Commentary:

The importance of exploring dose-dependent, subtype-specific, and age-related effects of maltreatment on the HPA axis and the link to psychopathology? A response to Fisher (2017)

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We greatly appreciate Dr. Fisher's commentary that provides an excellent backdrop and well-considered perspective on our findings. We agree that our results mesh well with previous work documenting hypocortisolism among youth who experienced early adversity, especially neglect. Moreover, as also perceptively noted by Dr. Fisher, our cross-sectional data provide support for the notion that hypocortisolism is not simply a transient phenomenon, but, rather, a persistent pattern characterizing maltreated youth. Specifically, the consistency of the between group effect (from age 9.69 onwards) on a multi-month index of cumulative cortisol and the dose-dependent gradient of hypocortisolism within the maltreated group which was related to the length of time that children and adolescents were affected by maltreatment lend weight to this view.

To the extent that our data support a mediating role of diminished HPA axis activity for the link between maltreatment and externalizing symptoms, this may certainly relate to the maltreatment-associated neurobehavioral disinhibition documented elsewhere (e.g., Fisher, Lester, et al., 2011). As noted by Dr. Fisher, this is particularly intriguing given that most adult research has linked HPA axis dysregulation among maltreated individuals to affective disorders. Hence, this also calls for more longitudinal research on heterotypic pathways, to explore trajectories from maltreatment to hypocortisolism and early externalizing problems which may, in turn, predict adult anxiety and mood disorders (Moffitt, 2006).

Dr. Fisher’s comment that hypocortisolism may represent an ‘evolutionarily conservative’ response of the child to the absence of “good enough” caregiving also merits further research. Given that the caregiver typically provides a source of interpersonal emotion regulation for the child (Cassidy, 1994; Crittenden & Ainsworth, 1989; Fonagy, Gergely, Jurist, & Target, 2002; Zaki & Williams, 2013), a limited capacity of the caregiver to do so – as indexed by (certain forms of) neglect – may reinforce the child in developing a suboptimal self-reliant strategy that may ultimately give rise to hypocortisolism. To identify the exact determinants of insufficient care that predict hypocortisolism should thus be the subject of detailed future analyses of parent-child interactions, among others.

In the final section, Dr. Fisher noted that our age-related effects – whereby hypocortisolism only emerged among maltreated youth from 9 ½ years onwards –may prove “somewhat of an artifact”. Indeed, he is correct in pointing out that allostatic load is more likely to have accumulated among older children and may have therefore crossed a critical “threshold in which the proposed downregulation of the HPA axis occurs”. Revisiting our data, we did indeed document an association between age and maltreatment chronicity within our maltreated sample (r = -.299, p < .001). However, in a regression analysis performed within the maltreated group that included age (β = .007, *p* =. 918, ΔR2 = .000) and maltreatment chronicity in Step 2 (β = -.068, *p* =. 314, ΔR2 = .004), we still found a significant interactive effect of chronicity x age on hair cortisol concentrations in Step 3 (β = -.227, *p* < .001; ΔR2 = .051; see Figure 1). We interpret this as preliminary evidence that it is neither chronicity nor age alone that can explain the pattern of our findings, but merely the interaction of these variables. While we concur with Dr. Fisher that our cross-sectional data can merely provide limited evidence either way, we still believe that future research should tackle the issue of age-dependent effects of maltreatment, especially as many studies suggest that the HPA axis undergoes important developmental changes in middle childhood and puberty (Gunnar & Vazquez, 2006).

Finally, we fully agree with Dr. Fisher that there is a pressing need for longitudinal studies assessing cortisol at multiple time-points across childhood and adolescence. Optimally, prospective designs will help reconcile our age-related effects of maltreatment with studies showing early occurring hypocortisolism in preschool (Bruce, Fisher, Pears, & Levine, 2009; Dozier et al., 2006; Fisher, Kim, Bruce, & Pears, 2011). As Dr. Fisher’s research elegantly shows, the latter pattern has primarily emerged from samples of children adopted or fostered from different settings (including institutional care), and may therefore reflect a distinct pattern related to early deprivation or separation, potentially akin to an ‘energy-sparing phenotype’ (Del Giudice, Ellis, & Shirtcliff, 2011). It is safe to say that the deprivation and adversity documented in these samples presumably diverges (e.g., in terms of quality and/ or magnitude) from that typically experienced by children in our maltreated sample – who, for example, usually grew up with a constant caregiver and in an environment with ample social and health-care services at their disposal, including child protection service interventions.

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*Figure 1.* Interaction of age and chronicity to predict HCC within the maltreated group.