Psychoneuroendocrinology 95 (2018) 145–148

Contents lists available at ScienceDirect

Psychoneuroendocrinology

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

Short Communication

Maternal distress and hair cortisol in pregnancy among women with elevated adverse childhood experiences

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ARTICLE INFO

Keywords:
Pregnancy
Distress
Cortisol
Early childhood adversity

ABSTRACT

Life-course exposure to stress is associated with a wide-range of health outcomes. Early childhood adversity may affect an individual's future response to stress. This is of particular concern during pregnancy as *early* maternal stress may impact the stress response in pregnancy, altering fetal exposure. We therefore hypothesized maternal childhood adversity may interact with distress experienced in pregnancy affecting maternal cortisol accumulation in pregnancy. Analyses were conducted within the PRegnancy and Infant Development (PRIDE) Study, a cohort of mother-infant pairs participating in Every Child Succeeds, a home visiting program in Cincinnati, Ohio. Thirty (of 53) healthy pregnant mothers contributed a hair sample and completed a battery of psychologic and stress measures including the Adverse Childhood Experiences (ACE) Scale. We used linear models to estimate the association between symptoms of depression, anxiety, somatization, both pregnancy and perceived stress and cortisol deposition; we generated multiplicative interaction terms generated and models stratified by the dose of ACEs ($\geq 2/ < 2$). Although overall the associations between maternal psychological distress were not associated with hair cortisol, among women who experienced ≥ 2 ACEs, depressive, somatic, and anxiety symptoms and perceived stress during pregnancy were positively (and significantly for depressive and somatic) correlated with cortisol accumulation. Pregnancy-specific stress was inversely associated with cortisol and also varied by ACEs. Interactions were non-significant (p values 0.11–0.51). We identified an association between measures of distress in pregnancy and hair cortisol *only* among mothers who experienced high levels of childhood adversity demonstrating importance of recognizing life-course stress.

1. Introduction

Stress throughout the life-course is associated with a wide-range of adverse health outcomes. Accumulating evidence from animal and several human studies suggests that maternal distress and adversity experienced during pregnancy, including depression, anxiety, general and pregnancy-specific stress can increase the risk for impaired infant development (Talge et al., 2007). Families in poverty, such as those participating in home visiting intervention programs, carry a high burden of adversity including increased early life stressors and family exposure to psychosocial stressors (e.g., violence, residential instability, food insecurity) and psychological distress (e.g., maternal depression, anxiety). The increased parental exposure to adversity contributes to disproportionate risks for offspring developmental delays (Rosenberg et al., 2008), impaired language and literacy (Fernald et al., 2013), and negative social-emotional function (Steele et al., 2015). Prior studies have evaluated the association between measures of adversity in pregnancy and hair cortisol with conflicting results. For example, in 25 healthy pregnant women, hair cortisol was positively associated with perceived stress (Kalra et al., 2007). However a large study of n = 768 mothers of newborns found no association between stress, anxiety, or depressive symptoms and hair cortisol (Braig et al., 2016).

The response to distress experienced in pregnancy may be dependent on prior adverse exposures. The Adverse Childhood Experiences (ACE) Study demonstrated the profound impact of early adversity, and the dose thereof, on subsequent outcomes ranging from mental health

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https://doi.org/10.1016/j.psyneuen.2018.05.024
Received 20 November 2017; Received in revised form 2 May 2018; Accepted 15 May 2018

to obesity (Felitti et al., 1998). Early adversity may alter a mother's cortisol response systems. For example, an altered cortisol response (reactivity) to stress, as measured by changes in salivary cortisol, has been shown among individuals who experienced adversity in childhood (Carpenter et al., 2007). This altered reactivity could have profound effects in pregnancy if it affects fetal exposure. Maternal distress experienced in pregnancy may also interact (be moderated) with early life adversity to elicit more intense or blunted maternal biological responses, potentially modulating fetal exposure to the toxic effects of stress. For example, cumulative childhood stress predicted birth timing in a cohort of African American mothers independent of later stress (Gillespie et al., 2017). In addition, childhood trauma experienced prior to 18 years of age was shown to modify the effect of prenatal mood on birthweight in a predominantly low-income, inner-city population (Blackmore et al., 2016). These alterations to the maternal stress response system affect cortisol reactivity and consequent cortisol accumulation. Our objective was therefore to determine the combined effect of maternal early life adversity and pregnancy-specific measures of distress on maternal hair cortisol accumulation during pregnancy.

2. Material and methods

2.1. Population

Analyses were conducted within the PRegnancy and Infant Development (PRIDE) Study, a longitudinal cohort of pregnant women, which aims to evaluate the association between maternal life-course distress and offspring development in a population of women with high sociodemographic risk. The PRIDE Study enrolled women who were participating in Every Child Succeeds (ECS), a home visiting program serving Greater Cincinnati, Ohio. First-time mothers, who are single, have low income, and/or initiate prenatal care late (after the start of the third trimester), may enroll prenatally in ECS and are provided weekly, bi-weekly, or monthly home visits depending on their gestational week. Approximately 25% of eligible mothers in the region participate in the ECS program. The PRIDE Study enrolled fifty-five healthy pregnant mothers participating in ECS.

2.2. Exposure measures

Women were enrolled in PRIDE mid-pregnancy, contributed a hair sample 3-cm in length and completed a battery of psychometric assessments including The Brief Symptom Index-18 (BSI-18), The Pregnancy Experience Scale (PES), the Perceived Stress Scale (PSS) and the Adverse Childhood Experiences (ACE) scale. To avoid methodologic problems associated with cortisol measures including those within plasma, urine, or saliva, we measured maternal hair cortisol to capture long term cortisol accumulation (D'Anna-Hernandez et al., 2011). While plasma and saliva provide a 'snapshot' of cortisol response, hair provides a measure over an extended period of time, as each centimeter of hair growth represents approximately one-month of cortisol accumulation. The BSI-18 is used to screen for common psychiatric disorders including depression, anxiety, and somatization (Derogatis, 2000). The PES Brief version measures pregnancy-specific contributors to psychological state using the top 10 items from the original scale with comparable validity and reliability (DiPietro et al., 2004). The PSS is the most widely used instrument to measure perceived stress (Cohen and Hoberman, 1983), was designed for community samples, and is easily interpreted. The 10-item ACE scale measures childhood abuse, neglect and household dysfunction before the age of 18 years.

2.3. Hair cortisol

We collected 3 cm of hair from 30 women, at the occipital vertex, as close to the scalp as possible, using a standard protocol for measurement of cortisol. Of the 25 women without a hair sample, a majority were willing, but unable to provide natural hair (wearing a wig or weave). Our laboratory methods for measuring hair cortisol have been described previously and include duplicate analyses and rigorous quality control standards (Meyer et al., 2014). Briefly, hair is weighed on an analytical balance and washed with isopropanol to remove external contamination. The isopropanol is then dried and the sample is ground to a fine powder to break up the hair keratin matrix and increase surface area. Cortisol is then extracted with methanol, and the methanol is evaporated using a vacuum evaporator. Cortisol is then reconstituted and measured using a commercial enzyme immunoassay (Salimetrics) and converted to pg per mg of hair. Samples with cortisol levels below the limit of detection (LOD) were replaced with the LOD/$\sqrt{2}$ (Hornung and Reed, 1990). The LOD for the enzyme immunoassay is 0.007 μg/dl according to the manufacturer"s specifications. However, to determine hair cortisol concentrations the assay readout is converted to pg cortisol per mg sample weight. Consequently, an LOD taking into account sample weight was calculated for each individual hair sample that, when reconstituted and analyzed, yielded a cortisol value below the overall assay LOD (n = 3). Intra- and inter-assay coefficients of variation for this assay are both < 10%.

2.4. Statistical analyses

We compared participants who were and were not able to provide a hair sample on demographic characteristics and psychometric measures using Wilcoxon rank sum tests for continuous variables and Fishers exact or chi-square tests for categorical variables. We summarized characteristics of the analytic population (those with a measure of hair cortisol) using means (standard deviations) and number (percent) for continuous and categorical variables, respectively. Spearmen correlations and linear models determined the association between symptoms of depression, anxiety, somatization, both pregnancy and perceived stress and cortisol accumulation. Interaction was evaluated using multiplicative interaction terms and stratification by the mean dose of ACEs (≥ 2 or < 2). While prior studies have dichotomized ACE scores at ≥ 4 or < 4, we had few participants with ≥ 4 given the small sample size. The Institutional Review Board at Cincinnati Children's Hospital Medical Center approved this work and informed consent was obtained from all participants.

3. Results

Participants who were (n = 30) and were not (n = 25) able to provide a hair sample differed significantly by race (p = 0.001) (Table 1). Participants who were black were less likely to provide a hair sample. While one of 15 white participants did not provide hair, 22 of 35 black participants were unable to provide natural hair. Mean summary variables for psychometric testing did not vary by participants who did and did not provide a hair sample. Overall scores on psychometric testing were slightly higher than standard populations. While 76.4% of our sample experiences one or more ACE, 59.4% of a general population sample reported one or more ACE (Bynum et al., 2010). Normative mean (standard deviation) values of the BSI-18 among a college-aged sample were 1.7 (2.3), 0.9 (1.6), 1.6 (1.9) (Lancaster et al., 2016) for somatic symptoms, depression, and anxiety, respectively, while among our population scores were 5.4 (3.8), 4.3 (4.6), and 4.4 (5.3). The ratio of the intensity of hassles to uplifts was 0.77 among a low risk population at 33–35 weeks (DiPietro et al., 2008), while the ratio was 1.8 in our sample. Finally, the normative mean for the PSS among young adults age18-29 was 14.2 (6.2) (Cohen et al., 1983) while our sample was 16.5 (8.7) (Table 1).

Among the analytic population (n = 29 after excluding one outlier with hair cortisol = 67.7 pg/mg), the mean maternal age was 21.6 years (± 3.5), and the race distribution was as follows: 13 (43.3%) black/African American, 14 (46.7%) white, and 3 (10%) multi-racial. Three samples were below the LOD. The mean hair cortisol