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Pregnancy anxiety and prenatal cortisol trajectories

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ABSTRACT

Pregnancy anxiety is a potent predictor of adverse birth and infant outcomes. The goal of the current study was to examine one potential mechanism whereby these effects may occur by testing associations between pregnancy anxiety and maternal salivary cortisol on 4 occasions during pregnancy in a sample of 448 women. Higher mean levels of pregnancy anxiety over the course of pregnancy predicted steeper increases in cortisol trajectories compared to lower pregnancy anxiety. Significant differences between cortisol trajectories emerged between 30 and 31 weeks of gestation. Results remained significant when adjusted for state anxiety and perceived stress. Neither changes in pregnancy anxiety over gestation, nor pregnancy anxiety specific to only a particular time in pregnancy predicted cortisol. These findings provide support for one way in which pregnancy anxiety may influence maternal physiology and contribute to a growing literature on the complex biological pathways linking pregnancy anxiety to birth and infant outcomes.

1. Introduction

Pregnancy anxiety is a highly specific type of maternal psychological distress defined as anxiety concerning a mother's own health, the baby's health, and labor and delivery in the context of a specific pregnancy (Dunkel Schetter, 2011). It is a potent and often more consistent predictor of birth, infant and child outcomes than general forms of psychological distress (Buss, Davis, Muftuler, Head, & Sandman, 2009; Dunkel Schetter & Glynn, 2011; Kramer et al., 2009; Lobel et al., 2008; Roesch, Dunkel Schetter, Woo, & Hobel, 2004). For example, pregnancy anxiety predicts preterm birth and gestational length (Kramer et al., 2009; Mancuso, Dunkel Schetter, Rini, Roesch, & Hobel, 2004; Roesch et al., 2004), infant mental and psychomotor development (Buitelaar, Huisink, Mulder, de Medina, & Visser, 2003; Davis & Sandman, 2010; Huizink, De Medina, Mulder, Visser, & Buitelaar, 2002), child temperament (Blair, Glynn, Sandman, & Davis, 2011; Huizink et al., 2002; Sandman, Davis, Buss, & Glynn, 2012), and brain morphology in young children (Buss et al., 2009). However, little is known about the biological mechanisms that explain these effects.

Alterations in the maternal hypothalamic–pituitary–adrenal (HPA) axis and placenta are hypothesized to be an explanatory mechanism (Seckl & Holmes, 2007; Van den Bergh, Mulder, Mennes, & Glover, 2005). Strong evidence from animal models demonstrates that maternal distress predicts increased fetal glucocorticoid exposure via synthesis and release of maternal glucocorticoids (Maccari et al., 2003; Weinstock, 2005), but similar evidence in humans linking pregnancy anxiety (or general maternal distress) to increased levels of maternal cortisol during pregnancy is lacking. Thus, it is unclear if and how pregnancy anxiety is associated with maternal cortisol during pregnancy. The purpose of this study was to determine whether pregnancy anxiety is associated with cortisol levels and trajectories over the course of pregnancy in an effort to better understand the broader processes linking pregnancy anxiety to birth, infant and child outcomes.

During pregnancy, maternal cortisol increases 2- to 4-fold (Glynn, Dunkel Schetter, Chicz-DeMet, Hobel, & Sandman, 2007; Mastorakos & Ilias, 2003; Meulenberg & Hofman, 1990) and passes through the placenta. However, the amount of maternal cortisol that crosses the placental barrier is limited because its passage is regulated by the enzyme 11β-hydroxysteroid dehydrogenase (11β-HSD2: Benediktsson, Calder, Edwards, & Seckl, 1997). Still,

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maternal cortisol accounts for approximately 30–40% of the variability in fetal concentrations of cortisol (Gitau, Cameron, Fisk, & Glover, 1998; Gitau, Fisk, Teixeira, Cameron, & Glover, 2001).

Maternal cortisol levels can affect birth and infant outcomes in multiple ways. For one, cortisol stimulates the synthesis and release of placental corticotrophin-releasing hormone (pCRH) (King, Smith, & Nicholson, 2001). In humans, elevated cortisol early in pregnancy predicts pCRH levels later in pregnancy (Sandman et al., 2006) and pCRH predicts preterm birth (Mclean & Smith, 2001). Maternal cortisol also acts directly on the fetus and its developing nervous system (for reviews, see Davis & Sandman, 2006; Sandman et al., 2012). For example, results of prospective studies have documented that relatively high levels of prenatal maternal cortisol predict greater behavioral and physiological stress reactivity in fetuses, infants and children (Davis, Glynn, Waffarn, & Sandman, 2011; De Weerth, Van Hees, & Buitelaar, 2003), decreased cognitive ability in infants (Davis & Sandman, 2010; Huizink, Robles de Medina, Mulder, Visser, & Buitelaar, 2003), increased affective problems in young girls (Buss et al., 2012), and altered amygdala volumes in young girls (Buss et al., 2012).

In the literature, the association between pregnancy anxiety and maternal cortisol is inconsistent at best. For example, a study of 603 women found that worries about pregnancy-related complications were associated with high evening maternal cortisol late in pregnancy (Obel et al., 2005), but with lower morning cortisol early in pregnancy. Several other studies reported no associations between maternal cortisol and pregnancy anxiety (Bolten et al., 2011; Davis & Sandman, 2010; Goedhart et al., 2010; Harville, Savitz, Dole, Herring, & Thorp, 2009; Kivlighan, Dipietro, Costigan, & Laudenslager, 2008; Pluess, Bolten, Pirke, & Hellhammer, 2011; Sikkema et al., 2001). However, the majority of these studies assessed maternal cortisol at only 1 or 2 time points during pregnancy, conducted only cross-sectional analyses, or did not test changes in levels or trajectories of cortisol, thus limiting their ability to detect potential effects.

The specific aim of the present study was to test predicted links between pregnancy anxiety and both maternal cortisol levels at specific time points in pregnancy and cortisol trajectories across pregnancy using multilevel modeling techniques. We hypothesized that higher levels of pregnancy anxiety would be associated with higher levels of cortisol and steeper increases in cortisol trajectories over pregnancy. We further hypothesized that pregnancy anxiety would be an independent predictor of cortisol after adjusting for other commonly studied measures of psychological distress (i.e., state anxiety and perceived stress).

2. Method

2.1. Study design and procedure

Study participants were women from a prospective longitudinal study assessing prenatal psychosocial and behavioral factors in pregnancy, the Multi-Site Behavior in Pregnancy Study (MSBIPS). Women were recruited in the Los Angeles area by research nurses at prenatal clinics in two large urban medical centers. Data for this study were collected on 4 occasions over the course of pregnancy separated by six week intervals (T1: 18–20 weeks, $M = 19.29$, $SD = .80$, T2: 24–26 weeks, $M = 24.98$, $SD = .83$, T3: 30–32 weeks, $M = 30.98$, $SD = .76$, and T4: 36–38 weeks, $M = 36.75$, $SD = .70$). At each assessment, women completed semi-structured interviews, questionnaires and provided one saliva sample for cortisol assessment. All study protocols and procedures were approved by each institution's Institutional Review Boards.

2.2. Participants

Inclusion criteria for the sample were 18 years of age, English ability, and singleton intrauterine pregnancy. Exclusion criteria were tobacco, alcohol, or drug use during pregnancy, and medical conditions involving dysregulated neuroendocrine, cardiovascular, hepatic or renal functioning.[1] Sixty-three percent of the 1189 women screened met eligibility criteria and 67% of these women consented to participate in the study ($N = 498$). The primary reasons for declining to participate in the study included work or school conflict, scheduling difficulties, child care issues and lack of interest. Participants were included in the current analysis if they had cortisol and pregnancy anxiety data for at least one time-point during the course of the study ($N = 494$).[2] Forty six women were excluded from the current sample due to missing demographic data or missing medical risk factor variables. Therefore, 448 women comprised the final sample.[3]

Table 1
Sample socio-demographics and medical history.

Variables	*N* (%)
Age at Time 1	$M = 30$ ($SD = 5.20$, range = 18–43)
Ethnicity	
Non-Hispanic White	221 (49.3%)
Latina	99 (22.1%)
African-American	61 (13.6%)
Asian	40 (8.9%)
Multi-ethnic/other	27 (6.9%)
Income	
<$10,000	20 (4.5%)
$10,001–30,000	67 (15.0%)
$30,001–50,000	87 (19.4%)
$50,001–70,000	91 (20.3%)
$70,001–90,000	60 (13.4%)
>$90,000	123 (27.5%)
Education	
High School or less	70 (15.6%)
Some college	175 (39.1%)
Bachelor's degree	123 (27.5%)
Graduate degree	80 (17.9%)
Married or cohabitating	396 (88.4%)
Parity	
Nulliparous	242 (54.0%)
Multiparous	206 (46.0%)
Current obstetric risk factors	$M = 1.15$ ($SD = 1.40$, range = 0–7)
Historical obstetric risk factors	$M = 0.75$ ($SD = .99$, range = 0–6)
Medical history risk factors	$M = 1.20$ ($SD = 1.14$, range = 0–5)

Note: $N = 448$.

Table 1 shows demographic and medical risk data for this sample. Participants were 30 years of age on average. The sample was composed of 49% non-Hispanic white, 22% Latina, 14% African American, and 9% Asian and was fairly socioeconomically diverse. The majority of the women were married or cohabitating (88%). Slightly over half of the women were carrying their first child (54%).

2.3. Measures

2.3.1. Maternal cortisol

Saliva samples were scheduled for collection at least 1 h after the participant had eaten. The samples were collected using a cotton gauze pad placed into a syringe and then clarified by depressing the plunger. They were then stored at −20 °C until assayed. Mean collection time for the samples was 2:20 pm ($SD = 1.92$ h). Thawed samples were centrifuged at 3000 rpm for 15 min before assay. All samples were assayed in duplicate using a competitive solid-phase radioimmunoassay (Coat-A-Count; Diagnostic Product Corp.). The test has a minimum detectable level of 0.02 μg/dl and the intra- and inter-assay coefficients of the variance were 5.5% and 7.6%, respectively. Cortisol data were log-transformed [ln(cortisol × 27.6)] and values outside ± 4 standard deviations from the mean were removed from the current analyses (2 data points were removed from T1, 1 from T2, 2 from T3 and 1 from T4).

[1] Despite screening procedure efforts, it was revealed from information abstracted from medical records and self-report questionnaires that a few ($n = 28$) women smoked up to the first assessment (Time 1). By the 2nd assessment (Time 2), no women reported any smoking. Because they were already enrolled in the study and occasional smokers, these women were retained in the study. A dummy coded variable was created, 1 (smoking) and 0 (no smoking) and entered into all analyses. The results remained unchanged and smoking was not a significant predictor of initial cortisol levels or cortisol trajectories. This variable was, therefore, not reported in the analyses.

[2] Three participants were removed due to lack of cortisol data. One participant was removed due to lack of pregnancy anxiety data.

[3] Women not included in the final sample were not significantly different from women who were included in the final sample on any study variables (all $ps > .10$).