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Interactions between salivary cortisol and alpha-amylase as predictors of children's cognitive functioning and academic performance

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ABSTRACT

We examined relations between salivary cortisol, alpha-amylase (sAA), and children's cognitive and academic functioning. Of interest were curvilinear and interactive effects of these salivary measures on cognitive and academic performance. Data were based on a sample of 28 boys and 36 girls (ages 8 and 9) in the Southeastern U.S.A. Children provided resting afternoon saliva samples. Children completed standardized tests of Intellectual Ability and schools provided academic achievement information. Regression analyses demonstrated significant curvilinear relations and interactions between cortisol and sAA in the prediction of child functioning. Contrary to current models of interactions among biological systems, findings indicated some of the highest and lowest scores were predicted at moderate levels of physiological arousal. For example, children with moderate sAA and either higher or lower cortisol had low predicted scores for Reading Ability. Children with moderate cortisol and lower sAA had the highest predicted scores for Intellectual Ability. Findings suggest that the study of interactions between biological stress response systems should not be based on models of rectilinear interactions.

1. Introduction

Biobehavioral models are increasingly applied in developmental science in an attempt to clarify perennial problems facing children. In many of these models, dynamic interactions involving physiological, behavioral, and social contextual variables are explored, with primary outcome areas of socio-emotional adjustment [1,2]. Research extending biobehavioral models to understanding variation in children's cognitive functioning and academic achievement has been more scarce [3]. In accord with calls in the literature to examine interactions between multiple physiological systems [4], the goal of this study is to examine individual differences in the activity of the autonomic nervous system (ANS) and the hypothalamic–pituitary–adrenal (HPA) axis as they relate to children's cognitive functioning and academic performance. These systems are among the principal components of the psychobiology of stress response [5], and contemporary theory suggests that individual differences in the regulation of, and coordination between, these systems have implications for child adaptation [3].

Research with non-humans indicates that chronic HPA axis activation adversely affects areas of the brain known to be involved in many aspects of cognitive performance [6–10]. Studies with adult humans indicate that cortisol is linked to cognitive performance, which may be impaired after administration of corticosteroids [11–13]. Patients with Cushing's syndrome, a disease characterized by chronic elevation of cortisol, have deficits in cognitive functioning [14,15]. Further, long-term elevations in cortisol may underlie the well-documented cognitive declines associated with aging [16,17]. Fewer studies have found cortisol administration to have a facilitative effect on cognitive functioning [18,19]. The proposition of a U-shaped distribution with highest and lowest levels of cortisol leading to more impaired cognitive function is often cited as a possible way that discrepancies in findings may be resolved [20]. Thus it is important to examine potential curvilinear associations between cortisol and child developmental outcomes.

Despite several studies with adults, few studies have examined relations between cortisol and children's cognitive performance. Existing evidence is mixed with some reports of no significant relations [21]. In the same study, higher diurnal cortisol levels at home and mean levels over the course of a laboratory visit were associated with better performance on tasks of inhibitory control. Recent studies documented that higher morning cortisol levels are associated with worse performance on a memory speed task [22], and greater cortisol reactivity is correlated with academic difficulties and attention problems in a sample of 5- to 12-year-olds [23]. Other reports indicate that higher basal cortisol levels facilitate spatial learning in 2- and 3-year-old children [24]. In a sample of 6 to 16 year old children, differences

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in basal cortisol levels associated with SES were *not* related to cognitive functioning [25]. As these few studies indicate, the relation between cortisol levels and performance on cognitive tasks in children remains unclear.

The SNS may play an important role in the effects of cortisol on cognitive performance. Research linking the activity of the autonomic nervous system (ANS) to cognitive functioning in adults has focused on the catecholamine neurotransmitter norepinephrine. Those studies have yielded some contradictory findings, with some showing increased, and some decreased, cognitive performance associated with higher levels of norepinephrine [25], a further indication that curvilinear associations may be important to examine. Research suggests that adult plasma norepinephrine concentrations increase during difficult cognitive tasks such as mental arithmetic [26]. Disruption of norepinephrine transmission is associated with memory impairment in rats [27]. However, Birnbaum and colleagues [28] found that stimulation of norepinephrine receptors adversely affected memory performance in rats. Greater electrodermal activity – an alternative measure of SNS activity – has been considered an indication of attention, meta-memory, and memory recall in adults [29,30]. Furthermore, damage to frontal lobes is associated with attenuated skin conductance activity [31]; the frontal lobe plays an important role in skills necessary for cognitive performance, such as decision making and higher-order thinking. To our knowledge, there are no studies of SNS activity and cognitive performance in children. However, research with adults and animal models indicates the SNS plays a complex role in cognitive performance and may interact with the HPA axis [32].

While it is clear that the HPA and ANS systems work in coordination to generate the physiologic changes associated with the stress response, the exact nature of the coordination (e.g., additive or interactive; opposing or complementary) is not well-understood. These subsystems are activated in response to different situational demands (i.e., defense vs. defeat) [33], and are differentially activated depending on a confluence of experiential, person, and contextual variables. Therefore, examining the associations and dissociations between concurrent actions across these systems in relation to children's cognitive and academic performance may allow a better understanding of the stress-response systems — child functioning link.

For this reason, there is a growing number of studies which incorporate both cortisol and salivary alpha-amylase as a predictor of functioning [34]. Salivary alpha-amylase (sAA) is a digestive enzyme that is secreted in response to SNS activity [35]. Stress-related increases in sAA can be inhibited by the adrenergic blocker, propranolol [36]. Because sAA and cortisol can both be measured in saliva, they permit examination of psychophysiological stress response in the same organ system. In a study with adults, both cortisol and salivary alpha-amylase were associated with performance on an attentional inhibition task thought to be modulated in the prefrontal cortex [37]. Specifically, sAA increased substantially after a stressor, and subjects who had higher cortisol concentrations had greater reductions in attentional inhibition.

The concept of allostatic load may be important to understanding why sAA and cortisol may interact in the prediction of child cognitive and academic performance. Allostasis is the process through which stress response systems work together to promote adaptation [38,39]. Malfunctioning in allostatic systems can take a toll on the body; this condition is known as allostatic load. Parts of the brain that have numerous receptors for the effector molecules of the SNS and HPA axis are especially vulnerable. The hippocampus is one of the vulnerable neural areas, and is involved in memory and perception of threat. Prolonged exposure to glucocorticoids and norepinephrine can lead to neural atrophy and even neural death in the hippocampus [40]. Allostatic load may be characterized by dissociation and dysregulation across multiple stress response systems rather than manifested in individual systems [4]. Thus, consideration of the co-influence of activity across both systems is likely to yield to a better understanding of child adaptation [4].

There are several possible patterns of interaction that may lead to increased risk for allostatic load and cognitive impairment. First, Bauer et al. [4] indicated that the HPA and ANS systems are complementary in their influences, and that symmetry between the two systems is likely to be related to optimal outcomes. Symmetry refers to the condition in which the two systems are working in the same direction on arousal. High levels of cortisol and sAA are expected to increase arousal, and therefore a high/high combination would be symmetric. Similarly, low levels of cortisol and sAA are expected to decrease arousal, and therefore a low/low combination would also be symmetric. Conversely, Bauer et al. [4] proposed that activation asymmetries would be related to adjustment problems. Such patterns would include the combination of high cortisol and low sAA, or low cortisol and high sAA. Asymmetry may reflect a form of allostatic load in which stress responses systems have lost the ability to adaptively coordinate. While the terms symmetry and asymmetry may connote a category of response, in fact sAA and cortisol levels fall along a continuum. As a result, symmetry/asymmetry also falls along a continuum, with varying degrees of symmetry or asymmetry being possible. Categorizing individuals on truly continuous variables attenuates associations, decreases power, and can also lead to spurious interactions [41]. We therefore preserve the continuous nature of sAA and cortisol in the present study.

Second, McEwen [38] proposes that either under or over reactive systems will be associated with allostatic load. Following this view, the high/high pattern may characterize especially high levels of arousal, leading to allostatic load. On the other hand, the low/low pattern may characterize a state of under-arousal, also leading to allostatic load. Bauer and colleagues [4] refer to this as an "additive model" of allostatic load. Conversely, patterns considered asymmetric, in which the systems are working in opposition, may lead to moderate levels of arousal that are more adaptive. Also adaptive would be patterns in which the SNS and HPA axis are each only moderately active. In the present study we examine interactions between cortisol and sAA in the prediction of different types of cognitive functioning in young elementary school children. Examinations of interaction effects between sAA and cortisol are limited [42–44] and to our knowledge, this is the first such examination of how those systems relate to cognitive functioning in school-age children.

The few examinations of interactions between the activity of the ANS and HPA in the prediction of children's adjustment have yielded data supportive of the importance of examining sAA × cortisol interactions [43,45–47]. In some studies, interactions between cortisol and sAA were associated with child internalizing and externalizing behaviors, such that higher cortisol levels and higher ANS/SNS activity (indexed by either sAA or skin conductance level) were associated with maladjustment [42]. This is consistent with the additive model. Berry and colleagues [48] found that lower cortisol and higher sAA were associated with better executive functioning in early childhood. This is consistent with the notion that moderate levels of arousal may be more beneficial. Although interactions between cortisol and sAA are typically found when examined, the shape of the interactions and the corresponding pattern of effects have not been uniform across all studies. The nature of the samples (e.g., clinical versus community), sample sizes, tasks used to evoke reactivity, and outcome measures have varied greatly across studies testing interactions between sAA and cortisol and likely influence the pattern of effects.

In the present study, we examined afternoon resting levels of sAA and cortisol. Based on prior research, we hypothesized that the combination of higher cortisol and higher sAA would be associated with worse cognitive performance and academic achievement. We expected moderate levels of cortisol and sAA to be associated with better