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Regular Article

Prenatal maternal subjective distress predicts higher autistic-like traits in offspring: The Iowa Flood Study

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Abstract

Autism spectrum disorder prevalence more than quadrupled in the United States between 2000 and 2020. Ice storm-related prenatal maternal stress (PNMS) predicts autistic-like trait severity in children exposed early in gestation. The objective was to determine the extent to which PNMS influences the severity and trajectory of autistic-like traits in prenatally flood-exposed children at ages 4–7 years and to test moderation by sex and gestational timing. Soon after the June 2008 floods in Iowa, USA, 268 women pregnant during the disaster were assessed for objective hardship, subjective distress, and cognitive appraisal of the experience. When their children were 4, 5½, and 7 years old, mothers completed the Social Communication Questionnaire (SCQ) to assess their children's autistic-like traits; 137 mothers completed the SCQ for at least one age. The final longitudinal multilevel model showed that the greater the maternal subjective distress, the more severe the child's autistic-like traits, controlling for objective hardship. The effect of PNMS on rate of change was not significant, and there were no significant main effects or interactions involving sex or timing. Prenatal maternal subjective distress, but not objective hardship or cognitive appraisal, predicted more severe autistic-like traits at age 4, and this effect remained stable through age 7.

Keywords: Autism; autistic-like traits; natural disaster; prenatal maternal stress; subjective distress

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Introduction

Autism spectrum disorder (ASD) is a neurodevelopmental syndrome reflecting both genetic and environmental influences (Lyall et al., 2017). It encompasses conditions with varying degrees of social behavior and communication impairment (WHO, 2022), as well as restricted and repetitive behaviors and interests (American Psychiatric Association, 2013). In the United States in 2020, 1 in 36 eight-year-olds was diagnosed with ASD, a rate that had more than quadrupled since 2000 (Maenner et al., 2023). Boys were four times more likely to be diagnosed than girls (Maenner et al., 2023).

Given that the distribution of autistic-like traits is common and continuous in the general population (Constantino & Todd, 2003), it has been argued that ASD etiology may be similar along the full continuum from "autistic traits" to "severe phenotype" (Lundstrom et al., 2012) (Robinson et al., 2011; Ronald & Hoekstra, 2011). This warrants the study of risk factors that explain variance in the full range of sub-clinical and clinical symptoms (Constantino & Todd, 2003), as well as individual variation in the trajectory of autistic-like traits across development (Fountain et al., 2012; Gotham et al., 2012; Lord et al., 2015) which, moreover, may be sexually dimorphic (Davis & Pfaff, 2014).

The estimated heritability of autism is approximately 80%, leaving 20% of the variance in ASD risk due to environmental/nongenetic factors (Bai et al., 2019). The premise, according to the Developmental Origins of Health and Disease (DOHaD) paradigm (Barker & Osmond, 1986; Barker et al., 1989), that the accumulation of environmental factors such as maternal and fetal perinatal complications contributes to atypical neurodevelopment, has received empirical support (Bölte et al., 2019; Getahun et al., 2017; Willfors et al., 2017). Several other putative nongenetic factors have been shown to impact the severity of ASD, potentially moderated by child sex (Holmboe et al., 2014). In particular, more severe prenatal maternal stress (PNMS) has consistently been associated with adverse child outcomes: regardless of how PNMS has been operationalized (stressful life events, maternal psychopathology, environmental exposures), greater PNMS has been associated with greater symptom severity along the neurotypical-to-ASD continuum in children (Van den Bergh et al., 2020).

Prenatal exposure to natural disasters, in particular, has been associated with increases in ASD risk. Kinney et al. (2008) reported that autism rates in Louisiana increased in a dose–response fashion according to the severity of prenatal exposure to tropical storms and hurricanes, with the greatest effects of exposure severity occurring during mid- and very late pregnancy (Kinney et al., 2008;

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Kinney et al., 2008). However, findings from other studies do not agree on which gestational period is most vulnerable to the effects of PNMS on autism (Beversdorf et al., 2005; Class et al., 2014). Moreover, Kinney's population-based results using administrative data provide only limited insight into aspects of maternal stress (such as objective aspects of exposure, or psychological distress) that influence children's development. This underlines the need for individual-level data to better understand the maternal stress experience and its association with child outcomes.

The Stress in Pregnancy International Research Alliance (SPIRAL, www.mcgill.ca/spiral) conducted a series of natural experiments using natural disasters to prospectively assess the impact of different aspects of PNMS on child development (King & Laplante, 2015). Importantly, natural disasters are considered "independent" life events, that is, their occurrence is independent of the pregnant woman's propensity to create or exacerbate difficulties in her life as a function of heritable temperament or personality traits. Based on the Lazarus and Folkman (1984) model of stress and coping, SPIRAL studies differentiate dimensions of PNMS: objective hardship, subjective distress, and cognitive appraisal of the disaster (King et al., 2005). As the onset of natural disasters is well defined, the exact time the exposure occurred during pregnancy can be determined (King et al., 2012).

In one SPIRAL study, Walder et al. (2014) found that maternal objective hardship ($r = 0.43$) and subjective distress ($r = 0.45$) levels following the 1998 Quebec Ice Storm were positively associated with children's autistic-like traits at 6½ years, with the greatest effect observed in children exposed during the first trimester. Given the sex-differentiated stress-response trajectory proposed by Davis and Pfaff (2014), it is noteworthy that, on average, autistic-like trait scores were higher in boys than in girls, but that sex did not moderate the effects of PNMS (Walder et al., 2014). In a follow-up study of the same cohort at age 19, Li et al. (2023) observed that all three aspects of PNMS (objective hardship, subjective distress, and cognitive appraisal) predicted different aspects of self-reported autistic-like traits in both boys and girls. In contrast, in another SPIRAL cohort that experienced severe flooding, greater positive maternal mental health assessed post-flood predicted less severe autistic-like traits in their 30-month-old children (Laplante et al., 2019).

This study aimed to replicate and extend the findings of Walder et al. (2014) to assess the longitudinal effects of prenatal maternal disaster-related PNMS on the severity of children's autistic-like traits at age 4 and on the rate of trajectory change between ages 4, 5½, and 7 while controlling for potential confounders. Secondary objectives were to examine the extent to which gestational timing and/or fetal sex moderate associations between PNMS and autistic-like traits in children.

The sample was drawn from SPIRAL's Iowa Flood Study (2008; https://www.mcgill.ca/spiral/iowa-flood-study). In June 2008, record rainfall in the Midwest caused one of the worst American disasters to date. In Iowa alone, more than 38,000 people were evacuated from their homes, businesses reported more than $5 billion in damage, 85 of Iowa's 99 counties were declared disaster areas, several hundred blocks of Cedar Rapids were underwater, and 24 people lost their lives due to the floods. The peak of flooding was on June 15, 2008.

Methods

Participants

A total of 268 women were recruited from obstetric clinics or from WIC (Women's, Infant and Children's health) clinics located in the flood-affected area. Inclusion criteria included being 18 years or older at the time of recruitment and English-speaking. For the current study, we added two additional criteria: pregnant on June 15, 2008 (excluding 49 participants who were exposed in preconception, postnatal or without trimester information) and having at least one measurement of autistic-like traits. The final sample included 137 mother–child dyads (Table 1), of which 92 responded to at least 2 out of 3 measurement times, and 69 to 3 out of 3. For more information on the original protocol, please refer to Nylen et al. (2013).

Procedures

At recruitment, PNMS measurements, birth or due date, demographics, and maternal mental health measures were collected. Most of the 268 participants (94.8%) completed these questionnaires within 2.1 months (range: 0–9 months) of June 15, 2008. These measures were re-administered an average of 22.2 months after the flood (range: 21–33 months) to complete specific information regarding objective hardship. Obstetrical data were extracted from medical records. When the children were 4, 5½, and 7 years old, mothers reported on their children's autistic-like traits.

Outcome: autistic-like traits

Mothers completed the 40-item Social Communication Questionnaire (SCQ; Rutter et al., (2003)). For each item, mothers reported whether the listed behavior was observed in their children during the past 3 months. Items are summed to obtain a total score. In a German population, the SCQ demonstrated good internal validity (Cronbach's $\alpha = 0.83$) and test–retest reliability ($r = 0.76$) (Bölte et al., 2008). For the present study, we obtained a Cronbach's alpha calculated at 5 ½ years ($n = 126$, $\alpha = 0.69$) (Hogan, 2019). As a screening for autism in children under 8 some authors recommend a cutoff of ≥11 (Allen et al., 2007; Corsello et al., 2007), with a sensitivity of 100% and a specificity of 62% for children aged 3–6 (Allen et al., 2007). With respect to replication with other SPIRAL studies, Project Ice Storm used the Autism Spectrum Screening Questionnaire (ASSQ; Ehlers et al. (1999)) to assess autistic-like traits. According to one comparison study (Norris & Lecavalier, 2010), the dimensions assessed by the SCQ and the ASSQ are similar: reciprocal social interaction, communication, language, and patterns of repetitive and stereotypical behaviors.

Predictors

Objective hardship

Objective hardship was measured using four dimensions of disaster experiences (Bromet & Dew, 1995): threat, loss, change, and scope. The threat dimension measured the level of threat to the mothers and/or their families (e.g., "Were you physically hurt?", "Were you in danger of lack of food?"). The loss dimension measured the amount of material and financial loss (e.g., "Was your home damaged?", "Did you experience loss of personal income?"). The change dimension measured the extent of change to daily life during the disaster (e.g., "Did your family stay together?", "Experience difficulty in accessing prenatal care?"). The scope dimension measured the duration and magnitude of the disaster on the mothers (e.g., "To what extent was your neighborhood affected?", "How many days were you deprived of electricity?"). The possible score for each dimension ranged from 0 (no exposure) to 25 (severe exposure). The dimensions were

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Table 1. Descriptive analysis and participant characteristics

	Sample size (n)			Mean			Standard deviation			Range		
Age:	4	5½	7	4	5½	7	4	5½	7	4	5½	7
Outcomes												
SCQ												
Total	86	130	95	3.95	4.06	3.69	2.57	3.84	2.81	0 - 12	0 - 26	0 - 15
Boys	45	63	47	4.13	4.78	4.13	2.75	4.03	4.35	0 - 12	0 - 25	0 - 15
Girls	41	67	48	3.76	4.04	3.27	2.37	3.64	3.37	0 - 12	0 - 26	0 - 10
Age at assessment												
Total	87	130	95	4.19	5.60	7.26	0.26	0.21	0.25	4.01 - 5.54	5.46 - 6.48	7.03 - 7.85
Boys	46	63	47	4.21	5.60	7.26	0.26	0.11	0.18	4.01 - 5.54	5.48 - 6.03	7.04 - 7.85
Girls	41	67	48	4.17	5.61	7.27	0.13	0.15	0.15	4.04 - 4.61	5.46 - 6.48	7.03 - 7.62
		Sample size (n)				Mean or percent			Standard deviation			
Prenatal maternal stress												
Objective hardship		137				7.93			8.69			
Subjective distress		137				−0.02			0.84			
Cognitive appraisal		137				2.50			0.69			
Timing of exposure (days)		137				140.83			81.38			
1st trimester		43				31.4%						
2nd trimester		49				35.8%						
3rd trimester		45				32.8%						
Maternal covariates												
Positive mental health		137				49.39			12.47			
Socioeconomic status		137				52.72			10.30			
Obstetric complications		136				6.17			2.91			
Child covariates												
Child sex		137										
Boys		69				50.4%						
Girls		68				49.6%						
Gestational age (weeks)		136				39.28			1.28			
Breathing prob. at birth		135										
yes		30				22.2%						
Hyperbilirubinemia		135										
yes		5				3.7%						
APGAR<8 at 5 min		135										
yes		5				3.7%						

(*Continued*)

Table 1. (*Continued*)

Maternal demographics					
Ethnicity	Asian	Black	Caucasian	Hispanic	Native
$N = 136$	2.9%	2.9%	92.6%	0.7%	0.7%
Marital status	Single	Partnership	Married	Divorced	
$N = 136$	10.3%	2.9%	85.3%	1.5%	
Socioeconomic status	Lower-middle	Middle	Upper-middle	Upper	
$N = 135$	3.7%	7.4%	42.2%	46.7%	
Maternal education	Technical	High school	College	Bachelor	Graduate
$N = 136$	14.0%	3.7%	19.1%	36.0%	27.2%
Household income	< $40k	$40k – $50k	$50k – $60k	$60k – $70k	> $70k
$N = 133$	28.6%	9.0%	8.3%	15.8%	38.3%

summed to create a total objective hardship score, the Iowa Flood 100 (or IF100) with a maximum score of 100. See Yong Ping et al. (2015) for more details.

Subjective distress

Posttraumatic distress symptoms: At recruitment, the severity of current post-traumatic stress disorder (PTSD)-like symptoms was assessed with the 22-item Impact of Events Scale-Revised (Weiss & Marmar, 1997). The IES-R has good internal consistency ($\alpha = .93$) and satisfactory test–retest reliability ($r = .76$) (Brunet et al., 2003).

Peritraumatic symptoms: Distress and dissociative experiences at the worst moment of the disaster, as recalled at the time of recruitment, were assessed with the 13-item Peritraumatic Distress Inventory (PDI; Brunet et al. (2001)) and the 10-item Peritraumatic Dissociative Experiences Questionnaire (PDEQ; Marmar et al., (1997)). The PDI and PDEQ have good internal consistency, test–retest reliability, and convergent and divergent validity (Brunet et al., 2001; Birmes et al., 2005; Bunnell et al., 2018).

Scores from these three questionnaires were combined to capture subjective distress: the Composite Score for Mothers' Subjective Stress (COSMOSS). COSMOSS, based on 268 participants, was calculated from the total scores of the IES-R, the PDI, and the PDEQ using principal component analysis which resulted in a single factor with a standardized mean of 0 and standard deviation of 1 that accounted for 76.4% of the overall variance in scores (0.380 * standardized IES-R) + (0.388 * standardized PDI) + (0.376 * standardized PDEQ).

Cognitive appraisal

A single item was used to assess cognitive appraisal: "Overall, what were the consequences of the flood on you and your family?". Response options were on a five-point scale of "Very negative," "Negative," "Neutral," "Positive" and "Very positive." This item has demonstrated its predictive validity in other SPIRAL studies by predicting DNA methylation in adolescence (Cao-Lei et al., 2015, 2016), C-Peptide secretion (Cao-Lei et al., 2018), and autistic-like traits (Laplante et al., 2019).

Timing of exposure in pregnancy

The timing of flood exposure during pregnancy was defined as the number of days between June 15, 2008, and the baby's due date. Third-trimester exposure corresponded to due dates between 0 and 93 days after June 15; second trimester, 94–186 days; and first trimester, 187–280 days.

Control variables

Obstetric complications

An abbreviated version of the Peripartum Events Scale (PES) was used to assess obstetric complications during pregnancy, labor, delivery, and the postpartum period. Each complication was rated as present or absent. PES items showed high inter-rater agreement for data extraction from medical records by two obstetricians (kappa = 0.91). In conjunction with the women's medical records, obstetric complications were divided into eleven domains (O'Hara et al., 1986). While the literature argues that the accumulation of complications for the mother during the perinatal period is linked to ASD (Lyall et al., 2012), we used a subscale reflecting maternal medical risk factors and obstetric complications to estimate maternal obstetric complications. This

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represents eight subscales containing a total of 55 items (e.g., hypertension, diabetes, chemical abuse, vaginal bleeding, duration of labor, etc) computed into a single score. For neonatal complications we selected specific items reflecting neonatal complications that have been associated with ASD risk: presence of neonatal respiratory problem (Froehlich-Santino et al., 2014); hyperbilirubinemia (Cordero et al., 2020); 5-minute APGAR score below 8 (Modabbernia et al., 2019); and gestational age at birth below 37 weeks or above 41 weeks were used (Cordero et al., 2020).

Maternal variables

Women's positive mental health was assessed post-flood by the Mental Health Continuum-Short Form (MHC-SF). The MHC-SF provides a total score and three dimension scores: emotional, psychological, and social well-being (Keyes et al., 2008). It demonstrates good internal consistency for the emotional ($\alpha = 0.84$), social ($\alpha = 0.88$), and psychological ($\alpha = 0.88$) subscales and, for the total score ($\alpha = 0.92$) (Rafiey et al., 2017). The total score was used in the analyses. Household socioeconomic status (SES) at the time of recruitment was determined using the four components of the Hollingshead Social Position Scale: maternal and paternal education and occupational status; higher scores represent higher SES (Hollingshead, 1975).

Statistical analyses

Statistical analyses were performed using IBM's Statistical Package for the Social Sciences (SPSS) version 28. Untransformed means and standard deviations for all variables are presented in Table 1. The objective hardship variable was log-transformed to correct for positive skewness. Any missing data for the predictors were imputed using multiple regression. All assumptions underlying multilevel longitudinal analyses were met. The restricted maximum likelihood (REML) approach was used for estimations with a Satterthwaite correction.

Multilevel linear modeling

Multilevel linear modeling (MLM) was used to test the longitudinal effect of PNMS on autistic-like traits. MLM considers the linear trajectory of outcomes over time from three measurement points, which for the present study was performed at 18-month intervals between the ages of 4 and 7 years (mean ages of 4⅙, 5½, and 7¼ years). We chose to treat age as a continuous variable for the precision it provides and for the variability it allows in terms of inter-individual differences in initial status. For interpretation, we centered the time variable at 4.01 years, the lowest age of participants.

MLMs are most effective when the number of predictors is limited, and they are weakly correlated with each other. A series of models were proposed, tested, and pruned to find the most parsimonious model. Our approach was to remove nonsignificant interactions from the various models, without removing important covariates. Fit indices that favor models with fewer parameters (deviance, AIC, and BIC) were used to justify the choice of the different variables kept in the final model (Tabachnick & Fidell, 2013). No imputation was performed on the autistic-like trait scores (SCQ) since MLM allows for an unequal number of observations.

Results

Descriptive statistics

Means and standard deviations, or percentages, for all outcome, predictor, and control variables can be found in Table 1. Mothers were predominantly from upper or upper-middle-class families (88.9%), non-Hispanic white (92.6%), living in couples or married (88.2%), and highly educated (83.3% graduated college or above) and had a household income of $60,000 or more (54.10%). The sample was much better educated, with a higher proportion of married couples, than the Iowa population in general. The SCQ scores at all ages did not differ significantly between boys and girls. The percentage of children meeting SCQ clinical criteria was higher at age 5½ (4.6%) than at ages 4 (2.4%) and 7 (2.1%).

Correlations

The Pearson correlation coefficients between the variables are shown in Table 2. Objective hardship and subjective distress were significantly correlated ($r = 0.394$, $p < 0.001$). SCQ scores at 4, 5½, and 7 years were also correlated with each other, with the highest coefficient between scores at 4 and 5½ years ($r = 0.567$, $p < 0.001$). SCQ scores were significantly correlated with objective hardship and subjective distress for at least one of the three ages.

Multilevel linear modeling

The multilevel modeling results are presented in Table 3. The assessment of the linearity of individual trajectories indicated that a linear model was adequate. The first step of the hierarchical MLM – Unconditional Mean Model (Level 1; see Model A) – estimated the grand mean of autistic-like traits to be 4.12 ($p < 0.001$). The intraclass correlation coefficient of 0.53 computed from this model confirmed that the multilevel approach was appropriate.

The second step – Unconditional Growth Model (Level 2; see Model B) – used time-structured data by adding the child's exact age. The average SCQ score at 4 years was 4.25 ($p < 0.001$). The proportion of variance in SCQ scores explained by this model was calculated from the unconditional mean ($\sigma^2\varepsilon = 4.12$; $p < 0.001$) and the estimate of intra-individual variation in the mean change trajectory ($\sigma2\varepsilon = 3.80$; $p < 0.001$). This allowed us to estimate that 7.6% of the change of autistic-like traits between 4 and 7 years was explained by age (Pseudo $R2\varepsilon = 0.076$). The random effect for the rate of change (age) was not significant ($p = 0.333$) and was removed from further steps. The random effect of the intercept was significant in all models.

The third step added the PNMS predictor variables into the model individually. The fixed effects estimates for objective hardship (0.71, $p = 0.011$) and for subjective distress (0.89, $p < 0.001$) were significant, but not for cognitive appraisal (Model C.1.1–C.3.1). No interactions between assessment age and PNMS variables were significant (Model C.1–C.3). Figure 1 illustrates the main effect of subjective distress on initial status at age 4 and the lack of interaction between subjective distress and child age resulting in a lack of differentiation among the trajectories of the severity of autistic-like traits over time for different levels of distress (model C.2).

Step four added all PNMS predictors into the same model (Model D). The fixed effects solution estimated a constant of 3.56 ($p = 0.002$) at 4 years old when the predictor variables were zero. Higher estimated mean SCQ levels were associated with

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Table 2. Correlation coefficients among outcome and predictor variables

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
Outcomes																		
1	SCQ 4y	–																
2	SCQ 5½y	**.567*****	–															
3	SCQ 7y	**.383****	**.424*****	–														
Prenatal stress																		
4	Objective$^{\alpha}$	.147	**.221***	.065	–													
5	Subjective	**.215***	**.206***	.162	**.394*****	–												
6	Cognitive	.009	–.134	.012	–**.282*****	–.078	–											
7	Timing	.027	–.140	–.124	.129	–.074	.015	–										
Child covariates																		
8	Sex (Males = 0)	–.074	–.096	–.153	–.109	–.118	–.037	–.036	–									
9	Gestational age	–.144	–.051	–.059	–.003	.053	.022	–.040	.007	–								
10	Breathing prob.	**.304****	**.204***	**.255***	–.066	–.024	.023	.006	–.095	–**.277****	–							
11	Hyperbilirubin.	.037	**.249****	–.116	.067	.063	.142	.022	–.035	–.130	–.010	–						
12	APGAR<8 at 5	.007	–.032	–.003	–.105	.008	.085	.096	–.113	–**.179***	**.367*****	**.169***	–					
13	Age at ass. 4y	–.189	–.009	–.015	.162	**.276****	–.072	–**.216***	–.115	.083	.089	.080	–.030	–				
14	Age at ass. 5½y	–.016	–.080	.068	.005	–.104	–.053	.168	.035	–.067	.002	–.081	–.051	.033	–			
15	Age at ass. 7y	.073	.060	.098	**.258***	.027	–.150	**.516*****	.015	–.181	**.203***	–.128	.019	.084	.073	–		
Maternal covariates																		
16	Pos. m. health	–.069	–**.294*****	–.187	–.052	–.140	–.042	.060	–.149	–.075	.018	.094	.078	–.023	.002	.005	–	
17	SES	–**.245***	–**.311*****	–.171	–.165	–.112	**.219***	.079	–.037	–.042	.058	–.033	.161	–.027	–**.178***	.002	**.223****	–
18	Obstetric comp.	–.001	.069	–.088	.031	.089	.057	–.022	–.063	–.151	**.269*****	.029	.150	.073	–.127	.033	.097	–.081

Breathing prob.: baby's breathing problems at birth; Hyperbilirubin.: hyperbilirubinemia; APGAR<8 at 5: at 5 minutes after birth; Pos. m. health: the mother's score on the Mental Health Continuum; SES: Socioeconomic status; Obstetric comp.: the obstetric complications mother's score from the Peripartum Events Scale (PES).

Significance levels are uncorrected for multiple tests.

$^{\alpha}$ Log-transformed scores.

***The correlation is significant at the $p < 0.001$ level (two-tailed).

**The correlation is significant at the $p < 0.01$ level (two-tailed).

*The correlation is significant at the $p < 0.05$ level (two-tailed).

Table 3. Multilevel linear modeling estimation – fixed effects solution

Fixed effects solution[a]								
						95% CI [LL, UL]		Pseudo[b]
Effect	β	SE	df	*t* test	Pr > |t|	LL	UL	R^2
Model A. Unconditional mean								n/a
Intercept	4.116	0.219	119.951	18.757	<0.001	3.682	4.551	
Model B. Unconditional Growth model								0.001
Intercept	4.254	0.266	99.639	16.014	<0.001	3.727	4.781	
Age	−0.088	0.102	81.980	−0.855	0.395	−0.291	0.116	
Model C.1. PNMS individually age*objective hardship								0.057
Intercept	2.964	0.672	236.198	4.410	<0.001	1.640	4.288	
Objective hardship	0.696	0.334	241.202	2.082	0.038	0.038	1.354	
Age	−0.102	0.259	181.484	−0.393	0.695	−0.613	0.409	
Age*Objective hardship	0.006	0.130	180.307	0.044	0.965	−0.252	0.263	
Model C.1.2 Objective hardship								0.057
Intercept	2.948	0.571	141.009	5.163	<0.001	1.819	4.077	
Objective hardship	0.705	0.273	124.223	2.583	0.011	0.165	1.245	
Age	−0.091	0.100	181.071	−0.915	0.361	−0.288	0.106	
Model C.2. PNMS individually age*subjective distress								0.036
Intercept	4.272	0.262	241.598	16.309	<0.001	3.756	4.787	
Subjective distress	0.801	0.330	275.507	2.427	0.016	0.151	1.451	
Age	−0.074	0.102	181.211	−0.730	0.466	−0.276	0.127	
Age*Subjective distress	0.059	0.145	185.560	0.409	0.683	−0.226	0.345	
Model C.2.1 Subjective distress								0.036
Intercept	4.281	0.261	239.872	16.424	<0.001	3.767	4.794	
Subjective distress	0.886	0.257	138.203	3.443	<0.001	0.377	1.394	
Age	−0.083	0.100	181.295	−0.829	0.408	−0.280	0.114	
Model C.3. PNMS individually age*cognitive appraisal								0.005
Intercept	5.341	1.058	250.065	5.050	<0.001	3.258	7.423	
Cognitive appraisal	−0.426	0.403	244.054	−1.057	0.292	−1.220	0.368	
Age	−0.408	0.395	187.662	−1.031	0.304	−1.188	0.372	
Age*Cognitive appraisal	0.124	0.152	187.261	0.815	0.416	−0.176	0.424	
Model C.3.1 Cognitive appraisal								0.004
Intercept	4.839	0.859	135.939	5.634	<0.001	3.140	6.537	
Cognitive appraisal	−0.230	0.323	122.900	−0.712	0.478	−0.870	0.410	
Age	−0.096	0.100	178.048	−0.960	0.338	−0.294	0.102	
Model D. PNMS								0.066
Intercept	3.564	1.128	124.054	3.161	0.002	1.332	5.796	
Objective hardship	0.422	0.296	114.545	1.422	0.158	−0.166	1.009	
Subjective distress	0.739	0.275	128.924	2.684	0.008	0.194	1.284	
Cognitive appraisal	−0.028	0.323	121.081	−0.086	0.932	−0.667	0.612	
Age	−0.084	0.100	180.704	−0.842	0.401	−0.281	0.113	
Model E. PNMS and covariates								0.226
Intercept	13.764	6.459	112.485	2.131	0.035	0.966	26.562	
Subjective distress	0.591	0.257	123.682	2.297	0.023	0.082	1.100	
Objective Hardship	0.424	0.274	106.513	1.545	0.125	−0.120	0.968	

(*Continued*)

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Table 3. (*Continued*)

	Fixed effects solution[a]							
						95% CI [LL, UL]		Pseudo[b]
Effect	β	SE	df	*t* test	Pr > |t|	LL	UL	R^2
Cognitive appraisal	0.051	0.303	113.693	0.169	0.866	−0.550	0.652	
Gestational age (wks)	−0.115	0.157	111.871	−0.730	0.467	−0.426	0.196	
Breathing prob. at birth	1.966	0.516	110.838	3.809	<0.001	0.943	2.989	
Hyperbilirubinemia	1.935	1.151	147.326	1.681	0.095	−0.340	4.210	
APGAR<8 at 5	−1.543	1.172	124.529	−1.316	0.191	−3.864	0.778	
Positive mental health	−0.042	0.017	125.275	−2.456	0.015	−0.075	−0.008	
Socioeconomic status	−0.071	0.021	113.436	−3.435	<0.001	−0.113	−0.030	
Obstetric complications	−0.081	0.069	106.525	−1.167	0.246	−0.218	0.056	
Age	−0.061	0.098	183.533	−0.622	0.535	−0.255	0.133	
Model G. Final model								0.234
Intercept	14.581	6.428	110.520	2.268	0.025	1.843	27.318	
Subjective distress	0.557	0.256	122.193	2.174	0.032	0.050	1.063	
Objective hardship	0.372	0.274	104.490	1.356	0.178	−0.172	0.915	
Cognitive appraisal	0.027	0.301	111.608	0.090	0.929	−0.570	0.624	
Gestational age (wks)	−0.120	0.156	110.181	−0.768	0.444	−0.428	0.189	
Breathing prob. at birth	1.934	0.512	108.734	3.774	<0.001	0.918	2.949	
Hyperbilirubinemia	1.991	1.144	146.168	1.741	0.084	−0.269	4.252	
APGAR<8 at 5	−1.743	1.170	123.760	−1.489	0.139	−4.059	0.573	
Positive mental health	−0.045	0.017	123.434	−2.668	0.009	−0.079	−0.012	
Socioeconomic status	−0.070	0.021	111.790	−3.417	<0.001	−0.111	−0.030	
Obstetric complications	−0.083	0.069	105.111	−1.215	0.227	−0.220	0.053	
Child sex	−0.626	0.392	109.493	−1.597	0.113	−1.403	0.151	
Age	−0.059	0.098	183.316	−0.598	0.551	−0.253	0.135	

[a]Dependent variable: SCQ.
[b]Marginal pseudo R2: Fixed effects only.

significantly higher maternal subjective distress levels ($p < 0.01$) controlling for objective hardship and cognitive appraisal. None of the other PNMS variables nor age were significantly associated with SCQ.

In step 5, mother and child covariates were added (Model E). Again, higher maternal subjective distress levels were associated with higher SCQ levels ($p = 0.023$). Having experienced breathing problems at birth was associated with higher SCQ levels at 4 years old ($p < 0.001$) while, in contrast, greater positive maternal mental health ($p = 0.015$) and higher SES ($p < 0.001$) were associated with lower SCQ levels.

In steps 6 and 7, the effects of child sex (Model F; supplementary material Table 3.1) and gestational timing of stress exposure (Model H.1–H.3; linear (timing) and quadratic (timing^2); supplementary material Table 3.1) on the SCQ score were not significant, nor were their interactions with age, indicating that neither sex nor timing of exposure had a significant effect on SCQ scores. Three-way interactions between PNMS variables, fetal sex and age were also not significant (Model F.1 to F.3; supplementary material Table 3.1). The final model (Model G) included the variables of Model E and controlled for the child's sex. According to the marginal pseudo R^2, this model explained 23% of the variance and had the lowest fit indices (Table 4). All previously significant variables remained significant after adjustment for the child's sex (subjective distress: $p = 0.031$; breathing problems: $p < 0.001$; positive maternal mental health: $p = 0.009$; SES: $p < 0.001$).

Discussion

The present study aimed to examine the effects of various dimensions of PNMS (i.e., objective hardship, subjective distress, and cognitive appraisal) experienced during the 2008 Iowa floods on children's autistic-like traits at 4 years of age, and on the rate of change in the severity of these traits between the ages of 4 and 7 years. The extent to which gestational timing of exposure, and/or child sex influences the association between PNMS and autistic-like traits was also examined. The results suggest that the greater the mothers' subjective distress following the floods, the more severe their children's autistic-like traits at age 4, and that the effect of subjective distress on the severity of the traits remains on a stable trajectory until at least 7 years of age. Neither child sex nor gestational timing of the flood exposure significantly predicted

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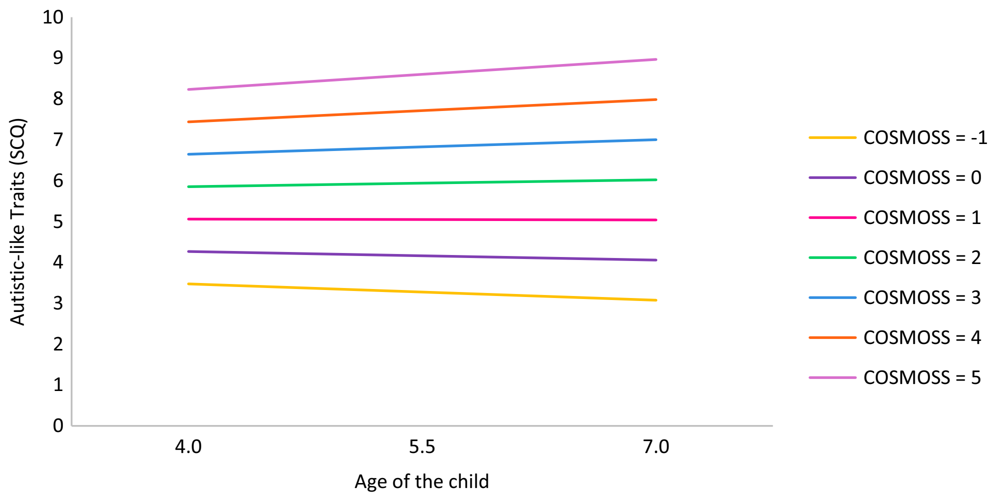

Figure 1. Predicted linear associations between different levels of maternal prenatal subjective distress (COSMOSS) and autistic-like traits score (SCQ) between 4 and 7 years.

autistic-like traits, nor did they significantly moderate the effects of PNMS on autistic-like traits.

Prenatal maternal stress effects

Consistent with the results of Walder et al. (2014), we observed that, individually, greater objective hardship and greater subjective distress predicted higher scores for autistic-like traits, while cognitive appraisal (which was not included in the Walder et al. (2014) analyses) did not (see C1–C3 models). However, when considering the PNMS dimensions within the same model (model D), only the influence of subjective distress remained a significant predictor of SCQ scores in the current study, in contrast to Walder et al.'s (2014) where both objective hardship and subjective distress were significantly associated with autistic-like traits. It is difficult to explain this discrepancy since objective hardship and subjective distress have similar correlations with each other in Project Ice Storm ($r = 0.38$; Walder et al. (2014)) and in this Iowa Flood Study ($r = 0.39$). These differences in results may, in part, reflect the nature of the events (i.e., ice storm versus flood) between the Project Ice Storm and Iowa Flood Study. All pregnant women experienced objective hardship to varying degrees during the 1998 ice storm, whereas in 2008, only women directly affected by the flooded areas experienced objective hardship as we measured it. Nevertheless, all women in both populations were likely to feel more or less affected by these disasters in their area, and to experience distress, especially as they were about to give birth to a child in this environment. Nonetheless, PTSD-like symptoms were significantly lower in the Iowa Flood Study cohort than in Project Ice Storm (King et al., 2021). Moreover, compared to Project Ice Storm, in which subjective distress was operationalized only by current PTSD symptoms at the time of recruitment, the Iowa Flood Study included questionnaires about recollections about experiences at the time of flooding (i.e., PDI, PDEQ). This latter method may have provided a better assessment of the state of distress during the disaster and, therefore, of the effect of distress on the fetus.

Prenatal maternal stress effects on the rate of change of autistic-like traits

PNMS did not influence the trajectory of autistic-like traits between the ages of 4 and 7 years. This is consistent with research showing that 80% of individual autism trajectories are stable across development (Gotham et al., 2012; Pellicano, 2012). Since, in general, there is little variance in trajectories of symptoms over time this leaves little variance to explain. Our results suggest that whatever variation there may be in individual trajectories of autistic-like traits across early childhood, PNMS does not explain it. Nevertheless, it would be interesting for a future study to consider the trend shown in Figure 1, which might suggest that the severity of prenatal maternal distress could influence the rate of change of autistic-like traits over time at later ages.

Gestational timing effects

Our finding that when the flood occurred during the pregnancy did not influence the association between PNMS and autistic-like traits contrasts with other findings (Beversdorf et al., 2005; Class et al., 2014; Kinney et al., 2008; Walder et al., 2014). According to the DOHaD model, the effects of any teratogen, including PNMS, will be seen in those fetal organs that were in a period of rapid development at the time of the exposure; thus, gestational timing of exposure ought to moderate the effects of PNMS (Charil et al., 2010; Hamada & Matthews, 2018; Veru et al., 2014). This was not supported by our data. ASD is a grouping of developmental problems with heterogeneous symptoms related to different parts of the brain that may have their own windows of susceptibility to the impact of the PNMS (Cattane et al., 2020; Paquin et al., 2021; Rakers et al., 2017). This could explain why studies observing the influence of gestational timing of the onset of PNMS on risk for autism or children's autistic-like traits differ in the vulnerable periods identified, and cover all trimesters, from the 1st (Walder et al., 2014), 2nd (Beversdorf et al., 2005; Kinney et al., 2008), to the 3rd (Class et al., 2014; Kinney et al., 2008). This difference could also reflect methodological differences across studies, including methods of assessing traits, children's ages and stressors studied. That said, Holmboe et al. (2014) found in their trajectory study that the proportion of variance in autistic-like traits due to environmental factors appeared to be influenced by different variables at different ages; thus, the effects of the same teratogen on an outcome could differ depending on the age of the children at assessment. This could explain why in Project Ice Storm, the influence of timing was present at age 6½ in Walder et al. (2014) but was no longer visible at age 19 (Li et al., 2023).

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Table 4. Fit indices

	Model A	Model B	Model D	Model E	Model G
No. of parameters	3	6	7	14	15
Deviance	1485.139	1486.737	1475.275	1428.579	1426.081
AIC	1489.139	1494.737	1479.275	1432.579	1430.081
BIC	1496.612	1509.670	1486.723	1439.953	1437.448

Model A: Unconditional mean; Model B: Unconditional Growth model; Model D: Prenatal Maternal Stress variables; Model E: Prenatal Maternal Stress variables and covariates; Model G: Final model; Without Model C: Prenatal Maternal Stress variables individually and each in interaction with age; Model F: Prenatal Maternal Stress variables, covariates, sex, and interaction between age and sex; Model F.1.–3: F-Model plus triple interaction (PNMS X age X sex); Model H.1.–3: PNMS variables separately in interaction with Timing of exposure.

Sex effects

The child's sex did not significantly moderate the relationship between PNMS and autistic-like traits, nor did sex interact with age to influence different trajectories of symptoms over time in boys and girls. These results are consistent with those of Walder et al. (2014) suggesting that boys and girls have the same level of risk of developing autistic-like traits due to PNMS. Nevertheless, in the Project Ice Storm cohort, Walder et al. (2014) showed a significant sex difference in autistic-like trait scores (boys had higher scores), which was not observed in the current cohort nor in that of Laplante et al. (2019) in an Australian PNMS cohort that also experienced flooding (Queensland, Australia, January 2011). The latter, did, however, find that children's genotype (i.e., serotonin transporter 5-HTTLPR (ls or ss) polymorphism) moderated the effects of subjective flood-related distress on autistic-like traits and did so differently by sex. Whether autistic-like traits might be more influenced by genetics in boys (Holmboe et al., 2014), and whether PNMS may be more detrimental as a function of genotype (Laplante et al., 2019) is an interesting line for future inquiry.

Obstetric complications

Some research suggests that obstetrical complications might mediate the relationship between PNMS and various psychopathologies, including schizophrenia and autism (Paquin et al., 2021). We did not, however, test this model; the maternal total score for prenatal and perinatal complications (including hypertension, diabetes, duration of labor, etc.) was not significantly correlated with either PNMS or autistic-like traits at any age, nor was it significant in our regression model.

Limitations and strengths

Although particular attention was paid to recruiting a sample covering a wider range of SES, our sample was composed primarily of families belonging to the upper or upper-middle socioeconomic classes (85%). It is, therefore, possible that the effects of the disaster on low-SES families are underestimated. Although the Iowa Flood Study is missing an unexposed control group and cannot make case–control comparisons, we can consider its design to be valid for testing dose–response associations, especially given its quasi-experimental nature since the severity of objective hardship was quasi-randomly distributed and uncorrelated with SES. Concerning the trajectory of the children's autistic-like traits, we had no information on whether any children had received clinical intervention during our assessment period, that is, between 4 and 7 years of age, which could have influenced the outcome (Pellicano, 2012). Also relevant to the trajectory analyses, it would have been beneficial to have a 4th assessment of autistic-like traits at a later age (Lord et al., 2006), since the data from the three assessments in the Iowa Flood Study limited us to a linear evaluation of the trajectory. According to Russell et al. (2012), there is an inflection point just before age 7 in the trajectory of autistic-like traits that flattens the curve. With an additional assessment at, for example, 8½ years, it would have been interesting to identify this point of inflection and to determine if it differed according to PNMS levels.

Several strengths of the study merit mention. First, the Iowa Flood Study was very quickly appended to an ongoing project at the University of Iowa, the Emotional Experiences of Women during Pregnancy Study, which was studying the effects of maternal psychosocial characteristics on obstetrical outcomes (Nylen et al., 2013). As such, a greater percentage of women in this study were pregnant at the time of recruitment than in other SPIRAL studies reducing possible recall bias. The Iowa Flood Study also included a scale of positive mental health (Mental Health Continuum – Short Form (MHC-SF)) which was a significant predictor of autistic-like traits in this study; prenatal stress studies tend to favor including maternal psychopathology as predictor while here and elsewhere (Laplante et al., 2019) we found positive mental health to be protective. Moreover, a major element that differentiates the SPIRAL studies from other studies of PNMS is the use of natural disasters as the source of stress; because the severity of the objective hardship experienced tends to be outside of the family's control (that is, an "independent" stressor), any effects of their subjective distress or cognitive appraisal can be isolated from their objective degree of hardship. In addition, because disasters have a clear date of onset, the assessment of the influence of gestational timing of the onset of the stressor on the fetus can be tested with great precision. It is worth noting that the gestational timing of the natural disaster is evenly distributed in our sample across the three trimesters of pregnancy, as is the fact that the sample has an equal number of boys and girls. Finally, multilevel linear models are a powerful tool for the study of trajectories. They respond to the problems of longitudinal estimates, in particular concerning the independence of the scores. While analyzing repeated observations of the same individuals over time violates the assumption of independence of error in general linear models, multilevel models are designed to overcome this problem. In addition, classical analyses estimate mean effects, while multilevel models allow variability of data at the intra-individual and inter-individual levels. Furthermore, these models allow for an unequal number of observations at each time point which makes it possible to manage the missing data inherent in longitudinal studies.

Clinical implications

Data suggest that the earlier in development a child receives intervention for ASD traits, the more beneficial it is (Rojas-Torres et al., 2020). By evaluating environmental risk factors early in pregnancy, it becomes possible to identify vulnerable children who

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may benefit from intervention programs. However, it may be preferable to protect the mother–fetus dyad from significant exposure to stress. In this sense, studies on doula support during the various perinatal periods show interesting results for reducing anxiety and stress with positive effects on birth outcomes (Sobczak et al., 2023). In a world where natural disasters are increasingly frequent and severe, the implementation of intervention protocols at the time of disasters, to reduce objective hardship and maternal distress, should become an important public health concern.

Conclusion

To our knowledge, this study is the first to assess the trajectory of autistic-like traits as a function of different levels of PNMS from a natural disaster. To summarize, our results suggest that both disaster-related prenatal maternal subjective distress and, to a lesser extent, objective hardship are correlated with the severity of autistic-like traits in their children between the ages of 4 and 7 years, but that PNMS has little effect on the trajectories of those traits between those ages. This study replicates and extends knowledge concerning the influence of PNMS on variation in autistic-like traits. It underscores the urgent need to rethink perinatal public health strategies, especially as natural disasters continue to increase in frequency.

Supplementary material. The supplementary material for this article can be found at https://doi.org/10.1017/S0954579424001494.

Author contributions. All authors contributed to the study conception and design. Material preparation, data collection, and analysis were performed by Suzanne King, Michael W. O'Hara, David P. Laplante, Guillaume Elgbeili, and Mylène Lapierre. The first draft of the manuscript was written by Mylène Lapierre, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.

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Competing interests. None.

Ethical approval. All procedures were approved by the Institutional Review Board at the University of Iowa and by the Comité d'éthique de la recherche en éducation et en psychologie at the University of Montreal. The procedures used in this study adhere to the tenets of the Declaration of Helsinki.

Consent to participate. Parents provided written informed consent for all phases of the study.

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