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### Publication Date

2015-04-01

### DOI

10.1016/j.psyneuen.2015.01.020

Peer reviewed

HHS Public Access

Author manuscript

*Psychoneuroendocrinology*. Author manuscript; available in PMC 2015 April 03.

Published in final edited form as:

*Psychoneuroendocrinology*. 2015 April ; 54: 103–114. doi:10.1016/j.psyneuen.2015.01.020.

# Differential associations between childhood trauma subtypes and adolescent HPA-axis functioning

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## Summary

Studies examining the association between childhood trauma exposure and neuroendocrine functioning have returned inconsistent findings. To date, few studies have accounted for the role exposure to different types of childhood trauma may have on different neuroendocrine adaptations, and no study has examined this association using multiple indices of hypothalamic—pituitary—adrenal axis (HPA-axis) functioning. The purpose of this study was to characterize the unique associations between exposure to physical abuse, emotional abuse, and non-intentional trauma, and multiple indices of HPA-axis functioning.

**Methods—**A community sample of 138 youth (aged 9—16) completed the Socially Evaluated Cold Pressor Task (SE-CPT) while their parents completed the Early Trauma Inventory (ETI). All youth then collected 4 diurnal salivary cortisol samples at home across 2 consecutive weekdays.

**Results—**High reported exposure to non-intentional trauma was associated with intact diurnal regulation but elevated cortisol at bedtime, physical abuse was associated with faster reactivity to acute stress, and emotional abuse was associated with delayed recovery of cortisol following acute stress. Taken together, there was a heterogeneous relationship among different indices of HPA-axis functioning and trauma subtype.

**Discussion—**Different types of childhood trauma exposure are related to distinct anomalies in HPA-axis functioning. This study underscores the importance of research incorporating multiple indices of HPA-axis functioning to inform our understanding of the underlying neuroendocrine dysregulation that may later lead to stress-related psychopathology.

### Keywords

Childhood trauma; Adolescent; HPA-axis; Cortisol

## 1. Introduction

Approximately 10% of children in the United States are maltreated (Finkelhor et al., 2009) and 66% report a major traumatic event before adulthood (Read et al., 2011). Exposure to



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**Conflict of interest statement**: The authors have no conflict of interest to declare.

trauma during childhood increases the risk for lifelong physical and mental health problems (Chapman et al., 2007; Dube et al., 2003). The hypothalamic—pituitary—adrenal-axis (HPA-axis) modulates multiple biological, affective, behavioral and cognitive responses to stress (Lupien et al., 2009), thus dysregulation of the HPA-axis may be one mechanism through which stress impacts health. Animals (Pryce et al., 2002) and humans (Gunnar and Quevedo, 2007) exposed to early life stress exhibit anomalies in HPA-axis functioning, although this research in youth has been equivocal. For example, trauma exposure has been linked to both diurnal HPA-axis hyper- and hypo-activity (Lupien et al., 2009; McEwen, 1998), as well as hyper- and hypo- reactivity to stress (MacMillan et al., 2009; Peckins et al., 2012; Saltzman et al., 2005; Trickett et al., 2014). The inconsistencies may be accounted for by different subtypes of childhood trauma contributing to different HPA-axis anomalies.

Traumatic events rarely occur in isolation (Finkelhor et al., 2007), yet the majority of published studies have either isolated one subtype of trauma exposure, such as parental loss (Kaplow et al., 2013) and marital violence (Saltzman et al., 2005), or collapsed subtypes of childhood trauma into a single category (e.g., adversity; Gustafsson et al., 2010). Both approaches limit our understanding of how different types of stress influence the HPA-axis. Neglect, physical abuse, and natural disaster may demand different physiological responses to promote learning and survival (Miller et al., 2007). Repeated exposure to any one of these categories could result in divergent processes (e.g., inhibiting emotional responses vs. responding quickly to a physical threat), reflecting different patterns of HPA-axis activation over time, and whose output may influence the long-term regulation of the system. Therefore, previous inconsistencies linking childhood trauma to the HPA-axis may reflect the heterogeneity of effects by different types of trauma.

The HPA-axis indices most commonly examined among youth include cortisol awakening response (CAR), diurnal regulation, and stress reactivity. These indices represent underlying neuroendocrine processes that may have different biopsychosocial meaning (Tsigos and Chrousos, 2002), but our understanding of how different types of trauma impact these indices is limited. CAR refers to a surge in cortisol following awakening and is used increasingly as a stress biomarker as it may reflect chronic, daily stress and affected physiological systems (Fries et al., 2009). In adults, greater CAR is most consistently associated with recent stress (Chida and Steptoe, 2009). Yet, surprisingly few studies have examined the relationship between childhood trauma and CAR. One study found that 1—2 adverse childhood events predicted greater CAR compared with none (Gustafsson et al., 2010), suggesting that any exposure may sensitize CAR. However, associations between number of adversities and CAR are not consistently observed (Michels et al., 2012), while singular experiences such as death of a caregiver have been linked to decreased CAR (Meinlschmidt and Heim, 2005). Thus, the previous inconsistencies may be explained by the type of childhood adversity examined which may be more critical to our understanding of the impact of stress on CAR than number of adversities.

More studies have examined the association between childhood trauma and diurnal regulation, but results have also been mixed. Cortisol follows a circadian pattern, with highest concentrations in the morning and lowest at night. Decline in cortisol throughout the day is a marker of the physiological capacity to maintain homeostasis (Tsigos and Chrousos,

2002), and deviation from this pattern is a predictor of risk for poor health (e.g., Sephton et al., 2000; Sjögren et al., 2006). Childhood maltreatment, inclusive of physical, sexual, and emotional abuse has been linked to high cortisol during the day (Cicchetti and Rogosch, 2001), specifically in the afternoon (Bevans et al., 2008; Hart et al., 1996). Similarly, children in foster care do not exhibit a decline in cortisol across the day (Linares et al., 2008), while some groups of maltreated youth do not exhibit anomalies in diurnal cortisol regulation at all (MacMillan et al., 2009; Ouellet-Morin et al., 2011). These conflicting findings may suggest that comparing maltreated and non-maltreated youth, or using a variable that collapses across multiple types of abuse and neglect does not inform our understanding of HPA-axis function or development. Thus, the simultaneous examination of trauma subtypes within the same sample may help us clarify how different types of maltreatment are associated with diurnal cortisol regulation.

Similar inconsistencies emerge among investigations of acute HPA-axis responses to stress. For example, greater cortisol reactivity to laboratory stress has been shown in school-aged youth exposed to any traumatic events (Ivanov et al., 2011), marital violence (Saltzman et al., 2005), and victims or witnesses of violence in the past year (Peckins et al., 2012). This is not surprising given the abundance of animal research suggesting sensitization of the axis in response to aversive events (Pryce et al., 2002) and that the presence of physical threat is a robust activator of the HPA-axis (Miller et al., 2007). Compared with emotional abuse and accidental trauma, physical abuse may be more likely to sensitize the axis to stressors. However, youth exposed to maltreatment, such as chronic abuse and neglect, demonstrate blunted reactivity to laboratory stress (MacMillan et al., 2009; Trickett et al., 2014). Therefore frequent exposure to adversity during childhood may accumulate to dampen the axis, although which types of stress drive this phenomenon are currently unknown. Here, we aimed to identify the contribution of physical abuse, emotional abuse, and non-intentional trauma to multiple indices of neuroendocrine functioning (CAR, diurnal regulation, acute reactivity) hypothesizing that each trauma subtype would be associated with distinct anomalies in neuroendocrine functioning such that physical abuse exposure may sensitize the HPA-axis to acute stress, while emotional abuse and neglect may be associated with impaired diurnal regulation of glucocorticoids.

## 2. Methods

### 2.1. Participants

Participants were 121 youth (51% male), ages 9—16 ($M_{age}$ = 12.8; $SD_{age}$ = 2.3) from a study aimed to characterize the mechanisms that underlie adolescent anxiety and depression. Participants were recruited from communities in and around Southeast Michigan via flyers, referrals from clinicians and primary care providers, and advertisements on websites targeting parents of adolescents who have concerns about their child's mental health. Participants in this study were 70% Caucasian, 10% biracial, 6% African American, 3% Latino, 2% Asian, 6% other, and 3% did not to respond. Participants were from educated families, where maternal education for 76% of the participants was a Bachelor's degree or higher, and 71% of youth lived in families with both biological parents. Families who were interested in participating first completed a phone screen during which their eligibility for

the study was determined. Participants were excluded from the larger study if parents indicated that the child had a history of a pervasive developmental disorder, were currently taking medications for asthma, were experiencing psychotic symptoms, or currently had any significant medical conditions. All eligible participants and their parents provided signed consent to participate in the study and all participants were compensated for their time.

## 2.2. Measures

**2.2.1. Trauma exposure—**Each child's parent completed the Early Trauma Inventory (ETI) about their child as a paper and pencil questionnaire (Bremner et al., 2007). In this inventory, the parent indicated whether their child had been exposed to 50 potentially traumatic events, when these exposures occurred, and their durations. These potentially traumatic events included four subtypes: non-intentional traumatic events such as witnessing an accident or exposure to a natural disaster; physical abuse such as being hit to the point of bruising or injury; sexual abuse such as being forced to engage in sexual acts; or emotional abuse such as persistently being ridiculed or insulted by a caregiver. This inventory produced a total score for each subtype of abuse that reflects the total number of abuse events multiplied by the frequency or duration (in years) of each of those events. Each subtype total score can be then summed to create a proxy for total trauma exposure that represents not only quantity, but chronicity and duration of trauma exposure.

**2.2.2. Clinical interview—**Following the completion of informed consent, each parent and child separately completed a semi-structured diagnostic interview (ISCA-D; Sherrill and Kovacs, 2000). These interviews were conducted by trained, advanced doctoral students who were directly supervised by a licensed clinical psychologist. These interviews were then scored by the clinician, reviewed by the licensed clinical supervisor, and discussed with a team of clinicians according to best estimate practices (Leckman et al., 1982).

## 2.3. Procedures

**2.3.1. Cortisol awakening response (CAR) and diurnal cortisol regulation—**During the week after completing the laboratory visit, each participant provided two consecutive weekdays of home saliva samples to assess for diurnal HPA-axis functioning. Samples were collected via passive drool using salivette tubes immediately after waking, 45min after waking, just before dinner, and immediately before bed. Participants were asked to refrain from eating or drinking for 1 h before each saliva sample, store saliva samples in a freezer until returning to the laboratory, and keep a log on the days of their home saliva sampling including the time each sample was taken, sleep and wake times, and whether the day included any significant stressors.

**2.3.2. Acute stress reactivity—**All visits began between 1:00pm and 4:00pm and consisted of a 30-min baseline phase, a 5-min stress task, and a 60-min regulation/recovery period for a total of 95min. Eight saliva samples were collected. *Baseline phase*. A 30-min baseline phase was used to allow for the regulation of the stress response to any stressors that occurred prior to arrival, including any stress associated with visiting a university laboratory. Participants were encouraged to read or play with puzzles and blocks during this phase and were discouraged from using their mobile phones. *Stress task*. The stress task

used in this study was the Socially-Evaluated Cold Pressor Task, which was specifically designed and validated for the activation of the HPA-axis in laboratory settings by combining thermal stress and social evaluation (Schwabe et al., 2008). In this task, participants immersed their non-dominant hand into a large bucket of ice water (33—39 °F) for up to 3 min, and were instructed to look directly into a video-camera approximately 12-in. from their face so that their "facial expressions could be recorded." A research assistant stared stoically and redirected participants' attention towards the camera if needed. If the participant removed their hand before 10s passed, the research assistant (RA) asked the participants to repeat the task until 30 s of immersion were reached. *Regulation phase*. Immediately following the stress task, participants watched one of four 60-min *National Geographic* documentaries, "Appalachian Trail", "Ocean Drifters", "The Ballad of the Irish Horse", or "Rainforest." These videos were selected for their lack of significant emotionally arousing content. *Stress reactivity*. Seven samples were collected via passive drool at 30 min before the task (−30), immediately before the task (0) and at 25, 35, 45, 55, and 65 min after the start of the task. Sixty seven percent of our participants exhibited at least a 10% increase in cortisol from baseline to peak. These times were selected because they maximize our ability to capture the cortisol peak in saliva, which are observed between 25 and 45 min post-stress initiation (Dickerson and Kemeny, 2004; Lopez-Duran et al., 2014). Samples were stored at −20 °C until assayed using an enzyme immunoassay kit (Salimetrics™). The inter-assay and intra-assay coefficients of variability were 5% and 9%, respectively. The sensitivity of the assay was .01 lg/dl. All samples from the same child were assayed in the same batch. Duplicates varying more than 15% were re-assayed. A total of 49 samples (. 02% of all study samples) had duplicate values varying more than 15%. These samples were re-assayed in duplicate, and the mean cortisol value from the 2nd assay was used. For all but 3 of the 49 samples, the second assay resulted in less than 15% variation. For those 3 samples where variation between duplicate values was >15%, the mean cortisol value results of the 2nd assay were used.

### 2.4. Data analysis

All data analyses were conducted in SPSS 20.0. Raw salivary cortisol values were transformed using the Box—Cox transformation to optimally address issues of skewness and kurtosis (Miller and Plessow, 2013). In each model, we first tested the association between sex and age on each index of HPA-axis functioning: cortisol awakening response (CAR), diurnal regulation, and acute stress reactivity. If age or sex were predictors of patterns of cortisol change even at trend levels ($p < .10$), the impact of age or sex on that pattern of cortisol regulation or reactivity was included as a covari-ate in all further models. We also examined whether there were significant associations between race/ethnicity, parent marital status, maternal education, and presence of an externalizing disorder (such as ADHD or ODD) and our indices of HPA-axis functioning. None of these were significantly associated with differences in CAR ($p > .63$), AUCi ($p > .25$), or diurnal cortisol ($p > .21$).

To determine the unique association between subtypes of childhood trauma and adolescent HPA-axis functioning, we conducted separate analyses for CAR, diurnal cortisol regulation, and acute stress reactivity. For the CAR analyses, we measured CAR magnitude across both days of collection using the regressor method (Vickers and Altman, 2001). Thus, we

conducted adjusted and unadjusted mixed linear regression models predicting the 45 min post awakening sample from the awakening samples and other factors (e.g., trauma subtypes). In the diurnal cortisol regulation analyses, we conducted unadjusted and adjusted growth curve models using linear mixed modeling predicting waking cortisol (intercept) and slope of diurnal cortisol regulation to dinner and bedtime from each trauma subtype. For all models, each subtype of trauma exposure was log transformed and centered at the mean. All models included random intercept and slopes.

To determine the association between childhood trauma subtypes and acute stress reactivity, we used a modified version of Growth Curve Analysis using landmark registration (Lopez-Duran et al., 2014), where we modeled slope of cortisol *activation* to the stress task, peak cortisol (intercept), and the slope of *recovery* from the stress task simultaneously. Landmark registration is a process of identifying each individual's peak in the stress reactivity curve and anchoring each individual's reactivity curve to this peak (Ramsay and Li, 1998), thus controlling for individual differences in peak time in response to the stress task. The mode (35%) peak cortisol was reached 45 min after the onset of our stress task. Within these stress reactivity analyses, we modeled each trauma subtype individually, and then all three trauma subtypes simultaneously. For each mixed model, we used an unstructured covariance matrix to allow for variation in the correlation between cortisol at different samples, accounted for the impact of baseline cortisol on stress reactivity, and the random effects for every model were the intercept and the linear slope of that specific model.

## 3. Results

### 3.1. Childhood trauma exposure and adolescent HPA-axis functioning

Per parent report, 85% of youth in our sample were exposed to at least one traumatic event where 71% reported at least one non-intentional trauma, 48% reported at least one incident of physical abuse, 31% reported at least one emotional abuse experience, and 6% of our sample reported at least one sexual abuse experience. Among the participants exposed to non-intentional trauma, the most frequently endorsed non-intentional traumatic events were: serious personal injury or illness (25%), family mental illness (24%), separation or divorce of parents (20%), death of a friend (18%), and witnessing violence (14%). See Table 1 for descriptive information correlations between study variables. There were no sex differences in exposure to physical abuse, $F(1, 110) = 1.81$, $p = 18$, emotional abuse, $F(1,112) = .15$, $p = 69$, or non-intentional trauma, $F(1, 100) = .35$, $p = 35$.

### 3.2. Trauma exposure and cortisol awakening response

We examined whether frequency or duration of trauma subtypes were associated with CAR using unadjusted and adjusted models where abuse subtypes were included as predictors of cortisol 45 min after awakening while controlling for awakening levels. Age and sex were not significant predictors of awakening response ($p > .10$). Therefore age and sex were not included in any of the subsequent models predicting CAR. In unadjusted models, physical and emotional abuse were not associated with the CAR, $p = .23$ and $p = .09$, while non-intentional trauma was associated with a greater CAR, $b = .20$, $t(91) = 2.24$, $p = .02$.

However, in an adjusted model accounting for all three types of trauma simultaneously, the effect of non-intentional trauma exposure was not significant, $b = .16$, $t(90) = 1.57$, $p = .12$.

**3.2.1. Trauma exposure and diurnal cortisol regulation—**We first examined unconditional linear and quadratic growth models of diurnal cortisol using waking cortisol as the intercept. The quadratic model was the best fit to the data (linear model AIC = 310.8 vs. quadratic model AIC = 309.7). There was a linear decrease in cortisol over time, Time $b = -.068$, $t(122.1) = -5.57$, $p < .001$, but this decrease decelerated later in the day, Time$^2$ $b = .001$, $t(102.5) = 1.77$, $p = .08$, suggesting that the decline in cortisol throughout the day became less pronounced between dinner and bedtime. Sex did not impact cortisol at wakening or the linear decline of diurnal cortisol. However, males showed less deceleration of the diurnal decline later in the day (between dinner and bedtime) than females, Sex × Time$^2$ $b = -.003$, $t(97.5) = -2.09$, $p = .04$. Age was not associated with waking cortisol (intercept) or cortisol trajectory throughout the day. Therefore, in all further diurnal cortisol models, we included the effects of sex on the intercept and slopes of diurnal cortisol as covariates.

Table 2 presents the results of the unadjusted models of trauma subtypes predicting diurnal cortisol. Physical and emotional abuse did not impact cortisol upon waking (intercept) or the diurnal trajectory. In contrast, non-intentional trauma exposure was associated with a steeper linear decline during the day, Non-Intentional × Time $b = -.037$, $t$ (103.3) = −2.36, $p = 02$, and a greater deceleration between dinner and bedtime, Non-Intentional × Time$^2$ $b = .002$, $t(88.0) = 2.16$, $p = 03$, leading to greater cortisol at bedtime among those exposed to non-intentional trauma (See Fig. 1).

In fully adjusted models, we found no associations between physical or emotional abuse on waking cortisol or cortisol trajectories over time, while non-intentional trauma exposure continued to impact the linear decline, Non-Intentional × Time $b = -.044$, $t(102.3) = -2.49$, $p = .015$, and later deceleration over time, Non-Intentional × Time$^2$ $b = .002$, $t(87.2) = 2.19$, $p = .03$.

### 3.3. Trauma exposure and acute stress reactivity

We first examined cortisol trajectories without predictors from the start of the task towards and away from the peak (intercept). A model with quadratic slopes of activation and recovery was the best fit to the data (linear model AIC = −343.9 vs. quadratic model AIC = −399.4). Cortisol values increased linearly toward the peak, Time $b = .007$, $t(405.1) = 5.97$, $p < .001$, and this increase accelerated over time, Time$^2$ $b = .0002$, $t(411.2) = 6.82$, $p < .001$. Cortisol values decreased linearly away from the peak, Time $b = -.013$, $t(480.5) = -9.63$, $p < .001$, and this decrease decelerated overtime, Time$^2$ $b = .0002$, $t(463.8) = 5.27$, $p < .001$.We then conducted conditional unadjusted models for age and sex. Age and sex were not associated with peak cortisol or slopes of activation and recovery, and thus were not included in subsequent models.

In unadjusted models, more physical abuse was related to greater acceleration as individuals approached their peaks, PA × Time$^2$ $b = .0001$, $t(439.5) = 2.41$, $p = .02$, but physical abuse was not related to peak cortisol, PA $b = .024$, $t(123.3) = .66$, $p = .51$. Physical abuse

exposure was also not associated with differences in the linear or quadratic decline of cortisol away from peak, PA × Time $b$ = .002, $t$(462.5) = 1.36, $p$ = .18 and PA × Time$^2$ $b$ = .0001, $t$(469.9) = −1.49, $p$ = .14. This suggests that PA was associated with a more intense activation but it did not impact peak levels or recovery slopes. Emotional abuse was not related to differences in the peak response to the task, EA $b$ = −.006, $t$(121.8) = −.21, $p$ = .84, or changes in cortisol approaching those peaks, EA × Time $b$ = −.001, $t$(355.9) = −.40, $p$ = .69 and EA × Time$^2$ $b$ = −.00001, $t$(443.6) = −.30, $p$ = .77. However, emotional abuse was related to less deceleration of cortisol over time during the post-peak recovery, EA × Time$^2$ $b$ = −.0001, $t$(470.7) = −2.18, $p$ = .03. This suggests that EA was associated with a longer time to recovery. Non-intentional trauma was not related to linear, Non-Intentional × Time $b$ = −.001, $t$(337.4) = −.50, $p$ = .62, or quadratic slope of cortisol increase to peak, Non-Intentional × Time$^2$ $b$ = .00001, $t$(407.7) = .33, $p$ = .74, peak values, Non-Intentional $b$ = −.032, $t$(110.8) = −.94, $p$ = .35, or differences in the decline in cortisol from peak, Non-Intentional × Time $b$ = .001, $t$(412.6) = .57, $p$ = .57 or Non-Intentional × Time$^2$ $b$ = −.00001, $t$(414.9) = −.14, $p$ = .89, respectively.

Table 3 presents the results of the adjusted model of the HPA-axis response to acute stressors. Consistent with the unadjusted models, higher reported physical abuse continued to be associated with steeper acceleration of cortisol toward peak after accounting for exposure to emotional abuse and non-intentional trauma. Likewise, more emotional abuse exposure continued to be associated with less deceleration of cortisol during the recovery phase, again suggesting that youth exposed to more emotional abuse in this sample exhibited elevated cortisol longer than their peers (See Fig. 2).

## 4. Discussion

In this study, we characterized the association between different types of childhood trauma exposure and HPA-axis functioning. More non-intentional trauma exposure was associated with greater CAR, however not when controlling for exposure to physical and emotional abuse. Youth with reported exposure to more non-intentional trauma throughout their childhood demonstrated a steeper decline in cortisol from morning to evening, and higher cortisol at bedtime compared to youth with less exposure to non-intentional trauma. Furthermore, more physical abuse was associated with a more accelerated HPA-axis activation to our stress task. Additionally, more emotional abuse was associated with a less intense post-peak recovery leading to higher cortisol during the recovery period. Overall, our findings suggest that different subtypes of childhood trauma exposure are associated with distinct anomalies in HPA-axis functioning, which are not better accounted for by age, sex, or depression. These findings may explain previous inconsistencies in findings linking trauma and HPA-axis in childhood and can provide insight into the mechanisms by which trauma may modulate long term changes in HPA-axis functioning.

Exposure to physical and emotional abuse were not associated with CAR in this sample, while non-intentional traumatic events were associated with higher CAR, although only when not accounting for other forms of childhood trauma. This suggests that high reported exposure to stress during childhood may not be associated with factors that underlie CAR variability among adolescents. In the past, high reported exposure to physical abuse and

neglect has been related to blunted CAR among 12—13 year old post-institutionalized youth, but only for those who were in the pre- or early stages of puberty compared with youth in the mid- to late stages (Quevedo et al., 2012). Additionally, parentally bereaved children (aged 7—12) exhibited blunted CAR if they were also experiencing symptoms of depression or anxiety (Kaplow et al., 2013). The lack of association between childhood trauma subtypes and CAR may have been due to the older age of our sample compared with previous studies, or the lower incidence of psychopathology, however we observed no associations in this sample between age or psychopathology and CAR. Given that our sample endorsed mostly very distal events (mean age = 4.22 years, SD = 3.4), it is also possible that elevated CAR is more closely related to recent or ongoing stress as is the case among adults samples (Chida and Steptoe, 2009), rather than distal stress.

We found that reported exposure to more non-intentional traumatic events was associated with anomalies in diurnal regulation of cortisol, while physical and emotional abuse were not. Specifically, youth with high reported exposure to non-intentional traumatic events demonstrated a steeper decline in cortisol from morning to evening but elevated cortisol at bedtime. The presence of elevated cortisol at night may indicate chronic anticipatory anxiety that accompanies living in an unpredictable environment, similar to those with community violence or insufficient caregiving. This is in contrast to unsafe environments that are predictable, such as those marked with repeated physical abuse potentially resulting in different physiological responses. In the absence of other indicators of diurnal dysregulation, cortisol elevation at bedtime among youth exposed to more non-intentional traumatic events may indicate increased stress associated with separation from parents, fear of the dark at bedtime, or difficulties falling or staying asleep, which may be a consequence of chronic sleep problems (e.g., insomnia; Vgontzas et al., 2001), secondary to living under conditions of unpredictable stress. Exposure to unpredictable non-intentional traumatic stress during childhood may also result in physiological alterations to the circadian regulation of the HPA-axis that lead to impaired down-regulation of cortisol at the end of the day (see Buckley and Schatzberg, 2005 for a review).

In the reactivity task, more exposure to physical abuse was associated with a steeper activation slope, which is consistent with previous studies showing that childhood exposure to violence is associated with hyperreactivity to acute stress (Ivanov et al., 2011; Peckins et al., 2012; Saltzman et al., 2005), and extends these findings to adolescents. Furthermore, physical abuse was not associated with peak cortisol, suggesting that physical abuse does not impact regulatory processes associated with the deactivation of the response and the recovery after peak. Specifically, the rapid activation of the HPA-axis likely also resulted in a more rapid activation of regulatory systems (as expected in an intact system; see Lopez-Duran et al., 2014), preventing youth exposed to physical abuse from reaching greater peaks than their peers. Thus the impact of physical abuse appears to be specific to excitatory processes. Although our data do not speak to the mechanisms, at least two potential processes merit further study. Exposure to repeated physical abuse may facilitate enhanced cognitive processing of threat in the environment (Gaab et al., 2005), thus enabling the HPA-axis to respond more rapidly in the presence of stress. Alternatively, repeated activation of the HPA-axis during physical abuse may lead to sensitization or priming of the axis (e.g., greater pituitary sensitivity to CRH, or adrenal sensitivity to ACTH), resulting in

faster secretion of cortisol early in the stress response. For example, in an animal model of stress sensitivity, exposure to a single inescapable stressor sensitized the glucocorticoid response to stress for up to 10 days (Johnson et al., 2002).

We also found that emotional abuse was associated with a slower decline in cortisol following peak responses to acute stress. That is, emotional abuse was uniquely associated with less efficient recovery of the HPA-axis after stress. Given that emotional abuse is unlikely to occur in the absence of other forms of trauma, very few studies have focused on the association between emotional abuse and HPA-axis functioning while controlling for other types of abuse. Adults reporting exposure to emotional abuse during childhood demonstrate a blunted response to the DST/CRH test (Carpenter et al., 2009), which is inconsistent with our present findings. However, Carpenter etal. (2009) suggested that this finding may become apparent with older age as the interpersonal difficulties perpetuated by being emotionally abused contribute to more subsequent interpersonal stress across the lifespan. However, impaired down-regulation of the HPA-axis response to acute stress has been previously shown in children exposed to low maternal warmth (Kuhlman et al., 2014). Maternal care behaviors in rodents are related to increased density of glucocorticoid receptors (GRs) in the brain which facilitate down-regulation of the stress response, while maternal separation leads to lower GR density (Meaney, 2001). Similarly, maternal depression during pregnancy is associated with variability in the methylation of GR genes and hypersecretion of cortisol during infancy (Oberlander et al., 2008). This may lead to impaired HPA-axis regulatory processes. Taken together, emotional abuse, compared with physical abuse and non-intentional trauma, may represent HPA-axis functioning in the absence of maternal warmth. It is possible that emotional abuse has an impact on GR-mediated regulatory processes resulting in a less efficient regulatory system, which can prolong the exposure to higher levels of cortisol during recovery.

Finally, previous studies linking childhood trauma and HPA-axis have varied significantly in critical methodological factors that may contribute to past inconsistencies, ranging from the assessment of adversity, to the inclusion/exclusion of participants with psychiatric diagnoses. For example, among the studies examining childhood trauma and CAR, two of the three studies used measures of childhood life stress that were limited to socioeconomic adversity or exposure to unpredictable, non-intentional trauma (Gustafsson et al., 2010; Michels et al., 2012), while the other only examined loss of a caregiver (Meinlschmidt and Heim, 2005). Furthermore, the study by Michels et al. (2012) only included events occurring within the past year. Therefore, no study of CAR to date accounted for domains of maltreatment, such as abuse, likely obscuring clarity in their findings. Similarly, among studies aimed at clarifying the role of maltreatment in HPA-axis development, inconsistencies in the literature may be accounted for by the recruitment procedure. Early investigations of diurnal cortisol in maltreated youth have relied upon dichotomous categorization of maltreated and non-maltreated youth conducted with post-institutionalized youth (Kertes etal., 2008), foster children (Linares et al., 2008), and children participating in day camps for disadvantaged youth (Cicchetti and Rogosch, 2001), who may all systematically differ in type and distribution of trauma exposure in childhood. Finally, the presence of psychopathology has likely been a source of considerable variability. For example, several studies have shown that psychopathology moderates the association

between trauma exposure and HPA-axis dysregulation (Harkness et al., 2011; Hart et al., 1996), while many studies to date have excluded youth from studies for the presence of psychopathology (e.g., Ivanov et al., 2011) or did not account for symptoms in their models of HPA-axis functioning (e.g., Saltzman et al., 2005). Therefore, the present study addresses these past limitations by assessing child trauma exposure in multiple domains, used trauma exposure as a continuous predictor, and recruited a community sample with a wide range in age, while accounting for the presence of psychopathology.

### 4.1. Limitations

The contribution of these findings should be considered within the context of several strengths and limitations. First, this study is cross-sectional and no causality can be inferred. Our theoretical model implies that exposure to childhood trauma influences later HPA-axis functioning, however it is also possible that individual differences in physiological stress reactivity may play a role in the generation of stressful experiences from the environment. We did not collect data on pubertal status which has been identified as a critical contributor to HPA-axis functioning (Gunnar et al., 2009; Hankin et al., 2010), specifically post-pubertal female gonadal hormones are thought to regulate the HPA-axis (Kirschbaum et al., 1999), and puberty may be a devel-opmentally critical period for the reprogramming of the HPA-axis following early care experiences (Quevedo et al., 2012). For example, studies conducted specifically to disentangle differences in diurnal cortisol regulation and pubertal status have found divergence between males and females that increased after puberty (e.g., Netherton et al., 2004). We attempted to account for some of this variability by accounting for age and sex in all of our models, however future efforts at replication of these findings would benefit from directly assessing pubertal status among youth. Furthermore, we did not examine the role that age of trauma onset may play in the association between childhood trauma and HPA-axis functioning and acknowledge that there may be key developmental factors involved that warrant further investigation. Childhood trauma exposure was provided retrospectively by the parents of our participants. More than 80% of child abuse and neglect is perpetrated by primary caregivers (Sedlak et al., 2010), therefore rates of abuse and neglect may be under-reported here. However, reports of abuse and trauma exposure in our sample did not differ from nationally representative studies (Flaherty et al., 2009). No objective methods were used to assess the integrity of the timing of diurnal cortisol samples beyond self-report. Therefore, it is possible that HPA-axis indices such as the CAR which are highly sensitive to timing in relation to waking are not accurate reflections of the CAR. Replication of these diurnal findings should be conducted using objective measures of insuring the validity of these data. The SE-CPT was selected for this study to confine the psychosocial stressor to fewer than 5min. This confers advantages for interpreting the timing of HPA-axis activation based on slopes to and from peak cortisol. However, this is the first study to our knowledge to use the SE-CPT in a youth sample, where most existing studies have used the TSST-C (Buske-Kirschbaum et al., 1997), and it will be important to replicate these findings using other tasks. Our response rate to this task (67%) was comparable to that of the original validation of the task in adults (70%; Schwabe et al., 2008) and similar to those obtained in adults and children with the TSST-C (60—70%; Foley and Kirschbaum, 2010; Gunnar etal., 2009), therefore our studies suggests that the SE-CPT may be a viable, short, and cost effective option for acute HPA-axis research in adolescents in the future.

Finally, this study was composed of mostly Caucasian participants, with in-tact families and educated parents which was consistent with the composition of the local community. Therefore, future investigations should be conducted to test these associations in other geographic locations with more diversity.

### 4.2. Conclusions

To date, this is the first study to characterize the profiles of neuroendocrine functioning associated with the duration and frequency of different types of childhood trauma exposure. Specifically, repeated exposure to physical abuse may influence the sensitivity of HPA-axis *activation* to stress in the environment, chronic emotional abuse may impair the *recovery* of that acute stress response, and cumulative unpredictable stress may disrupt regulatory ability around specific, daily stressors such as bedtime or may impact mechanisms responsible for circadian regulation. Previous investigations of the HPA-axis dysregulation associated with childhood trauma exposure have been limited by two methodological factors: examination of only one index of HPA-axis functioning and not examining childhood stress by subtype. Our findings have several important implications. First, we found consistent associations between subtypes of abuse and HPA-axis functioning in our unadjusted models as well as when accounting for exposure to other forms of trauma. This is further evidence that different subtypes of trauma have unique associations with HPA-axis functioning and that stress during childhood is a heterogeneous construct. Methodologically, the findings of this study emphasize the importance of assessing multiple indices of HPA-axis functioning according to the recommendations described in Clements (2012). Additionally, many previous studies examining the relationship between childhood trauma and HPA-axis dysregulation have collapsed across several forms of childhood stress (e.g., maltreatment). Our findings emphasize the importance of assessing multiple forms of childhood trauma in future studies in order to differentiate which childhood trauma experiences play a role in specific profiles of HPA-axis functioning that may have implications for health. As more clarity on the HPA-axis dysregulation that develops as a function of childhood trauma exposure emerges, more nuanced considerations can be made regarding other potential moderators, such as age of onset and psychopathology. For example, age of trauma exposure has been associated with structural and functional differences in the central nervous system (Andersen and Teicher, 2008), suggesting that age of onset will be an important consideration to make in future studies on the association between childhood trauma exposure and HPA-axis functioning.

## Acknowledgments

This research was funded by the Blue Cross Blue Shield of Michigan Foundation, Barabara A. Oleshansky Memorial Award, American Psychological Foundation Elizabeth Munsterberg-Koppitz Award, and The University of Michigan Rackham Graduate School. We also thank the faculty and fellows of the International Max Planck Research School “The Life Course: Evolutionary and Ontogenetic Dynamics” for valuable feedback on this work.

**Role of the funding source**: The sponsors of this research had no involvement in study design, data collection, analysis or interpretation of data, composition of this manuscript, or the decision to submit the article for publication.

## References


Andersen SL, Teicher MH. Stress, sensitive periods and maturational events in adolescent depression. Trends Neurosci. 2008; 31:183–191. http://dx.doi.org/10.1016/j.tins.2008.01.004. [PubMed: 18329735]

Bevans K, Cerbone A, Overstreet S. Relations between recurrent trauma exposure and recent life stress and salivary cortisol among children. Dev Psychopathol. 2008; 20:257. http://dx.Doi.org/10.1017/S0954579408000126. [PubMed: 18211737]

Bremner JD, Bolus R, Mayer EA. Psychometric properties of the early trauma inventory-self report. J Nerv Ment Dis. 2007; 195:211–218. http://dx.doi.org/10.1097/01.nmd.0000243824.84651.6c. [PubMed: 17468680]

Buckley TM, Schatzberg AF. On the interactions of the hypothalamic—pituitary—adrenal (HPA) axis and sleep: normal HPA axis activity and circadian rhythm, exemplary sleep disorders. JCEM. 2005; 90:3106–3114. http://dx.doi.org/10.1210/jc.2004-1056. [PubMed: 15728214]

Buske-Kirschbaum A, Jobst S, Wustmans A, Kirschbaum C, Rauh W, Hellhammer D. Attenuated free cortisol response to psychosocial stress in children with atopic dermatitis. Psychosom Med. 1997; 59:419–426. [PubMed: 9251162]

Carpenter LL, Tyrka AR, Ross NS, Khoury L, Anderson GM, Price LH. Effect of childhood emotional abuse and age on cortisol responsivity in adulthood. Biol Psychiatry. 2009; 66:69–75. http://dx.doi.org/10.1016/j.biopsych.2009.02.030. [PubMed: 19375070]

Chapman DP, Dube SR, Anda RF. Adverse childhood events as risk factors for negative mental health outcomes. Psyc-hiatr Ann. 2007; 37:359–364.

Chida Y, Steptoe A. Cortisol awakening response and psychosocial factors: a systematic review and meta-analysis. Biol Psychol. 2009; 80:265–278. http://dx.doi.org/10.1016/j.biopsycho.2008.10.004. [PubMed: 19022335]

Cicchetti D, Rogosch FA. Diverse patterns of neuroendocrine activity in maltreated children. Dev Psychopathol. 2001; 13:677–693. http://dx.doi.org/10.1017/S0954579401003145. [PubMed: 11523854]

Clements AD. Salivary cortisol measurement in developmental research: where do we go from here? Dev Psychobiol. 2012; 55:205–220. http://dx.doi.org/10.1002/dev.21025. [PubMed: 22488016]

Dickerson SS, Kemeny ME. Acute stressors and cortisol responses: a theoretical integration and synthesis of laboratory research. Psychol Bull. 2004; 130:355–391. http://dx.doi.org/10.1037/0033-2909.130.3.355. [PubMed: 15122924]

Dube SR, Felitti VJ, Dong M, Giles WH, Anda RF. The impact of adverse childhood experiences on health problems: evidence from four birth cohorts dating back to 1900. Prev Med. 2003; 37:268–277. http://dx.doi.org/10.1016/S0091-7435(03)00123-3. [PubMed: 12914833]

Finkelhor D, Ormrod RK, Turner HA. Poly-victimization: a neglected component in child victimization. Child Abuse Negl. 2007; 31:7–26. http://dx.doi.org/10.1016/j.chiabu.2006.06.008. [PubMed: 17224181]

Finkelhor D, Turner H, Ormrod R, Hamby SL. Violence, abuse, and crime exposure in a national sample of children and youth. Pediatrics. 2009; 124:1411–1423. http://dx.doi.org/10.1542/peds.2009-0467. [PubMed: 19805459]

Flaherty EG, Thompson R, Litrownik AJ, Zolotor AJ, Dubowitz H, Runyan DK, English DJ, Everson MD. Adverse childhood exposures and reported child health at age 12. Acad Pediatr. 2009; 9:150–156. http://dx.doi.org/10.1016/j.acap.2008.11.003. [PubMed: 19450774]

Foley P, Kirschbaum C. Human hypothalamus— pituitary—adrenal axis responses to acute psychosocial stress in laboratory settings. Neurosci Biobehav Rev. 2010; 35:91. [PubMed: 20109491]

Fries E, Dettenborn L, Kirschbaum C. The cortisol awakening response (CAR): facts and future directions. Int J Psychophysiol. 2009; 72:67–73. http://dx.doi.org/10.1016/j.ijpsycho.2008.03.014. [PubMed: 18854200]

Gaab J, Rohleder N, Nater UM, Ehlert U. Psychological determinants of the cortisol stress response: the role of anticipatory cognitive appraisal. Psychoneuroendocrinology. 2005; 30:599–610. http://dx.doi.org/10.1016/j.psyneuen.2005.02.001. [PubMed: 15808930]

Gunnar, MR.; Quevedo, KM. Early care experiences and HPA axis regulation in children: a mechanism for later trauma vulnerability. In: De Kloet, R.; Oitzl, MS.; Vermetten, E., editors. Progress in Brain Research. Elsevier B.V.; Amsterdam, The Netherlands: 2007. p. 137-149.

Gunnar MR, Talge NM, Herrera A. Stressor paradigms in developmental studies: what does and does not work to produce mean increases in salivary cortisol. Psychoneu-roendocrinology. 2009; 34:953–967. http://dx.doi.org/10.1016/j.psyneuen.2009.02.010.

Gustafsson PE, Anckarsäter H, Lichtenstein P, Nelson N, Gustafsson PA. Does quantity have a quality all its own? Cumulative adversity and up- and down-regulation of circadian salivary cortisol levels in healthy children. Psychoneuroendocrinology. 2010; 35:1410–1415. http://dx.doi.org/10.1016/j.psyneuen.2010.04.004. [PubMed: 20444551]

Hankin BL, Badanes LS, Abela JRZ, Watamura SE. Hypothalamic—pituitary—adrenal axis dysregulation in dysphoric children and adolescents: cortisol reactivity to psychosocial stress from preschool through middle adolescence. Biol Psychiatry. 2010; 68:484–490. http://dx.doi.org/10.1016/j.biopsych.2010.04.004. [PubMed: 20497900]

Harkness KL, Stewart JG, Wynne-Edwards KE. Cortisol reactivity to social stress in adolescents: role of depression severity and child maltreatment. Psychoneuroendocrinology. 2011; 36:173–181. http://dx.doi.org/10.1016/j.psyneuen.2010.07.006. [PubMed: 20688438]

Hart J, Gunnar M, Cicchetti D. Altered neuroendocrine activity in maltreated children related to symptoms of depression. Dev Psychopathol. 1996; 8:201–214. http://dx.doi.org/10.1017/S0954579400007045.

Ivanov I, Yehuda R, Greenblatt E, Davidow J, Makotkine I, Alfi L, Newcorn JH. The effect of trauma on stress reactivity in aggressive youth. Psychiatr Res. 2011; 189:396–402. http://dx.doi.org/10.1016/j.psychres.2011.05.046.

Johnson JD, O'Connor KA, Deak T, Spencer RL, Watkins LR, Maier SF. Prior stressor exposure primes the HPA axis. Psychoneuroendocrinology. 2002; 27:353–365. http://dx.doi.org/10.1016/S0306-4530(01)00057-9. [PubMed: 11818171]

Kaplow JB, Shapiro DN, Wardecker BM, Howell KH, Abelson JL, Worthman CM, Prossin AR. Psychological and environmental correlates of HPA axis functioning in parentally bereaved children: preliminary findings. J Trauma Stress. 2013; 26:233–240. http://dx.doi.org/10.1002/jts.21788. [PubMed: 23526635]

Kertes DA, Gunnar MR, Madsen NJ, Long JD. Early deprivation and home basal cortisol levels: a study of internationally adopted children. Dev Psychopathol. 2008; 20:473–491. http://dx.doi.org/10.1017/S0954579408000230. [PubMed: 18423090]

Kirschbaum C, Kudielka BM, Gaab J, Schommer NC, Hellhammer DH. Impact of gender, menstrual cycle phase, and oral contraceptives on the activity of the hypothalamus—pituitary—adrenal axis. Psychosom Med. 1999; 61:154–162. [PubMed: 10204967]

Kuhlman KR, Olson SL, Lopez-Duran NL. The development of preadolescent internalizing symptoms: examining the interplay between parenting and neuroendocrine stress reactivity. Dev Psychobiol. 2014; 56:908–923. http://dx.doi.org/10.1002/dev.21166. [PubMed: 24009085]

Leckman JF, Sholomskas D, Thompson D, Belanger A, Weiss-man MM. Best estimate of lifetime psychiatric diagnosis: a methodological study. Arch Gen Psychiatry. 1982; 39:879–883. [PubMed: 7103676]

Linares LO, Stovall-McClough KC, Li M, Morin N, Silva R, Albert A, Cloitre M, et al. Salivary cortisol in foster children: a pilot study. Child Abuse Negl. 2008; 32:665–670. http://dx.doi.org/10.1016/j.chiabu.2007.06.012. [PubMed: 18582935]

Lopez-Duran NL, Mayer SE, Abelson JL. Modeling neuroendocrine stress reactivity in salivary cortisol: adjusting for peak latency variability. Stress. 2014; 17:285–295. http://dx.doi.org/10.3109/10253890.2014.915517. [PubMed: 24754834]

Lupien SJ, McEwen BS, Gunnar MR, Heim C. Effects of stress throughout the lifespan on the brain, behaviour and cognition. Nat Rev Neurosci. 2009; 10:434–445. http://dx.doi.org/10.1038/nrn2639. [PubMed: 19401723]

MacMillan HL, Georgiades K, Duku EK, Shea A, Steiner M, Niec A, Tanaka M, Gensey S, Spree S, Vella E, Walsh CA, De Bellis MD, Van der Meulen J, Boyle MH, Schmidt LA. Cortisol response to stress in female youths exposed to childhood maltreatment: results of the youth mood project.

Biol Psychiatry. 2009; 66:62–68. http://dx.doi.org/10.1016/j.biopsych.2008.12.014. [PubMed: 19217075]

McEwen BS. Stress, adaptation, and disease: allosta-sis and allostatic load. Ann N Y Acad Sci. 1998; 840:33–44. http://dx.doi.org/10.1111/j.1749-6632.1998.tb09546.x. [PubMed: 9629234]

Meaney MJ. Maternal care, gene expression, and the transmission of individual differences in stress reactivity across generations. Annu Rev Neurosci. 2001; 24:1161–1192. http://dx.doi.org/10.1146/annurev.neuro.24.1.1161. [PubMed: 11520931]

Meinlschmidt G, Heim C. Decreased cortisol awakening response after early loss experience. Psychoneuroendocrinology. 2005; 30:568–576. http://dx.doi.org/10.1016/j.psyneuen.2005.01.006. [PubMed: 15808926]

Michels N, Sioen I, Huybrechts I, Bammann K, Vanaelst B, De Vriendt T, Iacoviello L, Konstabel K, Ahrens W, DeHenauw S. Negative life events, emotions and psychological difficulties as determinants of salivary cortisol in Belgian primary school children. Psychoneuroendocrinology. 2012; 37:1506–1515. http://dx.doi.org/10.1016/j.psyneuen.2012.02.004. [PubMed: 22385686]

Miller GE, Chen E, Zhou ES. If it goes up, must it come down? Chronic stress and the hypothalamic—pituitary—adrenocortical axis in humans. Psychol Bull. 2007; 133:25. [PubMed: 17201569]

Miller R, Plessow F. Transformation techniques for cross-sectional and longitudinal endocrine data: application to salivary cortisol concentrations. Psychoneuroendocrinology. 2013; 38:941–946. http://dx.doi.org/10.1016/j.psyneuen.2012.09.013. [PubMed: 23063878]

Netherton C, Goodyer I, Tamplin A, Herbert J. Salivary cortisol and dehydroepiandrosterone in relation to puberty and gender. Psychoneuroendocrinology. 2004; 29:125–140. http://dx.doi.org/10.1016/S0306-4530(02)00150-6. [PubMed: 14604596]

Oberlander TF, Weinberg J, Papsdorf M, Grunau R, Misri S, Devlin AM. Prenatal exposure to maternal depression, neonatal methylation of human glucocorticoid receptor gene (NR3C1) and infant cortisol stress responses. Epigenetics. 2008; 3:97–106. http://dx.doi.org/10.4161/epi.3.2.6034. [PubMed: 18536531]

Ouellet-Morin I, Odgers CL, Danese A, Bowes L, Shakoor S, Papadopoulos AS, Caspi A, Moffitt TE, Arseneault L. Blunted cortisol responses to stress signal social and behavioral problems among maltreated/bullied 12-year-old children. Biol Psychiatry. 2011; 70:1016–1023. http://dx.doi.org/10.1016/j.biopsych.2011.06.017. [PubMed: 21839988]

Peckins MK, Dockray S, Eckenrode JL, Heaton J, Susman EJ. The longitudinal impact of exposure to violence on cortisol reactivity in adolescents. J Adoles Health. 2012; 51:366–372. http://dx.doi.org/10.1016/j.jadohealth.2012.01.005.

Pryce CR, Rüedi-Bettschen D, Dettling AC, Feldon J. Early life stress: long-term physiological impact in rodents and primates. Physiology. 2002; 17:150–155. http://dx.doi.org/10.1152/nips.01367.2001.

Quevedo K, Johnson AE, Loman ML, LaFavor TL, Gunnar M. The confluence of adverse early experience and puberty on the cortisol awakening response. Int J Behav Dev. 2012; 36:19–28. http://dx.doi.org/10.1177/0165025411406860. [PubMed: 22383860]

Ramsay JO, Li X. Curve registration. J R Stat Soc: Ser, B (Stat Methodol). 1998; 60:351–363. http://dx.doi.org/10.1111/1467-9868.00129.

Read JP, Ouimette P, White J, Colder C, Farrow S. Rates of DSM—IV—TR trauma exposure and posttraumatic stress disorder among newly matriculated college students. Psychol Trauma: Theor Res Pract Policy. 2011; 3:148–156. http://dx.doi.org/10.1037/a0021260.

Saltzman KM, Holden GW, Holahan CJ. The psychobiology of children exposed to marital violence. J Clin Child Adolesc Psychol. 2005; 34:129–139. http://dx.doi.org/10.1207/s15374424jccp3401_12. [PubMed: 15677287]

Schwabe L, Haddad L, Schachinger H. HPA axis activation by a socially evaluated cold-pressor test. Psychoneuroendocrinology. 2008; 33:890–895. http://dx.doi.org/10.1016/j.psyneuen.2008.03.001. [PubMed: 18403130]

Sedlak, AJ.; Mettenburg, J.; Basena, M.; Peta, I.; McPherson, K.; Greene, A. Fourth National Incidence Study of Child Abuse and Neglect (NIS-4). Vol. 9. US Department of Health and Human Services; Washington, DC: 2010. p. 2010

Sephton SE, Sapolsky RM, Kraemer HC, Spiegel D. Diurnal cortisol rhythm as a predictor of breast cancer survival. JNCI J Natl Cancer Inst. 2000; 92:994–1000. http://dx.doi.org/10.1093/jnci/92.12.994.

Sherrill JT, Kovacs M. Interview schedule for children and adolescents (ISCA). J Am Acad Child Adoles Psychiatr. 2000; 39:67–75. http://dx.doi.org/10.1097/00004583-200001000-00018.

Sjögren E, Leanderson P, Kristenson M. Diurnal saliva cortisol levels and relations to psychosocial factors in a population sample of middle-aged swedish men and women. Int J Behav Med. 2006; 13:193–200. http://dx.doi.org/10.1207/s15327558ijbm1303_2. [PubMed: 17078769]

Trickett, PK.; Gordis, E.; Peckins, MK.; Susman, EJ. Stress reactivity in maltreated and comparison male and female young adolescents. Child Maltreat. 2014. http://dx.doi.org/10.1177/1077559513520466

Tsigos C, Chrousos GP. Hypothalamic—pituitary—adrenal axis, neuroendocrine factors and stress. J Psychosom Res. 2002; 53:865–871. http://dx.doi.org/10.1016/S0022-3999(02)00429-4. [PubMed: 12377295]

Vgontzas AN, Bixler EO, Lin HM, Prolo P, Mastorakos G, Vela-Bueno A, Kales A, Chrousos GP. Chronic insomnia is associated with nyctohemeral activation of the hypothalamic—pituitary—adrenal axis: clinical implications. J Clin Endocrinol Metab. 2001; 86:3787–3794. [PubMed: 11502812]

Vickers AJ, Altman DG. Analysing controlled trials with baseline and follow up measurements. BMJ. 2001; 323:1123–1124. [PubMed: 11701584]

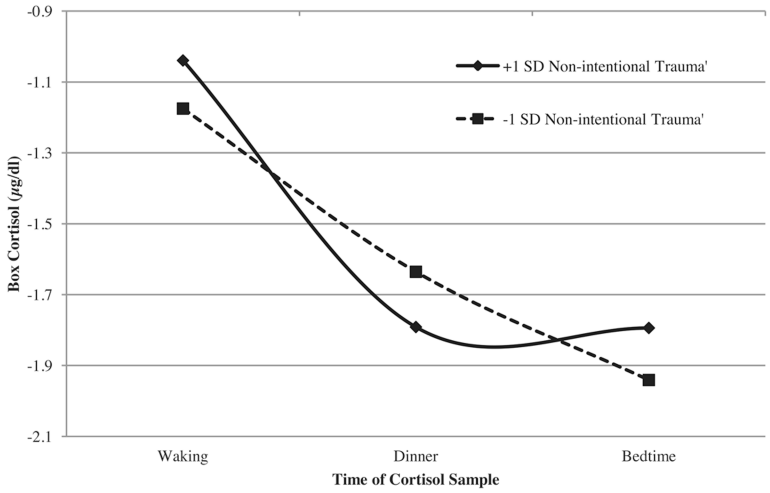


**Fig. 1.**

Diurnal cortisol regulation comparing youth with high and low exposure to non-intentional trauma during childhood.

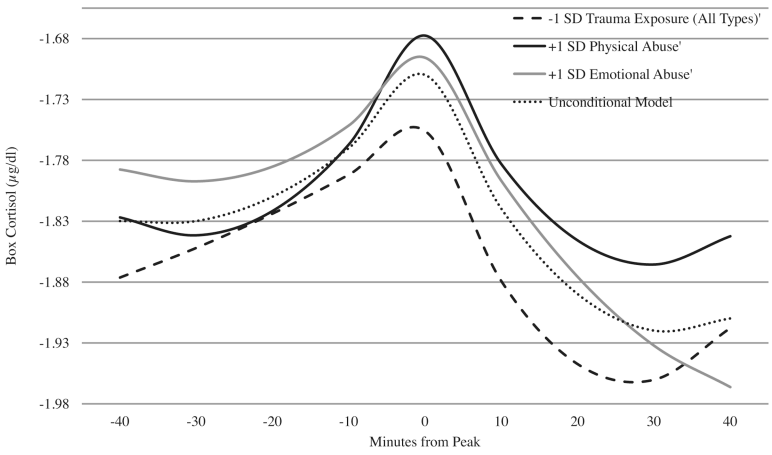


**Fig. 2.**

Adjusted growth curve model for HPA-axis activation to and recovery from to peak cortisol by childhood abuse exposure.

**Table 1**

Means, standard deviations and correlations between demographic, trauma exposure, and HPA-axis functioning indicators.

| M (SD) | | Correlations | | | | | | | | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | | **1** | **2** | **3** | **4** | **5** | **6** | **7** | **8** | **9** | **10** | **11** | **12** | **13** | **14** | **15** |
| 1. Age | 12.8 (2.3) | 1.0 | | | | | | | | | | | | | | |
| 2. Female (49%) | — | −.056 | 1.0 | | | | | | | | | | | | | |
| 3. Physical Abuse[a] | 1.53 (3.4) | −.002 | .127 | 1.0 | | | | | | | | | | | | |
| 4. Emotional Abuse[a] | 1.90 (4.5) | .160† | −.037 | .403** | 1.0 | | | | | | | | | | | |
| 5. Non-Intentional Trauma[a] | 2.55 (3.9) | .250* | −.059 | .272** | .425** | 1.0 | | | | | | | | | | |
| 6. Current Depression (20%) | — | .236* | −.033 | −.038 | .297** | −.042 | 1.0 | | | | | | | | | |
| 7. CDI-Parent[a] | 12.3 (6.7) | .289** | −.013 | .044 | .340** | .181 | .459** | 1.0 | | | | | | | | |
| 8. CDI-Self | 8.71 (9.3) | .364** | −.274** | −.019 | .275** | .241* | .527** | .488** | 1.0 | | | | | | | |
| 9. Baseline cortisol[b,c] | .146 (.27) | .152† | .020 | .046 | .059 | .058 | .087 | .121 | .124 | 1.0 | | | | | | |
| 10. AUCg[b,c] | 9.07 (17.6) | .082 | −.018 | .042 | .069 | −.009 | .076 | .130 | .119 | .892** | 1.0 | | | | | |
| 11. Peak cortisol[b,c] | .189 (.56) | .037 | −.040 | .049 | .071 | −.037 | .053 | .111 | .112 | .760** | .961** | 1.0 | | | | |
| 12. AUCi[b,c] | 1.55 (8.4) | −.096 | −.032 | .058 | .009 | −.119 | .015 | .040 | −.050 | −.010 | .399** | .559** | 1.0 | | | |
| 13. Waking Cortisol[b,c] | .297 (.15) | −.119 | .044 | .074 | −.007 | .125 | −.070 | −.057 | −.084 | .065 | .074 | .043 | .085 | 1.0 | | |
| 14. CAR[b,c] | .096 (.24) | .128 | −.016 | .104 | .168 | .163 | .037 | −.024 | .035 | −.149 | −.101 | −.059 | .005 | −.299** | 1.0 | |
| 15. Dinner Cortisol[b,c] | .123 (.149) | −.014 | −.100 | .026 | .030 | −.149 | .012 | −.095 | .027 | .269** | .429** | .464** | .219* | .033 | .161† | 1.0 |
| 16. Bedtime cortisol[b,c] | .114 (.144) | −.136 | −.351** | .054 | .041 | .055 | .025 | −.125 | .113 | .128 | .265** | .306** | .151 | .037 | .016 | .559** |

† $p < .10$.

* $p < .05$.

** $p < .01$.

[a] Log transformed for multivariate analyses.

[b] Box transformed for multivariate analyses.

[c] µg/dl.

**Table 2**

Unadjusted and adjusted growth curve models of diurnal cortisol regulation predicted by childhood trauma exposure by subtypes.

| | **Unadjusted physical abuse model (AIC = 285.5)** | | **Unadjusted emotion al abuse model (AIC = 287.0)** | | **Unadjusted ntional non-inte trauma model (AIC = 269.8)** | | **Adjusted (AIC = 278.model 8)** | |
|---|---|---|---|---|---|---|---|---|
| | ***β*** | ***t*** | ***β*** | ***t*** | ***β*** | ***T*** | ***β*** | ***t*** |
| Intercept | −1.12 | −20.6** | −1.13 | −20.8** | −1.14 | −19.4** | −1.14 | −19.3** |
| Hours | −.09 | −4.75** | −.09 | −4.70** | −.08 | −4.15** | −.08 | −4.11** |
| Hours$^2$ | .003 | 2.85** | .003 | 2.78** | .003 | 2.37* | .003 | 2.36* |
| Physical abuse | .023 | .43 | | | | | .019 | .31 |
| Physical abuse × hours | −.011 | −.64 | | | | | −.012 | −.58 |
| Physical abuse × hours$^2$ | .001 | .79 | | | | | .001 | .69 |
| Emotional abuse | | | −.006 | −.14 | | | −.046 | −.87 |
| Emotional abuse × hours | | | .001 | .05 | | | .021 | 1.22 |
| Emotional abuse × hours$^2$ | | | .0001 | .09 | | | −.001 | −1.03 |
| Non-intentional Trauma | | | | | .058 | 1.23 | .081 | 1.51 |
| Non-intentional trauma × hours | | | | | −.037 | −2.36* | −.044 | −2.49* |
| Non-intentional trauma × hours$^2$ | | | | | .002 | 2.16* | .002 | 2.19* |

* $p < .05$.

** $p < .01$.

## Table 3

Estimates of fixed effects for adjusted growth curve models of acute HPA-axis reactivity predicted by childhood trauma exposure by subtypes.

| | Acute stress reactivity adjusted model (AIC = −549.7) | |
|---|---|---|
| | ***B*** | ***t*** |
| Intercept | −.41 | −7.60** |
| Baseline | .78 | 28.42** |
| Minutes to peak | .007 | 5.35** |
| Minutes to peak$^2$ | .0001 | 6.18** |
| Minutes from peak | −.013 | −9.08** |
| Minutes from peak$^2$ | .0002 | 5.58** |
| Physical abuse minutes to Peak | .005 | 2.31* |
| Physical abuse × minutes to peak$^2$ | .0001 | 3.08** |
| Physical abuse | .044 | 1.01 |
| Physical abuse minutes from Peak | .0004 | .18 |
| Physical abuse × minutes from peak$^2$ | .00002 | −.29 |
| Emotional abuse × minutes to peak | −.0004 | −.23 |
| Emotional abuse × minutes to peak$^2$ | .00001 | −.53 |
| Emotional abuse | .016 | .42 |
| Emotional abuse × minutes from peak | .002 | 1.24 |
| Emotional abuse × minutes from peak$^2$ | −.0001 | −2.24* |
| Non-intentional trauma × minutes to peak | −.002 | −1.24 |
| Non-intentional trauma × minutes to peak$^2$ | −.00003 | −.90 |
| Non-intentional Trauma | −.051 | −1.30 |
| Non-intentional trauma minutes from peak | .0001 | .05 |
| Non-intentional trauma × minutes from peak$^2$ | .00005 | .94 |

* $p < .05$.

** $p < .01$.