Published in final edited form as:

Child Abuse Negl. 2012 ; 36(0): 596–601. doi:10.1016/j.chiabu.2011.12.002.

Intimate partner violence exposure, salivary cortisol, and childhood asthma

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Abstract

Objectives—Neuroendocrine alterations may help explain health differences between intimate partner violence (IPV) exposed children and non-exposed children. We sought to determine the feasibility of having families, recruited at a child asthma visit, collect at home and return via mail child salivary samples, and whether socio-demographic variables were associated with sample return. For those returning samples, we examined whether past-year IPV exposure was associated with total cortisol output (AUC) and the magnitude of the cortisol awakening response (CAR), and whether these cortisol values were associated with asthma control.

Methods—Fifty five families with an asthmatic child of any age were recruited from 2 pediatric asthma clinics. At the time of the visit, parents completed a survey packet which included a modified version of the Conflict Tactics Scale to assess IPV. Parents were given supplies to collect 3 child salivary cortisol samples (awakening, 30-minutes after awakening, bedtime) at home on a typical day, and return them via mail. Medical records also were abstracted.

Results—Fifty-three percent ($n = 29$) returned child salivary samples. Families who returned samples typically returned them within two weeks, most commonly before we made a reminder call. Parental male sex was associated ($p = .06$) with increased rate of return at the trend level. In multivariable models, a one-unit increase in IPV was significantly associated with a .93 SD increase in root-transformed total cortisol output (AUC) (un-standardized beta = 2.5; SE .59; $p = 0.001$). The odds of uncontrolled asthma were marginally higher for every nmol/l increase in CAR (OR 1.04; 95% CI 1.0, 1.1; $p = .06$).

Conclusions—This study provides support for the feasibility of obtaining a moderate return of salivary specimens from a convenience sample. Findings that IPV was associated with elevated total cortisol output and uncontrolled asthma was marginally associated with cortisol awakening response suggest that future studies should investigate whether cortisol mediates the IPV-child asthma relationship.

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Introduction

Around 275 children worldwide are exposed to violence at home (UNICEF, 2006). In the US, over 15 million children are exposed to intimate partner violence (IPV) each year (McDonald, Jouriles, Ramisetty-Mikler, Caetano, & Green, 2006). Some researchers have explored the IPV exposure-child health association for conditions like asthma that are known to be affected by stress-related alterations in the hypothalamic-pituitary-adrenal (HPA) axis (Miller, Gaudin, Zysk, & Chen, 2009). Chronic stress impacts asthma in part by altering HPA reactivity, leading to elevated cortisol (Chen & Miller, 2007). In response to prolonged cortisol elevations, the body down-regulates cortisol receptors on immune cells. Fewer cortisol receptors increase inflammatory response, including elevated cytokine production, eosinophil chemotaxis, and airway hyper-reactivity (Chen & Miller, 2007; Miller et al., 2009).

Four studies have reported that IPV-exposed children were more likely than their peers to develop asthma (Breiding & Ziembroski, 2010; Subramanian, Ackerson, Subramanyam, & Wright, 2007; Suglia, Duarte, Sandel, & Wright, 2010; Suglia, Enlow, Kullowatz, & Wright, 2009). However, none of these studies had access to physiological data that may have provided insight about underlying mechanisms. Obtaining physiological data, however, can be challenging because basal cortisol should be assessed at multiple points over the day.

It is unclear how likely a convenience sample enrolled during a pediatric medical visit would be to return multiple salivary specimens that they must collect from their child at home. Therefore, in this pilot study enrolling families during a pediatric asthma visit, we first sought to determine whether participating families would collect child salivary samples at home and return them via mail, and whether socio-demographic variables were associated with the likelihood of sample return. For those returning samples, we then sought to determine whether the number of acts of past-year parental IPV, controlling for other sources of stress, was associated with total cortisol output across the day and the magnitude of the cortisol awakening response (CAR), and whether these cortisol values were associated with asthma control.

Methods

Setting and sample

This study was approved by the authors' institutional review board. Families were recruited from 2 pediatric asthma clinics associated with an urban, tertiary care hospital. Eligibility criteria included: 1) English-speaking family with only 1 parent present at the appointment (for safety asking IPV questions); and 2) any age child born at 37 weeks gestation with physician-diagnosed asthma.

Data collection

Survey packet—Families were approached during their child's asthma visit. Informed consent, including consent to abstract the child's medical record, was obtained from parents, and verbal assent was obtained from children 7 years. Trained research assistants (RAs) asked parents to complete questionnaires during this visit, offering assistance with reading questions if needed. Parents were remunerated with a \$10 gift card; children received a book. Questionnaires included demographic questions as well as: 1) *IPV*: IPV was assessed using the first 44-items of the Revised Conflict Tactics Scale (CTS2) (Straus, Hamby, Boney-McCoy, & Sugarman, 1996). The first 44 items only were used because, due to a clerical error, 31 participants only completed the first 44 questions; the remaining 24 completed the entire 78-item CTS2. Of the 24 who completed the entire CTS2, three

disclosed IPV and 21 reported no IPV. Of the 3 who reported IPV, 2 reported all of the acts of past 12-month IPV within the first 44 questions (thus continuous scores did not change when the full scale was examined). The third participant answered affirmatively to IPV items throughout the measure; her total count of IPV acts increased when the full scale was examined. None of the 24 participants reported IPV only in the last 34 questions. Thus, it is unlikely that participants who answered only the first 44 questions and were negative for IPV were misclassified. Those who were positive using the first 44 questions may have reported an increased count of IPV acts if the full CTS2 had been used. This error would most likely lead to an underestimate of the reported associations. Two questions--- “I made my partner have sex without a condom” and “My partner did this to me”---were omitted for during analyses because respondents who answered affirmatively wrote in that they did not use condoms in their relationship; thus it was evident that the respondents misunderstood the question, and therefore the responses were unreliable. The 42 CTS2 items included questions about emotional, physical and sexual abuse. The CTS asks respondents about the number of times they have used tactics, including physical and sexual violence, to resolve disagreements over the past 12 months. Response options are categorical including: once, twice, 3–5 times, 6–10 times, 11–20 times, more than 20 times, and never. Responses were re-coded as follows (Straus et al., 1996): 3–5 times was coded as 4, 6–10 as 8, 11–20 as 15, and >20 times as 25. A continuous score was then created by summing the total number of all acts of physical and sexual abuse (including perpetration and victimization) (Straus et al., 1996). Alpha reliability coefficients for the husband to wife physical aggression scale range from 0.79–0.91 and wife to husband 0.82. Adequate discriminant and predictive validity have been demonstrated (Straus et al., 1996); 2) *Parental psychosocial functioning*: Parents’ perceived stress and coping were evaluated using the 10-item Perceived Stress Scale (PSS) and the 26-item Coping Self-Efficacy Scale (CSE), respectively (Chesney, Neilands, Chambers, Taylor, & Folkman, 2006; Cohen, Kamarack, & Mermelstein, 1983; Cole, 1999). The PSS asks about the respondent’s feelings over the past month, determining the degree to which she believes that life is unpredictable, uncontrollable or overloaded. Internal reliability (Cronbach’s alpha 0.67–0.86), predictive and concurrent validity are adequate (Cohen et al., 1983). The CSE measures perceived self-efficacy in managing daily challenges. Internal reliability (Cronbach’s alpha 0.80–0.91), concurrent and predictive validity are adequate (Chesney, Chambers, Taylor, Johnson, & Folkman, 2003). Responses for both are summed, with higher scores indicating more stress and better coping self-efficacy, respectively; and 3) *SES*: In addition to income and education, subjective social status (SSS) was measured. Participants ranked themselves on two 10-rung ladders (higher rungs indicate higher perceived status), one of their community and the other of the US (Singh-Manoux, Adler, & Marmot, 2003).

Saliva collection—Salivary cortisol measures basal levels of active, unbound cortisol (Schwartz, Granger, Susman, Gunnar, & Laird, 1998). At the pediatric asthma visit, families were given a packet of materials to collect 3 child saliva samples on any “typical” weekday: T1: upon awakening; T2: 30-minutes after awakening; and T3: bedtime. Packets included pictorial and written instructions, saliva collection supplies and a self-addressed mailer to return samples. RAs demonstrated saliva collection, emphasizing the importance of accurate sample timing and reporting. Children on oral steroids were advised to wait 2 weeks after finishing the medicine to collect saliva.

Parents were instructed to have children avoid eating, drinking, or brushing teeth for 30 minutes before providing samples (Granger et al., 2007). Saliva was collected using a Salivette device (Sarstedt, Newton, NC) or, among children 4 years, a cotton rope (Salimetrics, State College, PA). Parents were told to have their Children held the salivette/rope, under their tongue, for at least 1 minute (Granger et al., 2007). At each collection, parents completed a questionnaire including time and date, recent medication use, sleep/

wake times, stress experienced by the child on the collection day, and when the child had last eaten or drunk. Samples were kept frozen until they were returned. RAs made up to 2 reminder calls. Families were mailed a \$20 gift card for samples.

Salivary cortisol assays—Returned saliva samples were centrifuged at 1500g for 15 minutes, aliquoted, and stored frozen at -80°C . Samples were assayed using an FDA-approved enzyme immunoassay (Salimetrics, State College, PA) with a sensitivity of $<0.003\text{ }\mu\text{g/dL}$ and average intra- and inter-assay coefficients of variation of less than 10% and 15%, respectively.

Medical record abstraction—Child age, sex, height, weight, and medications were abstracted. Study staff also abstracted the 11-item Pediatric Asthma Control & Communication Instrument (PACCI), which parents complete during clinic visits. The PACCI classifies asthma symptoms using the National Institutes of Health (NIH) asthma severity categories including intermittent, and mild persistent, moderate and severe persistent, which then were dichotomized as controlled (intermittent) or uncontrolled (mild, moderate and severe persistent) (Okello et al., 2009; Okello et al., 2008; Patino et al., 2008).

Statistical analyses

Socio-demographic variables and asthma control in families with and without IPV were compared using Student's t-test and Fisher's exact test (Table 1). In separate bivariable models, we tested the relationship between sample return and socio-demographics.

Cortisol secretion typically exhibits a diurnal pattern, with levels high at awakening, a peak shortly after awakening, and declining values over the afternoon; however, there is significant inter-individual variability (Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003). After exploring individual cortisol values (i.e., T1, T2, T3), analyses examined: 1) total cortisol output across the all 3 time points using the area under the curve with respect to ground approach (AUC) (Pruessner, et al., 2003) ; and 2) the magnitude of the cortisol awakening response (CAR)—such as, AUCg for T1 & T2 only. To address distributional skew, values were square-root transformed where appropriate before inclusion in parametric models (Kelly, Young, Sweeting, Fischer, & West, 2008).

Separate multivariable linear regression models assessed the relationship between IPV and cortisol values. Multivariable logistic regression models assessed the relationship between cortisol values and asthma control. Given our sample size, we were not powered to conduct models testing whether cortisol values mediated the IPV-asthma control relationship. All multivariable models included covariates known to influence cortisol values including wake time (and/or collection time, if different), sleep duration, and child age and sex (Kelly et al., 2008). Multivariable models also included inhaled corticosteroid use (dichotomous) because of its potential to affect cortisol; the magnitude of this effect, however, is not well established in children (Ninan, Reid, Carter, Smail, & Russell, 1993). Body mass index was evaluated as a covariate, but was collinear with age, and therefore not included. Because the objective of the IPV-cortisol models was to examine the IPV-cortisol associations controlling for other sources of psychosocial stress, the initial multivariable linear regression models contained all socio-demographic variables. Covariates that were not significant at the trend level ($p = 0.10$) were dropped, beginning with the least significant. Remaining covariates included parental age, community ladder, income and education. For all results, statistical significance was defined as $p < 0.05$; trend-level significance, defined as $p < .10$, was also evaluated given our small pilot sample and the hypothesis generating goals of the study (Cummings & Koepsell, 2010).

Results

Sixty-eight potentially eligible families were approached. Eight families (12%) declined participation, leaving a sample of 60. One family asked during a reminder phone call to be withdrawn, and medical record abstraction revealed that 3 children were premature and 1 did not have an asthma diagnosis; these 5 families were excluded, leaving a sample of 55. Six out of the 55 (11%) parents reported past-12 month IPV. The socio-demographic characteristics of the sample, by IPV, are presented in Table 1. Based on PACCI responses for the entire sample, 43% of children had controlled asthma, and 57% had uncontrolled asthma.

Cortisol sample return

Twenty-nine out of the 55 families (53%) returned cortisol samples. Of the 26 families *not* returning samples, 5 were reminded once, 13 were reminded twice, 1 was inadvertently reminded 3 times, and the remaining 7 were not able to be reached; 5 caregivers provided information about why they had not returned the samples with 3 stating the child refused to provide saliva, and 2 stating that they kept forgetting.

Of the 29 families who returned samples, RAs made 1 reminder phone call prior to the return of samples for 3 families, and 2 reminder phone calls for 3 families. The remaining 23 families sent in samples before we were able to make the reminder calls. Families collected saliva samples a mean of 12.1 days (range 1–52) after the clinic visit during which they enrolled. Three parents of the 29 children returning samples (10%) reported IPV, 11 (38%) children had uncontrolled asthma and 25 (86%) were on an inhaled corticosteroid. Children accompanied to their visit by their fathers were more likely, at the trend level, to return samples compared to those accompanied by mothers (86% versus 48%; $p=0.06$). Returning cortisol samples was not significantly associated with other socio-demographic characteristics.

One child provided insufficient sample for T1 analyses and a second child at T2. One T1 sample was more than 3 standard deviations (SD) from the mean and was therefore treated as missing. Thus, cortisol analyses included 27 samples for T1, 28 for T2, and 29 for T3.

IPV and cortisol

A 1-unit increase in IPV was significantly associated with a .93 SD increase in root-transformed total cortisol output (AUC) [un-standardized beta (β)=2.5 SE .59; $p=0.001$]. IPV and CAR were not significantly associated ($\beta=.22$ SE: .22; $p=NS$).

Asthma control and cortisol

There was no significant relationship between AUC and asthma control (OR 1.0 CI .99–1.0, $p=NS$). At the trend level, the odds of uncontrolled asthma were higher for every nmol/l increase in CAR (OR 1.04; 95% CI 1.0, 1.1 $p=.06$).

Peak cortisol

Peak cortisol did not always occur at T2 (despite 85% compliance with the timing protocol). Thus, in addition to CAR, we examined associations between the magnitude of peak cortisol and IPV and asthma control. A 1-unit increase in IPV was associated with a .86 SD increase in peak cortisol ($\beta=.52$, SE: .12, $p=0.001$); the odds of uncontrolled asthma were 1.4 times higher for every unit increase peak cortisol (95% CI: 1.0, 1.9, $p=0.05$).

Discussion

Fifty-three percent of a diverse convenience sample enrolled at a pediatric asthma clinic visit returned child saliva samples collected at home on a typical day, with only modest resources dedicated to facilitating this return. This provides some anecdotal evidence that a moderate rate of return is feasible. Families who returned samples typically returned them within 2 weeks, most commonly before a reminder call was made.

For children returning samples, IPV was significantly associated with total cortisol output and higher peak cortisol. In separate models, children with uncontrolled asthma exhibited a significantly larger peak cortisol and a trend toward larger CAR. These observations deserve further evaluation in larger samples to determine if this represents a potential causal pathway or spurious findings. Our study is similar to prior pilot cortisol studies. Amongst a sample of 21 foster care children, Linares found that 4 out of 5 with an atypical cortisol patterns had been IPV-exposed, as compared to 2 out of 16 children with typical diurnal patterns (Linares et al., 2008). Additionally, our results concur with a growing body of research indicating that childhood stress, including IPV exposure, leads to physiologic alterations in the HPA axis (Gunnar & Quevedo, 2007), and that dysregulation of the HPA axis can adversely impact immune, behavioral, and psychological functioning (Granger, Granger, & Granger, 2006).

Several limitations should be considered. We did not measure child abuse, parental depression, or substance use. We did have information about parental stress and coping, hypothesized mechanisms by which depression and substance abuse affect child health and alter risk for maltreatment. Only the first 44 (out of 78) items on the CTS2 were used for analyses; based on our evaluation of participants completing the entire 78 items, however, we believe that it is unlikely those who were negative for IPV on the 44-item scale were misclassified. Those who were positive using the first 44 questions may have reported increased IPV on the full CTS2 which would most likely lead to an underestimate of the impact of IPV. It would be ideal to have 2 or more successive days of saliva collection (Wolf, Nicholls, & Chen, 2008). However, the study was designed to be a feasibility study to determine how likely families were to collect and return samples given a minimal, yet valid, protocol. Finally, given the small sample size, we did not have the power to conduct mediation or moderation analyses. This hinders our ability to directly examine the potential influence of cortisol in the IPV-asthma association; larger future studies are needed to explore this potential mechanism.

A moderate number of parents recruited during a pediatric asthma visit returned child salivary cortisol specimens, lending support to the feasibility of obtaining salivary specimens in cross-sectional studies of convenience samples. Findings that IPV and uncontrolled asthma were both associated with elevated peak cortisol are hypothesis-generating and suggest that future larger studies should investigate how cortisol mediates the IPV-child asthma relationship. This type of future research would provide significant insight into the mechanisms underlying the well-documented link between adverse life experiences and poor health across the lifespan (Felitti et al., 1998; Flaherty et al., 2009). Future research should also consider how different patterns of IPV (including severity, directionality and type of IPV) differentially impact this relationship.

Acknowledgments

The current study was funded by the Johns Hopkins Center for Mind and Body Research (R24 AT004641, J.A. Haythornthwaite, PI). Dr Bair-Merritt is funded by a Career Development Award (K23HD057180) sponsored by the National Institute of Child Health and Human Development. Dr. Johnson is funded by a Career Development Award from the National Institute on Drug Abuse (K01DA027229)

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Table 1**Sample Sociodemographic Characteristics by Intimate Partner Violence (IPV)**

	No IPV N=49 (89%)	IPV N=6 (11%)	<i>p</i> value^a
Caregiver Demographics n (%)			
Female	42 (86)	6 (100)	1.00
Marital Status			.53
Married	28 (57)	3 (50)	
Single	15 (31)	2 (33)	
Other	6 (12)	1 (17)	
Race			
Non-Hispanic Black	28 (57)	0 (0)	.02
Hispanic Black	3 (6)	0 (0)	
Non-Hispanic White	16 (33)	5 (83)	
Asian/Other	2 (4)	1 (17)	
Education			
<12 th grade	4 (8)	1 (17)	.51
High school graduate	6 (13)	1 (17)	
GED/trade school/some college	22 (46)	1 (16)	
College/post-graduate	16 (33)	3 (50)	
Income			
<\$10,000	4 (9)	1 (17)	.94
\$10–19,999	2 (4)	0 (0)	
\$20–49,999	13 (29)	1 (17)	
\$50–79,999	6 (13)	1 (17)	
>\$80,000	20 (45)	3 (50)	
Caregiver Demographics; mean (standard deviation [SD])			
Age (years)	36.2 (7.8)	29.5 (5.1)	.05
Perceived Stress Scale ^b	13.6 (5.7)	17.3 (5.99)	.14
Coping Self Efficacy ^c	197.4 (45.7)	148 (84.0)	.03
US Ladder ^d	5.8 (1.6)	4.8 (2.5)	.18
Community Ladder ^d	6.8 (1.8)	5.3 (2.5)	.08
Child Demographics; n (%) unless otherwise specified			
Female	18 (37)	3 (50)	.67
Age (years); mean (SD)	7.4 (4.4)	5.0 (2.4)	.19
Uncontrolled asthma	27 (56)	4 (67)	1.00

^aFischer's exact test for categorical variables and Student's *t* test for continuous variables

^bBased on 10-item measure with higher scores indicating higher levels of stress

^cBased on a 26-item measure with higher scores indicating more better coping skills

^dMeasure of subjective social status compared to others in the nation and in ones community (range 0–10) with higher scores indicating higher perceived social status.