

The effects of maternal stress and illness during pregnancy on infant temperament: Project Ice Storm

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BACKGROUND: To determine whether disaster-related prenatal maternal stress and maternal illness during pregnancy predict maternal-rated temperament status in 6-mo-old infants.

METHOD: The temperamental status of 121 infants (60 boys and 61 girls) exposed *in utero* to varying degrees of maternal stress and/or illness during either first ($n = 40$), second ($n = 43$), or third ($n = 38$) trimester of pregnancy was assessed using the Infant Characteristics Questionnaire.

RESULTS: Higher levels of maternal subjective distress and illness were primarily independently associated with poorer temperamental status in the infants. Maternal subjective distress explained 3.4, 3.1, and 9.8% and early pregnancy illness explained 4.3, 5.8, and 2.9% of the variance of the infants' fussy/difficult, dullness, and needs attention temperament dimensions, respectively.

CONCLUSION: This is the first study to assess whether temperament status is influenced by disaster-related prenatal maternal stress. Moreover, this is the first study to assess whether maternal stress and illness during pregnancy interact to determine infant temperament status. The findings suggest that while both factors predict temperament status at 6 mo, they do so primarily in an independent manner. These results suggest that pathways through which maternal stress and illness during pregnancy influence temperament status differ.

There is a growing body of literature linking measures of maternal stress during pregnancy and adverse infant/child outcomes. For example, higher levels of prenatal maternal stress (PNMS) are associated with poorer intellectual, linguistic, and behavioral outcomes (1). It is widely believed that heightened levels of stress during pregnancy increase maternal cortisol secretion to levels that become neurotoxic to the developing fetal brain, thereby resulting in less than optimal developmental outcomes during infancy and childhood (2). However, other mechanisms, such as maternal immune functioning, may also influence fetal development and subsequent postnatal functioning (3).

Temperament, although not universally defined, usually refers to differences in behavioral tendencies that are stable

across age and situations and are thought to be predictive of later psychological functioning (4). While there exists strong evidence that temperament is under some form of genetic control, there is equal evidence that environmental factors play a role in the expression of temperamental traits (5).

In terms of infant temperament, mothers who experience a greater number of major life events during pregnancy, or who report higher levels of pregnancy-specific anxiety or depression, report their children as having more difficult temperaments (6–8). One study that assessed the effect of maternal exposure to a natural disaster found that while hurricane-related experiences (i.e., damage to home, life in danger, walking through floodwaters) were unrelated to temperament status, increased number of hurricane-related post-traumatic stress disorder symptoms were related to more difficult infant temperaments (9). Furthermore, high levels of maternal cortisol during pregnancy have also been shown to be associated with poorer infant temperaments either directly (10) or by its effect on birth weight (11).

A second, less well-studied intrauterine event, particularly in humans, that has been linked to poorer outcomes throughout development is maternal illness or infection. Animal research has demonstrated that maternal infection is associated with fetal growth restriction, altered brain functioning, and deficits in prepulse inhibition, spatial and associative learning, memory, locomotion, and social interaction (see Boksa (12) for a review). It is believed that these adverse outcomes do not stem from the maternal infection itself, but from the mother's immune system, in particular the increased production of cytokines, in response to the infection (13). Human research indicates that maternal infection during pregnancy is associated with higher rates of schizophrenia and autism among offspring (14–17).

Since maternal illness and/or infection is associated with fetal growth restriction (12) and since fetal growth restriction has been linked to temperament (18–20), it is possible that maternal illness and/or infection has an indirect influence on temperament. To our knowledge, only one article has been published that looked at the direct link between maternal illness and infant temperament. Dombrowski *et al.* (21), using the Helsinki Longitudinal Project cohort, established

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Table 1. Correlation coefficients and means and SDs for outcome and predictor variables

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | Means | SD | |
|---------------------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|-------------------|--------------------|---------|--------|--------------------|-------------------|--------------------|-------|-------|-------|-------------------|-------------------|---------|-------|------|
| Temperament dimensions | | | | | | | | | | | | | | | | | | | | | |
| 1 Fussy/difficult | --- | | | | | | | | | | | | | | | | | | 2.5 | 0.9 | |
| 2 Unadaptable | 0.41 [†] | --- | | | | | | | | | | | | | | | | | 2.3 | 1.0 | |
| 3 Dull | 0.46 [‡] | 0.35 [‡] | --- | | | | | | | | | | | | | | | | 2.2 | 0.9 | |
| 4 Needs attention | 0.63 [‡] | 0.32 [‡] | 0.58 [‡] | --- | | | | | | | | | | | | | | | 3.7 | 1.7 | |
| Maternal characteristics | | | | | | | | | | | | | | | | | | | | | |
| 5 Anxiety | 0.15 | 0.02 | -0.04 | 0.17 | --- | | | | | | | | | | | | | | 2.3 | 2.1 | |
| 6 Major life events | 0.20* | 0.11 | 0.13 | 0.15 | 0.18* | --- | | | | | | | | | | | | | 5.4 | 3.3 | |
| 7 Postpartum depression | 0.17 | 0.11 | 0.14 | 0.20* | 0.32 [‡] | 0.14 | --- | | | | | | | | | | | | 6.3 | 4.8 | |
| 8 Obstetric complications | 0.01 | -0.01 | 0.06 | 0.09 | 0.08 | -0.05 | 0.06 | --- | | | | | | | | | | | 4.0 | 2.9 | |
| 9 Age at child's birth (years) | 0.11 | 0.11 | 0.25** | 0.17 [†] | 0.01 | 0.06 | -0.10 | 0.12 | --- | | | | | | | | | | 30.1 | 4.7 | |
| 10 Number of previous children | 0.11 | 0.13 | -0.10 | -0.04 | 0.04 | 0.10 | 0.09 | -0.17 [†] | 0.24** | --- | | | | | | | | | 1.6 | 1.2 | |
| 11 Socioeconomic status | 0.01 | -0.02 | -0.02 | 0.02 | 0.05 | -0.03 | 0.15 [†] | -0.06 | -0.24** | 0.09 | --- | | | | | | | | 28.8 | 12.8 | |
| Infant characteristics | | | | | | | | | | | | | | | | | | | | | |
| 12 Gestational age (weeks) | -0.05 | -0.12 | 0.05 | -0.02 | -0.02 | 0.01 | 0.01 | -0.17 [†] | 0.06 | -0.05 | 0.13 | --- | | | | | | | 39.5 | 1.7 | |
| 13 Birth weight (g) | 0.07 | -0.01 | -0.00 | 0.00 | 0.03 | -0.11 | 0.08 | -0.22* | -0.08 | 0.12 | 0.15 | 0.63 [‡] | --- | | | | | | 3,450.0 | 534.3 | |
| 14 Ponderal index | 0.07 | -0.13 | -0.09 | 0.04 | 0.08 | -0.02 | -0.02 | -0.19* | -0.24** | 0.08 | 0.22* | 0.19* | 0.41** | --- | | | | | 27.8 | 3.3 | |
| Maternal illness | | | | | | | | | | | | | | | | | | | | | |
| 15 First trimester | 0.12 | 0.13 | 0.26** | 0.17 [†] | -0.12 | 0.02 | -0.05 | -0.02 | 0.06 | 0.02 | -0.07 | -0.06 | -0.17 [†] | -0.08 | --- | | | | 0.3 | 0.6 | |
| 16 Second trimester | 0.16 [†] | 0.13 | -0.13 | 0.10 | 0.11 | 0.10 | 0.05 | -0.11 | -0.09 | 0.20* | 0.01 | -0.01 | 0.09 | 0.14 | -0.14 | --- | | | 0.3 | 0.7 | |
| 17 Third trimester | 0.06 | -0.03 | -0.01 | 0.14 | 0.15 | 0.16 [†] | 0.07 | 0.14 | 0.04 | 0.15 | -0.03 | 0.01 | 0.04 | 0.03 | -0.02 | -0.08 | --- | | 0.2 | 0.4 | |
| Disaster-related factors | | | | | | | | | | | | | | | | | | | | | |
| 18 Objective hardship | 0.10 | -0.01 | 0.14 | 0.16 [†] | 0.01 | 0.19 [†] | -0.10 | -0.01 | 0.01 | -0.05 | 0.09 | 0.03 | -0.01 | 0.23* | 0.19* | 0.20* | 0.01 | --- | 11.0 | 4.4 | |
| 19 Subjective distress | 0.24** | 0.07 | 0.15 | 0.31 [†] | 0.34 [‡] | 0.19 [†] | 0.23* | 0.04 | -0.14 | -0.05 | 0.16 [†] | -0.08 | 0.02 | 0.08 | -0.05 | 0.19* | 0.18 [†] | 0.34 [‡] | --- | 11.2 | 11.5 |
| 20 Timing of exposure | -0.21* | 0.01 | 0.01 | -0.06 | -0.04 | -0.13 | -0.11 | 0.04 | 0.08 | -0.22* | -0.19 [†] | -0.21* | -0.21* | 0.06 | 0.02 | 0.06 | -0.12 | 0.28** | -0.02 | 136.8 | 80.2 |

The diagonal dashes indicate correlations of same variables.
[†]*P* < 0.05; [‡]*P* < 0.01; **P* < 0.1; ^{††}*P* < 0.001.

Table 2. Summary of hierarchical linear regression analyses

| Predictor variables | Values in final model | | | Values after entry of each variable | | | | | |
|---|-----------------------|-------------|------------------|-------------------------------------|-----------------------|--------------|----------|------------|--------------------|
| | <i>B</i> | SE <i>B</i> | <i>B P</i> value | β | <i>R</i> ² | ΔR^2 | <i>F</i> | ΔF | $\Delta F P$ value |
| <i>Fussy/difficult dimension</i> | | | | | | | | | |
| (constant) | 2.177 | 0.277 | | | | | | | |
| Major life events | 0.041 | 0.024 | 0.094 | 0.198 | 0.039 | | 4.874* | | |
| Timing of exposure | < 0.001 | 0.001 | 0.967 | -0.187 | 0.074 | 0.034 | 4.695* | 4.378 | 0.039 |
| Maternal illness (first trimester) | -0.551 | 0.372 | 0.141 | 0.116 | 0.087 | 0.013 | 3.723* | 1.721 | 0.196 |
| Maternal illness (second trimester) | 0.213 | 0.111 | 0.057 | 0.175 | 0.117 | 0.030 | 3.830** | 3.878 | 0.051 |
| Objective hardship | -0.022 | 0.022 | 0.321 | 0.083 | 0.122 | 0.006 | 3.202* | 0.724 | 0.397 |
| Subjective distress | 0.041 | 0.013 | 0.002 | 0.204 | 0.157 | 0.034 | 3.530† | 4.662 | 0.033 |
| Objective hardship × maternal illness (first trimester) | 0.058 | 0.027 | 0.031 | 0.576 | 0.186 | 0.029 | 3.691† | 4.081 | 0.046 |
| Subjective distress × timing of exposure | 0.000 | 0.000 | 0.024 | -0.421 | 0.223 | 0.036 | 4.008† | 5.255 | 0.024 |
| <i>Dullness dimension</i> | | | | | | | | | |
| (constant) | 0.393 | 0.529 | | | | | | | |
| Maternal age | 0.050 | 0.017 | 0.003 | 0.250 | 0.063 | | 7.941** | | |
| Maternal illness (first trimester) | 0.357 | 0.123 | 0.004 | 0.241 | 0.121 | 0.058 | 8.094† | 7.794 | 0.006 |
| Subjective distress | 0.014 | 0.007 | 0.040 | 0.0178 | 0.152 | 0.031 | 6.986† | 4.315 | 0.040 |
| <i>Need attention dimension</i> | | | | | | | | | |
| (constant) | 0.439 | 0.977 | | | | | | | |
| Postpartum depression | 0.052 | 0.031 | 0.091 | 0.196 | 0.038 | | 4.763* | | |
| Maternal age | 0.075 | 0.030 | 0.015 | 0.187 | 0.072 | 0.034 | 4.641* | 4.384 | 0.038 |
| Maternal illness (first trimester) | 0.469 | 0.222 | 0.037 | 0.167 | 0.101 | 0.029 | 4.362** | 3.600 | 0.060 |
| Subjective distress | 0.048 | 0.013 | <0.000 | 0.325 | 0.199 | 0.098 | 7.205† | 14.249 | <0.000 |

P* < 0.05; *P* < 0.01; †*P* < 0.001.

a link between maternal illness and maternal ratings of their children's temperament at 6 mo and 5 y. Mothers reporting the presence of a fever due to flu or illness during the second trimester of pregnancy rated their 6-mo-old infants as exhibiting greater distress to novelty compared to mothers who either did not have an illness during pregnancy or who had an illness at other times during their pregnancies. Moreover, these same mothers rated their 5-y-old children as being more inhibited, having more negative emotionality, and lacking task persistence.

Most research on the effects of maternal illness is from animal research. Although these studies provide useful information, generalizing their results to humans is limited by differences in gestation length, *in utero* developmental time line, maturation status at birth, and differences in interspecies physiology (22). Research on maternal stress during pregnancy is also limited due to methodological constraints. Most human studies do not allow stressful events to be randomly assigned during pregnancy, and thus may lack internal validity. Moreover, measures of pregnancy-specific anxiety and/or major life events, such as divorce, job loss, or family and marital discord, may not be independent of the woman's own personality, which may also be passed on to her children genetically.

Interestingly, research on fetal exposure to stress and other factors that may impact postnatal development typically focus on only one aspect of the fetal experience. To date, the most widely examined prenatal risk factor studied is maternal

anxiety and/or "stress", particularly pregnancy-related stress. This research generally suggests that elevated anxiety/stress levels affect the developing fetus by exposing the fetus to higher-than-normal levels of maternal cortisol. However, maternal stress may also affect the fetus through other means, directly or indirectly, such as by alterations in diet and immune function (3). These alternative pathways through which maternal stress is believed to impact fetal development and thus subsequent postnatal development may work independently or in harmony with the cortisol pathway. However, no such research has been conducted to investigate how these different pathways may potentially interact. It is also possible that pathways other than maternal cortisol may exist even when maternal stress is not present.

The 1998 Québec ice storm provided a unique situation for determining whether an independent stressor arising from a natural disaster influences infant temperament in a manner similar to that observed with other pregnancy-related distress. The crisis affected a large population of pregnant women at various stages of pregnancy, and severity of exposure was independent of the women's age, education, socio-economic status, personality traits, and current psychological functioning. Moreover, because the ice storm was a naturally occurring, independent event, two forms of PNMS could be identified: objective hardship and subjective distress. Our objective hardship scale assessed the severity of specific storm-related events experienced by the pregnant women (e.g., number of days

without electricity, staying in a shelter). Our subjective distress measure assessed the pregnant women's distress in response to these events. In addition, because the exact parameters of the ice storm are well documented (e.g., days on which the power was lost and re-established for each household are well known), we were able to pinpoint the exact week or weeks of pregnancy during which the pregnant women experienced the effects of the ice storm. Finally, we were able to assess whether the women experienced any illness during each trimester of their pregnancies.

The goal of the present study was to extend the findings of previous research on the effects of PNMS and maternal illness on infant temperament by (i) exploring the impact of two components of PNMS (i.e., objective hardship and subjective distress) stemming from a natural disaster (i.e., the 1998 Québec ice storm); (ii) by exploring the impact of maternal illness; and (iii) by exploring the potential additive and multiplicative effects of PNMS and maternal illness on temperament outcomes. We were also interested in determining whether the timing in pregnancy of the exposure to the ice storm moderated any potential relationships between PNMS and/or illness and infant temperament ratings.

RESULTS

Prevalence of Maternal Illness

Overall, 61 mothers (50.4%) had an illness or infection at any time during their pregnancies. Twenty-eight mothers (23.2%) had at least one health condition during the first trimester of their pregnancies, 25 (20.6%) during the second trimester, and 16 (13.2%) during the third trimester. Eight mothers (6.6%) had at least one condition during two trimesters of their pregnancies. Three mothers had at least one condition during both the first and second trimesters of their pregnancies, three during the second and third trimesters, and two during the first and third trimesters.

The correlation matrix, and the means and SDs of all variables, can be found in [Table 1](#). As expected, the temperament dimensions are moderately-to-highly correlated with each other. Of the main predictor variables, life events experienced by the mothers, subjective distress levels, timing of exposure of the fetus to the ice storm, and maternal illness/infection during the second trimester ($P < 0.1$) were related to the infants' fussy/difficult scores. Maternal age at the time of delivery and maternal illness/infection during the first trimester were related to the infants' Dull scores. Maternal postpartum depression levels, subjective distress levels, maternal age at delivery ($P < 0.1$), maternal illness/infection during the first trimester ($P < 0.1$), and objective hardship levels ($P < 0.1$) were related to the infants' Needs Attention scores. Finally, no predictor or control variables were related to the infants' Unadaptable scores.

Hierarchical Linear Regression Models

The regression analysis outcomes can be found in [Table 2](#).

Fussy/difficult. Maternal life events, timing of exposure, maternal illness/infection during the second trimester, subjective

distress, and the objective hardship \times maternal illness/infection during the first trimester and subjective distress \times timing of exposure interaction terms all were significantly related to the infants' fussy/difficult scores upon entry into the model and explained 3.9, 3.0, 3.4, 2.9, and 3.6% of the variance, respectively. Mothers who experienced higher levels of maternal life events and who had a greater number of illness/infection conditions during their second trimester of pregnancy rated their children as being more difficult. Inspection of the objective hardship \times maternal illness/infection during the first trimester interaction indicated that mothers who experienced higher levels of objective hardship and a greater number of illness/infection symptoms during their first trimester of pregnancy rated their infants as more difficult. Finally, women who were in their early stages of pregnancy during the ice storm and reported higher levels of subjective distress rated their infants as more difficult. The final model explained 22.3% of the variance of the infants' fussy/difficult scores.

Dullness. Maternal age, maternal illness/infection during the first trimester, and subjective distress were significantly related to the infants' dullness scores upon entry into the model and explained 6.3, 5.8, and 3.1% of the variance, respectively. Older mothers, mothers who experienced a greater number of illness/infection conditions during their first trimester of pregnancy, and mothers who experienced more subjective distress following the ice storm reported their infants as being less responsive. Together, these variables explained 15.2% of the variance of the infants' Dullness scores.

Unadaptable. None of the control or ice storm variables were significantly associated with this dimension, and so, these results were not included in the table.

Needs Attention. Postpartum depression, maternal age, maternal illness/infection during the first trimester, and subjective distress were significantly related to the infants' Needs Attention scores upon entry into the model and explained 3.8, 3.4, 2.9, and 9.8% of the variance, respectively. Mothers who experienced higher levels of postpartum depression, were older, and experienced a greater number of illness/infection conditions during their first trimester of pregnancy, and mothers who experienced more subjective distress following the ice storm, reported their infants as requiring more attention.

DISCUSSION

The goal of the present study was to determine whether PNMS, resulting from a natural disaster, and maternal illness/infection during pregnancy, uniquely or in combination, contributed to the development of the exposed infants' temperament at 6 mo of age after controlling for other maternal and pregnancy factors known to influence the development of temperament during early infancy.

The results indicate that of our two measures of PNMS, subjective distress was consistently related to infant temperament. While our subjective PNMS measure is undoubtedly more

reflective of the women's personalities and propensity to experience distress than our objective hardship measure, it should be remembered that it specifically measured ice storm-related symptoms and was predictive of temperament status after controlling for the women's levels of postpartum depression (needs attention), major life events (fussy/difficult), and maternal age (dullness and needs attention). The contribution of subjective distress to infant temperament was equal to or greater than that of maternal life events or postpartum depression. Overall, these findings are similar to previous literature indicating that pregnancy-related anxiety, stress, and/or life events are associated with temperamental status in infancy (6–8).

Interestingly, the present results are in line with those obtained for women who became pregnant post-Hurricane Katrina by Tees *et al.* (9): in both studies, objectively defined disaster-related experiences had no direct effects on temperament status. However, in the present study, objective hardship combined with maternal illness/infection to explain a portion of the infants' fussy/difficult ratings.

The other consistent predictor of temperament status in the present study was maternal illness/infection. Maternal illness/infection during the first trimester directly accounted for between 1.3 and 5.8% of the variance in three of the four temperament dimensions. Second trimester maternal illness/infection accounted for an additional 3.0% of the variance of the fussy/difficult dimension. These findings are consistent with the outcomes of animal studies (12) and human studies on the effect of prenatal infection on the development of schizophrenia (23). Moreover, our findings are similar to those obtained by Dombrowski *et al.* (21) and suggest that the effects of prenatal maternal illness/infection wane with increased gestational age. However, it must be noted that our measure of maternal illness was derived not only from the women's hospital records but also from their own personal recall of having experienced either a cold, flu, and/or fever during their pregnancies. As such, it was not always possible to determine the severity of the women's illness. This is important since the literature clearly indicates that maternal illness/infection leading to severe inflammation is one of the leading causes of preterm birth (24) and abnormal white matter development in exposed fetuses (25).

Interestingly, multiplicative effects of PNMS and maternal illness/infection on temperament status were only observed for the mothers' ratings of their infants fussy/difficult scores, explaining an additional 2.9% of the variance. This suggests that these two adverse prenatal events had mostly unique and independent effects on the infants' temperaments. Because biological materials (i.e., maternal/fetal blood, placentas) are extremely difficult to obtain in disaster research, direct assessment of the mechanisms which might be involved in the transmission of PNMS and/or maternal illness to the developing fetus could not be conducted. However, based on previous animal (1,12,22) and human (1,22,26) studies, it is believed that PNMS influences the developing fetus via heightened maternal cortisol levels, which influence fetal HPA development and/or functioning (2,27,28), while maternal illness affects fetal

development via activation of the maternal immune system, and by an influence on white matter development in the developing fetal brain (25,29,30). These differences in the manner by which PNMS and maternal illness influence fetal development might explain why only one minor multiplicative effect of the two teratogens was observed. Regardless, our findings demonstrate that both PNMS and maternal illness were moderately related to temperament ratings. In both instances, higher levels were related to more difficult temperaments.

This study was limited by the relatively small sample size, by a lack of a nonexposed control group, by assessing maternal PNMS 5–6 mo after the crisis, by the absence of a direct, third-party evaluation of infant temperament, by direct biological measures of the severity of any infection, and by a lack of biological material from birth that might clarify the biological mechanisms of the PNMS effects on infant temperament. Finally, the internal consistency of the Dull subscale was low suggesting that this temperament dimension may not be as stable as the others.

Despite these limitations, however, this is the first prospective longitudinal study to evaluate the effects of two dimensions of disaster-related prenatal stress and maternal illness on the mothers' perception of their infants' temperaments. The results suggest that early term exposure to any level of PNMS, and *in utero* exposure to either high levels of maternal subjective distress or maternal illness in early gestation are associated with poorer temperaments in infants, at least as measured by their own mothers. Since negative temperaments are predictive of poorer psychological functioning later in development (4), the present findings suggest that psychological intervention may be appropriate for women who experience high levels of subjective distress following a natural disaster in the hopes of mitigating the long-term effects that PNMS may have on the developing fetus. Moreover, these results suggest that treatment for any maternal illness, particularly of illness that occurs in conjunction with a natural disaster or other major stressful event, should not be ignored but treated quickly in order to potentially reduce the risk on the developing fetus.

METHODS

Participants

The Research Ethics Board of the Douglas Hospital Research Centre approved the research protocols for this study. Subjects were white French-Canadian women who were 18 y of age or older, pregnant, and living in the Montréal region southeast of Montreal, Québec during the ice storm. Eligible women were identified by their physicians who agreed to mail Project Ice Storm consent forms and questionnaires to them. Details pertaining to the identification and recruitment of subjects have been presented elsewhere (31). An initial sample of 176 women available for follow-up, of whom approximately one-quarter were not yet pregnant at the time of the ice storm, completed postal questionnaires 6 mo postpartum. Thus, the present study consisted of 121 infants (60 boys and 61 girls) of women who were in their first ($n = 40$), second ($n = 43$), or third ($n = 38$) trimester of pregnancy on 9 January 1998, the peak of the ice storm. Analyses comparing dyads in the present sample and dyads for which full recruitment ($n = 16$; excluding "preconception" dyads) and partial 6 mo ($n = 35$; incomplete temperament data) revealed significant differences in terms of the number of children in the household ($P = 0.003$) and ponderal index ($P = 0.007$). Women who completed the temperament scale had

more children (including the child in the present sample) and their child in the study was heavier at birth for his/her length compared to children whose mothers did not complete the temperament scale. Participants and nonparticipants did not differ on any other factor.

Instruments

Outcome Measure

Infant temperament. The Infant Characteristics Questionnaire (32) was used to assess infant temperament at 6 mo. The Infant Characteristics Questionnaire provided scores on three dimensions: fussy/difficult, unadaptable, and dull. We also used one of the supplementary questions to assess the level of attention the infants required (needs attention). The authors report that the internal consistency of the scale dimensions range from 0.39 (dull) to 0.79 (fussy/difficult); the test–retest reliability scores ranged from 0.47 (needs attention) to 0.75 (unadaptable) (32). Mothers completed each item using a seven-point Likert scale that ranged from 1 (very easy) to 7 (very difficult).

Predictor Measures

Objective hardship. Because each natural disaster presents unique experiences to the exposed population, questions pertaining to each of the four categories must be tailor-made. We assessed objective hardship using the mothers' responses to questionnaire items tapping into categories of exposure used in other disaster studies: Threat, Loss, Scope, and Change (33). Each of the four dimensions was scored on a scale of 0–8, ranging from no exposure to high exposure (31). A total objective hardship score (Storm 32) was computed by summing scores from all four dimensions using McFarlane's approach (34). See Laplante et al. (31) for a list of items and the details of scoring.

Subjective. Distress was assessed using the French version (35) of the widely used Impact of Event Scale—Revised (36). The 22-item IES-R describes symptoms from three categories relevant to post-traumatic stress disorder: Intrusion (thoughts and images), Hyperarousal, and Avoidance. The IES-R instructions for respondents allow investigators or clinicians to “write in” the traumatic event in question. Participants, thus, responded on a five-point Likert scale, from “Not at all” to “Extremely”, the extent to which each item described how they felt over the preceding 7 d in response to the ice storm crisis. The internal consistency of the total score was 0.93 (35). We used the total score in all analyses.

Maternal illness. Maternal illness/infection was defined as a summation of the presence of otitis, pertussis, sinus infection, tonsillitis, hyperemesis gravidarum, group B streptococcus, chlamydia, candida, herpes simplex, pre-eclampsia, hypothyroidism, pneumonia, flu, fever, or cold with cough during each trimester of pregnancy. Data were derived from the mothers' medical files. Mothers also self-reported the presence of flu, fever, or cold with cough. Scores ranged from 0 to 3.

Trimester of Exposure to the ice storm by the fetus was determined using the number of days between each mother's anticipated due date and 9 January 1998, the date corresponding to the peak of the ice storm.

Control Measures

Maternal anxiety was assessed using the anxiety subscale on a validated French version (35) of the General Health Questionnaire-28 (37). Using a four-point Likert scale, mothers indicated the degree to which each anxiety, dysfunction, somatization, and depression symptom was experienced in the preceding 2 wk.

Maternal life events that occurred during pregnancy were assessed using the Life Experiences Survey (38). Respondents indicated, first, whether the event occurred or not, then the approximate date of the event, and then rated the impact of the event (if it occurred) on a seven-point Likert scale ranging from “Extremely Negative” to “Extremely Positive”. We reduced the number of experiences to 29 events by eliminating items not likely to have occurred in this sample (such as “combat experience”). The total number of different life events was used in the analyses in the present study.

Postpartum depression was assessed using the 10-item Edinburgh Postpartum Depression Scale (39,40). Mothers responded to each question using a four-point Likert scale, from “Not at all” to “Very much”. The total score was calculated by summing all items.

Obstetric complications, excluding flu with fever, was determined by maternal recall using an adaptation of the scale used by Kinney (41) and verified using hospital records. We used the total number of obstetric complications experienced by the women that were rated as moderate-to-severe using the McNeil-Sjöström Scale for obstetric complications (42).

Information on maternal and paternal age, education, job classification, and number of children in the household (including child in present study) were collected in the June 1998 questionnaire. Socio-economic status was computed using the Hollingshead Index criteria (43).

Measures of fetal growth included birth weight, ponderal index (birth weight/birth length³) and head circumference to body length ratio. These measures were calculated using information transcribed from the “Vaccination Booklet”, which all mothers in Quebec receive from the hospital upon discharge with their newborn. Gestational age at birth was also obtained from this booklet.

Procedures

Objective hardship, subjective distress, maternal anxiety, due date data, and demographics were collected in a questionnaire packet mailed to the mothers by their obstetricians on 1 June 1998. The remaining data were collected in a questionnaire packet mailed to the mothers 6 mo after each woman's expected due date. For each assessment period, the mothers were asked to complete the questionnaire within 2 wk of reception and return it using the self-addressed stamped envelope provided.

Statistical Analysis

Person Product–Moment correlations were used to assess the relationships between the predictor measures and the four temperament dimensions. The results of these analyses were used to select which of our potential control predictors would be included in the subsequent regression analyses.

The initial hierarchical multiple linear regression analyses conducted were similar for the four temperament dimensions. Control predictors demonstrating a significant association with the temperament dimensions were allowed to enter into the model during the first block in a stepwise manner. The timing of exposure was forced into the model during the second block. Maternal illness/infection during the first trimester was forced into the model during the third block. Maternal illness/infection during the second and third trimesters was allowed to enter into the model during the fourth block in a stepwise manner. Objective hardship was forced into the model during the fifth block. Subjective distress was forced into the model during the sixth block. Interaction terms between objective hardship and maternal illness/infection during the first trimester and subjective distress and maternal illness/infection during the first trimester were allowed to enter into the model during the seventh block in a stepwise manner. Finally, interaction terms between objective hardship and subjective distress, objective hardship and timing of exposure, and subjective distress and timing of exposure were allowed to enter into the model during the final block in a stepwise manner. Because of the relatively small sample, the equations were trimmed of any nonsignificant variables that were forced into the equation (unless they were included in a significant interaction) and rerun. Furthermore, additional regression models were created that first forced maternal illness/infection during the second trimester into the equation during the third block, allowed maternal illness/infection during the first and third trimester into the model during the fourth block in a stepwise manner, and allowed the interaction terms between objective hardship and maternal illness/infection during the second trimester and subjective distress and maternal illness/infection during the second trimester into the model during the seventh block in a stepwise manner. Once again, all nonsignificant variables were removed from the model where appropriate and the models rerun. The same procedure was used for maternal illness/infection during the third trimester.

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REFERENCES

- Weinstock M. The long-term behavioural consequences of prenatal stress. *Neurosci Biobehav Rev* 2008;32:1073–86.
- Avishai-Eliner S, Brunson KL, Sandman CA, Baram TZ. Stressed-out, or in (utero)? *Trends Neurosci* 2002;25:518–24.
- Beijers R, Buitelaar JK, de Weerth C. Mechanisms underlying the effects of prenatal psychosocial stress on child outcomes: beyond the HPA axis. *Eur Child Adolesc Psychiatry* 2014;23:943–56.
- Rettew DC, McKee L. Temperament and its role in developmental psychopathology. *Harv Rev Psychiatry* 2005;13:14–27.
- Werner EA, Myers MM, Fifer WP, et al. Prenatal predictors of infant temperament. *Dev Psychobiol* 2007;49:474–84.
- McGrath JM, Records K, Rice M. Maternal depression and infant temperament characteristics. *Infant Behav Dev* 2008;31:71–80.
- Austin MP, Hadzi-Pavlovic D, Leader L, Saint K, Parker G. Maternal trait anxiety, depression and life event stress in pregnancy: relationships with infant temperament. *Early Hum Dev* 2005;81:183–90.
- Huizink AC, de Medina PG, Mulder EJ, Visser GH, Buitelaar JK. Psychological measures of prenatal stress as predictors of infant temperament. *J Am Acad Child Adolesc Psychiatry* 2002;41:1078–85.
- Tees MT, Harville EW, Xiong X, Buekens P, Pridjian G, Elkind-Hirsch K. Hurricane Katrina-related maternal stress, maternal mental health, and early infant temperament. *Matern Child Health J* 2010;14:511–8.
- Davis EP, Glynn LM, Schetter CD, Hobel C, Chiciz-Demet A, Sandman CA. Prenatal exposure to maternal depression and cortisol influences infant temperament. *J Am Acad Child Adolesc Psychiatry* 2007;46:737–46.
- Baibazarova E, van de Beek C, Cohen-Kettenis PT, Buitelaar J, Shelton KH, van Goozen SH. Influence of prenatal maternal stress, maternal plasma cortisol and cortisol in the amniotic fluid on birth outcomes and child temperament at 3 months. *Psychoneuroendocrinology* 2013;38:907–15.
- Boksa P. Effects of prenatal infection on brain development and behavior: a review of findings from animal models. *Brain Behav Immun* 2010;24:881–97.
- Shi L, Tu N, Patterson PH. Maternal influenza infection is likely to alter fetal brain development indirectly: the virus is not detected in the fetus. *Int J Dev Neurosci* 2005;23:299–305.
- Patterson PH. Maternal infection and immune involvement in autism. *Trends Mol Med* 2011;17:389–94.
- Atladóttir HO, Thorsen P, Østergaard L, et al. Maternal infection requiring hospitalization during pregnancy and autism spectrum disorders. *J Autism Dev Disord* 2010;40:1423–30.
- Patterson PH. Immune involvement in schizophrenia and autism: etiology, pathology and animal models. *Behav Brain Res* 2009;204:313–21.
- Dreier JW, Andersen AM, Berg-Beckhoff G. Systematic review and meta-analyses: fever in pregnancy and health impacts in the offspring. *Pediatrics* 2014;133:e674–88.
- Pesonen AK, Räikkönen K, Kajantie E, Heinonen K, Strandberg TE, Järvenpää AL. Fetal programming of temperamental negative affectivity among children born healthy at term. *Dev Psychobiol* 2006;48:633–43.
- Roza SJ, van Lier PA, Jaddoe VW, et al. Intrauterine growth and infant temperamental difficulties: the Generation R Study. *J Am Acad Child Adolesc Psychiatry* 2008;47:264–72.
- Schlotz W, Jones A, Godfrey KM, Phillips DI. Effortful control mediates associations of fetal growth with hyperactivity and behavioural problems in 7- to 9-year-old children. *J Child Psychol Psychiatry* 2008;49:1228–36.
- Dombrowski SC, Martin RP, Huttunen MO. Association between maternal fever and psychological/behavior outcomes: a hypothesis. *Birth Defects Res A Clin Mol Teratol* 2003;67:905–10.
- Charil A, Laplante DP, Vaillancourt C, King S. Prenatal stress and brain development. *Brain Res Rev* 2010;65:56–79.
- Brown AS, Derkits EJ. Prenatal infection and schizophrenia: a review of epidemiologic and translational studies. *Am J Psychiatry* 2010;167:261–80.
- Christian LM. Psychoneuroimmunology in pregnancy: immune pathways linking stress with maternal health, adverse birth outcomes, and fetal development. *Neurosci Biobehav Rev* 2012;36:350–61.
- Hagberg H, Peebles D, Mallard C. Models of white matter injury: comparison of infectious, hypoxic-ischemic, and excitotoxic insults. *Ment Retard Dev Disabil Res Rev* 2002;8:30–8.
- Wadhwa PD. Psychoneuroendocrine processes in human pregnancy influence fetal development and health. *Psychoneuroendocrinology* 2005;30:724–43.
- Huizink AC, de Medina PG, Mulder EJJ, Visser GHA, Buitelaar JK. Prenatal maternal stress, HPA axis activity, and postnatal infant development. *Int Congr Ser* 2002;1241:65–71.
- Harris A, Seckl J. Glucocorticoids, prenatal stress and the programming of disease. *Horm Behav* 2011;59:279–89.
- Harry GJ, Lawler C, Brunssen SH. Maternal infection and white matter toxicity. *Neurotoxicology* 2006;27:658–70.
- Elovitz MA, Brown AG, Breen K, Anton L, Maubert M, Burd I. Intrauterine inflammation, insufficient to induce parturition, still evokes fetal and neonatal brain injury. *Int J Dev Neurosci* 2011;29:663–71.
- Laplante DP, Zelazo PR, Brunet A, King S. Functional play at 2 years of age: Effects of prenatal maternal stress. *Infancy* 2007;12:69–93.
- Bates JE, Freeland CA, Lounsbury ML. Measurement of infant difficulty. *Child Dev* 1979;50:794–803.
- Bromet E, Dew MA. Review of psychiatric epidemiologic research on disasters. *Epidemiol Rev* 1995;17:113–9.
- McFarlane AC. Relationship between psychiatric impairment and a natural disaster: the role of distress. *Psychol Med* 1988;18:129–39.
- Brunet A, St-Hilaire A, Jehel L, King S. Validation of a French version of the impact of event scale-revised. *Can J Psychiatry* 2003;48:56–61.
- Weiss DS, Marmar CR. The Impact of Event Scale - Revised. In: Wilson JP, Keane TM, eds. *Assessing Psychological Trauma and PTSD: A Practitioner's Handbook*. New York: Guilford, 1997. pp. 399–411.
- Goldberg DP. *The Detection of Psychiatric Illness by Questionnaire: A Technique for the Identification and Assessment of Non-Psychiatric Illness*. London: Oxford University Press, 1972.
- Sarason IG, Johnson JH, Siegel JM. Assessing the impact of life changes: development of the Life Experiences Survey. *J Consult Clin Psychol* 1978;46:932–46.
- Cox JL, Chapman G, Murray D, Jones P. Validation of the Edinburgh Postnatal Depression Scale (EPDS) in non-postnatal women. *J Affect Disord* 1996;39:185–9.
- Cox JL, Holden JM, Sagovsky R. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *Br J Psychiatry* 1987;150:782–6.
- Jacobsen B, Kinney DK. Perinatal complications in adopted and non-adopted samples of schizophrenics and controls. *Acta Psychiatr Scand* 1980;62:337–46.
- McNeil TF, Sjöström K. *The McNeil-Sjöström OC Scale: a Comprehensive Scale for Measuring Obstetric Complications*. Department of Psychiatry, Lund University, Malmö General Hospital: Malmö, Sweden, 1995.
- Hollingshead AB. *Four-Factor Index of Social Status*. New Haven: Yale University Press, 1973.