beyond those inherent in a natural disaster as nearly every stressful experience includes aspects of objective hardship and subjective distress. Using an "independent" stressor such as a disaster

allows us to tease apart components of mothers' stress experiences. We suggest that interventions aimed at reducing both the degree of hardship and the distress experienced by pregnant women will benefit the unborn child, no matter the nature of the prenatal stress.

In summary, the current results show that objective PNMS negatively influenced infant problem solving and personal-social development at 6 months of age, independent of potential covariates such as birth outcomes, maternal demographics, other life events, and mental health status. Girls seemed particularly vulnerable to the negative effects of subjective PNMS compared to boys, whose problem solving skills exceeded those of girls with higher maternal subjective PNMS. Finally, results suggest that late pregnancy may be a particularly sensitive period for infant personal-social development. However, PNMS did not appear to affect infant communication skills at this age. The QF2011 study continues to monitor the development of these children and will report on the effects of flood-related PNMS on development at later ages.

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