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# Preconception and prenatal maternal stress are associated with broad autism phenotype in young adults: Project Ice Storm

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## Original Article

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## Abstract

Studies show associations between prenatal maternal stress (PNMS) and child autism, with little attention paid to PNMS and autism in young adulthood. The broad autism phenotype (BAP), encompassing sub-clinical levels of autism, includes aloof personality, pragmatic language impairment and rigid personality. It remains unclear whether different aspects of PNMS explain variance in different BAP domains in young adult offspring. We recruited women who were pregnant during, or within 3 months of, the 1998 Quebec ice storm crisis, and assessed three aspects of their stress (i.e., objective hardship, subjective distress and cognitive appraisal). At age 19, the young adult offspring ($n = 33$, 22F / 11M) completed a BAP self-report. Linear and logistic regressions were implemented to examine associations between PNMS and BAP traits. Up to 21.4% of the variance in BAP total score and in BAP three domains tended to be explained by at least one aspect of maternal stress, For example, 16.8% of the variance in aloof personality tended to be explained by maternal objective hardship; 15.1% of the variance in pragmatic language impairment tended to be explained by maternal subjective distress; 20.0% of the variance in rigid personality tended to be explained by maternal objective hardship and 14.3% by maternal cognitive appraisal. Given the small sample size, the results should be interpreted with caution. In conclusion, this small prospective study suggests that different aspects of maternal stress could have differential effects on different components of BAP traits in young adults.

## Introduction

Autism spectrum disorder (ASD) is a group of neurodevelopmental disorders characterized by social and communication deficits and restricted, repetitive behaviors.[1] The broad autism phenotype (BAP)[2] describes three core domains associated with autistic-like behaviors: aloof personality, pragmatic language impairment and rigid personality.[3] The BAP domains are milder but qualitatively similar to the three defining ASD domains (i.e., social and communication deficits and restricted, repetitive behaviors).[4,5]

Prenatal maternal stress (PNMS) is an established risk factor for neurodevelopmental disorders.[6] Research has shown associations between in-utero exposure to maternal depression,[7-10] anxiety,[11] stressful life events[12-16] and natural disasters[17] and child autism[7-10,13-17] and autistic-like traits.[11,12] While PNMS has been specifically linked to communication deficits in autistic children,[16] its ability to relate to subclinical levels of social deficits and restricted, repetitive behaviors has yet to be examined.

Evidence from animals and humans has shown that maternal stress during the preconception period affects offspring neurodevelopment.[18] In addition, preconception stress typically persists into pregnancy.[19] For example, depressive and anxious symptoms in the preconception phase are closely associated with those during pregnancy, with the symptom profiles remaining largely unchanged from preconception into pregnancy,[19,20] warranting the need to examine the effect of stress across preconception and pregnancy periods.

The study of sudden-onset natural disasters can complement other PNMS research. Disaster-related PNMS can determine whether associations between PNMS and autistic-like traits are due more to a pregnant woman's objective degree of exposure, her level of subjective distress (i.e., post-traumatic stress symptoms), or her cognitive appraisal of the event.

In January 1998, three separate weather systems in southern Quebec produced five continuous days of freezing rain and left up to 100 mm of ice on the region. The weight of the ice toppled electrical poles, high-tension power lines and pylons, leaving more than 1.5 million households without power for as long as 45 days. In June 1998, we launched the world's first prospective longitudinal disaster-related PNMS cohort: Project Ice Storm. This project recruited women who were pregnant during the crisis or became pregnant within 3 months following the

crisis. In Project Ice Storm children, greater prenatal maternal objective hardship and subjective distress were associated with more severe mother-rated autistic-like traits at 6½ years of age.[21]

It remains unclear whether effects of PNMS on autistic-like traits extend beyond those observed in childhood. The present study explored long-lasting effects of disaster-related PNMS on the severity of autistic-like traits by assessing BAP traits in the Project Ice Storm young adults. The comprehensive assessment of three aspects of PNMS (i.e., objective hardship, subjective distress, and cognitive appraisal) allowed us to determine the active ingredient in pregnant women's stress associated with BAP traits. We hypothesized that higher levels of maternal objective hardship, subjective distress, and/or more negative cognitive appraisal of the disaster, would be associated with more severe BAP traits and greater risk for clinically significant traits (caseness) in the young adult offspring. We anticipated that different aspects of PNMS would explain variance in the severity of different domains of BAP traits and caseness.

## Methods

### Ethical approval

This study was approved by the Douglas Institute Research Centre Ethics Board. We obtained written informed consent from all participants at each time point.

### Participants

Following the ice storm in January 1998, we contacted physicians who delivered babies in the four regional hospitals of the Montérégie, an area southeast of Montreal that was most affected by the crisis and asked for their help in contacting eligible women. On June 1, 1998, we mailed 1144 postal surveys to eligible women who were pregnant on January 9, 1998, or who became pregnant within the following three months. The surveys assessed their levels of PNMS (i.e., objective hardship, subjective distress and cognitive appraisal). Among the 1144 surveys, 224 women responded of whom 176 agreed to further contact. At age 19 (18.74 ± 0.37 years, range = 18.10–19.62 years), 33 young adult offspring (22 females/11 males) self-reported their BAP levels.

### Outcome variables

The Broad Autism Phenotype Questionnaire (BAPQ)[2] was designed to assess BAP in non-clinical populations and was validated against direct clinical assessment of BAP.[4] The self-report BAPQ includes 36 questions assessing three subscales of 12 questions each: aloof personality, pragmatic language impairment and rigid personality. Aloof personality is defined as a lack of interest in, or enjoyment of, social interaction (corresponding to social deficits of autism). Pragmatic language impairment refers to deficits in social aspects of language, resulting in difficulties communicating effectively or in holding a fluid, reciprocal conversation (corresponding to communication deficits of autism). Rigid personality is defined as little interest in change or difficulty adjusting to change (corresponding to restricted, repetitive behaviors of autism).[3] Questions are rated using a 6-point Likert scale ranging from "very rarely" (1) to "very often" (6),[4] and mean ratings are calculated for each score. The following scores are used as clinical cutoffs for the total score (female: 3.25; male: 3.35), aloof personality (female: 3.00; male: 3.25), pragmatic language impairment (female: 2.70; male: 2.95) and rigid personality (female: 3.25; male: 3.65).[3] A clinical composite diagnosis of BAP is defined as the presence of two or three BAP domains above the cutoffs.

### Predictor variables

#### Objective hardship

In June 1998, the severity of maternal objective hardship was assessed using four domains of exposure: Threat (e.g., injuries), Loss (e.g., loss of personal income), Scope (e.g., days without electricity), and Change (e.g., temporary shelter).[22] Items were scored so that a maximum of 8 points was attributed to each domain, which were then summed to create the total score: Storm32. The detailed scoring of Storm32 is presented elsewhere.[23]

#### Subjective distress

In June 1998, maternal subjective distress was assessed using a validated French version[24] of the 22-item Impact of Event Scale – Revised (IES-R).[25] This scale provides a total score and three domain scores: Intrusive Thoughts (8 items), Hyperarousal (6 items), and Avoidance (8 items). Each item is rated on a 5-point scale from 0 to 4. The log-transformed values of the total score were used in the current study due to a skewed distribution.

#### Cognitive appraisal

In June 1998, maternal cognitive appraisal of the ice storm was assessed using a single question: "Overall, what were the consequences of the ice storm on you and your family?". Response options were coded into three levels: "negative" ("−1"), "neutral" ("0"), and "positive" ("1").

#### Timing of exposure

In June 1998, timing of in-utero ice storm exposure was defined as the number of days between the estimated date of conception (the woman's due date minus 280 days) and January 9, 1998, the date at which the ice storm peaked. Negative values indicate preconception exposure.

### Control variables

The following maternal and offspring variables were considered as potential confounders as they have been reported to relate to both PNMS and autism.

Maternal variables: Socioeconomic status (SES) at child's birth was assessed using the higher of the two parental scores on the Hollingshead Scale[26] that included educational attainment and occupational prestige; lower scores correspond to higher SES. Maternal psychological problems, including anxiety (e.g., Have you felt constantly under strain?), depression (e.g., Have you felt that life is not worth living?), somatic complaints (e.g., Have you felt that you are ill?) and dysfunction (e.g., Have you been taking longer over things you do?), were assessed using the General Health Questionnaire–28.[27] Each of its 28 items was scored on a 4-point Likert scale for how much the women had experienced it in the preceding 2 weeks. The number of life events (e.g., death, illness or serious injury, major financial change), other than the ice storm, that occurred to the mothers during pregnancy was assessed with the Life Experience Survey[28] short form. The total number of obstetric complications (e.g., hypertension, preeclampsia, cold or flu) experienced by the mothers that were rated as moderate to severe using the McNeil-Sjöström Scale for Obstetric Complications[29] was used in the current study. Information on smoking and alcohol habits during pregnancy was collected from

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mothers who were asked to indicate the number of cigarettes smoked per day and the number of drinks consumed per week.

Offspring variables: Mothers reported on gestational age at birth and birth weight. Current full-scale intelligence quotient was assessed with the Wechsler Adult Intelligence Scale–Third Edition short form.[30] Age at BAP assessment was also calculated.

### Comparisons between age 19 and the recruitment sample

We compared the predictor and control variables between the present sample (i.e., responder) and those who were included in the recruitment sample but who failed to participate in 19-year-old BAP assessment (i.e., non-responder). Results are shown in Supplementary Table S1. The two samples did not differ in any covariate or PNMS variables except that non-responders had lower SES levels and more severe maternal psychological problems at recruitment than the 19-year-old responders.

### Statistical analysis

All analyses were conducted using IBM SPSS version 26.[31] First, boxplots were used to detect univariate outliers (above Q3 + 3*IQR or below Q1 – 3*IQR).[32] Second, descriptive analyses including mean, standard deviation (SD) and range were computed for all variables, and Pearson correlation analyses were conducted among all variables.

All analyses were conducted for BAP total score and each of the three domain scores. Given that PNMS may influence offspring autism in a sex-specific manner, and given sex-specific prevalence in autism, we controlled for child sex in all analyses. To examine the association between PNMS and the severity of BAP traits, hierarchical linear regressions were conducted: child sex entered in the first step, the control variables that were significantly correlated with BAP traits entered in the second step, followed by objective hardship. The same regression model was rerun for subjective distress and cognitive appraisal. As shown in Table 1, the only control variable significantly correlated with BAP traits was SES, such that the lower the SES level, the more severe the young adults' pragmatic language impairment. Considering the small sample size, p-values of the control variables for enter and removal were set at 0.05 and 0.1, respectively. For each regression model, Mahalanobis Distance was used to identify multivariate outliers ($p < 0.001$).[33]

Binary logistic regressions were conducted to examine the association between PNMS and the occurrence of clinical levels of BAP traits (i.e., total score, three domains and composite diagnosis). In order to identify control variables correlated with the outcome variables, independent-samples t-tests were conducted to identify any that discriminated significantly between cases and non-cases. A crude logistic regression model (Model 1) was conducted with PNMS variables alone. Then, an adjusted model (Model 2) was conducted with PNMS variables, child sex and the control variables that discriminated significantly between cases and non-cases for the given domain. As shown in Supplementary Table S2, no control variables discriminated significantly between cases and non-cases, and thus Model 2 was conducted with PNMS variables and child sex. Hosmer–Lemeshow tests were conducted to test the goodness of fit of the models.

To test the stability of the hierarchical linear regression and logistic regression results, sensitivity analyses were conducted by omitting the preconception exposed young adults ($n = 8$). The hierarchical linear regression results were false discovery rate (FDR)-corrected for 12 comparisons based on three PNMS and four BAP traits variables (i.e., total score and three domains). The logistic regression results were FDR-corrected for 15 comparisons based on three PNMS and five BAP caseness variables (i.e., total score, three domains and composite diagnosis).

## Results

### Descriptive information

We did not identify any univariate or multivariate outliers. There were, however, two participants whose objective hardship scores were 2–3 SD above the mean even though they did not meet the predefined criteria as outliers. Nonetheless, readers are cautioned that some results may be overestimated. To verify the estimation of associations between maternal objective hardship and the severity of BAP traits, the bootstrapping analysis[34] of 10,000 resamplings was applied to the hierarchical linear regression models.

Descriptive results are presented in Table 1. Among the 33 families, 27.3% (9/33) were middle class; 48.5% (16/33) were upper middle class; and 24.2% (8/33) were upper class. When the ice storm peaked on January 9, 1998, 24.2% (8/33) were within 3-month of conception; 27.3% (9/33) were in the 1st trimester of pregnancy; 27.3% (9/33) were in the 2nd trimester; and 21.2% (7/33) were in the 3rd trimester.

At 19 years of age, 15.2% (5/33, 4 females; 1 male) of the young adults met BAP total score cutoffs; 42.4% (14/33, 10 females; 4 males) met aloof personality cutoffs; 21.2% (7/33, 6 females; 1 male) met pragmatic language impairment cutoffs; and 48.5% (16/33, 14 females; 2 males) met rigid personality cutoffs. There was a significantly higher proportion of females (63.6%, 14/22) meeting rigid personality cutoffs than males (18.2%, 2/11) ($p = 0.026$). Finally, 36.4% (12/33) presented two or three BAP domains thus meeting criteria for a composite diagnosis of BAP.

### Associations between PNMS and the severity of BAP traits controlling for child sex

As shown in Table 2, each of the four BAP traits variables was significantly ($p < 0.05$) associated with at least one PNMS variable, although these associations fell to the trend level ($q < 0.10$) after FDR correction as explained below.

Total score: The greater the mothers' objective hardship, the higher the young adults' BAP total score ($B = 0.078$, 95%CI [0.022, 0.134], $\beta = 0.467$, $\Delta R^2 = 0.214$, $p = 0.008$). The bootstrapping result showed that there was no change to the significance of the association between objective hardship and BAP total score (bootstrap 95%CI [0.010, 0.128]). However, this association fell to the trend level after FDR correction ($q = 0.060$). Although no association was observed between maternal subjective distress and BAP total score, there was a negative trend-level association for cognitive appraisal ($B = -0.269$, 95%CI [−0.565, 0.028], $\beta = -0.333$, $\Delta R^2 = 0.102$, $p = 0.074$), such that the more negative the cognitive appraisal, the greater the BAP total score, but it failed to approach significance after FDR correction ($q = 0.127$). Comparing the standardized coefficients ($\beta$), the effect of objective hardship on BAP total score was about 30% greater than that of cognitive appraisal, and more than twice the effect of subjective distress.

Aloof personality: The greater the mothers' objective hardship, the more severe the young adults' aloof personality ($B = 0.097$, 95% CI [0.017, 0.178], $\beta = 0.413$, $\Delta R^2 = 0.168$, $p = 0.020$). The bootstrapping result showed that there was no change to the significance of the association between objective hardship and

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**Table 1.** Descriptive information for 33 mother-young adult dyads and Pearson correlation coefficients among all variables

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11 | 12 | 13 | 14 | 15 | 16 | 17 | 18 | 19 | mean | SD | Range |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 - Objective exposure | – | | | | | | | | | | | | | | | | | | | 11.00 | 4.14 | 1–24 |
| 2 - Subjective distress[a] | 0.223 | – | | | | | | | | | | | | | | | | | | 1.90 | 1.11 | 0–3.71 |
| 3 - Cognitive appraisal | **−0.396*** | −0.201 | – | | | | | | | | | | | | | | | | | 0.12 | 0.86 | −1–1 |
| 4 - Timing of exposure (days) | −0.098 | 0.168 | 0.074 | – | | | | | | | | | | | | | | | | 90.08 | 99.40 | −73.02–274.02 |
| 5 - SES[b] | −0.130 | 0.317 | 0.140 | −0.011 | – | | | | | | | | | | | | | | | 25.01 | 10.50 | 11–47 |
| 6 - Maternal age (years) at birth | 0.048 | −0.069 | 0.009 | 0.210 | −0.195 | – | | | | | | | | | | | | | | 30.66 | 4.78 | 20.23–41.17 |
| 7 - Smoking per day | 0.076 | 0.240 | −0.019 | **−0.385*** | 0.264 | −0.162 | – | | | | | | | | | | | | | 1.50 | 4.81 | 0–25 |
| 8 - Alcohol per week | −0.058 | −0.176 | 0.067 | −0.031 | 0.081 | 0.154 | −0.003 | – | | | | | | | | | | | | 0.09 | 0.38 | 0–2 |
| 9 - Obstetric complications | −0.191 | −0.115 | −0.019 | −0.125 | 0.013 | 0.108 | 0.194 | −0.024 | – | | | | | | | | | | | 3.85 | 2.65 | 0–12 |
| 10 - Life events | **0.355*** | **0.477**** | −0.070 | 0.260 | −0.197 | 0.174 | 0.210 | −0.162 | −0.117 | – | | | | | | | | | | 6.24 | 4.12 | 1–17 |
| 11 - Psychological symptoms | 0.118 | 0.322 | −0.288 | 0.169 | −0.041 | 0.144 | 0.306 | −0.016 | 0.162 | 0.271 | – | | | | | | | | | 0.15 | 0.16 | 0–0.68 |
| 12 - Gestational age (weeks) at birth | 0.191 | 0.133 | −0.144 | −0.013 | −0.063 | 0.342 | −0.036 | −0.066 | **−0.418*** | 0.123 | 0.043 | – | | | | | | | | 39.55 | 1.35 | 33.43–41.00 |
| 13 - Birth weight (grams) | −0.039 | 0.135 | 0.002 | −0.002 | −0.065 | 0.164 | −0.086 | 0.062 | **−0.380*** | −0.053 | −0.024 | **0.611**** | – | | | | | | | 3520.64 | 491.01 | 1850–4432 |
| 14 - Age (years) at BAP assessment | −0.008 | 0.143 | 0.077 | **0.733**** | −0.029 | 0.038 | −0.105 | −0.002 | −0.305 | 0.263 | 0.259 | −0.051 | −0.065 | – | | | | | | 18.74 | 0.37 | 18.10–19.62 |
| 15 - IQ[c] | −0.230 | −0.289 | 0.003 | −0.122 | **−0.381*** | 0.035 | −0.269 | −0.230 | 0.007 | 0.025 | −0.209 | −0.058 | −0.116 | −0.114 | – | | | | | 113.32 | 11.15 | 90–137 |
| 16 - BAP total score | **0.457**** | 0.197 | −0.312 | −0.113 | 0.085 | −0.025 | 0.067 | −0.260 | 0.027 | 0.198 | −0.161 | 0.095 | −0.137 | −0.074 | 0.070 | – | | | | 2.80 | 0.69 | 1.53–4.44 |
| 17 - Aloof personality | **0.416*** | 0.101 | −0.225 | −0.040 | −0.045 | −0.041 | −0.125 | −0.224 | 0.103 | 0.199 | −0.186 | 0.007 | −0.158 | −0.047 | 0.143 | **0.914**** | – | | | 2.95 | 0.97 | 1.33–4.73 |
| 18 - Pragmatic language impairment | 0.320 | **0.386*** | −0.175 | 0.025 | **0.349*** | 0.006 | 0.070 | −0.203 | −0.263 | 0.084 | −0.268 | 0.260 | 0.124 | 0.071 | −0.068 | **0.775**** | **0.578**** | – | | 2.30 | 0.68 | 1.00–4.33 |
| 19 - Rigid personality | **0.426*** | 0.060 | **−0.401*** | −0.275 | −0.027 | −0.018 | 0.276 | −0.235 | 0.172 | 0.211 | 0.037 | 0.017 | −0.282 | −0.201 | 0.064 | **0.847**** | **0.682**** | **0.466**** | – | 3.17 | 0.77 | 1.83–4.83 |

BAP, Broad Autism Phenotype; IQ, Intelligence quotient; SD, standard deviation; SES, socioeconomic status; –, not applicable.
[a]Log-transformed values of IES-R total score
[b]Lower SES scores correspond to higher SES.
[c]IQ was assessed at 19 years of age using the Wechsler Adult Intelligence Scale–Third Edition short form
*$p < 0.05$
**$p < 0.01$

**Table 2.** Summary of hierarchical linear regression analyses for the association between PNMS and the severity of BAP traits in young adults when controlling for child sex

| | Values in final model | | | | | Values after entry of each variable | | | |
|---|---|---|---|---|---|---|---|---|---|
| | *B* | SE of B | *β* | *p* value | *q* value | $R^2$ | $\Delta R^2$ | *F* | $\Delta F$ |
| **(1) Total score** | | | | | | | | | |
| Constant | 1.764 | 0.534 | | | | | | | |
| Child sex | 0.111 | 0.235 | 0.077 | 0.642 | | 3.15E-04 | | 0.010 | |
| Objective hardship | 0.078 | 0.027 | 0.467 | **0.008**** | 0.060 | 0.214 | 0.214 | 4.095 | 8.179 |
| Constant | 2.466 | 0.52 | | | | | | | |
| Child sex | 0.060 | 0.260 | 0.041 | 0.820 | | 3.15E-04 | | 0.010 | |
| Subjective distress | 0.126 | 0.112 | 0.202 | 0.272 | 0.363 | 0.040 | 0.040 | 0.631 | 1.252 |
| Constant | 3.556 | 0.609 | | | | | | | |
| Child sex | −0.109 | 0.260 | −0.075 | 0.679 | | 3.15E-04 | | 0.010 | |
| Cognitive appraisal | −0.269 | 0.145 | −0.333 | 0.074 | 0.127 | 0.103 | 0.102 | 1.718 | 3.426 |
| **(2) Aloof personality** | | | | | | | | | |
| Constant | 1.942 | 0.773 | | | | | | | |
| Child sex | −0.040 | 0.341 | −0.019 | 0.908 | | 0.005 | | 0.160 | |
| Objective hardship | 0.097 | 0.039 | 0.413 | **0.020*** | 0.074 | 0.173 | 0.168 | 3.138 | 6.091 |
| Constant | 2.995 | 0.743 | | | | | | | |
| Child sex | −0.123 | 0.372 | −0.061 | 0.742 | | 0.005 | | 0.160 | |
| Subjective distress | 0.082 | 0.161 | 0.094 | 0.612 | 0.668 | 0.014 | 0.009 | 0.210 | 0.263 |
| Constant | 4.081 | 0.874 | | | | | | | |
| Child sex | −0.297 | 0.373 | −0.146 | 0.433 | | 0.005 | | 0.160 | |
| Cognitive appraisal | −0.302 | 0.208 | −0.266 | 0.158 | 0.237 | 0.070 | 0.065 | 1.132 | 2.099 |
| **(3) Pragmatic language impairment** | | | | | | | | | |
| Constant | 1.618 | 0.566 | | | | | | | |
| Child sex | 0.055 | 0.249 | 0.038 | 0.827 | | 7.00E-06 | | 2.17E-04 | |
| Objective hardship | 0.054 | 0.029 | 0.325 | 0.072 | 0.127 | 0.104 | 0.104 | 1.737 | 3.473 |
| Constant | 1.737 | 0.484 | | | | | | | |
| Child sex | 0.062 | 0.242 | 0.043 | 0.800 | | 7.00E-06 | | 2.17E-04 | |
| Subjective distress | 0.242 | 0.105 | 0.391 | **0.028*** | 0.074 | 0.151 | 0.151 | 2.668 | 5.336 |
| Constant | 2.756 | 0.626 | | | | | | | |
| Child sex | −0.080 | 0.267 | −0.056 | 0.767 | | 7.00E-06 | | 2.17E-04 | |
| Cognitive appraisal | −0.152 | 0.149 | −0.191 | 0.316 | 0.379 | 0.033 | 0.033 | 0.520 | 1.039 |
| **(4) Rigid personality** | | | | | | | | | |
| Constant | 1.723 | 0.596 | | | | | | | |
| Child sex | 0.312 | 0.263 | 0.193 | 0.245 | | 0.019 | | 0.584 | |
| Objective hardship | 0.084 | 0.030 | 0.451 | **0.010**** | 0.060 | 0.218 | 0.200 | 4.194 | 7.677 |
| Constant | 2.676 | 0.586 | | | | | | | |
| Child sex | 0.234 | 0.293 | 0.145 | 0.431 | | 0.019 | | 0.584 | |
| Subjective distress | 0.054 | 0.127 | 0.077 | 0.674 | 0.674 | 0.024 | 0.006 | 0.375 | 0.181 |
| Constant | 3.853 | 0.659 | | | | | | | |
| Child sex | 0.042 | 0.281 | 0.026 | 0.882 | | 0.019 | | 0.584 | |
| Cognitive appraisal | −0.355 | 0.157 | −0.394 | **0.031*** | 0.074 | 0.162 | 0.143 | 2.891 | 5.121 |

BAP, Broad Autism Phenotype; PNMS, prenatal maternal stress; SE, standard error.
*q* value represents corrected *p* values.
*$p < 0.05$
**$p < 0.01$

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aloof personality score (bootstrap 95%CI [0.008, 0.159]). This significant effect fell to the trend level after correction ($q = 0.074$). No associations were observed for maternal subjective distress or cognitive appraisal.

Pragmatic language impairment: The greater the mothers' subjective distress, the more severe the young adults' pragmatic language impairment ($B = 0.242$, 95%CI [0.028, 0.456], $\beta = 0.391$, $\Delta R^2 = 0.151$, $p = 0.028$), with the significant effect falling to a trend after correction (q = 0.074). There was a positive trend-level association for maternal objective hardship ($B = 0.054$, 95%CI [−0.005, 0.113], $\beta = 0.325$, $\Delta R^2 = 0.104$, $p = 0.072$), with the bootstrap 95%CI of [−0.024, 0.112]; this trend failed to survive correction ($q = 0.127$). No association was observed for maternal cognitive appraisal.

Rigid personality: The greater the mothers' objective hardship, the more severe the young adults' rigid personality ($B = 0.084$, 95% CI [0.022, 0.146], $\beta = 0.451$, $\Delta R^2 = 0.200$, $p = 0.010$). The bootstrapping result showed that there was no change to the significance of the association between objective hardship and rigid personality score (bootstrap 95%CI [0.035, 0.130]). The effect fell to the trend level after correction ($q = 0.060$). In addition, the more negative the mothers' cognitive appraisal, the more severe the young adults' rigid personality ($B = -0.355$, 95%CI [−0.676, −0.035], $\beta = -0.394$, $\Delta R^2 = 0.143$, $p = 0.031$), although this also fell to the trend level after correction ($q = 0.074$). No association with rigid personality was observed for maternal subjective distress.

### Association between PNMS and BAP clinical cutoffs controlling for child sex

The results of logistic regressions, showing associations between PNMS and BAP caseness, are presented in Supplementary Table S3. Despite significant initial results, none of the associations approached significance following FDR correction as described below.

Total score caseness: Maternal objective hardship was associated with BAP total score caseness (OR = 1.294, 95%CI [1.007, 1.663], $p = 0.044$), which failed to survive FDR correction ($q = 0.220$). Hosmer–Lemeshow test of goodness of fit indicated that the model adequately fit the data ($\chi^2 = 9.675$, $p = 0.289$). No associations were observed for maternal subjective distress or cognitive appraisal.

Aloof personality caseness: The severity of PNMS was not associated with aloof personality caseness.

Pragmatic language impairment caseness: Maternal subjective distress was associated with pragmatic language impairment caseness (OR = 4.826, 95%CI [1.252, 18.599], $p = 0.022$), which failed to survive FDR correction ($q = 0.218$). Hosmer–Lemeshow test of goodness of fit indicated that the model adequately fit the data ($\chi^2 = 3.462$, $p = 0.902$). No associations were observed for maternal objective hardship or cognitive appraisal.

Rigid personality caseness: Maternal objective hardship was associated with rigid personality caseness (OR = 1.290, 95%CI [1.026, 1.622], $p = 0.029$); however, this association did not survive FDR correction ($q = 0.218$). Hosmer–Lemeshow test of goodness of fit indicated that the model adequately fit the data ($\chi^2 = 5.814$, $p = 0.668$). No association was observed for maternal subjective distress. For maternal cognitive appraisal, a more negative cognitive appraisal by the mother was associated with an increased risk of rigid personality caseness (OR = 0.408, 95%CI [0.168, 0.995], $p = 0.049$) although this association became non-significant (OR = 0.478, 95%CI [0.184, 1.246], $p = 0.131$) after controlling for child sex. In addition, females were more likely to meet caseness for BAP clinical rigid personality than males regardless of three PNMS levels, however, this sex difference did not survive FDR correction regardless of levels of maternal objective hardship ($q = 0.113$), subjective distress ($q = 0.113$) or cognitive appraisal ($q = 0.235$).

Composite diagnosis of BAP caseness: The severity of PNMS was not associated with a composite diagnosis of BAP.

### Sensitivity analysis

After omitting the young adults in the preconception group (i.e., using the pregnancy sample only), there were no substantial changes to the hierarchical linear regression (Supplementary Table S4) or logistic regression results (Supplementary Table S5).

## Discussion

The goal of this study was to determine the extent to which objective, subjective and cognitive aspects of preconception and PNMS explain variance in different components of BAP traits in young adults using a prospective, natural experiment. Our findings support the preconception and prenatal developmental origins of BAP traits. Overall, greater maternal objective hardship tended to be associated with higher BAP total score. Regarding the three BAP domains, we found that distinct aspects of PNMS tended to explain between 14.3% and 20.0% of the variance in BAP traits, with maternal objective hardship and cognitive appraisal associated with personality difficulties, and maternal subjective distress associated with language impairments. These results extend our earlier findings at age 6½,[21] suggesting that exposure to disaster-related PNMS may influence autistic-like traits at least into young adulthood.

Despite the strengths inherent in this quasi-experimental study, the interpretations of the results that we present here must be taken with caution given the small sample size; the results summarized above were significant ($p < 0.05$) at uncorrected levels but fell to trend levels ($q < 0.10$) after FDR correction. Despite the lack of statistical univariate outliers, the small sample size also led to two high values of objective hardship scores that were somewhat beyond the rest. The two cases do not meet criteria for multivariate outliers and lie in the general trajectory of the swarm; as legitimate members of the population under study, these may be clinically-relevant examples of the effects of high exposure to early life stress. The results of bootstrapping analyses suggest that the confidence intervals[34] are not unduly biased by the two high values of objective hardship scores. However, these results must still be considered preliminary, potentially informing hypotheses to be tested in larger samples.

We found that higher maternal objective hardship to the 1998 ice storm tended to be associated with more severe aloof personality which parallels the social deficits of autism. Social functioning deficits, including a lack of social responsiveness, difficulty recognizing others' emotions and intentions and inability to form friendships in a reciprocal manner, have been considered as the most universal and principal feature of autism.[35] Our results echo animal research showing the effect of prenatal restraint stress on social behavior deficits in adult rats.[36] Emerging results from

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neuroimaging research have also partially explained the neurological mechanisms: social impairments may be partly attributed to the vulnerability of the amygdala, hippocampus and prefrontal cortex involved in social information processing.[37,38]

We also observed a tendency for higher maternal objective hardship and more negative maternal cognitive appraisal to be associated with more severe rigid personality. This trait parallels the restricted, repetitive behaviors of autism. To the best of our knowledge, this study is the first to investigate the predictive role of disaster-related PNMS on the severity of restricted, repetitive behaviors. In addition, despite failing to survive FDR correction, a female-biased prevalence was observed in rigid personality, and females in our sample were more likely to display these behaviors than males regardless of PNMS exposure levels. This seems somewhat unexpected given that males typically exhibit restricted, repetitive behaviors more often than females.[39] A possible explanation is that restricted, repetitive behaviors encompass two subdomains: repetitive sensory motor behaviors and insistence on sameness,[39] and rigid personality refers mainly to a desire for sameness.[3,4] Studies have shown a high percentage of internalizing symptoms and executive functioning deficits in girls with autism,[40,41] which may increase sameness behaviors in those affected girls. Furthermore, a recent study supports our female bias finding by showing that girls have greater insistence on sameness than boys.[39] Previous studies have proposed several neural correlates of insistence on sameness in adults with autism: low levels of the protein transporter for serotonin in the thalamus,[42] and increased prefrontal and caudate nucleus volumes.[43] Future research is needed to identify the probable neurological mediators between PNMS and offspring repetitive behaviors.

In contrast to the effects of objective hardship (and to a lesser extent cognitive appraisal) on aloof and rigid personalities, we found a trend suggesting that greater maternal subjective distress was associated with more severe pragmatic language impairment. This trait parallels the communicative deficits of autism. A previous study reported that prenatal stressful life events were associated with deficits in language and communication in children with autism.[16] Our finding extends the previous research by specifying that it may be the subjective distress, and the genetic propensity to experiencing symptoms of post-traumatic stress disorder 5–6 months following a life event, rather than the objective degree of the exposure, that is predictive of offspring communication deficits.

Our findings raise a question about why distinct aspects of PNMS seem to be associated with distinct BAP traits. While there is no consensus on an explanation, it has been established that offspring neurodevelopment and behaviors vary according to different aspects of PNMS.[44] For example, prenatal depression[7] and prenatal exposure to natural disasters[17] are both associated with child autism, whereas other studies found that child autism was not associated with prenatal exposure to life events such as deaths, accidents, serious illness or intimate partner abuse.[45,46] Moreover, our previous Project Ice Storm findings have demonstrated distinct pathways of the transgenerational transmission of the three aspects of PNMS to offspring development and behaviors. For example, greater maternal subjective distress was associated with more externalizing behaviors at 11½ years via larger amygdala volume[47] while maternal objective hardship[48] and cognitive appraisal[49] were associated with body mass index scores and central adiposity at 13½ years via DNA methylation. However, further investigation is needed to identify the specific mediators via which each of the three aspects of PNMS differentially affects distinct BAP traits.

The results of our sensitivity analyses suggest that associations between disaster-related stress and the severity of BAP traits are similar in young adults whether exposed in the preconception or prenatal periods. These findings are similar to those reported by Beijers et al.[50] indicating that war exposure during the preconception period was associated with increased internalizing and externalizing problems in young children. However, Class et al.[14] reported that while increased levels of preconception bereavement were associated with marginally higher rates of adult bipolar disorder and schizophrenia, no associations were found for childhood ASD or ADHD. Our finding provides additional support for extending the developmental origins of disease to three months preconception. Research has shown that preconception stress is associated with prenatal and postnatal maternal distress,[19] poor birth outcomes[18] and infant emotional reactivity.[51] Therefore, early screening of maternal mental health problems in women attempting to conceive may be a valuable tool to prevent severe child outcomes. Future studies are needed to determine the long-lasting detrimental influences of preconception stress on offspring behaviors.

There were several limitations. First, our sample is small due to loss to follow-up during the 19-year period, although no meaningful differences in the three aspects of PNMS levels were found between the sample included in this study and the original recruitment sample. Future studies with larger sample sizes are needed to replicate our findings. Second, the SES of the families in this study is higher than the median of the population in the region from which they were recruited in 1998, such that the current results may not generalize to lower class populations.

There were several strengths of this current study. First, our study took advantage of a sudden-onset natural disaster, which was independent of parental characteristics (e.g., SES and psychopathology), as the source of prenatal stress and which, thus, lends itself more easily to interpretations between objective hardship from the disaster and BAP traits. As well, this study was prospective in nature with most mothers reporting on their ice storm experiences while they were still pregnant. Our approach to studying PNMS, by assessing objective hardship, subjective distress, and cognitive appraisal, adds important nuances to the field that are difficult to accomplish in other naturalistic contexts. Finally, we assessed BAP traits through self-report, extending our understanding of BAP from studies of first-degree relatives of ASD patients, to a non-clinical population without a family history of ASD.

In conclusion, our results demonstrate the relevance of assessing not only maternal distress in pregnancy but also the objective severity of exposure to an independent life event, and of assessing the cognitive appraisal of those events, when explaining variance in distinct aspects of BAP traits in young adults.

**Supplementary materials.** For supplementary material for this article, please visit https://doi.org/10.1017/S2040174423000156

**Data availability statement.** Data are available upon request.

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**Conflicts of interest.** None.

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