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Cumulative Effects of Early Poverty on Cortisol in Young Children: Moderation by Autonomic Nervous System Activity

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Abstract

The relation of the cumulative experience of poverty in infancy and early childhood to child cortisol at age 48 months was examined in a prospective longitudinal sample of children and families (N=1,292) in predominantly low-income and rural communities in two distinct regions of the United States. Families were seen in the home for data collection and cumulative experience of poverty was indexed by parent reported income-to-need ratio and household chaos measures collected between child ages 2mos and 48mos. For the analysis presented here, three saliva samples were also collected over an approximate 90 minute interval at child age 48mos and were assayed for cortisol. ECG data were also collected during a resting period and during the administration of a mildly challenging battery of cognitive tasks. Mixed model analysis indicated that child cortisol at 48 months decreased significantly over the sampling time period and that cumulative time in poverty (number of years income-to-need less than or equal to 1) and cumulative household chaos were significantly related to a flatter trajectory for cortisol change and to an overall higher level of cortisol, respectively. Findings also indicated that respiratory sinus arrhythmia derived from the ECG data moderated the association between household chaos

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and child cortisol and that increase in respiratory sinus arrhythmia during the cognitive task was associated with an overall lower level of cortisol at 48 months.

A large literature has shown that children growing up in poverty face substantially increased risk for early learning difficulties and behavior problems (Bradley & Corwyn, 2002; Brooks-Gunn & Duncan, 1997). One potential mechanism of this effect involves stress. A growing literature suggests that one way in which poverty adversely affects children's development is by altering levels of stress hormones (Blair et al., 2011; Evans, 2003; Lupien, King, Meaney & McEwen., 2001). Alteration of stress hormone levels through factors present in the context of poverty is of substantial concern given that these hormones modulate activity in brain areas that underlie the control of attention and emotion (Arnsten, 2009; Floresco, 2013). At moderate levels of increase, catecholamines and glucocorticoids stimulate synaptic activity in areas of prefrontal cortex associated with working memory, executive function, and the regulation of attention and emotion (Alexander et al., 2007; Lupien et al., 1999; Ramos & Arnsten, 2007). Consequently, stress hormones can shape the circuitry of the brain, both developmentally and in adulthood. Human and animal models have shown that prenatal and postnatal stress as well as stress in adulthood alters cortical morphology and connectivity and functional activity in areas of PFC and associated limbic regions that underlie self-regulation and executive cognitive abilities (Bock, Riedel, & Braun, 2012; Liston et al., 2006; Hanson et al., 2012). As such, examinations of the effects of the environment, particularly the early environment, on stress hormone levels in children provide support for the idea that one pathway through which poverty increases risk for behavioral and learning difficulties in children is through effects on brain structure and function.

Examinations of child stress physiology in the context of poverty have frequently focused on the glucocorticoid hormone cortisol, usually as obtained from saliva samples. Cortisol is the end product of a cascade of activity in the hypothalamic-pituitary-adrenal (HPA) axis in which stimulation initiates the release of corticotropin releasing hormone (CRH) from the paraventricular nucleus of the hypothalamus leading to the secretion of adrenocorticotropic hormone from the pituitary and resulting release of cortisol from the adrenals. In part, the focus on cortisol in research on stress physiology and child development reflects the fact that the HPA axis is the slower acting branch of the stress response system. Notably, effects of glucocorticoids on development are primarily gene mediated (de Kloet, Karst, & Joels, 2008; Joels & Baram, 2009), meaning that glucocorticoids stimulate activity at the cell nucleus that can shape downstream physiological activity with implications for psychological development. As such, cortisol may be a robust indicator of longer term effects of experience on development. Alterations to resting levels may lead to variation in gene activity and to alterations in brain structure and function in ways that shape the development of physical and mental health (McEwen & Gianoros, 2011).

Although few published studies have examined the relation of poverty to stress physiology in children, those that do form a relatively coherent picture. In one study, lower parent reported income was associated with higher single time point cortisol levels in a cross sectional sample of 6 – 10 year old children but not 11 – 16 year old children (Lupien, King,

McEwen, & Meaney, 2000). A second study with a sample of 9 – 11 year old children examined multiple aspects of the stress response including overnight levels of norepinephrine and epinephrine as well as cortisol. These measures, combined with others (blood pressure, body mass index) into an index of allostatic load, were positively and linearly related to a cumulative index of psychosocial and physical risk factors in the home (Evans, 2003). A third study (Miller et al., 2009) using genome wide transcriptional profiling found that low SES in childhood was associated with up regulation of genes associated with adrenergic neural receptor function and down regulation of genes associated with glucocorticoid receptor function in adulthood; a pattern consistent with an expected higher level of reactivity and less prototypically effective regulation of physiological reactivity in individuals experiencing poverty in early childhood. A fourth study, with a sample of children 13–18 years of age found that SES was inversely associated with cortisol increase over two years and that family disorganization as assessed by a measure of household chaos was a relevant aspect of this effect (Chen, Cohen, & Miller, 2010).

In addition to the aforementioned studies, previous findings from the longitudinal early childhood sample used in this analysis (N=1,292) have shown high levels of resting or basal cortisol at 7 through 48 months of age for children facing early socioeconomic disadvantage (Blair et al., 2011a) and shown that observed parenting behavior partially mediated effects of socioeconomic disadvantage on cortisol levels in children (Blair et al., 2011b). Findings from this sample have also shown that sensitive parenting behavior observed when children are infants is associated with a higher level of cortisol reactivity to an emotionally arousing situation when children are 7 months old and with an overall lower level of cortisol in response to emotional arousal when children are 15 months old (Blair et al., 2008). Findings from that previous analysis also indicated that child temperament, namely distress to novelty, was associated with a higher level of cortisol at age 15 months. It may be that child characteristics are relevant to examinations of the effect of poverty on child stress physiology, and we examine temperament as well as child intelligence as additional or alternative explanations for any effects of the environment on child cortisol.

Given the small but consistent literature on poverty and stress physiology in childhood, it is of interest to separately examine distinct but related aspects of early disadvantage, including income to need but also characteristics of the home such as chaos that covary with but are not identical with poverty. It is also of interest to examine indicators of child sympathetic and parasympathetic activity simultaneously with cortisol. It may be that activity in the autonomic nervous system augments or moderates relations between disadvantage and cortisol. Stress response physiology is complex and composed of multiple interacting systems that communicate or mediate information from the environment to the organism. Monoamines (dopamine, norepinephrine) released in response to stress can enhance attentional focus and support psychological and behavioral strategies to maintain stress arousal in an acceptable range. Importantly, CRH also stimulates monoamine release, which can potentially have beneficial as well as negative consequences for the stress response (Meaney, Brake, & Gratton, 2002).

Alpha amylase obtained from saliva (sAA) is one marker of autonomic nervous system (ANS) activity that might be important for understanding the relation of psychosocial

disadvantage to cortisol (Granger, Kivlighan, El-Sheikh, Gordis, & Stroud, 2007; Rohleder & Nater, 2009). Levels of sAA increase during times of acute experiential stress (Chatterton, Vogelsong, Lu, Ellman, & Hudgens, 1996; Engert et al., 2011; Gordis et al., 2006) and are correlated with multiple indicators of ANS activity, including plasma norepinephrine (Rohleder, Nater, Wolf, Ehlert, & Kirschbaum, 2004), preejection period (Bosch et al., 2003; West et al., 2006), and skin conductance (El-Sheikh et al., 2008). As such, higher sAA might indicate monoamine increase in response to stress that could lead to higher cognitive and behavioral regulation and to lower cortisol levels.

Respiratory sinus arrhythmia (RSA) is another relevant indicator of ANS activity that can potentially inform the relation of psychosocial disadvantage to cortisol. RSA is a measure of parasympathetic influence on variability in heart rate occurring during respiration associated with the tenth cranial nerve, the vagus. RSA is presumed to work in a coordinated fashion with SNS and HPA systems to regulate responses to stimulation (Porges, 2001). Higher resting level of RSA, indicating greater influence of the vagus nerve on the heart, is understood to be indicative of a calm resting state and to indicate the potential to modulate heart rate as needed in response to stress (Porges, 1998, 2001). Reductions in RSA, referred to as vagal suppression or withdrawal, provide an index of the adaptive and flexible regulation of heart rate in response to cognitive or social challenges. Through increased regulation of physiological state, higher levels of RSA and of RSA change in response to stimulation may be associated with reduced cortisol in response to stress. Several studies have shown that low resting RSA and/or the absence of RSA change in response to challenge, whether increase (augmentation) or decrease (suppression) are associated with behavior problems and problems with the regulation of attention and emotion (Calkins, Graziano, & Keane, 2007; Huffman et al, 1998; Moore, 2010).

No studies of which we are aware have directly examined possible moderation of effects of early disadvantage on levels of cortisol in children by measures of ANS system activity. In addition to what is known about the physiological interaction of stress response systems (Joels & Baram, 2009), support for such a moderating hypothesis is provided by several studies showing that levels of ANS activity moderate the effects of stressful experience on behavioral outcomes with which cortisol is associated. In one study, higher level of resting RSA was associated with reduced behavior and attention problems for children in homes characterized by high levels of marital conflict (El-Sheikh & Whitson, 2006). Similarly, prior studies have shown that the relation of cortisol to behavioral and cognitive outcomes in children was moderated by sAA. In these studies, the combination of low cortisol and high sAA is associated with reduced internalizing and externalizing behavior (El-Sheikh, Erath, Buckhalt, Granger & Mize, 2008) and higher executive function (Berry et al., 2012). Of course, the timing of activity in stress response physiology is critical for understanding interactive effects (Joels & Baram, 2009; Joels & Kruger, 2007). Field-based research generally, however, does not allow for the careful control of the timing of experience when coming to conclusions about interaction among branches of the stress response system.

Prior studies indicate effects of early disadvantage such as that associated with poverty on stress physiology in children (Calkins, Graziano, Berdan, Degnan, & Keane, 2008; Evans, 2003) yet relatively few have examined effects of early disadvantage in a large sample using

a prospective longitudinal design. Therefore, in keeping with prior studies that make use of naturally occurring contexts as opposed to direct stress manipulations to examine stress physiology in children (e.g., Davis, Bruce, & Gunnar, 2002; Evans, 2003; Watamura, Donzella, Alwin, & Gunnar, 2003), we examined change in cortisol in response to the data collection session at age 48 months as a function of earlier adverse experience and child and family characteristics. In addition, given growing attention to the need for multiple indicators of the stress response system in the prediction of behavioral outcomes, it is important to examine several indicators simultaneously to determine whether relations between disadvantage and a physiological parameter such as cortisol can be more precisely specified with the inclusion of measures of ANS activity. Accordingly, we examine relations among salivary cortisol, sAA, and RSA in a population-based longitudinal sample of children at age 4 years in predominantly low-income and rural communities. our objective was to determine the extent to which higher levels of sAA, resting RSA, and RSA change as indicators of ANS activity might be related to lower levels of cortisol. Further, we were interested in the extent to which ANS activity might moderate effects of disadvantage, as indicated by measures of income-to-need and household chaos, on child cortisol levels.

Method

Participants

The Family Life Project (FLP) was designed to study young children and their families in two of the four major geographical areas of the United States with high poverty rates. Specifically, three counties in Eastern North Carolina and three counties in Central Pennsylvania were selected to be indicative of the Black South and Appalachia, respectively. The FLP adopted a developmental epidemiological design in which sampling procedures were employed to recruit a representative sample of 1,292 children whose families resided in one of the six counties at the time of the child's birth. Low-income families in both states and African American families in NC were over-sampled (African American families were not over-sampled in PA because African Americans made up < 5% of the population of the target communities).

At both sites, recruitment occurred seven days per week over the 12-month recruitment period spanning September 15, 2003 through September 14, 2004. Of those families selected to participate in the study, 1292 (82%) families completed a home visit at 2 months of child age, at which point they were formally enrolled in the study. Interested readers are referred to other papers summarizing study recruitment strategies and detailed descriptions of participating families and their communities (Burchinal, Vernon-Feagans, Cox, and the Family Life Project Investigators, 2008; Vernon-Feagans, Cox, and the FLP Investigators, in press).

Of the 1292 families completing a home visit at child age 2 months, N=1204, N=1169, N=1144, N=1123, and N=1066 participated in the age 7, 15, 24, 36, and 48 month visits. Participants in the current analysis included N=986 of 1,066 children seen at the 48 month home visit for data collection who had at least one cortisol value. These participants matched the composition of the original sample in that 51% of children were male, 43% were of African American ethnicity, and 40% resided in Pennsylvania. Of these participants,

286 children were missing ECG data. Reasons for missing cortisol data were primarily due to insufficient volumes of saliva for assays or participant refusal. Reasons for missing ECG data had to do primarily with occasional technical problems with the ECG recording equipment or participant refusal. Examination of missing data indicated few if any systematic associations among variables. Participants with and without ECG data did not differ in terms of income or maternal education. Participants missing cortisol data tended to come from higher income homes (income to need > 1.00), $\chi^2(1, 1{,}236) = 1.641$, $p = .11$.

Procedures

Families participating in the study were visited at their homes for data collection at approximately annual intervals beginning at child age 7 months. At each time point, families were visited in the home by highly trained research assistants, and the child's primary caregiver, in 99% of cases the mother, was administered questionnaires on household and demographic characteristics and also completed questionnaires on child temperament and behavior. At home visits for data collection at 7, 15, and 24 months, saliva samples were collected from children prior to and at two 20 minute intervals following the administration of emotion inducing tasks. At the home visit for data collection at child age 48 months, the primary source of data for the analyses presented here, the procedure involved first collecting physical measurements (height, weight, body temperature, and presence of ear fluid). A saliva sample was then collected followed by the collection of resting (baseline) ECG for the analysis of RSA. Children then completed a battery of 6 executive function tasks, for the first approximately 7 minutes of which ECG data were again collected to examine change in RSA associated with engagement in the cognitive tasks. Following the conclusion of the battery, a second saliva sample was collected, approximately one hour after the first sample (M = 61.1mins, SD = 18.9). Children then completed additional procedures following which a third saliva sample was collected, approximately 30 minutes after the second sample (M = 30.8mins, SD = 21.7). Given that families were seen at different times during the day, time of day of sample collection was included as a covariate in the analysis.

Measures

Poverty—During the home visits at each time point, child ages 7, 15, 24, 36, and 48 months, the primary caregiver answered questions about household demographics and income. Income-to-need ratio was calculated at each time point based upon reported income and reported number of persons in the household.

Household Chaos—Composites of household disorganization and instability developed by Vernon-Feagans, Garrett-Peters, Willoughby, & Mills-Koonce (2011) were used to assess household chaos. Data from 10 indicators collected at 2, 7, 15, 24, 36, and 48 months were shown using principal components analysis to factor into two dimensions composed of five variables each. *Household Instability* included the number of people moving in and out of the household, the total number of people in the household, the number of household moves, the number of changes in the primary caregiver, and the number of changes in the secondary caregiver. *Household Disorganization* included household density, the numbers of hours of TV viewing, the preparation for home visits, the cleanliness of the home, and

neighborhood noise. These 10 indicators were standardized (M = 0, SD = 1) and averaged to create two composite scores.

Child temperament—Selected subscales of the revised version of Rothbart's Infant Behavior Questionnaire (IBQ-R; Gartstein & Rothbart, 2003) were administered to parents during one of the home visits at the infant visit. Parents completed the fear/distress to novelty (16 items), distress to limitations (16 items), approach (12 items), duration of orienting (12 items) and falling reactivity/recovery from distress (13 items) subscales. A 7-point Likert scale ranging from never (1) to always (7) was used to rate the frequency with which their child exhibited the behaviors in the last two weeks.

Intelligence—The receptive verbal ability and block design subscales of the Wechsler Preschool and Primary Scales of Intelligence (WPPSI; Wechsler, 2002) were used to estimate child full scale IQ at age 36 months.

RSA—Mindware Technologies software (Gahanna, Ohio) was used to apply an algorithm to the time series of heart period data. The algorithm uses a moving polynomial to de-trend periodicities in heart period that are slower than RSA. A band-pass filter then extracts the heart rate variability within the frequency band of spontaneous respiration in children, .24 to 1.04 Hz, which is commonly studied to index vagal functioning in infants and young children (see Huffman et al., 1998; Stifter & Corey, 2001; Calkins & Keane, 2004). The software then derives an RSA estimate by calculating the natural log of specified heart period variability and is reported in units of ln(ms)2. Trained coders edited the ECG heart period records for movement artifact where possible, marking the R spike if identifiable on the record. Mean RSA was calculated for each 30 seconds of the baseline and reactivity tasks. RSA change was calculated by subtracting the RSA estimate during the task from the RSA estimate at baseline.

Salivary cortisol—All samples were assayed for salivary cortisol using a highly sensitive enzyme immunoassay US FDA 510k cleared for use as an in vitro diagnostic measure of adrenal function (Salimetrics, State College, PA). The test used 25 μl of saliva (for singlet determinations), had a range of sensitivity from .007 to 1.8 μg/dl, and average intra-and inter-assay coefficients of variation of less than 10%. All samples were assayed in duplicate. The criterion for repeat testing was variation between duplicates greater than 20%, and the average of the duplicates was used in all analyses. The cortisol distributions were subject to log transformation to correct positive skew. We examined child temperature, time since eating, time since sleeping, and use of medications (e.g., acetaminophen) as influences on child cortisol levels and found no relations.

Salivary alpha amylase—Following Granger et al. (2007), samples were assayed for sAA using a commercially available kinetic reaction assay (Salimetrics, State College, PA). Results are computed in U/ml of alpha-amylase using the formula: [absorbance difference per minute X total assay volume (328 ml) X dilution factor (200)]/[millimolar absorptivity of 2-chloro-p-nitrophenol (12.9) X sample volume (.008 ml) X light path (.97)]. Square root transformations were used to reduce positive skew.

Intra- and inter-assays for cortisol (ug/dL) and sAA (U/mL) were, on average, less than 10% and 15% respectively. All samples were assayed in duplicate. The criterion for repeat testing was variation between duplicates greater than 20%, and the average of the duplicates was used in all analyses.

Data analysis—The three cortisol values collected at the 48mos assessment were modeled using SAS PROC MIXED with time of day of sample collection, race, state, sex, age at assessment, maternal education, and child resting cortisol measured at age 7 months as covariates. We examined effects for RSA, RSA change, household instability, household disorganization, and cumulative time in poverty as indicated by the number of time points (7–48mos) in which the primary caregiver reported income-to-need ratio <= 1.00. We examined within subjects effects for each variable (interactions with time) and also examined between subjects interactions of RSA, RSA change, and sAA with household instability and household disorganization. In these models we excluded interactions not contributing to the model. Missing data were addressed using multiple imputation. SAS PROC MI was used to generate 15 data sets yielding efficiency in the estimates for each variable greater than 98%. Regression coefficients from the analysis of each of the data sets were combined using SAS MIANALYZE.

Results

Table 1 presents the means, standard deviations, range, and number of participants with values for each of the variables in the analysis. The average value for change in the untransformed variable in Table 1 is .07 ug/dl, which is substantially greater than the inter-assay coefficient of variation, indicating a meaningful decrease in cortisol in the sample as a whole. The sample is predominantly low income with a mean number of years in poverty of 1.8. Sixty percent of the sample reported income to need below the poverty level at one assessment or more, with 13% reporting poverty at all 5 assessment time points. Number of time points in poverty was moderately correlated with household disorganization, $r = .57$, $p < .0001$, and less so with household instability, $r = .37$, $p < .0001$. Disorganization and instability were moderately correlated, $r = .40$, $p < .0001$.

Results from the mixed model analysis of cortisol change in Table 2 indicated a random intercept and fixed linear and quadratic effects for time of sample collection (baseline, post1, and post2). A between subjects effect for time of day indicated that cortisol levels were lower on average for individuals seen later in the day. A between subjects effect was also observed for cortisol measured at 7 months of age, indicating some rank order stability in child cortisol from infancy through age 4 years. In addition, we also observed a between subjects effect for child IQ measured at age 36 months, in which higher IQ was associated with lower cortisol. Child temperamental reactivity to novelty at age 7 months was marginally positively associated with level of cortisol at age 48 months.

We observed an effect on the linear slope for cumulative time in poverty assessed as the number of data collection time points at which families reported income to need at or below the poverty line. Greater length of time in poverty was associated with a flatter trajectory for cortisol across the approximate 90 minutes of the data collection. Children with a longer

period of time in poverty had lower baseline values of cortisol and higher values at the second posttest. This association is presented in Figure 1 in which children never in poverty are contrasted with children whose families reported income to need below the poverty line at each time point.

We also observed a between subjects effect in which a positive association between cumulative household disorganization and cortisol was moderated by resting RSA. Notably, the positive association between household disorganization and child cortisol was only seen among children with lower resting RSA. For children with higher resting RSA, household disorganization was unrelated to cortisol. This association is presented in Figure 2. No effects were observed for household instability, individually or in interaction with resting RSA. Given moderate correlation between household disorganization and cumulative time in poverty, we also examined the model with only the poverty variable included and observed no change in the coefficient for cumulative poverty, indicating that its effect is distinct from that associated with household disorganization. Cumulative poverty was not moderated by resting RSA.

A between subjects effect was also observed for RSA change. In this instance, RSA decrease from baseline (vagal suppression) was associated with an overall higher as opposed to lower level of cortisol across the 90 minutes of the data collection procedure, on average. This finding indicates that individuals who responded to the data collection by decreasing RSA, an indicator of effort and increased attention associated with regulation of state through the PNS, had an overall higher level of HPA activity as indicated by cortisol. RSA change did not interact with either household disorganization or household instability. As well, no between or within subjects effects of sAA on cortisol were observed.

Given that our data are longitudinal and cumulative, we also examined potential effects of the timing of income to need at the poverty level and household disorganization on cortisol. We also examined whether change in poverty status or change in household disorganization was associated with variation in child cortisol at age 48 months. For both variables, we did not find any association with timing, comparing early (cumulative poverty and disorganization prior to 24 months) versus late (post 24 months). Change in both was also unrelated to child cortisol levels.

Finally, we also examined whether RSA and RSA change as well as sAA might also be affected by poverty and household chaos in ways similar to cortisol. In these analyses, we predicted RSA, RSA change, and sAA in separate equations from child characteristics and the cumulative measures of income to need and household disorganization and household instability. Findings indicated no associations of the indicators with the outcome variables. Effects were observed only for child race, in which African American children had lower resting RSA, and for state, in which children in North Carolina had lower resting RSA and sAA.

Discussion

This paper examined the association of early disadvantage with children's cortisol levels at age 48 months in a prospective longitudinal sample beginning at birth. Overall, findings are consistent with a growing literature suggesting that cumulative experience of poverty and disorganization in the home environment in early childhood is associated with elevations in measures of stress physiology, such as cortisol. These effects were observed over and above child characteristics, including intelligence and temperament as well as resting or basal child cortisol level at age 7 months. Key contributions of this analysis are the demonstration of distinct effects for income to need and household chaos on cortisol and the demonstration of effects for measures of ANS activity on child cortisol. Findings indicated that the cumulative experience of disadvantage as assessed by the number of years in which the family reported income to need at or below the poverty line was associated with a flatter trajectory for cortisol over an approximately 90 minute period in response to the presumed mild stress of participating in the data collection procedure. In contrast, children in more chaotic homes tended to have higher levels of cortisol overall, however, this was the case only if children also had lower levels of resting heart rate variability as indexed by RSA. Notably, we did not observe any effect for the timing of poverty exposure or household disorganization, however, both are highly stable in the sample.

Poverty and psychosocial disadvantage in early childhood

This study adds to an emerging literature examining relations between early disadvantage such as that occurring in the context of poverty and stress physiologically in children. Prior studies have considered poverty in terms of income to need and global measures of SES or through risk indices that examine the cumulative effect of several different aspects of the environment. Few prior studies, however, have examined distinct characteristics of socioeconomic disadvantage to determine relevant aspects of children's experience that may be proximal influences on cortisol levels. For example, Chen and colleagues (Chen, Miller & Cohen, 2010) found that a questionnaire measure of household chaos accounted for some of the effect of poverty, measured by family savings, on increases in child diurnal cortisol over a two year period in a small sample of 9–18 year olds. In contrast, in our sample of children followed over the first four years, we found that poverty as assessed by income to need and a measure of household chaos derived from an observational composite had distinct effects on child cortisol at age 48 months. This suggests that while there is an appropriate focus on effects of poverty on stress physiology in children, effects generalize beyond this context.

The generalizability of effects seen in this and other analyses points to questions about proximal influences through which disadvantage affects child stress physiology. To this end, further analyses with this and other data sets can help to address questions about the extent of malleability and potential for recovery and change in child stress response systems. Notably, the inclusion of child resting cortisol at age 7 months in this analysis helps to address the issue of endogeneity and the extent to which characteristics of the child might account for some of the association between disadvantage and cortisol levels. The finding of moderate stability in cortisol between 7 and 48 months helps to strengthen inference

concerning the influence of the environment on child cortisol levels at 48 months. As well, the inclusion of measures of temperament and intelligence help to rule out concerns about endogenous characteristics of the child as alternative explanations for the findings.

The complexity of stress physiology

The inclusion of measures of ANS activity in the assessment of the effects of disadvantage on cortisol levels in children is important given limited prior examinations of multiple aspects of stress physiology in such samples. Previous studies of the effects of poverty on child stress physiology have either examined cortisol individually (Chen et al., 2010; Fernald & Gunnar, 2010; Lupien et al., 2001) or have combined multiple measures of stress physiology in a cumulative index (Evans, 2003). The finding of interaction between measures of ANS activity and environmental characteristics in the prediction of child outcomes, however, is not without precedent. As noted in the introduction, higher resting RSA and RSA suppression have been shown to moderate the effects of marital conflict on attention and behavior problems in children (El-Sheikh et al., 2008). Similarly, lower resting RSA has been associated with increased externalizing and internalizing behavior in homes characterized by parental problem drinking (El-Sheikh, 2005).

Our finding for resting RSA as a moderating factor in the study of environmental risk is generally consistent with the prior literature on RSA. In contrast, our finding that increase as opposed to decrease in RSA from baseline (RSA augmentation) in response to the moderate demand of the cognitive task was associated with lower cortisol is somewhat less consistent with prior studies of RSA change. Prior studies have tended to indicate that decrease rather than increase in RSA is an adaptive in response to challenge (El-Sheikh & Witson, 2006; Graziano, Keane, & Calkins, 2007). RSA increase in response to moderate challenge, however, can also be seen as an adaptive response, particularly in social interaction of the type occurring in response to an experimenter in a data collection session. RSA increase, indicating increased influence of the vagus on the heart is thought to be indicative of increased social interaction ability. In theory, vagal influence on heart rate variability, that associated with the ‘smart’ or mammalian vagus originating in the nucleus ambiguus of the medulla, modulates cardiac output to meet metabolic demand during social interaction without incurring high metabolic cost associated with sympathetic or HPA activation (Porges, 1998). Through relations of the smart vagus with cranial nerves associated with breathing, facial expression, and vocalization, vagal regulation allows for the coordination of activities crucial to social interaction. Accordingly, higher RSA and increases in RSA in infants and toddlers have been associated with increased sociability and emotion regulation (Blair & Peters, 2003; Moore, 2009, 2010). Our finding for a relation between RSA increase and lower cortisol in children is likely indicative of a higher level of sociability and engagement.

Findings for RSA and RSA change in this analysis are in contrast to null findings for sAA. It may be that as children mature, regulation of state through RSA becomes a more prominent influence on physiology and behavior. Although we do not have complete RSA data at earlier time points in this sample, it may be future analyses examining relations between earlier and later measures of stress reactivity in infancy and toddlerhood can address

questions about developmental relations among cortisol, sAA, and RSA. As well, it may be that sAA, as an indicator of ANS activity is relatively independent of cortisol as an indicator of HPA activity and may interact with cortisol in the prediction of child outcomes. As noted in the introduction, previous analyses, including our own have shown that sAA interacts with cortisol in the prediction of executive function and behavior problems in children (Berry et al., 2012; El-Sheikh et al., 2008).

A related point concerns our finding of an absence of relations of measures of psychosocial disadvantage with RSA and sAA. It may be that other aspects of experience affect these systems in ways similar to that seen for the effect of cumulative time in poverty and cumulative household disorganization on cortisol. Alternatively, it may be that ANS activity as assessed by RSA and sAA is more trait-like and less influenced by experience, at least by age 4 years. Such an interpretation would be consistent with the idea that measures of RSA and sAA can effectively moderate effects of environmental disadvantage on child cortisol.

Strengths, limitations, and implications

Overall, findings indicating the unique effects of measures of disadvantage on child cortisol are bolstered by the size of the sample and the longitudinal nature of the data. By analyzing the data longitudinally we were able to estimate the extent to which accumulated experience of socioeconomic adversity is associated with variation in child cortisol at age 48 months, a time of rapid growth and development. As such, findings to some extent are consistent with the idea that accumulated experience over time is understood to alter set points for physiological stress response systems such as the HPA axis. It is important to recognize that estimates of the relation of disadvantage to child cortisol may be underestimates to some extent, given that the sample is predominantly low income. Further work with samples that span the socioeconomic spectrum or with convenience samples using an extreme groups approach to contrast children from high and low SES homes might indicate larger effects of disadvantage on stress physiology in young children.

Issues of effect size estimation and generalizability are particularly relevant to the interaction of RSA and household disorganization. This significant interaction was only one of several tested and as such may be sample specific. The analysis is further limited by a lack of specificity in the nature of the stressor and cortisol response in the sample. Saliva samples were collected over the course of a data collection session, a presumed stressor in which the child interacts over an extended period of time with strangers, albeit in the child's own home. Presumably this is somewhat stressful for children but of course the extent to which this is the case is indeterminate and as we show, partly attributable to child characteristics. In this, the analysis is similar to other studies that make use of naturalistic contexts, including data collection (e.g., Davis, Bruce, & Gunnar, 2002) but also child care (e.g., Watamura, Donzella, Alwin, & Gunnar, 2003) or experience in school (Bruce, Davis, & Gunnar, 2002) to assess change in children's cortisol levels.

Although limited in a number of ways, the current analysis adds to the growing literature demonstrating that one way in which early adversity influences child outcomes is by getting under the skin to alter physiological functioning in ways that can lead to longer term learning and health related problems. It is to be hoped that through repeated demonstrations

of the finding that poverty specifically and adversity generally affects the whole child, including the internal milieu as well as behavior and psychological function, that comprehensive action to bring about social change can be sustained. In doing so, however, it is essential to view results within a normative framework of environmental influences on child stress physiology and to avoid pathologizing of behavior in children facing early disadvantage. Data from this study indicate conditions that are nonoptimal but within the normal range of what children typically face. In theory, the expectation is that these environmental conditions effectively tune or shape stress response physiology to support behaviors and modes of thinking and feeling that are appropriate for the context in which development is occurring. Blair and Raver's (2012) experiential canalization model and Del Guidice, Ellis, and Shirtcliff's (2011) adaptive calibration model are two theories that specifically address the idea that environment and physiology combine to produce biological and psychological development to maximize individual efficacy within a given context. A pressing issue for both of these theories, however, is the extent of plasticity and malleability of physiology and the potential for alteration by environmental change. To this end, exemplary randomized, controlled trials of innovative programs for children facing early disadvantage provide promising evidence that improvements to family circumstances and to the quality of caregiving can produce positive change in stress response physiology and in outcomes with which it is associated (Brotman, Gouley, Huang, Kamboukos, Fratto, & Pine, 2007; Fisher, Gunnar, Dozier, Bruce, & Pears, 2006). Further research of the type seen in these exemplary experimental studies can help to more definitively establish relations between environmental change and child stress physiology and inform efforts to comprehensively support the development of children at risk.

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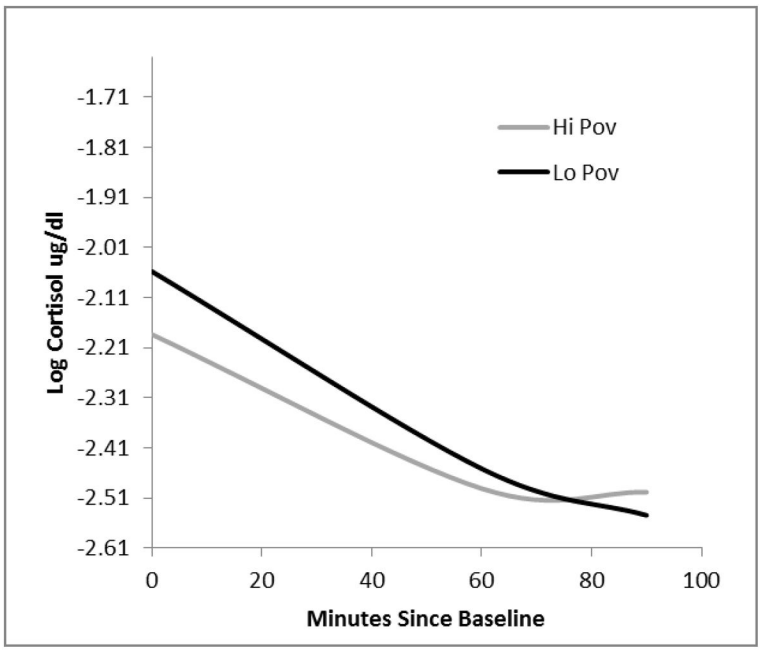

Figure 1.

Cortisol change as a function of cumulative experience of poverty. Dark line = income to need at or below poverty level at all 5 time points; Light line = income to need above the poverty level at all 5 time points.

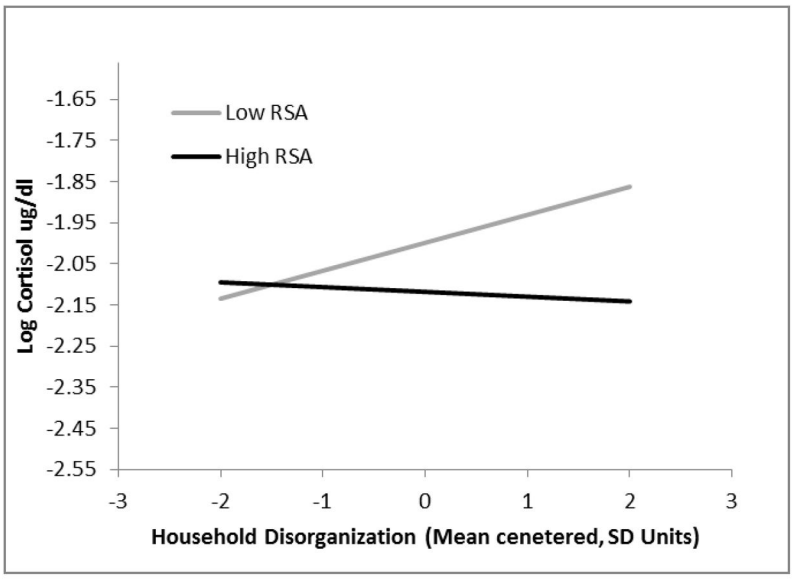

Figure 2.

Average cortisol as a function of household chaos (disorganization ± 1 SD) and resting heart rate variability (± 1 SD).

Table 1

Descriptive statistics for variables in the analysis.

	N	Min	Max	Mean	SD
RSA baseline	734	2.79	8.98	5.87	1.18
RSA during task	706	1.77	9.31	6.19	1.24
RSA difference	700	−2.72	2.80	−.32	.69
Cortisol baseline	962	.01	3.61	.17	.20
Cortisol post1	970	.01	2.50	.12	.20
Cortisol post2	970	.01	1.72	.10	.18
Salivary alpha amylase	830	.99	19.51	7.22	2.86
Household disorganization	984	−1.50	2.37	.012	.66
Household instability	984	−1.12	4.58	.004	.74
Years in poverty	919	0	5	1.8	1.8
Time of day	985	7:52	20:10	13:24	2:53
Child age	970	46	57	48	1.5
Maternal education years	984	5	22	15.04	2.63
Cortisol baseline 7 months	901	.02	4.66	.23	.39
Distress to novelty 7 months	924	1.00	6.50	2.81	1.00
Child IQ 36 months	921	45	142	93.85	16.41

Table 2

Mixed model predicting change in cortisol.

Parameter	Estimate	Std Error	t	Pr > |t|
Time	−0.5433	0.0447	−12.16	<.0001
Time X time	0.1501	0.0214	7.1	<.0001
Time of day	−0.0796	0.0054	−14.69	<.0001
State (PA = 1, NC = 0)	0.0050	0.0515	0.1	.9233
Race (Black = 1, White = 0)	0.0209	0.0509	0.41	.6828
Household disorganization	0.0421	0.0373	1.13	.2649
Household instability	−0.0244	0.0247	−0.99	.3271
RSA baseline	−0.0500	0.0144	−3.46	.0011
RSA change	0.0787	0.0349	2.26	.0333
Salivary alpha amylase	0.0016	0.0062	0.26	.7931
Cortisol at age 7 months	0.0902	0.0260	3.52	.0011
Maternal education	−0.0024	0.0076	−0.32	.7502
Child age	0.0022	0.0122	0.18	.8582
Sex (male vs female)	0.0028	0.0292	0.1	.9242
Child IQ 36 months	−0.0028	0.0011	−2.52	.0135
Distress to novelty 7 months	0.0326	0.0184	1.77	.0818
RSA baseline X disorganization	−0.0498	0.0233	−2.14	.0404
Time in poverty	−0.0251	0.0142	−1.77	.0821
Time in poverty X time	0.0172	0.0068	2.53	.0124