



Pregnancy anxiety predicts shorter gestation in Latina and non-Latina white women: The role of placental corticotrophin-releasing hormone

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ABSTRACT

Objective: Previous research has shown that a woman's anxiety about her pregnancy predicts gestational length. Placental corticotrophin-releasing hormone (CRH) is a stress-responsive peptide proposed as a mechanism. We examined placental CRH as a physiological mediator of the association between pregnancy anxiety and gestational length in Latina and non-Latina White women to replicate evidence of associations between pregnancy anxiety, placental CRH and gestational length; to test whether placental CRH levels or changes mediate effects of pregnancy anxiety on gestational length; to examine ethnic differences in pregnancy anxiety, placental CRH, and gestational length; and to explore whether the effects of pregnancy anxiety on gestational length as mediated by placental CRH vary by ethnicity.

Methods: In a prospective study of 337 pregnant Latina and non-Latina White women, participants completed in-person interviews that included a 10-item measure of pregnancy anxiety and provided blood samples assayed using radioimmunoassay at three timepoints (19, 25, and 31 weeks gestation).

Results: Pregnancy anxiety at 19 and 31 weeks and levels of placental CRH at 31 weeks predicted gestational length. Tests of indirect effects were consistent with mediation such that both pregnancy anxiety at 19 weeks and increases from 19 to 31 weeks predicted placental CRH at 31 weeks, which in turn predicted gestational length. Tests of moderated mediation by ethnicity showed that the mediated effect of placental CRH at 31 weeks was significant for Latinas only.

Conclusions: These findings add to growing evidence of the involvement of pregnancy anxiety in the timing of birth, address mechanisms, and suggest possible ethnic differences.

1. Introduction

Pregnancy anxiety, an emotional state rooted in concerns specific to the current pregnancy, has been implicated in the etiology of preterm birth and shortened length of gestation (Dole et al., 2003; Kramer et al., 2009; Lobel et al., 2008; Rini et al., 1999). Pregnancy anxiety refers to worries and fears experienced by pregnant women about their current pregnancy, including concern about the health of the baby, childbirth, health-care experiences, labor and delivery, and the maternal role (Dunkel Schetter, 2010; Guardino and Dunkel Schetter, 2014). Several large prospective studies have shown that this contextually-rooted form of anxiety reliably predicts shorter length of gestation. For example, one

prospective study of 2000 Black and White pregnant women revealed that pregnancy anxiety predicted spontaneous preterm birth (Dole et al., 2003). Another large study assessed many types of acute and chronic stressors in 5000 pregnant women including relationship strain and job-related stress, and found that only pregnancy anxiety predicted preterm birth in controlled analyses (Kramer et al., 2009).

Although the physiological pathways underlying the associations between pregnancy anxiety and birth outcomes have not been fully determined, the interrelated activities of the hypothalamic-pituitary-adrenal (HPA) axis and especially of placental corticotrophin-releasing hormone (CRH) are potential mechanisms explaining this association (Hobel et al., 1999). In the non-pregnant state, CRH is secreted by the

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hypothalamus and is not detectable in peripheral blood at concentrations of 10–20 pg/ml (McLean et al., 1995; Smith et al., 2009). During pregnancy, however, the placenta synthesizes and secretes CRH (referred to as placental CRH) into maternal and fetal circulation as early as the seventh week of gestation (McLean et al., 1995). As pregnancy progresses, levels of placental CRH increase exponentially, reaching high levels in maternal and fetal compartments during late pregnancy, and peak concentrations of 1000–10,000 pg/ml at term and in labor (Hillhouse and Grammatopoulos, 2002; Lindsay and Nieman, 2005; McLean et al., 1995). Several studies have shown that circulating CRH acts on CRH receptors in the myometrium to influence contractility (Cong et al., 2009; Jin et al., 2007; Zhang et al., 2008; Sandman and Glynn, 2009). Thus, the sharp rise of placental CRH in late pregnancy may initiate a cascade of events ultimately resulting in myometrial activation.

Only one published study has examined whether placental CRH mediates the link between pregnancy anxiety and length of gestation (Mancuso et al., 2004). The results of this study showed indirect effects of pregnancy anxiety reported at 28–30 weeks on length of gestation via levels of placental CRH measured at 28–30 weeks. Similar effects were not observed for measures of perceived stress or state anxiety, suggesting that pregnancy anxiety may be a particularly important construct for understanding stress processes underlying preterm birth. These results are consistent with the premise that pregnancy anxiety accelerates placental CRH trajectories during late pregnancy, thereby increasing risk for preterm birth through the triggering of labor and delivery pathways. However, the study did not collect measures of pregnancy anxiety before the time of placental CRH collection, nor did it examine changes in pregnancy anxiety or placental CRH over pregnancy.

Although some of the study samples in prior research on pregnancy anxiety are ethnically diverse, analyses typically adjust for ethnicity rather than examine it as a variable of interest. However, differences in attitudes about child-bearing and motherhood between Latina and non-Latina White women may contribute to differing levels of pregnancy anxiety (Campos et al., 2007; Engle et al., 1990; Fleuriet and Sunil, 2014; Scrimshaw et al., 1997). The authors of one qualitative study on the pregnancy behaviors of Puerto Rican women living in New York and pregnant Mexican immigrant women living in Los Angeles, speculated that Latinas expressed concerns about dying and leaving their babies motherless, and about their infant dying during childbirth (Scrimshaw et al., 1997). However, this study did not investigate these concerns in non-Latina women. In another study, Mexican-immigrant women living in South Texas reported higher levels of pregnancy anxiety compared to Mexican-American women (Fleuriet and Sunil, 2014). The limited available evidence demonstrating that Latinas may experience higher levels of pregnancy anxiety is noteworthy because of the implications for risk of preterm birth¹. However, additional research is needed to better understand how biopsychocultural factors operate in the etiology of preterm birth for the growing subgroup of Latinas in the United States population.

In sum, pregnancy anxiety has been shown to predict the length of gestation and has been shown to be higher among Latinas in a few studies. Furthermore, the physiological mechanisms linking pregnancy anxiety and birth outcomes are under active investigation. The present study examined whether pregnancy anxiety differed between Latina and non-Latina White women, tested indirect pathways (mediation) by placental CRH, and considered whether indirect or mediational

processes differed between these two ethnic groups.

We examined these issues in a sample of pregnant women who identified as Latina or non-Latina White. The first aim was to examine whether pregnancy anxiety, placental CRH, or changes in placental CRH predict the length of gestation. Based on prior research, we hypothesized that higher pregnancy anxiety and higher levels of placental CRH late in pregnancy would predict shorter length of gestation. We further hypothesized that placental CRH in pregnancy (19 and 25 weeks) and rate of change in placental CRH from mid to late pregnancy would predict the length of gestation. Second, we tested for ethnic differences between Latina and non-Latina White women in these variables (pregnancy anxiety, placental CRH at 19, 25, and 31 weeks, and changes in placental CRH from 19 to 31 weeks and 25 to 31 weeks). We expected that Latinas would show higher levels of pregnancy anxiety. No hypotheses were made for ethnic differences in length of gestation or ethnic differences in placental CRH in light of past conflicting evidence (Glynn et al., 2007; Ruiz et al., 2002; Siler-Khodr et al., 2003). Finally, we examined whether there were indirect pathways between pregnancy anxiety and length of gestation via levels of and changes in placental CRH, and whether ethnicity moderated any indirect effects.

2. Materials and methods

2.1. Protocol

This study utilized data from a prospective longitudinal study on psychosocial and behavioral factors in pregnancy. We recruited participants at two large medical centers, and obtained blood samples and interviewed women at three timepoints in pregnancy separated by six week intervals: T1 (M = 19 weeks, SD = .85); T2 (M = 25 weeks, SD = .85); and T3 (M = 31 weeks, SD = .80). Birth outcome data were abstracted from medical charts. Each institution's Institutional Review Board approved all protocols and procedures.

2.2. Subjects

Eligibility criteria were that a woman had to be 18 years of age or older, English speaking, and carrying a singleton intrauterine pregnancy. Exclusion criteria were no current tobacco, alcohol, or drug use, and no medical conditions involving dysregulated neuroendocrine, cardiovascular, hepatic, or renal functioning. The latter were to collect biomarkers that would be unaffected by these medical conditions.

A total of 63% of the 1189 women who were screened for the larger study met the eligibility criteria, and 67% of these women consented to participate in the study (N = 498). The primary reasons for declining to participate were having work or school conflict, scheduling difficulties, childcare issues, and lack of interest. For the present study, we consider only the subset of 337 participants who self-identified as Latina (n = 107) or non-Latina White (n = 230).

Among the 107 Latina women, 34 were foreign-born (32%), mainly born in Mexico (n = 23) but also Guatemala (n = 3), El Salvador (n = 3), Cuba (n = 1), the Dominican Republic (n = 1), Panama (n = 1), and other unspecified Latin American countries (n = 2). Foreign-born Latina women had been living in the United States for an average of 18 years (SD = 8.58, Range = 1–35).

2.3. Measures

2.3.1. Pregnancy anxiety

Pregnancy anxiety was measured with the 10-item Pregnancy-Related Anxiety Scale (Rini et al., 1999). This scale has been used in previous studies of pregnant English and Spanish speaking women (e.g., Rini et al., 1999) with good to excellent reliability and validity in both languages. Participants rated the extent to which they worried or felt concerned about their own health, their baby's health, labor and

¹ In a prior study of a subset of the present cohort examining familism, social support, perceived stress, pregnancy anxiety, and infant birthweight, there was an incidental finding on ethnic differences in pregnancy anxiety, which were not the focus of that study (Campos et al., 2008). The present study uses a larger cohort and different predictors and outcomes. Only the analysis of ethnic differences in pregnancy anxiety is common between them.

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