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Research paper

Maternal prenatal stress and infant emotional reactivity six months postpartum

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ABSTRACT

Background: Maternal prenatal stress has been related to infant negative affect. However, it is still unclear how different sources of maternal prenatal stress such as depressive, anxiety and pregnancy-specific anxiety symptoms are associated with reactivity outcomes. This study aimed to test the associations between different sources of maternal prenatal stress and the aspects of infant emotional reactivity at six months.

Method: Our study population (n=282) was drawn from the FinnBrain Birth Cohort Study. Prenatal stress was measured by questionnaires on maternal depression, general anxiety and pregnancy-specific anxiety at three time points across pregnancy (gwk 14, 24, 34). Based on the symptom scores, the sample was divided into mothers with high stress during pregnancy (n=110) and mothers with low stress during pregnancy (n=172). Mother-reported infant emotional reactivity and its subscales were measured six months postpartum.

Results: After controlling for background variables and maternal postnatal symptoms, overall negative emotional reactivity ($\beta=0.20$, $p<0.01$), and its aspects fearfulness ($\beta=0.15$, $p=.057$) and falling reactivity ($\beta=-0.22$, $p<0.01$), were predicted by only pregnancy-specific anxiety. No significant predictors were found for infant positive reactivity after adjusting for confounders.

Limitations: Mother reports of both maternal symptoms and infant reactivity were used, which might increase the risk of reporting bias.

Conclusions: The findings suggest that mothers experiencing stress should be provided intervention during pregnancy, and that screening should have a particular focus on pregnancy-related worries.

1. Introduction

Emotional reactivity or temperament refers to biologically based individual differences in affectivity, activity and self-regulation (Rothbart and Bates, 2006). Reactivity is generally divided into dimensions of negative and positive reactivity, of which the former refers to the tendency to experience and express negative emotions in relation to stimuli, whereas the latter refers to positive forms of reactivity, such as tendency for positive emotions, higher activity level, approach behaviors and vocal reactivity. The current evidence suggests that early individual differences in both positive and negative emotional reactivity are influenced by maternal stress during gestation, possibly through "programming" effects (Sandman et al., 2011). Specific studies of prenatal stress that examine programming influences on children's emotional reactivity have included perceived maternal stress, symptoms of depression, anxiety or pregnancy-specific anxiety (or some combination of these sources of stress).[1] Collectively, these sources of prenatal stress have been found to predict higher negative

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[1] In the present study, these symptoms are collectively referred to as prenatal stress given the general way of their use as measures of prenatal stress in the current literature, and the distress nature of mother's experience of pregnancy-specific anxiety (in comparison with pure mood symptoms).

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reactivity, including negative affect (e.g. fear, sadness, and distress/frustration) in both infants (Henrichs et al., 2009; Pesonen et al., 2005; Rouse and Goodman, 2014) and young toddlers (Agrati et al., 2015; Blair et al., 2011), and more irritability and low rhythmicity (Austin et al., 2005; Della Vedova 2014; Tees et al., 2010). Consistent with this research, prenatal stress measured as the functioning of HPA-axis (e.g. maternal prenatal cortisol or corticotrophin-releasing hormone level) has been found to predict higher infant reactivity, especially negative affect (Davis et al., 2007; de Weerth et al., 2003). In some studies, prenatal stress has also been linked to overall higher reactivity covering both positive and negative reactivity (Lin et al., 2014; Pesonen et al., 2005) or activity level (Blair et al., 2011; de Weerth et al., 2003; Henrichs et al., 2009; Werner et al., 2007), suggesting that prenatal stress might affect young children's tendency not only for negative but also for positive or overall reactivity to environmental stimuli.

While prenatal programming effects on individual differences in infant reactivity are important in their own right, in light of links between infant reactivity and later psychopathology, there also are implications for models of developmental psychopathology. For example, higher negative emotional reactivity and higher activity level have been found to be associated with both internalizing and externalizing problems in childhood, including depression and anxiety, attention deficit hyperactivity disorder (ADHD), conduct disorder (CD), oppositional defiant disorder (ODD), and even autism spectrum disorders (De Pauw and Mervielde, 2010; Putnam and Stifter, 2005; Sanson et al., 2004; Sayal et al., 2014). Furthermore, both maternal psychological and physiological stress during pregnancy are related to later mental health outcomes of the child, such as depression and anxiety (Davis and Sandman, 2012; Capron et al., 2015; Pearson et al., 2013). Thus, differences in infant emotional reactivity might be one mechanism linking fetal exposure to high maternal stress and psychopathology during childhood.

However, not all studies have found evidence for an association between prenatal stress and infant emotional reactivity (Baibazarova et al., 2013; Bhat et al., 2015; Rouse and Goodman, 2014). In a few cases, opposite findings have been reported by studies wherein it is shown that prenatal stress is related to lower infant fearfulness (Möhler et al., 2006), or that infant reactivity was associated with lower, not higher, levels of maternal stress during pregnancy (Rothenberger et al., 2011). These results suggest that the effects of prenatal stress are not consistently identified, which may be related to methodological differences in timing and the measures used. However, there are two rarely considered additional possibilities that may contribute to inconsistent findings in existing works. First, most of the studies in the field have focused on broad reactivity factors such as negative affect or single subscales of negative affect such as fearfulness, but have not considered the fine-grained aspects of the emotional reactivity (e.g. sadness, fearfulness) simultaneously. In studies that have found associations with reactivity *and* have taken into account different reactivity attributes, prenatal stress has been associated with higher infant activity level (Henrichs et al., 2009; Werner et al., 2007), higher distress to limitation and sadness (Henrichs et al., 2009), and fearfulness (Bergman et al., 2010; Henrichs et al., 2009).

Second, the source or type of prenatal stress might also explain the different outcomes across studies in relation to prenatal stress. Some studies suggest that pregnancy-specific anxiety might be an especially strong predictor of child outcomes, such as cognitive development, anxiety and brain morphology, in comparison with other prenatal psychiatric symptoms (Buss et al., 2011, 2010; Davis and Sandman, 2010, 2012; Huizink et al., 2003). Similar results have been reported between pregnancy-specific anxiety and infant emotional reactivity, including higher infant negative affect (Huizink et al., 2002) and activity level (Gutteling et al., 2005) after controlling for maternal depressive and general anxiety symptoms during pregnancy. However, some studies have not found associations between pregnancy-specific anxiety and infant emotional reactivity (Baibazarova et al., 2013; de Weerth et al., 2013; McMahon et al., 2013), and several have reported associations with maternal general anxiety (Austin et al., 2005; Braithwaite et al., 2013; Pluess et al., 2011; van den Heuvel et al., 2015) or depressive symptoms (Davis et al., 2007; Melchior et al., 2012; Rouse and Goodman, 2014), and infant reactivity, even in addition to pregnancy-specific anxiety (Henrichs et al., 2009). Even though there are studies that have considered many types of maternal mood or anxiety during pregnancy, most studies have focused on a single source, or type of stress, and the number of studies that have considered distinct aspects maternal prenatal distress simultaneously as predictors is small, especially with regard to simultaneous consideration of different infant reactivity attributes and the use of several assessments during the pregnancy. Investigating the relative role of pregnancy-specific anxiety (and other maternal prenatal psychological symptoms) on postnatal infant emotional reactivity might provide opportunities for more targeted screening of prenatal stress and optimizing infant developmental trajectories.

To summarize, existing work suggests that prenatal stress predicts higher negative emotional reactivity in infants, although there are some gaps in the current literature. Only a few studies have considered several fine-grained aspects of infant emotional reactivity (e.g. fearfulness, sadness). Furthermore, some studies suggest that pregnancy-related anxiety might be a distinct predictor of infant behavior in comparison with general anxiety or depressive symptoms, but the state of the research is currently mixed. The main aim of the present study is to extend this line of research by examining (1) the associations between prenatal stress and infant emotional reactivity in two groups of mothers and infants exposed to different levels of stress during pregnancy in a longitudinal birth cohort setting. Our hypothesis is that exposure to high prenatal stress will be associated with higher infant negative reactivity and all of its aspects (fearfulness, sadness, distress to limitations, and recovery from emotion), and, possibly, also to higher positive reactivity/activity level. Second, (2) the association between the type of maternal prenatal stress, including depressive, general anxiety and pregnancy-specific anxiety symptoms, and infant emotional reactivity is examined. It is hypothesized that pregnancy-related anxiety symptoms will be a predictor of infant negative emotional reactivity in addition to prenatal depressive or general anxiety symptoms. Third, we investigate (3) how different aspects of maternal prenatal stress are related to the more fine-grained aspects of reactivity (for example, if anxiety is more strongly related to infant fearfulness than other aspects of negative reactivity).

2. Method

2.1. Study design and participants

The sample consists of a subsample of Finnish families participating the FinnBrain Birth Cohort Study that was gathered from December 2011 through March 2014. All families attending the first trimester ultrasound visit (gestational week [gwk] 12) were informed about the study by a research nurse, and those giving their written informed consent were enrolled in the study. In all, 67% of those informed about the study gave consent. The study sample consists of 282 mothers who were qualified either as “cases” of psychological prenatal stress (n=110) or “controls” (n=172). The participant was defined as a case when she scored above the highest 94% in any two of the eight possible assessments

during pregnancy (three options for general anxiety and depressive symptoms, and two for pregnancy-related anxiety). Of the entire FinnBrain sample, cases comprise 18% of the participants. Controls were subjects scoring under the highest 67% in all of the eight assessments, and comprised 23% of the FinnBrain sample. The cut-points for the symptom questionnaires were selected based on analyses on the first 500 FinnBrain study subjects with an aim to define the highest and lowest 20th percentile of the sample with regard to the measured symptoms. Further, only subjects who returned the six-month study questionnaires including the long version of the IBQ-R (Gartstein and Rothbart, 2003) were included in the data. Subsequently, IBQ-R in study protocol was changed to short version (Putnam et al., 2014).

Data were gathered with postal and electronic questionnaires at four time points (first, second and third trimester and six months postpartum): at the end of the first trimester (gwk 14–16) mothers completed background information questionnaires, the Edinburgh Postnatal Depression Scale (EPDS) and the Symptom Checklist –90 (SCL) anxiety subscale. During the next two trimesters (gwk 24 and 34), mothers completed EPDS, SCL-90 and Pregnancy-Related Anxiety Questionnaire Revised 2 (PRAQ-R2). At six months, infant emotional reactivity was assessed with the Infant Behavior Questionnaire Revised (IBQ-R) filled in by the mother, and postnatal depression and anxiety were controlled with EPDS and SCL-90. The Joint Ethics Committee of the University of Turku and South-Western Hospital District approved the study protocol.

2.2. Measures

2.2.1. Maternal prenatal and postnatal stress

Maternal prenatal stress was assessed at gwk 14 using the Edinburgh Postnatal Depression Scale and Symptom Checklist-90 and at gwks 24 and 34 with the EPDS, SCL-90 and the Pregnancy-Related Anxiety Questionnaire 2. The EPDS is a widely used measure of both postnatal and prenatal depression (Cox et al., 1987) and consists of ten items rated from 0 to 3 (higher scores indicate more depressive symptoms). The anxiety subscale of Symptom Checklist 90 (SCL-90) is a reliable and valid measure of anxiety symptoms in both clinical and research settings (Derogatis 1983; Derogatis et al., 1973; Holi et al., 1998) and consists of 10 items rated from 0 to 5. The PRAQ-R2 is a recently revised version (Huizink et al., 2015) of the sensitive measure of pregnancy-specific anxiety (Huizink et al., 2004), and consists of 10 items rated from 1 to 5. PRAQ-R has previously been used as a predictor of postnatal outcomes independent of general anxiety (Huizink et al., 2002, 2003).

All measures showed good internal consistency throughout the study (0.88 for EPDS,0.91–0.93 for SCL-90 anxiety subscale, and 0.91 for PRAQ-R2) and were used both as a basis for defining high and low prenatal stress groups (see Study design and participants) and as continuous variables. Postnatal stress was measured at three months postpartum with the EPDS and SCL-90 anxiety subscale, with both measures again showing good internal consistency (0.86 for EPDS and 0.87 for SCL-90). Postnatal symptom questionnaires were used as continuous variables in this study.

2.2.2. Infant emotional reactivity

The Infant Behavior Questionnaire Revised (IBQ-R), a widely used, reliable and valid measure for assessing infant temperament (Gartstein and Rothbart, 2003), was completed by mothers when children reached six months of age. The IBQ-R has 191 items and is designed to measure temperament and emotional reactivity in children between the ages of 3 and 12 months. Mothers rate their infants' observed behavior during the past week or past two weeks on a scale from one to seven. Higher scores on each scale reflect higher levels of a particular temperament characteristic. The questionnaire contains three broad dimensions, of which Negative affectivity and Surgency/Positive affectivity, including the ten subscales comprising these two dimensions, were used in this study. The terms "Negative reactivity" (consisting of subscales Distress to limitations, Fearfulness, Sadness and reversed scale of Falling reactivity that describes recovery from negative emotions) and "Positive reactivity" (consisting of subscales Activity level, Smiling and laughter, High intensity pleasure, Perceptual sensitivity, Approach and Vocal reactivity) were used to refer to the two main dimensions of the IBQ-R. Each dimension and subscales demonstrated adequate internal consistency (alphas ranging from 0.68–0.89) in this investigation.

2.2.3. Background information

Maternal age at mid-gestation was calculated from the birth date given by mothers at the point of recruitment. Information about maternal education, income, parity and civil status was gathered in the first trimester questionnaire. Maternal education was measured on a scale from 1 to 10 and was further divided to four categories (1="part of secondary or secondary school", 2="high school or vocational school", 3="university/polytechnics degree", 4="higher"). Monthly income of the mother was reported on a scale from 1 to 9 (1="less than 500 euros per month", 9="more than 4000 euros per month") and was transformed to a four-category variable (1="less than 1000 euros per month", 2="from 1000 to 2000 euros per month", 3="2000 to 3000 euros per month", 4="more than 3000 euros per month"). Furthermore, mothers were asked about parity (1=primiparous, 2=multiparous) and civil status (1=married, 2=in a relationship, 3=divorced/separated, 4=widow, 5=civil partnership, 6=not in a relationship), which was then transformed into two categories (1=married/in a relationship, 2=not in a relationship). Information on the length of gestation and infant gender was based on hospital records collected continuously when the children in the sample were born. Maternal education and infant gender were used as covariates in the analyses. Other information was used only for purposes of describing the sample characteristics.

2.2.4. Statistical analyses

First, we examined the differences between non-responders and responders with independent *t*-tests and Chi-square statistics. A similar procedure was done in comparing the demographical differences of mothers with high stress (cases) and low stress (control) and their infants.

Next, the normality of the dependent variables was checked. The broad reactivity dimensions were normally distributed, but negative reactivity *subscales* fearfulness, sadness and falling reactivity, and positive reactivity *subscales* high intensity pleasure and approach were skewed. These variables were transformed with logarithm transformations, using recommendations made for treating skewed data (Tabachnick and Fidell, 2007).The associations between the study variables were investigated with zero-order Pearson correlations. Subsequently, *t*-tests were performed between case and control groups for both reactivity dimensions and their ten subscales to find out if case and control groups differed in terms of infant emotional reactivity.

Third, the centered overall means of each symptom scale assessment across pregnancy were used as a predictor of infant reactivity in regression models. The value of pregnancy mean was calculated separately for SCL-90, EPDS and PRAQ-R2 to form predictors of each symptom scale, and the linearity of the associations between symptoms scales and infant reactivity was checked. Standard multiple regression analyses were performed to examine predictors of infant negative and positive emotional reactivity, and additionally, of the reactivity subscales in which the *t*-test group

differences were significant or near-significant (distress to limitations, sadness, fearfulness, falling reactivity, smiling and laughter, perceptual sensitivity and vocal reactivity). In the first step of each model, we included infant gender and maternal education to control for background factors. In the second step of each model, postnatal depression and anxiety were added, and finally, prenatal psychiatric symptom averages were added to the third step of each model.

2.2.5. Missing data

The missing data analysis was done based on the first 2000 families recruited in the FinnBrain Birth Cohort. Of these, 675 belonged to the focus cohort, and 170 (25%) had missing data on six month questionnaires (including the IBQ-R). Non-respondent mothers were not different in terms of parity ($p=0.635$), but had attained lower education levels ($p<0.001$), were somewhat younger ($p<0.05$) and had higher levels of depression ($p<.001$) and anxiety ($p<0.001$) in the first trimester than the mothers who responded to the six month questionnaires.

3. Results

3.1. Sample characteristics

The demographic variables for the sample are shown in the Table, 1. The case and control groups did not differ in terms of maternal age, civil status, gestational age at birth or infant gender. There was a difference between the groups in maternal income and maternal education, with control mothers being more highly educated and earning higher incomes in relation to case mothers.

3.2. Zero-order correlations

In correlational analyses, mother-reported infant negative emotional reactivity was associated positively with all prenatal and postnatal stress measures at each assessment point (see Table, 2). Moreover, negative emotional reactivity *subscales* showed a similar pattern of associations with one exception: falling reactivity was correlated with depressive and pregnancy-specific anxiety symptoms, but correlations with general anxiety were modest and non-significant. Infant positive emotional reactivity was positively associated with first trimester maternal depressive and anxiety symptoms, and depressive and general anxiety throughout the pregnancy. Moreover, there were a few specific associations within positive reactivity subscales: Activity level was positively associated with pregnancy-specific anxiety throughout during each trimester; infant smiling and laughter was positively associated with the first trimester general anxiety symptoms and general anxiety mean throughout the pregnancy; and perceptual sensitivity was positively associated with all prenatal and postnatal stress measures at each assessment. There were no other significant associations between prenatal and postnatal stress measures and other infant positive reactivity subscales. Moreover, the correlations between prenatal stress measures were investigated, and they ranged from moderate to high for trimester scores (0.45–0.75), for pregnancy means (0.55–70), and for postnatal and prenatal measures (0.40–0.65).

3.3. Group differences in emotional reactivity

There was a statistically significant difference in both mother-reported infant negative and positive emotional reactivity between the groups (See Table, 3): the infants of the mothers with

Table 1
Subject characteristics (n=282).

Characteristics	Sample n=282		Cases n=110		Controls n=172		p
	n (%)	Mean (SD)	n (%)	Mean (SD)	n (%)	Mean (SD)	
Maternal age, years		30.6 (4.4)		30.1 (4.5)		30.9 (4.2)	n.s.
Maternal income							< 0.05
< 1000 e	70 (25)		34 (32)		36 (21)		
1000–2000	137 (49)		56 (52)		81 (47)		
2000–3000	61 (22)		15 (14)		46 (27)		
> 3000	12 (3)		3 (3)		9 (5)		
Maternal education							< 0.01
Secondary school or less	10 (4)		7 (6)		3 (2)		
High school/vocational	85 (30)		43 (40)		42 (24)		
University/polytechnics	171 (61)		54 (50)		117 (68)		
Higher	14 (5)		4 (4)		10 (6)		
Civil status, married/in a relationship	270 (99)		104 (99)		166 (99)		n.s.
Length of gestation		39.7 (1.7)		39.8 (1.9)		39.7 (1.7)	n.s.
Infant gender, boy	156 (55)		65 (59)		91 (53)		n.s.
Maternal stress							
EDPS mean (0–30)		4.5 (4.11)		8.8 (3.6)		1.9 (1.3)	< 0.001
EPDS gwk 14		4.9 (4.8)		9.1 (4.9)		2.1 (1.7)	
EPDS gwk 24		4.7 (4.7)		8.9 (4.6)		1.9 (1.7)	
EPDS gwk 34		4.3 (4.4)		8.3 (4.3)		1.8 (1.7)	
SCL-90 anx.mean (0–50)		3.5 (4.6)		8.0 (4.9)		0.8 (0.8)	< 0.001
SCL-90 gwk 14		3.6 (5.3)		7.7 (6.9)		1.0 (1.2)	
SCL-90 gwk 24		3.9 (5.6)		8.5 (6.4)		0.9 (1.2)	
SCL-90 gwk 34		3.3 (5.4)		7.6 (6.8)		0.7 (1.0)	
PRAQ-R2 mean (10–50)		22.2 (7.2)		29.0 (6.0)		18.1 (3.8)	< 0.001
PRAQ-R2 gwk 24		22.3 (7.9)		29.4 (7.4)		18.0 (4.1)	
PRAQ-R2 gwk 34		22.2 (7.3)		28.7 (6.6)		18.2 (4.4)	
EPDS at 6 months (0–30)		3.99 (4.2)		7.1 (4.6)		2.0 (2.4)	< 0.001
SCL-90 at 6 months (0–50)		2.4 (3.8)		5.1 (4.8)		0.6 (1.2)	< 0.001

Table 2
The Pearson correlations for maternal prenatal and postnatal stress and infant emotional reactivity: negative emotional reactivity, positive emotional reactivity, and the subscales.

	Negative reactivity	Distress	Fear	Sadness	Falling reactivity	Positive reactivity	Activity level	Smiling	High intensity pleasure	Perceptual	Approach	Vocal
First trimester												
EPDS	.26**	.23**	.16**	.20**	−.16**	.15*	.07	.10	.05	.19*	.10a	.10
SCL-90	.17**	.12a	.12a	.14*	−.10a	.13*	.06	.12*	.05	.12*	.07	.10a
Second trimester												
EPDS	.31**	.28**	.17**	.24**	−.19**	.10a	.06	.06	−.01	.15*	.09	.03
SCL-90	.27**	.21**	.24**	.20**	−.11a	.12*	.06	.09	−.02	.15*	.07	.08
PRAQ-R2	.30**	.24**	.19**	.19**	−.23**	.07	.12*	.01	.04	.12*	.04	.01
Third trimester												
EPDS	.27**	.23**	.15*	.26**	−.14*	.11a	.05	.04	−.01	.18**	.07	.06
SCL-90	.21**	.18**	.11a	.21**	−.07	.10	.02	.07	.03	.13*	.07	.04
PRAQ-R2	.28**	.22**	.16**	.17**	−.24**	.08	.12a	−.01	.04	.14*	.01	.03
Postpartum												
EPDS 6 months	.27**	.28**	.13*	.23**	−.12a	.09	.03	.01	.05	.18**	.04	.05
SCL 6 months	.24**	.24**	.14*	.21**	−.08	.10	.01	.01	.04	.19**	.07	.05
Pregnancy means												
EPDS	.30**	.27**	.17**	.25**	−.16**	.14*	.08	.09	.05	.19**	.09	.07
SCL-90	.23**	.18**	.19**	.19*	−.09	.14*	.07	.13*	.04	.15*	.07	.09
PRAQ-R2	.29**	.23**	.18**	.18**	−.24**	.09	.12*	.01	.06	.13*	.02	.03

Distress= Distress to limitations, Fear=Fearfulness, Smiling =Smiling and laughter, Perceptual=Perceptual sensitivity, Vocal =Vocal reactivity.
* $p < .05$.
** $p < .01$.
a $p < .10$.

Table 3
The means and mean differences between the case group (infants exposed to high maternal prenatal stress) and the control group (infants exposed to low prenatal stress).

	Mean (SD)		t (df)	p
	Cases	Controls		
Negative emotional reactivity	3.09 (0.64)	2.76 (0.60)	4.278 (279)	0.000
Distress to limitations	3.42 (0.88)	3.04 (0.80)	3.69 (279)	0.000
Fearfulness	2.69 (0.97)	2.34 (0.98)	3.31 (271)	0.001
Sadness	3.46 (0.99)	3.10 (0.90)	3.05 (277)	0.003
Falling reactivity	5.23 (0.78)	5.43 (0.73)	2.21 (279)	0.030
Positive emotional reactivity	4.93 (0.64)	4.69 (0.68)	2.97 (280)	0.003
Activity level	4.57 (0.75)	4.42 (0.76)	1.62 (280)	0.106
Smiling and laughter	4.78 (1.18)	4.54 (1.08)	1.76 (277)	0.079
High intensity pleasure	6.08 (0.71)	5.99 (0.74)	.94 (274)	0.351
Perceptual sensitivity	4.05 (1.13)	3.60 (1.25)	3.10 (280)	0.002
Approach	5.66 (0.66)	5.48 (0.83)	−1.54 (272)	0.124
Vocal reactivity	4.51 (0.98)	4.23 (1.03)	2.28 (280)	0.023

Table 4
The standard multiple regression for infant negative emotional reactivity.

	adj. R^2	ΔR^2	β	Partial r
Step 1	−0.00	0.00		
Maternal education			0.04	0.04
Infant gender			0.06	0.04
Step 2	0.04**	0.05**		
Maternal education			0.07	0.07
Infant gender			0.08	0.10
EPDS at 6 months			0.16a	0.13*
SCL at 6 months			0.09	0.07
Step 3	0.10**	0.06**		
Maternal education			0.11a	0.11a
Infant gender			0.12a	0.12a
EPDS at 6 months			0.03	0.02
SCL at 6 months			0.02	0.01
Prenatal EPDS mean			0.15	0.08
Prenatal SCL mean			0.00	0.00
PRAQ-R2 mean			0.20**	0.16**

* $p < 0.05$.
** $p < 0.01$.
a $p < 0.10$.

high stress during pregnancy were higher in both positive and negative emotional reactivity compared to the infants of mothers with low stress during pregnancy. The difference between the groups was also significant across all negative reactivity subscales. There was a significant difference in positive reactivity *subscales* perceptual sensitivity, approach and vocal reactivity, with infants of mothers who experienced high stress during pregnancy having higher scores in all three subscales. The difference between groups in infant smiling and laughter approached significance.

3.4. Associations between different psychiatric symptoms and infant emotional reactivity

The regression analysis for different maternal psychiatric symptoms and infant negative reactivity is presented in Table 4. After adjusting for covariates, only pregnancy-specific anxiety was significantly associated with infant negative emotional reactivity; higher pregnancy-specific anxiety symptoms throughout the second and third trimesters predicted higher negative emotional

reactivity. Pregnancy-specific anxiety symptoms were held as the only significant predictor ($\beta=0.16$, $p=0.028$) even when leaving out all background factors and postnatal depressive and general anxiety symptoms, which might have diminished the variance of prenatal depressive and general anxiety symptoms as predictors. For positive emotional reactivity, no significant predictors were found.

We repeated the regression analyses for the negative and positive reactivity *subscales* in which the case and control groups differed from each other based on *t*-test analyses to determine which factors explained each reactivity attribute. In the analyses of the negative reactivity subscales, infant distress to limitations and infant sadness were not predicted by any of the prenatal stress measures. Infant fearfulness was positively predicted by maternal pregnancy-specific anxiety mean ($\beta=0.15$, $p=0.057$) along with female gender ($\beta=0.24$, $p<0.001$). Infant falling reactivity was also negatively predicted by maternal pregnancy-specific anxiety mean ($\beta=-0.22$, $p=.005$), suggesting that there was an association between higher pregnancy-specific anxiety and lower infant recovery from negative emotions. None of the prenatal stress measures significantly predicted infant smiling and laughter, perceptual sensitivity, approach or vocal reactivity.

4. Discussion

In this study, the association between maternal prenatal stress and mother-reported infant emotional reactivity was examined by investigating differences between infants exposed to high or low maternal stress during pregnancy. Moreover, the relation of pregnancy-specific anxiety with infant emotional reactivity in addition to general anxiety and depressive symptoms was investigated to gain a more nuanced understanding of the contributions of distinct sources of maternal prenatal stress in predicting infant outcomes, and, distinct aspects of infant reactivity. In line with earlier research, it was found that infants of mothers with severe prenatal stress were rated higher in negative emotional reactivity. Moreover, maternal pregnancy-specific anxiety was found to predict infant negative emotional reactivity when controlling for background factors and other prenatal and postnatal symptoms experienced by mothers. When fine-grained aspects of infant negative emotional reactivity were considered, only perceived infant fearfulness and falling reactivity were predicted by pregnancy-specific anxiety. Prenatal stress was not found to predict any other aspects of infant emotional reactivity after controlling for covariates.

The main findings of the present study support earlier findings in showing that infants of the mothers with high prenatal stress are rated higher in negative emotional reactivity. However, our findings extend existing work in several notable ways. First, our findings suggest that maternal pregnancy-specific anxiety might be a distinct aspect of maternal prenatal stress in predicting infant negative emotional reactivity outcomes (see also Blair et al., 2011). Second, it was found in the present study that the effects of pregnancy-specific anxiety seem to be restricted to specific, fine-grained aspects of infant negative emotional reactivity, a possibility rarely considered in prior studies. However, the underlying mechanisms behind the differences between the sources of stress are unclear. It might be that pregnancy-specific anxiety captures specific stress experienced by a group of mothers who are more strongly affected by pregnancy and other life-changing events, in relation to mothers with either low emotional reactivity or more general experience of negative mood in different situations of life. Pregnancy-specific anxiety might be a marker of reactivity in this group of mothers and thus, a tendency that might affect the way that these mothers rate their infants or, a trait that is transferred to the children of these mothers via genetic or environmental pathways (e.g. through parenting). For the mothers with high pregnancy-specific anxiety, the pregnancy-related changes in the nervous system might also be more substantial, and this way, the experience of stress may more consistently be related to infant outcomes. For these reasons, the factors predicting higher levels of pregnancy-specific anxiety, including maternal temperament and personality traits, should be more thoroughly investigated.

In addition, the observation of the course of maternal prenatal stress in this investigation (see Table 1) shows that maternal depressive and general anxiety symptoms tend to decrease slightly between the second and third trimesters, but the experience of pregnancy-specific anxiety stays stable both in case and control groups. Previous studies have shown that even though maternal stress hormone levels rise throughout the pregnancy (Majzoub and Karalis, 1999), the maternal experience of stress diminishes (Glynn and Sandman, 2011; Glynn et al., 2004). In addition, some studies have suggested that pregnancy-specific anxiety should decrease towards the delivery as maternal concerns about the survival and development of the fetus are minimized (McMahon et al., 2013). However, this pattern does not seem to fit with the change of pregnancy-specific anxiety in our sample (see Table 1 in Results section). It may be that some pregnancy-specific stressors, such as worries related to delivery, become more prominent towards the end of the pregnancy and explain some of the more state-specific nature of pregnancy-specific anxiety and associations with infant outcomes.

Second, although infants exposed to high prenatal stress were consistently higher in all aspects of negative reactivity and lower in recovery from negative emotions, only infant falling reactivity and fearfulness were predicted by maternal symptoms of pregnancy-specific anxiety. In one previous study (Henrichs et al., 2009), pregnancy-specific anxiety was related to fearfulness. However, contrary to our findings, Henrichs et al. (2009) found that prenatal general anxiety also predicted activity level and sadness, and uniquely infant distress. The inconsistencies in the findings may be related to the use of slightly different outcome measures, different measures of pregnancy-specific anxiety, and differences in the sample sizes. However, the findings from both of these studies propose that different reactivity attributes are related, assessed and perhaps also programmed differently according to maternal symptom profiles. For instance, in both studies, only pregnancy-specific anxiety predicted infant fearfulness, which in turn is known to be related to children's later anxiety symptoms (Clauss and Blackford, 2012). In our study, fearfulness was also predicted by infant gender, with girls being assessed as more fearful by mothers than boys, which is a common finding in reactivity studies (Else-Quest et al., 2006; Gartstein et al., 2010). Consistent with the earlier studies that rarely have shown an association between prenatal stress and positive emotional/overall reactivity, we found no association between prenatal stress and positive emotional reactivity after adjusting for confounders. This suggests that individual differences of positive emotional reactivity in this study were explained by factors other than exposure to prenatal maternal stress. Moreover, this finding adds to the growing evidence that infant negative emotionality reactivity may be selectively affected by maternal prenatal stress.

It must be noted that the effect size found for prenatal stress and negative emotional reactivity in the present study was small, and prenatal stress explained only 6% of the variance in infant negative emotional reactivity. This is in line with previous studies (Davis et al., 2007; Henrichs et al., 2009; Huizink et al., 2002) and supports the line of reasoning that prenatal stress has a modest effect in the multifactorial origins of infant emotional reactivity. This also suggests that the lack of consistency in findings in previous studies might be at least partly due to the small effect size

that might easily disappear in the presence of other confounding factors, or when small sample sizes are used in such studies.

Clinically, our findings support the view that the prevention of early negative reactivity, and possibly, early externalizing and internalizing disorders, should be started during the pregnancy period. This would also help to minimize the risk of later externalizing and internalizing symptoms that are predicted by higher emotional reactivity in infancy. The most salient way of intervention would be a community-based treatment of maternal depressive, anxiety and especially pregnancy-specific anxiety symptoms experienced during pregnancy. If the anxiety experienced by the mothers is specific to pregnancy or delivery, these should be given particular attention in the screening, and the intervention should be targeted to diminish these worries.

Our study has several strengths. We used a longitudinal approach in a large cohort study, which made it possible to consider prenatal stress at several different time points to measure overall levels of maternal symptoms during pregnancy and during the postnatal period. Only a fraction of previous studies have assessed maternal stress several times across pregnancy (e.g. Braithwaite et al., 2013; Davis et al., 2007; Huizink et al., 2002), whereas most have collected data at a single time point. As the reliability of maternal distress measurement is strengthened by multiple assessments, a need for longitudinal research has been articulated in the literature (Blair et al., 2011). Furthermore, we used valid and reliable self-report methods in the assessment of both maternal pre- and postnatal stress and infant emotional reactivity. However, there are also several limitations that should be considered in future work. First, we used only mother reports of infant reactivity which we associated with mother's report of her own symptoms, which increases the risk of reporting bias. However, this concern is somewhat mitigated by the longitudinal approach (e.g., mothers completed measures of prenatal stress long before they completed measures of infant emotional reactivity). Moreover, parent reports of infant emotional reactivity have been found to reflect infant behavior relatively well (Kochanska et al., 1997), and parents are able to provide insights regarding infant emotional reactivity across a wider-range of situations relative to observational measures obtained in a laboratory setting (Gartstein and Marmion, 2008). The analyses in this study also revealed that the effect of prenatal stress was not mediated by maternal postnatal mental health symptoms, which means that maternal prenatal symptoms seem to have unique effects on infant behavior. Still, our modeling could not rule out the possible bias especially in case of depressive and general anxiety symptoms which were measured both pre- and postnatally. Third, our sample was relatively well-educated. We also had relatively high attrition at the six month questionnaire, which might have affected the results given that non-respondents seemed to differ from respondents in terms of socioeconomic factors, age, and depressive and anxiety symptoms. However, because of the use of a case-control-design, adequate numbers of mothers with high levels of prenatal stress were included in the sample.

To conclude, consistent with the earlier research, maternal prenatal stress and specifically pregnancy-specific anxiety predicted infant negative emotional reactivity and several of its subscales (fearfulness, falling reactivity) after adjusting for covariates. This suggests that prenatal stress and especially pregnancy-specific worries are related to the origins of infant negative emotional reactivity, placing children at higher risk of later externalizing and internalizing symptoms. The prevention of higher negative emotional reactivity should be focused on the mothers during pregnancy (van den Heuvel et al., 2015), and stress symptoms related to the pregnancy and delivery should be given particular attention in the screening and intervention. The ongoing research has already proposed that interventions might be effective in reducing prenatal stress (Hall et al., 2015) which suggests that pregnancy-related worries might be not only important, but also favorable ground for intervention.

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