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Arch Womens Ment Health. Author manuscript; available in PMC 2014 April 01.

Published in final edited form as:
Arch Womens Ment Health. 2013 April ; 16(2): 101–108. doi:10.1007/s00737-012-0321-z.

Concurrent levels of maternal salivary cortisol are unrelated to self-reported psychological measures in low-risk pregnant women

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Abstract

Associations between salivary cortisol and maternal psychological distress and well-being were examined prospectively on 112 women with normally progressing, singleton pregnancies between 24 and 38 weeks gestation. At each of 5 visits, conducted in 3-week intervals, women provided a saliva sample and completed questionnaires measuring trait anxiety, depressive symptoms, pregnancy-specific hassles and uplifts, and psychological well-being. Maternal salivary cortisol was unrelated to psychological measures with the exception of minor associations detected with measures of anxiety and depressive symptoms between 30 and 32 weeks only. Findings indicate that self-reported maternal psychological distress and well-being are not associated with significant variation in maternal salivary cortisol levels during the second half of gestation. This suggests that studies that measure psychological factors in pregnancy but do not measure maternal cortisol should exercise caution in assuming activation of the maternal hypothalamic-pituitary-adrenal (HPA) axis is the mechanism through which maternal psychological factors are transduced to the fetus.

Keywords

Cortisol; Pregnancy; Maternal stress; Fetal programming

Introduction

> No discussion of the growth and development of the baby would be complete without consideration of the old belief that the mental condition of the mother may modify the development of the unborn infant, or, as they say, “mark” it.” (Eastman 1951, p.36)

The notion that maternal emotional state during pregnancy – worry, sadness, or happiness – impacts the developing fetus has long-standing historical origins. There is tremendous

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DISCLOSURE: None of the authors have a conflict of interest.

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current academic interest in the relation between maternal psychological factors and pregnancy and infant outcomes. Although immune and inflammatory mechanisms have been proposed as potential links between maternal psychological factors and birth outcomes, most studies that detect associations implicate the physiological action of the hypothalamic pituitary adrenal (HPA) axis as the putative link (Cottrell and Seckl 2009; Kramer et al. 2009; Mulder et al. 2002; Sandman et al. 1997; Wadhwa et al. 2011). The HPA axis regulates the production of maternal cortisol. While a substantial proportion of cortisol (80-90%) is metabolized by the placenta during gestation, maternal concentrations have significant impact on fetal levels and cortisol in excess may directly reach the fetus unmetabolized (Gitau et al. 1998). As such, maternal cortisol has been termed the 'culprit prenatal stress variable' (Field and Diego 2008).

Regulation of the maternal HPA axis changes dramatically during pregnancy. Baseline cortisol levels increase across gestation, reaching levels that are two to fourfold greater than pre-pregnancy concentrations prior to delivery (Allolio et al. 1990; Mastorakos and Ilias 2003; Sandman et al. 2006). Placental production of corticotropin-releasing hormone (CRH) is an antecedent for observed elevations in maternal cortisol secretion during late pregnancy. Placental CRH exerts a strong regulatory influence on maternal adrenal function via hypothalamic inputs of the central nervous system, stimulating a positive feedback loop between hormone outputs of the maternal HPA axis and placenta (Chan et al. 1993; Petraglia et al. 1996; Stalla et al. 1989). At the same time, increased circulating maternal cortisol acts to down regulate hypothalamic production of CRH, inducing a negative feedback loop within the maternal central nervous system, and contributes to a dampening of the maternal physiological activation to external stressors with advancing gestation (Magiakou et al. 1996). Thus, the degree to which maternal emotions or psychological factors may affect the amount of cortisol to which the fetus is exposed is unknown.

A number of studies have failed to detect positive associations between a variety of measures of maternal psychological distress and maternal cortisol levels (Davis and Sandman 2010; Goedhart et al. 2010; Gutteling et al. 2006; Harville et al. 2009; King et al. 2010; Petraglia et al. 2001; Rothenberger et al. 2011; Sikkema et al. 2001). While most have focused on negative psychological factors in so far as they are theorized to increase maternal cortisol, a few have examined the physiological benefit of behavioral well-being during pregnancy. Results revealed a modest inverse association between positive life events and lower maternal awakening cortisol in late pregnancy and, consistent with others, no association with negative life events (Pluess et al. 2012). Both general and pregnancy specific social support are also modestly and inversely related to maternal cortisol in mid-gestation (Wadhwa et al. 1996).

Despite this, maternal HPA activity continues to be the proposed link between prenatal psychological stress and birth outcome in numerous conceptual models (Dunkel-Schetter 2011; Gennaro and Hennessy 2003; Wadhwa 2005). Some of the null findings of the lack of association between cortisol and psychological distress measures cited in the previous paragraph are buried in results describing other relationships with outcomes and not the focus of that report. Others involve study designs which may be viewed as limited in their ability to detect such associations due to the inclusion of only a single measure to assess maternal psychological function (Petraglia et al. 2001) or only one or two data points (Harville et al. 2009; Sikkema et al. 2001). The current study provides a multidimensional assessment of maternal psychological factors using five standard measures that assess both negative and positive maternal characteristics including trait anxiety, depressive symptoms, pregnancy-specific hassles and uplifts, and psychological well-being. These data were collected at each of five successive visits during pregnancy concomitant with measurement of maternal salivary cortisol utilizing a staggered-cohort design spanning 24 to 38 weeks

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gestation. We hypothesize that a) there will be intraindividual stability in measures of maternal cortisol and psychological functioning within pregnant women over time, and b) variation in maternal cortisol level will be unrelated to variation in maternal psychological factors.

Materials and Methods

Participants

Participants were 112 normotensive, non-smoking women with normally progressing, singleton pregnancies and no pre-existing medical complications known to complicate pregnancy (e.g., Type 1 diabetes) or infant outcome (e.g., malformations). Women were recruited through advertisements posted in a local university and hospital. During the course of the study, five participants developed gestational diabetes, six women developed pregnancy induced hypertension (PIH), and four women delivered mildly preterm (*M* = 36.2 weeks, *range* = 35 to 36 weeks). Table 1 presents sociodemographic characteristics which reflect a sample of well-educated, mature, married, and predominantly primiparous women. Pregnancy dating was based on last menstrual period and early confirmation by ultrasound. As expected from the nature of the sample, pregnancy was diagnosed relatively early (*M* = 4.8 weeks, *SD* = 1.2) followed by clinical confirmation (*M* = 8.1 weeks, *SD* = 2.0). Fifty-one percent of the offspring were female and all had normal birth outcomes (*M* gestational age at delivery = 39.4 weeks, *SD* = 1.2; *M* birth weight = 3443 grams, *SD* = 436). Approximately one quarter of the infants were delivered via Cesarean section (*N* = 26, 23%).

Procedure

To fully represent the gestational age span from 24 to 38 weeks gestation, participants were stratified into three cohorts with staggered entry into the protocol between 24 and 26 weeks gestation and tested in 3-week intervals. Each cohort included between 34 and 39 participants. Prenatal visits were scheduled at 13:00 h or 15:00 h. During each of the 5 prenatal visits, women provided saliva samples and completed five psychological questionnaires (described below), in addition to participating in a maternal-fetal monitoring period as part of the larger protocol, reported elsewhere (DiPietro et al. 2010). The study was approved by the university's Institutional Review Board and women provided written, informed consent.

Measures

Salivary cortisol—Saliva was collected approximately 0.5 h after arrival to the laboratory at each visit. Participants were instructed to eat no more than 1.5 h prior to arrival and to restrict fluid intake upon visit arrival prior to collection to avoid the possibility of contaminating substances in the saliva. Participants moistened a filter paper strip (2.5 cm x 9.0 cm, Whatman Grade 42) which was subsequently air dried and stored at room temperature. This procedure has been validated, showing cortisol remains stable in this dried format and yields comparable recovery rates (92%) to whole saliva (Neu et al. 2007), and has been used previously in pregnant women (Kivlighan et al. 2008). Salivary cortisol concentration is unaffected by saliva flow rate (Vining and McGinley 1987). Dried filters were cut and extracted in assay buffer using a commercial high sensitivity EIA kit (Salimetrics, LLC) that detects cortisol levels in the range of 0.003—3.0 micrograms/dl (0.083—82.77 nmol/L). The detection limit after accounting for the extraction dilution was 0.018 micrograms/dl (0.50 nmol/L). Inter-assay coefficients of variation were less than 9.0% for high and low range laboratory controls. Intra-assay coefficients of variation for duplicate determinations were less than 4.5% in this laboratory. Raw values were log transformed for data analyses.

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Psychological functioning

The following psychological questionnaires were administered at each visit:

Anxiety—Trait anxiety was evaluated by the Spielberger Trait Anxiety Scales (Y-2; STAI), one of the most extensively validated self-administered anxiety measures and the most commonly used measure of anxiety in studies of pregnancy (Spielberger 1983). The STAI includes twenty items, scored on a 4-point Likert scale, ranging from 1 (*almost never*) to 4 (*almost always*) where higher scores reflect greater trait anxiety. A median alpha reliability coefficient of 0.90 for this scale has been reported (Spielberger 1983).

Depressive symptoms—The Center for Epidemiologic Survey Depression Scale (CES-D) was used to index depressive symptoms (Radloff 1977). The CES-D is a widely-used 20-item self-report measure of depressive symptoms experienced over the past week. Each item is rated on a 4-point scale ranging from 0 (*rarely or none of the time*) to 3 (*most or all of the time*) and summed to create a total score. The CES-D has been used in numerous studies of the perinatal period, and Cronbach alpha values ranging from 0.83 to 0.88 reflect high internal reliability during pregnancy (Mercer and Ferketich 1988; Mosack and Shore 2006).

Pregnancy-specific hassles and uplifts—Pregnancy-specific stress was assessed by a shortened form of the previously validated Pregnancy Experiences Scale (PES) (DiPietro et al. 2004). The PES-Brief includes the 10 most frequently endorsed hassles and uplifts from the long form of the PES, each rated on the original 4-point scale, ranging from 0 (*not at all*) to 3 (*a great deal*). Items were scored and averaged to derive perceived intensity of hassles and uplifts, with higher values reflecting greater intensity. The abbreviated PES-Brief demonstrates comparable psychometric integrity to the original version; internal reliability alphas were equal or greater to .80 (DiPietro et al. 2008).

Well-being—Emotional well-being was assessed using the World Health Organization Five Well-being Index (WHO-5) (WHO 2008), a 5-item self-report measure that has been validated in non-pregnant samples (de Wit et al. 2007; Heun et al. 1999).

Statistical analyses

Preliminary analyses evaluated the role of pregnancy risk factors and sociodemographic variables including maternal race, education and parity as potential confounders using *t*-tests and Pearson correlation coefficients, as appropriate. Descriptive information regarding change over gestation for maternal cortisol and psychological measures was provided using hierarchical linear models (HLM; SAS Mixed). Data analysis was focused on examining the interrelationship among the five individual psychological measures and their stability over time as well as the association between maternal cortisol values and the psychological measures utilizing Pearson correlation coefficients. Exploratory analyses revealed that time of day of saliva sample collection was associated with cortisol values (rs = -0.21 to -0.31, $p < 0.05$), such that collection in the earlier afternoon time slot showed slightly higher salivary cortisol concentrations. As a result, partial correlations between cortisol and psychological measures, adjusted for time of day, were also conducted.

Computing individual correlation coefficients at each of the 15 gestational weeks with each of the five psychological measures would significantly inflate the possibility of detecting spurious associations and minimize ns; as a result data analysis was conducted by collapsing the cohorts into five gestational periods. That is, period 1 included data collected at 24, 25, or 26 weeks gestation; period 2 included data collected at 27, 28, or 29 weeks gestation; and so on. There was minor variation in sample size per gestational period due to missed visits or missing data by some participants at some gestational ages (see Table 2).

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Results

Sample means and standard deviations for maternal cortisol and psychological measures at each visit are reported in Table 2. Raw cortisol values are presented for interpretation; log-transformed cortisol values to correct for skew were used in all data analyses. Examination of cortisol and psychological values for the four women that delivered mildly preterm revealed no pattern of outliers among these cases and comparable means to that of the larger sample (e.g., cortisol 33 to 35 weeks: *M* mild preterm = 0.19, *SD* = 0.13, *M sample* = 0.22, *SD* = 0.13; anxiety 33 to 35 weeks: *M* slight preterm = 32.5, *SD* = 8.0, *M sample* = 31.4, *SD* = 8.5), and as such they were not excluded from the analyses. Cortisol and psychological measures were similarly unrelated to the development of pregnancy-induced hypertension (*n* = 6). The five women with gestational diabetes showed higher cortisol levels at the first visit ($t(103) = -2.54$, $p < 0.05$) but not thereafter; there were no differences in report of psychological distress and well-being in these women compared to the larger sample. With respect to sociodemographic variables, maternal cortisol and psychological factors were unrelated to either maternal race or parity at any gestational period with one exception: African-American women ($n = 15$) reported higher pregnancy uplifts in the first two gestational periods (24 to 26 weeks and 27 to 29 weeks GA, ps < .05). At two gestational periods (27 to 29 weeks and 33 to 35 weeks GA), higher maternal education was associated with lower CESD scores and, and at a single gestational period (27 to 29 weeks GA) with lower trait anxiety and cortisol level (ps < .05). Adjusting for the partial correlation of maternal education did not impact the magnitude or significance of associations between maternal psychological measures and cortisol. As a result, sociodemographic variables were not included in the final models.

Change in maternal salivary cortisol and psychological measures across gestation

HLM analyses were conducted to examine change across the second half of gestation; data are presented in Table 2. Gestational trends for cortisol (DiPietro et al. 2011) and select psychological measures (i.e., anxiety and pregnancy-specific hassles and uplifts) (DiPietro et al. 2010) or composite measures only (Mendelson et al. 2011), have been reported previously. Maternal cortisol increased significantly from 24 to 38 weeks, controlling for time of day of saliva collection. Of the measures of maternal distress, only the CESD, which includes items reflective of normal consequences of pregnancy including fatigue and restless sleep significantly increased across the second half of gestation. With respect to positive emotions, maternal pregnancy uplifts significantly increased while general emotional well-being declined.

Associations among psychological measures

At each measurement, measures of distress (i.e., anxiety, depressive symptoms and PES hassles) were positively correlated with each other ($rs = 0.40$ to 0.84, $p < 0.01$), as were measures of well-being (i.e., WHO and PES uplifts; $rs = 0.27$ to 0.42, $p < 0.01$). Distress and well-being measures (exclusive of the PES-Brief) were negatively related ($rs = -0.55$ to -0.77, $p < 0.01$). Because of the strong interrelations between positive and negative attributes and the presumption that any individual measure does not fully reflect psychological distress, the individual psychological measures were Z-scored (i.e., normalized) and averaged to create composite measures of maternal psychological distress (STAI, CES-D, PES-Brief Hassles) and well-being (WHO-5, PES-Brief Uplifts).

Across measurement occasions, there was considerable stability in maternal cortisol levels (range rs = 0.44 to 0.68) such that while these levels increased across pregnancy for all women, individuals generally retained their rank. Psychological measures were also stable within individual women: trait anxiety (range rs = 0.74 to 0.92), depressive symptoms

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(range *r*s = 0.52 to 0.81), pregnancy-specific hassles (range *r*s = 0.44 to 0.77), well-being (range *r*s = 0.63 to 0.81), and pregnancy-specific uplifts (range *r*s = 0.68 to 0.79).

Associations between maternal cortisol and psychological measures

Table 3 shows the unadjusted inter-correlations between maternal salivary cortisol levels and psychological measures of distress and well-being at each visit. The only significant, albeit modest, correlations between measures of maternal psychological distress and cortisol levels were found during the third gestational period. Women who reported more anxiety or depressive symptoms between 30 to 32 weeks gestation had higher cortisol levels (*rs* = 0.21 and 0.23, respectively). No other associations, for individual measures or either composite, reached significance at any gestational period. Adjustment for diurnal salivary cortisol trends related to time of day yielded a small reduction in the strength of these two significant correlations (anxiety: $r = 0.20$, $p = 0.05$; depressive symptoms: $r = 0.22$, $p < 0.05$) and an overall similar pattern of negligible associations with the remaining variables and at other gestational ages.

Discussion

Maternal salivary cortisol and measures of maternal psychological distress and well-being show significant within-person stability during the second half of pregnancy suggesting that both may exert chronic influence on the intrauterine context. However, in contrast to the common assumption that maternal psychological characteristics, as measured by paper and pencil assessments, are transduced to the fetus via action of the maternal HPA axis, levels of salivary cortisol were essentially unrelated to self-reported maternal anxiety, depressive symptoms, and pregnancy-specific stress or to measures of well-being.

Despite perhaps a general perception to the contrary, these results are consistent with those reported previously which failed to detect significant associations between cortisol and psychological functioning in samples of pregnant women (Davis and Sandman 2010; Gutteling et al. 2006; Harville et al. 2009; Petraglia et al. 2001). Harville et al. (2009) found no correlations larger than $r = 0.15$ between salivary cortisol and a wide range of psychosocial measures including perceived stress, state-trait anxiety, coping style, life events, social support, and pregnancy-specific anxiety measured during two gestational windows (15 to 19 weeks and 25 to 29 weeks). Similarly, Petraglia and colleagues (2001) did not find any evidence for a significant relationship between serum cortisol and psychological stress at 28 weeks gestation. Studies that included either a greater number of samples across a wider gestational window (i.e. 15 to 37 weeks) (Davis and Sandman 2010) or multiple cortisol assessments during the course of a day to assess diurnal decline (Gutteling et al. 2006), also failed to detect significant associations.

The current study detected significant associations between salivary cortisol and trait anxiety and depressive symptoms between 30 and 32 weeks (*rs* = 0.21 to 0.23). The magnitude of these relations is consistent with a significant finding reported elsewhere of correlations between maternal cortisol and perceived stress (*rs* = 0.18) measured in the first and second trimesters (Rothenberger et al. 2011). With respect to indicators of maternal well-being, we did not find evidence to suggest a significant association between emotional well-being and pregnancy uplifts with salivary cortisol (highest $r = -0.19$), although the direction of the association followed the same inverse patterns observed elsewhere (Pluess et al. 2012; Wadhwa et al. 1996). Although these associations may attain statistical significance at times, they reflect less than 6% of shared variance. Correlations of this magnitude are of questionable physiological significance, particularly in light of background normative changes in the regulation of the maternal HPA axis during pregnancy (Allolio et al. 1990; Mastorakos and Ilias 2003). The typical top-down regulation of the maternal HPA axis via

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hypothalamic inputs of the central nervous system is subject to the ascending influence of placental CRH (Chan et al. 1993; Petraglia et al. 1996; Stalla et al. 1989). Placental CRH stimulates HPA activity, resulting in uniform elevations in maternal baseline cortisol measured in serum and saliva, independent of the maternal psychological environment.

The data presented here, based on 15 individual samples spanning from the 24th week of gestation to term with repeated measurement of five psychological dimensions including measures of stress and well-being, represent one of the most comprehensive assessments to date of the association between maternal psychological factors and cortisol during pregnancy. However, it is not without its limitations, including methodological issues related to the timing of saliva collection both in terms of gestational period and time of day. Reliance on an initial measurement point mid-way through pregnancy raises the possibility that significant associations may have been evident earlier in gestation. There is one report of a near significant ($p = 0.06$) association between cortisol levels in early pregnancy (8 to 19 weeks gestation) and more negative life events (Obel et al. 2005) and another significant relation between cortisol and trait anxiety ($p < .05$) (Pluess et al. 2010) during a similar gestational time window (10 to 20 weeks gestation). Significant associations did not persist when evaluated again later in pregnancy in either study. In contrast, other studies that have included evaluation of these associations as early as 13 weeks (Goedhart et al. 2010), 15 weeks (Davis and Sandman 2010; Harville et al. 2009), or 17 weeks (Sikkema et al. 2001) have not found significant associations between cortisol and psychological measures and therefore an overall answer to this question in early pregnancy remains unclear.

In addition, the current study relied on cortisol samples collected in mid-afternoon. Individual variation in HPA axis activity is most optimally indexed by multiple measurements reflective of the cortisol awakening response or diurnal secretory pattern, both of which are maintained during pregnancy (Allolio et al 1990; de Weerth and Buitelaar 2005a; Harville et al 2007). The studies which found associations earlier in pregnancy included a morning cortisol sample (Obel et al. 2005) or multiple measures to assess the cortisol awakening response (Pluess et al. 2010). Although, another study that employed a highly intensive cortisol sampling design (i.e., 7 samples per day, collected every 2 h from 8 a.m. to 8 p.m.) yielding morning levels and diurnal slope estimates during three gestational periods (i.e., 15 to 17 weeks, 27 to 28 weeks, and 37 to 38 weeks) failed to reveal any significant associations between cortisol values and maternal stress measures (Gutteling et al. 2006).

It is also possible that studies of the type reported here which involve measurement under baseline conditions do not adequately reflect situations in which the HPA axis is sufficiently activated to reveal an association with measures of maternal psychological state. However, in a study of pregnant women awaiting amniocentesis, during which one would assume significant activation of the stress response system, serum cortisol levels were only modestly associated with maternal state anxiety ($r = 0.18$) (Sarkar et al. 2006). Further, HPA axis reactivity to physical and psychological stressors is attenuated with advancing gestation (de Weerth and Buitelaar 2005b; de Weerth et al. 2007; Entringer et al. 2010; Fink et al. 2010; Magiakou et al. 1996; Nierop et al. 2008), and thus may limit observed variation in reactivity compared to that measured in a non-pregnant sample.

Further, it is important to reiterate that the current findings are generated from a sample of healthy women of relative socioeconomic advantage, raising questions of generalizability to either clinical psychiatric populations or those under economic duress. There may be a behavioral distress threshold below which the activity of the HPA and distress measures is uncoupled but above which there is a significant change in one is associated with changes in the other. Results based on clinical or disadvantaged groups are mixed. Salivary cortisol

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levels at 36 weeks gestation were not elevated in a sample of women with diagnosed depression and anxiety disorders compared to controls, although a small sub-sample of women with comorbid diagnosis ($n = 9$) had higher levels of cortisol than controls or either group with a single diagnosis (Evans et al. 2008). Another study comparing the cortisol awakening response at 25 and 33 weeks gestation revealed no differences between women who were clinically depressed and non-depressed controls (Shea et al. 2007). With respect to differences related to demographic factors, a large epidemiological study of nearly 1,600 pregnant women found that the higher levels of stress reported by unmarried, African-American, or young women was not reflected by differences in cortisol levels (Harville et al. 2009).

In summary, empirical evidence is lacking in support of a dose-response association between maternal cortisol and self-reported psychological state either earlier in pregnancy, when measured at different time of day, or in women who are exposed to more chronic psychological or socioeconomic risk and does not contraindicate the findings reported here. However, this should not be interpreted to suggest that maternal cortisol itself may not provide the fetus with an important signal as there is evidence of meaningful linkages between maternal cortisol and development which have only recently begun to be fully explored. Maternal cortisol has been shown to have facilitative effects on maturation of the fetal brain and timing of delivery (Sandman et al. 2006; Buss et al. 2009) and impacts infant behavioral and physiological responses to stress (Davis et al. 2011). Higher maternal cortisol in late pregnancy has been associated with more advanced physical and neuromuscular maturation in the neonate and mental development scores on the Bayley Scales at 12 months (Davis and Sandman 2010; Ellman et al. 2008) while the direction of these associations is reversed earlier in pregnancy (Davis and Sandman 2010). The potential influence of maternal cortisol is underscored by findings of the current study for the moderate to strong intra-individual stability in cortisol between 24 and 38 weeks gestation, and in other studies that have measured cortisol longitudinally beginning earlier in pregnancy (Davis and Sandman 2010; Gutteling et al. 2006).

Transduction of maternal psychological functions to the intrauterine environment requires a physiological signal. This study adds to the existing, but generally unacknowledged literature, that maternal salivary cortisol does not necessarily correspond to self-reported maternal psychological stress or well-being during pregnancy. This suggests that any observation of links between self-reported maternal psychological state and infant developmental outcomes requires additional hypotheses to identify potential mediating pathways.

Acknowledgments

This research was supported by National Institute of Child Health and Human Development grant 2R01 HD27592, awarded to J. A. DiPietro.

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Table 1

Maternal sociodemographic characteristics (n = 112)

Variable	%	M ± SD
Maternal age (years)		31.2 ± 4.6
Maternal education (years)		17.2 ± 2.1
Pre-pregnancy body mass index		23.6 ± 4.3
Maternal race		
Caucasian	80	
African-American	13	
Asian	7	
Married	91	
Primiparous	72	

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Table 2

Descriptive information for maternal measures and change over time

	24-26 wks[a] *M (SD)*	27-29 wks[b] *M (SD)*	30-32 wks[c] *M (SD)*	33-35 wks[d] *M (SD)*	36-38 wks[e] *M (SD)*	*t* *	*p value*
Salivary cortisol (*ug/dl*)	0.18 (0.09)	0.20 (0.10)	0.20 (0.10)	0.22 (0.13)	0.25 (0.11)	5.56	< 0.001
Psychological factors							
Trait anxiety	31.19 (6.64)	31.68 (7.79)	31.17 (7.65)	31.41 (8.45)	31.94 (8.02)	1.08	0.283
Depressive symptoms	6.06 (4.65)	8.71 (7.85)	8.93 (7.26)	9.25 (7.28)	10.33 (7.10)	6.80	< 0.001
Pregnancy-specific hassles	1.37 (0.43)	1.38 (0.43)	1.42 (0.48)	1.40 (0.46)	1.43 (0.43)	1.30	0.196
Emotional well-being	13.01 (2.92)	12.83 (3.31)	12.52 (3.33)	12.36 (3.63)	12.24 (3.50)	−2.76	0.007
Pregnancy-specific uplifts	2.31 (0.47)	2.34 (0.46)	2.44 (0.45)	2.38 (0.48)	2.40 (0.46)	2.38	0.019

[a] n = 105-107

[b] n = 98-100

[c] n = 94

[d] n = 98-101

[e] n = 86-87

* n = 112 for hierarchical linear modeling (HLM) test of change over time

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Table 3

Interrelationships of maternal cortisol and psychological status

	Maternal salivary cortisol (*ug/dl*)				
	24-26 wks	**27-29 wks**	**30-32 wks**	**33-35 wks**	**36-38 wks**
Psychological measures					
Trait anxiety	−0.02	0.06	0.21*	0.09	0.21†
Depressive symptoms	−0.01	0.13	0.23†	0.18†	0.08
Pregnancy-specific hassles	0.06	0.05	0.10	0.06	0.09
Distress composite	0.02	0.09	0.20†	0.11	0.15
Emotional well-being	0.11	−0.01	−0.10	−0.10	0.01
Pregnancy-specific uplifts	0.05	−0.05	−0.19†	0.13	−0.18†
Well-being composite	0.10	−0.04	−0.17	0.02	−0.11

† p<0.10

* p<0.05