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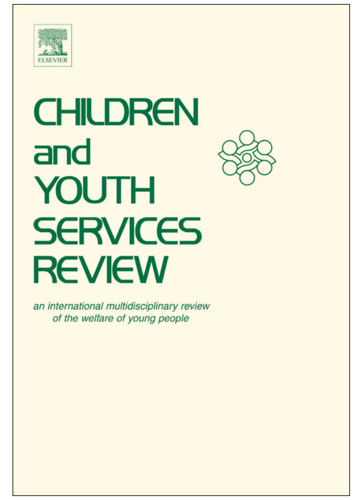

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Abstract

Little is known about the role of hypothalamic-pituitary-adrenal (HPA) axis functioning for children's cognitive development, especially among vulnerable groups. The current study explores the relationship between diurnal cortisol slope and cognitive outcomes among children at the ages of 5 and 6 who have been maltreated as infants and involved with child protective services, using data from the National Survey of Child and Adolescent Well-Being (NSCAW) I (N=158). Multiple regression analyses showed that a greater decline in salivary cortisol from morning to evening was positively associated with scores on applied problems and expressive communication, even after adjustment for confounding. It was also associated with lower odds of cognitive disability. There were null associations with letter-word identification, passage comprehension, auditory comprehension, matrices, and vocabulary. Results suggest that children involved with child protective services as infants, and thus exposed early to likely 'toxic' levels of stressors, may face dysregulation of the HPA axis and particular difficulties in some aspects of cognitive function. Potential explanations and implications for policy are discussed.

Keywords: NSCAW, salivary cortisol, child maltreatment, cognitive development, toxic stress

I. Introduction

Healthy development in the first years of life, a period of extreme vulnerability, is heavily dependent on sensitive and responsive care from a primary caregiver (Lucas & Richter, 2018). Maltreatment as well as the long-term absence of high-quality care in the early years can act as 'toxic' stress that raises the risk for later depression, anxiety, post-traumatic stress symptoms, eating disorders, substance abuse, and other chronic conditions (Doom et al., 2014). Past research has shown that these adverse outcomes may occur via disrupting the function of the hypothalamic-pituitary-adrenal (HPA) axis, a major neuroendocrine system that regulates reactions to stress and other important physical functions (Herman et al., 2016). The present study aimed to observe whether differences in HPA axis functioning were associated with meaningful differences in cognitive functioning among young children who had been maltreated as infants. To date, the existing research on this topic has mostly highlighted the role of HPA axis functioning in the association between toxic stress and cognitive functioning among adults (Suor et al., 2015). Such research is yet to be thoroughly conducted with young children, particularly those with experiences of maltreatment and/or neglect, who have been known to be at great risk of cognitive difficulties. This study was carried out to fill this gap and aimed to understand whether and how different domains of cognitive development in childhood are associated with the diurnal cortisol slopes of children who had been maltreated as infants.

1. The role of maltreatment in HPA axis functioning

The HPA axis is the main part of the stress-response system, and impacts neural activity and the development of brain structures. Functioning of the HPA axis and patterns of its end product, cortisol, have been found to be disrupted for children who experienced adversity because the functioning of the HPA axis is vulnerable to dysregulation during conditions of acute stress, such as neglect and abuse. To illustrate, children who have experienced maltreatment show progressively lower levels of morning cortisol over the ages of 19, 26, and 38 months (Cicchetti et al., 2011). Lower basal levels of cortisol have also been reported among children in institutions caring for those with an experience of neglect or abuse (Lupien et al., 2009). When early adversity becomes long-term, as is typically experienced by children involved with child protective services, it produces the type of chronic stress that the HPA axis is not accustomed to manage (Reilly & Gunnar, 2019). The HPA axis of children is highly susceptible to dysregulation particularly in the early years, a time when they are entirely dependent on external support to regulate physical and emotional stress (Fisher et al., 2007). Overall, accumulating evidence has indicated that children who have experienced chronic and toxic levels of stress are at risk for structural and functional alterations of the brain, mainly in the brain regions of the hippocampus, prefrontal cortex, and amygdala, through the release of glucocorticoids, such as cortisol, and HPA axis hyperactivity (Wesarg et al., 2020).

HPA axis functioning has generally been measured by the hormone cortisol (Herman et al., 2016). Typically, cortisol shows a distinct diurnal pattern throughout the day. Cortisol levels are highest in the morning, peaking about 30 minutes after wake-up. Cortisol then decreases throughout the day until it reaches a nadir near bedtime (Hirotsu et al., 2015). However, cortisol patterns fluctuate greatly. In general, cortisol patterns are established during early infancy (Groschl et al., 2003), but definitive reference values for salivary cortisol in healthy children have just begun to be established (Groschl et al., 2003). Although fluctuations in cortisol values continue to occur among children, the use of salivary cortisol is a useful and non-invasive method for measuring toxic stress and understanding its role in children's developmental outcomes.

In the early years, toxic stress is typically examined by family risk theories (Cowan & Cowan, 2002; Fox et al., 2002), which increasingly focus on the role of biological mechanisms as mediators. For example, allostasis and allostatic load (McEwen, 1998) provide a helpful lens to guide examination of how biological mechanisms of the stress-response system may mediate the negative effects of child and family-related adversity on health and developmental outcomes. A key concept, allostasis, represents the achievement of stability via physiological changes (e.g., in catecholamines, glucocorticoids, inflammatory cytokines) of the stress-response system (McEwen & Wingfield, 2003; Wesarg et al., 2020). Such physiological changes are temporarily adaptive for the individual, because they provide the necessary strength to deal with the stressful event. However, repetitive and continuous chronic stressors result in exhaustion of the response system, what is usually termed 'allostatic overload'. When allostatic overload ensues, dysfunctions and pathologies in the functioning of several physiological systems are likely to occur. In the context of child maltreatment, such a proximal family stressor may critically compromise the healthy development of children's stress-response systems as they are forced to adjust to chronically stressful and unsafe environments (Repetti et al., 2002). In the recent years, studies have indeed linked early exposure to serious family stressors and children's poor mental and physical health through aberrant HPA axis functioning and cortisol activity (Repetti et al., 2011).

2. The role of HPA axis functioning in cognition

Through alterations in critical brain structures and functions, early adversity and stress exposure have been associated with changes in the underlying cognitive processes related to the hippocampus, prefrontal cortex, and amygdala brain regions (Raymond et al., 2018; Tottenham & Sheridan, 2009). These areas are a critical target for stress hormones, and consequently may be crucial for a normally functioning HPA axis (Sandstrom et al., 2011). In adults for example, there is increasing evidence that chronic activation of the HPA axis is related to cognitive dysfunction (Keller et al., 2016). Among children, an inverted U-shape relationship has been found between cognitive functioning and glucocorticoids, such that typical amounts of cortisol appear to facilitate learning experiences and support the progress of cognitive abilities. However, chronically low or high levels of glucocorticoids are associated with impairment in several domains of cognition such as memory, attention, and spatial learning (Suor et al., 2015).

Thus, aberrant HPA axis functioning may mediate the association between maltreatment (and toxic stress in general) and poor cognitive outcomes in children. Family risk factors such as family instability (e.g., Vernon-Feagons et al., 2012), unsupportive and harsh parenting (e.g., Linver et al., 2002) and exposure to interpartner violence (e.g., Margolin & Gordis, 2004) have indeed been associated with difficulties in children's cognitive functioning. However, very little is known about the underlying biological mechanisms between family adversity and children's cognitive functioning (Suor et al., 2015). As discussed, chronic and toxic levels of stress induce steady levels of cortisol that may ensue in functional and structural alterations to the brain, compromising cognitive functioning (e.g., Suor et al., 2015). Such alterations may be of particular concern if they occur in childhood, a period of rapid change in cognitive capacities and abilities, due to the development of prefrontal and hippocampal brain regions (Hodel, 2018).

The current literature contends that knowledge on how exposure to early maltreatment affects young children's HPA axis functioning and cognitive functioning is still limited (Wesarg et al, 2020). While there is evidence that both HPA axis functioning and cognitive functioning can be disrupted by adversity (e.g., Edalati & Krank, 2016; Juruena et al., 2020), less is known about how the three processes associate with each other and shape developmental pathways. However, a better understanding of developmental pathways from early adversity to later outcomes is needed. Recent research has proposed a meaningful relationship between adversity-related HPA axis functioning changes and brain development, which then affects cognitive functioning (Raymond et al., 2018). Given that the importance of cognitive functioning amplifies in later development, an enhanced understanding of adversity-related processes in the first years of life is needed.

3. The present study

The present study aims to fill this gap by investigating the association between cognitive functioning and diurnal cortisol slope among 5-to 6-year-old children who were maltreated as infants, using data from the National Survey of Child and Adolescent Well-Being (NSCAW) I, which traces children involved with Child Protective Services (CPS). The diurnal cortisol slope is the linear degree of change in cortisol levels across the day, from morning to evening. A steeper decline is typically associated with better psychosocial and physical health (Adam & Kumari, 2009). Investigating this association in CPS-involved children is very important for two reasons. First, findings about maltreatment-related cortisol patterns in adults are not directly applicable to children. For example, the experience of child maltreatment is associated with blunting of HPA activity in adults but not always in children, suggesting that habituation of the stress response and hypocortisolism may begin in late adolescence and into adulthood (Doom et al., 2014). As such, research with children, particularly those in high-risk environments, is needed to understand the mechanisms underlying the link between HPA axis functioning and developmental outcomes. Second, the knowledge produced could help build targeted interventions to promote the academic outcomes of children who have experienced maltreatment, a group at very high risk for difficulties at school. To illustrate, the prevalence of language and cognitive delays among children in foster care has been reported to be 57% and 33% respectively, compared to 4% to 10% in the general population (Fry et al., 2017).

The cognitive outcomes we examined in this study are broad measures of executive function, language and memory, representing the type of cognitive functioning most related to areas of the brain that are heavily affected by increased levels of glucocorticoids during stressful situations, such as the hippocampus, prefrontal cortex, and amygdala (Llorens et al., 2022). There is indeed growing evidence that children exposed to maltreatment experience difficulty in tasks that require memory (Wunsch et al., 2019), executive functioning, selective attention (Raymond et al., 2018), verbal and visual working memory (Bos et al., 2009), and inhibitory control (Pollak et al., 2010). The primary research question of this study was to investigate what relationships exist between diurnal cortisol slope and these different domains of cognitive development among children maltreated as infants. We hypothesized that performance on assessments that require greater cognitive and memory load would be more strongly associated with diurnal cortisol slope. Performance on cognitive tasks that required the aforementioned abilities (e.g., memory, executive functioning, selective attention) to a varying degree was therefore examined as the main measures of interest. Thus, our study is an important addition to the current research because although the link from early maltreatment to difficulties in cognitive functioning via dysregulation of the HPA axis is probable (Raymond et al., 2018), it is still relatively unexplored in the early childhood population.

II. Methods

1. Study sample

The NSCAW is a national longitudinal study on the well-being of 5,501 children aged 14 years or younger in the United States who had contact with CPS within a 15-month period starting in October 1999. For the 'cortisol study' of NSCAW (at Wave 5), 1,186 children met the eligibility criteria of having been 5 or 6 years old at Wave 5 and infants when they were first investigated by CPS for maltreatment. The current study only uses data from Wave 5, which has been collected in 2006. Of these 1,186 children, 440 were selected for salivary cortisol sample collection, and 293 families agreed to collect the samples. Of those 293 families, 187 returned at least one saliva sample. This sample was further reduced to 158 children, as children who had missing information on either the wake or the bed time values (required for calculating diurnal slope) were also excluded. The analysis sample therefore included 158 children, aged 5 and 6 years old (M=5.26, SD=.44) at the time of cortisol collection (Wave 5). A total of 44.9% were male, 46.2% White, 35.4% Black, 8.2% American Indian, 2.5% Asian/Hawaiian/Pacific Islander, and 7.6% some other race.

2. Procedure

The NSCAW study follows all children investigated for maltreatment during the sampling period. Data was collected from a maximum of five possible respondents: the child, caregiver, caseworker, teacher, and former caregiver. Depending on the out-of-home status and age of the child, respondents were administered different interviews. For data collection, NSCAW field representatives mailed information brochures and letters to obtain consent and cooperation for the interview. For children under the age of seven, the child's legal guardian gave signed consent, and children between the ages of seven and fourteen were asked for their assent to interview. More information on the data collection procedures can be found in Dowd et al., 2008.

The 'cortisol study' sits within the larger NSCAW study, and has been conducted with a subset of the NSCAW sample at Wave 5, as explained. A number of precautions have been taken to ensure the reliability of the saliva sample collection. For example, a recent study (Wesarg et al., 2022) that investigated the reliability of cortisol measurement found that cortisol samples collected between 30 and 80 minutes after awakening and shortly before going to bed were considered a reliable collection of cortisol samples among young children. The salivary cortisol collection procedures in our study follow these reliability protocols. Moreover, caregivers were trained to take saliva samples from their children by NSCAW field representatives.

The High Sensitivity Salivary Cortisol Enzyme Immunoassay Kit was used for sample collection on three consecutive, typical weekdays (Salimetrics, State College, PA). All saliva samples from each child were included in the same assay batch to minimize within-subject variability. The saliva samples were assayed and averaged by the NSCAW team. Any duplicates varying by more than 15% were assayed again. The intra-assay coefficient of variance and the inter-assay coefficient of variance were 2% and 9%, respectively. To control for differences in substance use and collection procedures (both of which may influence cortisol levels), caregivers completed a brief questionnaire about their children's use of medication and sampling times on each of the sampling days. The questionnaires were inspected to ensure compliance with salivary cortisol collection guidelines. Saliva samples that failed to comply were excluded from analyses. Salivation was stimulated by chewing the Trident Original sugarless gum, which has been found to not affect cortisol levels by previous research (Schultheiss, 2013). After stimulation of saliva, salivettes were placed in the children's mouths to be saturated. Once saturated, the salivettes were placed in prelabeled plastic vials. Caregivers were then instructed to refrigerate the saliva samples until they were shipped to the laboratory. Previous research has found that cortisol levels are not influenced by the mailing processes (Kirschbaum & Hellhammer, 1989). The saliva samples were stored at -5°F until examined.

3. Measures

1) Diurnal cortisol slope

Diurnal cortisol slope was calculated by subtracting values of cortisol in the evening (30 minutes before going to bed but before brushing teeth; mean time 8:30 p.m.) from values in the morning (30 minutes after wakeup but before eating breakfast; mean time 7:31 a.m.), and dividing this by the number of hours separating the two samples. This approach appropriately adjusts for variations in the total time awake, and hence the total number of hours over which cortisol has the opportunity to decline.

2) Cognitive functioning

The present study uses scores on seven assessments to measure cognitive functioning: auditory comprehension and expressive communication within the Preschool Language Scale-3 assessment (PLS-3; Zimmerman et al., 1992), letter-word identification, comprehension, and applied problems within the Mini-Battery of Achievement assessment (M-BA; Woodcock et al., 1994), and vocabulary and matrices within the Kaufman Brief Intelligence Test (K-BIT; Kaufman & Kaufman, 1990). It also used a dichotomized measure of whether or not the child is diagnosed with a cognitive disability. All assessments have been agestandardized by the NSCAW team. PLS-3 measures prelinguistic skills such as attention, vocal development, and social communication, and language skills such as syntax, morphology, vocabulary, and concept development, measured via the expressive communication scale and the auditory comprehension scale. The auditory comprehension scale requires children to respond to verbal questions of increasing complexity by a motor response such as pointing or nodding, revealing the child's perception of language. The expressive communication scale requires children to express themselves verbally and evaluates the child's semantics, vocabulary, integrative thinking skills, and syntax. The M-BA test measures children's reading and math skills, through the letter-word identification, passage comprehension, and applied problems tests (Coohey et al., 2011). The letter-word identification test assesses the child's ability to read letters and words. The passage comprehension test assesses the child's ability to understand written text. Last of the three, the applied problems test assesses the child's ability to listen to a math problem and carry out the appropriate calculations. K-BIT is a brief, individually administered measure of verbal and nonverbal intelligence composed of two subtests, vocabulary and matrices, thus allowing the assessment of verbal-nonverbal ability discrepancies. The vocabulary test assesses knowledge of vocabulary and verbal concepts through verbal responses. The matrices test assesses non-verbal intelligence by using visual stimuli to ask children problem-solving questions. Finally, the cognitive disability measure is a dichotomous variable deposited by NSCAW. Children with scores less than 70 on either the K-BIT or the PLS-3 were coded as having a cognitive disability.

3. Confounding variables

The confounding variables for this study were child's gender (1=*male* and 2=*female),* race/ethnicity (0= *Non-White* and 1=*White*), age in months at entry into the study, number of out-of-home placements (0= *1 or fewer* and 1= *2 or more*), and severe abuse (0= *No* and 1=*Yes*). Age at entry into the study was derived using two existing variables: investigation close date (the CPS investigation that qualified the child to be in the NSCAW study) and child's date of birth.

4. Data analysis

Prior to the main data analysis, descriptive statistics summarizing the characteristics of the sample and a correlation analysis of the study variables with diurnal slope were carried out first. Next, to answer the main research question of whether there were significant associations between children's diurnal cortisol slopes and domains of cognitive functioning, adjusted and unadjusted linear and logistic regression analyses using multiple imputation to handle missing data were used. Multiple imputation predicts missing data based on the other known variables available on the same child. After several repetitions of this procedure, the standard errors and estimates of the resulting multiply imputed datasets are pooled into one overall dataset. The main advantages of multiple imputation over conventional methods for dealing with missing data such as listwise deletion, are that greater sample size and statistical power is preserved, correct standard errors are produced in consideration of missing data uncertainty, and unbiased results are given when data are missing at random (MAR) (de Goeij et al., 2013; Van Ginkel et al., 2020). Although multiple imputation may not be appropriate in certain scenarios where large numbers of variables are missing or when data is not missing at random (NMAR), this is not the case for the current study. We have therefore made the informed decision to use multiple imputation, given that our data meets the prerequisites for appropriate use of this method. Because only a small subsample of children was included, the weighted data and complex survey design typically used in analyses involving the NSCAW sample were not appropriate and so all analyses were conducted with unweighted data (Dowd et al., 2008).

III. Results

The descriptive statistics of the study variables can be found in Table 1 and 2 below. As expected, the study sample represents a high-risk group, with near a third of children having experienced severe abuse (32.3%) and at least two out-of-home placements (29.7%). The study sample had a mean age of 5.26 years (SD=.44) and was composed of slightly more girls (55.1%) than boys (44.9%). Children were between the ages of 0 to 13 months (M=7.25, SD=3.15) when they first entered the larger NSCAW study, which affirms that our study sample was exposed to maltreatment during infancy. Relatively few children had a diagnosis of cognitive disability (12.7%).

(Insert Table 1)

(Insert Table 2)

Table 3 below shows the correlation analysis between the variables included in the study. As Table 3 shows, steeper diurnal slopes, more likely in females (-.16, $p<.05$) and those without a cognitive disability (-.23, $p<.01$), were associated with better performance in applied problems (-.17, $p<.05$), expressive communication (-.20, $p<.05$) and letter-word identification (-.16, $p<.05$).

(Insert Table 3)

The effects of diurnal cortisol slope on each of the measures of cognitive functioning are shown in Table 4 in both adjusted and unadjusted regression models. As can be seen, in the model without any confounders, a greater cortisol decline was positively related to scores on applied problems ($\beta = -0.17$, $p<.05$), expressive communication ($\beta = -0.17$, $p<.05$) and letter-word identification ($\beta = -0.16$, $p<.05$), and was related to lower odds of having a cognitive disability (B=-35.86, SE=12.91, $p<.01$). In adjusted models, diurnal cortisol slope was related only to applied problems ($\beta = -0.18$, $p<.05$), expressive communication ($\beta = -0.16$, $p<.05$), and cognitive disability (B=-35.35, SE=13.56, $p<.01$).

(Insert Table 4)

IV. Discussion

The goal of the present study was to explore the cross-sectional association between diurnal cortisol slope and cognitive development at ages 5 and 6 years among children maltreated and investigated by Child Protective Services (CPS) as infants. Our results showed some associations but also evidence for significant outcome specificity. We found that after adjusting for key individual and care characteristics, a greater cortisol level decline from morning to evening was positively associated with scores on applied problems and expressive communication, and lower odds of cognitive disability. Its effect on letter-word identification was only significant before adjustment. Scores on passage comprehension, auditory comprehension, matrices, and vocabulary tests were not significantly associated with diurnal cortisol slope even before adjustment.

The reasons for this outcome specificity are unclear but we could speculate about a role of HPA axis functioning in working memory in the developing brain. Working memory is an important cognitive function that, in adults, is particularly affected by stress. Such a link has been less well-explored in children, but our study suggests, alongside other recent research (Wunsch et al., 2019), that it may exist in children too. In our sample we only observed an effect in the cognitive domains of applied problems and expressive communication, both heavily reliant on working memory, which, as a prefrontal-cortex-dependent executive resource, can be deleteriously impacted by stress (Lupien et al., 1999; Otto et al., 2013; Qin et al., 2009; Schoofs et al., 2009). In the present study, the expressive communication test examined the child's ability to express him- or herself verbally. Verbal working memory, the capacity to retain and manipulate information over temporary periods to conduct an immediate oral response, is required for this ability (Smith et al., 1998). Verbal working memory is related to receptive and expressive skills, the acquisition of new vocabulary, and the coherence and complexity of speech production (Evans & Saffran, 2009). On the other hand, the applied problems scale required children to solve mathematical word problems in response to orally presented problems. To solve each problem, the child is required to listen to it and understand it, decide on the procedure to be followed, and then perform calculations. Because many of the problems include extraneous information, the child needs to also determine what information is relevant and needed. All these processes involve working memory, requiring children to temporarily store new information (temporary storage), ignore irrelevant information (executive functioning, inhibition), and decide which mathematical operations should be used to solve the problem (high processing demands).

In contrast, performance on the vocabulary, matrices, letter-word identification, auditory comprehension, and passage comprehension tests may not require as large working memory capacity or be as heavily reliant on active processing, an important dimension according to the continuity model of working memory by Cornoldi and Vecchi (2003). This asserts the existence of two dimensions. The horizontal continuum refers to the various characteristic domains (e.g., verbal, visual, and spatial), and the vertical continuum refers to a distinction between passive storage (which requires recalling information in the previously presented format) and active processing (which requires integrating and revising previous information). The tests showing null associations in our study with diurnal cortisol slope require passive storage of working memory, with relatively fewer demands on active processing. For example, the vocabulary test requires children to retrieve stored information of words that they know. The matrices test again requires minimal processing and storage, and the letter-word identification test mainly requires phonological awareness. Although some capacity of working memory may be required when retrieving phonological information from the mental lexicon (i.e., the store of word knowledge) and decoding sounds, the task is still a single-step that does not require high-levels of active processing. Finally, the auditory and passage comprehension tests, both testing receptive language skills, also require storage primarily. Compared to expressive communication, these skills may be less demanding on processing activity and reflective thinking.

These null associations however should not compromise the novelty and importance of this study. Much of the research to date on the association between HPA axis functioning and cognitive functioning is with disadvantaged groups (predominantly in chronic poverty) in adulthood, with findings about the association in children lacking consistency (Bernard et al., 2015; Blair et al., 2005; Blair et al., 2011; Lupien et al., 2011). In addition, while the existing evidence asserts that experiences of child maltreatment are critical risk factors for psychopathology, our understanding of the psychobiological mechanisms that underlie this relationship is currently limited, and the relationship between specific risk factors early in life and later HPA axis dysfunction is not clearly established during the first five years of life (Wesarg et al., 2020). Still, there is adequate research evidence to conclude that early childhood is a critical developmental period when the HPA axis is at risk of being dysregulated when exposed to certain stressful experiences. Recent research suggests that toxic and chronic stressful experiences may act as a fundamental mechanism connecting experiences of early maltreatment to later cognitive difficulties (Blair & Raver, 2012; Raymond et al., 2018), and on this we built the rationale for our study.

As for the mechanism we proposed (aberrant HPA axis functioning), this is in line with findings from neurobiological research which asserts that glucocorticoids, the primary component of stress-response systems, affect the structural and neural development of the brain. To illustrate, the brain regions that are concentrated with glucocorticoid receptors such as the hippocampus, prefrontal cortex, and amygdala have been found to experience alterations in structure and function after adverse experiences (Lupien et al., 2009; McCrory et al., 2010; Raymond et al., 2018). In turn, evidence also demonstrates that the prefrontal cortex is an important part of the regulation of behavior, emotion, and cognition (Miller & Cohen, 2001; Ochsner & Gross, 2005). Overall, there is evidence to support the proposition that early experiences of adversity may place children's cognitive development at risk via mechanisms related to HPA axis functioning.

Our study also has some limitations that should be recognized. First, cortisol levels were concurrently measured with children's cognitive skills. A more robust study design would assess cortisol before and after the experience of the negative life event. This, however, was not possible as the present study used secondary data and cortisol data was only collected once at Wave 5. Despite this limitation, the children in the sample had been investigated by CPS as infants, indicating that they were at risk of abuse and/or neglect during infancy (US DHHS, 2009). As such, a flattened diurnal cortisol slope in our study can be understood as a marker of exposure to stressors occurring before cognitive functioning was tested. Carefully administered longitudinal studies examining the relationship between cortisol rhythm, chronic and early adversity, and resilient paths of development in high-risk groups of children will be very valuable. Second, our group may be too heterogeneous as it includes both substantiated and unsubstantiated CPS cases. However, past research has found that unsubstantiated reports pose the same risk for negative outcomes (Holbrook & Hudziak, 2020). Lastly, the lack of investigation of prenatal factors is a limitation of the study, as the existing evidence suggests that the development and functioning of the HPA axis can be affected by many types of extraneous factors, including intrauterine exposure to drugs and alcohol (Beijers et al., 2014; Kapoor et al., 2008), maternal mental conditions such as depression (Barker et al., 2013), and stress and trauma (King & Laplante, 2005). Children involved in CPS investigations, our sample, may have been exposed prenatally to 'toxic' stressors such as these, which have been found to co-occur with child maltreatment (Smith et al., 2007; Seay, 2015). Also related to controlling for variables which may confound the results, the dichotomization of the severe abuse measure is not ideal, as it leads to loss of information as well as the risk that confounding remains (Altman & Royston, 2006). Given these limitations, causal assumptions or conclusions are not possible.

In conclusion, the present study suggests that children with maltreatment exposure as infants may have experienced HPA axis dysregulation and impairment in cognitive development, particularly in domains related to working memory, at age 5. It also builds the evidence on the developmental outcomes of an important and substantial group of children in the field of child welfare research, those involved with child protective services very early in life. Recent reports of child victims' demographics, for example, document that the youngest children are the most susceptible and vulnerable to maltreatment, with those under the age of one suffering the highest rate of victimization compared to any other age group in the United States (25.1 per 1,000 children; U.S. Department of Health & Human Services et al., 2022). Future research should investigate the associations between stress hormones and different aspects of early cognitive development, including working memory, among CPS-involved children as well as among other high-risk child populations, with the aim of informing intervention strategies. There is some empirical evidence, for example, that children's cortisol levels have successfully been 'normalized' after parenting interventions, whereby children in the treatment group mirrored cortisol levels of a low-risk comparison group post treatment (Bernard et al., 2015; Cicchetti et al., 2011; Dozier et al., 2006). Such results have been demonstrated among children between birth and aged five in foster care (Dozier et al., 2006), neglected (Bernard et al., 2015), and maltreated (Cicchetti et al., 2011) populations. Findings from such interventions have substantial implications about the malleability of developmental trajectories. For instance, interventions for high-risk infants that aim to normalize HPA functioning by aiding children's capacities to appropriately perceive threat and regulate their neurobiological systems to avoid hypersensitivity to stressful experiences could be very effective (Cicchetti & Rogosch, 2007). Future research should also consider tracking the development of cognitive functioning of maltreated children over time and testing whether and, if so, how HPA axis functioning has a role to play in it. This knowledge can then contribute towards an empirical base which informs the design of interventions that alleviate the adverse effects of early maltreatment.

References

Adam, E. K., & Kumari, M. (2009). Assessing salivary cortisol in large-scale, epidemiological research. *Psychoneuroendocrinology, 34,* 1423-1436. https://doi.org/10.1016/j.psyneuen.2009.06.011

Alloway, T. P., Gathercole, S. E., & Pickering, S. J. (2006). Verbal and visuospatial short-term and working memory in children: Are they separable? *Child Development, 77*(6), 1698-1716. https://doi.org/10.1111/j.1467-8624.2006.00968.x

Altman, D. G., & Royston, P. (2006). The cost of dichotomizing continuous variables. *BMJ, 332*(7549), 1080.

Archibald, L. M. D., & Gathercole, S. E. (2006). Short-term and working memory in specific language impairment. *International Journal of Language & Communication Disorders, 41*(6), 675-693. https://doi.org/10.1080/13682820500442602

Barker, E. D., Kirkham, N., Ng, J., & Jensen, S. K. G. (2013). Prenatal maternal depression symptoms and nutrition, and child cognitive function. *The British Journal of Psychiatry, 203,* 417-421. doi: 10.1192/bjp.bp.113.129486

Beijers, R., Buitelaar, J. K., & de Weerth, C. (2014). Mechanisms underlying the effects of prenatal psychosocial stress on child outcomes: Beyond the HPA axis. *European Child & Adolescents Psychiatry, 23,* 943-956. https://doi.org/10.1007/s00787-014-0566-3

Bernard, K., Dozier, M., Bick, J., & Gordon, M. K. (2015). Intervening to enhance cortisol regulation among children at risk for neglect: Results of a randomized clinical trial. *Development and Psychopathology, 27*(3), 829-841. https://doi.org/10.1017/S095457941400073X

Bernard, K., Hostinar, C. E., & Dozier, M. (2015). Intervention effects on diurnal cortisol rhythms of child protective services- referred infants in early childhood. *JAMA Pediatrics, 169*(2), 112-119. 10.1001/jamapediatrics.2014.2369

Berninger, V. W., & Abbott, R. D. (2010). Listening comprehension, oral expression, reading comprehension, and written expression: Related yet unique language systems in grades 1, 3, 5, and 7. *Journal of Educational Psychology, 102*(3), 635-651. https://doi.org/10.1037/a0019319

Blair, C., Granger, D., & Razza, R. P. (2005). Cortisol reactivity is positively related to executive function in preschool children attending Head Start. *Child Development, 76*(3), 554-567. https://doi.org/10.1111/j.1467-8624.2005.00863.x

Bos, K. J., Fox, N., Zeanah, C. H., & Nelson III, C. A. (2009). Effects of early psychosocial deprivation on the development of memory and executive function. *Frontiers in Behavioral Neuroscience, 3*(16), 1-7. https://doi.org/10.3389/neuro.08.016.2009

Blair, C., Granger, D. A., Willoughby, M., Mills-Koonce, R., Cox, M., Greenberg, M. T., … & the FLP Investigators. (2011). Salivary cortisol mediates effects of poverty and parenting on executive functions in early childhood. *Child Development, 82*(6), 1970-1984. https://doi.org/10.1111/j.1467-8624.2011.01643.x

Blair, C., & Raver, C. C. (2012). Child development in the context of adversity: Experiential canalization of brain and behavior. *American Psychology, 67*(4), 309-318. https://doi.org/10.1037/a0027493

Bourdin, B., & Fayol, M. (1994). Is Written Language Production More Difficult than oral language production? A working memory approach. *International journal of Psychology, 29*(5), 591-620. https://doi.org/10.1080/00207599408248175

Bourdin, B., & Fayol, M. (2000). Is graphic activity cognitively costly? A developmental approach. *Reading and Writing: An Interdisciplinary Journal, 13*, 183-196. https://doi.org/10.1023/A:1026458102685

Campen, C. A. N. K., Segers, E., & Verhoeven, L. (2018). How phonological awareness mediates the relation between working memory and word reading efficiency in children with dyslexia. *Dyslexia, 24,* 156-169. https://doi.org/10.1002/dys.1583

Cicchetti, D., & Curtis, W. J. The developing brain and neural plasticity: Implications for normality, psychopathology, and resilience. In: Cicchetti, D., Cohen, D. J. (Eds.). Developmental psychopathology: Developmental neuroscience. 2nd. Vol. 2. Wiley; New York: 2006. p. 1-64.

Cicchetti, D., & Rogosch, F. A. (2007). Personality, adrenal steroid hormones, and resilience in maltreated children: A multi-level perspective. *Development and Psychopathology, 19*(3), 787-809. https://doi.org/10.1017/S0954579407000399

Cicchetti, D., Rogosch, F. A., Toth, S. L., & Sturge-Apple, M. L. (2011). Normalizing the development of cortisol regulation in maltreated infants through preventive interventions. *Development and Psychopathology, 23*(3), 789-800. https://doi.org/10.1017/S0954579411000307

Coohey, C., Renner, L. M., Hua, L., Zhang, Y., & Whitney, S. D. (2011). Academic Achievement despite child maltreatment: a longitudinal study. *Child Abuse and Neglect, 35*(9), 688-699. https://doi.org/10.1016/j.chiabu.2011.05.009

Cowan, P. A., & Cowan, C. P. (2002). Interventions as tests of family systems theories: Marital and family relationships in children's development and psychopathology. *Development and Psychopathology, 14*(4), 731-759. https://doi.org/10.1017/S0954579402004054

de Goeij, M. C. M., van Diepen, M., Jager, K. J., Tripepi, G., Zoccali, C., & Dekker, F. W. (2013). Multiple imputation: Dealing with missing data. *Nephrology Dialysis Transplantation, 28*(10), 2415-2420.

Doom, J. R., Cicchetti, D., & Rogosch, F. A. (2014). Longitudinal patterns of cortisol regulation differ in maltreated and nonmaltreated children. *Journal of the American Academy of Child & Adolescent Psychiatry, 53*(11), 1206-1215. https://doi.org/10.1016/j.jaac.2014.08.006

Dowd, K., Kinsey, S., Wheeless, S., Thissen, R., Richardson, J., Suresh, R., … Smith, K. (2008). *National survey of child and adolescent well-being (NSCAW) combined waves 1-5 data file user's manual-restricted release version.* Ithaca, NY: National Data Archive on Child Abuse and Neglect, Cornell University.

Dozier, M., Peloso, E., Lindheim, O., Gordon, M. K., Manni, M., Sepulveda, S., … Levine, S. (2006). Developing evidence-based interventions for foster children: An example of a randomized clinical trial with infants and toddlers. *Journal of Social Issues, 62*(4), 767-785. https://doi.org/10.1111/j.1540-4560.2006.00486.x

Edalati, H., & Krank, M. D. (2016). Childhood maltreatment and development of substance use disorders: a review and a model of cognitive pathways. *Trauma, Violence, & Abuse, 17*(5), 454–467. https://doi.org/10.1177/1524838015584370

Elliott, J. G., Gathercole, S. E., Alloway, T. P., Holmes, J., & Kirkwood, H. (2010). An evaluation of a classroom-based intervention to help overcome working memory difficulties and improve long-term academic achievement. *Journal of Cognitive Education and Psychology, 9*(3), 227-250. https://doi.org/10.1891/1945-8959.9.3.227

Evans, J. L. & Saffran, J. R. (2009). Statistical learning in children with specific language impairment. *Journal of Speech Language and Hearing Research, 52*(2), 321-335. https://doi.org/10.1044/1092-4388(2009/07-0189)

Fisher, P. A., Stoolmiller, M., Gunnar, M. R., & Burraston, B. O. (2007). Effects of a therapeutic intervention for foster preschoolers on diurnal cortisol activity. *Psychoneurodocrinology, 32*(8-10), 892-905. https://doi.org/10.1016/j.psyneuen.2007.06.008

Fox, G. L., Benson, M. L., DeMaris, A. A., & Van Wyk, J. (2002). Economic distress and intimate violence: Testing family stress and resource theories. *Journal of Marriage and Family, 64*(3), 793-807. https://doi.org/10.1111/j.1741-3737.2002.00793.x

Fox, N. A., & Leavitt, L. A. (1995). *The Violence Exposure Scale for Children- VEX (preschool version).* College Park: Department of Human Development, University of Maryland.

Fry, C. E., Langley, K., & Shelton, K. H. (2017). A systematic review of cognitive functioning among young people who have experienced homelessness, foster care, or poverty. *Child Neuropsychology, 23*(8), 907-934. https://doi.org/10.1080/09297049.2016.1207758

Groschl, M., Rauh, M., & Dorr, H. G. (2003). Circadian rhythm of salivary cortisol, 17{alpha}-hydroxyprogesterone, and progesterone in healthy children. *Clinical Chemistry, 49,* 1688-1691. https://doi.org/10.1373/49.10.1688

Hatcher, R. C., Breaux, K. C., Liu, X., Bray, M. A., Ottone-Cross, K. L., Courville, T., … Langley, S. D. (2017). Analysis of children’s errors in comprehension and expression. *Journal of Psychoeducational Assessment, 35*(1-2), 57-73. https://doi.org/10.1177/0734282916669019

Herman, J. P., McKlveen, J. M., Ghosal, S., Kopp, B. Wulsin, A., Makinson, R., …Myers, B. (2016). Regulation of the hypothalamic-pituitary-adrenocortical stress response. *Comprehensive Physiology, 6*(2), 603-621. https://doi.org/10.1002/cphy.c150015

Hirotsu, C., Tufik, S., & Andersen, M. L. (2015). Interactions between sleep, stress, and metabolism: From physiological to pathological conditions. *Sleep Science, 8*(3), 143-152. https://doi.org/10.1016/j.slsci.2015.09.002

Hodel, A. S. (2018). Rapid infant prefrontal cortex development and sensitivity to early environmental experience. *Developmental Review, 48,* 113-144. https://doi.org/10.1016/j.dr.2018.02.003

Holbrook, H. M. & Hudziak, J. J. (2020). Risk factors that predict longitudinal patterns of substantiated and unsubstantiated maltreatment reports. *Child Abuse and Neglect, 99,* 1-12. https://doi.org/10.1016/j.chiabu.2019.104279

Juruena, M. F., Eror, F., Cleare, A. J., & Young, A. H. (2020). The role of early life stress in HPA axis and anxiety. *Anxiety Disorders,* 141-153.

Kapoor, A., Petropoulos, S., & Matthews, S. G. (2008). Fetal programming of hypothalamic-pituitary-adrenal (HPA) axis function and behavior by synthetic glucocorticoids. *Brain Research Reviews, 57*(2), 586-595. https://doi.org/10.1016/j.brainresrev.2007.06.013

Keller, J., Gomez, R., Williams, G., Lembke, A., Lazzeroni, L., Murphy Jr., G. M., & Schatzberg, A. F. (2016). HPA axis in major depression: cortisol, clinical symptomatology and genetic variation predict cognition. *Molecular Psychiatry, 22,* 527-536. https://doi.org/10.1038/mp.2016.120

King, S., & Laplante, D. P. (2005). The effects of prenatal maternal stress on children's cognitive development: Project Ice Storm. *Stress, 8*(1), 35-45. https://doi.org/10.1080/10253890500108391

Kirschbaum, C., & Hellhammer, D. H. (1989). Salivary cortisol in psychobiological research: An overview. *Neuropsychobiology, 22*(3), 150-169. https://doi.org/10.1159/000118611

Linver, M. R., Brooks-Gunn, J., & Kohen, D. E. (2002). Family processes as pathways from income to young children's development. *Developmental Psychology, 38,* 719-734. https://doi.org/10.1037/0012-1649.38.5.719

Llorens, M., Barba, M., Tottalbas, J., Nadal, R., Armario, A., Gagliano, H., … Labad, J. (2022). Stress-related biomarkers and cognitive functioning in adolescents with ADHD: Effect of childhood maltreatment. *Journal of Psychiatric Research, 149,* 217-225. https://doi.org/10.1016/j.jpsychires.2022.02.041

Loosli, S. V., Buschkuehl, M., Perrig, W. J., & Jaeggi, S. M. (2012). Working memory training improves reading processes in typically developing children. *Child Neuropsychology, 18*(1), 62-78. https://doi.org/10.1080/09297049.2011.575772

Lucas, J. & Richter, L. (2018). Care for child development: an intervention in support of responsive caregiving and early child development: Care for child development. *Child Care Health and Development, 44*(1), 41-49. https://doi.org/10.1111/cch.12544

Luciana, M., Conklin, H. M., Hooper, C. J., & Yarger, R. S. (2005). The development of nonverbal working memory and executive control processes in adolescents. *Child Development, 76*(3), 697-712. https://doi.org/10.1111/j.1467-8624.2005.00872.x

Lupien, S. J., King, S., Meaney, M. J., & Mcewen, B. S. (2001). Can poverty get under your skin? Basal cortisol levels and cognitive function in children from low and high socioeconomic status. *Development and Psychopathology, 13*(1), 653-676. https://doi.org/10.1017/S0954579401003133

Lupien, S. J., McEwen, B. S., Gunnar, M. R., & Heim, C. (2009). Effects of stress throughout the lifespan on the brain, behavior, and cognition. *Nature Reviews Neuroscience, 10*(6), 434-445. https://doi.org/10.1038/nrn2639

Margolin, G., & Gordis, E. B. (2004). Children's exposure to violence in the family and community. *Current Directions in Psychological Science, 13,* 152-155. https://doi.org/10.1111/j.0963-7214.2004.00296.x

McCrory, E., Brito, S. A. D., & Viding, E. (2010). Research review: The neurobiology and genetics of maltreatment and adversity. *Journal of Child Psychology and Psychiatry, 51*(10), 1079-1095. https://doi.org/10.1111/j.1469-7610.2010.02271.x

McDonald, S., Gowland, A., Randall, R., Fisher, A., Osborne-Crowley, K., & Honan, C. (2014). Cognitive factors underpinning poor expressive communication skills after traumatic brain injury: Theory of Mind or Executive function? *Neuropsychology, 28*(5), 1-11. http://dx.doi.org/10.1037/neu0000089

McEwen, B. S. (1998). Stress, adaptation, and disease: Allostasis and allostatic load. *Neuroimmunomodulation: Molecular Aspects, Integrative Systems, and Clinical Advances, 840*(1), 33-44. https://doi.org/10.1111/j.1749-6632.1998.tb09546.x

McEwen, B. S., & Wingfield, J. C. (2003). The concept of allostasis in biology and biomedicine. *Hormones and Behavior, 43*(1), 2-15. https://doi.org/10.1016/S0018-506X(02)00024-7

McFayden, R. G. & Kitson, W. J. H. (1996). Language comprehension and expression among adolescents who have experienced childhood physical abuse. *Journal of Child Psychology and Psychiatry, 37*(5), 551-562. https://doi.org/10.1111/j.1469-7610.1996.tb01441.x

Miller, E. K., & Cohen, J. D. (2001). An integrative theory of prefrontal cortex function. *Annual Review of Neuroscience, 24*(1), 167-202. https://doi.org/10.1146/annurev.neuro.24.1.167

Ochsner, K. N., & Gross, J. J. (2005). The cognitive control of emotion. *Trends in Cognitive Sciences, 9*(5), 242-249. https://doi.org/10.1016/j.tics.2005.03.010

Raymond, C., Marin, M., Majeur, D., & Lupien, S. (2018). Early child adversity and psychopathology in adulthood: HPA axis and cognitive dysregulations as potential mechanisms. *Progress in Neuropsychopharmacology and Biological Psychiatry, 85*, 152-160. https://doi.org/10.1016/j.pnpbp.2017.07.015

Reilly, E. B. & Gunnar, M. R. (2019). Neglect, HPA axis reactivity, and development. *International Journal of Developmental Neuroscience, 78*(1), 100-108. https://doi.org/10.1016/j.ijdevneu.2019.07.010

Repetti, R. L., Robles, T. F., & Reynolds, B. (2011). Allostatic processes in the family. *Development and Psychopathology, 23,* 921-938. https://doi.org/10.1017/S095457941100040X

Repetti, R. L., Taylor, S. E., & Seeman, T. E. (2002). Risky families: Family social environments and the mental and physical health of offspring. *Psychological Bulletin*, 128, 330– 366. doi:10.1037/0033-2909.128.2.330

Riva, V., Cantiani, C., Dionne, G., Marini, A., Mascheretti, S., Molteni, M., & Masrino, C. (2017). Working memory mediates the effects of gestational age at birth on expressive language development in children. *Neuropsychology, 31*(5), 475-485. https://doi.org/10.1037/neu0000376

Rubin, R. D., Watson, P. D., Duff, M. C., & Cohen, N. J. (2014). The role of the hippocampus in flexible cognition and social behavior. *Frontiers in Human Neuroscience, 8*(742), 1-15. https://doi.org/10.3389/fnhum.2014.00742

Passolunghi, M. C. & Mammarella, I. C. (2010). Spatial and visual working memory ability in children with difficulties in arithmetic word problem solving. *European Journal of Cognitive Psychology, 22*(6), 944-963. https://doi.org/10.1080/09541440903091127

Pollak, S. D., Cicchetti, D., Hornung, K., & Reed, A. (2000). Recognizing emotion in faces: developmental effects of child abuse and neglect. *Developmental Psychology, 36*(5), 679-688. DOI: 10.1037//0012-1649.36.5.679

Sandi, C. (2013). Stress and cognition. *Wiley Interdisciplinary Reviews: Cognitive Science, 4,* 245-261. https://doi.org/10.1002/wcs.1222

Sandstrom, A., Peterson, J., Sandstrom, E., Lundberg, M. Nystrom, I. R., Nyberg, L., & Olsson, T. (2011). Cognitive deficits in relation to personality type and hypothalamic-pituitary-adrenal (HPA) axis dysfunction in women with stress-related exhaustion. *Scandinavian Journal of Psychology, 52,* 71-82. https://doi.org/10.1111/j.1467-9450.2010.00844.x

Schultheiss, O. C. (2013). Effects of sugarless chewing gum as a stimulant on progesterone, cortisol, and testosterone concentrations assessed in saliva. *International Journal of Psychophysiology, 87*(1), 111-114. https://doi.org/10.1016/j.ijpsycho.2012.11.012

Seay, K. (2015). How many families in child welfare services are affected by parental substance use disorders? A common question that remains unanswered. *Child Welfare, 94*(4), 19-51.

Smith, E. E., Jonides, J., Marshuetz, C., & Koeppe, R. A. (1998). Components of verbal working memory: Evidence from neuroimaging. *Proceedings of the National Academy of Sciences, 95*(3), 876-882. https://doi.org/10.1073/pnas.95.3.876

Smith, D. K., Johnson, A. B., Pears, K. C., Fisher, P. A., & DeGarmo, D. S. (2007). Child maltreatment and foster care: Unpacking the effects of prenatal and postnatal parental substance use. *Child maltreatment, 12*(2), 150-160. https://doi.org/10.1177/1077559507300129

Suor, J. H., Sturge-Apple, M. L., Davies, P. T., Cicchetti, D., & Manning, L. G. (2015). Tracing differential pathways of risk: Associations among family adversity, cortisol, and cognitive functioning in childhood. *Child Development, 86*(4), 1142-1158. https://doi.org/10.1111/cdev.12376

Tottenham, N. & Sheridan, M. A. (2009). A review of adversity, the amygdala and the hippocampus: A consideration of developmental timing. *Frontiers in Human Neuroscience, 3*(68), 1-18. https://doi.org/10.3389/neuro.09.068.2009

U. S. Department of Health and Human Services, Administration for Children, Youth and Families. (2009). Child Maltreatment 2007. U.S. Government Printing Office, Washington, D. C.

U.S. Department of Health & Human Services, Administration for Children and Families, Administration on Children, Youth and Families, Children's Bureau. (2022). *Child Maltreatment 2020.* Available from https://www.acf.hhs.gov/cb/data-research/child-maltreatment.

Van Bodegom, M., Homberg, J. R., & Henckens, M. J. A. G. (2017). Modulation of the Hypothalamic-Pituitary-Adrenal Axis by Early Life Stress Exposure. *Frontiers in Cellular Neuroscience, 11*(87), 1-33. https://doi.org/10.3389/fncel.2017.00087

Van Ginkel, J. R., Linting, M., Rippe, R. C. A., & van der Voort, A. (2020). Rebutting existing misconceptions about multiple imputation as a method for handling missing data. *Journal of Personality Assessment, 102*(3), 297-308. https://doi.org/10.1080/00223891.2018.1530680

Vernon-Feagans, L., Garrett-Peters, P., Willoughby, M., & Mills-Koonce, R. (2012). Chaos, poverty, and parenting: Predictors of early language development. *Early Childhood Research Quarterly, 27,* 339-351. https://doi.org/10.1016/j.ecresq.2011.11.001

Wesarg, C., Van den Akker, A. L., Hoeve, M., Wiers, R. W., & Oei, N. Y. L. (2022). Reliability of salivary cortisol levels in toddlers. *European Journal of Developmental Psychology, 19*(3), 419-437. https://doi.org/10.1080/17405629.2021.1926230

Wesarg, C., Van Den Akker, A. L., Oei, N. Y., Hoeve, M., & Wiers, R. W. (2020). Identifying pathways from early adversity to psychopathology: A review on dysregulated HPA axis functioning and impaired self-regulation in early childhood. *European Journal of Developmental Psychology,* 1-20. https://doi.org/10.1080/17405629.2020.1748594

Woodcock, R. W., McGrew, K. S., & Werder, J. K. (1994). *Woodcock-McGrew-Werder Mini-Battery of Achievement.* Chicago: Riverside Publishing Company.

Wunsch, K., Meier, M., Ueberholz, L., Strahler, J., & Kasten, N. (2019). Acute psychological stress and working memory performance: the potential of physical activity to modulate cognitive functions in children. *BMC Pediatrics, 19,* 271. https://doi.org/10.1186/s12887-019-1637-x

Zimmerman, I. L., Steiner, V. G., Pond, R. E. (1992). *Preschool Language Scale, 3rd edition.* San Antonio, TX: The Psychological Corporation.

Table 1. Descriptive statistics of categorical study variables

Variable	Category	N	Percent
Gender	Male	71	44.9
	Female	87	55.1
	Total	158	100.0
Age	5 years	117	74.1
	6 years	41	25.9
	Total	158	100.0
	*Age Mean(SD) = 5.26(.44)		
Race/Ethnicity	American Indian	13	8.2
	Asian/Hawaiian/Pacific Islander	4	2.5
	Black	56	35.4

	White	73	46.2
	Other	12	7.6
	Total	158	100.0
Number of out-of-home placements	2 or more	47	29.7
	1 or fewer	111	70.3
	Total	158	100.0
Severe abuse	Yes	51	32.3
	No	107	67.7
	Total	158	100.0
Cognitive disability	Yes	20	12.7
	No	138	87.3
	Total	158	100.0

Table 2. Descriptive statistics of continuous study variables

Variable	Category	N	Mean(SD)	Min, Max
Age at study entry (in months)		138	7.25(3.15)	0, 13
Diurnal slope		158	-.03(.02)	-.09, .03
K-BIT[a]				
	Vocabulary	157	94.08(13.14)	55, 121
	Matrices	158	95.24(14.08)	40, 160
PLS-3[b]				
	Auditory Comprehension	115	97.79(19.10)	50, 126
	Expressive Communication	115	95.91(21.54)	50, 124

M-BA[c]				
	Letter Word Identification	158	102.90(13.79)	57, 142
	Passage Comprehension	158	98.75(13.17)	62, 132
	Applied Problems	158	93.03(16.98)	29, 130

a. K-BIT- Kaufman Brief Intelligence Test, ***b.*** PLS-3- Preschool Language Scale-3, ***c.*** M-BA- Mini-Battery of Achievement

Table 3. Correlations between the study variables

Measure	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15
1. Diurnal slope	-	-	-	-	-	-	-	-	-	-	-	-	-	-	-
2. 2 or more placements	-.01	-	-	-	-	-	-	-	-	-	-	-	-	-	-
3. Age at study entry	.10	-.27**	-	-	-	-	-	-	-	-	-	-	-	-	-
4. Age at cortisol (and cognitive measures) collection	.03	-.28***	.21*	-	-	-	-	-	-	-	-	-	-	-	-
5. White	.05	-.10	.07	.09***	-	-	-	-	-	-	-	-	-	-	-
6. Female	-.16*	-.08	.05	-.01	.001	-	-	-	-	-	-	-	-	-	-
7. Severe abuse	-.06	-.09	-.21*	-.22**	-.22**	.06	-	-	-	-	-	-	-	-	-
8. No cognitive disability	-.23**	.06	.07	.12***	.07***	-.006	-.06	-	-	-	-	-	-	-	-
9. Vocabulary[a]	-.003	.12	.001	.03	.20***	-.04*	-.18*	.50***	-	-	-	-	-	-	-
10. Matrices[a]	-.11	.05	-.12	.13***	.09***	-.01	.003	.52***	.52***	-	-	-	-	-	-
11. Auditory Comprehension[b]	-.11	.09	.05	.01	.20***	.05	-.09	.56***	.57***	.42***	-	-	-	-	-
12. Expressive Communication[b]	-.20*	.15	.08	.06	.09*	.06	-.08	.66***	.53***	.34***	.61***	-	-	-	-
13. Letter-Word Identification[c]	-.16*	.16*	.01	-.09**	.05**	.03	-.12	.43***	.61***	.51***	.41***	.37***	-	-	-
14. Passage Comprehension[c]	-.06	.15*	-.10	-.23***	.04**	.02	-.01	.40***	.57***	.51***	.13***	.15***	.78***	-	-
15. Applied Problems[c]	-.17*	.07	-.02	.10***	.09***	-.02	-.19*	.48***	.56***	.55***	.56***	.54***	.65***	.63***	-

a. K-BIT- Kaufman Brief Intelligence Test, ***b.*** PLS-3- Preschool Language Scale-3, ***c.*** M-BA- Mini-Battery of Achievement
*$p < 0.05$
**$p < 0.01$
***$p < 0.001$

Table 4. Regression analyses (after multiple imputation)

Dependent Variable	Independent Variables	Unadjusted Model B	S.E.	*Beta*	*t*	Adjusted Model B	S.E.	*Beta*	*t*
Vocabulary [a]	Diurnal slope	-2.31	48.80	-.003	-0.039	-12.56	47.19	-0.02	-0.29
	Female					0.17	2.06	0.01	0.12*
	2 or more placements					1.13	0.67	0.15	1.84
	Age at study entry					0.08	0.22	0.03	0.43
	White					5.71	2.11	0.23	2.88
	Severe abuse					-7.28	2.30	-0.25	-3.13**
		B	**S.E.**	***Beta***	***t***	**B**	**S.E.**	***Beta***	***t***
Matrices [a]	Diurnal slope	-74.18	54.48	-.11	-1.36	-83.60	55.78	-0.12	-1.45
	Female					-1.25	2.4 2	-0.04	-0.48
	2 or more placements					0.34	0.77	0.03	0.40
	Age at study entry					-0.23	0.25	-0.11	-1.32
	White					4.28	2.49	0.14	1.68
	Severe abuse					-0.95	2.69	-0.03	-0.38
		B	**S.E.**	***Beta***	***t***	**B**	**S.E.**	***Beta***	***t***
Auditory Comprehension [b]	Diurnal slope	-91.16	80.50	-0.06	-0.70	-74.34	79.20	-0.04	-0.55
	Female					6.54	3.03	0.16	1.96
	2 or more placements					1.35	1.02	0.08	0.98
	Age at study entry					0.39	0.33	0.04	0.48
	White					7.26	3.28	0.15	1.88
	Severe abuse					-4.47	3.33	-0.12	-1.40
		B	**S.E.**	***Beta***	***t***	**B**	**S.E.**	***Beta***	***t***
Expressive Communication [b]	Diurnal slope	-177.24	78.80	-0.17	-2.09*	-159.25	78.30	-0.16	-2.03*
	Female					5.58	3.58	0.08	1.05
	2 or more placements					1.28	1.15	0.06	0.72
	Age at study entry					0.46	0.34	0.08	0.95
	White					-0.64	3.52	-0.002	-0.02
	Severe abuse					-7.77	3.98	-0.17	-2.06*
Letter-		**B**	**S.E.**	***Beta***	***t***	**B**	**S.E.**	***Beta***	***t***

Word Identification[c]	Diurnal slope	-100.26	50.40	-0.16	-1.99*	-91.96	50.42	-0.14	-1.83
	Female					3.35	2.19	0.12	1.53
	2 or more placements					0.32	0.70	0.05	0.57
	Age at study entry					-0.05	0.21	0.02	0.29
	White					-3.46	2.25	-0.13	-1.58
	Severe abuse					-6.82	2.44	-0.23	-2.74**
		B	**S.E.**	***Beta***	***t***	**B**	**S.E.**	***Beta***	***t***
Passage Comprehension[c]	Diurnal slope	-34.45	48.67	-0.057	-0.71	-29.06	49.81	-0.39	-0.48
	Female					2.32	2.16	0.09	1.15
	2 or more placements					0.23	0.69	0.03	0.31
	Age at study entry					-0.29	0.23	-0.14	-1.66
	White					-1.99	2.22	-0.08	-0.98
	Severe abuse					-3.71	2.40	-0.13	-1.56
		B	**S.E.**	***Beta***	***t***	**B**	**S.E.**	***Beta***	***t***
Applied Problems[c]	Diurnal slope	-135.54	61.91	-0.17	-2.19*	-144.21	61.64	-0.18	-2.28*
	Female					1.79	2.67	0.06	0.74
	2 or more placements					-0.38	0.86	-0.04	-0.52
	Age at study entry					-0.35	0.28	-0.15	-1.89
	White					5.68	2.74	0.16	2.02*
	Severe abuse					-6.57	2.97	-0.19	-2.28*
		B	**S.E.**	**Wald**	**Exp(B)**	**B**	**S.E.**	**Wald**	**Exp(B)**
No cognitive disability	Diurnal slope	-35.86	12.91	7.72	0.00**	-35.35	13.56	6.80	0.00**
	Female					0.68	0.53	1.63	1.98
	2 or more placements					0.47	0.61	0.60	1.60
	Age at study entry					0.05	0.07	0.43	1.05
	White					0.31	0.54	0.32	1.36
	Severe abuse					-0.61	0.55	1.22	0.55

a. K-BIT- Kaufman Brief Intelligence Test, ***b.*** PLS-3- Preschool Language Scale-3, ***c***. M-BA- Mini-Battery of Achievement

CRediT author statement

1. **Jane Jiyoun Lee:** Formal analysis, Writing- Original draft
2. **Eirini Flouri:** Conceptualization, Supervision, Writing – Review & Editing

Highlights

- Exposure to toxic stressors contribute to HPA axis dysregulation risk.
- HPA axis dysregulation may be related to working memory capacities.
- Early maltreatment is related to future impaired cognitive functioning.