

Original Research Article

Early Origins of Health Disparities: Material Deprivation Predicts Maternal Evening Cortisol in Pregnancy and Offspring Cortisol Reactivity in the First Few Weeks of Life

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Objectives: Maternal hypothalamic pituitary adrenal-axis function regulates production of the stress hormone cortisol, which during pregnancy can cross the placenta and have lasting impacts on fetal growth and development. This article provides a preliminary test of the hypothesis that a woman's socioeconomic status (SES) predicts her cortisol during pregnancy and her offspring's cortisol during the early postnatal period among an ethnically diverse sample in Auckland, New Zealand to evaluate whether differences in cortisol contribute to the intergenerational inheritance of health disparities within this population.

Methods: Maternal saliva samples were collected at waking and prior to sleep on 2 days in late pregnancy (34–36 weeks gestation; $N = 55$), and a subset of offspring saliva was collected before ($N = 48$) and 20 min after a standard vaccination at 6 weeks of age ($N = 19$). SES was quantified using a locally validated index of material deprivation, the NZ Deprivation Index for individuals (NZiDep).

Results: We found that, after controlling for ethnicity and other covariates, women with higher NZiDep scores had significantly higher evening but similar morning cortisol, consistent with a pattern of chronic strain. Infants of women reporting greater material deprivation had elevated cortisol response to vaccination.

Conclusions: These findings suggest that maternal SES experience impacts maternal cortisol in pregnancy and offspring cortisol reactivity soon after birth, with potential long-term effects on offspring biology and health. Additional research is needed to clarify how biological and behavioral factors in both the prenatal and postnatal period facilitate this relationship. *Am. J. Hum. Biol.* 00:000–000, 2014. © 2014 Wiley Periodicals, Inc.

There is a growing interest in clarifying the social and biological mechanisms underlying the well-documented socioeconomic gradient in health (Adler et al., 1994; Adler and Rehkopf, 2008; Adler and Stewart, 2010; Marmot and Wilkinson, 2006; Nguyen and Peschard, 2003). One physiological system of particular interest is the hypothalamic pituitary adrenal (HPA)-axis, which regulates production of the hormone cortisol (Hertzman and Boyce, 2010). Research has shown that factors such as lower education, chronic job stress, stressful life events, anxiety, and financial strain tend to predict lower morning or higher evening cortisol, resulting in a flattening of the diurnal rhythm (Cohen et al., 2006; Kivlighan et al., 2008; Miller et al., 2007; Obel et al., 2005; Skinner et al., 2011). Such effects on HPA-axis function are important for understanding the socioeconomic gradient in health because they have been associated with increased risk for psychiatric illness, cardiometabolic diseases, and overall mortality (Corbalán-Tutau et al., 2012; Rosmond, 2005; Schoorlemmer et al., 2009).

Although there is a broad consensus that lower socioeconomic status (SES) and altered cortisol functioning affect adult health, there is growing evidence that these effects can, in some instances, transcend the current generation to influence biological systems and health in offspring (Boyce and Ellis, 2005; Flinn, 2006; Foster et al., 2000; Nepomnaschy and Flinn, 2009; Worthman and Kuzara, 2005). Experimental studies in diverse species have found that offspring of mothers who experience stress in pregnancy, such as predation pressure, go on to have elevated HPA-axis function themselves as adults (Mommer and Bell, 2013; Sheriff et al., 2010; Sheriff and

Love, 2013). Although data in humans are more limited, studies of prenatal stress have found significant effects of maternal stress in pregnancy on offspring HPA-axis function in infancy (Brennan et al., 2008; Davis et al., 2010; Diego et al., 2004; Grant et al., 2009; Tollenaar et al., 2011; Yehuda et al., 2005), childhood (de Brujin et al., 2009; Gutteling et al., 2004, 2005; O'Connor et al., 2005), adolescence (Huizink et al., 2008; O'Donnell et al., 2013; Van den Bergh et al., 2008), and early adulthood (Entringer et al., 2009).

If maternal social environment influences how offspring respond physiologically to stress, and modifications in stress physiology increase risk of developing chronic disease, this could help perpetuate an intergenerational pattern of health disparities (Drake and Walker, 2004; Kuzawa and Sweet, 2009). However, while human studies generally suggest an intergenerational effect of maternal stress on offspring HPA-axis function, they have tended to focus on ethnically homogenous and higher SES individuals (O'Connor et al., 2013; Tollenaar et al., 2011). It thus

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remains unclear how important these pathways might be as contributors to SES-based gradients in health disparities.

To clarify the possible intergenerational effects of HPA-axis variation in a nonclinical, economically heterogeneous sample, the present analysis has the following goals: (1) evaluate whether SES is associated with maternal cortisol measured in late pregnancy among a socioeconomically and ethnically diverse sample of women from Auckland, New Zealand; and (2) determine whether maternal SES predicts early postnatal cortisol in their infants. Auckland is an ethnically diverse city within a country that has marked social, economic, and health inequalities (Ajwani et al., 2003; Bramley et al., 2004; Craig et al., 2002, 2004), and thus provides a valuable study site to evaluate the potential effects of maternal social environment on offspring HPA-axis function.

MATERIALS & METHODS

Sample

Study participants were recruited from two antenatal clinic waiting rooms between October 2011 and January 2012 in Central and South Auckland, New Zealand. Women were excluded if they were not able to speak English ($N = 7$), if their due date was outside of the study period ($N = 143$) or if they did not intend to vaccinate their child ($N = 26$). Of 193 women eligible for the study, 153 women agreed to be contacted and prenatal interviews were successfully scheduled for 71 women. Prenatal interviews were completed for 64 of the women. Attrition was primarily attributed to inability to contact the women ($N = 24$), women being too busy ($N = 22$), or women deciding they were not interested ($N = 33$). There were no significant differences in ethnicity, age, or primiparity between women who were eligible for the study and those who were ultimately recruited (all $P > 0.12$). Ethnicity was defined using the NZ Ministry of Health ethnicity data protocols (Ministry of Health, 2004). However, it should be noted that each "ethnic group," with the exception of Māori, is actually composed of several different ethnicities (Harris et al., 2012). The sample characteristics (55% NZ European; 25% Pacific Islander, and Māori and 20% Asian) closely approximate Auckland population demographics (56%, 25%, and 19%, respectively; Statistics New Zealand, 2013). Because interviews required that women take time away from other duties, they were compensated \$15 NZ for each study appointment. This study was conducted under conditions of written consent and approved by the Northwestern Institutional Review Board and the New Zealand Upper South B Health and Disability Ethics Committee.

SES measure

SES was defined using the NZ Individual Deprivation Index (NZiDep) questionnaire, which has been validated for use in NZ and found to be a useful index of material deprivation (Salmond et al., 2006). Women were verbally administered the NZiDep during an interview in their homes between 34 and 36 weeks gestation. Women answered Yes or No to six questions indexing material deprivation, and the answers were summed to create a NZiDep score with a possible range from 0 to 6, with higher scores corresponding to greater deprivation and therefore lower SES.

Health variables:

Maternal height was measured during the prenatal in-home visit using standard anthropometric techniques (Lohman et al., 1988). Women were asked their prepregnancy weight to estimate prepregnancy body mass index (BMI). Maternal birth date was used to calculate maternal age at date of prenatal interview. Maternal medication use for thyroid, autoimmune, and depression-related disorders, respectively, were also recorded.

Stress Markers:

Women rated their neighborhoods using likert scales (1–4, Very Bad to Very Good) reflecting safety of property, personal safety, friendliness, cleanliness, schools, and access to recreation areas, with the values summed across variables to create a composite neighborhood score. Data were also collected on whether or not women owned their home and how many adults and children currently lived in their home. Significant life events during pregnancy were also assessed by asking women if they had experienced up to 19 significant life events in pregnancy, ranging from job loss to divorce to death of a friend or immediate family member, with women having two or more events compared with women who reported one or no events (Cochrane and Robertson, 1973). Abuse was assessed by asking whether women had ever been physically or emotionally abused by their partner or someone close to them.

Cortisol measurement

Saliva collection is a minimally invasive method for assessing cortisol that reflects the unbound, bioactive fraction of the hormone (Kirschbaum and Hellhammer, 1989). Following recruitment women were provided four 2.0 ml saliva tubes and instructions for saliva collection. Women passively drooled into each tube at waking and prior to going to sleep on two consecutive weekdays between 34 and 36 weeks gestation. Participants were instructed to not eat, drink, or brush their teeth in the 30 min prior to collecting samples, and they recorded start and stop times for saliva collection, mood and, for morning samples, sleep quality the previous night. Participants stored samples in their freezer until they were retrieved by the interviewer during a prenatal interview the following week. Following retrieval by the researcher, samples were stored at -80°C at a laboratory until analysis. Although 64 women were enrolled, sufficient saliva for cortisol measurement in both morning and evening samples was collected from 55 women. Women who did not provide sufficient saliva at both times of day did not differ in ethnicity ($P = 0.22$) but were more likely to have greater material deprivation ($P = 0.005$).

Since infants do not establish a diurnal rhythm until approximately 3 months after birth (Price et al., 1983), many studies of HPA-axis function in early infancy have measured the cortisol response to a stressor, such as heel prick, vaccination, a bath, or maternal separation (Albers et al., 2008; Jansen et al., 2010; O'Connor et al., 2013; Tollenaar et al., 2011). Following this work, we assessed cortisol reactivity by meeting mothers and infants ($N = 62$) at a clinic during the infant's routine vaccination at 6 weeks of age. Infant saliva was collected just prior to vaccination and again 20–25 min after the vaccination (mean = 22.6 min, standard deviation (SD) = 2.6 min)

TABLE 1. Characteristics of study participants

	Full sample (N = 64)	NZiDep = 0 (N = 33)	NZiDep ≥ 1 (N = 31)	P-value
Mother				
Age (years)	30.8 (4.8)	31.9 (4.6)	29.7 (4.7)	0.06
Ethnicity				0.01
NZ European	54%	62%	45%	
Pacific Islander/Maori	26%	12%	42%	
Asian	20%	27%	13%	
Immigrant	50%	60%	39%	0.08
Height (cm)	166.3 (7.1)	164.8 (6.4)	167.8 (7.5)	0.08
Prepregnancy weight (kg)	69.8 (20.8)	65.4 (21.2)	74.3 (19.8)	0.10
University degree	48%	58%	39%	0.13
Own home	47%	55%	37%	0.16
Household size	3.9 (2.3)	3.4 (1.3)	4.5 (3.0)	0.08
Primipara	25%	24%	29%	0.67
Infant				
Birth weight (g)	3487 (535)	3537 (566)	3430 (501)	0.44
Birth length (cm)	51.3 (2.3)	51.5 (2.5)	51.0 (2.1)	0.40
Head circumference at birth (cm)	34.9 (1.5)	35.2 (1.7)	34.6 (1.3)	0.23
Gestational age (weeks)	39.2 (1.4)	39.4 (1.2)	39.0 (1.5)	0.31
Cesarean section	32%	31%	32%	0.94
Agpar 1 min	8.6 (1.3)	8.9 (0.7)	8.3 (1.7)	0.15
Agpar 5 min	9.4 (0.9)	9.7 (0.6)	9.3 (1.1)	0.15
Unadjusted Cortisol measurements				
Waking cortisol (ng/ml)	3.2 (1.1)	3.2 (0.9)	3.3 (1.3)	0.55
Evening cortisol (ng/ml)	1.0 (0.7)	0.9 (0.6)	1.2 (0.9)	0.24
Infant baseline (ng/ml)	2.5 (4.6)	1.8 (2.3)	3.3 (6.4)	0.29
Infant 20 min after vaccination (ng/ml)	5.5 (8.2)	3.6 (2.9)	8.4 (12.2)	0.16

Mean (standard deviation) values reported for continuous variables, while percentages are presented for categorical variables. Two-tailed *t*-tests (continuous variables) and Pearson chi-squared tests (categorical variables) were used to evaluate differences between individuals with a NZiDep score = 0 and individuals with a NZiDep score ≥ 1.

using two Salimetrics Infant Swabs which were placed into Salimetrics Swab Storage tubes. These samples were then taken to the laboratory and stored at -80°C until analysis. Samples were thawed and spun to retrieve saliva. Sufficient saliva samples were collected from 48 infants at baseline and from 25 infants following the stressor, but sufficient saliva samples from both before and after the vaccination were retrieved from only 19 infants. The main reasons for not collecting post vaccination samples included infant fussiness, infants falling asleep, or infants not drooling enough. There were no differences between maternal SES, BMI, or ethnicity between the mothers of infants for whom saliva was collected at either time point and those that were not (all $P > 0.24$).

Cortisol samples were analyzed using triple quadrupole mass spectrometry at the Liggins Institute in Auckland, New Zealand. Cortisol assays were performed without knowledge of participant SES. Samples were run in duplicate, with all samples from each participant run in the same assay. Cortisol was extracted using 1 ml of ethyl acetate (Merck KGaA Darnstadt, Germany) (Rumball et al., 2008). After removal of the organic supernatant, samples were dried by vacuum concentration (Savant SC250EXP, Thermo Scientific, Asheville, NC), resuspended in 60 μl of mobile phase 72% methanol (Merck) and 28% water, and transferred to high-performance liquid chromatography (HPLC) injector vials. Twelve microliter was injected onto an HPLC mass spectrometer system consisting of an Accela MS pump and autosampler followed by an Ion Max atmospheric-pressure chemical ionization (APCI) source on a Finnigan TSQ Quantum Ultra AM triple quadrupole mass spectrometer all controlled by Finnigan Xcaliber software (Thermo Electron Corporation, San Jose, CA) (Rumball et al., 2008). The mobile phase was isocratic, flowing at 250 $\mu\text{l min}^{-1}$ through a Luna high speed technology (HST) 2.6 μm C18 (2) 100 \times 3.0 mm column at

40°C (Phenomenex, Auckland, New Zealand). Cortisol retention time was 3.1 min, ionization was in positive mode and Q2 had 1.2 m Torr of argon. The mass transitions followed were 363.2 \rightarrow 122.2 at 28 V. Coefficients of variation ranged from 3.4 to 12.1%.

Statistical Analysis

This analysis was conducted using Stata v.10.0 (College Station, Texas). A univariate analysis was initially conducted on all variables to evaluate normality using the Shapiro Wilk test. Maternal evening cortisol, infant baseline cortisol, and NZiDep score were non-normally distributed and were log transformed. Summary statistics were then generated, followed by a bivariate analysis of stress variables to evaluate associations with NZiDep. The study aims were then analyzed using linear regression. We first assessed the relationship between maternal cortisol and NZiDep. This model controlled for time of saliva collection, ethnicity, and medication use. We next evaluated the relationship between maternal NZiDep and both baseline offspring cortisol and offspring cortisol response. In each of these models, we controlled for birth weight, maternal ethnicity, and offspring sex. For all models, we assessed the assumption of homoscedasticity using the STATA estat hettest command. Conventional statistical thresholds were observed ($P < 0.05$).

RESULTS

Summary statistics

Sample characteristics are provided in Table 1. NZiDep scores ranged from 0 to 5 and were similarly distributed to that of the overall NZ population (Fig. 1). There were significant differences in ethnicity between women with high and low NZiDep scores, with Pacific Islander and Māori women significantly more likely to be in the high NZiDep group than NZ European or Asian women. Of the

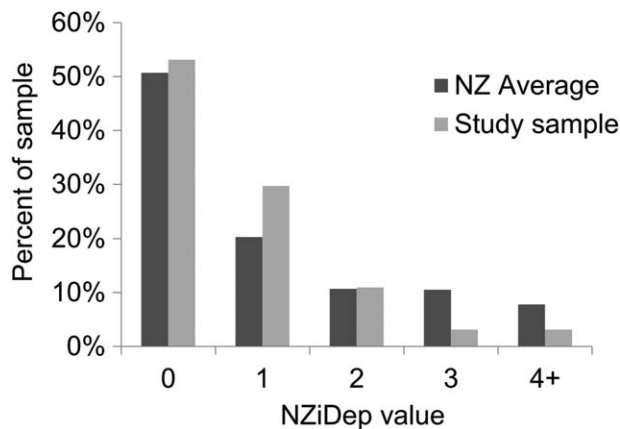


Fig. 1. Distribution of NZiDep values in study sample compared with national sample (national sample data from Salmond et al. 2006).

TABLE 2. Results of NZ individual deprivation index questionnaire

In the last 12 months have you:	Percent of sample who answered yes (%)
1. Personally been forced to buy cheaper food so that you could pay for other things you needed?	36
2. Put up with feeling cold to save heating costs?	16
3. Personally made use of special food grants or food banks because you did not have enough money for food?	9
4. Personally continued wearing shoes with holes because you could not afford replacement?	8
5. Personally gone without fresh fruit or vegetables, often, so that you could pay for other things that you needed?	3
6. Personally received help in the form of clothes or money from a community organization, like the Salvation Army?	3

different NZiDep measures, the largest number of women reported having to buy cheaper food to pay for other things that they needed (Table 2).

Women with higher NZiDep scores were significantly less likely to own a home and had significantly more people living in the home (Table 3). These women also reported more significant life events in pregnancy and were more likely to report having experienced abuse from their partner or someone close to them. There were no significant differences in neighborhood score by NZiDep.

Relationship between material deprivation and cortisol

Maternal diurnal cortisol profile in late pregnancy was not associated with NZiDep score ($P = 0.88$), but there was a trend toward women with higher NZiDep to have elevated morning cortisol ($P = 0.09$) (Table 4). Women experiencing more material deprivation had significantly higher evening cortisol in late pregnancy ($P = 0.02$) (Fig. 2). Among infants, higher maternal NZiDep was not associated with baseline cortisol ($P = 0.68$) but was associated

TABLE 3. Correlation between NZiDep and social stressors

	r^a	P -value
Household size	0.33	0.006 ^b
Household ownership	-0.34	0.006 ^b
Significant life events in pregnancy	0.44	0.0003 ^b
Neighborhood quality	0.11	0.38
History of abuse	0.39	0.003 ^b

^aPearson correlation coefficient.

^b $P < 0.01$.

TABLE 4. Multivariate regression predicting maternal cortisol in late pregnancy ($N = 55$)

	Beta	SE	t -statistic	P -value
Maternal diurnal cortisol decline				
Material deprivation	0.03	0.20	0.15	0.88
PI/Maori	-1.1	0.43	-2.67	0.01**
Asian	-0.45	0.38	-1.19	0.24
Medication use	0.89	0.33	2.71	0.009**
Model Adj. R^2	0.20			
Maternal waking cortisol				
AM collection time	0.13	14.1	0.01	0.99
Material deprivation	0.36	0.20	1.73	0.09
PI/Maori	-0.71	0.47	-1.53	0.13
Asian	-0.16	0.40	-0.41	0.69
Medication use	0.58	0.33	1.75	0.09
Model Adj. R^2	0.09			
Maternal evening cortisol				
PM collection time	-3.2	4.1	-0.77	0.45
Material deprivation	0.22	0.09	2.51	0.02*
PI/Maori	0.27	0.20	1.35	0.18
Asian	0.16	0.17	0.95	0.35
Medication use	-0.40	0.15	-2.70	0.01**
Model Adj. R^2	0.22			

* = $P < 0.05$; ** = $P \leq 0.01$.

with elevated cortisol response to vaccination ($P = 0.009$; Table 5; Fig. 3).

DISCUSSION

The effects of cortisol on health are increasingly well-documented (Flinn and England, 1997; Miller et al., 2007; Sapolsky, 2004). However, it is still poorly understood whether changes in cortisol during pregnancy or in the early postnatal period contribute to the maintenance of the social gradient in health across generations. In this multi-ethnic sample from Auckland, women reporting greater material deprivation had higher evening cortisol. These findings support a model in which maternal stress physiology is sensitive to socioeconomic conditions, including during pregnancy when HPA-axis function undergoes substantial regulatory changes. Importantly, there was a positive, continuous relationship between material deprivation and offspring cortisol response to vaccination measured 6 weeks after birth. These results are consistent with an intergenerational effect of maternal experience, and may operate through some combination of prenatal and postnatal environmental factors.

Prior studies evaluating the relationship between SES and cortisol have focused on nonpregnant individuals (Dowd et al., 2009). Consistent with most of this work, we found that lower SES predicted higher evening cortisol (Cohen et al., 2006; Skinner et al., 2011). Higher evening cortisol has previously been associated with chronic stress in pregnancy (Obel et al., 2005), early delivery (Buss

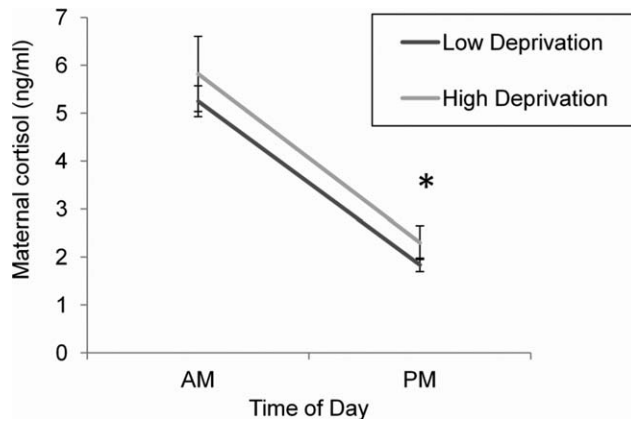


Fig. 2. Maternal morning (AM) and evening (PM) cortisol among women with high (NZiDep ≥ 2) and low (NZiDep < 2) material deprivation (values shown are mean (SE))(* = $P < 0.05$).

TABLE 5. Regression models evaluating relationship between maternal deprivation and offspring cortisol

	Beta	SE	<i>t</i> -Statistic	<i>P</i> -value
Baseline cortisol (<i>N</i> = 48)				
Collection time	-0.001	0.001	-0.79	0.43
Material deprivation	0.13	0.31	0.41	0.68
Pacific Islander/Maori	0.09	0.72	0.13	0.89
Asian	0.85	0.69	1.23	0.22
Birth weight	0.0004	0.0005	0.87	0.39
Female	-0.49	0.57	-0.87	0.39
Model Adj. <i>R</i> ²	-0.07			
Offspring cortisol response (<i>N</i> = 19)				
Baseline cortisol	0.20	0.80	0.25	0.80
Material deprivation	4.39	1.42	3.08	0.009*
Pacific Islander/Maori	-7.04	3.26	-2.16	0.05*
Asian	-3.73	2.92	-1.28	0.22
Birth weight	-0.005	0.002	-2.37	0.04*
Female	-7.41	3.15	-2.35	0.04*
Model Adj. <i>R</i> ²	0.24			

* = $P < 0.05$.

et al., 2009), and reduced fetal growth rate (Diego et al., 2006; Thayer et al., 2012). In contrast, morning cortisol was not significantly related to SES in this sample, although there was a trend toward higher morning cortisol among women with lower SES.

We found that offspring cortisol response to a standardized challenge (vaccination) was positively related to material deprivation in mothers, indicating that offspring raised by more deprived mothers tend to produce more cortisol when faced with a stressor. Experimental work in animal models has shown that maternal stress experienced in pregnancy can directly modify offspring HPA-axis function. For example, prenatal stress has previously been found to induce altered HPA-axis function in nonhuman primates (Clarke et al., 1994; Schneider et al., 2002), and maternal or experimental alterations of corticosteroid levels in eggs also induce HPA-axis changes in a variety of avian, reptilian, and amphibian species (Crespi and Denver, 2005; Denver, 2009; Love and Williams, 2008). Similar findings have been reported among prenatal stress studies in humans (O'Connor et al., 2013; Tollenaar et al., 2011), but never in relation to differences in stress expo-

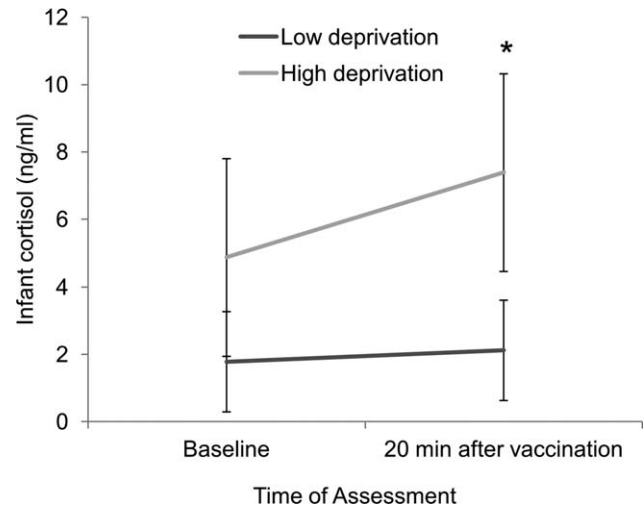


Fig. 3. Offspring cortisol response to vaccination stratified by high (NZiDep ≥ 2) and low material deprivation (NZiDep < 2) in mothers (values shown are mean (SE); * = $P < 0.05$).

sure related to SES specifically. This past work, coupled with the findings reported here, suggest that a mother's experience of SES during pregnancy may, through effects on maternal HPA-axis regulation, directly impact fetal growth during pregnancy and have long-term consequences on HPA-axis regulation in offspring after birth.

If offspring HPA-axis function is influenced by maternal environmental experience, as our results suggest, then the biological mechanisms that facilitate this effect remain unclear. One possibility is that hormonal characteristics of the intrauterine environment program offspring biology. As one example, placental corticotropin-releasing hormone, which is elevated among women reporting stress in pregnancy (de Weerth and Buitelaar, 2005; Hobel et al., 1999), can modify offspring HPA-axis function through changes in glucocorticoid receptor density and abundance (Meaney et al., 1996). Another possibility is that offspring cortisol reactivity is strongly affected by the activity of enzymes that regulate cortisol transfer from mother to offspring across the placenta, particularly 11 β -hydroxysteroid dehydrogenase type 2 (11 β -HSD2). Changes in the activity of this enzyme independent of circulating maternal cortisol levels has been associated with offspring outcomes such as fetal growth and blood pressure (Marsit et al., 2012; Murphy et al., 2006). Interestingly, a recent study found that individuals with lower SES have less methylation in the promoter region of the 11 β -HSD2 gene, which could result in increased expression of this enzyme and therefore a decrease in fetal cortisol exposure (Appleton et al., 2013).

A second possibility is that the relationship between maternal SES and offspring HPA reactivity reflects post-natal impacts on offspring HPA-axis function. For instance, maternal sensitivity and maternal-infant attachment have been found to influence offspring cortisol reactivity (Gunnar and Donzella, 2002; Nachmias et al., 1996; Spangler and Schieche, 1994). Notably, however, these findings have been limited to infants older than 3 months (Jansen et al., 2010). In addition, prior research has found that infant cortisol is associated with factors such as co-sleeping (Beijers et al., 2013; Tollenaar et al.,

2012), which may vary across the study sample. It is also notable that women who are stressed have been shown to secrete greater concentrations of cortisol in their breast milk, some of which is directly transferred to the developing breastfed infant (Brummelte et al., 2010; Flinn et al., 2011; Grey et al., 2013). In light of past work, it seems plausible that material deprivation could modify offspring HPA-axis function through some combination of altered gestational environment and changes in the rearing context in the first few weeks of life. In support of this possibility, a recent study found that depressive symptoms among both the biological mother and the adoptive mother were predictive of lower offspring cortisol in the morning and evening (Laurent et al., 2013).

Regardless of the specific timing of exposure or exposures that account for the changes in offspring cortisol reactivity that we document, our findings suggest that stressful social environments experienced by a mother impact offspring HPA-axis function and that this is already detectable in the first few weeks after birth. These findings point to an early origin in social disparity-based differences in biological function. Since changes in HPA-axis function established in early life can have downstream impacts on growth, cardiovascular, immune, reproductive, and cognitive systems (Nepomnaschy and Flinn, 2009; Nyberg et al., 2012), these intergenerational HPA-axis effects may contribute to an intergenerational cycle of health disparities (Kuzawa and Sweet, 2009; Wells, 2010).

The deep evolutionary history of HPA-axis sensitivity to environmental conditions suggests that this response has been strongly selected for across time. However, the types of stress exposures that we associate with lower SES and which impact cortisol in the present study, including home ownership and household crowding, are relatively novel from an evolutionary perspective. Large-scale social stratification has only emerged in recent millennia, which is a fraction of the evolutionary history of our species (Paynter, 1989). The presence of these factors, however, activates a system which has evolved to respond to ecological signals of a different sort, such as nutritional ecology or predator densities. Thus, any mechanisms that may have evolved to facilitate intergenerational transfer of information to improve the adaptive fit of offspring to their environment could be maladaptive in the contemporary ecology when activated in response to structural inequalities that result in chronic stress experience (Flinn et al., 2011; Gravlee, 2009; Sapolsky, 2004). Future research evaluating diverse sources of stress and a range of biological responses in offspring are necessary to clarify whether modifications in offspring biology actually reflect adaptation (Ellison, 2005; Kuzawa, 2005; Pike, 2005) or biological impairment (Ellison and Jasienska, 2007; Schell and Magnus, 2007).

Consistent with prior research, we had difficulty obtaining sufficient saliva from many of the infants (Egliston et al., 2007). Insufficient saliva was retrieved from infants who had fallen asleep after the vaccination or who were fussy, and sample collection was ceased when and if mothers requested it. In addition, our failure to find significant associations between NZiDep and morning cortisol, while consistent with prior studies which tend to suggest a stronger effect of the environment on evening cortisol (Obel et al., 2005), may have been influenced by the fact that women recorded time of sample collection at waking

and not actual waking time. Although instructed to collect saliva right at waking, women who may have waited between waking and collection could have captured the normal increase in cortisol associated with the cortisol awakening response (Clow et al., 2010). This could explain why there is much more variability in morning cortisol values compared with evening cortisol values. Despite these limitations, our ability to identify a significant linear trend between the mother's report of deprivation and maternal and offspring cortisol points to a robust biological effect with potentially important public health implications.

CONCLUSIONS

In summary, we found that women reporting greater levels of material deprivation had elevated evening cortisol in late pregnancy. Offspring born to these women exhibited an increased cortisol response to vaccination at 6 weeks of age, suggesting that early life environmental deprivation alters HPA-axis function. These changes in HPA-axis function are likely the result of a combination of lingering biological effects of maternal stress experience during pregnancy or deprivation-induced changes in maternal rearing behavior, infant attachment, or breast milk composition in the immediate postnatal period. Future research will be needed to replicate these results as well as to identify the underlying mechanisms of biological "memory" linking social experiences in one generation with biology and health in the next.

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