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Child maltreatment and gender interactions as predictors of differential neuroendocrine profiles

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Summary Child maltreatment is a potent stressor associated with neuroendocrine dysregulation and increased risk for mental and physical disorders throughout the lifespan. Gender differences in stress reactivity and adult psychopathology prevalence may be related to sex-specific responsivity to stress. The purpose of this study is to examine whether gender interacts with the stress of maltreatment to produce differential neuroendocrine profiles in children. Participants included 137 maltreated and 110 nonmaltreated low-income, racially and ethnically diverse children (range: 7.9—10.9 years; *M* = 9.42 years; 52% male) who attended a summer research day camp. Saliva was collected 3 times across the day for 5 days for cortisol and dehydroepiandosterone (DHEA) analysis. Department of Human Services records were examined to determine the type, severity, chronicity, onset, and recency of maltreatment for children in the maltreated group. Significant interactions between gender and maltreatment pervasiveness predicted diurnal cortisol, DHEA, and cortisol/DHEA ratio levels. Elevated daily cortisol levels were reported for boys compared to girls in the group with more pervasive maltreatment. Boys with less pervasive maltreatment had lower DHEA and higher cortisol/DHEA ratio levels than girls with similar experiences, nonmaltreated boys, and boys with more pervasive maltreatment. Further results are consistent with down-regulation of cortisol production in girls with more pervasive maltreatment and girls who experienced maltreatment that was early onset and not recent. The effectiveness of interventions for maltreated children may be improved with greater knowledge of how maltreatment differentially affects neuroendocrine regulation by gender.

1. Introduction

Chronic stress in childhood contributes to progressive wear and tear on the body that can have lasting effects on mental and physical health (Shonkoff et al., 2009). Child maltreatment significantly increases the risk for psychopathology across the lifespan (Cicchetti and Valentino, 2006), and atypical hypothalamic—pituitary—adrenal (HPA) regulation

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following maltreatment in childhood may contribute to this heightened vulnerability to poor mental health (Van Goozen and Fairchild, 2008). Increasing evidence indicates potential gender differences in neuroendocrine profiles in response to traumatic stress, especially in adults. Less work has been done in children, but different groups have hypothesized about stress system regulation in response to serious childhood stressors, such as maltreatment. Interestingly, both hyper and hypoactivation of the stress system have been documented in response to traumatic stress, and understanding patterns of neuroendocrine activity may elucidate mechanisms of stress system regulation. In this study, we will test the opposing hypotheses of the adaptive calibration model (ACM) (Del Giudice et al., 2011) and Kajantie and Phillips (2006), which predict differential responses to traumatic stress based on gender.

The ACM (Del Giudice et al., 2011) proposes that evolution may have led to stress system recalibration around the time of puberty due to differential life history strategies between males and females. Increasing sexual differentiation and rising adrenal hormones in middle childhood are hypothesized to underlie sex differences in stress reactivity and regulation, with environmental stress predicting the amount of divergence between sexes. Under a moderate amount of stress, individuals are hypothesized to have better physiological regulation and optimal engagement with the environment, resulting in only moderate sex differences. In highly stressful or threatening situations, boys are predicted to become more callous and unemotional, traits linked to low stress responsivity. Girls are predicted to become fearful and anxious and to develop internalizing symptoms, which are associated with high sympathetic and HPA reactivity. However, studies testing the ACM's gender hypothesis have not yet been conducted. In this study, we will test the ACM's hypothesis that traumatic stress will lead to low stress system responsivity in males compared to females.

Kajantie and Phillips (2006) would predict blunted cortisol levels for women who have experienced early trauma. A review of the literature suggests lower HPA and autonomic responses to stress in adult women versus men, with significant variation depending on the menstrual phase in women (Kajantie and Phillips, 2006). They suggest that modifiers such as estrogen, arginine vasopressin, and corticosteroid-binding globulin could be responsible for the sex differences observed in adults. The reason for physiological hyporesponsiveness in women could be an evolutionary pressure to protect a potential fetus from excess glucocorticoids, especially due to research reporting attenuated HPA responses in pregnant women.

1.1. Gender differences in neuroendocrine profiles

There is evidence that differences in HPA reactivity and basal activity, which result in production of the hormones cortisol and dehydroepiandosterone (DHEA) in the adrenal glands, are apparent between males and females, especially after puberty. In pre-pubertal children, there are generally no differences in baseline cortisol levels, but as children approach puberty, girls tend to mature faster and may show higher cortisol levels than boys (Netherton et al., 2004; Jessop and Turner-Cobb, 2008). Post-puberty, men are more likely to have elevated cortisol responses to stress than women (for review, Kudielka and Kirschbaum, 2005). On the other hand, DHEA levels are positively correlated with age, but not gender (Netherton et al., 2004).

1.2. Effects of child maltreatment on cortisol and DHEA

Child maltreatment is a potent moderator of stress-mediating systems. However, the literature on the exact effects of maltreatment on the HPA axis is mixed, and discrepancies are likely due to differential maltreatment experiences, environmental risk and protective factors, and concurrent psychiatric disorders (for review, see Tarullo and Gunnar, 2006; Van Voorhees and Scarpa, 2004). Depressed and non-depressed men and women maltreated as children have shown increased cortisol and adrenocorticotropic hormone (ACTH) reactivity to challenge (Heim et al., 2002, 2008). However, some studies in adults maltreated as children report attenuated cortisol and ACTH responses to stress in adults without psychopathology (Carpenter et al., 2007) and women with PTSD (Bremner et al., 2007).

The pattern of HPA axis regulation following maltreatment is often unclear in studies of children as well. For example, physical and sexual abuse have been associated with high morning cortisol levels in children, and those who have suffered multiple types of abuse are more likely to exhibit high morning and afternoon cortisol levels (Cicchetti and Rogosch, 2001a). Children with PTSD secondary to trauma have also exhibited elevated cortisol levels compared to controls (De Bellis et al., 1999). However, some physically abused children show low cortisol and a flattened diurnal slope compared to nonmaltreated children (Cicchetti and Rogosch, 2001a), and adolescent females with PTSD secondary to rape have demonstrated low cortisol levels (Bicanic et al., in press). Several studies have reported attenuated cortisol responses to stressors in maltreated boys and girls (Ouellet-Morin et al., 2011) and maltreated females specifically (De Bellis et al., 1994; MacMillan et al., 2009). Internalizing and externalizing symptomology may also play a role in HPA axis regulation. For example, school-age children experiencing physical and/or sexual abuse before age 5 have demonstrated an attenuated diurnal cortisol slope when accompanied by concurrent internalizing symptoms (Cicchetti et al., 2010). In addition, maltreated children may show high or low levels or flattening of the diurnal slope depending on the presence of internalizing or externalizing symptoms (Cicchetti and Rogosch, 2001b). In maltreated individuals, low cortisol could be related to subsequent PTSD, while high cortisol could be concurrent with depressive disorders (McCrory et al., 2011).

A review by Tarullo and Gunnar (2006) noted increased basal cortisol levels in maltreated children with internalizing problems while adults who were maltreated as children tend to show hyposecretion of cortisol and increased ACTH responsiveness, with puberty targeted as a potential time of stress system reorganization in these individuals. A recent study demonstrated that sexually abused girls who exhibited high cortisol levels in childhood showed attenuation in adolescence and transitioned to low cortisol levels in adulthood