

Pattern of Perceived Stress and Anxiety in Pregnancy Predicts Preterm Birth

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Objective: To determine whether the pattern of prenatal stress, as compared to prenatal stress assessed at a single gestational time point, predicts preterm delivery (PTD). **Design:** Perceived stress and anxiety were assessed in 415 pregnant women at 18–20 and 30–32 weeks' gestation. **Main Outcome Measures:** Gestational length was determined by last menstrual period and confirmed by early pregnancy ultrasound. Births were categorized as preterm (< 37 weeks) or term. **Results:** At neither assessment did levels of anxiety or perceived stress predict PTD. However, patterns of anxiety and stress were associated with gestational length. Although the majority of women who delivered at term exhibited declines in stress and anxiety, those who delivered preterm exhibited increases. The elevated risk for PTD associated with an increase in stress or anxiety persisted when adjusting statistically for obstetric risk, pregnancy-related anxiety, ethnicity, parity, and prenatal life events. **Conclusions:** These data suggest that the pattern of prenatal stress is an important predictor of PTD. More generally, the findings support the possibility that a decline in stress responses during pregnancy may help to protect mother and fetus from adverse influences associated with PTD.

Keywords: pregnancy, preterm birth, prenatal stress, anxiety, birth outcome

During pregnancy, profound physiological changes are essential to maintain a successful gestation and effect delivery. The placenta, a transient organ of fetal origin, plays a primary role in the regulation of the maternal–fetal endocrine milieu (Petraglia, Florio, Nappi, & Genazzani, 1996). It is not widely appreciated, however, that these hormonal alterations have implications that extend beyond the reproductive process; they also influence the maternal stress system, including psychological functioning during pregnancy (Glynn, Wadhwa, Dunkel-Schetter, Chicz-Demet, & Sandman, 2001; Glynn, Dunkel-Schetter, Wadhwa, & Sandman, 2004). The present study examines how reports of prenatal stress change during pregnancy and whether these alterations are associated with birth outcome.

Relation Between Psychosocial Stress and Pregnancy Outcomes

Preterm birth (delivery prior to 37 weeks' completed gestation) is a significant health problem accounting for approxi-

mately 12% of live births in the United States and is the leading cause of neonatal mortality in nonanomalous infants (Martin et al., 2003; Matthews, Menacker, & MacDorman, 2004). Despite advances in medical care, rates of preterm birth have increased by 30% over the past 25 years (Martin, Kochanek, Strobino, Guyer, & MacDorman, 2005). Recognized predictors of preterm birth include medical factors such as assisted reproduction, multiple gestations, low body mass index, and infections (Goldenberg, Hauth, & Andrews, 2000; Moutquin, 2003; Jackson et al., 2004; Institute of Medicine, 2006); behavior patterns such as tobacco use (Savitz, Dole, Terry, Zhou, & Thorp, 2001); sociodemographic characteristics such as race/ethnicity and maternal age (Cnattingius, Forman, Berendes, Graubard, & Iso-talo, 1993; Martin et al., 2005); as well as psychosocial factors including prenatal stress (Copper et al., 1996; Dole et al., 2003). Despite progress in understanding the etiology of preterm birth, in the majority of these births the causes are not known (Challis et al., 2001).

Children born preterm who do survive are at risk for a panoply of problems, including profound physical and mental handicaps as well as a wide variety of less severe, adverse outcomes. Premature children are at increased risk for cognitive deficits that manifest in low IQ scores and educational problems (Bhutta, Cleves, Casey, Cradock, & Anand, 2002; Goldenberg et al., 1996). Growth is more likely to be stunted in these children, and they experience poorer physical health on average (Cooke & Foulder-Hughes, 2003; Saigal, 1995). Premature birth is associated with delayed motor development (Cooke & Foulder-Hughes, 2003), and the spectrum of potential complications also includes social relation-

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ship and emotional problems. Premature children are more likely to exhibit delays in expressive behavior (van Beek, Hopkins, & Hoeksema, 1994) and tend to have more difficult temperaments (Gennaro, Tulman, & Fawcett, 1990).

As noted previously, findings suggest a role for prenatal stress in the occurrence of adverse birth outcomes including preterm birth (Copper et al., 1996; Dole et al., 2003; Hedegaard, Henriksen, Sabroe, & Secher, 1993). Despite the growing number of studies supporting this relation, the sizes of the effects on average are quite modest. Clearly, this may be due to the fact that the effects are small in size, but a more likely explanation is that the empirical work is not capturing optimally these relations for a variety of reasons. Two of the most influential reviews of the stress and birth outcomes literature (Lobel, 1994; Paarlberg, Vingerhoets, Passchier, Dekker, & Van Geijn, 1995) provide a number of reasons for the modest and sometimes inconsistent results. These factors include many aspects of the way in which prenatal stress is operationalized (e.g., instruments with poor construct validity, nonstandard assessments, inconsistencies among studies in which instruments are used), variations in the time frame of measurement during pregnancy, different and sometimes erroneous definitions of adverse birth outcome (studies lump together antepartum complications, preterm birth, and low birth weight—conditions that have different etiologies and perhaps different relations with stress), and failure to take into account other important factors associated with birth outcome such as medical risk, parity, and smoking.

The purpose of the present study is to examine a relatively unexplored factor that may help explain the inconsistent and modest findings of the existing prenatal stress studies—changes in maternal sensitivity to the environment that occur with advancing gestation. As pregnancy progresses, women are less physiologically and psychologically reactive to stress (Glynn et al., 2001, 2004; Matthews & Rodin, 1992; Schulte, Weisner, & Allolio, 1990). The implication of these findings is that the impact of stress during pregnancy is not uniform. Stressors experienced early in pregnancy have greater impact, on both physiological and psychological responses, than stress experienced later.

Stress Responses in Pregnancy

Both physiological and behavioral indices in animal models suggest that stress responses in pregnancy are altered. Pregnant mice, rats, and ewes show reduced fear and anxiety behavior in a variety of stressful situations compared to nonpregnant animals (Maestripieri & D'Amato, 1991; Viérin & Bouissou, 2001; Wartella et al., 2003). Neumann et al. (1998) have shown that animal models of physical and emotional stress result in reduced ACTH and corticosterone responses in pregnant rats compared to virgins. In addition, their work indicates that the ACTH response to the administration of exogenous corticotropin-releasing hormone (CRH) is reduced in pregnant versus virgin animals.

Two studies in humans have directly assessed changes in psychological responses to stress during pregnancy. Both examined affective responses to major life events (Glynn et al., 2001, 2004). In the first study, it was determined that the timing of a major earthquake during pregnancy was related to the magnitude of the stress response to that earthquake. Women who experienced the earthquake early in pregnancy rated it as more stressful than those who experienced it late. In a second study, responses to a wide

variety of life events were examined including job loss, problems in a romantic relationship, legal trouble, and threats of physical harm. Again, the data suggested that events occurring early in pregnancy were experienced as more stressful than those same events occurring later in pregnancy. Further, this effect was not limited to a few events. Fourteen of the 18 events showed the same pattern, with early events being rated as more stressful.

Studies examining physiological responses mirror the psychological findings, also indicating that the stress response is dampened as a result of pregnancy (see deWeerth & Buitelaar, 2005, for a detailed review). Administration of CRH, which stimulates the synthesis and release of ACTH, which in turn stimulates the release of cortisol in nonpregnant women, does not produce detectable responses in women the third trimester of pregnancy (Schulte et al., 1990). Cortisol responses to cold pressor challenge in pregnant women are similarly absent but are present in nonpregnant women (Kammerer, Adams, von Castelberg, & Glover, 2002). When presented either with a physical or psychological stressor at 21–23 weeks' gestation, pregnant women have reduced blood pressure responses compared to nonpregnant women (Matthews & Rodin, 1992). Heart period responses to challenge also are increased (indicating decreased responsivity) at 24 weeks' gestation compared to a nonpregnant state (DiPietro, Costigan, & Gurewitsch, 2005). Similarly, compared to the nonpregnant state, catecholamine responses to challenge are diminished when examined during the third trimester of pregnancy (Nisell, Hjemdahl, Linde, & Lunell, 1985). Taken together, the existing studies suggest that changes in the physiological stress response are present as early as late second trimester.

Why Examine Change in Responses to Stress During Pregnancy?

There is evidence that increased maternal stress during pregnancy is related to decreased gestational length and that pregnancy-associated changes in stress responses exist across a wide variety of species including humans. Given these findings, a next step is to ask whether meaningful individual differences in stress responses during the prenatal period exist. That is, if on average women become less responsive to stress during pregnancy, do differences in the propensity to exhibit this decline predict the outcome of pregnancy? Women who do not show a decline in stress responses may have increased cumulative susceptibility to stress across gestation. Because they are more likely to be influenced by the adverse effects of stress during the entire course of pregnancy, they may be more likely to deliver preterm. It also may be the case that a failure to exhibit a decline in stress responding is a marker of dysregulation in the parturition process associated with an increased likelihood of preterm delivery. Regardless of whether a change in stress responses during pregnancy might play a causal role in development of preterm birth outcome or whether it is a marker of some underlying pathophysiology, its utility as a predictor of adverse birth outcome remains to be assessed. With this study, we examined changes in prenatal maternal reports of stress (perceived stress and state anxiety) from mid to late pregnancy and determined whether these changes relate to preterm birth. We predicted that women who exhibit increases in measures of prenatal stress would be more likely to deliver preterm. In addition, we explored whether any changes in prenatal

stress responses observed during gestation might be due to three potential sources of stress: pregnancy anxiety, the experience of a medically high risk pregnancy, or a range of stressful life events.

Method

Participants

Participants were pregnant women who were receiving prenatal care from Cedars-Sinai Hospital in Los Angeles or the faculty obstetric practice at the University of California, Irvine Medical Center. All of the women were nonsmokers and had a singleton pregnancy. Of the total potential participants at each site (1,189), 63% met eligibility criteria. The most common reasons for ineligibility (in order of frequency) were non-English speaking, gestational age >18 weeks, multiple gestation, and smoking. Among the 754 eligible women, 67.5% (509) were consented and came for the initial visit. Our sample comprised the 415 women who had complete data through the last pregnancy study visit at 32 weeks' gestation and complete birth outcome data. The demographic characteristics of the sample can be seen in Table 1. Compared to those included in this study, women not included in the study sample were more likely to be parous and African American (both $p < .05$); there was a trend suggesting they also had lower incomes ($p = .06$). The two samples did not differ in maternal age or education levels (both $p > .15$).

Procedures

Data reported here were obtained at two prenatal visits in a longitudinal study of pregnancy. One visit occurred at 18–20 weeks' gestation ($M = 19.3$, $SD = 0.8$) and the other at 30–32 weeks' gestation ($M = 31.0$, $SD = 0.8$). Participants completed the assessments discussed later through structured interview and questionnaire.

Measures of Prenatal Stress

As suggested by Lobel (1994), we adopted an umbrella concept (Lazarus & Folkman, 1984) to characterize prenatal stress. This view includes both stress exposures and responses under the same framework of prenatal stress. Here we examine the latter component—reports of prenatal stress with measures of generalized stress and anxiety. We examined the measures of stress and anxiety separately because, although the measures are positively associated, the correlations are not perfect (in the current sample they were correlated in the .7–.8 range).

Generalized or nonspecific stress was assessed at each visit using a modification of the 10-item version of the Perceived Stress Scale (Cohen & Williamson, 1988). This modified 12-item measure,¹ referencing the previous 7 days, includes questions addressing how often women felt they are able to successfully handle day-to-day problems and hassles, how often they felt nervous and stressed, and how often they felt things are going well. Responses were given on a 5-point Likert scale ranging from *never* to *almost always*. The 12-item measure correlated .99 at both time points with the 10-item version; in the present study, the reliability was high (average alpha coefficient across the two time points was .92).

State anxiety was assessed at both visits with the 10-item state anxiety subscale of the State–Trait Personality Inventory (Spielberger, 1979). Various anxiety-related adjectives were rated on a 4-point scale ranging from *not at all* to *very much*. For example, women stated how often in the last few days they felt calm, worried, or jittery. This brief measure has been shown have acceptable psychometric properties when used in pregnant and non-pregnant populations (Gurung, Dunkel-Schetter, Collins, Rini, & Hobel, 2005; Spielberger, 1979); it also was found to be reliable in the current sample ($\alpha = .84$, average of the two study time points).

Preterm Birth

Length of gestation was determined by last menstrual period and confirmed by early pregnancy ultrasound. If the discrepancy between the last menstrual period date and the date by ultrasound exceeded 7 days, then the estimate was revised based on the ultrasound. Preterm birth (<37 weeks' gestation) was indicated with a dichotomous variable (0 = *term*, 1 = *preterm*).

Pregnancy Anxiety

A 10-item pregnancy anxiety scale, which assesses a woman's feelings about her health during pregnancy, the health of her baby, and her feelings about labor and delivery, was administered at both study visits. Answers were given on a 4-point scale and included items such as: "I am fearful regarding the health of my baby," "I am concerned or worried about losing my baby," and "I am concerned or worried about developing medical problems during my pregnancy." This reliable measure ($\alpha = .75$ –.85) was specifically developed for use in pregnancy research (Rini, Dunkel-Schetter, Wadhwa, & Sandman, 1999). In the present study, the alpha coefficient was .81.

Medical Risk Factors

Medical risk for preterm birth was defined as the presence of certain historical risk factors and medical conditions in the index pregnancy including previous history of preterm birth, vaginal bleeding, and pregnancy-induced hypertension (Hobel, 1982). Risk conditions were determined through interview and extensive medical chart review. Medical risk was coded as a dichotomous variable with 1 indicating the presence of at least one condition and 0 indicating the absence of any current or historical risk conditions.

Life Events

At the initial visit, participants reported on the presence or absence of 24 major life events that might have occurred in the previous year. At the 30–32 week visit, they reported on the occurrence of these same set of events since the first visit at 18–20

¹ The modified version consisted of the published 10-item version and two additional questions derived from the original 14-item Perceived Stress Scale (Cohen, Kamarck, & Mermelstein, 1983): "How often have you dealt successfully with day-to-day problems and hassles?" and "How often have you felt that you were coping well or effectively handling the important changes that were occurring in your life?"

Table 1
Sample Characteristics

	Complete sample (<i>N</i> = 415)	Term (<i>n</i> = 377)	Preterm (<i>n</i> = 38)	<i>F</i> or χ^2	Increased PS (<i>n</i> = 174)	Decreased PS (<i>n</i> = 241)	<i>F</i> or χ^2	Increased anxiety (<i>n</i> = 172)	Decreased anxiety (<i>n</i> = 243)	<i>F</i> or χ^2
Race/ethnicity				6.33*			1.68			2.29
Hispanic White	23%	22%	35%		22%	23%		24%	22%	
Non-Hispanic White	48%	50%	30%		51%	46%		51%	46%	
African American	14%	13%	19%		12%	15%		11%	16%	
Other	15%	15%	16%		16%	16%		14%	16%	
Education				1.74			0.37			4.5
High school or less	16%	15%	19%		16%	15%		15%	15.5%	
Some college	38%	38%	43%		38%	38%		40%	37%	
Four-year degree	28%	28%	27%		29%	28%		24%	32%	
Post-graduate degree	18%	19%	11%		17%	19%		21%	15.5%	
Annual household income	\$63,181	\$63,541	\$59,357	0.55	\$64,304	\$62,384	0.60	\$62,187	\$63,880	0.41
Maternal age at delivery	30.64	30.63	30.78	0.03	31.02	30.36	1.27	30.52	30.73	0.60
Parity (% nulliparous)	57%	58%	42%	3.66*	56%	58%	0.57	56%	58%	0.17
Small for gestational age	8%	7%	38%	7.22***	8%	6%	0.59	8%	7%	0.02

Note. PS = perceived stress.

* $p < .1$. *** $p < .01$

weeks. The life events instrument has been used successfully in previous studies of pregnant women (Glynn et al., 2004; Lobel, Dunkel-Schetter, & Scrimshaw, 1992). The number of events experienced during the period prior to the first assessment and the number of events experienced between the study visits each were summed to create two life events scores.

Analysis Plans

First, the data were examined using conventional methods in which the relations between preterm birth and the prenatal stress measures at 18–20 and 30–32 weeks were assessed. Then change in prenatal stress was assessed both as a continuous (score at 18–20 weeks subtracted from the score at 30–32 weeks) and dichotomous (direction of the change between time points, i.e., an increase or a decrease²) variable. To assess the possibility that demographic characteristics such as race/ethnicity, socioeconomic status, or parity might account for observed links between prenatal stress and preterm birth, we included any variables that showed a reliable relation ($p < .1$) with the prenatal stress variables or preterm birth as covariates in hierarchical logistic regression analyses. The sample characteristics considered as potential covariates are presented in Table 1.

In addition, three potential sources of stress—pregnancy anxiety, medical risk for preterm birth, and life events—were analyzed in conjunction with change in stress in the hierarchical logistic regression models used to predict preterm birth. These analyses were included to explore whether any association between changes in prenatal stress and preterm birth could be attributed to differences in pregnancy anxiety, the presence of medical conditions placing the woman at risk for a preterm birth, or to exposure to stressful life events.

Results

The means for the prenatal stress measures at the two time points for women who delivered preterm and at term are given in

Table 2. For women who delivered at term, the value for the third trimester was either the same or lower than that of the second trimester. In contrast, for those who delivered preterm, the mean was higher during the third trimester for both state anxiety and perceived stress. A two-way repeated measures analysis of variance (ANOVA; Group x Time) revealed a statistically significant interaction between group and time for state anxiety, $F(1, 413) = 3.87, p = .05$. However, the interaction term for perceived stress failed to achieve significance, $F(1, 413) = 3.26, p = .07$. There were no statistically significant main effects of time or group for either dependent measure (all $ps > .1$).

The point-biserial correlations between preterm birth and the stress and anxiety measures at 18–20 and 30–32 weeks' gestation are given in Table 3. There were no significant relations between perceived stress and state anxiety and preterm birth at either of the time points under study.

Analysis of Change

Analysis of the continuous change variables showed that changes in perceived stress and state anxiety were not associated with preterm delivery (see Table 3). The distribution of the dichotomous change variables comparing women who experienced an increase in the prenatal stress measures to those who experienced a decrease is shown in Figure 1. Women who delivered preterm were significantly more likely to show increases in perceived stress and state anxiety between 18–20 and 30–32 weeks (both χ^2 's (1, *N* = 415) $> 6.3, ps < .05$).

² For the perceived stress measure, 36 individuals showed no differences between the first and second time points; similarly, 23 individuals showed no difference for the state anxiety measure. These participants were included in the decrease group. The analyses were repeated without the inclusion of these participants, and results were not altered.

Table 2
Mean Stress and Anxiety Scores for Term ($n = 377$) and Preterm ($n = 38$) Pregnancies

	18–20 weeks' GA	30–32 weeks' GA
PS		
Term	2.25	2.25
Preterm	2.27	2.46
Anxiety		
Term	1.96	1.91
Preterm	1.96	2.10

Note. GA = gestational age; PS = perceived stress.

Although none of the demographic variables were associated with the dichotomous change variables (see Table 1), race³ and parity were associated with preterm birth and so they were entered into the first step of two hierarchical logistic regression models and the dichotomous change variables were entered second. Adjusting for race and parity, our analyses revealed that women who showed an increase in perceived stress were three times more likely to deliver preterm (odds ratio [OR] = 3.08, 95% confidence interval [CI] = 1.51–6.28) and those who showed an increase in state anxiety were more than twice as likely to have had a preterm delivery (OR = 2.49, 95% CI = 1.24–4.98).

To determine whether the change in perceived stress or state anxiety exerted effects independent of the absolute levels of these variables, a second set of hierarchical logistic regression analyses were conducted in which the race and parity variables were entered first, the level of perceived stress or state anxiety at the 18–20 week assessment was entered second, and then, in the third and final step, the dichotomous change variable was entered. These regression analyses were repeated with the level of perceived stress and state anxiety at the 30–32 week assessment entered in the second step. In all analyses, the dichotomous change variables for perceived stress and state anxiety remained statistically significant predictors even when the variance attributed to the demographic covariates and the values at the first and second assessments were held constant (all ORs > 2.36, $ps < .05$).

Alternate Explanations: Pregnancy Anxiety, Medical Risk, and Life Events

We next explored whether the observed associations between changes in prenatal stress and preterm birth could be attributed to differences in pregnancy anxiety, to the presence of medical conditions placing the woman at risk for a preterm birth, or to exposure to stressful life events. Pregnancy anxiety might influence both perceived stress and state anxiety and also be associated with preterm birth. Similarly, the experience of an “at risk” pregnancy (obstetric risk for preterm birth) could affect the measures of prenatal stress and also is more likely to result in a preterm birth. These two pregnancy-related variables were entered into the second step of the regression models seen in Table 4. Last, we addressed whether the associations between changes in perceived stress, state anxiety, and preterm birth could be attributed to the presence of significant life stressors. The number of life events experienced in the period prior to the first assessment and expe-

rienced during the study period were entered into the third step of the regression models (Table 4).

The results of the two regression analyses for perceived stress and state anxiety are found in Table 4. It is important to note that dichotomous change in perceived stress and state anxiety remained significant predictors after accounting for the variance attributed to pregnancy anxiety, medical risk status, and life events (ORs = 2.79 and 2.41, respectively). Not surprisingly, medical risk was a significant predictor of preterm birth in both of the models (both ORs > 3.49). In contrast, at neither time point was pregnancy anxiety a significant predictor of preterm birth in either of the analyses. The number of life events either before or during the study period also was not a significant predictor of preterm birth.

Independent Contributions of Perceived Stress and State Anxiety

In a final regression model, dichotomous change in both perceived stress and state anxiety were assessed conjointly to determine whether they were unique predictors of preterm birth. This model (not shown) was identical to that seen in Table 4, the only difference being that change both in perceived stress and in state anxiety were entered simultaneously in the fourth step. As with all of the other models, of the variables entered in the first three steps, only medical risk was a reliable predictor of preterm birth (OR = 3.46, 95% CI = 1.28–9.36). In the final step, only change in perceived stress remained a statistically significant predictor (OR = 2.26, 95% CI = 1.02–5.01) and change in state anxiety was rendered not significant (OR = 1.80, 95% CI = 0.83–3.97).

Discussion

These are the first data to show that the pattern of change in prenatal stress during the course of gestation is an important predictor of the adverse outcome of preterm birth. Whether or not a woman reported an increase in perceived stress or state anxiety during pregnancy was a better predictor of preterm birth than levels of these variables at either of the gestational time points under study. In this study, the size of the change was not as important as the simple presence of an increase or decrease. In the final statistical model, perceived stress was a superior predictor of preterm birth when compared to state anxiety.

It cannot be determined with certainty with the current data set whether the changes observed are due to the dramatic reductions in physiological stress responding seen in humans and a variety of other species, reflect alterations in pregnant women's environments, or result from modifications of attribution processes concerning stress exposures that are purely psychological in origin. However, we believe that the best available explanation for the changes in psychological stress responses during pregnancy is that they reflect the changes in the physiological milieu of the pregnant woman. This conclusion is based both on the data we present and on more general considerations. Our findings cannot be attributed to the fact that women who delivered preterm experienced in-

³ For all regression analyses, the three most common racial/ethnic groups (non-Hispanic White, African American, and Hispanic White), as defined by self-identification, were dummy coded and included as covariates (1 = membership in the racial/ethnic group, 0 = nonmembership).

Table 3
Correlations of Psychological Variables With Preterm Delivery

	1	2	3	4	5	6	7
1. Preterm delivery	—						
2. PS (18–20 weeks' GA)	.01	—					
3. PS (30–32 weeks' GA)	.09*	.53***	—				
4. Change in PS ^a	.09*	-.42***	.55***	—			
5. Anxiety (18–20 weeks' GA)	.00	.73***	.48***	-.20***	—		
6. Anxiety (30–32 weeks' GA)	.08*	.55***	.80***	.32***	.62***	—	
7. Change in anxiety ^a	.10*	-.14**	.43***	.60***	-.37***	.51***	—

Note. PS = perceived stress; GA = gestational age.

^a Change from 18–20 to 30–32 weeks' gestation (computed by subtracting the score at 18–20 weeks from the score at 30–32 weeks).

* $p < .1$. *** $p < .01$.

creases in stress and anxiety because they experienced medically complicated pregnancies that were more likely to result in a shortened gestation or to the fact that some women experienced heightened levels of pregnancy-related anxiety. It also does not appear that the changes in perceived stress and anxiety reflect the presence of significant environmental stressors for some women. The number of stressful life events prior to and during the study period did not predict preterm birth, and the relation between

preterm birth and the change in perceived stress and state anxiety variables remained unaltered when the life events variables were included in the statistical models. Further, our measures of change were not associated with sociodemographic factors such as parity, race, and socioeconomic status, characteristics that plausibly could have accounted for our findings due to their associations both with prenatal stress and preterm birth (Cnattingius et al., 1993; Kramer et al., 2001; Lu & Chen, 2004). Our measures did not, by any means, capture all aspects of the pregnant woman's environment. For the measures we did have, however, our data support the argument that the changes in prenatal stress profile are most likely related to the physiological processes that occur during pregnancy because they mirror the dampening of the physiological stress response. We believe that this conclusion is further strengthened by two additional considerations. First, our data are consistent with animal models of altered fear and anxiety behaviors during pregnancy that have been linked to underlying physiological mechanisms (Kinsely & Lambert, 2006; Wartella et al., 2003). Second, if the changes observed are veridical, then one would have to posit a plausible explanation for why stress exposures differ systematically as a function of pregnancy (specifically why, on average, they lessen). Future research will need to explore the issue of underlying mechanisms further by incorporating both more detailed measures of environmental factors, such as stress exposures, as well as measures of physiological stress responses.

We studied change in prenatal stress from 18–20 weeks' gestation to 30–32 weeks' gestation. Without measures of stress prior to 18 weeks, we are unable to draw any conclusions about change in stress beginning in the first trimester, for example, whether the change from early to late pregnancy might be a better predictor of length of gestation than change from mid to late pregnancy. The timing of our assessments also does not provide insight into risk for very early preterm births. However, unlike the etiology of later preterm birth, the factors involved in these very early preterm births already are quite well characterized: it is known that infection is the primary cause of most very early deliveries (Goldenberg et al., 2000). In contrast, as gestation progresses to 33 weeks, the incidence of preterm birth due to infection drops to below 10%; in the majority of preterm births, there is no known etiological agent (Challis et al., 2001). Growing evidence, including the data presented here, supports a role for psychological factors in the process leading to preterm birth (Copper et al., 1996; Dole et al., 2003; Hedegaard et al., 1993).

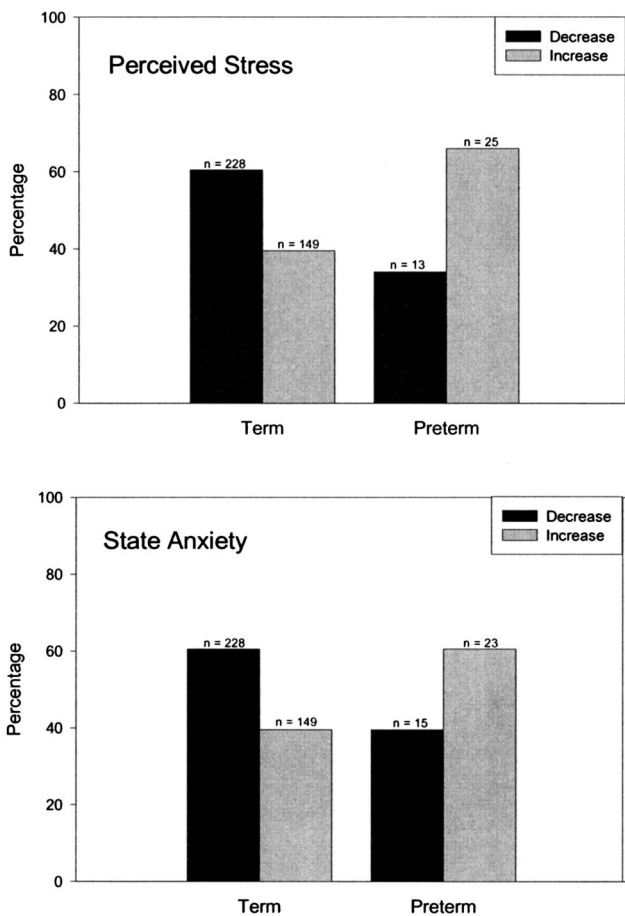


Figure 1. Percent of women delivering at term or preterm showing increases or decreases in stress and anxiety.

Table 4
Hierarchical Logistic Regression Models Used to Predict Preterm Birth

	Step 1		Step 2		Step 3		Step 4	
	OR	95% CI	OR	95% CI	OR	95% CI	OR	95% CI
Model 1								
Parity	1.64	0.80–3.36	1.47	0.70–3.10	1.46	0.69–3.07	1.44	0.68–3.01
African American	1.62	0.48–5.48	1.32	0.38–4.58	1.30	0.38–4.52	1.50	0.42–5.35
Non-Hispanic White	0.75	0.25–2.25	0.68	0.22–2.09	0.66	0.21–2.07	0.68	0.21–2.14
Hispanic White	1.83	0.61–5.45	1.76	0.58–5.37	1.73	0.56–5.32	1.85	0.59–5.78
Pregnancy events								
T1 PANX			0.93	0.85–1.03	0.94	0.85–1.03	0.95	0.86–1.04
T2 PANX			1.08	0.98–1.20	1.08	0.98–1.20	1.07	0.97–1.18
Med risk			3.63**	1.35–9.74	3.64**	1.35–9.78	3.49**	1.29–9.44
Life events								
T1 life events					1.03	0.88–1.20	1.05	0.90–1.23
T2 life events					0.96	0.78–1.17	0.92	0.75–1.13
Change in PS							2.79***	1.32–5.88
Model 2								
Parity							1.45	0.68–3.06
African American							1.40	0.40–4.92
Non-Hispanic White							0.63	0.20–1.99
Hispanic White							1.70	0.55–5.25
Pregnancy events								
T1 PANX							0.95	0.86–1.04
T2 PANX							1.07	0.97–1.18
Med risk							3.54	1.31–9.58
Life events								
T1 life events							1.03	0.88–1.21
T2 life events							0.93	0.76–1.14
Change in anxiety							2.41**	1.16–5.03

Note. OR = odds ratio; CI = confidence interval; T1 = 18–20 weeks' gestation; PANX = pregnancy anxiety; T2 = 30–32 weeks' gestation; Med risk = obstetric risk for preterm birth; PS = perceived stress.

Change from 18–20 to 30–32 weeks' gestation (dichotomous).

** $p < .05$. *** $p < .01$.

Methodological Implications for Stress Research

The implications of changes in stress responding during gestation for stress research during pregnancy are clear. The timing of stress appears to be critical in determining its effects. Early stressors may have the potential to influence outcomes more profoundly, particularly to the extent that they induce poststress ruminations (Glynn, Christenfeld, & Gerin, 2002). Further, a majority of women show decreases in response to stressors during pregnancy, and these changes seem to influence the effects of stress exposure in pregnancy (Glynn et al. 2001, 2004). With these data, we have shown that pregnant women who do not show the expected decline in stress and anxiety are at increased risk for preterm delivery. An increase in perceived stress or state anxiety was associated with more than a 2-fold increase in risk for preterm birth (the odds ratios ranged from 2.26 to 3.08 in the various regression models). These odds ratios translate into effect sizes ranging from .49 to .57 (Chin, 2000). Had we not taken change in stress responding into account and simply looked at the average of our prenatal stress measures, or at the levels at individual time points, we would not have detected a relation between prenatal stress and shortened gestation. A failure to take into account the variations in the potential for stressors to exert influences across gestation in design and analysis could serve to underestimate (or, in some cases, eliminate) the observed associations between pre-

natal stress and birth outcomes. Further, the effects related to timing of pregnancy described here and in other articles do render plausible the assertion that the inconsistent and modest results that characterize that stress and birth outcomes literature may be due in part to study designs that do not take timing of stress exposure into account.

Significance of a Decline in Stress Responses During Pregnancy

If the changes in responding we observed are related to the underlying physiological changes of pregnancy, it is not clear whether these alterations in psychological stress responses during pregnancy are merely epiphenomenal or whether they serve a function in themselves. In other words, are they purely a product of the physiological changes necessary to maintain a healthy pregnancy and effect a successful delivery, or do they serve some functional purpose? Work with animal models indicates that the fairly high reproductive failure rate in mammals exists for evolutionary reasons (Wasser, 1999). According to the adaptive reproductive failure model, failure is an adaptive mechanism evolved to minimize reproduction in times of environmental hardship. Failure can occur at many levels, including absence of menses, spontaneous abortion, or death of the infant (including premature birth,

abandonment, and infanticide; Wasser, 1999). There also exists evidence from work with humans that they, like other mammals, may have evolved so that reproductive failure is adaptive and that their fertility at all stages is affected by environmental cues (Copper et al., 1996; O'Hare & Creed, 1995; Rini et al., 1999; Wasser, Sewall, & Soules, 1993). In earlier work, it has been demonstrated that the later a major stressor occurs during pregnancy, the less likely it is to shorten gestation (Glynn et al., 2001; Lederman et al., 2004)—a finding that also supports the adaptive reproductive failure model in humans. The new data presented here suggest that women who do not show a potentially protective decline in responding are at greater risk of adverse birth outcomes. Early in pregnancy, it may be advantageous for the mother to respond to and transmit the effects of environmental stress to the fetal/placental unit thus increasing the probability of a pregnancy failure. However, the duration of human pregnancy is long and involves a significant investment on the part of the mother. Perhaps after a certain point, it may be adaptive to maintain the pregnancy even in times of environmental hardship. It is plausible that as maternal investment increases with gestation, environmental sensitivity decreases to ensure that environmental stress is less likely to result in an adverse birth outcome. Those who do not show this potentially adaptive decrease remain equally sensitive to the effects of stress across the gestational span and as a result are at greater risk for a preterm delivery. Future research will have to examine why individual differences in this phenomenon exist. It is possible that, for some women, remaining sensitive (or relatively more sensitive) to the effects of stress is adaptive. For example, perhaps in the face of adverse environmental circumstances, it might be more advantageous to terminate a pregnancy for women who have many children or for those who have had pregnancies in quick succession (a short interpregnancy interval). For women who have many children, or have a very young infant, maternal resources are relatively scarce and thus the cost of an additional child may be greater for them than for women with little or no commitment to offspring.

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