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Salivary alpha amylase diurnal pattern and stress response are associated with body mass index in low-income preschool-aged children

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Summary Physiological stress responses are proposed as a pathway through which stress can ''get under the skin'' and lead to health problems, specifically obesity. We tested associations of salivary alpha amylase (sAA) diurnal patterns and stress responses with body mass index (BMI) in young, low-income children (51% male; 54% non-Hispanic white). Diurnal saliva samples were collected three times per day across three days for 269 children (M age 50.8 months, SD 6.3). Individual sAA intercept and slope values were calculated using random effect models to represent morning sAA levels and rate of sAA change across the day. A subset of children ($n = 195$; M age 56.6 months, SD 6.9) participated in a lab-based behavioral stress protocol. Area under the curve increase (AUCI) across four timepoints was calculated to represent increase in sAA output during stress elicitation. Children were weighed and height measured and BMI *z*-score was calculated. Linear regression was used to evaluate associations of sAA intercept, sAA slope, and sAA AUCI with BMI *z*-score, controlling for child age, sex, and race/ethnicity; maternal weight status; and family income-to-needs ratio. Diurnal and stress—response sAA patterns were related to child adiposity: for each 1-standard deviation unit (SDU) decrease in morning

Abbreviations: BMI, body mass index; AUCI, area under the curve increase; sAA, salivary alpha-amylase; SNS, sympathetic nervous system; SDU, standard deviation unit.

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sAA level, the child's BMI z-score increased by 0.11 (SE 0.05) SDU's ($p < .04$); for each 1-SDU increase in sAA slope across the day, the child's BMI z-score increased by 0.12 (SE 0.05) SDU's ($p < .03$); and for each 1-SDU decrease in sAA AUCI during the stress elicitation, the child's BMI z-score increased by 0.14 (SE 0.06) SDU's ($p < .03$). Blunted stress responses and atypical diurnal patterns of sAA have been found following exposure to chronic life stressors such as poverty. Findings suggest that associations of stress, sAA, and elevated body mass index may develop very early in the lifespan.

1. Introduction

1.1. Salivary alpha amylase as a marker of sympathetic nervous system activity

The autonomic nervous system (ANS) consists of the sympathetic nervous system (SNS) and parasympathetic nervous system (PNS). The functioning of these two complementary systems is measured primarily via indices of cardiovascular physiology (e.g., heart rate, blood pressure) or catecholamines (epinephrine and norepinephrine) (Granger et al., 2007). Salivary alpha amylase (sAA) has been described as a marker of SNS basal activity and stress reactivity (Rohleder et al., 2004; Granger et al., 2007; Nater and Rohleder, 2009), although it is debated as to whether sAA signals pure SNS activity or a combination of SNS and PNS activation (Bosch et al., 2011; Ditzen et al., 2014). It is known that SNS stimulation promotes the secretion of norepinephrine, which in turn increases sAA secretion (Kuebler et al., 2014). The result is a robust diurnal pattern for sAA, defined by a pronounced decline within the first 30 min after awakening, steadily rising in the afternoon, and peaking in the late afternoon or evening (Rohleder et al., 2004; Nater et al., 2007). sAA is sensitive to psychological stressors (Nater et al., 2006; Thoma et al., 2012), in general rising in response to stressors (Rohleder et al., 2004).sAA reactivity in response to stress correlates with stress induced serum catecholamine levels (Ditzen et al., 2014; Thoma et al., 2012) and cardiac physiological changes observed in response to stress (Nater et al., 2006; El-Sheikh et al., 2008). Associations between basal sAA output and resting SNS activity have been examined less frequently; one recent study of adult males found stronger sAA-SNS associations under challenging compared to resting conditions (Ditzen et al., 2014). Thus, although the specific nature of sAA-SNS associations has yet to be determined, particularly with regard to resting SNS-sAA associations, evidence suggests that sAA may be a reasonable marker of SNS stress reactivity or at least of SNS dominance (Nater and Rohleder, 2009). The methods used to measure SNS functioning directly are typically fairly invasive (e.g., venipuncture, heart rate, skin conductance). As sAA is measured in saliva, it is more easily used in stress research with young children (Hill-Soderlund et al., 2014).

1.2. A conceptual model linking stress, behavior, sympathetic nervous system activity, and adiposity in children

As has been hypothesized with the hypothalamic—pituitary—adrenal axis (Gunnar and Vazquez, 2001), chronic activation of the SNS in the face of stress has been hypothesized to lead to down-regulation of the system (Lovallo, 2011; Pervanidou and Chrousos, 2012), such that chronic stress exposure is associated with low basal sAA activity and reduced sAA reactivity in response to challenge. Lower basal sAA patterns have been associated with chronic stress exposure in children (Hill-Soderlund et al., 2014; Wolf et al., 2008). Also in children, attenuated sAA reactivity in response to stress has been associated with more disruptive behavior (Granger et al., 2007; Susman et al., 2010; de Vries-Bouw et al., 2012), more anger and impulsivity (Spinrad et al., 2009), and weaker ability to delay gratification (Lisonbee et al., 2010). Both psychosocial stress exposure and these behavioral features have been associated with a higher risk of obesity in children (Lumeng et al., 2003; Seeyave et al., 2009; Lumeng et al., 2013; Leung et al., 2014). We therefore hypothesized that these blunted basal and stress—responsive sAA patterns linked with chronic stress exposure and poor emotional and behavioral regulation among children would also be associated with increased adiposity.

1.3. Assessment of the evidence base for the proposed conceptual model

Studies of adults provide support for the proposed conceptual model. Of the few studies that have considered SNS responses to stress in relation to adiposity, lower SNS stress responses assessed using cardiac measures were associated with greater adiposity (Carroll et al., 2008; Jones et al., 2012). One study assessing SNS reactivity to stress via sAA also found a trend for an association between lower sAA stress response and greater adiposity (Thoma et al., 2012).

Resting SNS activity as measured by cardiac physiology is also related to obesity risk, although evidence for the direction of association is more mixed. For example, cross-sectional studies have reported associations between obesity risk indicators and greater resting SNS activity (Tentolouris et al., 2006). However, low resting SNS activity has also been implicated in weight gain (Tataranni et al., 1997) and slower weight loss over time (Astrup et al., 1995). Two studies that examined diurnal sAA and adiposity found lower diurnal sAA associated with higher body mass index (BMI; Nater et al., 2007) or no association (Veen et al., 2012).

Fewer studies have been done in children and their results are more conflicting. The only study to examine cardiac reactivity to stress in relation to adiposity was in preschool-aged children, and found a negative association (Alkon et al., 2014). In studies of older children (ages