Posttraumatic Stress Symptoms Related to Community Violence and Children's Diurnal Cortisol Response in an Urban Community-Dwelling Sample

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Abstract

Background While community violence has been linked to psychological morbidity in urban youth, data on the physiological correlates of violence and associated post-traumatic stress symptoms are sparse. We examined the influence of child posttraumatic stress symptoms reported in relationship to community violence exposure on diurnal salivary cortisol response in a population based sample of 28 girls and 15 boys ages 7–13, 54% self-identified as white and 46% as Hispanic.

Methods Mothers' reported on the child's exposure to community violence using the *Survey of Children's Exposure to Community Violence* and completed the Checklist of Children's Distress Symptoms (CCDS) which captures factors related to posttraumatic stress; children who were eight years of age or greater reported on their own community violence exposure. Saliva samples were obtained from the children four times a day (after awakening, lunch, dinner and bedtime) over

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Harvard Medical School, Boston, MA, USA three days. Mixed models were used to assess the influence of posttraumatic stress symptoms on cortisol expression, examined as diurnal slope and area under the curve (AUC), calculated across the day, adjusting for socio-demographics.

Results In adjusted analyses, higher scores on total traumatic stress symptoms (CCDS) were associated with both greater cortisol AUC and with a flatter cortisol waking to bedtime rhythm. The associations were primarily attributable to differences on the intrusion, arousal and avoidance CCDS subscales.

Conclusion Posttraumatic stress symptomatology reported in response to community violence exposure was associated with diurnal cortisol disruption in these community-dwelling urban children.

Keywords Community violence · Cortisol rhythm · Posttraumatic stress symptoms

Introduction

Violence exposure among children growing up in the United States (US) is a leading pediatric public health problem [1]. Among youth living in urban communities in the US the prevalence of experiencing and witnessing serious and lethal violence is particularly high [2]. The majority of urban youth have witnessed violent events and, among older children, a third or more report being a direct victim of violence [3–5]. In addition to being highly prevalent, exposure to violence is increasingly recognized as a major cause of childhood morbidity in urban US communities [6]. Research on children experiencing violence suggests that a number of domains related to cognitive, social and emotional functioning are adversely affected by exposure to such stressors. Children who are

victims of violent acts or who witness violence have been found to have more externalizing and internalizing behavior problems, depressive symptoms, more aggression problems and are more likely to experience symptoms of posttraumatic stress disorder (PTSD) [7–11].

Chronic psychosocial stressors, including violence, may also result in physiologic alterations which may have even broader health effects [6]. Overlapping lines of evidence from both animal [12–14] and human [15, 16] studies support the notion that physiologic stress pathways may be altered by chronic stress and early traumatic experiences. The health effects of early traumatic experiences, such as witnessing or being a victim of violent events, may be mediated through activation of the stress-response system resulting in dysregulation of the hypothalamic–pituitary– adrenal (HPA) axis and poor regulation of cortisol, the final product of the HPA system.

Typically, cortisol levels among adults as well as children rise in the morning, approximately thirty minutes after awakening, and decrease throughout the day [16]. This pattern of cortisol activity has been observed in children as young as 2 months of age [16]. A growing number of studies have demonstrated altered cortisol secretion among maltreated and neglected children [17, 18]. For example, Cicchetti et al found higher morning and afternoon cortisol levels among maltreated children exhibiting internalizing symptoms (i.e., depression and anxiety disorders), compared to non-maltreated children experiencing symptoms [19]. Maltreated children with posttraumatic stress symptoms have also been shown to have elevated cortisol levels throughout the day [20]. Elevated daytime salivary cortisol levels have also been found among 6- to 12-year-old children reared in Romanian orphanages several years after adoption [21]. In contrast, other studies have found lower morning cortisol levels and a flattened daily cortisol rhythm among abused and maltreated children [22, 23]. Data on the diurnal cortisol rhythm in pediatric samples outside of these selective populations and clinical samples is sparse.

Only a few studies have begun to examine the impact of community violence exposure on physiologic markers of stress response in children [24–27]. Murali and Chen examined the effects of violence on laboratory assessments of cardiovascular and neuroendocrine measures, both at baseline and in response to an interpersonal laboratory stressor (a debate task or a puzzle task) in 115 urban high-school students aged 16 to 19 years. Increased frequency of lifetime violence exposure was associated with higher basal diastolic blood pressure, heart rate, and cortisol level. These relationships held even when they considered only remote exposure to violence (i.e., occurring more than a year ago). Higher levels of violence exposure also predicted decreased cardiovascular reactivity to the acute laboratory stressor based on the physiologic indicators (i.e., blood pressure,

heart rate, heart rate variability); there was no difference in the change in cortisol in relation to the acute laboratory stressor comparing those with high violence vs. low violence exposure [26]. Kliewer examined the association between salivary cortisol levels and exposure to violence in 101 African American youth [25]. Witnessed violence was associated with both lower baseline cortisol (measured in the laboratory) and with increases in cortisol in response to a mild stressor (viewing and discussing a video depicting community violence). These authors additionally assessed morning levels of cortisol in these adolescents taken in the home setting. Girls with higher levels of witnessed violence had atypical awakening response patterns (i.e., declining cortisol from awakening to 1 hour after awakening without a rise). These data link community violence exposure with disruption of stress reactivity pathways, including the HPA axis albeit neither considered diurnal variation in cortisol expression throughout the day in a non-laboratory setting.

Moreover, existing evidence on stress hormones in PTSD is based in clinical samples and samples of other selective populations [28]. Although a few studies have begun to examine the relationships among PTSD symptomatology and cortisol expression in community adult samples, [29, 30] none have assessed these associations in non-clinical urban samples of children.

We expand the literature in the current study which aims to examine the relationships among posttraumatic stress symptoms reported in relationship to community violence experiences, and basal diurnal salivary cortisol response among a community-based cohort of urban school-aged children.

Materials and Methods

Study Population

The study is nested in a larger community-based cohort of mothers and their children aimed at examining the influence of environmental factors, including chronic stress, on respiratory outcomes as previously described in detail [31]. In brief, pregnant women receiving prenatal care at an urban community health center in Boston, MA, were enrolled between March 1986 and October 1992 prior to the 20th week of gestation. Women who did not speak either English or Spanish, who did not plan to have pediatric follow-up at the clinic, and whose age was less than 18 years at the time of delivery were excluded. One thousand women were eligible and enrolled, of whom 848 continued participation and delivered a live-born infant. In November 1996, new study initiatives were implemented at which time approximately 500 women continued active follow-up in the parent study. Of them, 412 gave voluntary

written consent and completed a survey on their children's violence exposure. Those who did not participate in the violence assessment were more likely to be White Non-Hispanics and current smokers (Hispanics, 45% nonresponders vs. 52% responders; current smokers, 42% non-responders vs. 28% responders). The subsample presented in these analyses was randomly selected from the larger community-based study for the purpose of conducting a pilot study of a home-based collection protocol for salivary cortisol. Participants did not differ from non-participants based on demographics, violence exposure or distress symptoms. Fifty-five children were asked to participate and 43 completed the protocol. In the longitudinal study, detailed data had been ascertained through standardized questionnaires administered at baseline, clinic follow-up visits and medical record review as previously described [31]. The study protocol was approved by the human studies committees at both the Brigham & Women's Hospital and the Beth Israel Deaconess Medical Center.

Exposure to Violence

Violence exposure was ascertained when the children were between 4 and 10 years of age, using a modified version of the Survey of Children's Exposure to Community Violence (ETV) [32]. The ETV is a multi-item survey structured to gather data on direct victimization and witnessing violence as well as factors known to influence the impact of violence (e.g. familiarity with the perpetrator or victim, frequency of events and the setting of the exposure. i.e. whether the events occurred at home) [33]. The survey measured lifetime exposure to specific violent events including hearing gunshots, and witnessing and/or experiencing shoving, hitting or punching, knife attacks, shootings, and witnessing verbal abuse of their primary caregiver. Mothers were asked to report on their child's lifetime exposure to violence. In addition, children who were 8 years of age or greater (N=22) reported on their own community violence exposure. Acceptable internal consistency, test-retest reliability, and validity have previously been described for this scale [1, 33].

We implemented Rasch modeling techniques to summarize responses to the community ETV questionnaire into a continuous score as previously described [34]. The Rasch model produces two scores, one based on the parent's responses to the violence survey, the other on the child's responses to the survey. If a child is missing his or her selfreport the model predicts the Rasch score based on the existing correlation between the parent and child responses in the remainder of the cohort, so that all children have two scores. The final violence score is the average of the two Rasch scores [35, 36]. This is a desirable approach here as children are unlikely to be able to recall events occurring during very early childhood at the same time that parents may be more likely to underreport events that occur when children are older and violence occurs outside of the supervision of parents [37, 38].

Psychological Distress Symptoms

At the time of the violence assessment, mothers also reported on child posttraumatic stress symptoms over the past 6 months related to their exposure to community violence using the Checklist of Children's Distress Symptoms (CCDS) [39]. The CCDS which is based on diagnostic criteria described in the Diagnostic and Statistical Manual of Mental Disorders, Revised Third Edition [40] was originally developed to assess distress in youth related to community violence exposure. The 28-item scale assesses children's posttraumatic stress symptoms anchored to the experiences of community violence. Examples of symptoms assessed on this scale include difficulty with attention or sleep, intrusive thoughts, flashbacks, worries, and reminders of things that have happened in the past. Responses are based on a 5-point scale ranging from 1, "never" to 5, "most of the time". The scale includes subscales on intrusive thoughts, emotional numbness, avoidant behavior, arousal and hopelessness or despondency about the future [41, 42]. Many of these symptoms and behaviors including hypervigilance and emotional numbing as well as avoidant behavior and intrusive thoughts are defined components of PTSD while the despondency subscale is more closely related to depression and hopelessness [43]. An overall total CCDS score was considered in the analyses as well as the separate subscale scores. Higher scores correspond to more adverse psychological symptoms.

Cortisol Measures

During longitudinal follow-up, salivary cortisol was collected from the children when they were between 7 and 13 years of age. The protocol consisted of a home-based assessment of salivary cortisol collected by the passive drool technique on 3 days [44, 45]. Parents and their children were given verbal instructions by trained research staff when saliva tubes were supplied as well as brief daily diaries repeating these instructions for recording adherence to the collection protocol. Subjects were instructed not to eat, brush their teeth, or drink liquids for at least 15 min before taking a sample. They provided four samples each day of collection: 30 minutes after awakening ("when your eyes open and you are ready to get up"), before lunch, before dinner, and at bedtime ("right before getting into bed") similar to collection protocols in prior research [20]. They were also instructed to record the time that they woke up (in the log book) and the date and the exact time that each sample was taken (on the tube label and log book). After each collection, the tubes were placed in a home freezer. Samples were picked up in person by research staff on the fourth day and kept frozen in a cooler until they arrived at the Reproductive Ecology Laboratory at Harvard University where the cortisol assays were conducted. Salivary cortisol samples were assayed using radioimmunoassay (RIA) following procedures detailed by Ellison [46]. Data were analyzed using a computerized RIA program, which calculated cortisol concentrations (nmol/l) from the counts per minute. The inter- and intra-assay coefficients of variation were 10% and 7.37% respectively. The sensitivity limit (the lowest value of cortisol distinguishable from 0 with 95% confidence) averaged 8×10^{-4} pmol/l for all assays.

Forty-three children completed the saliva protocol and provided samples. To limit variation between collection times we restricted our analyses to samples that were taken during the following time windows: 30 min after awakening to 1.5 h (time 1), between 3 and 6.5 h after waking (time 2), 7.5 to 11.5 h after waking (time 3) and more than 11.5 h after waking (time 4). These time windows were selected a priori as previously done in other studies [47]. The variation in sampling times within each sampling interval appeared random in that they were not related to the level of community violence exposure or CCDS symptoms (Pearson correlation). The children provided 516 saliva samples, 88 samples were excluded from analyses because they did not meet the sampling time windows, leaving 428 samples for analyses.

Statistical Analyses

Guided by previously described methodologies [48], we examined the relationships among exposure to violence, child posttraumatic stress symptoms, and cortisol levels at each time point of collection as well as the area under the curve (AUC) and the diurnal slope over the waking day. Cortisol values were log transformed prior to analyses due to their skewed distribution. Diurnal slope is the slope of the log cortisol measurements over the course of the day. Slopes were estimated using the best linear unbiased predictor from a hierarchical mixed model that included random effects for subject and day within subject [47]. These estimates are "best" in the sense that they are unbiased and less variable than other linear estimators such as ordinary least squares estimates. The AUC was calculated as the area under a linear interpolation of the log cortisol measures over time for each day of measurement for each child.

Initially, Pearson correlation coefficients were performed to assess the relationships among community violence exposure, and posttraumatic stress symptoms assessed on the CCDS. To model the relationship between cortisol levels and posttraumatic stress symptoms we employed mixed models allowing for repeated diurnal slope and AUC measures (one per each day per each child). Additionally we used mixed models regression to estimate the effect of violence exposure and posttraumatic stress symptoms on log cortisol at each time point of measurement. All analyses were adjusted for race/ethnicity, socioeconomic status (maternal education), age and gender. While tobacco smoke exposure has been shown to alter cortisol secretion we did not adjust for tobacco exposure due to the high correlation with race/ethnicity in these data (i.e., of the 20 Hispanic women in our sample only one smoked during pregnancy, 35% of the White women smoked during pregnancy). All statistical analyses were done using SAS version 9.0 (SAS Institute, Cary, NC).

Results

Table 1 summarizes the demographic characteristics of the population and descriptive statistics for all other covariates. Of the 43 children, 65% were female, 54% white, 46% Hispanic and 42% had mothers with less than a high-school education. Means and standard deviations for the violence exposure scale, cortisol levels aggregated across the 3 days for each time interval of collection as well as summary variables, and the CCDS subscale scores are also depicted.

The community violence scale was modestly correlated with the overall posttraumatic stress symptoms score (Pearson correlation r=0.26 p=.09) as well as the subscales derived from the CCDS measure (r ranged from 0.07 to 0.31), similar to what has been found in other urban populations [41]. The community violence scale was most strongly correlated with intrusive symptoms (r=0.31, p=0.04) on the posttraumatic stress scale which also corroborates previous findings by Howard et al. [41]. The community violence scale was not significantly associated with the cortisol indicators.

We did find consistent and robust relationships between the overall posttraumatic stress symptom scale and subscale scores and cortisol disruption. In unadjusted analyses (data not shown), the posttraumatic stress symptom overall score from the CCDS was positively associated with cortisol AUC and diurnal slope as well as the cortisol measures taken at time 3 (before lunch) and time 4 (before dinner; all p < 0.05).

We assessed the relationship between the overall score and subscales on the CCDS (as a continuous measure) and cortisol outcomes, adjusting for socio-demographic factors (Table 2). A number of the posttraumatic stress symptom subscales as well as the overall score strongly predicted cortisol measures in these separate regression models. Diurnal slope was positively associated with the arousal,

Table 1 Population character- istics and descriptive statistics for covariates	Demographics	N	%	Mean	SD	Range		
	Child's age			10.3	1.8	7–13		
	Child's gender							
	Male	15	34.9					
	Female	28	65.1					
	Race/ethnicity							
	White	23	53.5					
	Hispanic/Black/other ^a	20	46.5					
	Mother's education level							
	Some college	7	16.3					
	High-school graduate/technical school	18	41.9					
	Less than high-school/no graduation	18	41.9					
	Cortisol measures ^b (time after awakening)							
	Time 1 (30 min to 1.5h)			5.23	4.13			
	Time 2 (3–6.5 h)			2.06	2.76			
	Time 3 (7.5–11.5 h)			1.88	2.94			
	Time 4 (11.5 h+)			1.04	1.78			
	Diurnal slope			-0.13	0.03			
	AUC			87.6	16.4			
	Checklist of child distress symptoms (CCDS)							
^a Seventeen children identified as Hispanic, one Black, and two as other race/ethnicity	CCDS overall score			1.73	0.70			
	Hopelessness			1.42	0.68			
	Numbness			1.3	0.50			
^b Units for cortisol in nmol/l; for	Arousal			2.1	0.87			
conversion to mg/dl divide by Intrusion				1.45	0.80			

avoidance and intrusion subscales and with the overall posttraumatic stress score indicating that higher CCDS scores associate with cortisol levels that do not decrease as quickly over the course of the day. In addition, the AUC was positively associated with the arousal, avoidance, and intrusion subscale and with the overall CCDS score indicating that those with higher posttraumatic stress symptom scores also had higher average cortisol levels over the course of the day. In analyses of the time-specific cortisol measures, cortisol levels were positively associated with the arousal, avoidance, intrusion, and numbness subscales and with the overall posttraumatic stress scores among measures obtained before dinner (time 3) and before bedtime (time 4). The adjusted association between posttraumatic stress symptoms overall score and cortisol is also shown in Fig. 1. Children with an overall posttraumatic

Table 2	Child distress symptoms	(per one unit change)) on cortisol response	(nMol/L) by time o	f collection, AUC, and diurnal slope
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	Time 1 (30 min to 1.5h)	Time 2 (3–6.5h)	Time 3 (7.5–11.5h)	Time 4 (11.5+ h)	AUC	Diurnal slope Estimate	
	Estimate	Estimate	Estimate	Estimate	Estimate		
CCDS ^a							
Overall score	0.1640	0.2720*	0.4556**	0.3883**	5.2632**	0.0102**	
Hopelessness	-0.0516	0.2379	0.2116	0.2880****	1.9227	0.0080	
Numbness	-0.0163	0.4206*	0.2589	0.4720**	4.5320	0.0099	
Arousal	0.1956	0.1988	0.3657**	0.2860**	4.7409**	0.0071*	
Avoidance	0.0538	0.2102*	0.3735**	0.2502**	3.6407**	0.0079**	
Intrusion	0.1316	0.2008	0.4867**	0.3916**	5.2831**	0.0114**	

Each line represents a separate regression model. All models are adjusted for age, gender, race/ethnicity, and maternal education

*p-value<0.10; **p-value<0.05

^a Checklist of Child Distress Symptoms

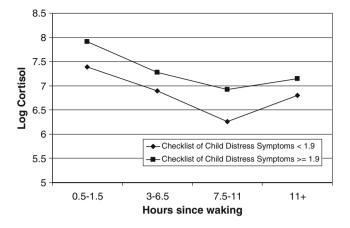


Fig. 1 Mean cortisol level (nmol/L) by severity of symptoms on the Checklist of Child Distress Symptoms and time of collection. Significant differences between CCDS groups were noted at time 1 and time 3 (p<0.05). Adjusted for age, gender, race/ethnicity, and maternal education

symptom score greater than 1.9 (highest quartile of CCDS score), had higher salivary cortisol levels throughout the day.

Given the variability in the timing of collection for the morning sample, it is possible that the peak value for the cortisol morning response is included for some subjects which may influence the diurnal slope [49]. We thus ran a sensitivity analysis calculating the diurnal slope excluding the morning value and found that the effect estimates shown in Table 2 changed only slightly and remained statistically significant (data not shown).

Discussion

In this urban community-dwelling sample of school-aged children higher levels of posttraumatic stress symptoms reported in response to community violence exposure predicted elevated cortisol levels, especially in the afternoon and evening samples, and a blunted diurnal slope, even when adjusting for race, gender, age, and socioeconomic status. Stronger associations were found for the numbness, avoidance, intrusion and arousal subscales, defined components of PTSD, and not with the hopelessness subscale which is more closely related with depression [42, 43].

These findings are strikingly similar to diurnal salivary cortisol patterns reported by Carrion et al. in a pediatric clinical sample who met criteria for a diagnosis of PTSD in which a parallel home salivary cortisol collection protocol with similar timing of collection was used [20]. Subjects were also similarly aged (mean 10.7 years, range 7 to 14 years). Unlike our community sample, children in that study were recruited from local social service departments and mental health clinics. In the clinical sample, all children

had been exposed to interpersonal trauma and met criteria for PTSD based on a score of 12 or greater on the PTSD Reaction Index [50]. The clinical sample had significantly higher cortisol levels later in the day (samples collected in the afternoon and evening) relative to age- and gendermatched archival controls. Moreover, these investigators found no differences between children meeting criteria for PTSD and children with sub-threshold symptoms in terms of elevated cortisol levels. These findings are also consistent with those of De Bellis et al. [51] who reported elevated levels of cortisol in 24-h urine collections in children with a history of maltreatment when compared to controls. However, they conflict with a number of studies of adults and older adolescents with trauma histories and PTSD [52]. This may reflect developmental differences given the ages across these studies as well as variation in cortisol collection procedures [17, 51]. While stress may elicit elevated cortisol levels among children [20, 21], under prolonged stress the stress-cortisol response may be further disrupted resulting in decreased cortisol expression in adulthood [53]. It could be that, if symptoms persist these children would later show lower cortisol levels if followed longitudinally. Future studies with repeated assessment related to traumatic stress exposure and the subsequent development of psychopathology and disrupted stress responses (e.g., HPA axis) will be needed to better delineate the natural history of the psychobiological stress response (e.g., cortisol) following exposures such as community violence.

As in any epidemiologic study we acknowledge a number of limitations. As is typical with longitudinal studies, there was significant reduction in the sample available from the original cohort over time. The nonparticipation of subjects from the longitudinal study may be seen as a limitation albeit there were no differences based on socio-demographics, violence exposure or distress symptoms, comparing those who had cortisol assessed versus those who did not among the participants who remained in follow-up. Thus, this unlikely influenced our findings. In addition, although the relatively small sample size was large enough to reveal significant effects, a larger sample size could increase the precision of our estimates. Moreover, a larger sample size may allow for the more formal testing of a mediation model, i.e., community violence events leading to PTSD leading to cortisol disruption.

Notably we demonstrated associations between posttraumatic stress symptoms and cortisol measures later in the day (afternoon and evening) but not in the morning. It is possible these associations reflect an aggregate effect of daily challenges making the afternoon measures more sensitive to chronic stressors [49]. Another explanation is that the association actually does occur across the day, but because the diurnal slope tend to be very steep from early morning to early afternoon, relatively small errors in the timing of samples (which is difficult to avoid in naturalistic studies) may result in large errors in cortisol measurement. Thus the explanation may lie more in the collection procedures. Indeed, while we asked mothers to provide the morning samples 30 min after the child awakened, only 75% of samples were collected within 25–35 min of awakening. Some of the morning samples were collected as close to 5 minutes after awakening while the rest were collected one hour after awakening with one additional sample collected one and a half hours after awakening. This wide sampling frame may include the peak morning cortisol response for some subjects which may influence the diurnal slope although a sensitivity analysis suggested this did not explain our results.

In summary, subclinical PTSD symptomatology reported in relation to community violence exposure significantly predicts cortisol disruption in this urban community-dwelling non-clinical pediatric sample. Moreover, the cortisol response among children with greater distress symptoms parallels diurnal cortisol patterns previously reported in a clinical sample of traumatized children with diagnosed PTSD in the same age range [20]. Further research to corroborate these preliminary findings is needed; if the posttraumatic stress symptoms are a result of the experiences these children encounter as exigencies of their urban environment (e.g., crime and violence), which is highly prevalent in these neighborhoods, a large number of children may be impacted. Psychological sequelae in this context may also result in physiologic alterations which may have even broader health effects [6].

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