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Chronic stress, salivary cortisol, and α-amylase in children with asthma and healthy children

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Abstract

The present study examined whether chronic stress is related to daily life levels of salivary α-amylase (sAA), a marker for sympathetic activity, and cortisol in healthy children versus children with asthma.

Children's sAA and cortisol levels were measured repeatedly over 2 days. Chronic stress measures included interviews with children about chronic home life stress and interviews with parents about one marker of socioeconomic status, parental education.

Among children with asthma, higher chronic stress was associated with lower daily sAA output, while among healthy children, higher chronic stress was associated with flatter cortisol slopes.

In conclusion, chronically stressed children with asthma showed lower salivary α-amylase output, indicating lower sympathetic activity, and implying a possible mechanism for increased susceptibility to symptom exacerbations. In contrast, higher cortisol levels in healthy children with chronic stress may indicate, for example, an increased risk for infectious diseases. This dichotomy emphasizes the different biological effects of chronic stress depending on illness status.

Keywords: Salivary α-amylase; Cortisol; Childhood asthma; Chronic stress; Socioeconomic status

1. Introduction

Stress is known to activate two major biological systems, the hypothalamus-pituitary-adrenal (HPA) axis and the sympatho-adrenal medullary (SAM) axis. In humans, activation of the hypothalamus-pituitary-adrenal axis results in an enhanced secretion of the hormone cortisol. Cortisol has a typical circadian pattern with higher levels in the morning and lower evening levels (Van Cauter, 1995). Activation of the SAM axis, on the other hand, results in the release of epinephrine and norepinephrine from the adrenal medulla as well as norepinephrine from nerve terminals of the sympathetic nervous system (Goldstein, 2000; Kvetnansky and McCarty, 2000). While both cortisol and catecholamines can be measured in plasma, the field of psychoneuroendocrinology (PNE) has sought to develop non-invasive markers of both axes. In the case of cortisol, salivary cortisol has become a widely used and important tool (Kirschbaum and Hellhammer, 1994). Salivary cortisol levels correlate highly with serum levels (Kirschbaum and Hellhammer, 2007) and reflect the free/unbound fraction of total cortisol, which is thought to be the biological active fraction (Mendel, 1992; Pearson-Murphy, 2000).

The search for a similar non-invasive and easily obtainable marker of the SAM axis has raised salivary α-amylase (sAA) as a promising candidate. Salivary α-amylase is an enzyme important for carbohydrate digestion and its secretion is under strong neurohormonal control (i.e., released upon sympathetic stimulation; Baum, 1993; Smith, 1996). Strong evidence for the assumption of salivary α-amylase reflecting sympathetic activity has come from pharmacological studies. van Stegeren et al. (2006) were able to reduce stress-induced salivary α-amylase increases by application of a β-adrenergic receptor blocker and Ehlert et al. (2006) recently reported that stimulation of the sympathetic nervous system using the α2-adrenergic receptor antagonist yohimbine increased salivary α-amylase levels. Hence, salivary cortisol levels reflect the activity of the HPA axis, whereas salivary α-amylase activity can be considered a marker of sympathetic activity.

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1.1. Relevance of salivary α-amylase and cortisol for health

Changes in salivary α-amylase and cortisol levels are thought to have implications for health. For example, two studies by Granger et al. (2006, 2007a) suggest a link between salivary α-amylase and disease. One study found that greater salivary α-amylase increases in response to laboratory challenges were observed in children with more parent-reported illnesses. The second study revealed that higher levels of salivary α-amylase after acute laboratory stressors were associated with increased health problems, such as respiratory problems, in children. With respect to cortisol, there is a large body of evidence linking it to disease. Changes in basal as well as stimulated cortisol levels are reported to be associated with different disease processes or susceptibilities towards different diseases (Chrousos, 1998), such that, for example, a decreased HPA axis activity is found in individuals with fibromyalgia (Chikanza et al., 1992) and atopic diseases (Buske-Kirschbaum et al., 1998).

In the present study, we compared salivary α-amylase and cortisol in children with asthma versus healthy children. Asthma was chosen because it is the most common chronic illness in childhood (Mannino et al., 1998), and has been linked to alterations in cortisol responses to acute laboratory stressors (Buske-Kirschbaum et al., 2003) as well as in autonomic nervous system activity (Kallenbach et al., 1985). Hence our first goal was to determine whether a chronic illness such as asthma would be associated with different patterns of daily life salivary α-amylase and cortisol in children.

1.2. Psychological factors linked to salivary α-amylase and cortisol

As mentioned above, psychological stress activates both the HPA axis as well as the SAM axis, which manifests as changes in cortisol and salivary α-amylase output. For example, salivary α-amylase has been found to respond to psychological stress (Bosch et al., 1996, 2003; Nater et al., 2006, 2005; Rohleder et al., 2006; Skosnik et al., 2000), a finding that is also true in children (summarized in Granger et al., 2006, 2007a,b). Interestingly, while a relatively large number of studies have investigated laboratory stress reactivity and salivary α-amylase, studies of salivary α-amylase variations during individuals' daily lives (basal levels) are relatively rare. Rohleder et al. (2004) reported salivary α-amylase in university students to show a diurnal pattern opposite that of salivary cortisol, with lowest values shortly after awakening followed by increases during the day. The same pattern was reported by others (Jenzano et al., 1987; Nater et al., 2007; Rantonen and Meurman, 2000). To our knowledge, however, there have been no studies investigating basal salivary α-amylase activity over the day in children and adolescents. Furthermore, not only are studies investigating basal salivary α-amylase levels rare, but even fewer studies have attempted to link it to psychological factors such as chronic stress. Only one study that we are aware of measured chronic stress and found a positive association with salivary α-amylase levels over the day in university students (Nater et al., 2007). One study that investigated differences in socioeconomic status (SES) in young children found salivary α-amylase reactivity to an acute stressor to be negatively associated with SES (Granger et al., 2006).

Many more studies have investigated the effects of acute stressors on cortisol secretion. Acute stressors are known to elicit a delayed increase in cortisol secretion with a slow decrease after the offset of the stressor, reaching baseline levels approximately 1 h later (for a review see Dickerson and Kemeny, 2004). However, the literature on the effects of chronic stress on basal cortisol levels is less consistent. Both elevated levels of diurnal cortisol output (Arnetz et al., 1987; Baum et al., 1983; Kosten et al., 1984; Schaeffer and Baum, 1984) as well as a reduced cortisol output (Heim et al., 2000; Miller et al., 2002; Vedhara et al., 2002; Yehuda, 2000) over the day were found to be associated with chronic stress. Furthermore, a recent meta-analysis highlighted the importance of taking stressor and person features into account (Miller et al., 2007). For example, stressors that elicited a flat diurnal cortisol profile with high afternoon and evening levels were characterized as ones that threatened physical integrity, involved trauma, and were uncontrollable.

The second aim of the present study was thus to compare the effects of chronic stress on basal salivary α-amylase and cortisol levels in children with asthma and healthy children, thus testing whether psychosocial factors could be linked to daily life profiles of these two biological markers.

1.3. Study aims

In summary, the goal of the present study was twofold. First, we aimed to compare basal salivary α-amylase activity and basal salivary cortisol levels in healthy children versus children with asthma. Second, we aimed to test the relationships between chronic stress and salivary α-amylase as well as cortisol. Chronic stress was defined in two ways in this study, the experiences of chronic stress in home life, as well as low family SES, based on parental education.

2. Methods

2.1. Subjects

A total of 92 children and adolescents were recruited from the Vancouver, BC community through advertisements in newspapers, magazines, and physicians' offices. 47 children and adolescents were physician-diagnosed with asthma according to NHLBI guidelines (NHLBI, 1997, 2002) and 45 children and adolescents were medically healthy. Children with any other chronic medical (besides asthma) or psychiatric illness were excluded. To assess this, during the telephone-screening interview, parents were asked about any chronic medical or psychiatric illnesses their child had as well as about any acute illnesses in the past month and any medications the child was taking. During their visit at the laboratory, parents were queried again about any major health problems, physical, emotional, or other types the child had. Furthermore, a differential blood count from the child was used to ensure that children were not having any acute health problems. Children with upper-respiratory illness during the past 4 weeks were rescheduled.