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Exposure to traumatic events in childhood predicts cortisol production among high risk pregnant women

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Abstract

Childhood exposure to traumatic events has a profound and disruptive impact on mental and physical health, including stress physiology. In the current study, we evaluate 90 pregnant women at risk for preterm delivery and assess the association between history of exposure to traumatic events and hair cortisol concentrations, an integrated measure of cortisol production. Exposure to more traumatic events in childhood and in adulthood independently predicted elevated hair cortisol concentrations in pregnancy. Notably, the impact of childhood exposure to traumatic events remained after accounting for more proximal traumatic events in adulthood. Further, there was a significant interaction between childhood and adult exposures. Traumatic experiences in adulthood were more strongly associated with hair cortisol concentrations among mothers with a history of greater childhood trauma. Findings suggest that not only do proximal adult exposures impact HPA-axis functioning during pregnancy, but that childhood traumatic experiences have persisting consequences for HPA-axis functioning during pregnancy. Maternal HPA- axis dysregulation in pregnancy has consequences for both maternal health and for fetal development. Therefore, we consider prenatal maternal HPA-axis functioning as a potential biological pathway underlying intergenerational consequences of childhood trauma.

Keywords

Cortisol; Pregnancy; Stress; Trauma; Early Life

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Introduction

Nearly 39% of children in the United States will experience a traumatic event before the age of 13 (Koenen, Roberts, Stone, & Dunn, 2010). This high prevalence is of public health concern, because early life exposure to traumatic events can have profound and lifelong consequences (Perry, Pollard, Blakley, Baker, & Vigilante, 1995). Broadly, adults with a history of childhood trauma are at elevated risk for a range of physical and mental health problems, including dysregulation of immune, cardiovascular, and endocrine systems (Baumeister, Akhtar, Ciufolini, Pariante, & Mondelli, 2016; Bush, Lane, & McLaughlin, 2016; Roy, Janal, & Roy, 2010; Teicher et al., 2003), and heightened risk for psychopathology (Heim & Nemeroff, 2001). Childhood exposure to trauma has implications not only for health across the lifespan, but also for the next generation (Narayan, Bucio, Rivera, & Lieberman, 2016). Offspring of mothers who experienced early life trauma and post-traumatic stress are at greater risk for adverse mental health outcomes, (Collishaw, Dunn, O'Connor, & Golding, 2007; Yehuda, Halligan, & Bierer, 2001) reduced intracranial volume (Moog et al., 2018), and altered stress physiology, including lower levels of cortisol (a key stress hormone and glucocorticoid) at baseline and over a 24 hour period in comparison to non-exposed controls (Brand et al., 2011; Yehuda, Halligan, & Grossman, 2001). Pathways proposed to underlie this transfer of risk from mother to offspring include shared environmental risk factors, parenting behaviors, and epigenetic inheritance (Buss et al., 2017; Bowers & Yehuda, 2016; Yehuda & Meany, 2018). Another complimentary but less frequently considered pathway is the biological embedding of mothers' early traumatic experiences on her stress physiology and the resulting impact on the prenatal environment (Buss et al., 2017; Bowers & Yehuda, 2016; Moog et al., 2016). This is a plausible pathway, because childhood traumatic experiences exert a lasting biological imprint that persists into adulthood (Heim et al., 2000; Heim et al., 2002). Thus, it is likely that these experiences will influence maternal hypothalamic pituitary adrenal (HPA) axis activity during pregnancy, with ensuing consequences for fetal development (Sandman & Davis, 2012).

Exposure to traumatic events in childhood disrupts the regulation of cortisol, the end product of the HPA-axis, one of the body's major stress systems (Carpenter, Shattuck, Tyrka, Geracioti, & Price, 2011; Selye, 1976). Dysregulation of the diurnal rhythm of cortisol, cortisol response to an acute stressor, and total cortisol production (indexed by hair), have been observed among adults with a history of child abuse, maltreatment, and early life adversity (Bublitz & Stroud, 2012; Carpenter et al., 2011; Heim & Nemeroff, 2001; Heim et al., 2000). Although the link between childhood trauma and subsequent HPA- axis dysregulation in adulthood is well supported (Heim et al., 2001), the directionality and strength of this association varies as a function of time from exposure to assessment (Weems & Carrion, 2007), experience of post-traumatic stress symptoms (Morris, Compas, & Garber, 2012), and type of maltreatment (Kuhlman, Geiss, Vargas, & Lopez-Duran, 2015), suggesting that the neurobiological sequalae of early life trauma is complicated and merits further investigation (Tarullo & Gunnar, 2006; Watts-English et al., 2006).

The stress sensitization hypothesis posits that exposure to stressful life events is more likely to lead to mental health problems among individuals who experienced trauma in childhood as compared to those who did not (Heim et al., 2002). According to the stress sensitization

hypothesis, early-life trauma alters the regulation of stress sensitive systems thereby increasing the impact of subsequent exposures. Support for this theory has been provided by studies of non-pregnant women. Heim and colleagues (2002) report that women with a history of child abuse who also experienced trauma as an adult, were more likely to exhibit a greater HPA-axis response to an acute stressor, compared to women who did not experience subsequent adulthood trauma (Heim et al., 2002). This study provides important evidence that childhood traumatic experiences sensitize the HPA-axis, increasing vulnerability to subsequent exposures.

Investigation of the consequences of childhood trauma on HPA-axis functioning in pregnancy is important as pregnancy represents a challenge to maternal stress systems. The maternal HPA-axis undergoes profound change over the course of pregnancy, with the pituitary gland nearly doubling in size by the time of delivery. However, perhaps the most drastic change is brought on by the development of a new fetal endocrine organ, the placenta, which synthesizes and releases corticotropin-releasing hormone (CRH) into both maternal and fetal circulation. As gestation progresses, levels of stress hormones in maternal circulation, including cortisol, normatively increase three to five-fold (Allolio et al., 1990; D'Anna-Hernandez, Ross, Natvig, & Laudenslager, 2011; Kirschbaum, Tietze, Skoluda, & Dettenborn, 2009; McLean et al., 1995). Individual differences in HPA-axis functioning may become exaggerated during the physiological challenge of pregnancy, revealing or exacerbating prior vulnerabilities, including the consequences of early life exposure to trauma.

Dysregulation in cortisol production during pregnancy may be of particular importance because perinatal HPA-axis activity has been associated with maternal well-being, including alterations in maternal cognitive functioning such as a decline in verbal memory recall (Glynn, 2010), onset of maternal behaviors such as greater attunement to the odor of her own newborn (Fleming, Steiner, & Corter, 1997), elevated risk for maternal postpartum depression (Glynn, Davis, & Sandman, 2013; Yim et al., 2009), and poor immunological functioning (Mastorakos & Ilias, 2003). In addition to impacting maternal health and behavior, maternal HPA-axis activity during pregnancy also has implications for the developing fetus. Exposure to maternal cortisol is a mechanism proposed to underlie the fetal programming of later health and disease (Duthie & Reynolds, 2013). Circulating maternal cortisol crosses the placental barrier and enters the fetal compartment (Mulder et al., 2002). Dysregulation of maternal cortisol production therefore has consequences, not only for the mother, but also for the developing fetus (de Weerth, van Hees, & Buitelaar, 2003; O'Connor, Bergman, & Sarkar, 2013; Sandman & Davis, 2012). The rate of fetal development far outpaces any other period of the lifespan, therefore fetal growth and development are highly susceptible to the influence of prenatal experiences and alterations to maternal stress hormones can have wide-ranging effects (Barker, 1998).

Although a growing body of work has explored the consequences of prenatal HPA-axis activity, relatively little is known about the impact of maternal childhood trauma on cortisol production during pregnancy (Bublitz, Parade, & Stroud, 2014; Bublitz & Stroud, 2012; Moog et al., 2016; Schreier, Enlow, Ritz, Gennings, & Wright, 2015; Shea et al., 2007; Thomas et al., 2018). Adverse maternal experiences, including maltreatment and sexual

abuse in childhood, predict lower baseline cortisol concentrations, an increasing cortisol awakening response (CAR), and a flattened diurnal slope over the course of gestation (Bublitz et al., 2014; Bublitz & Stroud, 2012; Shea et al., 2007; Thomas et al., 2018). Similarly, Schreier and colleagues (2015) report that women with a history of childhood abuse before age 11 had elevated third trimester hair cortisol concentrations. We are unaware of any studies which have explored if exposure to a broad range of traumatic events predicts prenatal cortisol production, or whether the experience of trauma in childhood sensitizes the HPA-axis, increasing the impact of subsequent adult exposures on prenatal HPA-axis functioning. Additional research is also needed to explore how childhood trauma may impact prenatal HPA-axis functioning within medically high-risk pregnancies, as women with a history of trauma are more likely to experience pregnancy and delivery complications (Lev-Wiesel, Chen, Daphna-Tekoah, & Hod, 2009), and limited work has been done to characterize how prior trauma relates to prenatal stress physiology within this high-risk population.

In the current study, we hypothesize that childhood traumatic events (defined as report of potentially traumatic experiences occurring before the age of 10) predict cumulative cortisol concentrations during pregnancy (measured in hair) within a sample of women at risk for preterm delivery. Women who have experienced prior traumas are at elevated risk for preterm delivery in comparison to those not exposed to trauma over their lifetimes (Leeners, Stiller, Block, Gorres, & Rath, 2010), thus the impact of childhood trauma may be particularly relevant within this at-risk population. As a secondary hypothesis, we predict that childhood traumatic events sensitize the individual to the consequences of exposure to subsequent trauma on cortisol concentrations during pregnancy.

Materials and Method

Participants

The sample of women was recruited for a study assessing outcomes of pregnancies at risk for preterm birth (although despite this elevated risk, 44% of participants in the sample delivered at term and 56% delivered preterm, <37 gestational weeks). Participants were recruited from a large university medical center in Southern California, where they had been admitted for risk of imminent preterm delivery (i.e. delivery within a week), which was determined by their attending physician and not in relation to the study protocol. Inclusion criteria were: a) 18 years of age or more, b) singleton pregnancy, and c) between 23 and 34 weeks pregnant. Exclusion criteria were: a) prior exposure to antenatal corticosteroids during the current pregnancy, b) known fetal genetic or congenital anomalies, and/or c) illicit drug use. We additionally excluded one participant for the presence of spina bifida, three participants for end-stage renal disease, and one participant for chronic pain and methadone use. Of the 121 eligible participants, we included the 90 pregnant women who provided a hair sample for cortisol analyses. The 31 women who did not provide hair did not differ on sociodemographic or obstetric factors, compared to women who consented to this procedure. Women in the sample were predominantly Hispanic (68.9%), 31.8% lived below the federal poverty line, and 45.5% had a high school education or less (Table 1). All study procedures

were approved by the Institutional Review Board for protection of human subjects, and each participant provided written and informed consent.

Procedure

Women were assessed once during pregnancy while in the hospital (M = 28.60; SD = 3.20). A standardized interview was used to assess women's exposure to traumatic events and a hair sample was collected for cortisol analysis.

Sociodemographic and medical factors

Sociodemographic characteristics, including age, education, household income, cohabitation status (i.e. living with a partner), and ethnicity, were assessed. Obstetric risk was determined from medical record abstraction. The obstetric risk score accounted for prenatal infection, pregnancy-induced hypertension, gestational diabetes, oligohydromnios, polyhdramnios, preterm labor, vaginal bleeding, placenta previa, and anemia. A cumulative score assessing prenatal obstetric risk was derived from the sum of all present risk variables (Hobel, 1982).

Traumatic events

Women's report of traumatic events in childhood, adolescence, adulthood, and in her current pregnancy was recorded using the Life Events Checklist (Gray, Litz, Hsu, & Lombardo, 2004). The Life Events Checklist (LEC) is a validated diagnostic tool that assesses exposure to 16 potentially traumatic events (e.g. physical assault, sexual assault, exposure to a fire or explosion) (Gray et al., 2004). For each traumatic event a woman endorsed, she was asked to select the age range(s) during which the event occurred: childhood (0–10 years), adolescence (11–17 years), adulthood (18+ years) prior to the current pregnancy, and/or during the current pregnancy. Four sum scores were calculated based on the number of endorsed life events within each age group (childhood, adolescence, adulthood, current pregnancy). The LEC has good test-retest reliability (r = 0.82) (Gray et al., 2004) and has been widely used, including in pregnant women (Zhu, Tao, Hao, Sun, & Jiang, 2010). We used this standardized checklist to measure exposure to traumatic events, because prior studies suggest that this format, which does not rely on a subjective evaluation of a major adverse event, is minimally susceptible to recall bias (Hardt & Rutter, 2004).

Hair cortisol

Hair samples were collected from the posterior vertex region of the head and as close to the scalp as possible. The hair sample was then placed on top of 100% cotton paper, and the paper was folded around the hair and affixed with paper ties at both ends. Samples were stored in a dry and dark room until assayed.

The three centimeters closest to the root end of the hair samples were assayed for cortisol concentrations, providing a measure of cumulative cortisol production over the previous three months (Russell, Koren, Rieder, & Van Uum, 2012). Thus, a single hair sample provides an index of chronic cortisol production in contrast to momentary measures such as blood or saliva, which require repeated assessment to estimate chronic cortisol release (D'Anna-Hernandez et al., 2011). Hair cortisol was assayed by an independent laboratory (Behavioral Immunology and Endocrinology Lab) (Hoffman, Karban, Benitez, Goodteacher,

& Laudenslager, 2014) using a modified Salivary Cortisol Enzyme Immunoassay (Salimetrics, LLC, State College, PA). Hair was washed 2–3 times for 3 minutes each in 2.5 mL isopropanol, then pulverized with a Retsch ball mill at 25 Hz for 10 minutes. Samples were then extracted using 1 mL of methanol, then left to incubate for 24 hours at room temperature. Samples were shaken gently during extraction, then evaporated under a steady stream of nitrogen at 38°C for 30 minutes. Solvent was reconstituted using 400 μL of phosphate-buffered saline. Samples were centrifuged at 500 rpm during assay, and cortisol was quantified at wavelength 450nm. Two pooled hair samples from random hair clippings were created, ground, and separately mixed to create a high and low laboratory control. These two controls served as an internal assay control that was included in every assay for determination of intra-assay CVs. For the present study the mean intra-assay CVs were 3.8% and 8.3% for the low and high controls respectively. Inter-assay CV was 1.8%. The high control was spiked with known amounts of cortisol using Salimetrics standards between 0.11 and 3.00 micrograms/dl. Recovery for these standards averaged 92.5%. A limiting dilution of the high internal laboratory control from 1:1 to 1:64 showed near perfect linear dilution, R2 = .99, between expected and observed levels. Two participants were excluded from analyses, one because hair cortisol concentrations were >3 SD above the mean, and the other because hair cortisol levels were undetectable. Therefore, final analyses included 88 participants. None of the women in this sample used bleach or chemical hair straightener, which are known to affect hair cortisol (Hoffman et al., 2014). Consistent with prior literature, natural hair type, hair color, and dying hair were not associated with hair cortisol concentrations (Wosu, Valdimarsdottir, Shields, Williams, & Williams, 2013). Hair cortisol concentrations (M = 9.61 pg/mg; SD = 14.78) during pregnancy were positively skewed so hair cortisol values were log transformed. Prior work has shown that cortisol concentrations increase over gestation (Kirschbaum et al., 2009). Although not statistically significant in this sample, gestational week at time of hair sample collection was covaried in all analyses.

Statistical analyses

Partial correlations and ANCOVAs, covarying gestational week at time of hair sample collection, were used to identify socio-demographic and pregnancy factors (age, education, household income, ethnicity, cohabitation with a partner, obstetric risk, parity, fetal sex, and gestational length) that might influence hair cortisol concentrations. These factors, all of which were selected for theoretical reasons, were included in subsequent analyses if they were associated with hair cortisol at the $p \leq .10$ level of significance. As shown in Table 2, no variables met criteria for inclusion as a covariate. Partial correlations were conducted to explore the associations between childhood traumatic events and traumatic events in other age ranges (adolescence, adulthood, and during the current pregnancy). Partial correlations were also used to assess the associations between traumatic events endorsed in each age range and hair cortisol.

Linear regression was used to test the hypothesis that childhood traumatic events predict maternal cortisol concentrations during pregnancy. A second regression model evaluated the relative influence of childhood traumatic events on prenatal hair cortisol concentrations, when also accounting for events at later ages (traumatic events in adolescence and during the current pregnancy were not associated with hair cortisol concentrations, therefore only

adulthood traumatic events were included in the regression model; see Table 4). Finally, to test the secondary hypothesis that childhood exposure sensitizes the HPA-axis, increasing the effect of subsequent exposures on prenatal cortisol production, we tested the interaction between childhood traumatic events and later exposure (adulthood traumatic events, as it was the only time period outside of childhood in which traumatic events were associated with hair cortisol concentrations). Significant interactions were probed by calculating and plotting simple slopes, and inspecting regions of significance (Preacher, Curran, & Bauer, 2006).

Results

Descriptive Statistics

Descriptive characterization of exposure to traumatic events within each age range is presented in Table 3. The number of childhood traumatic events was significantly correlated with number of events endorsed during adolescence ($r = 0.49, p < 0.001$) and adulthood ($r = 0.29, p = 0.006$), but not with traumatic events experienced during pregnancy ($r = 0.03$, $p = 0.767$) (see Table 4).

Childhood Exposure to Traumatic Events and Cortisol Concentrations During Pregnancy

Regression analyses testing the primary hypothesis, revealed that exposure to more traumatic events in childhood predicted elevated hair cortisol concentration during pregnancy ($\beta = 0.32$, $t(87) = 3.06$, $p = 0.003$); $R^2 = 0.10$, $F(2, 85) = 4.82$, $p = 0.010$; see Model 1 in Table 5). A subsequent regression model revealed that a greater number of traumatic events experienced during childhood ($\beta = 0.23$, t(87) = 2.21, $p = 0.030$; see Model 2 in Table 5) and adulthood $\beta = 0.32$, $t(87) = 3.08$, $p = 0.003$), predicted elevated cortisol concentration during pregnancy, demonstrating that the effect of childhood traumatic events on prenatal HPA-axis activity persisted, even while accounting for exposure to traumatic events in adulthood ($R^2 = .193$, $F(3, 84) = 6.70$, $p < 0.001$).

Stress Sensitization and Prenatal Maternal Hair Cortisol Concentrations

A significant interaction was observed between childhood and adulthood exposure to traumatic events, indicating that adult exposure to trauma was more strongly associated with hair cortisol when women also experienced trauma during childhood ($\beta = 0.42$, $t(87) = 2.39$, $p = 0.019$; $R^2 = 0.25$, $F(4, 83) = 6.73$, $p < 0.001$; see Figure 1 and Model 3 in Table 5). Investigation of the region of significance found that adult traumatic events only predict prenatal maternal cortisol for women who experienced at least one event during childhood (region of significance boundary = 0.82 childhood traumatic events; see Figure 1).

Conclusions

Nearly four out of every ten individuals experience a traumatic event in childhood (Koenen et al., 2010). Rates are higher among women at risk for preterm birth (Leeners et al., 2010) and in our sample 54% of women experienced a traumatic event in childhood. We find that exposure to a greater number of traumatic events both in childhood and during adulthood independently predict elevated cortisol production in a group of pregnant women at risk for

preterm delivery. These findings indicate that the impact of childhood traumatic events persists, even after accounting for more proximal adulthood exposures. Further, childhood exposure to traumatic events enhances the consequences of adult exposures on prenatal cortisol production. These findings suggest that traumatic experiences early in life can have a lasting impact on cortisol production in pregnancy, a consequence which may be particularly relevant for women with high risk pregnancies and may have important implications for both the mother and the developing fetus.

It is widely recognized that adult exposure to traumatic events will have consequences for HPA- axis regulation (Sherin & Nemeroff, 2011). Our finding that proximal adult exposures are associated with prenatal cortisol is consistent with this literature. Less is known about the long-term consequences of exposure to traumatic events in early life. The relation between early experiences and prenatal cortisol production is consistent with literature linking childhood traumatic events to cortisol dysregulation in non-pregnant adults (Carpenter et al., 2011; Heim & Nemeroff, 2001; Heim et al., 2000) and in pregnant women (Bublitz et al., 2014; Bublitz & Stroud, 2012; Schreier et al., 2015; Shea et al., 2007). Our research expands upon previous findings by demonstrating that the association is not limited to survivors of childhood physical and sexual abuse— we find that exposure to a diverse range of early life traumatic events predicts cortisol production in pregnancy. Further, the current study adds new knowledge by demonstrating that the relation between childhood traumatic events and prenatal maternal cortisol persists even when considering more proximal exposures in adulthood. Importantly, child and adult traumatic events are only modestly correlated ($r = 0.29$), suggesting that the impact of childhood trauma on maternal prenatal cortisol is not solely due to the fact that individuals who reported childhood trauma are more likely to report additional traumas in adulthood (Desai, Arias, Thompson, & Basile, 2002). Thus, findings suggest that early-life exposure to trauma exerts a persisting influence on HPA-axis functioning beyond the impact of more proximal exposures in adulthood.

Novel to the present investigation is the observation that exposure to traumatic events in adulthood is a stronger predictor of elevated hair cortisol concentrations among women who previously experienced traumatic events in childhood. Data reported here are consistent with evidence that childhood exposure to traumatic events may sensitize the HPA-axis to the effects of exposure in adulthood among non-pregnant women (Heim et al., 2002). Our findings are consistent with the stress sensitization hypothesis which posits that exposure to childhood adversity increases the consequences of adult exposure to adversity on stress physiology, potentially increasing risk for psychopathology (Heim & Nemeroff, 2001; McLaughlin, Conron, Koenen, & Gilman, 2010). The present findings suggest that the effect of stress sensitization may have consequences for HPA-axis functioning during pregnancy.

We did not find that traumatic events in adolescence predicted maternal HPA-axis activity during pregnancy. This pattern of findings may be due to the strong and far-reaching influence of childhood trauma as early-life is a sensitive window when the environment exerts potent influences (Baram et al., 2012; Dunn, McLaughlin, Slopen, Rosand, & Smoller, 2013; Narayan et al., 2016). Consistent with this possibility, previous studies report that exposure to traumatic events occurring before the age of 10 predicts long-term outcomes

(Kaplow & Widom, 2007; Keiley, Howe, Dodge, Bates, & Pettit, 2001; Thomberry, Henry, Ireland, & Smith, 2010). Further, Dunn and colleagues (2013) report that early childhood maltreatment (i.e. ages 0 to 5) has relatively greater influence on adult outcomes than exposure in adolescence, suggesting that early-life may be a sensitive window to the consequences of traumatic events. Exposure to traumatic events in adulthood, on the other hand, may have a pronounced influence on prenatal physiology because adult events are more proximal to the time of hair sample collection. It may be for these reasons that childhood and adulthood exposures had a relatively stronger impact on prenatal HPA-axis activity than adolescent traumatic events.

One strength of the study is the use of hair cortisol as an integrated measure of maternal HPA- axis activity across the prior three months of pregnancy. Other methodologies, such as single blood and saliva samples, provide useful measurements of momentary cortisol production within a particular context (D'Anna-Hernandez et al., 2011). The use of hair however, is advantageous because it provides a robust metric of chronic HPA-axis activity. The relation between maternal traumatic events and prenatal cortisol concentrations was examined in a sample of women at elevated risk for preterm delivery. Although this characteristic of the study sample may limit generalizability to samples who do not demonstrate risk for preterm delivery, women with a significant trauma history are at elevated risk for preterm birth (Leeners et al., 2010). Therefore, it is particularly relevant to explore the impact of early life trauma within this at- risk population. Another potential limitation of the current study is the use of retrospective recall to assess lifetime exposure to and timing of traumatic events. Retrospective biases were reduced by using a standardized measure of traumatic life events that only asked whether the event occurred, rather than assessing the subjective details or severity of the events themselves. This method has been shown in prior work to reduce susceptibility to recall biases and provide a more reliable estimate of traumatic experiences in early life (Hardt & Rutter, 2004). Additionally, we assessed multiple types of traumas. Although this approach allowed us to capture a range of exposures, given limited statistical power we were unable to evaluate the impact of each exposure individually. Previous work suggests that different forms of traumatic events, such as the experiences of loss (e.g. death of a loved one) versus threat (e.g. physical and/or sexual assault), may differentially impact the HPA-axis (McLaughlin & Sheridan, 2016). Future work should evaluate the impact of type of traumatic events on HPA-axis functioning during pregnancy. On average, women within the sample also typically experienced a single occurrence or single type of traumatic event within each age range. Future work may therefore further assess the impact of multiple co-occurring and/or repeated traumas within higher risk samples. The current study also assessed maternal experience of potentially traumatic events and did not assess post-traumatic stress symptoms. Because non-pregnant individuals with post-traumatic stress disorder (PTSD) display hypocortisolism, future studies should assess cortisol production in pregnant women with childhood trauma and current symptoms of PTSD.

The effect of childhood traumatic events on cortisol concentrations during pregnancy can have important implications for both the mother (Fleming et al., 1997; Glynn, 2010; Glynn et al., 2013; Mastorakos & Ilias, 2003) as well as the developing fetus (Sandman & Davis, 2012) across multiple pregnancies (Fox, Sandman, Davis, & Glynn, 2015). Changes in

cortisol production across the prenatal period are essential for normative functioning and development in both the mother and the fetus (Davis & Sandman, 2010). However, cortisol can also have adverse consequences for the maternal-fetal pair when its production is elevated in relation to other pregnancies (Davis & Sandman, 2012; de Weerth et al., 2003; O'Connor et al., 2013). Pregnancy is a sensitive period for the mother, as dysregulation in prenatal HPA-axis functioning predicts elevated risk for postpartum depression as well as impairment in immunological and cognitive functioning (Glynn, 2010; Glynn et al., 2013; Mastorakos & Ilias, 2003). Prenatal HPA-axis activity also has important implications for the fetus, as the robust fetal programming literature documents the importance of prenatal stress hormones in shaping offspring physical and mental health (Sandman & Davis, 2012). Specifically, prenatal maternal cortisol, including hair cortisol, has been found to predict emotional and stress dysregulation, poor cognitive development, risk for developing psychopathology in childhood and adolescence, and poor physical health outcomes (Beijers, Jansen, Riksen-Walraven, & de Weerth, 2010; Buss et al., 2012; Davis & Sandman, 2010; Davis & Sandman, 2012; de Weerth et al., 2003; Karlen, Frostell, Theodorsson, Faresjo, & Ludvigsson, 2013; O'Connor et al., 2013). Prenatal maternal HPA-axis activity may therefore be a potential mechanism of action underlying the intergenerational impact of maternal traumatic experiences, as findings demonstrate that childhood traumatic experiences can have persisting effects on maternal cortisol production during pregnancy, and maternal HPA-axis activity during pregnancy has known programming effects on the developing fetus. Future work could evaluate whether the lasting biological imprint of maternal adversity prior to conception impacts the next generation.

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Highlights:

- Traumatic events in childhood predict cortisol levels in at risk pregnant women
- Childhood traumatic events predict prenatal cortisol after covarying adult trauma
- The relation between adult trauma and prenatal cortisol is moderated by child trauma
- Elevated prenatal maternal cortisol could have consequences for both mom and baby

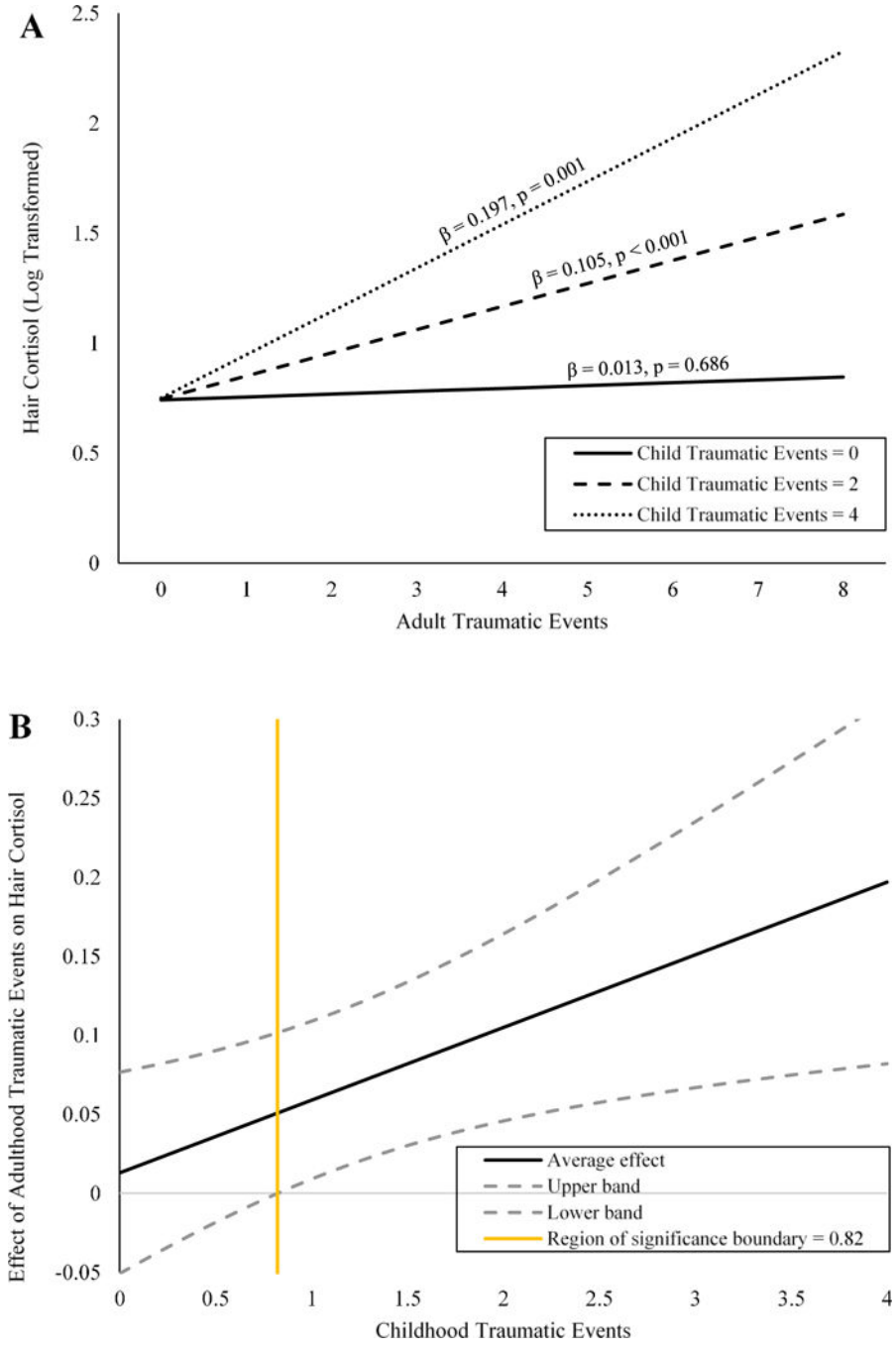

Fig. 1.

Effect of adulthood traumatic events on hair cortisol concentrations during pregnancy. **(A)** Data were analyzed continuously using regression and are depicted here as 0, 2, and 4 childhood traumatic events **(B)** The positive association between traumatic events in adulthood and hair cortisol concentrations during pregnancy, reached statistical significance when the reported number of traumatic events experienced in childhood was above an

average of 0.82 events (i.e., at least one event). Dashed lines indicate 95% confidence intervals. The vertical line at 0.82 indicates the region of significance boundary

Table 1.

Sample characteristics

Sample Characteristics (*N* = 90)	
Maternal Age *(M* ± SD)	30.0 ± 6.4; 18.5–45.5
Cohabitating (%)	76.7
Ethnicity (%)	
Non-Hispanic White	21.1
Hispanic	68.9
Household Income (%)	
$0-$30,000	37.8
$30,001-$60,000	27.8
$60,001-$100,000	11.1
Over $100,000	12.2
Education (%)	
High school or less	44.4
Technical or vocational school	6.7
Some college	22.2
Certificate	4.4
Associate degree	7.8
Bachelor's degree or higher	14.4
Parity (*M* ± SD; Range)	1.2 ± 1.2; 0–6
Gestational length (*M* ± SD; Range)	34.9 ± 4.4; 24.4–40.7
Preterm Delivery (less than 37 gestational weeks)	54.5
Hair cortisol pg/mol (*M* ± SD; Range)	9.6 ± 14.8; 1.7–115.9
Gestational week at time of hair sample collection (*M* ± SD; Range)	28.6 ± 3.2; 23.3–34.0
Childhood traumatic events (*M* ± SD; Range; % with 0 events)	0.6 ± 1.0; 0–4; 46
Adolescent traumatic events (*M* ± SD; Range; % with 0 events)	0.9 ± 1.2; 0–7; 61
Adulthood traumatic events (*M* ± SD; Range; % with 0 events	1.4 ± 1.0; 0–8; 30
Pregnancy traumatic events (*M* ± SD; Range; % with 0 events)	0.2 ± 0.5; 0–2; 78

Table 2.

Associations between participant characteristics and hair cortisol

Participant Characteristics	Test Statistic (p-value)
Obstetric risk	0.02^{a} (.83)
Education (in yrs.)	0.14^{a} (.20)
Maternal age	0.15^{a} (.18)
Household income	0.09^{a} (.45)
Ethnicity	1.40^{b} (.24)
Cohabitation status	2.39^{a} (.13)
Parity	-0.03^{a} (.79)
Fetal sex	1.24^{a} (.27)
Gestational length	-0.05^{a} (.64)
Hair color	0.88^{b} (.45)
Natural hair type	1.03^{b} (.36)
Hair dyed	0.01^{b} (.94)

Note: Reported test statistics are partial r for continuous variables and ANCOVA for group data, with gestational week at time of hair sample collection included as a covariate.

[a] partial r and

[b] F statistic

Table 3.

Frequency of traumatic events

Item	0–10	11–17	18+	Current Pregnancy
1. Natural disaster	8	8	5	1
2. Fire or explosion	4	2	0	0
3. Transportation accident	7	20	31	7
4. Serious accident at home, work, or recreational activity	4	5	5	0
5. Exposure to a toxic substance	1	0	1	0
6. Physical assault	4	11	11	3
7. Assault with a weapon	0	3	6	0
8. Sexual assault	5	4	6	1
9. Other unwanted or uncomfortable sexual experiences	5	3	9	0
10. Combat or exposure to a war-zone	1	0	0	0
11. Captivity	2	1	1	0
12. Life-threatening illness or injury	3	1	8	0
13. Severe human suffering	1	2	5	1
14. Sudden, violent death of someone close to you	0	4	4	2
15. Sudden, unexpected death of someone close to you	8	13	29	6
16. Serious injury, harm, or death you caused to someone else	0	1	0	0
Total number of traumatic events	53	78	121	21

Table 4.

Partial correlations between hair cortisol and maternal traumatic events at each age range

	1	2	3	4	5	6
1. Hair Cortisol[a,b]	--	0 37***	0.32**	0.08	0.38***	0.06
2. LEC-Any Age	--	--	0.66***	0.66***	0 73***	0.32**
3. LEC-Childhood	--	--	--	0 49***	0.29**	0.03
4. LEC-Adolescence	--	--	--	--	0.19	0.09
5. LEC-Adult	--	--	--	--	--	0.33**
6. LEC-Current Pregnancy	--	--	--	--	--	--

Note: LEC = Life Events Checklist

[a] Hair cortisol was log transformed

[b] Analyses adjusted for gestational week at time of hair sample collection

* $p < .05$

** $p < .01$

*** $p < .001$

Table 5.

Regression models examining the association between childhood traumatic events and hair cortisol concentrations during pregnancy

	Model 1: Childhood			**Model 2: Childhood and Adulthood**			**Model 3: Interaction**		
Variable	*B*	*SE B*	*β*	*B*	*SE B*	*β*	*B*	*SE B*	*β*
Gestational Week	0.002	0.01	0.02	−0.002	0.01	−0.02	−0.005	0.01	−0.05
LEC-Childhood	**0.10** **	0.03	0.32	**0.07** *	0.03	0.23	−0.003	0.05	−0.01
LEC-Adulthood				**0.07** **	0.02	0.32	0.03	0.03	0.13
LEC-Childhood * LEC-Adulthood							**0.04** *	0.02	0.42
R^2	0.10			0.19			0.25		
F	4.82 *			6.70 ***			6.73 ***		

Note: Hair cortisol was log transformed. LEC = Life Events Checklist. B = unstandardized coefficient. β= standardized coefficient

* $p < .05$

** $p < .01$

*** $p < .001$