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Research paper

Patterns of cortisol and alpha-amylase reactivity to psychosocial stress in maltreated women

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ABSTRACT

Background: Childhood maltreatment can trigger enduring changes in major stress response systems, particularly in the context of major depressive disorder (MDD). However, the relative impact of maltreatment versus MDD on hypothalamic-pituitary-adrenal axis and sympathetic-adrenal-medullary system stress reactivity is not well understood.

Method: This study examined salivary cortisol and alpha-amylase responses to the Trier Social Stress Test (TSST) in 26 maltreated (15 with current MDD) and 26 non-maltreated (17 with current MDD) women.

Results: Maltreated women showed greater anticipatory cortisol reactivity during the TSST protocol compared to non-maltreated women. Maltreated women also showed rapid deceleration in cortisol levels. Whereas non-maltreated women showed initial declines in alpha-amylase levels but rapidly increasing alpha-amylase levels during the TSST protocol, maltreated women did not exhibit changes in alpha-amylase levels during the TSST protocol. Contrary to expectation, MDD did not impact cortisol or alpha-amylase responses.

Limitations: The present study is limited by retrospective report of childhood maltreatment, cross-sectional design, and modest sample sizes.

Conclusions: These findings suggest that childhood maltreatment plays a greater role driving alterations in cortisol and alpha-amylase stress reactivity than MDD. Understanding the biological embedding of maltreatment is critical for elucidating mechanisms linking these experiences to risk for negative mental and physical health outcomes.

1. Introduction

Maltreatment affects as many as 1 in 4 children in the United States and resulted in an estimated 3.6 million referrals for cases of suspected abuse or neglect and 1,580 childhood maltreatment-related deaths in 2014 (U.S. Department of Health and Human Services, 2016; Finkelhor et al., 2013). Exposure to childhood maltreatment (including physical, sexual or emotional abuse, physical or emotional neglect, and exposure to domestic violence) can produce enduring changes in stress response systems such as the hypothalamic-pituitary-adrenal (HPA) axis and sympathetic-adrenal-medullary system (SAM), and can increase vulnerability to major depressive disorder (MDD) and posttraumatic stress disorder (PTSD) (Heim et al., 2008; Pervanidou, 2008). Girls are more likely than boys to report maltreatment in general (U.S. Department of Health and Human Services, 2012), and sexual abuse in particular (Centers for Disease Control and Prevention, 2005). In retrospective studies, women are twice as likely as men to develop trauma-related conditions such as MDD in their lifetimes (Kessler et al., 1993).

Neurodevelopmental traumatology models emphasize the importance of both the developmental timing of trauma exposure as well as compensatory adaptations that occur over time. Unfortunately, time since maltreatment is confounded with age of maltreatment onset in most studies (Morris et al., 2012). Regarding timing of trauma exposure, the impact of childhood trauma on physical and mental health outcomes is particularly devastating due to the adverse consequences of dysregulated stress response systems on brain development during critical vulnerability periods (De Bellis et al., 1999, 2011).

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For example, earlier onset of sexual abuse has been linked to smaller intracranial volume and greater PTSD symptom severity (De Bellis et al., 1999). Regarding time elapsed since trauma exposure, theoretical models describe an attenuation of HPA activity over time triggered by developmental alterations and compensatory adaptations of the HPA axis: children recently exposed to maltreatment exhibit increased diurnal cortisol secretion and reactivity to stress, but over time show a progressive downregulation of HPA (re)activity (De Bellis et al., 2011; Gunnar and Vazquez, 2001; Heim et al., 2008; Susman, 2006). Support for these models comes from a longitudinal study of youth with a history of sexual abuse (Trickett et al., 2010). In this longitudinal study of females from childhood through early adulthood, both abused and non-abused groups showed a linear increase in morning basal cortisol levels with development, but this trend leveled off in their early 20s. Abused females exhibited slower increases in cortisol levels over time (as they became older and time since abuse increased) compared to non-abused females.

It is challenging to interpret findings from studies of maltreated youth and adults examining HPA reactivity to psychosocial stress due to the host of genetic, developmental, personality, environmental and methodological factors that influence HPA function in general, and the stress response in particular (Allen et al., 2014). Nevertheless, one consistent theme in the literature has been the importance of accounting for psychiatric comorbidity such as MDD. Youth studies have reported elevated cortisol reactivity in boys and girls with mild-to-moderate depression but blunted cortisol reactivity in those with moderate-to-severe depression (Harkness et al., 2011) and elevated cortisol responses in depressed youth with early-life adversity (Rao et al., 2008). A third study that excluded youth who met diagnostic criteria for MDD reported blunted cortisol reactivity in adolescent girls regardless of depressive or PTSD symptoms (MacMillan et al., 2009). Adult studies have generally reported enhanced HPA reactivity to stress in maltreated individuals with MDD (Heim et al., 2000, 2002), PTSD (Bremner et al., 2003; Elzinga et al., 2003) or social anxiety disorder (Elzinga et al., 2010) compared to non-maltreated controls. In contrast, studies examining HPA responses to stress in maltreated adults without PTSD or MDD have generally reported blunted cortisol reactivity to stress (Carpenter et al., 2007, 2011; Elzinga et al., 2008; Voellmin et al., 2015; see also DeSantis et al., 2011; Luecken and Appelhans, 2006).

The SAM responds within seconds of stressor exposure by releasing norepinephrine and epinephrine from the adrenal medulla, which triggers a number of peripherally measurable physiological changes. Salivary alpha-amylase levels increase in response to psychosocial stressors, correlate positively with cardiovascular responses, and can be used as non-invasive indicators of SAM activation (Nater et al., 2006). Increased SAM activity following childhood trauma exposure has been proposed as a risk factor for developing PTSD (Pervanidou, 2008). However, it remains unclear whether individuals with a history of childhood maltreatment exhibit enduring changes in SAM reactivity similar to those observed for the HPA axis, and if these alterations differ according to the presence of MDD. The present study addressed this critical gap in the literature by simultaneously examining HPA and SAM reactivity to psychosocial stress in women exposed to childhood maltreatment, some of whom developed MDD while others were free from psychopathology.

Although enhanced SAM reactivity to stress appears to characterize trauma-exposed individuals with and without PTSD (for reviews see Morris and Rao, 2013; Pole, 2007), the impact of childhood maltreatment on SAM responses to psychosocial stressors has not been well characterized. One study in youth found an association between maltreatment history and cardiovascular parameters thought to reflect a threat (or withdrawal) response: blunted cardiac output reactivity and greater peripheral resistance (McLaughlin et al., 2014). Adult studies examining cardiovascular responses to stress tasks have reported elevated blood pressure in men and women with early parental loss (Luecken,1998), as well as elevated heart rate in women with PTSD due to childhood sexual abuse (Orr et al., 1998) or women with MDD in the context of childhood sexual or physical abuse (Heim et al., 2000) compared to non-maltreated controls. In contrast, a study of healthy women found more attenuated heart rate reactivity to a stressor among women with more adverse childhood experiences (Voellmin et al., 2015). Two studies examining relations between HPA and SAM reactivity to stress found an asymmetry between salivary cortisol and alpha-amylase responses in maltreated youth (Gordis et al., 2008) or higher ratios of alpha-amylase to cortisol responses in adults with more early-life adversity (Ali and Pruessner, 2012). Unfortunately, neither of these studies were able to parse the relative influence of maltreatment and trauma-related psychopathology.

The purpose of the present study was to examine the unique effects of childhood maltreatment and current MDD on salivary cortisol and alpha-amylase responses to a psychosocial stressor in women. We hypothesized that cortisol responses would be higher in maltreated women with current MDD and blunted in maltreated women without current MDD compared to non-maltreated women. We further hypothesized that alpha-amylase responses would be greater in maltreated women with current MDD compared to those without past maltreatment.

2. Methods

2.1. Participants

The participants were recruited through advertisements in local newspapers and universities as part of a larger programmatic study on depression. Participants for the present study were selected from this larger sample if they were 18 years or older, had completed a psychosocial stress task, and met further inclusion/exclusion criteria described below. The sample included 26 women with a history of maltreatment before the age of 10 (15 with current MDD) and 26 women with no history of maltreatment (17 with current MDD). Depressed women with a lifetime history of mania, hypomania, schizophrenia, schizoaffective disorder, or autism, or with a family history of bipolar disorder, were excluded from the study. All participants were medically healthy and free from psychotropic medication (for a minimum of 8 weeks but most of them were psychotropic-naive), other medications that can impact HPA and SAM activity (with the exception of oral contraceptives), and alcohol or illicit drug use, as determined by physical examination, laboratory investigations, and urine drug screens. All participants provided written informed consent and all procedures were approved by the institutional review board.

2.2. Measures

2.2.1. Maltreatment

The Childhood Adversity Interview (CAI; Dienes et al., 2006; Rao et al., 2008; Raposa et al., 2014) is a semi-structured interview that was administered by trained raters. Seven subtypes of childhood adversity occurring before age 10 were assessed: separation/loss; life-threatening illness or injury; physical neglect; emotional abuse; physical abuse or assault; witnessing domestic violence; and sexual abuse or assault. Summary scores for each subtype were tabulated using ratings on a 5-point scale (1=*none*, 5=*most severe*). The presence of maltreatment (dummy variable: 1=present; 0=absent) was determined by a score of three or greater on at least one of the following subscales: physical abuse/assault, sexual abuse/assault, and witnessing domestic violence. The CAI has demonstrated good inter-rater and test-retest reliability (Hammen et al., 2000). Inter-rater reliability scores in this sample computed for a randomly selected 25% of CAI interviews were adequate (κ's≥.85).