



Maternal trait anxiety, emotional distress, and salivary cortisol in pregnancy

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ABSTRACT

Animal models suggest that stress-induced hormonal changes in the mother during pregnancy lead to enduring changes in the fetus and empirical links between prenatal maternal stress and negative child development have been discerned repeatedly in human studies. But the role of heritable personality traits has received little attention in the latter work. The goal of the current study was to investigate the relationship between maternal personality, psychological measures of maternal distress and maternal salivary cortisol during pregnancy. Maternal reports of personality (16 PF) and stress-related psychological measures (depression, pregnancy-related anxiety, perceived stress, negative life events) as well as salivary cortisol samples of 66 healthy pregnant women were collected in early and late pregnancy. Maternal trait anxiety proved related to all stress-related psychological measures and high anxiety predicted low baseline cortisol awakening levels in early pregnancy. Maternal trait anxiety is related to both psychological and biological stress measures during pregnancy.

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A growing body of evidence links maternal emotional distress during pregnancy with negative child functioning in the behavioral, emotional, and cognitive domain (for review of the literature see: Huizink et al., 2004; Ruiz and Avant, 2005; Van den Bergh et al., 2005b; Rice et al., 2007). Prenatal programming of fetal stress reactivity is the most often suggested mechanism responsible for this association. More specifically, the fetal programming hypothesis suggests that elevated levels of maternal cortisol in response to psychological or physical stressors produce permanent alterations of the hypothalamic–pituitary–adrenal (HPA) axis of the developing fetus (Barker, 1998; Egliston et al., 2007). Consequently, such elevated stress reactivity – an individual physiological trait expected to extend across childhood into adult life (Kofman, 2002; Huizink et al., 2004; Weinstock, 2005) – contributes to negative child development (Van den Bergh et al., 2005b). Because experimental studies with animals prove generally consistent with such prenatal programming, it is assumed that the same mechanisms operate in humans.

While animal studies allow for the experimental induction of stress across randomized groups and thus afford precise control of stress exposure and other important variables, human studies on prenatal stress effects are generally limited by being observational. Due to this methodological constraint, the discerned relationship

between prenatal stress and child development in human studies could be an artifact of enduring maternal personality traits, reflective of underlying heritable mechanisms given the highly heritable nature of personality (Jang et al., 1996), influencing not only maternal reports of stress during pregnancy but also the child's postnatal functioning by means of shared genes. Thus, enduring personality characteristics of mothers may account for the putative causal – and compromising – influence of prenatal stress on children's development. It is not difficult to imagine, in fact, that personality traits specifically related to stress reactivity and sensitivity (e.g., neuroticism, trait anxiety) may influence a pregnant woman's reporting and/or experiencing of prenatal stress (e.g., cortisol reactivity). If this is so, it would compromise any causal interpretation of associations linking prenatal stress with postnatal child well-being. Thus, the purpose of the research reported herein is to explore links between stress-related personality traits of pregnant women and measures of their prenatal stress, including cortisol levels. It is predicted that neuroticism/trait anxiety would be reflected in both psychological and physiological measures of prenatal stress.

Neuroticism, reflecting proclivities to experience negative affect (Costa and McCrae, 1992), to arouse quickly when stimulated and inhibit slowly, and to appraise events as stressful (Widiger et al., 1984), is one personality trait often associated with response to stress (Costa and McCrae, 1992). Behavior-genetic studies reveal it to be 40–50% heritable (Plomin et al., 1994; Jang et al., 1996; Eaves et al., 1999). Many studies chronicle links between neuroticism and psychological distress and emotional disorders (Bolger and Schilling,

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1991; Kendler et al., 1993; Engelhard et al., 2006; Hettema et al., 2006). Empirical evidence also chronicles links between neuroticism and biological stress response in humans, such that high neuroticism is associated with dysregulated autonomic nervous system functioning (e.g., lower heart rate variability, see Riese et al., 2006) and altered HPA axis functioning. Highly neurotic individuals manifest a blunted cortisol response when exposed to stress (Oswald et al., 2006), a higher range of dose-dependent cortisol response after the application of naloxone, an opioid receptor antagonist (Mangold and Wand, 2006), and enhanced early morning cortisol levels 30 min after awakening (Portella et al., 2005). As it turns out, neuroticism also proves related to exposure to stressful situations, with individuals scoring high on neuroticism experiencing more stressful life events than do those scoring low (Bolger and Zuckerman, 1995; Kendler et al., 2003).

Considered together, findings such as those just summarized raise the very real possibility that maternal personality traits contribute to the phenomenological and biological experience of stress during pregnancy. Indeed, it seems eminently plausible that maternal personality may influence (1) self-reported psychological stress measures (e.g., depression, anxiety), (2) biological measures of stress (e.g., cortisol levels), and even (3) exposure and reaction to stressful situations and experiences (e.g., negative life events, natural disasters).

Surprisingly, personality measures, apart from a study by Mohler et al. (2006), have generally not been included in research on prenatal programming via prenatal maternal distress, though several well designed studies have controlled for *postnatal* anxiety and depression, two fundamental facets of neuroticism, in attempt to distinguish emotional stress experienced during fetal life and postnatal exposure (e.g., Huizink et al., 2002; O'Connor et al., 2003; Davis et al., 2004; Van den Bergh et al., 2005a). What such research designs cannot do, however, is disentangle putative effects of prenatal stress from maternal personality characteristics such as neuroticism which may influence both the predictors and outcomes of prenatal programming studies.

Given this background, the main objective of the work reported herein was to investigate the relationship between maternal personality, psychological measures of distress, and maternal salivary cortisol, all measured during pregnancy. To this end, we analyzed data from a prospective longitudinal study (see Rieger et al., 2004; Wurmser et al., 2006) in which personality, several measures of psychological distress, and the cortisol awakening response were assessed in healthy women both in early and late pregnancy. This work is thus conceptualized as a first step in exploring, eventually, the role of personality, measured prenatally, in accounting for effects of prenatal stress on child well being. Based on the preceding analysis, we expected maternal personality – specifically trait anxiety (i.e., neuroticism) – to be positively related to maternal self-report measures commonly used in the research of prenatal stress effects (perceived stress, depression, pregnancy anxiety, and negative life events) and with maternal cortisol levels of the cortisol awakening response during pregnancy.

1. Method

1.1. Overview

The present work is based on data from a prospective longitudinal study on the effects of prenatal maternal stress on early postnatal infant development employing several assessment points during pregnancy and the early postpartum period (Rieger et al., 2004; Wurmser et al., 2006). For the present study only data collected during the prenatal period was considered. Subject recruitment and data collection took place in Trier, Germany.

1.2. Sample and procedure

Subjects were recruited in collaboration with local obstetricians/gynecologists in private practice, clinic departments of gynecology and obstetrics, information

centers for pregnant women, and by advertisements in local newspapers. Women that met inclusion criteria (age of 16 years or older and fluency in German) were contacted by phone and briefly informed about the study's research protocol. Exclusion criteria were: (a) severe medical complications (acute or chronic physical diseases, such as gestational diabetes, metabolic diseases, hypertension, thyroid hyper function), (b) signs of fetal malformation, (c) multi-fetal pregnancies, and (d) psychiatric problems (women were excluded if their answer to the screening question "Are you currently suffering from a psychiatric disorder or do you receive medical or psychological treatment for psychological problems?" was positive). After providing informed consent for participation eligible women were invited for a first assessment at 10–20 weeks gestation (early pregnancy) and a second assessment at 32–34 weeks gestation (late pregnancy).

Originally, a total of 94 women were recruited into the study. One woman was excluded due to being pregnant with twins, 6 women denied further participation after the introductory interview at first contact, 11 women did not complete the personality assessment, 5 women lacked cortisol measurements at both assessment points, 4 women were excluded due to other patterns of missing data and one woman due to extremely high cortisol levels. Consequently, data of 66 (70.2%) women were available for the present study. Comparisons between the selected sample of 66 and the 28 excluded women indicated no significant differences between the two groups on demographic, biological, or psychological variables. Eight of the 66 included women reported smoking during pregnancy with a mean consumption of 10.29 cigarettes per day ($SD = 9.16$) and eight women reported drinking alcohol during pregnancy ($M = 1.80$ times per month, $SD = 1.79$). Demographic characteristics of the complete sample and the low and high trait anxiety subgroups (split across the median) are displayed in Table 1.

Eleven women joined the study after 20 weeks of gestation and were consequently excluded from analyses of the early pregnancy as were two women lacking cortisol values for this period. Women of the remaining early pregnancy subsample ($n = 53$) were at 14.62 ($SD = 3.57$) weeks of gestation at first assessment. For the late pregnancy assessment 6 women had to be excluded due to missing cortisol values resulting in a subsample of $n = 60$. Sample sizes for the different analyses varied additionally due to different patterns of missing data.

All women were paid 200 Euro for their time and efforts in participating in the initial project. The study protocol was approved by the Ethical Committee of the University of Trier and is consistent with the revised Helsinki Declaration of 1975.

1.3. Instruments

1.3.1. Structured interviews

Structured interviews were conducted by trained female research assistants at both assessment points and inquired about sociodemographic (e.g., age, education, occupation, income, marital status) and medical information. During the interview in early pregnancy women were asked whether they were currently smoking (and if yes, how many cigarettes per day), consuming alcohol (and if yes, how often per month), and whether they experienced severe psychological stress since the beginning of the pregnancy.

1.3.2. 16 Personality Factor Questionnaire (16-PF)

The 16PF Questionnaire is a 184-item self-report instrument that measures the sixteen personality dimensions proposed by Cattell et al. (1970). Each item represents a statement (e.g., "I believe I worry less than most people") which the respondent has to rate on a three-point scale as "true", "not true", or "?" ("?" is an open answer that could stand for "unsure", "sometimes" and the like). From subject responses to the questionnaire, scores are derived for each of the sixteen personality factors of which scores for five Global Factors are computed. The Global Factors are extraversion (tendency to be sociable, assertive, active), anxiety (tendency to be easily upset, worried, overwhelmed; in the current study this global factor is referred to as trait anxiety in order to avoid confusion with other anxiety measures), tough-mindedness (tendency to focus on objectivity, to prefer logical, realistic solutions), independence (tendency to be dominant, fearless, skeptic of others), and self-control (tendency to be conscientious, restrained, organized). The 16PF Global Factor anxiety correlates with the neuroticism dimension of the NEO-FFI questionnaire (Costa and McCrae, 1992) at $r = .64$, the 16PF extraversion with the NEO-FFI extraversion at $r = .67$ and the 16PF self-control with the NEO-FFI conscientiousness at $r = .50$. Internal consistencies of the 16PF Global Factors range from $\alpha = .73$ to $.87$ (for Global Factor anxiety $\alpha = .84$), retest-reliabilities from $r = .83$ to $.90$. The validated German version of the 16PF uses "standardized ten" (sten) score scales ranging from 1 to 10, with a mean of 5.5 and a standard deviation of 2, which relates individual scores to the scores of a normative German sample of 669 adult women (Schneewind and Graf, 1998). 16PF stens of 4–7 are considered within the "average" population range. The 16PF was administered in late pregnancy.

1.3.3. Perceived Stress Scale (PSS)

The PSS (Cohen et al., 1983) is the most widely used psychological instrument for measuring the perception of stress designed to provide a global measure of context free stress. This 14-item scale assesses the frequency of experiencing a situation as unpredictable, uncontrollable, or overloading. Participants indicate on a five-point scale from "never" to "very often" how frequently they experienced subjective affective and cognitive stress reactions, subjective effectiveness of and confidence

Table 1
Demographic characteristics of the sample.

Variables	Full sample <i>n</i> = 66, <i>n</i> (%)	Low trait anxiety subgroup <i>n</i> = 33, <i>n</i> (%)	High trait anxiety subgroup <i>n</i> = 33, <i>n</i> (%)
Age at first contact (years)	<i>M</i> = 30.7, <i>SD</i> = 4.8 (range: 16–39)	<i>M</i> = 32.4, <i>SD</i> = 3.5 (range: 24–38)	<i>M</i> = 29.0, <i>SD</i> = 5.4 (range: 16–39)
Living situation			
Living with partner	60 (90.9%)	32 (97.0%)	28 (84.8%)
Living without partner	6 (9.1%)	1 (3.0%)	5 (15.2%)
Education			
<High school	26 (39.4%)	11 (33.3%)	15 (45.5%)
High school graduate	20 (30.3%)	9 (27.3%)	11 (33.3%)
College graduate	20 (30.3%)	13 (39.4%)	7 (21.2%)
Monthly income per household			
<750 Euro	4 (6.2%)	1 (3.0%)	3 (9.4%)
750–1500 Euro	9 (13.8%)	4 (12.1%)	5 (15.6%)
1500–3000 Euro	30 (46.2%)	16 (48.5%)	14 (43.8%)
>3000 Euro	22 (33.8%)	12 (36.4%)	10 (31.3%)
Parity			
Primiparous	27 (40.9%)	13 (39.4%)	14 (42.4%)
Multiparous	39 (59.1%)	20 (60.6%)	19 (57.6%)
Planned pregnancy			
Planned	47 (71.2%)	25 (75.8%)	22 (66.7%)
Unplanned	19 (28.8%)	8 (24.2%)	11 (33.3%)
Wanted pregnancy			
Wanted	58 (87.9%)	31 (93.9%)	27 (81.8%)
Unwanted	8 (12.1%)	2 (6.1%)	6 (18.2%)
Smoking during pregnancy	8 (12.1%)	1 (3.0%)	7 (21.2%)
Alcohol during pregnancy	8 (12.1%)	2 (6.1%)	6 (18.2%)
Severe stress during pregnancy	7 (10.6%)	1 (3.0%)	6 (18.2%)

about coping efforts, and subjective controllability of potential stressors during the past month. Internal consistency ranges between $\alpha = .84$ and $.86$. The PSS (German Version) was administered at both assessment points of the study.

1.3.4. Life Experiences Survey (LES)

The LES (Sarason et al., 1978) lists 47 life changes that require adjustment (e.g., marriage, severe illness, relocation). Subjects are required to indicate whether the listed life events occurred during the preceding 12 months and rate the impact on a bipolar seven-point scale ranging from “extremely negative” to “extremely positive”. Summing up the occurrences with negative impact ratings yields a measure for negative life events. The LES is a widely used, validated instrument with a test–retest reliability of $r = .88$ for the negative sum score. The LES (German Version) was administered only in early pregnancy.

1.3.5. Edinburgh Postnatal Depression Scale (EPDS)

The EPDS (Cox et al., 1987) is a widely used 10-item measure inquiring about the mother’s mood in the past 7 days. Each item (e.g., “In the last seven days I felt so unhappy that I cried”) is rated on a four-point scale from “most of the time” to “not at all” and refers to depressed mood, anhedonia, guilt, anxiety, and suicidal ideation. The split-half reliability of the German scale is $r = .82$, and its internal consistency coefficient is $\alpha = .81$ (Bergant et al., 1998). Women with EPDS scores of 13 or more are suspected to suffer from clinical depression (Bergant et al., 1998; Matthey et al., 2006). The EPDS (German Version) was administered at both assessment points of the study.

1.3.6. Prenatal Distress Questionnaire (PDQ)

The PDQ (Yali and Lobel, 1999) is a 12-item self-report questionnaire designed to assess worries and anxiety of the pregnant mother regarding pregnancy and birth. The 12 items describe pregnancy specific worries (e.g., medical complications, physical changes, birth, health of the baby) that have to be rated on a five-point scale ranging from “not at all worried” to “extremely worried”. Internal consistency of the English version is $\alpha = .81$. We administered our own German translation at both assessment points of the study. Internal consistency of our German version was $\alpha = .81$.

1.3.7. Salivary cortisol

Subjects were instructed to collect saliva at home with specially designed test tubes (Salivette[®], Sarstedt, Germany) right after awakening and 30, 45, and 60 min thereafter and to store the samples in the freezer until the next study assessment. In early pregnancy subjects were asked to collect salivary samples during two consecutive workdays following the study assessment. In late pregnancy the participants collected saliva samples on 1 day during the 35th and 1 day during the 36th week of gestation. Handed in saliva samples were stored at $-20\text{ }^{\circ}\text{C}$ until analysis. After thawing, samples were centrifuged at $2000 \times g$ at $10\text{ }^{\circ}\text{C}$ for 10 min.

Salivary cortisol was analyzed using a commercial competitive luminescence immunoassay (LIA; IBL, Hamburg, Germany). Intra- and inter-assay coefficients of variation were both below 10%. Every tenth sample was assayed twice.

1.4. Data analysis

Exploratory data analysis included examination of variables for missing data, normality, and outliers. Missing value analysis did not reveal any systematic patterns of missing data. Missing questionnaire items were replaced by the mean of the corresponding scale/subscale of the individual if applicable. Differences on demographic characteristics, salivary cortisol levels and psychological measures between included and excluded study participants and between high and low trait anxiety groups were tested by multiple *t*- and χ^2 -tests (alpha adjusted according to Bonferroni). Unadjusted associations between the different measures were evaluated using bivariate correlations (Pearson, two-tailed). Salivary cortisol values were averaged across the 2 days per assessment period. For the multiple regression analyses, variables without normal distribution were log transformed. Differences in the cortisol awakening response between high and low trait anxiety groups were tested by repeated measures analysis of variance (ANOVA) using log transformed cortisol values. Due to not fulfilling sphericity requirements results were Huynh–Feldt corrected (uncorrected dfs reported). Area under the curve (AUCg) of the cortisol awakening response was calculated using the trapezoid method with respect to ground (Pruessner et al., 2003). The level of significance for all analyses was set at $\alpha = .05$. All statistical analyses were carried out using the Statistical Package for the Social Sciences, version 16.0 for Windows (SPSS, 2007).

2. Results

2.1. Psychological measures

Mean, standard deviation and range for all psychological variables are displayed in Table 2. Negative life events across the 12 months preceding the first measuring point were assessed only in early pregnancy and personality measures only in late pregnancy. According to the presented data women reported more stress ($t(53) = -.98$, $p = .33$) and depressive symptoms ($t(52) = -1.04$, $p = .31$) in late pregnancy compared to the early pregnancy period, yet these differences did not reach statistical significance (paired samples *t*-tests, two-tailed). Eight women (15.1%) in early and 11 women (18.6%) in late pregnancy were

Table 2
Descriptive values for maternal psychological measures.

Variables	Early pregnancy				Late pregnancy				
	M	SD	Range	n	M	SD	Range	n	
Extraversion (16PF)	–	–	–	–	5.18	1.79	–.1 to 8.9	66	
Trait anxiety (16PF)	–	–	–	–	5.79	1.94	2.5–10.0	66	
Self-control (16PF)	–	–	–	–	5.29	1.68	.8–8.3	66	
Independence (16PF)	–	–	–	–	5.60	1.88	.4–11.5	66	
Tough-mindedness (16PF)	–	–	–	–	3.85	1.89	.1–10.6	66	
Depression (EPDS)	6.38	4.81	0–18	56	7.22	5.74	0–21	63	
Perceived stress (PSS)	24.56	9.77	6–47	55	25.51	9.12	9–47	65	
Pregnancy anxiety (PDQ)	1.24	.67	.2–2.8	55	1.23	.65	.1–2.7	60	
Negative life events (LES)	4.00	3.41	0–15	66	–	–	–	–	

classified as suffering from clinical depression based on EPDS score of 13 or more (Bergant et al., 1998; Matthey et al., 2006). However, most participating women had EPDS scores of less than 13 (84.9% in early and 81.4% in late pregnancy).

2.2. Associations between personality and psychological measures of distress

Table 3 presents unadjusted bivariate correlations between personality traits and psychological measures of prenatal distress (depression, perceived stress, negative life events, pregnancy anxiety). Trait anxiety was positively and significantly associated with all stress-related psychological measures. Questionnaires that were administered repeatedly (perceived stress, depression, and pregnancy anxiety) were highly correlated across the two assessment periods ($r(49–54) = .41–.75, p < .01$).

2.3. Associations between salivary cortisol and demographic variables

Cortisol levels (AUCg) between early and late pregnancy were significantly and positively correlated with $r(51) = .67, p < .01$. Unadjusted bivariate correlations between cortisol measures and demographic variables yielded several significant associations: between awakening cortisol in early pregnancy and smoking during pregnancy ($r(52) = -.28, p < .05$), alcohol consumption during pregnancy ($r(52) = -.37, p < .01$), and severe psychological stress during pregnancy ($r(52) = -.28, p < .05$) and between planned pregnancy and cortisol 30 min after awakening in late pregnancy ($r(60) = .37, p < .01$) and AUCg in late pregnancy ($r(60) = .28, p < .05$). Maternal BMI before pregnancy, child gender, gestational age of the fetus at early pregnancy assessment and all other demographic characteristics were not associated with cortisol levels and were therefore not included in consequent multivariate analyses.

Table 3
Unadjusted associations between personality and psychological measures.

Measures	E	TA	SC	I	TM	LES	PSS 1	PSS 2	EPDS 1	EPDS 2	PDQ 1
Extraversion (E)	–										
Trait anxiety (TA)	–.12	–									
Self-control (SC)	–.44**	–.21	–								
Independence (I)	.18	–.24*	.07	–							
Tough-mindedness (TM)	–.39**	–.12	.40**	.13	–						
Negative life events (LES)	.10	.33**	–.38**	–.07	–.27*	–					
Perceived stress (PSS 1)	–.14	.58**	–.12	–.23	–.13	.44**	–				
Perceived stress (PSS 2)	–.03	.62**	–.11	–.26*	–.11	.40**	.67**	–			
Depression (EPDS 1)	–.04	.32*	–.08	–.13	–.19	.38**	.70**	.53**	–		
Depression (EPDS 2)	.07	.49**	–.25	–.18	–.20	.40**	.45**	.63**	.41**	–	
Pregnancy anxiety (PDQ 1)	.03	.31*	–.16	.06	–.14	.32*	.26	.18	.34*	.16	–
Pregnancy anxiety (PDQ 2)	.13	.40**	–.22	–.09	–.16	.37**	.24	.37**	.33*	.18	.75**

Note: 1 = Early pregnancy; 2 = late pregnancy.

* $p < .05$.

** $p < .01$.

2.4. Associations between salivary cortisol and psychological measures

Bivariate unadjusted correlations between salivary cortisol and psychological measures in early pregnancy revealed significant associations between trait anxiety and cortisol levels at awakening ($r(52) = -.43, p < .01$), and between trait anxiety and cortisol levels at 30 min after awakening with $r(52) = -.28, p < .05$. No further correlations between salivary cortisol and psychological measures in early pregnancy reached significance. In late pregnancy cortisol levels at 30 min after awakening were significantly correlated with negative life events at $r(60) = -.28, p < .05$. There were no other significant associations between cortisol and psychological measures in late pregnancy.

2.5. Trait anxiety and salivary cortisol

In order to further investigate the significant associations between trait anxiety and cortisol we ran separate multiple regression analyses with cortisol levels at awakening and 30 min after awakening, both from the early pregnancy assessment, as outcome variables and trait anxiety as predictor, controlled for smoking, alcohol, and severe stressful experiences since the beginning of the pregnancy. Trait anxiety significantly predicted awakening cortisol in early pregnancy ($\beta = -.29, p < .05$) but the association between trait anxiety and cortisol 30 min after awakening was only marginally significant ($\beta = -.26, p < .10$) and the total model did not reach significance. Results of the multiple regression analyses are displayed in Table 4. In order to verify that significant results of the regression analyses are not a function of the 11 women that reported smoking and alcohol consumption during pregnancy we repeated the multiple regression models excluding these women. Results remained unchanged. In addition, we ran a model excluding women who may be

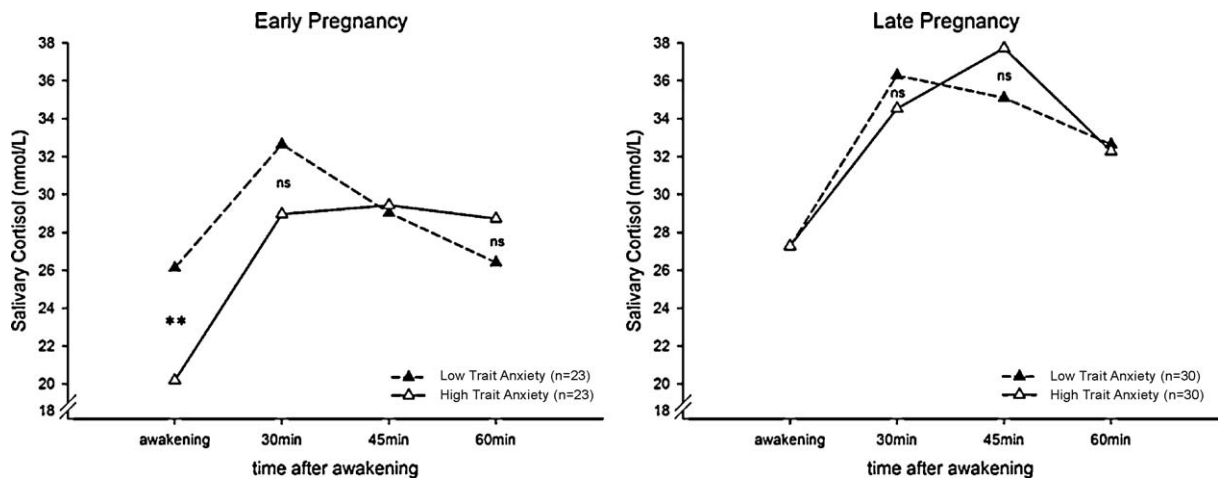


Fig. 1. Cortisol awakening response in early and late pregnancy. *t*-Tests between low and high trait anxiety group; ns, not significant. * $p < .05$, ** $p < .01$.

Table 4

Summary of multiple regression analysis (early pregnancy).

Predictors	Awakening cortisol β	Cortisol 30min after awakening β
Smoking ^a	-.12	.04
Alcohol ^b	-.34**	-.04
Stress ^c	-.18	-.04
Trait anxiety (16PF)	-.29*	-.26#

Note: Awakening cortisol: $n = 52$; adjusted $R^2 = .31$; $F(4, 51) = 6.64^{**}$; cortisol 30min after awakening: $n = 52$; adjusted $R^2 < .01$; $F(4, 51) = .28$.

^a 0 = Not smoking during pregnancy; 1 = smoking during pregnancy.

^b 0 = Not drinking alcohol during pregnancy; 1 = drinking alcohol during pregnancy.

^c 0 = No stressful experiences during pregnancy; 1 = stressful experiences during pregnancy.

$p < .10$.

* $p < .05$.

** $p < .01$.

suffering from clinical depression – indicated by EPDS score of 13 or more – in order to confirm that significant results are not a function of depression. Again results remained unchanged.

To compare women with different trait anxiety scores we split the sample across the median in a high and a low trait anxiety group. A two-way repeated measures analysis of variance (ANOVA) was performed, separately for early and late pregnancy, with group as between-subject factor and time of the cortisol awakening response as the main within-subject factor (see Fig. 1). The early pregnancy ANOVA revealed a significant group-by-time interaction ($F(3, 132) = 4.95, p = .01$) and according to *t*-tests the cortisol values at awakening were significantly lower in the high trait anxiety group than in the low trait anxiety group, $t(44) = 3.27, p < .01$. However, after inclusion of alcohol, smoking and severe psychological stress, the group-by-time interaction at early pregnancy did not reach statistical significance anymore ($F(3, 120) = 1.09, p = .35$). At late pregnancy there was no significant interaction and no significant differences in cortisol levels between groups. Area under the curve of the cortisol awakening response (AUCg) did not differ between groups in early ($t(44) = 1.13, p = .26$) nor in late pregnancy ($t(58) = .02, p = .99$).

3. Discussion

The goal of the present study was to investigate associations between personality traits, stress-related psychological measures, and salivary cortisol of pregnant women. Not surprisingly, personality – and as predicted specifically trait anxiety – was

related to self-reported psychological measures of stress. Not only was trait anxiety significantly and positively associated with perceived stress, depression, and pregnancy anxiety – both during early and late pregnancy – it was also correlated with the number of negative life events the women reported. The high correlations between state measures of perceived stress, depression, and pregnancy anxiety which have been assessed at both assessment points suggest that there was little change regarding the basic psychological state of the expectant mothers across the course of the pregnancy and/or that these measures largely represent reflections of maternal personality traits. The same can be said of the cortisol levels which were also highly correlated between early and late pregnancy. However, associations between psychological measures and cortisol levels were low. It was only trait anxiety in early pregnancy and negative life events in late pregnancy that significantly predicted cortisol levels during pregnancy. Even though authors studying associations between self-reported maternal distress and child development often assume that high maternal cortisol, in response to psychological distress during pregnancy, reaches the fetus and influences its development, correlations between maternal stress and maternal cortisol levels during pregnancy have generally been weak according to the existing literature—if they were detectable at all. In a study by Wadhwa et al. (1996) a single measure of plasma cortisol at 28 weeks of gestation of 54 pregnant women was significantly associated with the personality trait hardiness and social support but not with life events stress, perceived stress, or pregnancy anxiety. After controlling for socio-demographics and stress measures the association between social support and hardiness with plasma cortisol was only marginally significant. Field et al. (2006) assessed urinary cortisol and mood states during early and late pregnancy in 353 women and found significant associations between cortisol levels and self-report measures of depression and anxiety, not controlling for any covariates, however. Psychological and cortisol measures were highly correlated across pregnancy. Controlling for smoking and time of saliva collection Obel et al. (2005) found that women ($n = 650$) had lower morning cortisol levels in early pregnancy if they reporting pregnancy-related stress due to complications and higher evening cortisol levels in late pregnancy if they felt very stressed by life events and were worried regarding existing pregnancy complications. The only other study we are aware of that investigated the cortisol awakening response in pregnant women in relation to stress found significant associations between baseline awakening cortisol levels at 20 weeks of gestation and early life trauma, but not with depression or anxiety (Shea et al., 2007). Hence, the present findings of rather limited associations – or lack thereof –

between cortisol and psychological measures of stress during pregnancy are in line with other empirical work. Nevertheless, cortisol in early pregnancy was significantly associated with trait anxiety, even when controlled for a range of covariates (smoking, alcohol, and severe stress during pregnancy). However, in late pregnancy this was not the case anymore. Previous studies also failed to find associations between psychological measures of stress and morning cortisol in late pregnancy (Petraglia et al., 2001; Obel et al., 2005). Since cortisol levels are rising throughout the course of pregnancy, associations with personality may not be detectable anymore in later periods of the pregnancy. This masking effect may also explain the lack of a group-by-time interaction in late pregnancy.

Interestingly, trait anxiety was not associated with higher cortisol levels but with lower baseline concentrations at awakening and 30 min thereafter. This is consistent with previous studies which found decreased morning cortisol levels in women who were worried for their pregnancy and had complications in first trimester (Obel et al., 2005) and lower baseline awakening cortisol levels in pregnant women reporting early life traumata (Shea et al., 2007). Studies with non-pregnant individuals found decreased cortisol awakening responses in students that experienced early loss (Meinlschmidt and Heim, 2005) and flatter cortisol diurnal profiles in anxious adolescents (Van den Bergh et al., 2008). Consequently, the low cortisol levels at awakening which emerged in the present study in the case of the women with high trait anxiety suggest that trait anxiety may be characterized by a similar dysregulation of the HPA axis. Important to mention here also, however, is a recent investigation by Rademaker et al. (2009) detecting a higher cortisol awakening response and a higher cortisol increase after awakening in male soldiers high on personality traits self-directedness and harm avoidance.

Contrary to the findings of Rademaker et al. (2009) and Portella et al. (2005) we did not detect an enhanced awakening cortisol response in the high trait anxiety group and there was no significant difference in AUCg between the two groups. Our findings suggest, though, a trend of enhanced cortisol levels 60 min after awakening in the high trait anxiety group compared to the low trait anxiety group which is in accordance with Portella et al.'s group-by-time interaction.

3.1. Limitations

The results of the present study should be viewed in the context of several important methodological limitations: (1) the sample size was rather small and consequently these findings may not generalize to other samples; (2) our findings are based on correlational data which limits causal interpretation; (3) negative life events across the preceding 12 months were assessed only in early pregnancy and not in late pregnancy; (4) maternal personality, though treated as predictor of early pregnancy measures, was assessed only in late pregnancy. However, empirical evidence suggests that personality traits are reasonably stable in adulthood (McCrae and Costa, 1994; Caspi et al., 2005); (5) time (compliance) of exact cortisol sampling was not assessed and controlled for; (6) exclusion of participants with psychiatric problems was not based on validated clinical interviews and may have been insufficient; (7) not all factors that are known to affect the cortisol awakening response have been controlled for (e.g., sleeping patterns, caffeine, drug abuse).

While the findings of the current study appear to suggest important implications for the research of maternal prenatal stress effects they are limited by the design and sample size. Therefore, future studies with more adequate designs are required in order to confirm the significant relationships between maternal personality, prenatal stress, and maternal cortisol levels. Future studies

should also consider assessing maternal personality before pregnancy in order to investigate the possibility that the transition to parenthood – demarcated by pregnancy – may induce changes in maternal personality traits (e.g., see Paris and Helson, 2002).

4. Conclusion

Despite the study's limitations the results of the present study suggest that subjective measures of psychological distress and cortisol levels during pregnancy are related to maternal trait anxiety scores. Maternal prenatal stress has been defined and assessed differently across studies on the effects of maternal stress on child development with measures used ranging from single or multiple subjective psychometric state and/or trait measures to biological correlates of stress (e.g., salivary cortisol levels). While a small number of studies were able to use exposure to a natural disaster as a more objective measure of stress (Glynn et al., 2001; Laplante et al., 2004; Huizink et al., 2008), and a few studies assessed maternal levels of salivary cortisol (Huizink et al., 2002; Buitelaar et al., 2003; de Weerth et al., 2003; Davis et al., 2007), most other studies relied on self-reported psychological measures (e.g., state and trait anxiety, pregnancy-related anxiety, depression, perceived stress, stressful life events, and daily hassles). Based on the significant correlations between maternal trait anxiety and self-reported distress and the implied association between maternal trait anxiety and cortisol levels reported in this study, the question arises as to what extent measures of stress generally used in studies on prenatal stress effects are able to capture stress responses during pregnancy that are independent from mothers inherent disposition to respond more or less to stressful experiences. This distinction between state and trait is of crucial importance considering the significant heritable compound of neuroticism (Plomin et al., 1994; Jang et al., 1996; Eaves et al., 1999). Given that women scoring high on trait anxiety/neuroticism – as a function of their genetic make-up – are more likely to give birth to children that tend to exhibit similar personality traits, associations between mothers' reported stress exposure during pregnancy and offspring's stress reactivity may be confounded by shared genes. However, maternal trait anxiety/neuroticism may have a number of effects over and above genetics: (1) the enhanced stress reactivity of women with high trait anxiety/neuroticism may amplify the biological mechanisms of fetal programming (e.g., higher cortisol levels), (2) the greater number of stressful life events individuals with high trait anxiety/neuroticism typically experience may affect the child both pre- and postnatally, and (3) maternal personality may define a large amount of the postnatal environment's quality (e.g., parenting, marital quality).

In conclusion, the present study suggests that maternal trait anxiety is reflected in self-reported maternal stress measures and in maternal cortisol levels and that it predicts exposure to negative life events during pregnancy. It may, therefore, be advisable to include measures of maternal trait anxiety/neuroticism in studies investigating effects of maternal stress during pregnancy on child development.

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References

- Barker, D.J., 1998. In utero programming of chronic disease. *Clinical Science* 95 (2), 115–128.
- Bergant, A.M., Nguyen, T., Heim, K., Ulmer, H., Dapunt, O., 1998. Deutschsprachige Fassung und Validierung der "Edinburgh postnatal depression scale". *Deutsche medizinische Wochenschrift* 123, 35–40.
- Bolger, N., Schilling, E.A., 1991. Personality and the problems of everyday life: the role of neuroticism in exposure and reactivity to daily stressors. *Journal of Personality* 59 (3), 355–386.
- Bolger, N., Zuckerman, A., 1995. A framework for studying personality in the stress process. *Journal of Personality and Social Psychology* 69 (5), 890–902.
- Buitelaar, J.K., Huizink, A.C., Mulder, E.J., de Medina, P.G., Visser, G.H., 2003. Prenatal stress and cognitive development and temperament in infants. *Neurobiological Aging* 24 (Suppl. 1), S53–S60 (discussion S67–58).
- Caspi, A., Roberts, B.W., Shiner, R.L., 2005. Personality development: stability and change. *Annual Review of Psychology* 56, 453–484.
- Cattell, R.B., Eber, H.W., Tatsuoka, M.M., 1970. *Handbook for the Sixteen Personality Factor Questionnaire (16PF)*. Institute for Personality and Ability Testing (IPAT), Champaign.
- Cohen, S., Kamarck, T., Mermelstein, R., 1983. A global measure of perceived stress. *Journal of Health and Social Behavior* 24 (4), 385–396.
- Costa, P.T., McCrae, R.R., 1992. *Revised NEO Personality Factor Inventory (NEO PI-R) and NEO Five Factor Inventory*. Professional Manual. Psychological Assessment Resources, Odessa.
- Cox, J.L., Holden, J.M., Sagovsky, R., 1987. Detection of postnatal depression. Development of the 10-item Edinburgh Postnatal Depression Scale. *British Journal of Psychiatry* 150, 782–786.
- Davis, E.P., Glynn, L.M., Schetter, C.D., Hobel, C., Chicz-Demet, A., Sandman, C.A., 2007. Prenatal exposure to maternal depression and cortisol influences infant temperament. *Journal of the American Academy of Child and Adolescent Psychiatry* 46 (6), 737–746.
- Davis, E.P., Snidman, N., Wadhwa, P.D., Glynn, L.M., Schetter, C.D., Sandman, C.A., 2004. Prenatal maternal anxiety and depression predict negative behavioral reactivity in infancy. *Infancy* 6 (3), 319–331.
- de Weerth, C., van Hees, Y., Buitelaar, J.K., 2003. Prenatal maternal cortisol levels and infant behavior during the first 5 months. *Early Human Development* 74 (2), 139–151.
- Eaves, L., Heath, A., Martin, N., Maes, H., Neale, M., Kendler, K., et al., 1999. Comparing the biological and cultural inheritance of personality and social attitudes in the Virginia 30,000 study of twins and their relatives. *Twin Research* 2 (2), 62–80.
- Egliston, K.A., McMahon, C., Austin, M.P., 2007. Stress in pregnancy and infant HPA axis function: conceptual and methodological issues relating to the use of salivary cortisol as an outcome measure. *Psychoneuroendocrinology* 32 (1), 1–13.
- Engelhard, I.M., van den Hout, M.A., Schouten, E.G., 2006. Neuroticism and low educational level predict the risk of posttraumatic stress disorder in women after miscarriage or stillbirth. *General Hospital Psychiatry* 28 (5), 414–417.
- Field, T., Hernandez-Reif, M., Diego, M., Schanberg, S., Kuhn, C., 2006. Stability of mood states and biochemistry across pregnancy. *Infant Behavior and Development* 29 (2), 262–267.
- Glynn, L.M., Wadhwa, P.D., Dunkel-Schetter, C., Chicz-Demet, A., Sandman, C.A., 2001. When stress happens matters: effects of earthquake timing on stress responsiveness in pregnancy. *American Journal of Obstetrics and Gynecology* 184 (4), 637–642.
- Hettema, J.M., Neale, M.C., Myers, J.M., Prescott, C.A., Kendler, K.S., 2006. A population-based twin study of the relationship between neuroticism and internalizing disorders. *American Journal of Psychiatry* 163 (5), 857–864.
- Huizink, A.C., Bartels, M., Rose, R.J., Pulkkinen, L., Eriksson, C.J., Kaprio, J., 2008. Chernobyl exposure as stressor during pregnancy and hormone levels in adolescent offspring. *Journal of Epidemiology Community Health* 62 (4), e5.
- Huizink, A.C., de Medina, P.G., Mulder, E.J., Visser, G.H., Buitelaar, J.K., 2002. Psychological measures of prenatal stress as predictors of infant temperament. *Journal of the American Academy of Child and Adolescent Psychiatry* 41 (9), 1078–1085.
- Huizink, A.C., Mulder, E.J., Buitelaar, J.K., 2004. Prenatal stress and risk for psychopathology: specific effects or induction of general susceptibility? *Psychological Bulletin* 130 (1), 115–142.
- Jang, K.L., Livesley, W.J., Vernon, P.A., 1996. Heritability of the big five personality dimensions and their facets: a twin study. *Journal of Personality* 64 (3), 577–591.
- Kendler, K.S., Gardner, C.O., Prescott, C.A., 2003. Personality and the experience of environmental adversity. *Psychological Medicine* 33 (7), 1193–1202.
- Kendler, K.S., Neale, M.C., Kessler, R.C., Heath, A.C., Eaves, L.J., 1993. A longitudinal twin study of personality and major depression in women. *Archives of General Psychiatry* 50 (11), 853–862.
- Kofman, O., 2002. The role of prenatal stress in the etiology of developmental behavioural disorders. *Neuroscience and Biobehavioral Reviews* 26 (4), 457–470.
- Laplante, D.P., Barr, R.G., Brunet, A., Galbaud du Fort, G., Meaney, M.L., Saucier, J.F., et al., 2004. Stress during pregnancy affects general intellectual and language functioning in human toddlers. *Pediatric Research* 56 (3), 400–410.
- Mangold, D.L., Wand, G.S., 2006. Cortisol and adrenocorticotropic hormone responses to naloxone in subjects with high and low neuroticism. *Biological Psychiatry* 60 (8), 850–855.
- Matthey, S., Henshaw, C., Elliott, S., Barnett, B., 2006. Variability in use of cut-off scores and formats on the Edinburgh Postnatal Depression Scale: implications for clinical and research practice. *Archives of Women's Mental Health* 9 (6), 309–315.
- McCrae, R., Costa, P., 1994. The stability of personality: observation and evaluations. *Current Directions in Psychological Science* 3, 173–175.
- Meinlschmidt, G., Heim, C., 2005. Decreased cortisol awakening response after early loss experience. *Psychoneuroendocrinology* 30 (6), 568–576.
- Mohler, E., Parzer, P., Brunner, R., Wiebel, A., Resch, F., 2006. Emotional stress in pregnancy predicts human infant reactivity. *Early Human Development* 82 (11), 731–737.
- Obel, C., Hedegaard, M., Henriksen, T.B., Secher, N.J., Olsen, J., Levine, S., 2005. Stress and salivary cortisol during pregnancy. *Psychoneuroendocrinology* 30 (7), 647–656.
- O'Connor, T.G., Heron, J., Golding, J., Glover, V., 2003. Maternal antenatal anxiety and behavioural/emotional problems in children: a test of a programming hypothesis. *Journal of Child Psychology and Psychiatry* 44 (7), 1025–1036.
- Oswald, L.M., Zandi, P., Nestadt, G., Potash, J.B., Kalaydjian, A.E., Wand, G.S., 2006. Relationship between cortisol responses to stress and personality. *Neuropsychopharmacology* 31 (7), 1583–1591.
- Paris, R., Helson, R., 2002. Early mothering experience and personality change. *Journal of Family Psychology* 16 (2), 172–185.
- Petraglia, F., Hatch, M.C., Lapinski, R., Stomati, M., Reis, F.M., Cobelli, L., et al., 2001. Lack of effect of psychosocial stress on maternal corticotropin-releasing factor and catecholamine levels at 28 weeks' gestation. *Journal of the Society for Gynecologic Investigation* 8 (2), 83–88.
- Plomin, R., Owen, M.J., McGuffin, P., 1994. The genetic basis of complex human behaviors. *Science* 264 (5166), 1733–1739.
- Portella, M.J., Harmer, C.J., Flint, J., Cowen, P., Goodwin, G.M., 2005. Enhanced early morning salivary cortisol in neuroticism. *American Journal of Psychiatry* 162 (4), 807–809.
- Pruessner, J.C., Kirschbaum, C., Meinlschmidt, G., Hellhammer, D.H., 2003. Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. *Psychoneuroendocrinology* 28 (7), 916–931.
- Rademaker, A.R., Kleber, R.J., Geuze, E., Vermetten, E., 2009. Personality dimensions harm avoidance and self-directedness predict the cortisol awakening response in military men. *Biological Psychology* 81 (3), 177–183.
- Rice, F., Jones, I., Thapar, A., 2007. The impact of gestational stress and prenatal growth on emotional problems in offspring: a review. *Acta Psychiatrica Scandinavica* 115 (3), 171–183.
- Rieger, M., Pirke, K.M., Buske-Kirschbaum, A., Wurmser, H., Papousek, M., Hellhammer, D.H., 2004. Influence of stress during pregnancy on HPA activity and neonatal behavior. *Annals of the New York Academy of Sciences* 1032, 228–230.
- Riese, H., Rosmalen, J.G., Ormel, J., Van Roon, A.M., Oldehinkel, A.J., Rijdsdijk, F.V., 2006. The genetic relationship between neuroticism and autonomic function in female twins. *Psychological Medicine* 1–11.
- Ruiz, R.J., Avart, K.C., 2005. Effects of maternal prenatal stress on infant outcomes: a synthesis of the literature. *Advances in Nursing Science* 28 (4), 345–355.
- Sarason, I.G., Johnson, J.H., Siegel, J.M., 1978. Assessing the impact of life changes: development of the Life Experiences Survey. *Journal of Consulting and Clinical Psychology* 46 (5), 932–946.
- Schneewind, K.A., Graf, J., 1998. *Sixteen Personality Factor Questionnaire—German version*. Testzentrale, Goettingen.
- Shea, A.K., Streiner, D.L., Fleming, A., Kamath, M.V., Broad, K., Steiner, M., 2007. The effect of depression, anxiety and early life trauma on the cortisol awakening response during pregnancy: preliminary results. *Psychoneuroendocrinology* 32 (8–10), 1013–1020.
- SPSS, 2007. *SPSS for Windows (Version 16.0.2)* SPSS, Chicago.
- Van den Bergh, B.R., Mennes, M., Oosterlaan, J., Stevens, V., Stiers, P., Marcoen, A., et al., 2005a. High antenatal maternal anxiety is related to impulsivity during performance on cognitive tasks in 14- and 15-year-olds. *Neuroscience and Biobehavioral Reviews* 29 (2), 259–269.
- Van den Bergh, B.R., Mulder, E.J., Mennes, M., Glover, V., 2005b. Antenatal maternal anxiety and stress and the neurobehavioural development of the fetus and child: links and possible mechanisms. A review. *Neuroscience and Biobehavioral Reviews* 29 (2), 237–258.
- Van den Bergh, B.R., Van Calster, B., Pinna Puissant, S., Van Huffel, S., 2008. Self-reported symptoms of depressed mood, trait anxiety and aggressive behavior in post-pubertal adolescents: associations with diurnal cortisol profiles. *Hormones and Behaviour* 54 (2), 253–257.
- Wadhwa, P.D., Dunkel-Schetter, C., Chicz-DeMet, A., Porto, M., Sandman, C.A., 1996. Prenatal psychosocial factors and the neuroendocrine axis in human pregnancy. *Psychosomatic Medicine* 58 (5), 432–446.
- Weinstock, M., 2005. The potential influence of maternal stress hormones on development and mental health of the offspring. *Brain, Behavior, and Immunity* 19 (4), 294–308.
- Widiger, T.A., Hurt, S.W., Frances, A., Clarkin, J.F., Gilmore, M., 1984. Diagnostic efficiency and DSM-III. *Archives of General Psychiatry* 41 (10), 1005–1012.
- Wurmser, H., Rieger, M., Domogalla, C., Kahnt, A., Buchwald, J., Kowatsch, M., et al., 2006. Association between life stress during pregnancy and infant crying in the first six months postpartum: a prospective longitudinal study. *Early Human Development* 82 (5), 341–349.
- Yali, A.M., Lobel, M., 1999. Coping and distress in pregnancy: an investigation of medically high risk women. *Journal of Psychosomatic Obstetrics and Gynecology* 20 (1), 39–52.