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Reduced hair cortisol after maltreatment mediates externalizing symptoms in middle childhood and adolescence

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Abstract

Background—The enduring impact of childhood maltreatment on biological systems and ensuing psychopathology remains incompletely understood. Long-term effects of stress may be reflected in cumulative cortisol secretion over several months, which is now quantifiable via hair cortisol concentrations (HCC). We conducted a first comprehensive investigation utilizing the potential of hair cortisol analysis in a large sample of maltreated and nonmaltreated children and adolescents.

Method—Participants included 537 children and adolescents (3 to 16 years; 272 females) with maltreatment (n = 245) or without maltreatment histories (n = 292). Maltreated subjects were recruited from child protection services (CPS; n = 95), youth psychiatric services (n = 56), and the community (n = 94). Maltreatment was coded using the Maltreatment Classification System drawing on caregiver interviews and complemented with CPS records. Caregivers and teachers reported on child mental health. HCC were assessed in the first 3 cm hair-segment.

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Supporting information

Additional Supporting Information may be found in the online version of this article.

The authors have declared they have no potential or competing conflicts of interest in relation to this report.

Results—Analyses uniformly supported that maltreatment coincides with a gradual and dose-dependent reduction of HCC from 9-10 years onwards relative to nonmaltreated controls. This pattern emerged consistently from both group-comparisons between maltreated and nonmaltreated subjects (27.6% HCC reduction in maltreated 9 to 16-year-olds) and dimensional analyses within maltreated subjects, with lower HCC related to greater maltreatment chronicity and number of subtypes. Moreover, both group comparisons and dimensional analyses within maltreated youth revealed that relative HCC reduction mediates the effect of maltreatment on externalizing symptoms.

Conclusions—From middle childhood onwards, maltreatment coincides with a relative reduction of cortisol secretion, which, in turn, may predispose to externalizing symptoms.

Keywords

hair cortisol; maltreatment; neglect; externalizing symptoms

Introduction

Long-term changes in neurobiological systems are thought to provide a crucial mechanism to explain how early adversity gets “under the skin” to give rise to poor mental and physical health (Bush & Boyce, 2014). Ample research suggests dysregulated hypothalamic-pituitary-adrenal (HPA) axis functioning in maltreated or trauma-exposed youth compared to their unexposed counterparts (Lupien, McEwen, Gunnar, & Heim, 2009; Nemeroff, 2016). While initial data implied that child maltreatment gives rise to hyper-activation of the HPA axis, mounting evidence now also supports a hypo-activation hypothesis (Doom & Gunnar, 2013).

Given these opposing patterns the present research utilizes a new cortisol assessment technique in hair that reliably captures cumulative cortisol outflow over an extended period independent of moment-to-moment secretory fluctuations (Stalder & Kirschbaum, 2012). At the same time, this study aims to address potential modulators of neurobiological effects of adversity, specifically maltreatment characteristics and the developmental period of cortisol assessment (Gunnar & Quevedo, 2007). As both hyper- and hypocortisolism have been associated with psychiatric conditions in childhood and adolescence (e.g., Alink et al., 2008), this study also seeks to evaluate cortisol as a mediator of the effect of maltreatment on child mental health (e.g., Davies, Sturge-Apple, Cicchetti, & Cummings, 2007).

Regarding developmental and temporal factors, recent data suggest that trauma-related reduction of cortisol emerges gradually across development relative to typically developing children. For example, in maltreated girls, initial elevation of cortisol levels was followed by progressive relative cortisol reduction beginning in adolescence (Trickett, Noll, Susman, Shenk, & Putnam, 2010). This maps onto other child and adult data implying that after an initial hyperactive phase, HPA axis hypo-activation may ensue if stress persists (e.g., Jaffee et al., 2015; G. E. Miller, Chen, & Zhou, 2007; Steudte-Schmiedgen, Kirschbaum, Alexander, & Stalder, 2016). Subtype and pervasiveness of maltreatment are also deemed important (Doom, Cicchetti, Rogosch, & Dackis, 2013). Neglect, in particular, may give rise to hypocortisolism (e.g., Quevedo, Johnson, Loman, LaFavor, & Gunnar, 2012; van der

Vegt, van der Ende, Kirschbaum, Verhulst, & Tiemeier, 2009). Yet, with a few important exceptions, developmental work has rarely considered a broad array of maltreatment subtypes and characteristics in a single study.

Cortisol assessment techniques may act as another source of variance. Research on maltreated youth has previously relied almost exclusively on traditional cortisol assessment methods, optimal for capturing short-term variation in cortisol secretion (e.g., stress-responsivity) in the order of minutes (saliva, plasma) to hours (urine). Yet, assessment of cumulative cortisol secretion over extended periods using these methods is impacted and potentially confounded by acute influences, such as circadian rhythmicity, pulsatile cortisol secretion, and a range of situational factors (Stalder et al., 2016; Young, Abelson, & Lightman, 2004). In this regard, the assessment of cortisol in scalp hair may prove a major advance, affording a valid and robust retrospective index of cumulative cortisol secretion over several months (see Stalder & Kirschbaum, 2012; Staufenbiel, Penninx, Spijker, Elzinga, & van Rossum, 2013). Using this method, it has been shown that chronically stressed, severely traumatized and adult psychiatric populations exhibit altered hair cortisol concentrations (HCC) relative to controls (see Steudte-Schmiedgen, et al., 2016). Yet, despite initial data on HCC in traumatized children (Simmons et al., 2016), the unique potential of hair cortisol analysis of determining stable cumulative cortisol secretory patterns over an extended period has yet to be fully realized in a large-scale study on children and adolescents with a broad spectrum of maltreatment experiences.

In this study, we employed HCC measurements in a large, well-characterized group of maltreated and nonmaltreated youth across a broad age-range. Aforementioned theory and research (e.g., G. E. Miller et al., 2007) led us to predict that maltreatment would be associated with earlier HPA axis hyper-activation followed by progressive hypo-activation later in development. Moreover, we expected that early, more chronic and extensive maltreatment as well as neglect, in particular, would result in more pronounced cortisol reduction among maltreated relative to nonmaltreated youth. Also, in keeping with work on biological embedding of stress as a mechanism for later psychopathology (e.g., Lupien et al., 2009), we hypothesized that effects of maltreatment on psychiatric symptoms would be mediated by relative HCC reduction.

Method

Sample and Design

We recruited 537 children and adolescents (3 to 16 years; 272 females) as part of the AMIS project (see White et al. (2015) for a detailed description). In total, we included 245 maltreated and 292 nonmaltreated subjects. Maltreated subjects were referred by the child protection services (CPS; $n = 95$) and youth psychiatric services ($n = 56$). Additionally, we recruited subjects from daycare centers, general practitioners, and the registry office ($n=386$), yielding a further set of maltreated subjects ($n = 94$) and age and gender-matched nonmaltreated controls ($n=292$; see Table 1 for sample characteristics).

Ethical Considerations

Institutional Review Boards of the Universities of Leipzig and Munich provided ethical approval of the AMIS project. After describing the study to parents and children, we obtained informed written and oral consent (parents) and informed oral assent (children).

Maltreatment characteristics

The Maternal Maltreatment Classification Interview (Cicchetti, Toth, & Manly, 2003) was conducted with caregivers and videotaped for subsequent coding. The interview covers six maltreatment subtypes using screening questions: sexual abuse, physical abuse, emotional maltreatment, as well as the neglect subtypes failure to provide, lack of supervision, moral/legal/ educational maltreatment. Interviewers follow up positive screens to assess subtype, severity and developmental stage per incident. For CPS-referred children, case records were additionally retrieved and analyzed. Reported maltreatment incidents were coded by trained researchers from interviews and CPS records employing the Maltreatment Classification System (MCS; Barnett, Manly, & Cicchetti, 1993). One of the authors of the MCS provided on-site training. To resolve coding issues, raters consulted a group of senior researchers who met on a fortnightly basis and/ or contacted the MCS trainer, if necessary. The MCS has undergone extensive validation and reliability testing (e.g., Manly, Oshri, Lynch, Herzog, & Wortel, 2013). Coders rate each incident in terms of subtype, severity (1=low to 5 = high), and developmental period in which the incident occurred, i.e., infancy (0-1.4 years), toddlerhood (1.5-2 years), preschool age (3-5 years), early school age (6-7 years), late school age (8-12 years), and adolescence (13-18 years). Three dimensions (number of subtypes, chronicity, maximum severity) were derived. To yield an age-independent index of maltreatment chronicity, we computed the percentage of periods affected by maltreatment (affected periods relative to the total number of developmental periods of a child). For CPS-referred children, case-records and interview-data were integrated. Five caregivers from the CPS sample declined the interview. In these cases, ratings were based solely on CPS records.

Psychiatric symptoms

Caregivers completed the Child Behavior Checklist (CBCL; Achenbach, 1991). The CBCL is a comprehensive 113-item measure including scales to assess composite internalizing (withdrawn/depressed, somatic complaints, and anxious/depressed behavior) and externalizing syndromes (rule-breaking behavior, aggressive behavior, attention problems). In a subsample of 372 children and adolescents, teachers completed and returned the Strengths and Difficulties Questionnaire (R. Goodman, 1997), which yields composite scales for internalizing and externalizing symptoms (A. Goodman, Lamping, & Ploubidis, 2010).

Control variables and physical development

The number of non-abuse life adversities of subjects, children's hair-related variables (e.g., hair-washes), other HCC correlates (e.g., exercising), and sociodemographic variables (e.g., household income) were reported by caregivers. Body-mass-index (BMI) was also considered as a covariate based on previous reports of positive associations with HCC

(Stalder, Steudte, Alexander, et al., 2012). BMI values were referenced to a representative sample of children and adolescents to derive developmentally-sensitive standard deviation scores (BMI-SDS) and percentile values (Cole, Freeman, & Preece, 1995). Children aged nine and above self-reported their pubertal status using line drawings of the Tanner stages (Tanner, 1962).

Hair cortisol concentrations (HCC)

Hair strands (~3 mm diameter) were cut scalp-near at a posterior vertex locus. We determined cortisol concentrations in the first 3 cm hair segment which, given a growth rate of ~1 cm/month, is assumed to index cumulative cortisol exposure over the past three months (Stalder & Kirschbaum, 2012). Wash and cortisol extraction procedures followed a protocol described elsewhere (Stalder, Steudte, Miller, et al., 2012), with 7.5 mg of whole, nonpulverized hair washed with 2.5 mL isopropanol and steroid extraction with 1800 μ L methanol for 18 hours at 45°C. Cortisol concentrations were quantified using a commercially available immunoassay with luminescence detection (LIA, IBL-Hamburg, Germany). Intra- and interassay variance coefficients for this assay are below 8%.

Data-analytic plan

Hair cortisol data were power-transformed ($X^{.15}$) to reduce positive skew (R. Miller & Plessow). For illustrative purposes, untransformed mean HCC data are reported in figures and text. Outlying HCC (± 3 SDs from the mean) were winsorized ($n=6$). As a preparatory step, child characteristics, caregiver demographics, and hair-related variables were analyzed in relation to maltreatment status and HCC. The main analysis first employed a hierarchical linear regression model with HCC as outcome to analyze the effects of age and maltreatment status and their interaction. We used the PROCESS macro (Hayes, 2013) to implement the Johnson-Neyman technique in order to identify age-ranges where regression lines of maltreated and nonmaltreated subjects differed, i.e., potential regions of significance (ROS). Within ROS, maltreated and nonmaltreated subjects were compared using analysis of variance (ANOVA) and covariance (ANCOVA) to account for potential covariates. Next, maltreated subjects within ROS were submitted to correlational analyses to identify continuous relationships between HCC and maltreatment dimensions and psychiatric symptoms. The PROCESS macro (Hayes, 2013) was used to assess if HCC mediated effects of maltreatment on psychiatric symptoms. We conducted ordinary least squares (OLS) path analyses for subjects within ROS using 1,000 bootstrapping samples, a bias-corrected 95% confidence interval (CI), and Preacher and Kelley's (2011) κ^2 for effect size estimates (small: .01 - .089, intermediate: .09-.249, large: .25). Lastly, exploratory analyses were conducted based on the patterns observed outside the ROS.

Results

Table 1 provides descriptive data on maltreatment characteristics within the maltreated sample. Table 2 provides results from preliminary group comparisons of maltreated and nonmaltreated youth, yielding no differences on gender, age, BMI percentile, pubertal status, sports per week or recent physical illness in the last 3 months. Maltreated subjects experienced more non-abuse life adversities as well as more stressful events in the last 3

months and reported more frequent hair washing and hair-coloration compared to nonmaltreated youth. Resembling prior work (e.g., Gilbert et al., 2009; Scott, Smith, & Ellis, 2010) caregivers of maltreated youth exhibited lower levels of education and net-income, as well as higher levels of unemployment.

Preparatory analyses revealed that HCC did not differ as a function of gender ($p > .68$), number of non-abuse life adversities ($p > .71$), recent physical illness or stressful events in the past 3 months ($ps > .14$), exercise per week ($p > .78$), or hair-related variables ($ps > .18$), except the presence of curls ($r = .091$, $p = .036$). HCC were associated with child age ($r = .139$, $p = .001$), BMI-SDS ($r = .127$, $p = .004$), as well as caregivers' level of education ($r = .162$, $p < .001$), net-income ($r = .109$, $p = .014$), and employment status ($r = .128$, $p = .003$).

Figure 1a illustrates HCC as a function of maltreatment status and age. A hierarchical linear regression model yielded main effects of maltreatment (Step 1: $\beta = -.100$, $p = .021$, $R^2 = .010$) and age (Step 2: $\beta = .136$, $p = .002$, $R^2 = .018$) as well as a maltreatment X age interaction (Step 3: $\beta = -.177$, $p = .003$, $R^2 = .016$). The Johnson-Neyman technique revealed a region of significance (ROS) for all subjects aged 9.69 years and older (53.26% of subjects). Figure 1b displays the result of an ANOVA comparing subjects in the ROS regarding maltreatment, revealing 27.6%-lower HCC among maltreated subjects than nonmaltreated subjects, $F(1, 284) = 13.816$, $p < .001$, $\eta_p^2 = .046$. The effect of maltreatment in the ROS proved robust to co-varying for child gender, BMI-SDS, pubertal status, non-abuse life adversities, recent illness, recent stressful events, hair-related variables (for all ANCOVAs $ps < .001$), and sociodemographic variables of caregivers (for all ANCOVAs, $ps < .016$).

Next, we analyzed effects of specific maltreatment dimensions, subtypes and developmental periods affected by maltreatment among maltreated subjects in the ROS. Online Supplementary Fig S1 displays the inverse associations of HCC with maltreatment chronicity ($r = -.237$, $p = .008$) and number of subtypes ($r = -.315$, $p < .001$). No significant relationship of HCC with the maximum maltreatment severity emerged ($r = -.119$, $p = .183$). Subjects exposed to failure to provide (FTP) vs. other subtypes and moral-legal/ educational (MLE) maltreatment vs. other subtypes showed more pronounced decrements in HCC. Likewise, subjects who experienced maltreatment in infancy vs. other periods and maltreatment in adolescence vs. other periods exhibited more pronounced relative HCC reduction (see Supplementary Table S1 and S2). Subtype-specific effects were robust to controlling for variations in maltreatment chronicity (FTP: $p = .010$; MLE: $p = .031$), implying that subtype-specific effects were independent of variations in base-rates (chronicity) between subtypes.

In the ROS, the effect of maltreatment was not further moderated by age ($p = .135$) or gender ($p = .682$). However, in the ROS the effect of maltreatment varied as a function of pubertal status (see Figure 2). A hierarchical linear regression model yielded a main effect of maltreatment ($\beta = -.216$, $p < .001$, $R^2 = .041$), no main effect of pubertal status ($\beta = .049$, $p = .795$, $R^2 = .002$), but a maltreatment X pubertal status interaction ($\beta = -.426$, $p < .001$, $R^2 = .076$). The interaction between puberty and maltreatment was robust to controlling for age and gender ($\beta = -.354$, $p < .001$, $R^2 = .048$). Separate regression analyses for genders

showed that the interaction effects between pubertal status and age were significant both among females ($\beta = -.342, p = .001, R^2 = .062$) and males ($\beta = -.494, p = .003, R^2 = .069$). Yet, among maltreated subjects in the ROS, pubertal status did not moderate the influence of maltreatment chronicity ($\beta = -.005, p = .961, R^2 = .000$) or subtype number ($\beta = -.107, p = .373, R^2 = .006$), suggesting that the dimensional effects of maltreatment were comparable across pubertal stages.

Among subjects in the ROS, HCC were inversely related to externalizing symptoms reported by caregivers ($r = -.253, p < .001$) and teachers ($r = -.246, p = .001$) as well as internalizing symptoms reported by caregivers ($r = -.137, p = .021$) and teachers ($r = -.235, p = .001$; see Fig S1). As expected, maltreated youth also displayed higher levels of clinical-level psychiatric symptoms compared to nonmaltreated controls (see Table 2). We used OLS path analyses to evaluate whether relative HCC reduction mediates the effect of maltreatment on psychiatric symptoms. For maltreated and nonmaltreated subjects in the ROS, HCC reduction mediated the effect of maltreatment on externalizing symptoms in parent reports (CI: .209 to 1.287; $\kappa^2 = .037$; see Figure 3a) and teacher-reports (.040 to .796; $\kappa^2 = .043$), whereas no such effect emerged for internalizing symptoms in parent reports (CI: -.195 to .700; $\kappa^2 = .013$) or teacher reports (CI: -.063 to .752; $\kappa^2 = .038$). Moreover, within the maltreated group, HCC mediated the effects of maltreatment chronicity (CI: .357 to 4.431; $\kappa^2 = .045$) and number of subtypes (CI: .091 to 1.116; $\kappa^2 = .059$) on caregiver-reported externalizing symptoms (see Figures 3b and 3c).

Finally, exploratory analyses were conducted for children below the intersection point of the regression lines displayed in Figure 1 (7.91 years). HCC were comparable between maltreated subjects ($M = 15.37; SD = 14.83$) and nonmaltreated subjects ($M = 15.75; SD = 17.02$; $F(1, 199) = .295, p = .588, \eta_p^2 = .001$) below 7.91 years. Among maltreated subjects below 7.91 years, the following patterns emerged: HCC were positively associated with maltreatment chronicity ($r = .212, p = .039$); a trend emerged for a positive association with externalizing symptoms reported by parents ($r = .208, p = .056$); elevated HCC were also found for subjects with maltreatment in infancy ($M = 19.41; SD = 18.01$) vs. other periods ($M = 11.32; SD = 9.32$; $F(1, 94) = 7.85, p = .006, \eta_p^2 = .077$), but HCC did not vary as a function of other periods ($p > .480$) or subtypes ($p > .059$); HCC was not associated with maltreatment subtype number ($r = .030, p = .803$), with externalizing symptoms reported by teachers ($r = .106, p = .388$), or with internalizing symptoms reported by parents ($r = -.041, p = .706$) or teachers ($r = .039, p = .750$).

Discussion

This is the first comprehensive study to investigate the enduring impact of maltreatment on cumulative cortisol secretion over several months, indexed by HCC, and ensuing mental health problems in a large, well-characterized sample of maltreated and nonmaltreated children and adolescents. We observed a striking pattern of associations of HCC to maltreatment status, specific maltreatment characteristics, and psychiatric symptoms that varied markedly by age. Among subjects from middle childhood onwards (9.69 years), maltreatment history – especially more chronic and extensive maltreatment that occurred in infancy or adolescence, and neglect – was accompanied by a salient reduction of HCC

relative to nonmaltreated subjects that was robust to full covariate adjustments (e.g., non-abuse adversities, SES, BMI). This study further provides tentative evidence that this maltreatment-related relative reduction of cumulative cortisol levels reflects part of a biological mediating pathway that contributes to increased externalizing symptoms.

Our findings of maltreatment-related relative HCC reduction, which emerged consistently from group comparisons and associations within maltreated subjects, mesh well with adult data reporting similar effects of HPA axis blunting among those with childhood abuse (e.g., van der Vegt et al., 2009). Maltreatment-related HCC reduction surfaced in middle childhood and grew increasingly stronger with pubertal maturation relative to nonmaltreated youth, akin to prior data showing that adversity-related cortisol blunting emerges over the course of development (Trickett et al., 2010). Descriptively, it is noteworthy that HCC of maltreated youth did not decline with age. Rather, maltreated children beyond age nine did not evince the normative developmental increase in cortisol observed among nonmaltreated youth – the typical developmental pattern found in previous reports (e.g., Kiess et al., 1995; Trickett et al., 2010). Potentially, this indicates a thwarting or halting of a normative developmental process. At the same time, with pubertal maturation a similar incremental pattern emerged among nonmaltreated children while a decline of HCC emerged among maltreated children, suggesting that the HPA axis may potentially become hypo-active across pubertal development following maltreatment.

Notably, unlike previous work on sexually maltreated females, which detected progressive cortisol reduction beginning in adolescence (Trickett et al., 2010), we already document a relative reduction of HCC among maltreated children emerging from middle childhood onwards. Potentially, this difference may be attributable to methodological differences of hair cortisol analyses (e.g., increased sensitivity for assessing cumulative cortisol secretion over several months; Stalder & Kirschbaum, 2012) and/ or our broader focus on a wider spectrum of maltreatment subtypes that may potentially onset at earlier points in time, i.e., in our sample, failure to provide showed a markedly earlier modal age of onset (infancy) than sexual abuse (preschool age). Indeed, subtype analyses confirmed that HCC reduction was especially pronounced among neglected relative to other maltreated subjects, which converges with prior child and adult data (e.g., Dozier et al., 2006; Quevedo et al., 2012; van der Vegt et al., 2009).

Interestingly, in early childhood (3-7 years), exploratory analyses revealed a contrasting positive association between HCC and maltreatment chronicity and infant onset for maltreated children, though corresponding group-level effects were not observed. This pattern meshes with recent observations of elevations in HCC among primary school-aged children with increasing adversity load (Simmons et al., 2016) and studies comparing maltreated and nonmaltreated children using other cortisol measurement modalities (e.g., Gunnar, Morison, Chisholm, & Schuder, 2001; Trickett et al., 2010). However, a recent body of data documents hypocortisolism among young children under age 9 adopted or fostered from institutional care using salivary cortisol measures (McLaughlin et al., 2015; Koss, Milber, Donzella & Gunnar, 2016). Among populations with histories of institutional care, the pervasiveness of early deprivation is exceedingly high which may potentially contribute

to an earlier emergence of hypocortisolism in development compared to the pattern observed in our study.

The maltreatment-related pattern of relative HCC reduction in middle childhood and adolescence converges with adult data suggesting that cortisol secretion follows a non-linear time course after exposure to adversity, i.e., dose-dependent hypercortisolism in the initial phase, which reverts to hypocortisolism over time (see G. E. Miller et al., 2007). In accordance with this view, maltreatment onset in infancy predicted elevated HCC in early childhood, when infancy was still relatively recent, but relatively reduced HCC levels in older age groups, when infancy lay further in the past. One possibility is that chronic stress-exposure gives rise to adaptations at the level of the pituitary or increased glucocorticoid receptor sensitivity, promoting negative feedback on the HPA axis (Fries, Hesse, Hellhammer, & Hellhammer, 2005). However, the time-frame implied by links of HCC with maltreatment onset in infancy or chronicity in young children seems rather long to be termed 'initial phase'; i.e., even in the 3 to 7-year-olds the period of infancy lay at least two years in the past and high chronicity implied that maltreatment had taken place in at least two developmental periods. Based on adult meta-analytic data in the chronic stress context (G. E. Miller et al., 2007), the proposed mechanisms whereby adversity eventually gives rise to hypocortisolism may be suspected to occur more rapidly.

Thus, a phase-specific mechanism involving shifts in glucocorticoid regulation from early to middle childhood and adolescence in response to chronic adversity should also be considered. This view is also bolstered by our result that puberty additionally modulated maltreatment-related HCC reduction compared to nonmaltreated subjects. From this perspective, our data dovetail with recent proposals that middle childhood and puberty reflect crucial developmental switch points affecting stress hormone system functioning (Del Giudice, Ellis, & Shirtcliff, 2011). Yet, overall, longitudinal research in trauma-exposed youth is needed to provide conclusive data on potential switch points and mechanisms underlying endocrine changes following early adversity.

Besides this age-related shift, our data also corroborate the notion that maltreatment-related HPA axis dysregulation comprises part of a risk mechanism for developmental psychopathology, particularly externalizing symptoms (Susman, 2006). Intriguingly, the pattern of respective findings closely tracked the age-related shift in maltreatment associations, such that externalizing symptom-load was predicted by elevated HCC in early childhood (trend), but by reduced HCC in middle childhood and adolescence. Several studies link cortisol reductions to aggressive/ peer problems in maltreated and nonmaltreated children in middle childhood, with some evidence for elevated cortisol among younger children (Alink et al., 2008; Ouellet-Morin et al., 2011). Moreover, both group-comparisons and dimensional analyses within maltreated subjects were consistent with the idea that HCC may act as a mediator of the maltreatment effect on externalizing symptoms in middle childhood and adolescence, though longitudinal data are needed to confirm this effect. Our cross-sectional data therefore provide tentative support to the idea that HPA axis dysregulation may reflect a neurobiological pathway that partly accounts for maltreated youth's known risk for externalizing symptoms (e.g., Davies et al., 2007).

Some limitations of this study deserve consideration. First, this study employed a cross-sectional design. Therefore caution should be exercised, especially regarding the interpretation of the direction of mediation effects (Hayes, 2013). However, given that our within-group analyses suggested that maltreatment exerted its effects primarily when it was chronic and occurred in infancy, a longitudinal effect of maltreatment on HCC seems likely. Second, recruiting maltreated subjects from sources other than the CPS increased the variance in maltreatment exposure within our maltreated sample. This may have limited our chances to detect group-level differences in comparison with nonmaltreated subjects. Still, robust group effects were detected from middle childhood onwards. Moreover, our broad sampling strategy carried important benefits, ensuring a wide variance in maltreatment characteristics, which allowed for dimensional testing within maltreated subjects. Finally, compared to other cortisol measurement modalities, hair cortisol remains a relatively new measure that would profit from further validation confirming that it documents cumulative cortisol secretion over several months (Steudte-Schmiedgen et al., 2016), though recent detailed validation efforts have yielded promising results (e.g., Short et al., 2016).

In summary, our results reveal an intriguing pattern whereby experiences of maltreatment by caregivers promote a dose-dependent relative reduction of cumulative cortisol secretion, which begins to emerge from middle childhood onwards (between 9-10 years). This enduring cortisol reduction, in turn, appears to predispose maltreated youth to mental health problems, particularly increased externalizing symptoms. As such, these data illuminate a potentially important developmental pathway whereby early adversity becomes biologically embedded to explain the immense physical and mental health burden originating from maltreatment in childhood and beyond (e.g., Scott et al., 2010; Vachon, Krueger, Rogosch, & Cicchetti, 2015). New insights into developmental switch points for effects of maltreatment on the neuroendocrine stress systems may eventually inform targeted interventions.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Key points

- Ample studies using short-term cortisol measures suggest that maltreatment elicits dysregulated HPA axis functioning, but few studies address the factors influencing hyper- and hypocortisolism and link these patterns to development and mental health.
- We assessed hair cortisol - a robust index of cumulative cortisol secretion over several months - in a large carefully characterized sample of maltreated and nonmaltreated children and adolescents to elucidate factors accounting for disparate HPA axis functioning across development after maltreatment.
- From 9-10 years onwards, we detected that maltreatment coincided with a gradual and dose-dependent reduction of hair cortisol that, in turn, mediated the effect of maltreatment on externalizing symptoms.
- Given the immense physical and mental health burden originating from maltreatment, this study offers new insights into developmental switch points for effects of maltreatment on the neuroendocrine stress systems which may eventually inform targeted interventions.

Figure 1.

(a.) Associations between HCC (transformed) and age among maltreated subjects ($r = .003$, $p = .963$; $n = 245$) and nonmaltreated subjects ($r = .246$, $p < .001$; $n = 292$) with confidence intervals (thin curved lines) and cut-off point (9.69 years) illustrated above which the regression lines for maltreated and nonmaltreated children differed significantly. (b.) HCC for maltreated children ($n = 126$) and nonmaltreated children ($n = 160$) above the age cut-off with standard errors displayed.

Figure 2.

Associations between HCC (transformed) and pubertal stages among maltreated subjects ($r = -.224$, $p = .013$; $n = 122$) and nonmaltreated controls ($r = .330$, $p < .001$; $n = 160$) above the age-cut-off (9.69 years) with confidence intervals (thin curved lines).

Figure 3.

Within late childhood (9-9.69 years), HCC (transformed) mediated the effects of (a.) maltreatment status on externalizing symptoms in maltreated and nonmaltreated subjects, (b.) maltreatment chronicity on externalizing symptoms within maltreated subjects, and (c.) number of maltreatment subtypes on externalizing symptoms within maltreated subjects. Standardized path coefficients are presented to facilitate interpretation.

Table 1

Comparison of demographic, hair-related, maltreatment variables, and psychiatric symptoms of maltreated and nonmaltreated youth.

	Maltreated group (n=223-245)	Nonmaltreated group (n=272-292)	Test Statistic	p-value
<i>Child characteristics</i>				
Female (n, %)	113 (46.1)	159 (54.5)	$\chi^2(1) = 3.698$	.054
Age years (mean, SD)	9.86 (3.24)	10.08 (3.03)	$F(1,535) = .635$	.426
BMI percentile (mean, SD)	52.42 (30.56)	47.73 (29.71)	$F(1,521) = 3.146$	.077
Postpuberty (n, %)	102 (42.1)	104 (35.7)	$\chi^2(1) = 2.289$	.130
Sport per week (mean, SD)	3.30 (1.88)	3.39 (1.61)	$F(1,193) = .301$	.583
Non-abuse adversities (mean, SD)	6.50 (2.84)	4.46 (2.44)	$F(1,531) = 79.780$	<.001
Physical illness last 3 mths (n, %)	104 (43.9)	137 (47.2)	$\chi^2(1) = .593$	.441
Stressful event last 3 mths (n, %)	66 (27.7)	55 (19.0)	$\chi^2(1) = 5.686$	.017
<i>Demographics (caregiver):</i>				
Unemployed (n, %)	95 (40.6)	28 (9.8)	$\chi^2(1) = 67.642$	<.001
Net-income bracket (median)	1,000-1,500€	3,000-3,500€	$U(506) = 13343$	<.001
School education (median)	Upper secondary	High school diploma	$U(512) = 18885$	<.001
<i>Hair-related variables:</i>				
Washes per week (mean, SD)	2.89 (1.78)	2.37 (1.49)	$F(1,502) = 12.723$	<.001
Curls/ waves (n, %)	67 (28.4)	95 (32.9)	$\chi^2(1) = 1.223$	.269
Hair-dye (n, %)	10 (4.3)	7 (2.4)	$\chi^2(1) = 1.431$	.232
Bleaching/coloration (n, %)	25 (10.6)	16 (5.5)	$\chi^2(1) = 4.614$	.032
<i>Psychiatric Symptoms (above clinical cut-off):</i>				
Externalizing problems (n, %)	107 (46.9)	22 (7.9)	$\chi^2(1) = 100.389$	<.001
Internalizing problems (n, %)	126 (54.3)	65 (22.6)	$\chi^2(1) = 55.299$	<.001

BMI Percentile, Body mass index percentile within representative population.

Table 2

Maltreatment characteristics as indexed by the MCS within the maltreated sample (n=245).

<i>Maltreatment dimensions:</i>		
Number of subtypes (mean, SD)	2.26	(1.39)
Chronicity (mean, SD)	54.79	(30.19)
Maximum Severity (mean, SD)	2.94	(1.31)
<i>Subtypes of Maltreatment:</i>		
Physical abuse (n, %)	81	(33.1)
Emotional maltreatment (n, %)	191	(78.0)
Sexual abuse (n, %)	30	(12.2)
Overall neglect (n, %)	156	(63.7)
Failure to Provide (n, %)	82	(33.5)
Lack of Supervision (n, %)	123	(50.2)
Moral-legal/Educational (n, %)	46	(18.8)
<i>Timing of Maltreatment:</i>		
Infancy (n, %)	98	(40.0)
Toddlerhood (n, %)	119	(48.6)
Preschool (n, %)	159	(64.9)
Early school-age (n, %)	117	(53.7) ^a
Late school-age (n, %)	101	(68.2) ^b
Adolescence (n, %)	17	(33.3) ^c

^aValue refers to n = 218^bValue refers to n = 148^cValue refers to n = 51