Original Research Article

Developmental Origins of Flatter Cortisol Rhythms: Socioeconomic Status and Adult Cortisol Activity

AMY S. DESANTIS,[1]* CHRISTOPHER W. KUZAWA,[2,3] AND EMMA K. ADAM[3,4]
[1]*Department of Humanities and Social Sciences, Indian Institute of Technology, Gandhinagar, Gujarat, India*
[2]*Department of Anthropology, Northwestern University, Evanston, Illinois*
[3]*Cells to Society, The Center for Social Disparities and Health at the Institute for Policy Research, Northwestern University, Evanston, Illinois*
[4]*Department of Human Development and Social Policy, Northwestern University, Evanston, Illinois*

Objective: Low socioeconomic status (SES) is associated with increased psychosocial stress among low-income persons, which could contribute to differences in activity of the HPA axis (assessed by diurnal cortisol profiles). The current article investigates associations of SES from different developmental stages with cortisol profiles.

Methods: Using data from a large, socioeconomically diverse birth cohort ($N = 1{,}490$) in Cebu, Philippines, the current study compares the relative and joint contributions of SES from five developmental periods, between the prenatal/birth period and early adulthood, to adult cortisol, and examines the effects of chronic exposure to low SES.

Results: Chronically low SES from infancy through early adulthood predicts the highest bedtime cortisol levels, lowest cortisol awakening responses (CARs), lowest total cortisol levels across the day (area under curve or AUC), and the flattest cortisol rhythms between wake up and bedtime, a profile associated with poorer health. Results indicate that cumulative economic strain (between the prenatal period and early adulthood) predicts flatter cortisol rhythms more consistently than SES from any particular period.

Conclusion: Interventions focusing on the psychosocial stressors associated with economic deprivation during any period from infancy to adulthood may be helpful, but targeting interventions across multiple periods may have the greatest impact. Interventions aimed at improving economic conditions between infancy and early adulthood may have implications for long-term changes in HPA axis functioning. Am. J. Hum. Biol. 00:000–000, 2015.

Prolonged exposure to various forms of psychosocial stress has been found to be associated with altered activity of the hypothalamic pituitary adrenal (HPA) axis and its end-product, cortisol (Adam and Gunnar, 2001; Gunnar and Vazquez, 2001; Saxbe et al., 2008; Yehuda et al., 2005). Although periodic HPA system activation in response to stress helps individuals to cope with acute, time-limited stressors (Dickerson and Kemeny, 2004), frequent or chronic activation of the HPA axis is thought to be associated with adverse physical and mental health conditions (Chrousos and Gold, 1992; McEwen, 1998; Sapolsky et al., 2000).

One alteration of the HPA axis that appears to be associated with stress exposure and with chronic psychosocial stress in particular is a flattening of the basal/diurnal cortisol rhythm across the day (Adam and Kumari, 2009). Cortisol typically follows a strong diurnal rhythm in which levels are high upon waking, increase to a peak about 30 min postawakening (the cortisol awakening response, or CAR), and then decline across the day (Kirschbaum and Hellhammer, 1989; Pruessner et al., 1997). Flatter cortisol slopes across the waking day have been associated with many types of psychosocial stress exposure in children (Gunnar and Vazquez, 2001) and adults (Adam and Gunnar, 2001; Saxbe et al., 2008; Yehuda et al., 2005). Not surprisingly, lower socioeconomic status (SES) and financial hardship, pervasive sources of stress, are also associated with flatter diurnal cortisol slopes (slower rates of cortisol decline) across the waking day, due to either lower wake up or higher bedtime cortisol levels (Cohen et al., 2006b; Hajat et al., 2010; Kumari et al., 2010; Ranjit et al., 2005). Flatter cortisol rhythms are also associated with numerous adverse physical and mental health outcomes (Bower et al., 2005; Holt-Lunstad, and Steffen, 2007; Matthews et al., 2006; Rosmond and Bjorntorp, 2000; Sephton et al., 2000) in adults, as well as increased risk of depression in youth (Goodyer, 1996). Consequently, higher levels of psychosocial stress among low-income persons, and the effects of psychosocial stress on the hypothalamic-pituitary-adrenal (HPA) axis specifically, have been proposed as a potential pathway by which low socioeconomic status leads to problematic mental and physical health outcomes (Cohen et al., 2006a; Grzywacz et al., 2004; Hajat et al., 2010; Kumari et al., 2010; Li et al., 2007; Lupien et al., 2000, 2001; Turner and Avison, 2003).

Many early studies linking SES to HPA axis activity were cross-sectional or focused on average levels of

Conflict of interest: The authors report no potential conflicts of interest and have nothing to disclose

Contract grant sponsor: National Institutes of Health; Contract grant numbers: R01-HD19983A, R01-HD18880, P01-HD28076, R01-HD23182, R01-TW05596, R01-HL085144, R01-DK078150, R01-HD054501, and R03TW008133; Contract grant sponsors: Nestle Coordinating Center for Nutrition Research, Wyeth International, The Ford Foundation, The US National Academy of Science, The World Health Organization, The US Agency for International Development (via grants from Wellstart International, the International Center for Research on Women, Family Health International, MEASURE), The Asian Development Bank, The World Bank, The Thrasher Research Fund, The Mellon Foundation, Nestle Research Foundation, and The Carolina Population Center, Institute for Policy Research at Northwestern University (to A.S.D.), the Alumnae Dissertation Fellowship of Northwestern University, and the American Psychological Association Division 38 Graduate Student Research Award.

*Correspondence to: Amy DeSantis, Indian Institute of Technology, Gandhinagar, VGEC Complex, Chandkheda, Ahmedabad, Gujarat 382424, India. E-mail: desantis@iitgn.ac.in

Received 9 March 2014; Revision received 29 October 2014; Accepted 10 November 2014

DOI: 10.1002/ajhb.22668
Published online 00 Month 2015 in Wiley Online Library (wileyonlinelibrary.com).

cortisol at specific times of day (Lupien et al., 2000, 2001), average total daily cortisol output (Cohen et al., 2006a), or stress system reactivity and/or cortisol awakening responses (Wright and Steptoe, 2005). These studies have provided inconsistent results (Lupien et al., 2000; Dowd et al., 2011). In one of the few longitudinal studies of SES-cortisol associations, researchers found that SES differences in morning cortisol levels that were apparent during childhood were no longer significant in adolescence (Lupien et al., 2001). Prior research on SES in relation to cortisol slopes across the waking day has provided more consistent results, indicating that lower SES and/or greater material hardship are associated with flatter diurnal cortisol declines in multiple studies of middle age and older adults (Cohen et al., 2006a; Kumari et al., 2010; Hajat et al., 2010; Ranjit et al., 2005). However, to date, this parameter has not been examined in adolescents or emerging adults.

Research on SES and health has revealed that the chronicity of economic disadvantage across the life course, and low childhood SES in particular, predicts poor adult health independent of current SES (Chen et al., 2007; Galobardes et al., 2004; O'Rand and Hamil-Luker, 2005; Singh-Manoux et al., 2004). As a result, researchers have begun to question the importance of the chronicity and developmental timing of exposure to low SES, including the question of whether there are specific sensitive or critical periods during which the effects of SES on biological stress systems such as cortisol, and on health, may be particularly acute (Ben-Shlomo and Kuh, 2002). Thus, understanding the role of SES exposures during specific developmental periods, as well as chronic exposure to low SES, and how they impact HPA activity is an important and understudied issue in health disparities research.

Developmental timing

Early environmental influences, beginning during the prenatal period, are known predictors of adult health (Barker, 1998; Barker and Osmond, 1986; Kajantie, 2006). Altered activation of the HPA axis has been implicated as one potential mediator of the robust associations between low birth weight and adult health (Kajantie et al., 2007; Kajantie, 2006; Phillips et al., 2000). In particular, animal-based research indicates that exposure to prenatal stress, and maternal physiological stress system activation during pregnancy specifically, has implications for the fetus's intrauterine growth and HPA axis programming. The fetal/neonatal and even infant HPA axis may be particularly sensitive to environmental cues, as it still in the process of being set-up or "programmed" (Kapoor et al., 2006; Murphy et al., 2006). Evidence from human studies has shown influences of prenatal maternal stress on the HPA axis during infancy and later periods (Essex et al., 2002; Glover et al., 2010; Halligan et al., 2004).

On the other hand, stressors occurring during later developmental periods also predict cortisol rhythms. In particular, exposure to negative life events, chronic stress, loneliness, and trauma have been associated with flatter cortisol slopes across the day in children (Gunnar and Vazquez, 2001; Heim et al., 2004), adolescents (Doane and Adam, 2010; Doane et al., in press), and adults (Adam and Gunnar, 2001; Saxbe, et al., 2008; Yehuda et al., 2005).

Because associations between SES and cortisol in humans have primarily examined concurrent SES, the extent to which the developmental timing and chronicity of socioeconomic deprivation influence HPA axis activity remains unclear. The sole longitudinal developmental study of the associations between childhood SES and basal cortisol activity in adulthood (Li et al., 2007) used the very broad groupings of "childhood" (0–16 years old) and "adulthood," (23–42 years old) which did not allow identification of more specific "sensitive periods" during which associations between SES and HPA axis activity may be particularly strong. They also assessed childhood SES based solely on paternal occupational status and only examined cortisol changes between 45 min and 3 h 25 min postawakening, rather than assessing the diurnal cortisol decline across the full waking day. To our knowledge, there have been no prior studies linking prenatal SES to cortisol slopes across the full waking day in adulthood. In addition, prior studies have not accounted for potential confounding influences of cortisol slopes such as birth weight and gestational age at birth. A detailed examination of the developmental timing of SES during more specific, narrowly defined periods, including the prenatal period, may therefore improve our understanding of the relative contributions of SES during different developmental periods to adult cortisol activity.

To clarify the relative importance of developmental timing and the chronicity of economic strain, the current study analyzes data from a large population-based, longitudinal cohort study that has consistent repeated measurements of socioeconomic indicators between the prenatal period and young adulthood, and diurnal cortisol rhythms measured in young adulthood. The primary goal is to identify the developmental origins of altered cortisol rhythms and assess the relative contributions of SES during various developmental periods (from gestation to early adulthood), and to examine gender differences in these associations. We also investigate whether cumulative economic deprivation (i.e., summing the number of developmental periods an individual is below the median SES) predicts HPA functioning more strongly than does SES from individual periods. Because of the extensive literature on the importance of the prenatal and early postnatal periods (Gunnar and Vazquez, 2001; Kapoor et al., 2006), as well as the importance of concurrent psychosocial stress at the time of cortisol measurement for cortisol activity (Adam et al., 2006), we hypothesized that SES from these two periods would be most strongly associated with adult cortisol activity.

MATERIALS AND METHODS

Participants

Participants include young adults (ages 20–22 years) in the Cebu Longitudinal Health and Nutrition Survey (CLHNS), a 1-year birth cohort (n = 3,080 singleton liveborns) delivered from May 1983 to April 1984 in Cebu, Philippines (Adair et al., 2011). Random clustering methods were employed to select 33 communities (barangays) from the 243 barangays in the greater Cebu metropolitan area. During recruitment, all pregnant women identified in the selected barangays were invited to participate. Most women who consented were first interviewed during the 6th or 7th month of pregnancy. Eligibility criteria for follow-up included residence and delivery of a live singleton in a selected barangay or in any health facility in the greater Cebu Metropolitan area. Eighty-three percent of

eligible women consented to and completed prenatal and birth interviews. Data in the present analyses also avail of additional follow-up surveys conducted in 1991–1992, 1994, 1999, 2002, 2005, and 2007.

The Philippines is a country that has experienced significant economic development and increased urbanization in the 23 years between the inception of the study and the time of cortisol collection, making it a highly interesting site to examine the current research question. In addition, although the original research team opted to base the study in the country's second largest city, the metropolitan area included nearby rural and suburban areas (Adair et al., 2011). The country was in 1983, and continues to be, less economically developed than the highly industrialized countries where most other studies of this nature (on SES and cortisol) have been conducted (e.g., U.S., U.K., and Canada). Levels of low birth weight and infant mortality, as well as malnutrition and growth stunting were generally much higher in the Philippines at the study's inception, making it a different cultural and economic setting than the Western industrialized countries where prior studies of this nature have been conducted. The current study has relevance for understanding the physiologic pathways linking social environments and adverse health in other societies undergoing similar transitions, as well as for Asian and Pacific Island populations more generally. In addition, because the sample involves a large representative birth cohort, the full range of income of this country is included (including both very low and very high SES), which is an advantage compared with prior most prior studies, most of which have used convenience samples to examine associations between SES and cortisol. If results from the representative birth cohort in a society very different from the U.S. resemble those found in the U.S. and other Western populations, it would provide some evidence of the universality of the implications of low SES for HPA axis functioning.

Analytical sample

The analytic sample comes from wave 19 (2005), which included 1,912 participants. Of these, 1,788 (94%) provided saliva samples and information on wake and bedtimes, which were used to calculate rate cortisol decline (cortisol slope) from waking to bedtime. Excluding participants in the third trimester of pregnancy (Mastorakos, 2000) and those with highly atypical sleep patterns (Hennig et al., 1998), due to evidence that these factors dramatically alter HPA axis activity, resulted in an analytical sample of 1490 participants (676 women and 814 men: 78% of participants in this wave). Oral contraceptive use was also included as a covariate in all analyses. No participants in the remaining analytical sample reported using corticosteroid-based medications, which was our final exclusion criterion.

Socioeconomic status (SES). SES is measured in the study as a combination of income, education, and assets. Participants reported their *annual income* from all sources, including in-kind services, and the sale of livestock or other products created by household members during the prior year, which were summed to determine total household income. Incomes were deflated to 1983 levels, and logarithmically-transformed. Both *maternal and paternal education* (in years) were also reported. Participants also reported on nine *assets*, (coded 0, 1) and were selected to capture population-relevant aspects of social class, including electricity, televisions, refrigerators, air conditioners, tape recorder, electric fans, jeepneys, cars, and their residence. In addition, house construction type (i.e., light, mixed, permanent structure) was coded as 0, 1, and 2, respectively. Thus, asset scores ranged from 0 to 11. Additionally, participants were asked whether they resided with their parents, parents-in-law, or other adults, or whether they resided alone or with a spouse in the absence of other adults. Residing alone or with a spouse was also included as a covariate. The income during adulthood represents the household income, including parental income for participants who continued to reside with them.

Correlations between the various SES components (income in pesos, number of assets, and average of both parents' education levels) within each wave ranged from $r = 0.49$ to $r = 0.59$ ($P < 0.01$). For both genders, SES-cortisol associations were stronger for the composite SES measure than for any single component. Thus, SES is represented in analyses by a composite variable that included standardized household income, total assets, and average parental education (Chronbach α range = 0.64–0.74; mean $\alpha = 0.70$) for the various developmental periods. All SES components were identical at each wave, and individual components (income, assets, and education) were standardized before being averaged at each wave.

Developmental periods. SES indicators from multiple waves were grouped together by developmental stage. Because birth data (collected within 6 days postpartum) were highly correlated ($r = 0.95$) with prenatal SES data, they were averaged together to represent "prenatal/birth" SES. Toddler SES was calculated from 1986 data (2-year postpartum follow-up); middle childhood SES was represented by the average of 1991 and 1994 measures (ages 8–11); adolescent SES was calculated as the average of 1998 and 2002 data (ages 14–19); and early adulthood SES was represented by 2005 data (ages 22–23), concurrent with saliva sampling.

Cortisol analyses

Participants provided three saliva samples in the 19th wave of data collection (2005). The first was collected at bedtime, then upon awakening the next morning, and 30 min after waking. This protocol allowed us to capture both morning and evening cortisol levels in a compact amount of time; we believe any error (or additional state variation) introduced by sampling evening levels on one day and morning levels on the next day is compensated for by the large sample size (close to 1,500 participants) associated with this study (Adam and Kumari, 2009). Participants were instructed to provide the first saliva sample in a tube that was pre-labeled "sample 1" right before going to bed on the first night. They were further instructed to keep the other two empty tubes in the Ziploc bag beside their bed to more easily facilitate providing the second saliva sample in the tube prelabeled "sample 2" immediately upon waking. They were also given timers to set at this time for 30 min later, at which time they were

TABLE 1. CLHNS Demographic characteristics: Waves 1–19

	Mean or %	SD	Min	Max
Socioeconomic status (SES)				
Prenatal income	280.23	486.43	−6.7	9,924.12
Toddler income	237.53	487.74	0.15	19,363.83
Middle childhood income	442.78	359.23	20.45	6,296.16
Adolescent income	635.65	3,142.24	8.48	12,053.40
Early adult income	601.95	1,337.92	−6.19	40,246.76
Father's education (1983)	7.72	3.93	0	18
Mother's education (1983)	7.47	3.69	0	19
Reside with parents or other adults	87%		0	1
Reside alone or with spouse	13%		0	1
Birth outcomes				
Preterm births (<37 wk)	15%		0	1
Birth weight (g)	3,021	420	910	4,828
Covariates				
Gender (male)	55%		0	1
Body mass index (BMI)	20.69	3.08	13.93	41.17
Wake time	6:34 AM	1 h 8 min	5:00 AM	11:45 AM
Smoking	3%	0.16	0	1
Subjective stress (2005)	2.58	1.22	1	5
Use oral contraceptives	2.9%		0	1
Dependent variables				
Cortisol % decline/h	−0.10	0.07	−0.29	0.12
Area under the curve (nmol/l)	90.84	49.45	3.42	478.26
Cortisol awakening response (nmol/l)	1.98	4.85	−17.86	29.90
Wakeup cortisol (nmol/l)	7.52	4.22	0.21	61.01
Wakeup + 30 min Cortisol (nmol/l)	9.47	5.17	0.27	65.69
Bedtime Cortisol (nmol/l)	2.21	2.57	0.06	22.68

instructed to provide the third sample in the third empty tube for "sample 3." They were further instructed not to brush their teeth within 30 minutes before providing any samples. In addition to timers and the empty tubes, participants also were given article diaries in which they were instructed to record the date and exact time the samples were provided.

Slopes were calculated by subtracting wakeup cortisol levels from bedtime levels and dividing by the estimated length of the waking day using data from both days of saliva sampling. That is, an hourly rate of cortisol decline from morning levels to evening levels was calculated, with steeper slopes reflected by a larger, more negative rate of decline, and flatter slopes associated with a smaller negative decline or an increase in cortisol from morning to evening levels. Total cortisol output was determined by calculating the total "area under the curve" (AUC) with respect to ground in nmol/l from across the waking day, using the polygon method (Pruessner et al., 2003). The length of the waking day was estimated by subtracting the number of hours asleep from 24. The cortisol awakening response (CAR) was calculated by subtracting the wake up cortisol levels from the levels 30 min later, and then standardizing these values. All cortisol values were logarithmically transformed to correct strong positive skews, and measures were standardized such that effect sizes could be easily compared across different cortisol measures.

Saliva samples were shipped on dry ice to a laboratory at Northwestern University, and were stored frozen at −80°C before having the supernatant separated and divided into aliquots. Samples were shipped on dry ice to Trier, Germany, where they were assayed in duplicate for cortisol using a time-resolved immunoassay with fluorometric detection (DELFIA) (Dressendorfer et al., 1992). Intra-assay and inter-assays coefficients of variation (CVs) average less than 7% and 9.0%, respectively.

Covariates

All analyses included covariates for potentially confounding influences including gestational age at birth, birth weight, self-reported stress in 2005 (concurrent with cortisol testing, to ensure that results are not attributable to current, rather than past stress), and body mass index in 2005. Gestational age was calculated based on the mother's last menstrual period prior to the birth of the child. Under certain conditions, including reportedly premature birth or low birth weight (<2,500 g), the Ballard method was used to assess gestational age (Ballard et al., 1979). Birth weights (in grams) were recorded based on reports from birth helpers affiliated with the study or from hospital records. Subjective stress ratings in 2005 were assessed by asking participants to rate their levels of stress for the prior year on a scale of 1 to 5. To ensure cultural appropriateness, all stress related questions were pilot tested and refined in focus groups. All analyses covaried time of waking (Kudielka and Kirschbaum, 2003) and smoking within 30 min before providing the sample (Badrick et al., 2007). Time of waking and times that samples were provided were recorded by participants in diaries that they were given, along with instructions for saliva collection. Smoking status was determined by self-report, and participants had been advised not to smoke within 30 min of providing samples. Those who reported smoking during this time were distinguished from those who did not smoke using a dichotomous categorical variable. We also included use of oral contraceptives as a covariate.

Analytical plan. We conducted the following set of analyses using OLS regression: (a) associations between SES and cortisol for each developmental period (prenatal/birth, toddler, middle childhood, adolescent, and adult) in separate models; (b) average SES from across all five

TABLE 2. Correlations between psychosocial variables and cortisol activity

	Wakeup cortisol	Wake up + 30 mins	Bedtime cortisol	Slope	CAR	AUC
Wake up + 30 mins cortisol	0.49**					
Bedtime cortisol	0.17**	0.12**				
Cortisol slope	−0.40**	−0.13**	0.82**			
Cortisol awakening Resp	0.47**	0.54**	0.04	0.25*		
Cortisol AUC	0.41**	0.79**	0.48**	0.25**	0.40**	
Full-term birth	0.06*	0.01	−0.05*	−0.08**	−0.04	−0.00
Birth weight	0.02	0.01	0.00	−0.01	−0.04	−0.00
Male	−0.14**	−0.09**	0.04	0.10**	0.04	−0.06*
Prenatal SES composite	−0.01	0.04	−0.10**	−0.07**	0.05+	−0.02
Toddler SES composite	−0.02	0.04	−0.10**	−0.06*	0.05+	0.02
Middle childhood SES composite	−0.02	0.04	−0.11**	−0.07**	0.05+	0.01
Adolescent SES composite	−0.02	0.04	−0.12**	−0.07**	0.06*	0.02
Adult SES composite	−0.01	0.06*	−0.09**	−0.05*	0.06*	0.05*
SES low early-low late	0.01	−0.02	0.10**	0.07**	−0.03	−0.02
SES low early-high late	−0.00	0.00	0.03	0.03	0.00	0.03
SES high early-low late	−0.00	−0.05*	−0.01	−0.00	−0.05+	−0.06*
SES high early-high late	−0.01	0.05+	−0.11**	−0.08**	−0.06*	0.04
Live alone	0.00	−0.08**	−0.06*	−0.06*	−0.08**	−0.10**
Stress rating (2005)	0.06*	0.04	0.02	−0.01	−0.02	0.07**
BMI	−0.05+	−0.05+	−0.09**	−0.05+	−0.00	−0.05+
Wake time	−0.19**	−0.19**	−0.01	0.05*	−0.00	−0.20**
Smoking	−0.08**	−0.05+	0.04	0.07**	0.03	−0.05+
Oral contraceptives	0.04	−0.01	−0.05	−0.08**	−0.05+	−0.04+

Note: $+p < 0.10$; $*p < 0.05$; $**p < 0.01$.

periods (c) analyses of SES from all five periods simultaneously; (d) cumulative economic deprivation across all five periods (number of periods a participant was below the median SES); and (e) comparison of those who experience lower SES in early life (prenatal-middle childhood) and low SES later in life (adolescence through early adulthood) with those who experienced low SES in early life and higher SES later, those who experienced high SES in early life and lower SES later; and those who experienced high SES in early life and later. Because associations of HPA axis activity with SES and prenatal environments have been found to vary by gender (Kapoor et al., 2006; Li et al., 2007), and research on associations of prenatal environments with other biologic outcomes in this cohort have been found to differ by gender (Kuzawa and Adair, 2003), we tested for gender-SES interactions in analyses.

RESULTS

Participants in the study reflected a broad range of socioeconomic backgrounds (Table 1). Parental education ranged from zero to 19 years (means = 7.5 years and 7.7 years for mothers and fathers, respectively), throughout the course of the study. Although there was moderate to strong stability in levels of home ownership and housing quality, there were marked increases in the number of assets and deflated (to 1983 pesos) household income across the 22 years of the study, indicating a general shift upward in real income across the study period. Approximately 13% of participants were living alone and/or with spouses at this time. Average levels and distributions of covariates are summarized in Table 1.

Correlations

Simple correlations between cortisol parameters and covariates are presented in Table 2. SES was inversely correlated with slopes ($r = -0.06$ to $r = -0.08$, all P values <0.05), although the effect size was small. This was attributable primarily to associations with bedtime, rather than wake up cortisol levels. Adolescent and adult SES were also correlated with CAR ($r = -0.06$, $P < 0.05$); and only adult SES was correlated with AUC ($r = -0.06$, $P < 0.05$),

Regression analyses

Cortisol slopes. SES was significantly inversely associated with cortisol declines, i.e., those persons with higher levels of SES had more negative (steeper) hourly rates of decline from morning to bedtime, during every developmental period (Table 3). Changes in cortisol slopes associated with each 1 SD increase in SES ranged from $\beta = -0.08$ SD (1% steeper per hour) ($P < 0.01$) during the toddler period to $\beta = -0.10$ SD ($P < 0.01$) for SES during the adolescent period. Note that because diurnal rhythms are typically negative, with cortisol levels decreasing across the waking day, negative coefficients represent a relatively steeper rhythm, consistent with a healthier profile. Each 1 SD increase in average SES was associated with a −0.10 SD (1% steeper per hour) ($P < 0.01$) steeper slope. When we entered SES from all five periods simultaneously into one model to determine whether any particular periods independently predict cortisol rhythms, controlling for the others, we found that no one particular period predicted cortisol slopes, independent of the other SES measures when analyzed simultaneously (Table 3).

Next, we investigated whether the chronicity of economic deprivation (i.e., number of periods below the median SES) or the direction of one's SES trajectory (upward, downward, consistently high, and consistently low) better predicted cortisol slopes than did SES during the individual periods (Table 3). Those in the lower half of the SES distribution during four or five developmental periods had cortisol slopes that were 0.21 SD flatter ($P < 0.01$), relative to those who spent zero or one period in the lower half of the SES distribution. Analyses of SES trajectories were similar in that those who were consistently below the median SES had 0.21 SD (1.5% per hour) flatter slopes ($P < 0.01$) than those who were consistently above, but there were no significant differences between those who experienced either upward or downward

TABLE 3. Associations of cortisol slopes, cortisol awakening response, and cortisol area under the curve, with SES

	Cortisol slope			Cortisol awakening response (CAR)			Area under the curve (AUC)		
	(1) Individual periods	(2) All periods simultaneously	(3) No. periods low SES and trajectories	(4) Individual periods	(5) All periods simultaneously	(6) No. Periods low SES and trajectories	(7) Individual periods	(8) All periods simultaneously	(9) No. periods low SES and trajectories
Developmental period									
Prenatal	−0.09**	−0.06		0.05+	−0.01		0.05+	−0.00	
	(0.03)	(0.06)		(0.03)	(0.07)		(0.03)	(0.06)	
Toddler	−0.08**	0.03		0.05+	0.01		0.05+	0.03	
	(0.03)	(0.07)		(0.03)	(0.07)		(0.03)	(0.07)	
Mid childhood	−0.09**	−0.02		0.05+	−0.02		0.05+	−0.04	
	(0.03)	(0.08)		(0.03)	(0.08)		(0.03)	(0.08)	
Adolescence	−0.10**	−0.07		0.06*	0.05		0.05+	−0.05	
	(0.03)	(0.08)		(0.03)	(0.08)		(0.03)	(0.08)	
Adulthood	−0.09**	0.02		0.06+	0.02		0.08*	0.13+	
	(0.03)	(0.06)		(0.03)	(0.07)		(0.03)	(0.07)	
Average	−0.10**			0.06+			0.06*		
	(0.03)			(0.03)			(0.03)		
2–3 Periods low SES			0.06			−0.15*			−0.10
			(0.07)			(0.08)			(0.07)
4–5 Periods low SES			0.21**			−0.09			−0.08
			(0.06)			(0.06)			(0.06)
SES low early-high late			−0.04			0.01			0.14
			(0.10)			(0.10)			(0.10)
SES high early-low late			−0.12			−0.12			−0.11
			(0.10)			(0.10)			(0.10)
SES high early-high late			−0.21**			0.10			0.12*
			(0.06)			(0.06)			(0.06)
Male	−0.14**	−0.15**	−0.14**	−0.05	−0.04	−0.04	0.14**	0.13**	0.14**
	(0.05)	(0.05)	(0.05)	(0.05)	(0.06)	(0.05)	(0.05)	(0.05)	(0.05)
Term birth (37 wks)	−0.22*	−0.21*	−0.22*	−0.12	−0.12	−0.11	−0.06	−0.06	−0.05
	(0.07)	(0.07)	(0.07)	(0.08)	(0.08)	(0.08)	(0.07)	(0.07)	(0.07)
Birth weight	0.01	0.02	0.01	−0.07	−0.08	−0.07	0.03	0.03	0.03
	(0.06)	(0.06)	(0.06)	(0.06)	(0.06)	(0.06)	(0.06)	(0.06)	(0.06)
Live alone/spouse	−0.16*	−0.12	−0.13+	−0.16+	−0.17*	−0.18*	−0.29**	−0.28**	−0.33**
	(0.08)	(0.08)	(0.08)	(0.08)	(0.08)	(0.08)	(0.08)	(0.08)	(0.08)
Concurrent Stress	−0.01	0.00	0.00	−0.02	−0.02	−0.02	0.06*	0.07*	0.07*
	(0.03)	(0.03)	(0.03)	(0.03)	(0.03)	(0.03)	(0.03)	(0.03)	(0.03)
Body mass index	−0.02**	−0.02**	−0.02**	−0.00	−0.00	−0.00	−0.02+	−0.02+	−0.01+
	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)	(0.01)
Smoking	0.28+	0.29+	0.28+	0.12	0.12	0.12	−0.13	−0.13	−0.14
	(0.16)	(0.16)	(0.16)	(0.16)	(0.16)	(0.16)	(0.16)	(0.16)	(0.16)
Wakeup time	0.05*	0.05*	0.05*	−0.02	−0.02	−0.02	−0.20*	−0.20*	−0.19*
	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)	(0.02)
Oral contraceptives	−0.55*	−0.54*	−0.54*	−0.31	−0.31	−0.31	−0.30	−0.30	−0.30
	(0.23)	(0.24)	(0.23)	(0.24)	(0.24)	(0.24)	(0.23)	(0.23)	(0.23)
Constant	−0.07	−0.11	−0.19	0.52	0.52	0.56	1.27*	1.25*	1.27*
	(0.24)	(0.25)	(0.25)	(0.25)	(0.25)	(0.25)	(0.25)	(0.25)	(0.25)
R^2	0.03	0.03	0.03	0.01	0.01	0.01	0.07	0.07	0.07
N	1,490	1,490	1,490	1,461	1,461	1,461	1,461	1,461	1,461

Coefficients for each of the SES variables in models 1, 4, and 7 represent associations of SES and cortisol for each individual developmental period when *entered separately* in five different models. Coefficients for the covariates in models 1, 4, and 7 indicate associations of covariates with cortisol for models in which current adult SES is analyzed, but these values did not differ substantially from coefficients when SES for the other developmental periods were entered individually. In models 2, 5, and 8, SES from all developmental periods were entered simultaneously in one model.
All cortisol values are logarithmically-transformed. $+P < 0.10$; $*P < 0.05$; $**P < 0.01$.
Reference group for number of periods in the lower half of SES distribution is 0 or 1. Reference group for preterm birth is term birth (37 weeks). Reference category for models on SES trajectories is low SES in early life and low SES in later life. Standard errors are noted in parentheses below the coefficients to which they correspond.

trajectories, as compared with either of the two extreme groups or to one another.

Also of note, females had cortisol slopes that were 0.15 SD steeper, relative to males, in general. Individuals who were born at term (at least 37 weeks gestation) also had cortisol slopes that were −0.21 SD to −0.22 SD steeper, compared with those born preterm. In addition, higher body mass index (BMI) was associated with steeper cortisol slopes (−0.02 SD steeper) ($P < 0.01$).

Cortisol awakening response. When we investigated associations between SES and the cortisol awakening response (CAR), we found that when SES from each developmental period is entered into separate models, higher adolescent SES was significantly associated with higher CARs (Table 3). Coefficients ranged from $\beta = 0.05$ or 3% higher ($P > 0.05$) for SES during the prenatal period to $\beta = 0.08$ SD or 4% higher ($P < 0.05$) during adolescence. When SES periods were entered simultaneously in one model, cortisol was not associated with SES for any of one particular period, controlling for SES during other periods. Each 1 SD increase in average SES was marginally associated with a 0.06 SD (4%) higher CAR ($P < 0.10$).

The analyses of chronicity of economic deprivation and CARs found that those who were below the median SES for two to three of the five developmental periods had CARs that were 0.1 SD (9%) lower ($P < 0.05$); while those who consistently remained below the median SES (4 or 5 periods) did not differ significantly from those who were consistently in the upper SES distribution (i.e., zero or one period low-SES).

Area under curve. Higher levels of SES from each period were associated with marginal increases in total cortisol output (AUC) across the waking day for each developmental period when examined separately (Table 3). Associations between cortisol AUC and each 1 SD increase in SES from each period ranged from 0.05 SD (2.4 nmol/l) ($P < 0.10$) higher for SES during the prenatal period to 0.08 SD (3.7 nmol/l) higher AUC ($P < 0.01$) associated with SES in adulthood. Those with chronically high SES (early and later life) had AUCs that were 0.12 SD higher ($P < 0.05$), compared with those who experienced low SES in early and later life. Finally, those with later wake up times also had lower AUC on average.

Individual cortisol values. Finally, when associations between SES and cortisol values upon awakening and at bedtime were analyzed, higher SES was significantly associated with lower cortisol levels at bedtime, but was not associated with wakeup cortisol levels. Bedtime cortisol levels were inversely associated with SES; each 1 SD increase in SES across the five developmental periods was associated with bedtime cortisol levels that ranged from −0.11 SD ($P < 0.01$) (prenatal SES) to −0.14 SD lower ($P < 0.01$) (adolescent SES) (not shown). One SD lower average SES from across the five periods was associated with −0.14 SD ($P < 0.01$) lower bedtime cortisol levels. When SES from each time period was examined in the model simultaneously, no particular developmental period was more strongly associated with bedtime cortisol levels, relative to other developmental periods. Analyses of the chronicity of economic deprivation (i.e., number of periods in which a person was below the median SES level) revealed that people who were below the median SES for four or five periods had bedtime cortisol levels that were 0.28 SD higher ($P < 0.01$) than those who were below the median SES level for 0 or 1 period. Those of lower SES during early life and adulthood had bedtime cortisol levels that were 0.27 SD higher ($P < 0.01$), as compared with those of higher SES during both early and later life. Those who experienced either upward or downward shifts in SES between early and later life did not differ significantly from one another or from the chronically low or chronically high SES groups. Higher BMI and being born at term (at least 37 weeks gestation) also predicted significantly lower bedtime cortisol levels. Wakeup cortisol levels were not significantly associated with SES from any of the developmental periods, when examined individually or simultaneously (not shown).

We also investigated whether associations between cortisol and SES from different developmental periods differed according to gender by testing gender-SES interactions for all cortisol parameters, and found that interactions were not statistically significant.

DISCUSSION

We found consistent significant associations of higher SES with steeper diurnal cortisol slopes and lower bedtime cortisol levels, indicating a healthier profile overall. Additionally, higher SES in adulthood, and high average SES from infancy to adulthood were also associated with greater area under the curve (AUC), although SES during earlier individual periods was not related to adult cortisol. Those of higher SES during both early and later life had higher AUCs than those of lower SES across early and later life. CARs were positively associated with adolescent SES, but none of the other developmental periods. Those who experienced consistently (4+ periods) high SES had lower CARs than those who experienced two or three periods below the median. In addition, there were no significant differences in wakeup cortisol levels by SES in the current study, which was somewhat unexpected (Hajat et al., 2010), although null findings have been found previously (Cohen et al., 2006b; Kumari et al., 2010).

Associations between chronic socioeconomic deprivation (i.e., the number of periods below the median SES) and cortisol were generally greater than associations between cortisol and either average SES or SES from individual periods. Overall, there was no one particular developmental period that was more strongly related to adult cortisol than the others. Hence, our original hypothesis (that early childhood and current SES would be more strongly associated than intermediate periods) was not borne out by the data. Although it was unsurprising that cumulative disadvantage was related to current cortisol, it is surprising that neither early life nor concurrent SES were more strongly associated with adult cortisol, with the exception of adult SES and AUC. Thus, the cortisol-SES associations for individual developmental stages may be largely attributable to shared SES variance over time.

Flatter slopes have been associated with a number of adverse metabolic and cardiovascular health conditions, as well as depression and PTSD (Heim et al., 2004; Yehuda et al., 2005). On the other hand, research on associations of CARs and AUCs with health has been

equivocal. Higher AUCs are related to depression (Heim et al., 2004); while lower AUCs are related to chronic fatigue syndrome (Bower et al., 2005) and PTSD (Yehuda et al., 2005).

As mentioned, we tested whether associations between SES and gender differed significantly according to gender but found that interactions were not significant. Because prior studies of gender differences in associations between SES and cortisol have presented stratified results, comparisons with such studies are not entirely straightforward. These results are in contrast with Li et al. (2007), who found that adult SES mediated associations between childhood SES and male cortisol. They also found that SES in adulthood, but not childhood/adolescent SES, significantly predicted female cortisol declines. However, Li et al. (2007) analyzed two more broadly defined developmental periods (childhood: 0–16 years old versus adulthood: 23–42 years old), assessed SES based only on paternal occupation, and did not include data on birth outcomes or distinguish between prenatal and postnatal periods. Moreover, cortisol declines in those analyses were measured only between 45 min and 3 h 45 min postawakening, rather than across the entire day. Regardless, the current results replicate the few other studies to examine associations of SES with cortisol slopes (Cohen et al., 2006b; Hajat et al., 2010; Kumari et al., 2010), identifying significant associations between higher SES and steeper cortisol slopes, and finding that lower SES was associated with higher bedtime cortisol associations (Cohen et al., 2006b). It is difficult to directly compare effect sizes with prior studies. Cohen et al. (2006) present separate associations of education and income, with income divided into three categories, whereas Hajat et al. (2011) present an 9-point wealth index and divide the decline into early decline (30–120 min postawakening) and late decline (2–16 h postawakening). Finally, Kumari et al. (2011) found that British civil servants in the lowest grade had hourly declines that were 0.125 nmol/l/h versus those in the highest grades (0.125 nmol/l/h) ($P = 0.003$ for males). Different SES measures and methods of calculating slopes make it challenging to compare effect sizes. However, it is notable that all studies are in the same direction, and while absolute differences, as well as percent differences seem small, the clinical relevance of these effect sizes remains unclear.

Contrary to expectations, birth weight was not related to cortisol parameters in our study. This contrasts with some prior studies of birth weight-HPA activity associations. One possible source of this discrepancy is the use of animal models and/or stress reactivity paradigms in past research, and the fact that most past studies of humans focused on average cortisol levels from specific times of day, rather than studying cortisol slopes between wakeup and bedtime in naturalistic settings and in large community samples (Kapoor et al., 2006).

The current study focused on examining the relative contributions of SES during several developmental periods in relation to cortisol activity during one specific developmental period (young adulthood). Associations of SES with cortisol activity might differ if cortisol had been measured during a different developmental period. Currently, we cannot determine the specific mechanisms through which SES may operate to influence cortisol activity, or the extent to which this may be amenable to naturally occurring changes later in life or responsive to intervention. Additional measures of HPA axis activity at each of the developmental periods for which we have SES data would be an important extension of the current research.

Current psychosocial stress was associated with higher AUC, but no other cortisol parameters. The lack of associations with other cortisol parameters may be due to the fact that the question refers to the entire prior year. Because the HPA axis is sensitive to daily and other recent stressors, it may be the case that a question focusing on more recent specific periods would better capture associations with CAR, slopes, and individual points.

An important limitation of this study is that we did not include measures of maternal HPA axis activity during pregnancy or in the participants themselves during childhood or adolescence. Such information would permit direct examination of whether and how maternal HPA axis activity relates to birth outcomes, SES, and children's postnatal HPA axis functioning, and whether and when SES becomes "biologically embedded" in the form of cortisol changes.

Additionally, we collected cortisol from only one 24-h period, with the bedtime sample preceding the wakeup sample provided the following morning, which is unconventional, but was necessary to maximize efficiency in this large, representative sample for which home-based sample refrigeration was not always available. We also used a single sample to estimate each of wake up, wake up +30 min, and bedtime cortisol levels. We are nonetheless analyzing data as though waking, 30 min after waking, and bedtime samples were taken over the course of the same waking day, in order that our measures are more comparable to past measures of cortisol slopes across the day.

Finally, we did not assess mood states at the exact times of saliva sampling or electronically monitor compliance with sampling protocols. Because momentary- and day-level changes in emotions and stressors influence cortisol levels (Adam, 2006), multiple days of data collection would be preferable. Co-varying state influences on cortisol, and accounting for non-compliance with requested sample timings on the days of collection may have further strengthened associations between chronic stressors, such as low SES, and more stable components of the diurnal cortisol rhythm.

However, as with most cortisol protocols that assume that samples on any given day reflect at least some trait, rather than purely state or day-specific variance, any deviations from typical sleep patterns or cortisol levels would likely serve as a source of error that would attenuate our power to detect significant associations between past SES and cortisol, rather than systematic bias. Furthermore, as part of a large population-based study, errors in reliability due to this minimized protocol are likely to be reduced by the large sample size (Adam and Kumari, 2009). Because the study already included an extensive protocol, and was conducted overseas in a large metropolitan area and many surrounding rural communities, the research team felt that reduced reliability was a reasonable tradeoff for the large sample size that is a representative one-year birth cohort for the country's second-largest city. Moreover, we still found significant associations, attesting to the robustness of the identified SES-cortisol associations.

Our large population-based sample, comprehensive measurement of socioeconomic factors, and nuanced

measurement of the developmental timing of SES exposures, are unique strengths of the current study. No prior studies have included such fine-grained measures of SES, measured as consistently across such a diverse range of developmental periods in a cohort of this size. Our findings speak to the importance of life course experience of SES and support the idea that cumulative disadvantage may be more strongly associated with adult HPA axis activity than disadvantage during any particular "critical period." Notably, chronically low SES is associated with the greatest flattening of the diurnal cortisol slope, which in turn has been found to have important implications for mental and physical health (Heim et al., 2000; Sephton et al., 2000). Kumari et al. (2011) found that a 1-SD flatter slope predicted a 1.87 higher hazard risk (HR) of mortality from cardiovascular causes and a 1.3 higher HR of all-cause mortality, and higher bedtime cortisol, but not wake up cortisol or CARs, significantly predicted mortality in British civil servants. Sephton et al. (2000) divided cancer patients by median split into flatter and steeper cortisol slopes. They found 77% of those with flatter rhythms died, after an average of 3.2 years; while 60% of the patients with steeper rhythms died, but survived an average of 4.5 years. Matthews et al. (2006) found that in persons with coronary calcification, cortisol declined approximately 6% per hour in cortisol over the course of the day, whereas in those without coronary calcification it declined more than 8% per hour ($P = 0.003$).

Despite the challenges involved in estimating the effect sizes of the increased health risks associated with flatter cortisol slopes, and variations in sampling protocols and analytical methods across studies, a growing literature supports the notion that flatter cortisol rhythms are prospectively related to poorer health. Additional longitudinal research in younger, healthy, population-based samples would help to more precisely quantify the specific health risks associated with cortisol slopes of varying magnitudes. The current findings provide support for the theory that HPA axis activity may play a role in associations among SES, cumulative economic strain, and adult health, and offer further evidence that prevention of early poverty, and in particular chronic poverty across childhood, may be an important measure to consider to improve public health and developmental outcomes.

LITERATURE CITED

Adair LS. 1989. Low birth weight and intrauterine growth retardation in Filipino infants. Pediatrics 84:613–622.

Adair LS, Popkin BM, Akin JS, Guilkey DK, Gultiano S, Borja J, Perez L, Kuzawa CW, McDade T, Hindin MJ. 2011. Cohort profile: the Cebu longitudinal health and nutrition survey. Int J Epidemiol 40:619–25.

Adam EK, Gunnar MR. 2001. Relationship functioning and home and work demands predict individual differences in diurnal cortisol patterns in women. Psychoneuroendocrinology 26:189–208.

Adam EK. 2006. Transactions among adolescent trait and state emotion and diurnal and momentary cortisol activity in naturalistic settings. Psychoneuroendocrinology 31:664–679.

Adam EK, Kumari M. 2009. Assessing salivary cortisol in large-scale, epidemiological research. Psychoneuroendocrinology 34:1423–1436.

Adler NE. 1999. Socioeconomic status and health in industrial nations: social, psychological, and biological pathways. New York: New York Academy of Science.

Adler N, Boyce T, Chesney MA, Cohen S. 1994. Socioeconomic status and health: the challenge of the gradient. Am Psychol 4:15–24.

Adler N, Ostrove JM. 1999. Socioeconomic status and health: what we know and what we don't. Ann NY Acad Sci 896:3–15.

Badrick E, Kirschbaum C, Kumari M. 2007. The relationship between smoking status and cortisol secretion. J Clin Endocrinol Metab 92: 819–824.

Ballard JL, Novak K, Driver M. 1979. A simplified score for assessment of fetal maturation of newly born infants. J Pediatr 95:769–774.

Barker D. 1998. In utero programming of chronic disease. Clin Sci (Lond 1979) 95:115–128.

Barker DJP, Osmond C. 1986. Infant mortality, childhood nutrition, and ischemic heart disease in England and Wales. Lancet 1:1077–1081.

Bartels M, De Geus EJC, Kirschbaum C, Sluyter F, Boomsma DI. 2003. Heritability of daytime cortisol level in children. Behav Genet 33:421–433.

Ben-Shlomo Y, Kuh D. 2002. A life course approach to chronic disease epidemiology: conceptual models, empirical challenges and interdisciplinary perspectives. Int J Epidemiol 31:285–293.

Bower JE, Ganz PA, Dickerson SS, Petersen L, Aziz N, Fahey JL. 2005. Diurnal cortisol rhythm and fatigue in breast cancer survivors. Psychoneuroendocrinology 30:92–100.

Chen E, Martin AD, Matthews KA. 2007. Trajectories of socioeconomic status across children's lifetime predict health. Pediatrics 120:e297–e303.

Chrousos GP, Gold PW. 1992. The concepts of stress and stress system disorders. Overview of physical and behavioral homeostasis. J Am Med Assoc 267:1244–1252.

Cohen S, Doyle WJ, Baum A. 2006a. Socioeconomic status is associated with stress hormones. Psychosom Med 68:414–420.

Cohen S, Schwartz JE, Epel E, Kirschbaum C, Sidney S, Seeman TE. 2006b. Socioeconomic status, race and diurnal cortisol decline in the coronary artery risk development in young adults (CARDIA) study. Psychosom Med 68:41–50.

Davis EP, Sandman CA. 2010. The timing of prenatal exposure to maternal cortisol and psychosocial stress is associated with human infant cognitive development. Child Dev 81:131–138.

Dickerson SS, Kemeny ME. 2004. Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. Psychol Bull 130:355–391.

Dowd JB, Ranjit N, Do DP, Young EA, House JS, Kaplan GA. 2011. Education and levels of salivary cortisol over the day in US adults. Ann Behav Med 41:13–20.

Dressendorfer RA, Kirschbaum C, Rohde W, Stahl F, Strasburger C. 1992. Synthesis of a cortisol–biotin conjugate and evaluation as a tracer in an immunoassay for salivary cortisol measurement. J Steroid Biochem Mol Biol 43:683–692.

Essex MJ, Klein MH, Cho E, Kalin NH. 2002. Maternal stress beginning in infancy may sensitize children to later stress exposure: effects on cortisol and behavior. Biol Psychiatry 52:776–784.

Galobardes B, Lynch JW, Davey Smith G. 2004. Childhood socioeconomic circumstances and cause-specific mortality in adulthood: systematic review and interpretation. Epidemiol Rev 26:7–21.

Glover V, O'Connor T, O'Donnell K. 2010. Prenatal stress and the programming of the HPA axis. Neurosci Biobehav Rev 35:17–22.

Goodyer IM, Herbert J, Altham PME, Pearson J, Secher SM, Shiers HM. 1996. Adrenal secretion during major depression in 8-to 16-year-olds, I. Altered diurnal rhythms in salivary cortisol and dehydroepiandrosterone (DHEA) at presentation. Psychol Med 26:245–256.

Grzywacz JG, Almeida DM, Neupert SD, Ettner SL. 2004. Socioeconomic status and health: a micro-level analysis of exposure and vulnerability to daily stressors J Health Soc Behav 45:1–16.

Gunnar MR, Vazquez D. 2001. Low cortisol and a flattening of the expected daytime rhythm: potential indices of risk in human development. Dev Psychopathol 13:515–538.

Hajat A, Diez Roux AV, Franklin TG, Seeman T, Shrager S, Ranjit N, Castro C, Watson K, Sanchez BN, Kirschbaum C. 2010. Socioeconomic and race/ethnic differences in daily salivary cortisol profiles: the Multiethnic Study of atherosclerosis. Psychoneuroendocrinology 35:932–943.

Halligan SL, Herbert J, Goodyer IM, Murray L. 2004. Exposure to postnatal depression predicts elevated cortisol in adolescent offspring. Biol Psychiatry 55:376–381.

Heim C, Ehlert U, Hellhammer D. 2000. The potential role of hypocortisolism in the pathophysiology of stress-related bodily disorders. Psychoneuroendocrinology 25:1–35.

Heim C, Plotsky P, Nemeroff C. 2004. Importance of studying the contributions of early adverse experience to neurobiological findings in depression. Neuropsychopharmacology 29:641–648.

Hennig J, Kieferdorf P, Moritz C, Huwe S, Netter P. 1998. Changes in cortisol secretion during shiftwork: implications for tolerance to shiftwork? Ergonomics 41:610–621.

Holt-Lunstad J, Steffen PR. 2007. Diurnal cortisol variation is associated with nocturnal blood pressure dipping. Psychosom Med 69:339–343.

Kahn JR, Fazio EM. 2005. Economic status over the life course and racial disparities in health J Gerontol Psychol Sci Soc Sci 60:S76–S84.

Kajantie E. 2006. Fetal origins of stress-related adult disease. Ann NY Acad Sci 1083:11–27.

Kajantie E, Feldt K, Räikkönen K, Phillips DI, Osmond C, Heinonen K, Pesonen AK, Andersson S, Barker DJ, Eriksson JG. 2007. Body size at

birth predicts hypothalamic-pituitary-adrenal axis response to psychosocial stress at age 60 to 70 years. J Clin Endocrinol Metab 92:4094–4100.
Kapoor A, Dunn E, Kostaki A, Andrews MH, Matthews SG. 2006. Fetal programming of hypothalamo-pituitary-adrenal function: prenatal stress and glucocorticoids. J Physiol 572:31–44.
Kirschbaum C, Hellhammer DH. 1989. Salivary cortisol in psychobiological research: an overview. Neuropscyhobiology 22:150–169.
Kirschbaum C, Kudielka B, Gaab J, Schommer N, Hellhammer D. 1999. Impact of gender, menstrual cycle phase, and oral contraceptives on the activity of the hypothalamus-pituitary-adrenal axis. Psychosom Med 61: 154–162.
Kudielka BM, Kirschbaum C. 2003. Awakening cortisol responses are influenced by health status and awakening time but not by menstrual cycle phase. Psychoneuroendocrinology 28:35–47.
Kumari M, Badrick E, Chandola T, Adler NE. 2010. Measures of social position and cortisol secretion in an aging population: findings from the Whitehall II study. Psychosom Med 72:27–34.
Kumari M, Shipley M, Stafford M, Kivimaki M. 2011. Association of diurnal patterns in salivary cortisol with all-cause and cardiovascular mortality: findings from the Whitehall II study. J Clin Endocrinol Metab 96: 1478–1485.
Kuzawa CW, Adair LS. 2003. Lipid profiles in adolescent Filipinos: relation to birth weight and maternal energy status during pregnancy. Am J Clin Nutr 77;960–966.
Lemelin ET, Diez Roux AV, Franklin TG, Carnethon M, Lutsey PL, Ni H, O'Meara E, Shrager S. 2009. Life-course socioeconomic positions and subclinical atherosclerosis in the multi-ethnic study of atherosclerosis. Soc Sci Med 68:444–451.
Li L, Power C, Kelly S, Kirschbaum C, Hertzman C. 2007. Life-time socioeconomic position and cortisol patterns in mid-life. Psychoneuroendocrinology 32:824–833.
Lupien SJ, King S, Meaney MJ, McEwen BS. 2000. Child's stress hormone levels correlate with mother's socioeconomic status and depressive state. Biol Psychiatry 48:976–80.
Lupien SJ, King S, Meaney MJ, McEwen BS. 2001. Can poverty get under your skin? Basal cortisol levels and cognitive function in children from low and high socioeconomic status. Dev Psychopathol 13:653–676.
Marmot M, Smith GD, Stansfeld S, Patel C, North F, Head J, White I, Brunner E, Feeney A. 1991. Health inequalities among British civil servants: the Whitehall II study. Lancet 8754:1387.
Mastorakos G, Ilias I. 2000. Maternal hypothalamic-pituitary-adrenal axis in pregnancy and the postpartum period: postpartum-related disorders. Ann NY Acad Sci 900:95–106.
Matthews K, Schwartz J, Cohen S, Seeman TE. 2006. Diurnal cortisol decline is related to coronary calcification: CARDIA Study. Psychosom Med 68:657–661.
McEwen BS. 1998. Protective and damaging effects of stress mediators. N Engl J Med 338:171–179.
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 133:25–45.
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.
O'Rand AM, Hamil-Luker J. 2005. Processes of cumulative adversity: childhood disadvantage and increased risk of heart attack across the life course. J Gerontol Ser B Psychol Sci Soc Sci 60(Suppl Special Issue 2): S117–S124.
Phillips D, Walker BR, Reynolds RM, Flanagan D, Wood PJ, Osmond C. 2000. Low birth weight predicts elevated plasma cortisol concentrations in adults from 3 populations. Hypertension 35:1301–1306.
Pruessner JC, Kirschbaum C, Meinlschmid G, Hellhammer DH. 2003. Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. Psychoneuroendocrinology 28:916–931.
Pruessner JC, Wolf OT, Hellhammer DH, Buske-Kirschbaum A, von Auer K, Jobst S. 1997. Free cortisol levels after awakening: a reliable biological marker for the assessment of adrenocortical activity. Life Sci 61: 2539–2549.
Ranjit N, Young EA, Kaplan GA. 2005. Material hardship alters the diurnal rhythm of salivary cortisol. Int J Epidemiol 34:1138–1143.
Reynolds RM, Walker BR, Syddall HE, Andrew R, Wood PJ, Whorwood CB, Phillips D. 2001. Altered control of cortisol secretion in adult men with low birthweight and cardiovascular risk factors. J Clin Endocrinol Metab 86:245–250.
Rosmond R, Bjorntorp P. 2000. The hypothalamic-pituitary-adrenal axis activity as a predictor of cardiovascular disease, type 2 diabetes, and stroke. J Int Med 247:188–197.
Sapolsky RM, Romero LM, Munck AU. 2000. How do glucocorticoids influence stress responses? Integrating permissive, suppressive, stimulatory, and preparative actions. Endocr Rev 21:55–89.
Saxbe DE, Repetti R, Nishina A. 2008. Marital satisfaction, recovery from work, and diurnal cortisol among men and women. Health Psychol 27: 15–25.
Sephton SE, Sapolsky R, Kraemer HC, Spiegel D. 2000. Diurnal cortisol rhythm as a predictor of breast cancer survival. J Natl Cancer Inst 92: 994–1000.
Singh-Manoux A, Ferrie JE, Chandola T, Marmot M. 2004. Socioeconomic trajectories across the life course and health outcomes in midlife: evidence for the accumulation hypothesis? Int J Epidemiol 33:1072–1079.
Stroud LR, Papandonatos GD, Williamson DE, Dahl RE. 2004. Sex differences in the effects of pubertal development on responses to a corticotropin-releasing hormone challenge: the Pittsburgh psychobiologic studies. Ann NY Acad Sci 1021:348–351.
Turner RJ, Avison W. 2003. Status variations in stress exposure: implications for the interpretation of research on race, socioeconomic status, and gender. J Health Soc Behav 44:488–505.
Ward AM, Syddall HE, Wood PJ, Chrousos GP, Phillips DI. 2004. Fetal programming of the hypothalamic-pituitary-adrenal (HPA) axis: low birth weight and central HPA regulation. J Endocrinol Metab 89:1227–1233.
Wright CE, Steptoe A. 2005. Subjective socioeconomic position, gender and cortisol responses to waking in an elderly population. Psychoneuroendocrinology 30:582–590.
Yehuda R, Golier JA, Kaufman S. 2005. Circadian rhythm of salivary cortisol in Holocaust survivors with and without PTSD. Am J Psychiatry 162:998–1000.