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

Lars O. White,1,Marcus Ising,2,Kai von Klitzing,1,Susan Sierau,1, Andrea Michel,1,3, Annette M. Klein,1,Anna Andreas,1,Jan Keil,1,Leonhard Quintero,1, Bertram Muller-

Myhsok,2,4,5,Manfred Uhr,2,Ruth Gausche,6,Jody T. Manly,7,Michael J. Crowley,8,Clemens Kirschbaum,9 and Tobias Stalder9,10

1

Department of Child and Adolescent Psychiatry, University of Leipzig, Leipzig;

2

Max Planck Institute of Psychiatry, Munich;

3

Department of Developmental Psychology, University of Jena, Jena;

4

Munich Cluster for Systems Neurology (SyNergy), Munich, Germany;

5

Institute of Translational Medicine, University of Liverpool, Liverpool, UK;

6

University of Leipzig, Leipzig, Germany;

7

Mt. Hope Family Center, University of Rochester, Rochester, NY;

8

Yale Child Study Center, Yale University School of Medicine, New Haven, CT, USA;

9

Institute of Psychology, TU Dresden, Dresden;

10

Clinical Psychology, University of Siegen, Siegen, Germany

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 – 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.

Results:

Analyses uniformly supported that maltreatment coincides with a gradual and dose-dependent

reduction in HCC from 9 to 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 –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 in 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 hyperactivation of the HPA axis, mounting evidence now also supports a hypoactivation 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 child-hood and adolescence (e.g. Alink et al., 2008), thisstudy 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 in 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, Sus- man, Shenk, & Putnam, 2010). This maps onto other child and adult data implying that after an initial hyperactive phase, HPA axis hypoactivation may ensue if stress persists (e.g. Jaffee et al., 2015; 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. Miller et al., 2007) led us to predict that maltreatment would be associated with earlier HPA axis hyperactivation followed by progressive hypoactivation 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.