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Prenatal exposure to a natural disaster increases risk for obesity in 5½-year-old children

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INTRODUCTION: An adverse environment *in utero,* including exposure to prenatal maternal stress (PNMS), can result in poor birth outcomes such as low birth weight, which increases risk of later cardiometabolic diseases such as hypertension and obesity. It is unclear to what extent PNMS influences obesity risk independent of its impact on birth characteristics, especially among humans. Our objective was to determine whether PNMS resulting from a natural disaster influenced risk of childhood obesity.

RESULTS: Eight children with high objective PNMS exposure (14.5%) were obese compared to one child (1.8%) with low exposure (P = 0.02). Objective PNMS increased obesity risk (model 1, P = 0.02, odds ratio = 1.37) after controlling for other potential risk factors.

DISCUSSION: Results suggest that PNMS might be an independent risk factor in the development of childhood obesity.

METHODS: Participants included 111 women who were pregnant during the January 1998 Québec Ice Storm or who conceived within the following 3 months and their children. We tested associations between objective and subjective PNMS from the storm and childhood obesity status at age 5½, controlling for children's birth characteristics and breastfeeding status; household socioeconomic status; maternal obstetric complications, life events and smoking during pregnancy, psychological functioning, and height (model 1, n = 111) or BMI (for a subset of 69 participants, model 2).

A large body of evidence now implicates adverse conditions *in utero* with increased risk of chronic diseases in adulthood. Studies from both animals and humans suggest that nutrient restriction during pregnancy (1) and exposure to high levels of maternal stress or glucocorticoids (GC) *in utero* (2,3) are associated with low birth weight or intrauterine growth restriction, which are associated with increased risk for later cardiometabolic diseases such as hypertension, insulin resistance, and obesity (1,4). However, fetal growth patterns are unlikely to be the only causal factors in this chain of events. Rather, common underlying factors likely influence fetal and infant growth as well as adult physiology (5). Exposure to high levels of prenatal maternal stress (PNMS) or to exogenous GCs *in utero* is associated not only with poor fetal growth (6–8) but also with deregulation of the hypothalamic–pituitary–adrenal axis (9), which is involved in metabolic pathways (10) and likely represents a mediating mechanism in the developmental origins of adult diseases (2,3,11,12).

Animal studies show varying effects of PNMS on body weight, some suggesting decreased weight in adolescent and adult offspring (13), others increased (14,15), and some with no significant effects (16). These studies also suggest that PNMS exposure is associated with later hypertension (14) and features of insulin resistance (16). However, the impact of PNMS on cardiometabolic outcomes among humans is not entirely clear. Studies of the offspring of women whose nutrition was marginal during pregnancy, such as during the Dutch Famine, reveal associations among adverse conditions *in utero* and later adiposity, cardiovascular disease risk, and appetite homeostasis (17–19), with variations based on the timing of exposure during gestation (20). Maternal stress likely impacts outcomes (20), but it is difficult to determine the extent of its role independent of, or in association with, severe nutrient restriction. Another study demonstrated that maternal bereavement (e.g., due to the death of a spouse or child) during or shortly before pregnancy was associated with overweight among exposed children at ages 10–13, even after controlling for gestational age and birth weight (21). Further evidence comes from retrospective case–control studies of Entringer and colleagues (3,22), which indicated that BMI, percent body fat, and risk of insulin resistance were elevated among young adults whose mothers experienced stressful life events during pregnancy. Finally, one study in humans, Project Viva, has shown positive associations between higher levels of maternal corticotrophin-releasing hormone, which provides a marker of fetal GC exposure, and offspring adiposity at age 3 (23). Replication of these findings in other samples and with different types of stressors is necessary to clarify the programming effects of PNMS on cardiometabolic outcomes.

Project Ice Storm provides an opportunity to examine the effects of PNMS on a number of later health outcomes, including childhood obesity. In January 1998, an ice storm in Canada's St. Lawrence River Valley caused power outages for more than 1.4 million Québec households ranging from a few

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hours to more than 6 wk. The storm resulted in $1 billion in insurance claims, $3 billion of lost income to businesses, and $1 billion in hydroelectric infrastructure repairs, and has been described as Canada's most costly natural disaster in history (24). Shortly after the storm, we assessed levels of objective exposure and subjective distress dimensions of PNMS among women who were pregnant during the storm or who conceived within the following 3 months, when levels of stress hormones could still be elevated. We have since analyzed a number of physical, behavioral, and developmental measures among their children (25–29). Project Ice Storm differs in several important ways from other studies of PNMS among humans. First, the severity of exposure to hardship from the storm was fairly randomly distributed, such that there were no systematic associations between objective stress exposure and sociodemographic or physiological characteristics of the women. Second, we were able to distinguish between objective stress exposure (i.e., what happened) and subjective distress (i.e., how the women reacted), which is nearly impossible in studies of antenatal anxiety or nonindependent life events. Finally, because the exact parameters of the storm were well documented (e.g., date of onset, days during which power was out), we were able to pinpoint the exact week or weeks of pregnancy during which study participants were affected.

Our objective was to determine the extent to which exposure to PNMS due to the ice storm was associated with obesity risk among 5½-year-old children. We hypothesized that PNMS would predict obesity risk independent of the children's birth characteristics, maternal characteristics, and other risk factors.

RESULTS

Sample Characteristics

According to the SES scores, 3 families (2.7%) were in the lower class, 2 (1.8%) in the lower-middle class, 29 (26.1%) in the middle class, 58 (52.3%) in the upper-middle class, and 19 (17.1%) in the upper class. Prevalence of maternal overweight (24.6%) and obesity (14.5%) was similar to figures for Québec women of ages 18–44 in 2004 (23.9% and 18.8%) (http://www.hc-sc.gc.ca/fn-an/surveill/nutrition/commun/index-eng.php). Women who reported weight were more likely to have breastfed their children than women who did not report weight ($P = 0.02$) and had more moderate-to-severe obstetric complications (3.6 compared to 4.8, $P = 0.04$), but did not differ with respect to any other maternal variables (psychological functioning, life events, obstetric complications, smoking, SES, height), child variables (birth weight, birth length, gestational age), or storm-related variables (trimester of exposure, objective PNMS, subjective PNMS). Furthermore, women who were obese and not obese did not differ significantly for maternal variables, with the exception of BMI and life events: women who were obese reported significantly more life events (7.7 compared to 4.6, $P < 0.01$). Further analyses revealed no significant differences in the mean impact of these life events between groups ($P = 0.24$). There were no significant differences in child and storm-related variables among women who were obese and not obese.

Descriptive Analyses

Nine of the 111 children (8.1%) were classified as obese—four boys and five girls. Of the 55 children with high exposure to objective PNMS, 8 were obese (14.5%), compared to only 1 of 56 children (1.8%) from the low objective PNMS group ($P = 0.02$). One boy and three girls (3.6%) were slightly underweight (< 5th percentile); all were from the low objective PNMS group.

Table 1 presents means and standard deviations for continuous parental and child variables. Objective PNMS, life events scores, and maternal BMI (for the subset of 69 participants) differed between children who were obese and those of normal weights. Other parental variables did not differ between groups, nor did children's birth weight, length, or gestational age. Groups also did not differ with respect to trimester of exposure ($P = 0.24$), maternal smoking (cigarettes/day; $P = 0.56$), or breastfeeding status ($P = 0.39$).

Hierarchical Linear Regression

Maternal height entered into the equation and accounted for 3.7% of variance in children's BMI: shorter height was associated with larger BMI (Table 2). Birth weight accounted for a further 10.0% of variance: heavier birth weights predicted larger BMI among children. Finally, objective PNMS explained an additional 4.9% of variance in children's BMI: greater objective PNMS exposure was

Table 1. Characteristics of obese and normal-weight samples

Variable	Normal-weight sample ($n = 102$) Mean (SD)	Obese sample ($n = 9$) Mean (SD)	*P* value
Child's characteristics, age 5½			
Weight, kg	19.8 (2.3)	26.8 (2.8)	<0.01
Height, cm	112.7 (4.2)	116.0 (3.9)	0.03
BMI	15.6 (1.2)	19.9 (1.1)	<0.01
Prenatal maternal stress (PNMS)			
Objective	10.2 (4.1)	14.7 (5.1)	0.03
Subjective	10.0 (12.7)	13.6 (7.6)	0.42
Maternal characteristics			
Psychological functioning	5.8 (5.1)	5.1 (4.1)	0.68
Life events	5.0 (3.3)	7.6 (5.6)	0.04
Household socioeconomic status (SES)	27.9 (11.7)	26.3 (17.2)	0.72
Obstetric complications	4.3 (2.9)	4.8 (2.3)	0.62
Height, cm	163.0 (5.2)	160.1 (7.1)	0.12
BMI[a]	24.6 (5.2)[a]	34.0 (9.1)[a]	<0.01
Child's birth characteristics			
Birth weight, g	3,438.4 (574.9)	3,501.2 (597.5)	0.76
Birth length, cm	50.3 (2.9)	50.3 (2.2)	0.93
Gestational age, wk	39.6 (2.0)	39.9 (0.7)	0.64

[a]Based on a subset of participants. Normal-weight group, $n = 62$; obese group, $n = 7$.

Table 2. Hierarchical linear regression analysis between predictor variables and children's BMI: model 1 (parental height, $n = 111$)

Predictor variable	B	R	R^2	ΔR^2	F	ΔF
Step 1		0.192	0.037		4.172*	
Maternal height	−0.192*					
Step 2		0.370	0.137	0.100	8.544**	12.477**
Maternal height	−0.267**					
Birth weight	0.325**					
Step 3		0.431	0.186	0.049	8.144**	6.478*
Maternal height	−0.252**					
Birth weight	0.330**					
Objective prenatal maternal stress	0.223*					

*$P < 0.05$, **$P < 0.01$.

Table 3. Odds ratios and confidence intervals obtained from the multivariate logistic regression model 1 (including maternal height, $n = 111$)

Predictor variable	Odds ratio	Confidence interval	P value
Maternal variables			
Psychological functioning	0.82	0.64–1.05	0.11
Life events	1.26	0.99–1.60	0.06
Household socioeconomic status (SES)	0.95	0.88–1.03	0.24
Obstetric complications	1.19	0.85–1.67	0.31
Smoking[a]	1.49	0.39–5.60	0.56
Height	0.79	0.64–0.97	0.03
Child variables			
Birth weight	1.00	1.00–1.00	0.55
Birth length	1.24	0.74–2.07	0.42
Breastfeeding status[b]	0.36	0.04–3.14	0.36
Sex[c]	1.39	0.21–9.30	0.73
Storm-related variables			
Trimester of exposure[d]	1.38	0.66–2.89	0.39
Subjective prenatal maternal stress (PNMS)	1.01	0.92–1.11	0.84
Objective prenatal maternal stress (PNMS)	1.37	1.06–1.77	0.02

[a]0 = none, 1 = 1–5 cigarettes/day, 2 = 6–10, 3 = 11–15, 4 = 16–20, 5 = > 20. [b]0 = no, 1 = yes. [c]1 = boys, 2 = girls. [d]−1 = preconception exposure, 1 = 1st trimester, 2 = 2nd trimester, 3 = 3rd trimester.

associated with larger BMI. Together, these variables explained 18.6% of the variance in children's BMI values.

Logistic Regression

In model 1 (Table 3), when controlling for all other variables, shorter maternal height was predictive of childhood obesity ($P = 0.03$, odds ratio (OR) = 0.79) as well as greater objective PNMS ($P = 0.02$, OR = 1.37). We also observed a trend between greater number of maternal life events and increased obesity risk ($P = 0.06$, OR = 1.26). In model 2, using the smaller subset of participants with maternal BMI data (Table 4), higher maternal BMI predicted childhood obesity ($P = 0.03$, OR = 1.47), and we observed trends between higher SES (lower Hollingshead score) and obesity risk ($P = 0.07$, OR = 0.81), and greater risk among children who were not breastfed ($P = 0.07$, OR = 0.02). Finally, we observed a trend between higher objective PNMS scores and childhood obesity ($P = 0.09$, OR = 1.43) in the smaller subset of participants.

DISCUSSION

Results from animal studies suggest that PNMS can have programming effects independent of effects on fetal growth. For example, preweaning maternal stress (30) did not influence offspring birth weight but was associated with greater weight, BMI, and abdominal circumference among juvenile macaques (30). Furthermore, antenatal exposure to synthetic GCs resulted in increased subcutaneous fat thickness, decreased β-cell numbers, and increased blood pressure among juvenile vervet monkeys, despite the lack of impact on birth weight (31). However, similar findings among humans are limited. Some studies of the Dutch Famine suggest that early-gestation exposure was associated with obesity among women (32) and with an atherogenic lipid profile (33) independent of effects on size at birth. Similarly, maternal bereavement before or during pregnancy increases risk of offspring overweight independent of birth weight (21). Other human studies suggest that prenatal GC exposure is associated with increased blood pressure in adolescence (34) and with greater risk of insulin resistance in adulthood (35) independent of effects on birth weights. Thus, although PNMS has been shown to be associated with poor birth outcomes (2), a growing body of evidence suggests that exposure might play a role in long-term programming independent of these effects.

The ice storm provided an opportunity to examine the role of PNMS on children's health outcomes by randomly assigning pregnant women to greater or lesser degrees of objective hardship. Exposure was sufficient to have an impact on infant growth and development—higher levels of objective PNMS were associated with shorter infant length at birth (25)—and we postulated that it might also affect development at later ages. For example, increasing objective PNMS predicted poorer cognitive and linguistic functioning at 2 and 5½ years of age, all else being equal (28,29), and fingerprint asymmetry (27), which reflects disruptions in fetal development during gestation weeks 14–22.

Results from the present study suggest that objective PNMS increases obesity risk at age 5½ (OR = 1.37–1.43) and that these effects are independent of size at birth and several maternal characteristics, including size (height or BMI), which is a major predictor of childhood obesity (36). Models differ in other risk factor trends, likely reflecting small sample size and the small number of children with obesity (nine in model 1, seven in model 2). Furthermore, SES in our sample was skewed to higher SES—of the children with obesity, only one was in the

Table 4. Odds ratios and confidence intervals obtained from the multivariate logistic regression model 2 (including maternal BMI, $n = 69$)

Predictor variable	Odds ratio	Confidence interval	*P* value
Maternal variables			
Psychological functioning	0.91	0.71–1.18	0.49
Life events	1.00	0.69–1.45	1.00
Household socioeconomic status (SES)	0.81	0.64–1.01	0.07
Obstetric complications	0.72	0.38–1.36	0.31
Smoking[a]	3.49	0.65–18.66	0.14
BMI	1.47	1.04–2.07	0.03
Child variables			
Birth weight	1.00	1.00–1.00	0.78
Birth length	1.15	0.60–2.23	0.67
Breastfeeding status[b]	0.02	0.00–1.38	0.07
Sex[c]	2.63	0.19–36.93	0.47
Storm-related variables			
Trimester of exposure[d]	2.31	0.84–6.36	0.11
Subjective prenatal maternal stress (PNMS)	1.01	0.89–1.15	0.86
Objective prenatal maternal stress (PNMS)	1.43	0.94–2.16	0.09

[a]0 = none, 1 = 1–5 cigarettes/day, 2 = 6–10, 3 = 11–15, 4 = 16–20, 5 = > 20. [b]0 = no, 1 = yes. [c]1 = boys, 2 = girls. [d]–1 = preconception exposure, 1 = 1st trimester, 2 = 2nd trimester, 3 = 3rd trimester.

lower class (9.1%) and the rest were in the middle class (9.1%) or above (81.8%). Thus, the trend between higher SES and obesity risk, which is the opposite of that observed in most studies (36), must be interpreted cautiously. However, other trends mirror findings of past research, including potential effects of life events (3,21,22) and breastfeeding (36) on obesity risk.

The impact of objective PNMS in both analyses provides support for the position that prenatal psychosocial stress may have programming effects observed in physical growth. A number of pathways are likely involved, especially through the reorganization of neural pathways involved in appetite regulation and metabolism, and a subsequent "reprogramming" of energy balance (3,20,37), which could increase risk independent of known contributors to childhood weight status such as parental BMI and SES. Interestingly, there were no effects of maternal subjective distress on child obesity. There may be different biological mechanisms operating under conditions of acute environmental stress, such as during the ice storm, and under conditions of more long-standing subjective distress. As evidence grows for the programming effects of PNMS on childhood physical growth, more human studies investigating these relationships and mechanisms are necessary.

As noted above, one limitation of this study is a small sample with biased SES distribution. Furthermore, we lack data on maternal diet during the storm, which might have had an impact on children's growth patterns. Finally, self-reported maternal height and weight are less reliable than measured values, and analyses would be greatly strengthened by including measured maternal BMI for all children. However, severity of exposure was randomly distributed along SES levels within our sample, and we have no reason to suspect systematic associations between objective PNMS scores and maternal height or weight that might skew results. Replication of these findings in a larger, more representative sample is required to conclude that exposure to high levels of objective PNMS is a truly independent risk factor for children's obesity.

The effects of exposure to hardship induced by the ice storm highlight the vulnerability of the developing fetus to psychosocial stressors. Risk might be even further exacerbated among the children of women exposed to more severe events, emphasizing the need for more research on the long-term programming effects of PNMS.

METHODS

This study was approved by the Douglas Hospital Research Ethics Board. Informed parental consent and child assent were obtained from all study participants.

Participants

Shortly after the ice storm, we contacted obstetricians associated with the four major hospitals in the Montérégie, a region southeast of Montréal that endured the longest electrical power losses from the storm. These obstetricians identified patients who were pregnant during or conceived within 3 months of the storm and who were at least 18 years old. The first questionnaire, "Reactions to the storm," was mailed on 1 June 1998 to 1,440 women. Of 224 respondents, 178 consented to follow-up and were sent a second questionnaire, "Outcomes of the pregnancy," 6 months after their pregnancy due date. Of these, 177 returned the second questionnaire. Level of education was higher for respondents than in the Montérégie in general: 61.0% of respondents had a college degree or higher, and 33.1% a university degree or higher, compared to regional figures of 45.3% and 20.9%, respectively, for women of ages 20–44 in the 2001 census (http://www12.statcan.ca/english/census01/home/index.cfm).

In addition to other follow-up, families were contacted when the children were 5½ years old for a comprehensive in-home assessment of children's physical, cognitive, and behavioral development. We were able to contact 140 families from our original sample; 116 (82.9%) agreed to the assessment. During the assessment, standing height was measured to the nearest 0.5 cm, and weight was measured to the nearest 0.5 kg (using a Conair "Thinner" digital scale, Model HW118). Children were measured without shoes but with clothing; weights were not corrected for clothing weight. Weight and/or height was not recorded for five children, leaving a final sample of 111 children (56 boys, 55 girls) and their mothers who had been in their 1st (n = 29), 2nd (n = 29), or 3rd (n = 27) trimester of pregnancy during the storm or who became pregnant in the following 3 months (n = 26). Sex- and age-specific BMI scores were calculated for each child using Centers for Disease Control and Prevention norms (38). Obesity was defined as BMI ≥ 95th percentile. Maternal height was self-reported during the assessment. Missing values for five women were replaced with the sample mean height. Both height and weight were reported for 69 women, and BMI was calculated. All participants were Francophone Caucasians.

Predictor Variables

Objective PNMS was assessed in the first questionnaire using mothers' responses to items tapping into categories used in other disaster studies: threat, loss, scope, and change (39). Because each disaster presents unique experiences, questions must be tailor-made. Our scale (26)

included questions specific to the storm, such as days without electricity, danger due to falling ice or tree branches, and spending time in temporary shelters. Each dimension was scored on a scale of 0–8, from no exposure to high exposure. A total score was calculated by summing scores from all four dimensions using McFarlane's approach (40). In the current sample, scores ranged from 1–24 (median = 11). To obtain a discrete variable for some analyses, two groups were formed (low and high objective PNMS) based on a median split of the data set.

Subjective PNMS was assessed in the first questionnaire using a validated French version of the Impact of Event Scale–Revised (41), a 22-item scale describing symptoms relevant to posttraumatic stress disorder: intrusive thoughts, hyperarousal, and avoidance. Items were written to reflect symptoms relative to the storm. Women indicated on a 5-point Likert scale, from "not at all" to "extremely," the extent to which each behavior described how they felt over the preceding 7 d. The total score was used in analyses.

Trimester of exposure was based on trimester at 9 January 1998 (the storm peak) and coded as −1 (preconception exposure), 1 (1st trimester), 2 (2nd trimester), and 3 (3rd trimester).

Maternal psychological functioning. Maternal non-storm-related psychological functioning was assessed in the first questionnaire with the widely used General Health Questionnaire 28 (42), a self-report screening tool for psychiatric symptoms that includes seven items in each of the anxiety, depression, dysfunction, and somatization subscales. Items are scored on a 4-point Likert scale indicating the degree to which each symptom was experienced in the preceding 2 wk. Following Goldberg (42), each item was recoded as either 0 (a rating of 0 or 1) or 1 (a rating of 2 or 3). The total score was used in analyses.

Exposure to potentially stressful maternal life events was assessed in the second questionnaire using the Life Experiences Survey (43), a self-report measure that lists 57 life changes, such as death of a spouse or a work promotion. To keep the questionnaire length reasonable, we reduced this to 29 events by eliminating items not likely to have occurred in this sample (e.g., combat experience). Women indicated events that occurred in the preceding 18 months, that is, the 6 months since the baby's due date, 9 months of pregnancy, and 3 months before conception; gave the approximate date of each event; and rated the impact of each event on a 7-point Likert scale ranging from "extremely negative" to "extremely positive." The number of life events was used in analyses.

Information on maternal age, marital status, maternal and paternal education and job status, and household income were collected during the first questionnaire. Socioeconomic status (SES) was computed using the Hollingshead Social Position criteria (44); higher scores represent lower SES. Information on obstetric complications (including pregnancy, labor and delivery, and neonatal complications) was obtained in the second questionnaire from maternal reports with Kinney's checklist (45) and verified using hospital records. The McNeil–Sjöstörm Scale (46) was used to rate severity, and the number of moderate-to-severe complications was used in analyses. We also assessed maternal smoking during pregnancy in the second questionnaire (any smoking "yes/no" and cigarettes per day). We included cigarettes per day in analyses: 0 (no smoking), 1 (1–5 cigarettes/day), 2 (6–10), 3 (11–15), 4 (16–20), and 5 (> 20).

Children's birth weight, birth length, and gestational age were obtained from maternal reports and hospital records. These data, and information concerning whether the children were ever breastfed (0 = no, 1 = yes), were obtained from our second questionnaire.

Statistical analyses

Descriptive analyses were performed on both the outcome and predictor variables to identify differences in groups based on childhood obesity status. We also conducted descriptive statistics for maternal overweight (BMI ≥ 25) and obesity (BMI ≥ 30) and to identify differences between women who reported weight and those who did not. Hierarchical linear regression analysis was conducted on the children's BMI scores. Variables were allowed to enter the equation using a stepwise procedure with a P value of 0.05 to enter as criterion. Maternal and family factors (psychological functioning, life events, obstetric complications, smoking, SES, and maternal height (reported at the children's assessment at age 5½)) were allowed to enter during step 1, followed by child factors (birth weight, birth length, sex, and breastfeeding status) in step 2. Storm-related variables were allowed to enter in steps 3–5: trimester of exposure (step 3), objective PNMS (step 4), and subjective PNMS (step 5). A single-step logistic analysis was also used to determine whether obesity status could be predicted by the predictor variables (model 1). We repeated this analysis for the subset of participants for whom maternal BMI, calculated from measurements reported during the children's assessment at age 5½, was available (replacing maternal height, model 2). All analyses were completed with SPSS 18.0 (SPSS, Chicago, IL).

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