Child abuse, disruptive behavior disorders, depression, and salivary cortisol levels among institutionalized and community-residing boys in Mongolia

Brandon A. Kohrt1* MD PhD, Daniel J. Hruschka1† PhD MPH, Holbrook E. Kohrt2‡ MD PhD, Victor G. Carrion2 MD, Irwin D. Waldman3 PhD & Carol M. Worthman1 PhD

1 Department of Anthropology, Emory University, Atlanta, GA, USA
2 Department of Psychiatry and Behavioral Sciences, Child Development, Stanford University School of Medicine, Stanford, CA, USA
3 Department of Psychology, Emory University, Atlanta, GA, USA

Abstract

Introduction: Hypothalamic-pituitary-adrenal (HPA) axis activity is related to childhood disruptive behavior disorders and to exposure to abuse and neglect. This study explores the relationship of diurnal salivary cortisol levels with oppositional defiant disorder (ODD) and caregiver attitudes toward physical punishment among boys in Mongolia.

Methods: Salivary cortisol was collected in the home or institution 4 times daily for 4 days from 46 boys, aged 4–10 years, in Ulaanbaatar, Mongolia. Caregivers rated child disruptive behavior symptoms, attitudes toward physical punishment, and community violence exposures. Mixed effects models were used to estimate the association of psychopathology and caregiver attitudes with salivary cortisol levels.

Results: Boys meeting criteria for ODD displayed consistently lower diurnal salivary cortisol levels compared to boys without ODD diagnoses. Controlling for ODD diagnosis, boys with depression showed higher cortisol levels throughout the day. No other diagnosis was associated with cortisol levels. Psychiatric diagnosis accounted for 17% of between individual variations in cortisol levels unexplained by the covariates. In a separate model, caregivers’ beliefs regarding physical punishment accounted for 11% of between individual differences: boys with caregivers who stated physical punishment was necessary for discipline displayed hypocortisolism. Institutionalization did not associate with cortisol levels.

Discussion: Salivary cortisol data from a non-Western naturalistic setting support an association of reduced basal HPA activity with disruptive behavior disorders and caregiver attitudes toward discipline. These findings suggest HPA functioning may be a reflection of or mediate disruptive behavior disorders in children across ethnic and cultural settings.

Introduction

Childhood disruptive behavior disorders (DBD), including oppositional defiant disorder (ODD) and conduct disorder (CD), are risk factors for depression, anxiety, substance abuse disorders, antisocial personality disorder, and suicidality in adolescence and young adulthood (Waldman et al., 2006; Copeland et al., 2009; Rowe et al., 2010; Keren and Tyano, 2012). Aggression and other features of DBD co-occur with alterations in diurnal levels of cortisol, the product of the hypothalamic-pituitary-adrenal (HPA) axis. Hypocortisolism (low cortisol levels) may reflect decreased attention, learning, and memory, such as heightened false recognition memory on neuropsychological testing, which could impair
response to social cues, such as parental discipline and other socializing stimuli (McBurnett et al., 1996; King et al., 1998; Cicchetti et al., 2010b).

Boys with DBD display hypocortisolism similar to adults with antisocial personality disorder (Pajer et al., 2001; Kariyawasam et al., 2002; Popma et al., 2006; Susman et al., 2007). Aggression-related symptoms more strongly associate with hypocortisolism than non-aggression symptoms (Oosterlaan et al., 2005). Hypocortisolism predicts future aggression and externalizing disorders in longitudinal studies (Shoal et al., 2003; Shirtcliff et al., 2005). Other studies failed to associate hypocortisolism and DBD (Jansen et al., 1999; van Goozen et al., 2000; Scarpa et al., 2000; Klimes-Dougan et al., 2001; Snoek et al., 2002; Sondeijker et al., 2007).

One possible etiology associated with DBD and aberrant cortisol activity is exposure to trauma, particularly child abuse (Tennes and Kreye, 1985; Carrion et al., 2001, 2007; Gunnar and Vazquez, 2001; Yehuda et al., 2001; Gunnar and Donzella, 2002; Teicher et al., 2003; Watts-English et al., 2006; Shea et al., 2007; McGowan et al., 2009; McCrory et al., 2010). Hypocortisolism among maltreated children associates with higher rates of aggressive and disruptive behaviors (Ouellet-Morin et al., 2011; Alink et al., 2012). However, other studies find reversed associations between cortisol levels and stress exposure (Cooley-Quille et al., 2001; Schreier and Evans, 2003). Aberrant HPA functioning also has been identified in children with depression and other internalizing disorders, with some studies suggesting hypercortisolism (higher basal diurnal cortisol levels) and a flatter slopes (less decrease) across the day from morning to evening (Kagan, 1994; Granger et al., 1996; Gispen-de Wied et al., 2000; Van den Bergh and Van Calster, 2009; Cicchetti et al., 2010a; Harkness et al., 2011; Tyrka et al., 2012), which is supported by some findings in adults (Plotsky et al., 1998; Gold and Chrousos, 2002).

Institutionalization in former communist countries, most notably Romania, has been associated with child psychiatric symptoms and disorders, adverse attachment styles, and negative emotional reactivity (Fries et al., 2008; Rutter et al., 2010; Bos et al., 2011). Among institution-reared children in Bucharest, attention deficit hyperactivity disorder (ADHD), DBD, depression, and anxiety are more prevalent than among community comparison children; and, aberrant electroencephalogram findings are observed in institution-reared children suggesting delayed cortical maturation (McLaughlin et al., 2010). In one study, 22% of Romanian orphans living in Canada 6 years after adoption exhibited cortisol levels averaged over the day that exceeded the mean plus standard deviations compared to early-adopted children and Canadian-born children (Gunnar et al., 2001). In a study of international adoptees who had experienced pre-adoptive deprivation, the level of pre-adoptive deprivation associated with higher morning cortisol levels and a larger diurnal cortisol decrease (Kertes et al., 2008). Outcomes associated with institutionalization are poorer for boys and show less improvement after deinstitutionalization compared to girls (Zeanah et al., 2009).

One questions facing cross-cultural child psychiatry is whether disorders have universal biological mechanisms or markers (Canino and Alegria, 2008). The association of hypocortisolism with disruptive behavior has been observed in two studies in East Asia and one in South Asia (Kaneko et al., 1993; Hruschka et al., 2005; Yang et al., 2007). In Japan, greater than half of children with ADHD display atypical diurnal rhythms (Kaneko et al., 1993). In Nepal, aggression explains 11% of cortisol variance between boys, with hypocortisolism predicting aggression (Hruschka et al., 2005).

The purpose of this current study is to further assess the evidence base for potential diurnal cortisol level variation in association with DBD and child abuse in a non-Western cultural context.

Methods

Setting

Mongolia is a historically nomadic pastoralist society and a formerly communist nation located between China and Russia. Greater than 90% of the population belongs to the Khalkh ethnic group. In a United Nations Children’s Fund study of child maltreatment in 24 countries (Lansford and Deater-Deckard, 2012), 82% of caregivers worldwide reported witnessing violence against a child in the household in the past month. However, in Mongolia, 100% of the respondents reported witnessing violence against a child in the household in the past month. Psychiatric services are limited in Mongolia; traditional Mongolian medicine, including Buddhist medical traditions, Eastern European homeopathy, and shamanism, is widely used for mental health problems (Hruschka and Kohrt, 2004; Kohrt et al., 2004a).

Participants and sampling

The sample included 46 boys aged 4.3 to 10.3 years and comprised four groups: institutionalized children
(10 from a government nursery for abandoned children and six from an Australian managed Buddhist home for abandoned children), urban poor (11 children from a poor community in Ulaanbaatar), urban middle class (10 boys from middle-class households in Ulaanbaatar), and semi-rural (nine boys from a herding community 50 kilometers from Ulaanbaatar). Sixteen boys were institutionalized, and 30 were not. Children in institutional and low socioeconomic status environments were over-sampled because of the greater percentage of behavioral disorders in these populations in Western nations (Burke et al., 2002). Only boys were recruited because of sex differences in cortisol levels (Kirschbaum et al., 1992) and because the effects of institutionalization appear to be more detrimental and long-lasting compared to girls (Zeanah et al., 2009; Bos et al., 2011).

The Institutional Review Board of Emory School of Medicine approved the study. Informed consent was obtained from parents or legal institutional guardians. The study was conducted in cooperation with the Agency for the Protection and Prevention for Children from Abuse and Neglect, Ulaanbaatar.

**Measures**

Psychopathology was assessed with the Emory Combined Rating Scale (ECRS), which elicits questionnaire-based diagnoses for ADHD, CD, major depressive episode, generalized anxiety disorder (GAD), social anxiety disorder (SAD), and ODD (Waldman et al., 1998; Rhee and Waldman, 2004). The measure uses each criterion from the DSM-IV for these disorders. Caregivers rate children on a 5-point scale from 0–4 (never to always) on each criterion. A child rated 3 or 4 on any criterion was considered to have that symptom. Diagnoses were then made for any child exceeding the threshold of symptoms for that disorder. We used cutoffs considered “severe” (Waldman et al., 1998) to achieve higher specificity and decrease the probability of including false positive cases. For the present analysis, an ordinal score of severity determined by number of positive symptoms reported was employed. Further construct validation was assessed with reliability (Table 1) and inter-scale correlations. In two-way correlations, all externalizing scales correlated (Spearman correlations, *P* < 0.01) except the conduct disorder scale. Depression and generalized anxiety scales also correlated, (Spearman correlation = 0.545, *P* < 0.001). Because psychiatrists in Mongolia do not routinely perform child psychiatric diagnoses, we were unable to assess the reliability, sensitivity, or specificity of the measure against clinical diagnoses. The measures show strong external validity through their association with ecological risk factors in Mongolia (Kohrt et al., 2004b).

Caregivers were asked whether the child was exposed to community violence. Responses were coded categorically with all answers involving witnessing physical violence recorded as “1” (e.g., physical assault, mugging involving a weapon). All other responses were coded “0” (e.g., no violence, yelling by intoxicated men). Caregivers were asked if they felt physical violence was necessary to discipline boys. Caregivers who responded that it was never necessary were coded “0.” Caregivers who responded “sometimes” or “always” were coded as “1.” To clarify the coding, each caregiver’s definition of “physical violence” was recorded. For all caregivers, “spanking without an instrument” was not coded as physical violence. Responses coded as physical violence included kicking, whipping, beating, or spanking with a belt or stick.

**Salivary cortisol collection and analysis**

Saliva collection is minimally invasive, and levels of cortisol in saliva consistently correlate with serum levels (Kirschbaum and Hellhammer, 1994). Because changes in diurnal cortisol profiles have been associated with affective load and psychiatric risk in children (Dettling et al., 2000), collections were made four times per day: morning (within 90 minutes of waking), early afternoon (between 2 and 6 hours post-waking), late afternoon (between 6 and 10 hours post-waking), and evening (greater than 10 hours post-waking). Ideally, each participant contributed four morning, four early afternoon, four late afternoon, and four evening samples. Collections occurred in naturalistic settings, the child’s home, or institution. At each sampling period, recent diet,

<table>
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<tr>
<th>Scale</th>
<th>Number of items</th>
<th>Cronbach’s α</th>
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<tr>
<td>Inattention</td>
<td>10</td>
<td>0.85</td>
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<tr>
<td>Impulsivity</td>
<td>3</td>
<td>0.73</td>
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<tr>
<td>Hyperactivity</td>
<td>7</td>
<td>0.84</td>
</tr>
<tr>
<td>Oppositional defiant disorder</td>
<td>8</td>
<td>0.84</td>
</tr>
<tr>
<td>Conduct disorder</td>
<td>15</td>
<td>0.65</td>
</tr>
<tr>
<td>Generalized anxiety disorder</td>
<td>18</td>
<td>0.78</td>
</tr>
<tr>
<td>Major depressive disorder</td>
<td>20</td>
<td>0.82</td>
</tr>
<tr>
<td>All behavior disorder items</td>
<td>43</td>
<td>0.91</td>
</tr>
<tr>
<td>All internalizing disorder items</td>
<td>38</td>
<td>0.88</td>
</tr>
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activity, sleep behavior, current health, and tooth brushing were recorded. Attempts were made not to collect samples within 1 hour of food or drink consumption. All samples were collected by trained researchers to assure the accuracy of sample delivery and the correct recording of time and other contextual variables. After researchers’ arrival, children rinsed their mouths with clean water, waited 5 minutes, masticated a piece of Parafilm (Pechiney Plastic Packaging, Chicago, IL, USA) to generate saliva, and spit through a plastic funnel into sodium azide-treated test tubes which were then capped and refrigerated at 5°C.

Within 3 weeks of collection, samples were packed with freezer bags and shipped to the United States where they were frozen at −27°C until assayed at an Emory laboratory using solid phase Coat-A-Count Cortisol (Diagnostic Products Corporation, Los Angeles, CA) radioimmunoassays. The highly cortisol-specific antibody cross-reacts 1.4% with corticosterone, 1.5% with 11-deoxycorticosterone, and <1.0% with other related hormones. Procedures were conducted according to kit manufacturer specifications except for dilution of standards following the common modification for salivary use of the Coat-A-Count kit (Tunn et al., 1992; Raff et al., 1998) because concentrations of Coat-A-Count standards are intended for serum, plasma, or urine. Assay sensitivity is 0.06 mg/dL. Coefficients of variation (CV) for low, medium, and high commercial controls are 10.7%, 6.2%, and 7.7% for intra-assay and 11.3%, 8.2%, and 8.0% for inter-assay. The intra-assay and inter-assay CV for the saliva pool is 3.14% and 5.54%, respectively.

Statistical analysis

Mixed effects models were used (i) to describe children’s diurnal cortisol rhythms and (ii) to provide tests for the association of salivary cortisol levels and psychopathology, adjusting for child-level characteristics (age), observation-level variables (time since waking, day of observation, prior food intake), and interobservation covariance (Singer, 1998; Snijders and Bosker, 1999; Verbeke and Molenberghs, 2000). Mixed models offer several advantages in the analysis of repeated measures data, allowing the investigator to model a range of interobservation covariance structures and accommodating data, such as that considered in this analysis, in which observations are missing at random.

Although readings were collected over 4 days, the first day was excluded from the analysis due to the large number of missing morning values. This led to a maximum of 12 readings per child. Salivary cortisol values were right skewed at each of the four daily measurement periods so raw values were log transformed to satisfy the normality assumptions of the model (Smyth et al., 1997; McBurnett et al., 2000). Observations with high within-assay standard deviations (standard of log values > 0.25) were excluded, as were values below the assay’s sensitivity (<0.005 μg/dL). The general model in this paper included (i) fixed effects for “time since waking,” “food intake within 1 hour before measurement” (dichotomous), “waking within 30 minutes before measurement in the afternoon” (dichotomous), “child’s age” (four-level categorical), diagnoses of ODD, depression, ADHD, GAD, SAD, and conduct disorder, exposure to community violence, caregiver’s belief regarding physical violence, (ii) a random effect for child, and (iii) a random effect for child-day. The models followed this general format:

\[
\text{LNCORT}_{ijk} = \beta_0 + (\Sigma \beta_m \times \text{Fixed Effect}_m) + b_{io} + b_{ij} + \varepsilon_{ijk}
\]

Where LNCORT_{ijk} is the natural log of cortisol for the \(i^{th}\) person \((i = 1 \text{ to } 46)\) at the \(k^{th}\) observation \((k = 1 \text{ to } 4)\) on the \(j^{th}\) day \((j = 1 \text{ to } 3)\), \(\beta_0\) is the estimate of the population mean in the morning of the first day, \(\beta_m\) is the parameter estimate for the \(k^{th}\) fixed effect, \(b_{io}\) is an estimate of the child’s deviation from the population mean, and \(b_{ij}\) is an estimate of a particular day’s deviation for a given child.

Models were fit using SAS Proc Mixed (SAS Institute Inc, 2000). Covariance parameters were estimated using the default restricted maximum likelihood method (REML), while fixed effects were estimated using maximum likelihood (ML). The data were not completely balanced (e.g., there were missing values), so when testing hypotheses about fixed effects, the correct degrees of freedom were estimated using Satterthwaite’s approximation. Inferences about random components were made using the procedures outlined in Verbeke and Molenberghs (2000). The proportion of variance modeled by fixed effects was estimated with the method by Snijders and Bosker (1999), (c.f., Hruschka et al., 2005).

Initially, a baseline model was fit including the random effects for child and child-day and fixed effects for child’s age, recent food intake, time since morning waking, and recent afternoon waking. Diagnoses were added to the baseline model and retained when \(P < 0.05\). In a separate model, measures of exposure to violence were added to the baseline model and retained when \(P < 0.05\).
Results

Cortisol by time of day, individual, and group

Demographics are presented in Table 2. Mean values for cortisol were highest in the morning and lowest during the evening collection (Table 3). A base time model indicated that time of day accounted for a substantial portion of total variance (28%) that a significant component of the remaining variance (20%) could be attributed to between-child differences and that there was statistically significant correlations of cortisol values within child-days. Adding a random variable for residential setting did not improve model fit, as judged by corrected Akaike information criterion and log-likelihood ratio test. These results indicated correlation of cortisol levels within individuals, and within person-days, but not within groups, supporting the use of a three-level mixed model (with child, child-day, and measurement levels).

Age accounted for 9% of between-individual variation and was included in the model. Cortisol values were highest in children less than 5 years of age and exhibited a downward trend with increasing age. Eating within 1 hour of measurement and awakening from an afternoon nap within the last 30 minutes were not significantly associated with momentary cortisol values (at \( P < 0.05 \) level). Group differences between institutionalized and noninstitutionalized boys did not account for a statistically significant amount of variation.

Cortisol levels by psychopathology

There was a significant negative association between ODD and cortisol (\( \beta = -0.377 \), standard error [SE] = 0.125, \( F = 9.04, P = 0.004 \)), while depression showed a significant positive effect (\( \beta = 0.433, \text{SE} = 0.165, F = 6.93, P = 0.01 \)), and there was no significant interaction (at 0.05 level) between these and any other psychiatric diagnosis, nor with child’s age or time of day (Table 4). The negative association of ODD and positive association of depression with cortisol levels consistently emerged when examined at each individual day (days 2–4). Controlling for depression increased the effect of ODD (from \( \beta = -0.239, \text{SE} = 0.122, \text{to } \beta = -0.377, \text{SE} = 0.125 \)). Conversely, controlling for ODD doubled the effect of depression (from \( \beta = 0.229, \text{SE} = 0.163, \text{to } \beta = 0.433, \text{SE} = 0.165 \)). Figure 1 illustrates the mean log value and standard error for cortisol levels based on psychopathology and time of day. Regarding comorbidity for ODD and depression, six boys displayed ODD without depression, two qualified for depression without ODD, and four qualified for both depression and ODD.

Examining the estimates of between-individual variance, diagnoses of ODD and depression account for 17% of the between-child variation in cortisol levels not explained by time of day, day of measurement, child’s age, or premeasurement food consumption.

Cortisol levels by exposure to violence

Nineteen caregivers (41%) reported that physical violence was necessary for the proper discipline of a boy. Sixteen (35%) of caregivers reported that the children were exposed to community violence. Caregiver reports of violence in the community were not associated with cortisol levels. Children whose caregivers

| Table 2. Age, diagnoses, and number of salivary cortisol collections of participants (n = 46) |
|------------------------------------------|----------------|----------------|
| Age                                      | Number (%) of participants |
| <5 years                                  | 10 (22%)          |
| 5 to <6 years                             | 12 (26%)          |
| 6 to <7.5 years                           | 13 (28%)          |
| ≥7.5 years                                | 11 (24%)          |
| Diagnoses                                 |                   |
| Attention deficit hyperactivity disorder  | 11 (24%)          |
| Oppositional defiant disorder             | 10 (22%)          |
| Conduct disorder                          | 3 (7%)            |
| Generalized anxiety disorder              | 14 (30%)          |
| Major depressive disorder                 | 6 (13%)           |
| Number of salivary cortisol collections   |                   |
| 8 collections                             | 4 (9%)            |
| 9 collections                             | 1 (2%)            |
| 10 collections                            | 5 (11%)           |
| 11 collections                            | 12 (26%)          |
| 12 collections                            | 24 (52%)          |

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<th>Table 3. Distribution of observations and mean cortisol levels</th>
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<tr>
<td>Time of observation</td>
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<tr>
<td>Morning (&lt;1.75 hours post-waking)</td>
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<tr>
<td>Early afternoon (1.75–5.5 hours)</td>
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<tr>
<td>Late afternoon (5.5–10 hours)</td>
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<tr>
<td>Evening (&gt;10 hours)</td>
</tr>
<tr>
<td>Residence</td>
</tr>
<tr>
<td>Institution</td>
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<tr>
<td>Family</td>
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<tr>
<td>Afternoon waking within 30 minutes</td>
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<tr>
<td>Yes</td>
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<tr>
<td>No</td>
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<tr>
<td>Eating within 1 hour</td>
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<td>Yes</td>
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<td>No</td>
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deemed physical violence as necessary for child discipline had significantly lower levels of cortisol (β = −0.2727, SE = 0.1055, F = 6.68, P = 0.013). This variable was highly correlated with diagnosis of ODD (phi = 0.651, P < 0.001).

Examining the estimates of between-individual variance, caregiver attitudes towards physical violence accounted for 11% of the between-child variation in cortisol levels not explained by time of day, child’s age, or premeasurement food consumption.
Collinearity of ODD and caregivers’ endorsement of physical punishment

All caregivers of boys with ODD accepted physical violence as necessary for discipline of the child. Only 22% of other caregivers accepted physical violence as necessary for discipline of the child. Caregivers for the two children diagnosed with depression but without ODD did not endorse physical violence as necessary for discipline of the child. Due to this high degree of collinearity, we did not include psychopathology and parental attitudes toward physical violence in the same model.

Discussion

This study supports previous findings of diurnal hypocortisolism related to DBD, specifically ODD, and hypercortisolism related to depression, thus demonstrating dysregulation of the HPA axis associated with internalizing and externalizing behavior in a non-Western cultural setting among a central Asian ethnic population. There were no group differences based on institutionalization and residence (e.g., orphanage versus poor urban area versus rural area). ODD and depression together model a significant portion (17%) of between-individual variation in cortisol levels not explained by time of day, day of measurement, age of child, and premeasurement food consumption.

The relationship between one diagnosis and an external variable (in this case ODD and cortisol level) may be influenced by comorbidity (in this case depression). Controlling for depression increased the effect of ODD, with ODD associating with basal diurnal hypocortisolism. Conversely, controlling for ODD doubled the effect of depression, with depression associating with basal diurnal hypercortisolism. Such findings concur with other reports suggesting that comorbid conditions may contribute to cortisol profiles and confound analyses that do not separate children with comorbid diagnoses from children with a single diagnosis (McBurnett et al., 1991; Herbert et al., 1996; van Goozen et al., 2000). This is an important issue for both study designs and conceptual models in biological psychiatry. Depression and ODD are often comorbid, and ODD in childhood predicts depression in adolescence and adulthood (Copeland et al., 2009). Different pathways may be at play between ODD, depression, and comorbid conditions, with the latter potentially better understood as mood dysregulation or negative emotionality in which inability to control negative moods becomes misdiagnosed as ODD or other DBD. For example, in a study of 2,000 children and adolescents, no unique genetic influences on depressive disorder/conduct disorder comorbidity after accounting for negative emotionality; and there are common environmental and non-shared environmental influences for the comorbid condition (Singh and Waldman, 2010; Tackett et al., 2011).

Notably, ODD showed the strongest association with aberrant cortisol levels. Whether this is a characteristic of the disorder itself or of the measures employed, the finding suggests cross-cultural commonalities in DBD. However, we report null findings with regard to GAD, ADHD, and CD. Null findings for CD may result from only identifying three CD cases. It is also important to note that ODD and CD likely have distinct genetic etiologies, with half of genetic influences on CD unique to that disorder, whereas ODD lacks unique genetic risk factors and instead shares its risks with genetic profiles of other disorders (Lahey and Waldman, 2012). Regarding ADHD, which was more prevalent in the sample (n = 11), our data suggest that this disorder may not have the same underlying endocrinological profile as ODD. This may be because ADHD difference are related to a phase delay in cortisol rhythms rather than overall hyper- or hypocortisolism (Baird et al., 2012). However, the association of ADHD and hypocortisolism in meta-analyses (Scassellati et al., 2012) suggests that our negative outcome may be the result of cultural differences in detection and diagnosis of ADHD (Folmar and Palmes, 2009), rather than a population difference in the pathway. Our study failed to demonstrate a comorbidity effect of GAD on ODD on cortisol levels (McBurnett et al., 1991).

Caregivers’ attitudes toward physical discipline were associated with hypocortisolism, explaining 11% of the between-individual variation in cortisol levels. The cross-sectional nature of the study only provides associations without definitive information regarding causality. Because of the high collinearity of caregiver attitudes and ODD, we could not include them in same model.

This study demonstrated the need for multiple salivary cortisol levels across multiple days in order to control for within-individual variation. Between-individual variability accounts for less than a fourth of total variance in cortisol levels, and consequently ODD and depression model only 4.3% and physical violence models 2.8% in separate models of the total variance not attributable to other covariates. Without sampling and modeling strategies that address the tremendous within-individual variance in cortisol levels, it would be easy to miss or identify erroneous associations of cortisol with between-individual differences.
Attempts to develop more rigorous common protocols for sampling and statistical treatment will help elucidate the important interaction of HPA activity and child psychopathology (Hruschka et al., 2005).

Questionnaire-based diagnoses and unavailability of clinical cases limits the generalizability of this study. Transculturally validated measures would have better addressed the cultural equivalence of DBD (Kohrt et al., 2011). Additionally, the ECRS fails to address post-traumatic stress disorder (PTSD). Moreover, due to the lack of adequate histories for the institutionalized children, we were unable to determine PTSD prevalence. Past studies have associated PTSD with cortisol levels (Carrion et al., 2002; Carrion and Kletter, 2012). In particular, PTSD shows an association with increased bedtime cortisol (Weems and Kletter, 2012). Given the importance of comorbidity in our findings, it will be crucial to assess PTSD in future studies as well as ensure bedtime collection in naturalistic protocols.

One of the challenges in this type of study is collecting accurate reports of abuse history, as well as cultural differences in what is considered abusive child treatment (Korbin, 1991; Kohrt and Maharjan, 2009; Kohrt, 2014). In this study, we collected caregiver information regarding children’s exposure to community violence. However, for domestic violence and abuse, we only included caregiver attitudes toward what type of behaviors were considered appropriate for discipline. Parental self-reports of physical, emotional, and other forms of abuse may be unreliable; parent–child correlations of abuse were less than 0.3 in a large longitudinal study (Tajima et al., 2004). It is notable that using parental attitudes as proxy for child exposure to physical discipline still resulted in a significant finding. The association between hypocortisolism and ODD may be a reflection of abusive parenting because abusive parents are more likely to report disruptive behavior among their children (Lau et al., 2006). In our study, witnessing community violence was not associated with child cortisol levels, which suggests that more proximal zones of ecological development may have greater influence on psychoneuroendocrinological function in young children (Worthman, 2010).

Moreover, despite strong differences observed between institutionalized versus community dwelling children in Romania (Zeanah et al., 2009; McLaughlin et al., 2010; Bos et al., 2011), our study did not replicate any difference between institutionalized and community residing children. In Nepal, a study of boys recruited from four settings (urban homeless, urban squatter, urban school attending, and rural village), village boys displayed the highest allostatic load and lowest residual cortisol (Worthman and Panter-Brick, 2008). Given the expected associations between hypocortisolism and high-risk environment, the research showed unexpected findings with greater biological vulnerability among village boys living with their families compared to urban homeless and squatter boys. Taken together, these findings suggests that the type of setting where children live, exposures within that setting, and caregiver practices may vary considerably across context and culture, precluding a categorical generalization of settings such as institutions, residential communities, and homeless groups. Developmental, cultural, ecological frameworks are crucial for explaining within and between population differences in child health and behavior (Kohrt et al., 2010; Worthman, 2010).

The small sample size of only 46 boys constrains extrapolation of our findings. This a problem of the field in general where most samples are not greater than 60 boys in a single study (Targum et al., 1990; Stoff et al., 1992; Gispen-de Wied et al., 1998; van Goozen et al., 1998; McBurnett et al., 2000; Scarpa et al., 2000; Carrion et al., 2002; van de Wiel et al., 2004; Hruschka et al., 2005; Oosterlaan et al., 2005; Susman et al., 2007; Yang et al., 2007). Our study did have the advantage of analyzing 8 to 12 readings per child, whereas most studies based their claims of cortisol and psychopathology association on 3 or 4 cortisol readings per child. Of note, we did not assess IQ or other intelligence measures nor control for congenital adrenal hyperplasia, testosterone, or dehydroepiandrosterone, which could impact the association between cortisol and behavior (Herzog et al., 2001).

Given the small sample size of the study, we did not pursue more complex analyses to answer questions about mediation or effect moderation. However, future studies with larger sample sizes and with longitudinal components of longer duration may be designed to examine questions about specific causal pathways relating cortisol level, child abuse and morbidity, and how they might interact.

Our results suggest the association of cortisol levels with behavioral disorders and violence exposure is not limited to the laboratory setting, and that naturalistic settings can be used to assess HPA functioning in groups with psychopathology. Due to the high degree of intra-individual variation in cortisol levels, multiple daily assessments across multiple days should be used in conjunction with mixed effects models analysis. With numerous studies now supporting an association between basal HPA hypoactivity and DBD,
the clinical value of endocrine normalization through interventions should be further assessed (Fisher et al., 2000, 2006; Cicchetti et al., 2011). The cross-cultural association of exposure to violence, hypocortisolism, and psychopathology emphasizes the crucial need to advance global action against child maltreatment (Engle et al., 2011).

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