Biological Psychology 102 (2014) 38–43

Contents lists available at ScienceDirect

Biological Psychology

journal homepage: www.elsevier.com/locate/biopsycho

Pre-pregnancy obesity and maternal circadian cortisol regulation: Moderation by gestational weight gain

Nicki L. Aubuchon-Endsley[a,*], Margaret H. Bublitz[b,c], Laura R. Stroud[b,c]

[a] Department of Psychology, Idaho State University, 921 S 8th Avenue, Stop 8112, Pocatello, ID 83209, USA
[b] Centers for Behavioral and Preventive Medicine, 164 Summit Avenue, Providence, RI 02906, USA
[c] Department of Psychiatry and Human Behavior, Alpert Medical School of Brown University, Box G-BH, Providence, RI 02912, USA

ARTICLE INFO

Article history:
Received 1 March 2014
Accepted 3 July 2014
Available online 16 July 2014

Keywords:
Obesity
Weight gain
Cortisol
Pregnancy
Glucocorticoid

ABSTRACT

We investigated main and interactive effects of maternal pre-pregnancy obesity and gestational weight gain on circadian cortisol from the second to third trimester. A diverse sample of 215 pregnant women was enrolled. Maternal height and most recent pre-pregnancy weight were collected at study initiation (22% obese). Weight and circadian salivary cortisol samples were measured during second (24 ± 4) and third (35 ± 1 weeks) trimesters. During the third trimester, women who were obese prior to conception showed elevated evening cortisol versus normal weight women. This pattern was moderated by weight gain in excess of Institute of Medicine guidelines, such that women who were obese prior to conception and gained greater than 7.94 kg by the 35 ± 1 week visit displayed greatest elevations in evening cortisol. Given links between excessive prenatal glucocorticoid exposure and both poor maternal and offspring health outcomes, elevated maternal cortisol may be one mechanism underlying links between maternal obesity and adverse perinatal outcomes.

Over half of women of childbearing age are overweight or obese (Vahratian & Vahratian, 2009). Given the adverse consequences of maternal excessive gestational weight on perinatal health outcomes (Cogswell, Perry, Schieve, & Dietz, 2001; Mann, McDermott, Hardin, Pan, & Zhang, 2013; Siega-Riz, 2012; Van Lieshout, Taylor, & Boyle, 2011) and offspring risk of cardiometabolic and neurobehavioral deficits through adulthood, this represents a major public health concern (Baeten, Bukusi, & Lambe, 2001; Sen et al., 2012; Siega-Riz & Laraia, 2006). Given these notable health consequences, the Institute of Medicine (IOM) recommends limiting gestational weight gain in obese women to 4.99–9.07 kg (Rasmussen & Yaktine, 2009), though 60% of these women gain in excess of this recommendation (Rasmussen & Yaktine, 2009). This is particularly concerning given that the coupling of maternal pre-pregnancy obesity with excessive gestational weight gain may result in additional risk for fetal overgrowth (Jensen et al., 2005), poor pregnancy outcomes (Black, Sacks, Xiang, & Lawrence, 2013), and both maternal and offspring long-term obesity and cardiovascular disease (Jensen et al., 2005; Siega-Riz & Laraia, 2006). Although these studies highlight the additive risk of pre-pregnancy obesity and excessive gestational weight gain on maternal and offspring outcomes, few studies have examined mechanisms underlying these relations. However, relatively new literature supports the role of stress hormones.

During typical, healthy pregnancies, daily maternal stress hormone release changes, relative to non-pregnant women (Jansson et al., 2008). In particular, cortisol awakening responses (cortisol peak between awakening and approximately 30 min post-awakening) and maternal stress reactivity decline as pregnancy progresses (Entringer et al., 2010; Obel et al., 2005). Blunting of the cortisol awakening response is thought to protect against maternal and fetal morbidity associated with excessive prenatal glucocorticoid exposure (Ching-Yu & Pickler, 2010; Stroud et al., 2014). Elevated cortisol may also be associated with excessive maternal weight, given that glucocorticoids decrease basal metabolic rate (Heiman et al., 1997). However, maternal fat cells inhibit reciprocal negative relations between elevated cortisol and decreased metabolism by releasing leptin hormone, which inhibits the hypothalamic–pituitary–adrenal response to stress (Sen et al., 2012). This response, however, is altered in obese women. In particular, obesity leads to the development of leptin hormone resistance, which results in elevated circulating cortisol (Sen et al., 2012), which has been linked to poorer appetite control (Heiman et al., 1997). In fact, in non-pregnant samples, obesity-related disruptions

* Corresponding author. Tel.: +1 208 282 2462; fax: +1 208 282 4832.
E-mail addresses: Nicki_Aubuchon-Endsley@brown.edu, aubucho@ostatemail.okstate.edu (N.L. Aubuchon-Endsley), mbublitz@lifespan.org (M.H. Bublitz), Laura_Stroud@brown.edu (L.R. Stroud).

http://dx.doi.org/10.1016/j.biopsycho.2014.07.006
0301-0511/

in circadian cortisol have been supported. These disruptions were manifested as attenuated cortisol awakening responses (Abraham, Rubino, Sinaii, Ramsey, & Nieman, 2013; Champaneri et al., 2013) as well as less pronounced decreases in evening cortisol levels (Farag et al., 2008; Sedaghat, Rabiei, & Rastmanesh, 2012). These flatter circadian trajectories, in which cortisol stays elevated longer throughout the day, may account for hypercortisolism in obese samples (Farag et al., 2008).

Given support for links among obesity, weight gain, and dysregulation of circadian cortisol, in the current study, we investigated circadian cortisol levels over the second and third trimesters in obese and non-obese pregnant women. Our first aim was to investigate the influence of pre-pregnancy obesity versus normal weight on daily circadian cortisol at 24 ± 4 and 35 ± 1 weeks gestation. Given the previous studies of non-pregnant samples documenting the effects of obesity on elevated circulating glucocorticoids, we predicted that women who were obese prior to pregnancy would have the greatest daily cortisol output, manifested as a flatter daily cortisol rhythm (i.e., higher baseline values, attenuated awakening response, and higher evening values). Our second aim was to explore the interaction among maternal pre-pregnancy obesity, gestational weight gain, and circadian cortisol. Based on preliminary studies suggesting leptin resistance associated with obesity and reciprocal relations between maternal cortisol and gestational weight gain, we predicted that for obese women, greater gestational weight gain would be associated with greater daily cortisol release, manifested as a flatter daily cortisol rhythm.

1. Materials and methods

1.1. Participants

Participants were recruited as part of a larger study (Behavior and Mood in Mothers and Behavior in Infants; BAMBI) of maternal depression in relation to fetal/infant development. Recruitment took place in health centers, obstetrical offices, and hospitals in the Providence, Rhode Island region. Two-hundred and fifteen participants were enrolled. Following enrollment, four participants declined participation over the course of the study. After removing participants with missing pre-pregnancy weight data, there were a total of 173 participants within the current sample, who are described in Table 1. None of the participants utilized in data analyses had been diagnosed with an endocrine disease (e.g., diabetes mellitus, hypo/hyperglycemia, and hypo/hyperthyroidism), thus eliminating such disorders as potential confounds.

1.2. Procedure/Materials

The current study was approved by the Women and Infants Hospital and Lifespan Hospitals' Institutional Review Boards. Following an initial telephone screen for exclusion criteria, the first (24 ± 4 weeks) session included study review, consent, and interviews regarding participant demographics and health/weight history, including participant-reported most recent pre-pregnancy weight. Participants were given detailed instructions and tubes for circadian saliva collection for three days at awakening, 30 min post-awakening, and prior to sleep at night for both visits (i.e., 24 ± 4 and 35 ± 1 weeks gestation).

To increase circadian saliva collection compliance, (I) detailed written and oral instructions were provided at each visit, (II) a subsample of participants (13%) utilized Medication Event Monitoring System caps (AARDEX, Zurich, Switzerland) with robust associations between self-reported and MEMS sampling times at wake/30 min post (r's = .99–1.0) and before bed (r's = .87–1.0), (III) incentives were provided for each saliva sample, and (IV) saliva and Medication Event Monitoring System caps were obtained by study staff from participants' homes after each circadian collection. Saliva collection times were included as covariates in our subsequent analyses. Participants were instructed to avoid eating or brushing their teeth 1 h prior to sampling. Upon retrieving samples, they were frozen at −80 °C prior to analysis. Cortisol assays were performed using expanded range high-sensitive enzyme immunoassays (ER-HS-EIAs) completed at Dresden University. The intra- and inter-assay coefficients of variation were <8%.

Maternal pre-pregnancy BMI was calculated utilizing the following standard formula: BMI = weight (kg)/height (m) squared. This semi-continuous BMI variable was used for interaction analyses. Women were classified as obese (BMI ≥ 30) or not (BMI < 30; Rasmussen & Yaktine, 2009) for main effects and follow-up analyses examining direction of effects. Weight changes were calculated by subtracting pre-pregnancy weight from weight at respective visits (i.e., 24 ± 4 and 35 ± 1 weeks gestation). The semi-continuous variable was used for all primary analyses, while categories (i.e., above or below IOM recommendations, according to pre-pregnancy BMI) were used for follow-up analyses.

Potential covariates considered in the current sample included maternal age in years, education (percentage of participants with a high school diploma or more education), employment (percentage of participants unemployed), married (percentage), race (percentage non-white), ethnicity (percentage Hispanic), parity, household income (percentage low income defined as <$40,000/year or approximately twice the federal poverty threshold for a family of four), and planned pregnancy (percentage), all obtained via maternal self-report at the first prenatal visit. Additionally, prenatal depression diagnoses (percentage) were captured over the course of the study via the administration of the Structured Clinical Interview for DSM-IV (SCID) and the percentage of participants with drug use (i.e., nicotine, alcohol, cannabinoids, and opiates) and major medical conditions (i.e., gallstones, oligohydramnios, generalized epilepsy, Chrone's Disease, MRSA infection, and kidney infection with hospitalization) during pregnancy were assessed from maternal interview, medical chart review, and biochemical analyses of infant meconium (assayed for amphetamines, cannabinoids, carboxy-THC, cocaine, codeine, hydrocodone, hydromorphone, morphine, and cotinine), respectively. Birth outcomes, including gestational age at birth, birth weight, small for gestational age (SGA; weight <10th percentile for the gestational age), large for gestational age (LGA; weight >90th percentile for gestational age), and APGAR score at 5 min post delivery, were collected by medical chart review following delivery.

2. Data analysis

All data analyses were completed using Predictive Analytics SoftWare (PASW), version 18. At both prenatal time points (24 ± 4 weeks and 35 ± 1 weeks, individually), Conditional Growth Models were used to examine main (semi-continuous BMI) and interactive effects of pre-pregnancy weight (dichotomous obesity) and gestational weight gain (semi-continuous) on the circadian cortisol trajectories. Level 1 models included each cortisol collection time (awakening, 30 min post-awakening, and before bedtime each averaged from available data over the three collection days), while Level 2 included pre-pregnancy weight, gestational weight gain, and the interaction term. Full maximum likelihood and composite residuals for covariance structures were used to estimate all Conditional Growth Models. Follow-up repeated-measures ANOVAs were conducted to explore group differences in the direction of significant main or interactive effects of pre-pregnancy obesity (yes, no) and gestational weight gain (above or below IOM recommendations) on circadian cortisol (at awakening, 30 min post-awakening, and before bedtime averaged over the three collection days) identified in the growth models. The gestational weight gain variables used for follow-up tests were adjusted for average pregnancy duration at the time of the respective study session using IOM recommendations. In particular, it is suggested that normative weight and overweight women should gain at or below 3 kg in the first trimester. While normative weight women should gain at or below 0.5 kg/week in the second and third trimesters, overweight women should gain at or below 0.33 kg/week in the second and third trimesters (Rasmussen & Yaktine, 2009). Obese women are recommended to gain at or below 2 kg in the first trimester and at or below 0.27 kg/week in the second and third trimesters (Rasmussen & Yaktine, 2009). Results from these follow-up repeated-measures ANOVAs were used to model group effects in figures, though semi-continuous variables were used in Conditional Growth Models. Cortisol collection time served as the repeated-measures variable for the ANOVAs, which were conducted separately for each prenatal time point.

Sampling distributions of residuals were examined for normality and logarithmic transformations were applied for maternal cortisol variables at the first prenatal time point (24 ± 4 weeks gestation). No data transformations were applied at the second time point because data were normally distributed and none of the analyses simultaneously assess diurnal cortisol at both a time points. Morning cortisol samples that were collected <20 or >40 min apart were removed in order to assure accurate measurement of the cortisol awakening response. One-way ANOVAs and chi-square tests