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

ZANETA M. THAYER[1]* AND CHRISTOPHER W. KUZAWA[2,3]
[1]*Department of Anthropology, University of Colorado Denver, Denver, Colorado 80202*
[2]*Department of Anthropology, Northwestern University, Evanston, Illinois 60208*
[3]*Institute for Policy Research, Northwestern University, Evanston, Illinois 60208*

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. 26:723–730, 2014.

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 Bruijn 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

Contract grant sponsor: NSF Graduate Research Fellowship and Northwestern University Presidential Fellowship; Contract grant sponsor: Wenner Gren Foundation; Contract grant number: 8334; Contract grant sponsor: NSF Doctoral Dissertation Improvement Grant; Contract grant number: 7285514.

*Correspondence to: Zaneta M. Thayer, Department of Anthropology, University of Colorado Denver, Campus Box 103, PO Box 173364, Denver, CO 80217-3364. E-mail: zaneta.thayer@ucdenver.edu

Received 21 November 2013; Revision received 6 February 2014; Accepted 8 February 2014

DOI: 10.1002/ajhb.22532
Published online 6 March 2014 in Wiley Online Library (wileyonlinelibrary.com).

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/Māori	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 fusiness, 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 quadrapole 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 μl min^{-1} through a Luna high speed technology (HST) 2.6 μm C18 (2) 100 × 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 → 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

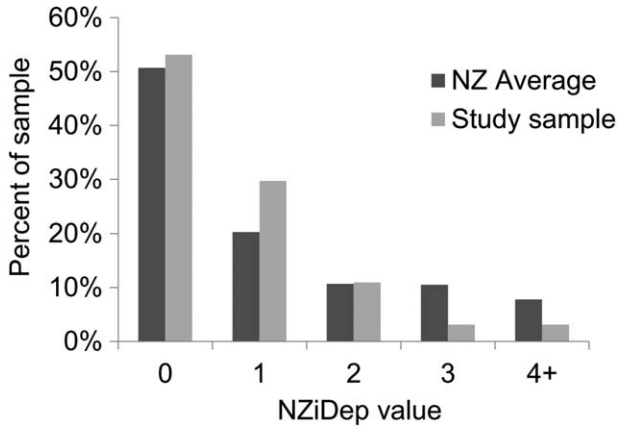

Fig. 1. Distribution of NZiDep values in study sample compared with national sample (national sample data from Salmond et al. 2006).

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

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]

[a]Pearson 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	020	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			

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

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

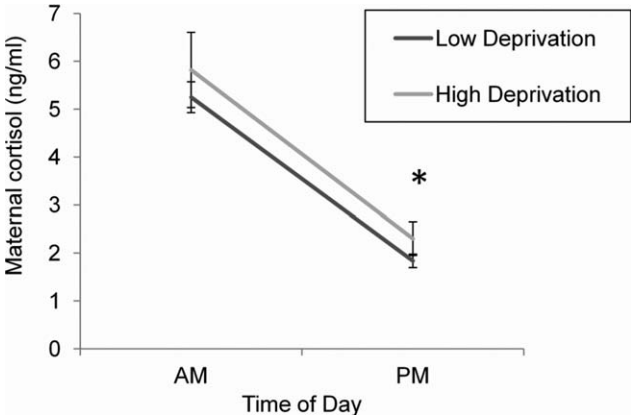

Fig. 2. Maternal morning (AM) and evening (PM) cortisol among women with high (NZiDep ≥ 2) and low (NZiDep < 2) material deprivation (values shown are mean (SE))(* = $P < 0.05$).

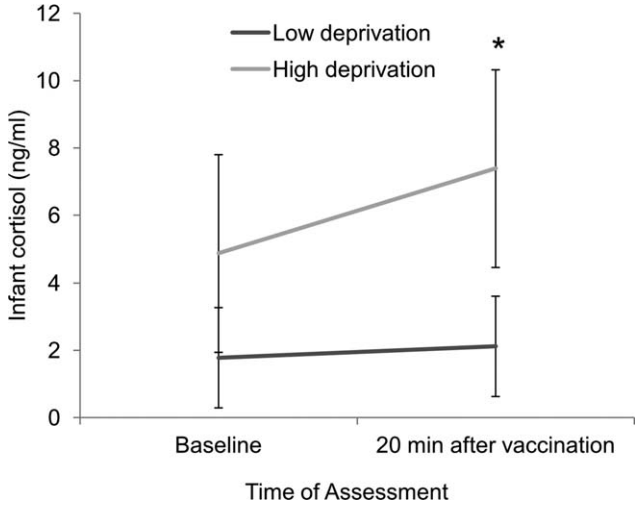

Fig. 3. Offspring cortisol response to vaccination stratified by high (NZiDep ≥ 2) and low material deprivation (NZiDep < 2) in mothers (values shown are mean (SE); * = $P < 0.05$).

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

	Beta	SE	*t*-Statistic	*P*-value
Baseline cortisol *(N = 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. R^2	−0.07			
Offspring cortisol response *(N = 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. R^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 exposure 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 11β-hydroxysteroid dehydrogenase type 2 (11β-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 methlyation in the promotor region of the *11β-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 postnatal 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.

ACKNOWLEDGMENTS

Special thanks to the study participants, SAMCL, Greenlane Medical Clinic and Whariki Health Research Group. An anonymous reviewer and Dr. Sievert helped improve the quality of this manuscript.

LITERATURE CITED

Adler NE, Boyce T, Chesney MA, Cohen S, Folkman S, Kahn RL, Syme SL. 1994. Socioeconomic status and health: the challenge of the gradient. Am Psychol 49:15–24.

Adler NE, Rehkopf DH. 2008. US disparities in health: descriptions, causes, and mechanisms. Annu Rev Public Health 29:235–252.

Adler NE, Stewart J. 2010. Health disparities across the lifespan: meaning, methods, and mechanisms. Ann N Y Acad Sci 1186:5–23.

Ajwani S, Blakely T, Robson B, Tobias M, Bonne M. 2003. Decades of disparity: ethnic mortality trends in New Zealand 1980–1999. Wellington: Ministry of Health.

Albers EM, Marianne Riksen-Walraven J, Sweep FCGJ, Weerth Cd. 2008. Maternal behavior predicts infant cortisol recovery from a mild everyday stressor. J Child Psychol Psychiatry 49:97–103.

Appleton AA, Armstrong DA, Lesseur C, Lee J, Padbury JF, Lester BM, Marsit CJ. 2013. Patterning in placental 11-B hydroxysteroid dehydrogenase methylation according to prenatal socioeconomic adversity. PloS one 8:e74691.

Beijers R, JM R-W, C dW. 2013. Cortisol regulation in 12-month-old human infants: associations with the infants' early history of breastfeeding and co-sleeping. Stress 16:267–277.

Boyce TW, Ellis BJ. 2005. Biological sensitivity to context: I. An evolutionary developmental theory of the origins and functions of stress reactivity. Dev Psychopathol 17:271–301.

Bramley D, Herbert P, Tuzzio L, Chassin M. 2004. Disparities in indigenous health: a cross-country comparison between New Zealand and the United States. Am J Public Health 95:844–850.

Brennan PA, Pargas R, Walker EF, Green P, Newport DJ, Stowe Z. 2008. Maternal depression and infant cortisol: influences of timing, comorbidity and treatment. J Child Psychol Psychiatry 49:1099–1107.

Brummelte S, Schmidt KL, Taves MD, Soma KK, Galea LA. 2010. Elevated corticosterone levels in stomach milk, serum, and brain of male

and female offspring after maternal corticosterone treatment in the rat. Dev Neurobiol 70:714–725.
Buss C, Entringer S, Reyes JF, Chicz-DeMet A, Sandman CA, Waffarn F, Wadhwa PD. 2009. The maternal cortisol awakening response in human pregnancy is associated with the length of gestation. Am J Obstet Gynecol 201:e1–e8.
Clarke AS, Wittwer D, Abbott D, Schneider M. 1994. Long term effects of prenatal stress on HPA axis activity in juvenile rhesus monkeys. Dev Psychobiol 27:257–269.
Clow A, Hucklebridge F, Stalder T, Evans P, Thorn L. 2010. The cortisol awakening response: more than a measure of HPA axis function. Neurosci Biobehav Rev 35:97–103.
Cochrane R, Robertson A. 1973. The life events inventory: a measure of the relative severity of psycho-social stressors. J Psychosom Res 17:135–139.
Cohen S, Schwartz JE, Epel E, Kirschbaum C, Sidney S, Seeman T. 2006. Socioeconomic status, race, and diurnal cortisol decline in the coronary artery risk development in young adults (CARDIA) study. Psychosom Med 68:41–50.
Corbalán-Tutau MD, Madrid JA, Nicolás F, Garaulet M. 2012. Daily profile in two circadian markers "melatonin and cortisol" and associations with metabolic syndrome components. Physiol Behav 123: 231–235.
Craig E, Thompson J, Mitchell E. 2002. Socioeconomic status and preterm birth: New Zealand trends, 1980 to 1999. Arch Dis Child Fetal Neonatal Ed 86:F142–F146.
Craig ED, Mantell CD, Ekeroma AJ, Stewart AW, Mitchell EA. 2004. Ethnicity and birth outcome: New Zealand trends 1980–2001. Part 1. Introduction, methods, results and overview. Aust N Z J Obstet Gynaecol 44: 530–536.
Crespi EJ, Denver RJ. 2005. Ancient origins of human developmental plasticity. Am J Hum Biol 17:44–54.
Davis EP, Glynn LM, Waffarn F, Sandman CA. 2010. Prenatal maternal stress programs infant stress regulation. J Child Psychol Psychiatry 52: 119–129.
de Bruijn A, van Bakel J, Wijnen H, Pop VJM, van Baar AL. 2009. Prenatal maternal emotional complaints are associated with cortisol responses in toddler and preschool aged girls. Dev Psychobiol 51:553–563.
de Weerth C, Buitelaar JK. 2005. Physiological stress reactivity in human pregnancy–a review. Neurosci Biobehav Rev 29:295–312.
Denver RJ. 2009. Stress hormones mediate environment-genotype interactions during amphibian development. Gen Comp Endocrinol 164:20–31.
Diego MA, Field T, Hernandez-Reif M, Cullen C, Schanberg S, Kuhn C. 2004. Prepartum, postpartum, and chronic depression effects on newborns. Psychiatry 67:63–80.
Diego MA, Jones NA, Field T, Hernandez-Reif M, Schanberg S, Kuhn C, Gonzalez-Garcia A. 2006. Maternal psychological distress, prenatal cortisol, and fetal weight. Psychosom Med 68:747–753.
Dowd JB, Simanek AM, Aiello AE. 2009. Socio-economic status, cortisol and allostatic load: a review of the literature. Int J Epidemiol 38:1297–1309.
Drake A, Walker B. 2004. The intergenerational effects of fetal programming: non-genomic mechanisms for the inheritance of low birth weight and cardiovascular risk. J Endocrinol 180:1–16.
Egliston K-A, McMahon C, Austin M-P. 2007. Stress in pregnancy and infant HPA axis function: conceptual and methodological issues relating to the use of salivary cortisol as an outcome measure. Psychoneuroendocrinology 32(1):1–13.
Ellison PT. 2005. Evolutionary perspectives on the fetal origins hypothesis. Am J Hum Biol 17:113–118.
Ellison PT, Jasienska G. 2007. Constraint, pathology, and adaptation: how can we tell them apart? Am J Hum Biol 19:622–630.
Entringer S, Kumsta R, Hellhammer DH, Wadhwa PD, Wüst S. 2009. Prenatal exposure to maternal psychosocial stress and HPA axis regulation in young adults. Horm Behav 55:292–298.
Flinn MV. 2006. Evolution and ontogeny of stress response to social challenges in the human child. Dev Rev 26:138–174.
Flinn MV, England BG. 1997. Social economics of childhood glucocorticoid stress response and health. Am J Phys Anthropol 102:33–53.
Flinn MV, Nepomnaschy PA, Muehlenbein MP, Ponzi D. 2011. Evolutionary functions of early social modulation of hypothalamic-pituitary-adrenal axis development in humans. Neurosci Biobehav Rev 35:1611–1629.
Foster HW, Wu L, Bracken MB, Semenya K, Thomas J. 2000. Intergenerational effects of high socioeconomic status on low birthweight and preterm birth in African Americans. J Natl Med Assoc 92:213–221.
Grant KA, McMahon C, Austin MP, Reilly N, Leader L, Ali S. 2009. Maternal prenatal anxiety, postnatal caregiving and infants' cortisol responses to the still face procedure. Dev Psychobiol 51:625–637.
Gravlee CC. 2009. How race becomes biology: embodiment of social inequality. Am J Phys Anthropol 139:47–57.
Grey KR, Davis EP, Sandman CA, Glynn LM. 2013. Human milk cortisol is associated with infant temperament. Psychoneuroendocrinology 38: 1178–1185.
Gunnar MR, Donzella B. 2002. Social regulation of the cortisol levels in early human development. Psychoneuroendocrinology 27:199–220.
Gutteling BM, de Weerth C, Buitelaar JK. 2004. Short communication: Maternal prenatal stress and 4–6 year old children's salivary cortisol concentrations pre- and post-vaccination. Stress 7:257–260.
Gutteling BM, Weerth Cd, Buitelaar JK. 2005. Prenatal stress and children's cortisol reaction to the first day of school. Psychoneuroendocrinology 30:541–549.
Harris R, Cormack D, Tobias M, Yeh L-C, Talamaivao N, Minster J, Timutimu R. 2012. The pervasive effects of racism: experiences of racial discrimination in New Zealand over time and associations with multiple health domains. Soc Sci Med 74:408–415.
Hertzman C, Boyce T. 2010. How experience gets under the skin to create gradients in developmental health. Ann Rev Public Health 31:329–347.
Hobel CJ, Dunkel-Schetter C, Roesch SC, Castro LC, Arora CP. 1999. Maternal plasma corticotropin-releasing hormone associated with stress at 20 weeks' gestation in pregnancies ending in preterm delivery. Am J Obstet Gynecol 180:S257–S263.
Huizink AC, Bartels M, Rose RJ, Pulkkinen L, Eriksson CJP, Kaprio J. 2008. Chernobyl exposure as stressor during pregnancy and hormone levels in adolescent offspring. J Epidemiol Commun Health 62:e5–e5.
Jansen J, Beijers R, Riksen-Walraven M, de Weerth C. 2010. Cortisol reactivity in young infants. Psychoneuroendocrinology 35:329–338.
Kirschbaum C, Hellhammer DH. 1989. Salivary cortisol in psychobiological research: an overview. Neuropsychobiology 22:150–169.
Kivlighan KT, DiPietro JA, Costigan KA, Laudenslager ML. 2008. Diurnal rhythm of cortisol during late pregnancy: associations with maternal psychological well-being and fetal growth. Psychoneuroendocrinology 33:1225–1235.
Kuzawa CW. 2005. Fetal origins of developmental plasticity: are fetal cues reliable predictors of future nutritional environments? Am J Hum Biol 17:5–21.
Kuzawa CW, Sweet E. 2009. Epigenetics and the embodiment of race: developmental origins of US racial disparities in cardiovascular health. Am J Hum Biol 21:2–15.
Laurent HK, Leve LD, Neiderhiser JM, Natsuaki MN, Shaw DS, Harold GT, Reiss D. 2013. Effects of prenatal and postnatal parent depressive symptoms on adopted child HPA regulation: Independent and Moderated Influences.Dev Psychol 49:876–886.
Lohman G, Roche A, Martorell R. 1988. Skinfold thicknesses and measurement technique. Anthropometric standardization reference manual. Champaign, IL: Human Kinetics Books. p 55–70.
Love OP, Williams TD. 2008. Plasticity in the adrenocortical response of a free-living vertebrate: the role of pre- and post-natal developmental stress. Horm Behav 54:496–505.
Marmot M, Wilkinson R. 2006. Social determinants of health. Oxford University Press, Oxford.
Marsit CJ, Maccani MA, Padbury JF, Lester BM. 2012. Placental 11-beta hydroxysteroid dehydrogenase methylation is associated with newborn growth and a measure of neurobehavioral outcome. PloS one 7:e33794.
Meaney MJ, Diorio J, Francis D, Widdowson J, LaPlante P, Caldji C, Sharma S, Seckl JR, Plotsky PM. 1996. Early environmental regulation of forebrain glucocorticoid receptor gene expression: implications for adrenocortical responses to stress. Dev Neurosci 18:61–72.
Miller GE, Chen E, Zhou ES. 2007. If it goes up, must it come down? Chronic stress and the hypothalamic-pituitary-adrenocortical axis in humans. Psychol Bull 133:25.
Ministry of Health. 2004. Ethnicity Data Protocols for the Health and Disability Sector. Wellington: Ministry of Health.
Mommer BC, Bell AM. 2013. A test of maternal programming of offspring stress response to predation risk in threespine sticklebacks. Physiol Behav 122:222–227.
Murphy VE, Smith R, Giles WB, Clifton VL. 2006. Endocrine regulation of human fetal growth: the role of the mother, placenta, and fetus. Endocr Rev 27:141–169.
Nachmias M, Gunnar M, Mangelsdorf S, Parritz RH, Buss K. 1996. Behavioral inhibition and stress reactivity: the moderating role of attachment security. Child Dev 67:508–522.
Nepomnaschy P, Flinn M. 2009. Early life influences on the ontogeny of neuroendocrine stress response in the human child. In: The endocrinology of social relationships, P Gray & P Ellison (Eds.) (Chapter 16 pp. 364–382). Cambridge, MA: Harvard University Press.
Nguyen V-K, Peschard K. 2003. Anthropology, inequality and disease: a review. Ann Rev Anthropol 32:447–474.
Nyberg CH, Leonard WR, Tanner S, Mcdade T, Huanca T, Godoy RA. 2012. Diurnal cortisol rhythms and child growth: exploring the life history consequences of HPA activation among the Tsimane'. Am J Hum Biol 24:730–738.

O'Connor TG, Ben-Shlomo Y, Heron J, Golding J, Adams D, Glover V. 2005. Prenatal anxiety predicts individual differences in cortisol in preadolescent children. Biol Psychiatry 58:211–217.
O'Connor TG, Bergman K, Sarkar P, Glover V. 2013. Prenatal cortisol exposure predicts infant cortisol response to acute stress. Dev Psychobiol 55:145–155.
O'Donnell KJ, Glover V, Jenkins J, Browne D, Ben-Shlomo Y, Golding J, O'Connor TG. 2013. Prenatal maternal mood is associated with altered diurnal cortisol in adolescence. Psychoneuroendocrinology 38:1630–1638.
Obel C, Hedegaard M, Henriksen TB, Secher NJ, Olsen J, Levine S. 2005. Stress and salivary cortisol during pregnancy. Psychoneuroendocrinology 30:647–656.
Paynter R. 1989. The archaeology of equality and inequality. Ann Rev Anthropol 18:369–399.
Pike IL. 2005. Maternal stress and fetal responses: evolutionary perspectives on preterm delivery. Am J Hum Biol 17:55–65.
Price DA, Close GC, Fielding BA. 1983. Age of appearance of circadian rhythm in salivary cortisol values in infancy. Arch Dis Child 58:454–456.
Rosmond R. 2005. Role of stress in the pathogenesis of the metabolic syndrome. Psychoneuroendocrinology 30:1–10.
Rumball C, Oliver M, Thorstensen E, Jaquiery A, Husted S, Harding J, Bloomfield F. 2008. Effects of twinning and periconceptional undernutrition on late-gestation hypothalamic-pituitary-adrenal axis function in ovine pregnancy. Endocrinology 149:1163–1172.
Salmond C, Crampton P, King P, Waldegrave C. 2006. NZiDep: a New Zealand index of socioeconomic deprivation for individuals. Soc Sci Med 62: 1474–1485.
Sapolsky RM. 2004. Social status and health in humans and other animals. Ann Rev Anthropol 33:393–418.
Schell LM, Magnus P. 2007. Is there an elephant in the room? Addressing rival approaches to the interpretation of growth perturbations and small size. Am J Hum Biol 19:606–614.
Schneider ML, Moore CF, Kraemer GW, Roberts AD, DeJesus OT. 2002. The impact of prenatal stress, fetal alcohol exposure, or both on development: perspectives from a primate model. Psychoneuroendocrinology 27: 285–298.
Schoorlemmer R, Peeters G, Van Schoor N, Lips P. 2009. Relationships between cortisol level, mortality and chronic diseases in older persons. Clin Endocrinol 71:779–786.
Sheriff MJ, Krebs CJ, Boonstra R. 2010. The ghosts of predators past: population cycles and the role of maternal programming under fluctuating predation risk. Ecology 91:2983–2994.
Sheriff MJ, Love OP. 2013. Determining the adaptive potential of maternal stress. Ecol Lett 16:271–280.
Skinner ML, Shirtcliff EA, Haggerty KP, Coe CL, Catalano RF. 2011. Allostasis model facilitates understanding race differences in the diurnal cortisol rhythm. Dev Psychopathol 23:1167.
Spangler G, Schieche M. 1994. Biobehavioral organization in one-year-olds: quality of mother-infant attachment and immunological and adrenocortical regulation. Psychol Beitr 36:30–35.
Statistics New Zealand. 2013. QuickStats About Auckland Region. Available at: http://www.stats.govt.nz/Census/2006CensusHomePage/QuickStats/AboutAPlace/SnapShot.aspx?tab=Culturaldiversity&id=1000002. Accessed on 24 February, 2014.
Thayer ZM, Feranil AB, Kuzawa CW. 2012. Maternal cortisol disproportionately impacts fetal growth in male offspring: evidence from the Philippines. Am J Hum Biol 24:1–4.
Tollenaar M, Beijers R, Jansen J, Riksen-Walraven J, de Weerth C. 2012. Solitary sleeping in young infants is associated with heightened cortisol reactivity to a bathing session but not to a vaccination. Psychoneuroendocrinology 37:167–177.
Tollenaar MS, Beijers R, Jansen J, Riksen-Walraven JMA, de Weerth C. 2011. Maternal prenatal stress and cortisol reactivity to stressors in human infants. Stress 14:53–65.
Van den Bergh BRH, Van Calster B, Smits T, Van Huffel S, Lagae L. 2008. Antenatal maternal anxiety is related to HPA-axis dysregulation and self-reported depressive symptoms in adolescence: a prospective study on the fetal origins of depressed mood. Neuropsychopharmacology 33: 536–545.
Wells JC. 2010. Maternal capital and the metabolic ghetto: an evolutionary perspective on the transgenerational basis of health inequalities. Am J Hum Biol 22:1–17.
Worthman CM, Kuzara J. 2005. Life history and the early origins of health differentials. Am J Hum Biol 17:95–112.
Yehuda R, Engel SM, Brand SR, Seckl J, Marcus SM, Berkowitz GS. 2005. Transgenerational effects of posttraumatic stress disorder in babies of mothers exposed to the World trade center attacks during pregnancy. J Clin Endocrinol Metab 90:4115–4118.