Published in final edited form as:
Ann N Y Acad Sci. 2011 August ; 1231: 56–64. doi:10.1111/j.1749-6632.2011.06151.x.

Blunted Diurnal Decline of Cortisol among Older Adults with Low Socioeconomic Status

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Abstract

Low socioeconomic status (SES) is associated with increased risk for adverse health outcomes; those with low SES are thought to experience more environmental disadvantage and exposure to chronic stress over the life course. The effects of chronic stress on health have been measured by cortisol levels and variations in their diurnal pattern. However, the patterns of association between SES and cortisol have been equivocal in older adults. This paper examined in 98 older adults participating in the Brain Health Substudy of the Baltimore Experience Corps Trial baseline patterns of diurnal variation in salivary cortisol associated with lower versus higher SES using total income and perceived SES relative to others. For each measure, participants stratified into lower vs. higher SES showed a more blunted rate of decline in diurnal salivary cortisol over the day in adjusted models (*P* values ≤ 0.05). There were no SES-related differences in awakening cortisol, cortisol awakening response, or area under the curve. These findings confirm prior evidence of a biologic pathway through which socioeconomic disadvantage is linked to biologic vulnerability, and through which the impact of volunteer service in Experience Corps may be measured.

Keywords

socioeconomic status; salivary cortisol; stress; diurnal pattern; HPA axis; resilience

Introduction

A key question researchers have sought to answer relates to the mechanism through which low socioeconomic status (SES) gets under the skin to affect health and aging. Previous studies have shown that SES has a significant impact on health outcomes in adulthood, predicting increased risk for chronic diseases and mortality.[1–6] The cumulative effects of SES are visible across multiple biological systems.[6, 7]

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The most widely studied pathway, or mechanism, by which low SES is thought to impact health is through chronic excitation of the stress response in the hypothalamic-pituitary-adrenal (HPA) axis, a major biological regulatory system. Evidence indicates that low SES is often associated with a shallower, or, blunted pattern of diurnal decline in cortisol secretion, sometimes resulting in persistently higher salivary levels over the course of the day.[8–11] Salivary cortisol is a noninvasive, surrogate marker for blood cortisol.[12] Among individuals with healthy patterns, levels rise steeply during the 30–45 minute period immediately after wake-up this is known as the cortisol awakening response (CAR) – and then decline gradually from this peak (with mild elevations at meal times) to reach a nadir at bed time. Various features of the daily cortisol profile have been examined, including cortisol levels at wake-up, CAR, area under the curve (AUC), and the diurnal slope.[8–11] There is a lack of consensus regarding those component measures of diurnal cortisol that relate most directly to health.[13] Conflicting results in prior studies may be due, in part, to the lack of standardization in the use of cortisol measures and compliance.[13] Low SES is often associated with a shallower or, blunted pattern of diurnal decline in cortisol secretion and persistently elevated levels of cortisol over the course of the day.[8–11]

Prior research on the association between SES and health have used measures of objective and perceived SES, including level of education attained, income, occupational status or level within an organization, and perceived SES relative to others. More recent measures of SES include annual combined household income, total savings, and home ownership to yield a more comprehensive index of the financial situation over years.

The majority of empirical evidence relating SES to cortisol is derived from young and middle-aged populations. In older populations, low SES has been associated with lower cortisol levels upon waking and flattened, or 'blunted', pattern of diurnal cortisol secretion.[14] In the Multi-Ethnic Study of Atherosclerosis, Hajat *et al.* examined objective measures of SES and reported that low SES groups and Blacks and Hispanics had lower levels of waking cortisol and a flattened decline during the early part of the day.[15] Wright and Steptoe examined subjective SES, gender, and CAR in an older population and found an association between low social status on the MacArthur Scale of Subjective Social Status [16] and a larger CAR after adjusting for biobehavioral and other factors that may mediate the relationship between SES and cortisol.[17] Although these results are consistent with the notion that SES is independently associated with various cortisol measures, few studies have investigated this relationship in a sample of majority lower SES, sociodemographically at risk, minority older adults.

Studying the relationship between SES and diurnal cortisol in older, socio-demographically at-risk adults is important for evaluating how SES over the life course influences vulnerability to chronic diseases, such as diabetes, stroke, heart disease, and dementia, which increases exponentially with age. Additionally, through the identification and use of sensitive measures of biologic susceptibility within lower SES groups, we will be better able to understand behaviors and factors that promote resilience despite environmental disadvantage.

This aim of this study was to explore the baseline relationship between measures of SES and salivary cortisol in individuals participating in the Baltimore Experience Corps Trial (BECT) Brain Health Substudy (BHS). We hypothesized that greater biologic susceptibility associated with lower SES would be associated with blunted decline in diurnal cortisol and elevated diurnal cortisol levels.

Methods

Study Population

Salivary cortisol and SES were measured on participants enrolled in the BHS, a substudy within the BECT. From 2006 to 2010, the BECT randomized a total of 702 older adults to volunteer service designed to improve the academic outcomes of children and increase older adults' health through increased physical, social, and cognitive activity. Participants randomized to the intervention volunteered for 15 hours per week over two academic years in Baltimore City public elementary schools, and were given standardized cognitive, psychological, physical, and functional health assessments at baseline and two annual follow ups. The study design and eligibility criteria for the BECT have been described elsewhere.[18] Inclusion criteria included a Wide Range Achievement Test (WRAT[19]) reading score above 44 (equivalent to 6th grade level) and a Mini-Mental State Examination (MMSE[20]) equal to or above 24. Additional enrollment criteria for BHS participants included: right-hand dominance, no prior history of a pacemaker or other ferrous metal objects in the body, and no history of brain cancer, brain aneurism, or stroke in the prior year. Protocol for data collection was approved by the Johns Hopkins School of Medicine Institutional Review Board, and all participants provided written, informed consent. We measured salivary cortisol levels in 114 of the 123 participants who were enrolled between 2006 and 2009. Based on criteria described in the next section, 16 participants were excluded from the final analysis, leaving 98 participants in this cross-sectional analysis. Those excluded did not differ from the final sample in socio-demographic characteristics including age, sex, race, and education (*P* values > 0.05).

Cortisol Data Collection

Salivary swabs were taken at home by participants immediately after their BHS baseline evaluation at four time points: (i) immediately after wake-up (before brushing), (ii) between 1/2-1 hour after wake-up, (iii) before dinner, and (iv) before bed. Participants were asked to record the time of sample collection. Saliva was collected on small cotton swabs housed in plastic vials (Salivettes, Sardstedt, Numbrecht, Germany) by asking subjects to chew each swab until the swab was saturated. Swabs were refrigerated until laboratory analysis. Cortisol was measured using a competitive immunoassay (HS-Cort Kit, Salimetic LLC, State College, PA) designed for quantitative measurement of salivary cortisol. We excluded 16 participants, noted above, who provided samples outside an acceptable window (>10mins after wake-up at first cortisol sample collection and >60mins between first and second sample collection), and participants who did not provide at least three samples (times i, ii, and iii/iv).

Outcome Measures and Independent Variables

Four measures of the diurnal cortisol pattern were used as outcomes: wake-up cortisol level, CAR (a measure of diurnal HPA axis activity), AUC (a summary measure that captures total diurnal cortisol secretion over the course of the day), and the rate of decline over the period during which samples 2–4 were collected. All salivary cortisol values were log-transformed in analyses except for AUC.

Two measures of socioeconomic status were examined. Perceived location on the SES ladder assessed a participant's perceived position relative to others in society as summarized by "high" SES (upper 5 rungs) or "low" SES (lower 5 rungs) and is thought to be more comprehensive than income or education alone.[16] In addition, participants reported total current, combined household yearly income before tax, which was dichotomized based on median split in the sample as less than $25,000 (low SES) and $25,000 or more (high SES). Covariates included in all models were identified based on prior research demonstrating

their association with cortisol levels and include: age, sex, body mass index (BMI; calculated using height and weight) and years of education.

Statistical Analysis

In depicting and modeling diurnal decline, we noticed variability in the times of sample collection (e.g. mean (range): time 2: 8:00 a.m. (4:45–12:20); time 3: 6:14 p.m. (4:00–9:55); time 4: 8:59 p.m. (7:00–12:30). Therefore, to better model individual rates of decline, we used a response feature analysis, or a two-stage analysis, to summarize cortisol samples at times 2–4 for each participant to a single biologically meaningful response that more sensitively captures variability in collection time. For each individual, we estimated the rate of decline as the slope of a linear regression of logarithm of the cortisol values at exact sample times 2–4. This methodology substantially improved model fit compared to standard linear regression methodologies that assume fixed collection times. In addition to all other cortisol measures, the rate of decline generated from the model was analyzed using fixed effects one-way analysis of variance (ANOVA) to model the relationship between cortisol and SES measures. We performed a univariate linear regression to test the unadjusted association between salivary cortisol measures and (1) position on the SES ladder and (2) combined household income before tax. We then included covariates and reported the significance of regression coefficients (Table 2). Analyses were performed using STATA 11.2 (StataCorp, College Station, TX).

Results

Table 1 shows baseline characteristics of the study sample. Participants were majority female (71.4%) and African American (90.8%) with a mean age of 66.8 years. Thirty-seven percent of participants had a high school or less education, the median income before tax was $30,000, and 23.5% fell below the poverty threshold using income/household size and based on 2011 Health and Human Services poverty guidelines.[21] Participants had a mean MMSE score of 28.4, and, based on self-reported health status, 74.2% had hypertension, 60.8% had osteoarthritis, and 30.9% had diabetes. Approximately 42% of participants placed themselves on the upper half of the SES ladder, and 56% reported incomes of $25,000 or more.

Table 2 shows the mean value of diurnal cortisol parameters by perceived SES position, the unadjusted and the adjusted (regression coefficients; *P*-values) measures of association between cortisol measures and perceived position on the SES ladder. Participants in the low SES group (mean rate of decline = −0.04) had a significantly blunted rate of decline in diurnal cortisol relative to those in the high SES group (mean rate of decline = −0.05) as evident by the unadjusted ($\beta = -0.02$; $P = 0.04$) and adjusted coefficients ($\beta = -0.03$, $P = 0.05$) (note: high SES used as the reference group). There were no group differences in awakening cortisol, CAR, and AUC before or after adjustment for age, sex, BMI and education ($P > 0.05$). Similar results are depicted in Table 3 when stratifying participants by combined household income before tax. Participants with a combined household income of less than $25,000 (mean rate of decline = −0.04) had a significantly blunted rate of decline in diurnal cortisol compared to those with a combined household income of $25,000 or more (mean rate of decline = −0.06) as evident by the unadjusted ($\beta = -0.002$; $P = 0.03$) and adjusted coefficients ($\beta = -0.04$, $P = 0.02$) (note: high SES used as the reference group). Again we did not observe significant group differences in awakening cortisol, CAR, and AUC.

Overall, whether defining low SES according to perceived location on the SES ladder or by combined household income, participants with low SES exhibited a blunted or slower decline in the diurnal pattern of cortisol secretion over the day.

Discussion

We explored in a socioeconomically at-risk cohort of urban-dwelling older adults enrolled in a large-scale trial of a social health promotion program the baseline associations between measures of diurnal variation in cortisol and SES. Whether classifying participants according to perceived location in the lower vs. upper half of the SES ladder or by combined current household income of above and below $25,000, we observed blunted decline in diurnal cortisol among participants in the lower vs. higher SES strata. These associations were unaltered when adjusting for age, sex, and BMI. We did not observe SES-related differences in awakening cortisol, CAR, or AUC. Our results confirm studies reporting a blunted decline in diurnal cortisol among lower vs. higher SES groups[22–24], extending this work to an older, community-dwelling sample of socioecomically at-risk adults. They suggest that one major biologic mechanism through which environmental disadvantage accumulates is through dysregulation, e.g. chronic elevation, in daily cortisol levels as demonstrated here by blunted diurnal decline.

Blunted diurnal cortisol appears to be a sensitive measure of decreased physiologic resilience under the concepts of frailty and disability, and, allostatic load (AL) and risk for chronic disease. Frailty has been conceptualized as a disease-independent state of impaired regulation across multiple systems and is associated with increased vulnerability to physical disability.[25–27] In earlier work among older women, we provided the first epidemiologic evidence that higher levels and blunted diurnal cortisol were associated with increasing frailty burden, whereas awakening was not.[28] AL has been described by Seeman *et al.* [6] as a biological pathway through which environmental risk factors over the life course cumulatively impose a significant physiological burden on multiple, interrelated body systems.[29–31]

Biological evidence for the deleterious effects of over-stimulation of the HPA-axis can be observed using numerous markers of brain health, including atrophy, deactivation, and cell death in the hippocampus [32], a region important to memory and risk for Alzheimer's Disease. Behaviorally, healthy older adults with increasing and elevated cortisol levels over the preceding four years exhibited poorer memory and attention relative to those with lower levels.[33] Elevated and increasing levels of cortisol were also associated with reduced hippocampal volumes.[34] These effects may be compounded, or exacerbated, in those experiencing chronic environmental disadvantage through low SES.

The socioeconomic composition of older adults participating in the BECT offers a critical opportunity to examine the intersection of aging and life time cumulative risk through low SES, given that these individuals are at elevated risk for disease and disability. Education was variable with 37% having a high school education or less. The median total income before taxes in our sample was $30,000, and often represents combined income in many participants who report living with others. The federal poverty guidelines commonly used by the Department of Health and Human Services (HHS) (2011) for a family of four is $22,350. In addition, the majority of participants are African-American, and represent a segment of the population experiencing increased financial strain that likely affects health.[35]

In this group, we nonetheless found numerous similarities across socioeconomic strata in diurnal cortisol levels for awakening, CAR, and AUC. Specifically, we did not observe a difference in awakening cortisol level according to perceived SES or combined household

income. Several studies have reported higher awakening cortisol levels among high SES participants[8, 9, 36] although few studies have reported the opposite association.[37, 38] Other studies, like ours, reported no difference in awakening cortisol by SES group.[14, 15, 37, 39, 40] These equivocal findings may reflect variability in socioeconomic strata studied, and variable sleep-wake patterns, as observed here with wake times ranging from 4:00 a.m. to 10:00 a.m. Similarly, for the CAR, results are inconclusive with some finding an association with SES.[14, 37, 41] We did not observe a difference in CAR by perceived SES and by total current household income, confirming reports from several other studies.[14, 36, 37, 41] Whereas a lower CAR has been associated with chronic health problems, posttraumatic stress disorder, chronic fatigue syndrome, and sleep disorders, day-to-day fluctuations in CAR have been observed.[42] Finally, AUC is a commonly used measure of total cortisol secreted with studies finding that lower SES was significantly related to a higher AUC.[15, 17, 43] However, our study showed no association between AUC and SES. This may be due, in part, to limited sensitivity of the AUC when two participants have the same AUC value but different patterns of diurnal secretion that may suggest chronically elevated levels.

An important factor in the assessment of diurnal cortisol that may partially explain equivocal findings is the variability in and accuracy with which one takes and reports collection at the indicated times. Differential adherence to timing contributes to artificial blunting of the diurnal cortisol pattern.[7, 41] However, few investigators report compliance rates in the collection of samples at designated times and this has a significant impact on the reported results.[7, 13, 14, 41, 43, 44] In modeling the data, we observed great variability in sample collection times and recognized the potential for measurement error by assuming fixed collection times. Therefore, we applied one fitted regression slope and incorporated time administered for samples 2–4, thus reducing the potential for measurement error and increasing sensitivity in detecting associations between SES and diurnal cortisol (see methods). The methodologic approach used here to model diurnal decline in cortisol represents a novel metric intended to mitigate the effect of this unmeasured variability and a represents a particular strength of the study.

This study identified biologic vulnerability among individuals with lower SES who are participating in a two-year randomized trial studying the effects of activity and environmental enrichment through volunteer service to elementary school children. Having collected annual follow-up cortisol samples over the two years of the BECT, we will now be able to examine whether this biologic link to chronic environmental deprivation and disadvantage over the life course can be partially reversed when these individuals volunteer in an enriched environment. Specifically, we will extend this work to determine how such vulnerability over the life course may be partially reversed through these same plastic regulatory pathways. Animal models show that enriched environments elicit neurogenesis or synaptogenesis (i.e., growth of new neurons or formation of new synapses between neurons), and reduced neuronal death, especially in hippocampal structures important to memory [45] and dementia risk. There is ample evidence of these neuroplastic changes in older animals.[46–50] However, this work has only recently begun to be translated to human studies of chronic stress [51], and remains to be explored in older adults who may have experienced decades of accumulated physiologic burden in multiple, interrelated systems.

There are a number of study limitations that warrant consideration. First, while the study sample was relatively small (N<100), but was nonetheless comparable to other studies examining diurnal cortisol in older adults and was sufficiently powered to observe SES-related differences in diurnal decline using two different measures. Second, our collection of cortisol samples was restricted to one day unlike other studies that obtained samples over three or more days.[14, 15, 52, 53] To address this limitation, we are currently administering a validation study to assess cortisol concentrations over two days. Third, we did not adjust for

the day of the week during which samples were obtained, as daily patterns may be less variable in retired adults. Nonetheless, this limitation suggests that our results may represent a conservative estimate of the association between cortisol and SES. Finally, regarding generalizability, these findings were from a study of participants willing to enroll in a two-year trial of high-intensity volunteer service. These individuals may represent the health-conscious members of their community, which again would lead to a conservative estimate of the association between SES and biologic vulnerability as measured by diurnal cortisol.

We used perceived position on the SES ladder as an SES measure to complement current total income; because most studies exploring this association have not used the SES ladder, we were unable to compare our results to multiple studies. However it should be noted that utilization of the SES ladder provides more information about the social status of an individual across multiple SES indicators compared to education and or current income especially in an older population.[16]

Conclusion

These cross-sectional findings contribute to our understanding as to how environmental disadvantage and social conditions ‘get under the skin’ to affect health and aging over the life course.54 Elevated cortisol levels in low SES older adults may be indicative of cumulative disadvantage and associated physiologic burden over the life course that leads to decreased biologic resilience in the face of additional insult. Although many studies have focused on the correlation between SES and salivary cortisol in children, adolescents, and adults, few have examined this association in older adults who may have experienced a life time of accumulated SES burden and who are entering an age of elevated risk for disease and disability. The results of this study among socioeconomically at-risk participants enrolled in a social health promotion model to promote cognitive, physical, and psychological health will provide further insight into how increased biologic vulnerability, as indexed by blunted diurnal cortisol levels, may be reversed along the same physiologic pathways through environmental enrichment and advantage.

Acknowledgments

This work was supported by the National Institute on Aging (NIA) BSR Grant # P01AG027735-03, by the NIA Claude D. Pepper Older Americans Independence Center Grant #P30AG021334, and by the Johns Hopkins Neurobehavioral Research Unit. Dr. Seplaki is supported by Mentored Research Scientist Development Award number K01AG031332 from the National Institute on Aging.

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Table 1

Baseline demographic, health, and cognitive characteristics of the Baltimore Experience Corps Trial (BECT) Brain Health Substudy.

Characteristics	N=98
Age, mean ± SD	66.8 ± 5.6
Female, %	70 (71.4)
Race (African American), n (%)	89 (90.8)
Education (≤ high school), n (%)	32 (37.1)
Household Income, median	$30,000
Income (below the poverty threshold *), n (%)	23 (23.5)
MMSE, mean ± SD	28.4 ± 1.5
Co-morbid conditions, n (%)	
Hypertension	72 (74.2)
Osteoarthritis	59 (60.8)
Diabetes	30 (30.9)
Perceived SES position, n (%)	
High SES	41 (41.8)
Low SES	57 (58.2)
Household Income, n(%	
≥ $25,000	55 (56.1)
< $25,000	43 (43.9)

* Determined by 2011HHS poverty guidelines (http://aspe.hhs.gov/poverty/11poverty.shtml)

Table 2

Mean values of diurnal cortisol response by perceived SES position with unadjusted and adjusted regression coefficients.

Cortisol Measure	Perceived SES Position		Unadjusted Regression Coefficient	P - value	Adjusted* Regression Coefficient	P - value
	Low (mean)	High (mean)				
Awakening level (nmol/l)	17.68	17.39	−0.03	0.84	−0.08	0.58
CAR (nmol/l)	3.45	2.96	0.01	0.97	−0.02	0.58
AUC	217	200	−15.20	0.90	−16.35	0.63
Rate of decline (nmol/l hr)	−0.04	−0.05	−0.02	0.04	−0.03	0.05

*Regression model adjusted for age, sex, BMI, and education.

Cortisol Measurements for all regression models were log-transformed except AUC; regression coefficients for Awakening level, CAR, and Rate of decline can be interpreted as the change in log-transformed cortisol measure for the high SES group compared to the low SES group.

CAR, cortisol awakening response; AUC, area under the curve.

Table 3

Mean values of diurnal cortisol response by combined household income before tax with unadjusted and adjusted regression coefficients.

Cortisol Measure	combined household income before tax		Unadjusted Regression Coefficient	P - value	Adjusted* Regression Coefficient	P - value
	< $25,000(mean)	≥ $25,000(mean)				
Awakening level (nmol/l)	16.54	18.36	−0.14	0.34	−0.03	0.83
CAR (nmol/l)	6.12	1.00	−0.28	0.47	−0.71	0.10
AUC	210	209	−19.25	0.90	−21.15	0.56
Rate of decline (nmol/l hr)	−0.04	−0.06	−0.02	0.03	−0.04	0.02

*Regression model adjusted for age, sex, BMI, and education.

Cortisol Measurements for all regression models were log-transformed except AUC; regression coefficients for Awakening level, CAR, and Rate of decline can be interpreted as the change in log-transformed cortisol measure for the high SES group compared to the low SES group.

CAR, cortisol awakening response; AUC, area under the curve