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Publication Date

2015-04-01

DOI

10.1016/j.psyneuen.2015.01.012

Peer reviewed

HHS Public Access

Author manuscript

Psychoneuroendocrinology. Author manuscript; available in PMC 2016 April 01.

Published in final edited form as:

Psychoneuroendocrinology. 2015 April ; 54: 14–23. doi:10.1016/j.psyneuen.2015.01.012.

Alpha-Amylase Reactivity in Relation to Psychopathic Traits in Adults

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Abstract

Recent investigations of the psychobiology of stress in antisocial youth have benefited from a multi-system measurement model. The inclusion of salivary alpha-amylase (sAA), a surrogate marker of autonomic/sympathetic nervous system (ANS) activity, in addition to salivary cortisol, a biomarker of the hypothalamic-pituitary-adrenal (HPA) axis functioning, has helped define a more complete picture of individual differences and potential dysfunction in the stress response system of these individuals. To the authors' knowledge, no studies have examined sAA in relation to antisocial behavior in adults or in relation to psychopathic traits specifically. In the present study, we examined sAA, in addition to salivary cortisol, in a relatively large sample (n = 158) of adult

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Conflict of Interest: *Disclosure Statement*: In the interest of full disclosure, DAG is founder and Chief Scientific and Strategy Advisor at Salimetrics LLC and Salivabio LLC (Carlsbad, CA) and these relationships are managed by the policies of the committee on conflict of interest at the Johns Hopkins University School of Medicine and the Office of Research Integrity and Adherence at Arizona State University.

Contributors: A.G., A.R., and D.G. conceptualized and designed the study. PCL-R interviews and scoring were performed by R.S. Implementation of the stressor task and sample acquisition was performed by Y.G. Analyses and interpretation of the data and initial drafting of the article were performed by A.G. and R.R.A.G., R.R., A.R., and D.G. revised the manuscript. All authors approved the final version of the article.

males (M age = 36.81, range = 22-67 years; 44% African-American, 34% Caucasian, 16% Hispanic) recruited from temporary employment agencies with varying levels of psychopathic traits. Males scoring highest in psychopathy were found to have attenuated sAA reactivity to social stress compared to those scoring lower in psychopathy. No differential relationships with the different factors of psychopathy were observed. In contrast to studies of antisocial youth, there were no interactions between sAA and cortisol levels in relation to psychopathy, but there was a significant interaction between pre-stressor levels of sAA and cortisol. Findings reveal potential regulatory deficits in the fast-acting, 'fight or flight', component of the stress response in adult males with psychopathic traits, as well as abnormalities in how this system may interact with the HPA axis.

Keywords

psychopathy; alpha-amylase; cortisol; stress; antisocial; hormone

Introduction

The stress response system is important to the biological understanding of psychopathy because it is involved in generating the body's responses to harmful or fearful situations, including punishment. When functioning properly, the stress response system increases the probability of withdrawal behavior by inducing fear and increasing sensitivity to punishment (van Honk & Schutter, 2006). Individuals with psychopathic traits have been described as fearless and insensitive to punishment (Lykken, 1995), suggesting that the stress response system may be impaired. Without proper responses to cues of threat, individuals may be more likely to engage in risky and antisocial behavior with little fear of consequences.

The two main physiological systems of the stress response system are the HPA axis and the sympathetic branch of the autonomic nervous system (ANS). These two systems are thought to interact to maintain homeostasis and normal responding to stress (de Kloet et al., 2005). The ANS is a fast-acting system involved in regulating critical functions on a moment-to-moment basis; ANS responses include an increase in heart rate, skin conductance, and the release of neurotransmitters, primarily norepinephrine (NE). The HPA axis is involved in a second, slower-acting response that includes the release of cortisol. Coordination of the two systems involved in the stress response occurs at several points in the brain where the ANS and HPA axis receive shared inputs and can be activated and inhibited simultaneously. Because of the interconnectedness of these systems, it may be necessary to assess both systems in order to understand the reduced stress responsivity observed in psychopathy, but to date, no studies have examined ANS and HPA axis functioning simultaneously in relation to psychopathy.

Several studies examining the stress response system in youth with antisocial behavior have recognized the importance of simultaneously assessing ANS and HPA axis functioning, and have included measures of sAA, in addition to measures of cortisol. Gordis et al. (2006) found an interaction between cortisol and sAA reactivity when predicting aggressive behavior in children; at high levels of alpha-amylase, cortisol was not related to aggression,

yet at low sAA levels, low cortisol was associated with increased aggression. Similarly, Chen et al. (2014) found an interaction such that lower cortisol levels were associated with higher externalizing behavior, but only at low levels of sAA. These results support an additive model, suggesting that low cortisol and sAA reactivity, when combined, may substantially increase the risk for aggression (i.e., a “double hit”). This interactive effect is consistent with the physiological under-arousal hypothesis explaining externalizing behavior in youth (van Goozen et al., 2007). This hypothesis states that when under-arousal in both systems is present, the activation threshold for a fear or avoidance responses is heightened such that more stimulation is required to elicit a withdrawal response.

In contrast to the above studies, de Vries-Bouw et al. (2012) did not find an interaction between sAA and cortisol reactivity in a sample of delinquent adolescents. The researchers found that concurrent low sAA and low cortisol reactivity was associated with the highest levels of disruptive behavior. While no interaction between sAA and cortisol was found, these results also support an additive model. Susman et al. (2010) found that low cortisol reactivity and low sAA reactivity were both related to higher rates of antisocial behavior in boys, but these findings were dependent on timing of puberty. These results are in line with the results of Gordis and colleagues (2006), although Susman and colleagues (2010) did not report interactions between cortisol and sAA.

Collectively, these studies suggest that an additive model of cortisol and sAA reactivity may explain the most variance in antisocial behavior in youth, with most evidence suggesting that low cortisol and low sAA reactivity is associated with higher levels of antisocial behavior. However, discrepancies exist. For example, El-Sheikh et al. (2008) also found an interaction between baseline cortisol and sAA levels when predicting externalizing behavior in children (aggression, impulsivity, disruptive behavior, delinquency, and noncompliance), but found that *higher* baseline cortisol levels were positively associated with higher externalizing problems among children with higher ANS activity (sAA levels), as compared to children with lower ANS activity. Overall, the discrepancies in these findings may result from sampling from different age ranges, the assessment of baseline levels versus reactivity, and the heterogeneity in externalizing/aggressive samples (e.g., including individuals with callous-unemotional traits as well as those with primarily reactive aggression).

The first goal of the present study was to assess both systems involved in the stress response via cortisol and sAA in relation to psychopathic traits specifically, thus reducing the problems associated with heterogeneity that occur when assessing antisocial behavior more broadly. The construct of psychopathy consists of several features, including manipulativeness, deceitfulness, reduced emotional responsiveness, impulsivity, stimulation seeking, and antisocial behavior. Some of these features are specific to psychopathy, whereas others are observed in antisocial individuals more generally. There may be reason to hypothesize differences in stress reactivity between those who demonstrate core features of psychopathy such as fearlessness and reduced emotional responsiveness compared to individuals who have externalizing behaviors without demonstrating these traits. Individuals characterized by fearlessness and reduced emotional responsiveness may exhibit blunted reactivity to stressors in the environment, whereas those who demonstrate externalizing problems as a result of poor emotion regulation or impulsivity may exhibit heightened

reactivity to a stressor. In the prior studies of youth, it is unclear what proportion of these youth may demonstrate the affective (e.g., callous-unemotional) features of psychopathy. Thus, in addition to examining relationships with total psychopathy scores, we aimed to gain a better understanding of the specificity of these relationships by examining the different factors of psychopathy.

The second goal of the study was to assess these systems in a sample of adults in order to determine whether some of the same patterns of findings observed in antisocial youth may also be present in adults. We predicted that adult psychopathy would be associated with low levels of *both* ANS and HPA axis functioning, measured by sAA and cortisol.

Methods

Participants

Participants (158 males, mean age = 36.81, *SD* = 8.57, range = 22-67 years, 43.7% African-American, 33.5% Caucasian, 15.8% Hispanic, 3.2% Asian, 3.8% other) were recruited from temporary employment agencies in the greater Los Angeles area. We previously analyzed saliva samples acquired from this sample for cortisol and found that the ratio between cortisol reactivity and baseline testosterone was associated with psychopathy scores (Glenn et al., 2011). In the present study, we analyzed the samples for sAA in order to simultaneously examine the two components of the stress response system. After giving informed consent, participants completed 2 days of assessments. A certificate of confidentiality was obtained from the Secretary of Health pursuant to Section 303(a) of Public Health Act 42 (U.S.C. 241[d]) prior to the start of data collection. Participants were informed that information they may provide during the study about uninvestigated crimes could not be subpoenaed by any United States federal, state, or local court. Participants were paid $100 for participating.

Psychopathy assessment

Psychopathy was assessed with the Psychopathy Checklist-Revised (PCL-R): 2nd edition (Hare, 2003) and was corroborated using 10 other data sources. The PCL-R: 2nd edition consists of 20 items and has been conceptualized in both two- and four-factor models. In the two-factor model, Factor 1 consists of interpersonal and affective traits (e.g., manipulativeness, lack of empathy), and Factor 2 consists of antisocial traits and behaviors (e.g., sensation-seeking, short-term relationships). In the four-factor model, facet 1 represents the interpersonal features, facet 2 represents the affective features, facet 3 represents the lifestyle features (e.g., irresponsibility, impulsivity) and facet 4 represents antisocial behaviors. Psychopathy assessments were conducted by an author (RS) trained in administering and scoring the PCL-R by Robert D. Hare and Adelle Forth. Training included completing a series of assessments on standardized videotaped cases of adult male offenders (correlations between rater's and standard criterion scores: PCL-R Total = .92, Factor 1 = .93, and Factor 2 = .91). Assessments were supervised by another author (AR) who has extensive experience in psychopathy assessment.

In order to successfully assess psychopathy in a community sample using the PCL-R, we used 10 additional sources of collateral data, including internet-based background check services. These collateral data sources provided additional background information for item evaluation on the PCL-R and also allowed for an assessment of discrepancies between the participant's report and objective data reports. This aids in assessing the extent of pathological lying and deception. The 10 collateral data sources were: (a) self-reported theft, drug offenses, and violent crime, assessed by an adult extension (Raine et al., 2000) of the delinquency measure (Elliot et al., 1983) from the National Youth Survey; (b) official state-level Department of Justice criminal records from California; (c) nationwide state-level criminal and court record database searches; (d) federal criminal records database search; (e) involvement in civil actions, liens, and other financial judgments; (f) personal history judgments including marriage and divorce, prior residences and relocations, relatives, and significant others; (g) data from, and observations derived during, the Structured Clinical Interview for DSM-IV Axis I Disorders (First et al., 1996); (h) the SCID Axis II Personality Disorders (First et al., 1997); both SCID diagnoses were made by the same research assistant, who was trained on the SCID (Ventura et al., 1998); (i) the Interpersonal Measure of Psychopathy (IM-P; Kosson et al., 1997), which provides an interviewer's ratings of psychopathic interpersonal behaviors, has demonstrated construct validity with the PCL-R in a prison sample, and has been validated with non-incarcerated, community samples as well (Kosson et al., 1997); and (j) independent IM-P ratings made by two different laboratory assistants at separate times of laboratory testing over the two day testing period.

Social stressor task

Subjects were asked to perform a social stressor task, which was designed to provoke negative emotions such as embarrassment and guilt (Damasio, 2000). Subjects were given two minutes to prepare a speech about the worst thing he/she has ever done, followed by a 2-minute speaking portion in which they delivered their speech to an experimenter while being videotaped. If the participant stopped speaking or had difficulty speaking continuously, the experimenter requested that he or she give specific examples in order to enhance the stressfulness of the task (Ishikawa et al., 2001; Raine et al., 2000). According to a meta-analysis of the effectiveness of stress tasks (Dickerson & Kemeny, 2004), uncontrollable psychological stressors with a social-evaluative aspect induce the greatest cortisol response to stress.

In the afternoon (between 1:00 and 6:00 p.m.) on one of the two days of testing, three saliva samples were collected to track cortisol and sAA responses to the public speaking stressor task. The first sample was collected prior to the public speaking stressor task. Prior to providing this baseline sample, participants completed a countdown task lasting 2-3 minutes, a tone aversiveness rating, an oddball task lasting 6-8 minutes, and completed the Positive and Negative Affect Schedule (PANAS). Although the countdown task was originally intended to induce stress, it was not effective in generating a stress response. No changes in sAA were found between a sample collected prior to these tasks (not used in this study) and the sample collected prior to the public speaking stressor task ($t = -.381$, $p = .70$, pre-countdown mean = 155.1 (SD = 89.7); post-countdown mean = 156.9 (SD = 97.9)), and cortisol levels declined significantly, as expected with the diurnal cycle ($t = 2.415$, $p = .02$,

pre-countdown mean = .14 (SD = .09); post-countdown mean = .13 (SD = .07)). Furthermore, the oddball task and PANAS that occurred immediately prior to the public speaking task were not stress inducing activities. Thus, the sample collected immediately prior to the public speaking task was considered a baseline measure. The second sample was collected approximately 20 minutes after the first sample (approximately 12 minutes after the end of the public speaking task. The third sample was collected approximately 20-25 minutes after the second sample, representing a return to baseline levels[1]. These will be referred to subsequently as sample 1, sample 2, and sample 3, respectively.

Determination of Salivary Analytes

For each saliva sample, participants deposited whole, unstimulated saliva by passive drool through a short straw into collection vials (Granger et al., 2007). Prior to sample donation, participants were asked to abstain from exercise, smoking, eating, and consuming caffeinated beverages or alcohol for 1 hr before. After collection, each sample was immediately frozen at -85° Celsius. Saliva samples were analyzed with commercially available enzyme immunoassay and kinetic reaction assay kits, following the manufacturer's recommended protocols (Salmetrics LLC, Carlsbad, CA). For cortisol, the test volume was 25 ul, sensitivity ranged from 0.007 to 3.0 μg/dL, and interassay and intraassay coefficients of variation were less than 5.0%. For sAA, saliva samples were assayed using a chromagnetic substrate, 2- chloro-*p*-nitrophenol, linked to maltotriose (Salimetrics LLC, Carlsbad, CA). Saliva samples (10μL) were diluted 1:200. 8μL test volume pipetted into individual wells of a microtiter plate. 320μL of the chromagnetic amylase substrate solution, preheated to 37 C, were added to each well and rotated at 500- 600 RPM at 37 C for 3 minutes. Optical density was read after exactly 1 and 3 minutes. Results were computed in U/mL of sAA using this formula: [Absorbance difference per minute × total assay volume (328 ml) × dilution factor (200)]/[millimolar absorptivity of 2-chloro-*p*-nitrophenol (12.9) × sample volume (.008 ml) × light path (.97)]. Sensitivity of the sAA kit is 0.01 U/mL to 400 U/mL, and intra-and inter assay coefficients of variation were less than 5% and 20%, respectively.

Statistical Analyses

Subjects were excluded from analyses if they were missing one or more sAA measurement. Twenty-eight participants were excluded on this basis. Additionally, 13 participants were excluded from analyses involving cortisol because they were missing one or more cortisol measurements.

Outliers more than 3 SD from the mean were also excluded from analyses. This resulted in 8 participants being removed from analyses due to cortisol or sAA data. This resulted in a final sample of 139 participants (122 males; 128 participants for cortisol analyses, due to missing data).

[1]The analysis of the public speaking task as a single stressor represents a change from the authors' previous publication on cortisol and testosterone (Glenn et al., 2011) as well as from the analyses presented in the first author's dissertation (publically available online), which combine the countdown and public speaking tasks into one stressor for analyses. Given the significant time between the stressors, we decided that combining the two tasks was not appropriate for the sAA data, given the faster response and recovery time of sAA.

Cortisol and sAA reactivity to the stressor was measured by calculating the area under the curve (AUC) with respect to the increase (Pruessner et al., 2003) for the three samples collected surrounding the stressor. The formula is given by the following:

$$AUC_I = \left(\sum_{i=1}^{n-1} \frac{(m_{(i+1)} + m_i) \cdot t_i}{2} \right) - \left(m_1 \cdot \sum_{i=1}^{n-1} t_i \right)$$

where t_i is the precise interval between sample i and sample $i + 1$, times which are specific for each participant and each interval, n is the total number of measurements, and m_i is the level of the hormone for sample i. This analysis results in one number representing a general index of reactivity for each participant, and allowed for variations in time between sample collections to be accounted for.

Cortisol and AA reactivity was also measured using the area under the curve with respect to the ground (AUCg) (Pruessner et al., 2003). The formula takes into account reactivity as well as baseline levels, and is given by the following:

$$AUC_G = \sum_{i=1}^{n-1} \frac{(m_{(i+1)} + m_i) \cdot t_i}{2}$$

Twenty participants were excluded from area under the curve analyses because precise timing information was not available for calculations.

For some analyses, participants scoring higher in psychopathy (PCL-R total score > 23; n = 53) were compared to participants lower in psychopathy (PCL-R total score < 14; n = 45). We selected this cut-off point to maintain consistency with several prior studies of psychopathy in community samples (Glenn et al., 2010; Ishikawa et al., 2001; Raine et al., 2004; Yang et al., 2005) that have yielded theoretically meaningful findings, and also because the PCL-R (which was developed in prison samples) may underestimate psychopathy scores in community samples in which we do not have access to the rich sources of collateral information obtained in institutionalized samples. However, supplementary analyses were also conducted using a cut-off score of 28.

Results

Descriptive Statistics

Descriptive statistics for all variables can be found in Table 1 and zero-order correlations between variables in Table 2. Age was negatively related to sAA area under the curve with respect to increase (AUC_i), but not to cortisol or psychopathy variables. The time in the afternoon that the task began was correlated with sAA levels for all three samples ($p < .05$) but not with cortisol levels (all $p > .4$).

Cortisol and sAA

We first examined the changes in sAA and cortisol over the course of the stressor task to determine whether the task resulted in significant changes. Repeated measures ANOVA revealed a main effect of time for sAA over the course of the stressor task, ($F(2,121) = 3.40$, $p = .035$). Post-hoc paired t- tests showed that there was no significant change in sAA levels from baseline to post-stressor ($t = -.52$, $p > 0.6$), but that sAA decreased significantly from post-stressor to the recovery sample ($t = 2.43$, $p < .05$). Similar results were observed for cortisol; there was a significant main effect of time ($F(2,110) = 10.99$, $p < .005$) and post-hoc paired t-tests revealed that cortisol did not differ significantly between sample 1 and sample 2 ($t = 1.55$, $p = .12$), but decreased significantly between sample 2 and sample 3 ($t = 2.04$, $p < .05$).

Relationships with Psychopathy

Because age and the start time of the stressor task were correlated with sAA AUC_i, they were controlled for in regression analyses. When controlling for start time and age, sAA AUC_i was not associated with total psychopathy scores ($\beta = -.15$, $p = .15$). Psychopathy group comparisons were performed using cut-off points of greater than 23 for entry into the "high" psychopathy group and less than 14 for entry into the "low" psychopathy group. A repeated measures ANOVA examining differences in sAA levels across saliva samples in males scoring higher versus lower in psychopathy, controlling for age and start time of the task, revealed a significant interaction ($F(2,138)=3.13$, $p = .03$). sAA levels for the two groups are plotted in Figure 1. Although pre-stressor sAA levels did not differ significantly between the groups ($t = .80$, $p = .43$), paired t-tests showed that males scoring lower in psychopathy show a significant increase in sAA in response to the stressor ($t = -3.59$, $p < .005$), whereas males scoring higher in psychopathy did not ($t = .37$, $p = .71$). Additionally, the difference score representing the change in sAA levels from pre- to post-stressor was significantly correlated with PCL-R total scores ($r = -.22$, $p = .02$). Analyses using a cut-off score of 28 produced similar results and are reported in the Supplementary Materials. sAA AUC_g and both AUC measures for cortisol were not associated with psychopathy scores.

Analyses of Psychopathy Factors

sAA AUC_i was not associated with Factor 1 ($\beta = -.10$, $p = .36$) or with Factor 2 ($\beta = -.16$, $p = .12$) when controlling for start time and age. It was not associated with any of the individual facets of psychopathy ($p > .19$). However, a repeated measures ANOVA examining differences in sAA levels across the three samples in males scoring in the top third (>10) versus bottom third (<6) of the sample on Factor 1 of psychopathy was significant ($F(2,64) = 3.97$, $p = .02$). Similar to analyses with total psychopathy scores, plots demonstrated that males scoring high on Factor 1 demonstrated reduced sAA responses compared to those scoring low on Factor 1. Although pre-stressor sAA levels did not differ significantly between the groups ($t = -1.39$, $p = .17$), paired t-tests showed that males low in Factor 1 show a significant increase in sAA in response to the stressor ($t = -3.13$, $p < .005$), whereas males high in Factor 1 did not ($t = .57$, $p = .57$).

A repeated measures ANOVA examining differences in sAA levels across the three samples in males scoring in the top third (>11.1) versus and bottom third (<7) of the sample on

Factor 2 of psychopathy was also significant ($F(2,42) = 3.74$, $p = .03$). A similar pattern was found in which paired t- tests showed that males low in Factor 2 show a significant increase in sAA in response to the stressor ($t = -2.54$, $p < .02$), whereas males high in Factor 2 did not ($t = .35$, $p = .73$). Pre-stressor sAA levels did not differ significantly between the groups ($t = -.42$, $p = .68$).

In addition to these analyses, partial correlations were computed to adjust for the correlation between Factors 1 and 2. Controlling for correlated variation in Factor 2, Factor 1 was not associated with sAA AUC_i ($r = .06$, $p = .57$). Similarly, controlling for correlated variation in Factor 1, Factor 2 was not associated with sAA AUC_i ($r = -.13$, $p = .21$).

Interactions with Cortisol

We examined the interactive effects of cortisol and sAA on psychopathy scores via multiple regression analyses. A multiple regression with psychopathy total scores as the dependent variable and with age, start time of the stressor, baseline sAA and baseline cortisol revealed a significant interaction ($\beta = -.21$, $p = .04$). We probed this interaction further by plotting the slope of the relation between baseline cortisol and psychopathy separately for males above and below the median on baseline sAA (examination of one standard deviation above and below the mean produced two few participants for analyses). For males above the median on sAA, baseline cortisol was significantly associated with psychopathy total scores ($\beta = -.27$, $p = .05$), controlling for age and start time of the stressor, such that males scoring higher in psychopathy had lower levels of baseline cortisol. For males below the median on sAA, baseline cortisol was unrelated to total psychopathy scores ($\beta = .08$, $p = .60$) (Figure 2).

A multiple regression with psychopathy total scores as the dependent variable and with age, start time of the stressor, sAA AUC_i and cortisol AUC_i revealed no significant interaction between sAA and cortisol reactivity ($p > .79$). Similarly, a regression with psychopathy total scores as the dependent variable and with age, start time of the stressor, sAA AUC_g and cortisol AUC_g revealed no significant interaction between sAA and cortisol reactivity ($p > .28$).

Discussion

To our knowledge, this is the first study investigating sAA reactivity in relation to psychopathy in adults, and also the first to examine potential interactions between autonomic nervous system functioning (measured via sAA) and HPA axis functioning (measured via cortisol) in adults with psychopathic traits. In this sample of adult males, dimensional analyses using the area under the curve measure for sAA did not reveal significant associations with psychopathy. However, categorical analyses of individuals scoring above and below particular cutoffs of psychopathy revealed that those scoring lower in psychopathy had significant increases in sAA in response to the stressor whereas those scoring higher in psychopathy did not. The reduction in sAA reactivity, though modest, is consistent with prior research suggesting that individuals with psychopathic traits may have deficits in autonomic nervous system functioning, as has been indicated by low resting electrodermal activity and reduced electrodermal reactivity (for meta- analysis, see Lorber, 2004).

Unlike findings from studies of youth with externalizing problems (Chen et al., 2014; El-Sheikh et al., 2008; Gordis et al., 2006), no interaction was detected between sAA and cortisol reactivity. In addition, we did not observe reductions in *both* sAA and cortisol reactivity, as reported in the study by de Vries-Bouw et al. (2012), who found that sAA reactivity and cortisol reactivity in response to a stress task were significantly lower in a group of adolescents and young adults with behavior disorders, compared to normal controls. However, we did observe an interaction between baseline sAA and baseline cortisol levels. For males with high baseline levels of sAA, lower baseline cortisol levels were associated with higher psychopathy scores. For males with low baseline levels of sAA, cortisol levels were unrelated to psychopathy scores. Figure 2 suggests that individuals scoring higher in psychopathy were those with either high sAA and low baseline cortisol, or those with low sAA and high baseline cortisol. This pattern of findings may support a theory proposed by Bauer et al. (2002), who suggest that asymmetry between the HPA axis and the SNS (i.e., inefficient or poor coordination) may contribute to behavioral problems (internalizing or externalizing). Bauer et al. (2002) suggest that although it is clear that the HPA axis and ANS work concurrently to generate the physiological changes associated with stress, there is evidence of differential activation and sometimes suppression between the two systems. For example, the ANS has been described as a “defense reaction” that responds more to controllable stressors and is more prominent in individuals with a personality tendency to exert high effort to obtain control. In contrast, activation of the HPA axis may be more of a “defeat reaction” – a passive response pattern characterized by emotional distress, behavioral withdrawal, and loss of control (Henry, 1992); activation of this system is especially likely to occur when situations are uncontrollable (Dickerson & Kemeny, 2004). Bauer et al. (2002) suggest that because the ANS and HPA systems can be activated in response to different situational demands and may be differentially activated depending on individuals' perception of events, there is potential for the responses of the two systems to become dissociated.

This is in contrast to the “additive” model, of which previous studies of youth with externalizing problems have found support. One possible reason for the discrepancy between our findings and findings in youth with externalizing problems is that the relationships between psychopathy and the stress response systems may change with age. Several studies have found developmental differences in sAA and cortisol responses to social stressors. A study by Strahler et al. (2010) compared children, young adults, and older adults on both sAA and cortisol reactivity. They found that children have higher baseline levels of sAA, and lower baseline levels of cortisol than adults. In addition, sAA responses are more blunted in children than adults. Within adults, they found age to be the strongest predictor of sAA responsivity (AUC_i), with younger adults exhibiting higher reactivity than older adults. Similarly, Yim et al. (2010) tested an identical laboratory stressor in both children and adults and found that adults demonstrated an sAA response, whereas children did not. Stroud et al. (2009) identified reductions in both cortisol and sAA responses to stress in children compared to adolescents. These changes in sAA and cortisol levels that occur from childhood throughout adulthood may partly explain the differences in the relationships observed in the present adult sample and previous findings involving youth. In

line with the findings of Strahler et al. (2010), in the present sample of adults we found age to be negatively correlated with baseline levels of sAA as well as sAA increases.

Another potential reason for these discrepant findings is that previous studies in youth examined externalizing problems more generally, whereas the current study focused specifically on relationships with psychopathic traits. However, when examining the individual factors of psychopathy, similar relationships were observed for both Factor 1 (Interpersonal-Affective) and Factor 2 (Lifestyle- Antisocial) of psychopathy. Specifically, individuals low on either factor showed a significant increase between pre- and post-stressor, whereas individuals high on either factor showed no such increase. Partial correlations accounting for the covariance between the two factors did not reveal significant associations between sAA and the unique variance of either factor. Overall, this suggests that the relationship observed with sAA is not specific to the affective and interpersonal features of psychopathy, but is associated with the variance in psychopathy that is shared between the two factors.

Some limitations should be considered. In this study, we used one post-stressor sample, measured twelve minutes after the end of the stressor task, to examine both sAA and cortisol reactivity. The collection of additional post-stressor saliva samples in shorter time intervals may have improved our ability to capture separate peak responses for sAA and cortisol. We did not observe significant increases in cortisol and sAA levels from baseline to post-stressor, suggesting that the stressor task used may have not been powerful enough to elicit a response in many participants. Although speculative, this may be in part due to the nature of our sample, which was recruited from temporary employment agencies rather than an undergraduate population. Individuals recruited from temporary employment agencies may have more significant stressors in their daily lives, and thus this type of stressor may be less effective at eliciting a response. However, significant increases in sAA were present in those scoring low in psychopathy. Another possibility is that higher rates of psychopathy in this population may have resulted in blunted responses in the group as a whole. It is also possible that individuals scoring higher in psychopathy took the task less seriously, or talked about more benign faults during the task in order to present themselves in a more positive light. Finally, our sample was limited to males, so we do not have information about how relationships between these hormones and psychopathy may differ in females.

In conclusion, a unique feature of this study is that sAA and cortisol were measured simultaneously. In youth, a growing body of literature has found that low reactivity of both the HPA axis and ANS is related to externalizing behavior. However, we did not find such effects in this study. Our results are consistent with the body of evidence suggesting dysfunction of the ANS in adults with psychopathic traits (Lorber, 2004). Future studies using longitudinal designs could further explore how the HPA axis and ANS, as well as the relationships between them, change with age, and how this may influence relationships with psychopathy and externalizing problems. In addition, studies specifically examining psychopathic traits in youth may help to clarify whether findings from previous studies apply to youth with psychopathic traits as well as those who may demonstrate primarily reactive forms of aggression.

Acknowledgments

We acknowledge Lori Lacasse, Janet Kim, and Avital Falk for assistance with sAA assays.

Role of the funding source: This study was supported by grants from the National Institute of Mental Health to Dr. Raine (Research Scientist Development Award No. K02 MH01114-01, Independent Scientist Award K02 MH01114-01, and Grant No. 5 R03 MH50940-02).

References

Bauer AM, Quas JA, Boyce WT. Associations between physiological reactivity and children's behavior: advantages of a multisystem approach. Journal of Developmental Behavioral Pediatrics. 2002; 23:102–113. [PubMed: 11943973]

Chen FR, Raine A, Soyfer L, Granger DA. Interaction of Adrenocortical Activity and Autonomic Arousal on Children's Externalizing and Internalizing Behavior Problems. J Abnorm Child Psychol. 2014

Damasio AR. Commentary: A Neural Basis for Sociopathy. Archives of General Psychiatry. 2000; 57:128–129.

de Kloet ER, Joels M, Holsboer F. Stress and the brain: from adaptation to disease. Nature Reviews: Neuroscience. 2005; 6(6):463–475.

de Vries-Bouw M, Jansen L, Vermeiren R, Doreleijers T, van de Ven P, Popma A. Concurrent attenuated reactivity of alpha-amylase and cortisol is related to disruptive behavior in male adolescents. Horm Behav. 2012; 62(1):77–85. [PubMed: 22587939]

Dickerson SS, Kemeny ME. Acute Stressors and Cortisol Responses: A Theoretical Integration and Synthesis of Laboratory Research. Psychological Bulletin. 2004; 130:355–391. [PubMed: 15122924]

El-Sheikh M, Erath SA, Buckhalt JA, Granger DA, Mize J. Cortisol and children's adjustment: the moderating role of sympathetic nervous system activity. Journal of Abnormal Child Psychology. 2008; 36:601–611. [PubMed: 18197472]

Elliot, DS.; Ageton, SS.; Huizinga, D.; Knowles, BA.; Canter, RJ. The prevalence and incidence of delinquent behavior: 1976-1980. Boulder, CO: Behavioral Research Institute; 1983.

First, MB.; Gibbon, M.; Spitzer, RL.; Williams, JBW.; Benjamin, LS. Structured Clinical Interview for DSM-IV Axis II Personality Disorders (SCID-II). Washington, DC: American Psychiatric Press; 1997.

First, MB.; Spitzer, RL.; Gibbon, M.; Williams, JBW. User's Guide for the Structured Clinical Interview for DSM-IV Axis I Disorders: SCID-I Clinician Version. Washington, DC: American Psychiatric Press; 1996.

Glenn AL, Raine A, Schug RA, Gao Y, Granger DA. Increased testosterone-to- cortisol ratio in psychopathy. J Abnorm Psychol. 2011; 120:389–399. [PubMed: 21133509]

Glenn AL, Raine A, Yaralian PS, Yang Y. Increased volume of the striatum in psychopathic individuals. Biol Psychiatry. 2010; 67:52–58. [PubMed: 19683706]

Gordis EB, Granger DA, Susman EJ, Trickett PK. Asymmetry between salivary cortisol and alpha-amylase reactivity to stress: Relation to agressive behavior in adolescents. Psychoneuroendocrinology. 2006; 31:976–987. [PubMed: 16879926]

Granger DA, Kivlighan KT, Fortunato C, Harmon AG, Hibel LC, Schwartz EB, Whembolua GL. Integration of salivary biomarkers into developmental and behaviorally-oriented research: problems and solutions for collecting specimens. Physiol Behav. 2007; 92:583–590. [PubMed: 17572453]

Hare, RD. Hare Psychopathy Checklist-Revised (PCL-R). 2nd. Toronto: Multi-Health Systems, Inc; 2003.

Henry JP. Biological basis of the stress response. Integrated Physiology and Behavioral Sciences. 1992; 27:66–83.

Ishikawa SS, Raine A, Lencz T, Bihrle S, Lacasse L. Autonomic stress reactivity and executive functions in successful and unsuccessful criminal psychopaths from the community. Journal of Abnormal Psychology. 2001; 110(3):423–432. [PubMed: 11502085]

Kosson DS, Kelly JC, White JW. Psychopathy-related traits predict self-reported sexual aggression among college men. Journal of Interpersonal Violence. 1997; 12:241–254.

Lorber MF. Psychophysiology of Aggression, Psychopathy, and Conduct Problems: A Meta-Analysis. Pychological Bulletin. 2004; 130(4):531–552.

Lykken, D. The antisocial personalities. Hillsdale, NJ: Erlbaum; 1995.

Pruessner JC, Kirschbaum C, Meinlschmid G, Hellhammer DH. Two formulas for computation of the area under the curve represent measures of total hormone concentration versus time-dependent change. Psychoneuroendocrinology. 2003; 28(7):916–931. [PubMed: 12892658]

Raine A, Ishikawa SS, Arce E, Lencz T, Knuth KH, Bihrle S, et al. Colletti P. Hippocampal structural asymmetry in unsuccessful psychopaths. Biological Psychiatry. 2004; 55:185–191. [PubMed: 14732599]

Raine A, Lencz T, Bihrle S, LaCasse L, Colletti P. Reduced prefrontal gray matter volume and reduced autonomic activity in antisocial personality disorder. Archives of General Psychiatry. 2000; 57:119–127. [PubMed: 10665614]

Strahler J, Mueller A, Rosenloecher F, Kirschbaum C, Rohleder N. Salivary alpha- amylase stress reactivity across different age groups. Psychophysiology. 2010; 47(3):587–595. [PubMed: 20070573]

Stroud LR, Foster E, Papandonatos GD, Handwerger K, Granger DA, Kivlighan KT, Niaura R. Stress response and the adolescent transition: Performance versus peer rejection stressors. Development and Psychopathology. 2009; 21(1):47–68. [PubMed: 19144222]

Susman EJ, Dockray S, Granger DA, Blades KT, Randazzo W, Heaton JA, Dorn LD. Cortisol and alpha amylase reactivity and timing of puberty: Vulnerabilities for antisocial behaviour in young adolescents. Psychoneuroendocrinology. 2010; 35(4):557–569. [PubMed: 19819639]

van Goozen SH, Fairchild G, Snoek H, Harold GT. The evidence for a neurobiological model of childhood antisocial behavior. Psychol Bull. 2007; 133(1):149–182. [PubMed: 17201574]

van Honk J, Schutter DJLG. Unmasking feigned sanity: A neurobiological model of emotion processing in primary psychopathy. Cognitive Neuropsychiatry. 2006; 11(3):285–306. [PubMed: 17354073]

Ventura J, Liberman RP, Green MF, Shaner A, Mintz J. Training and quality assurance with the Structured Clinical Interview for DSM-IV (SCID-I/P). Psychiatry Res. 1998; 79:163–173. [PubMed: 9705054]

Yang Y, Raine A, Lencz T, Bihrle S, Lacasse L, Colletti P. Volume reduction in prefrontal gray matter in unsuccessful criminal psychopaths. Biological Psychiatry. 2005; 15(57):1103–1108. [PubMed: 15866549]

Yim IS, Granger DA, Quas JA. Children's and adults' salivary alpha-amylase responses to a laboratory stressor and to verbal recall of the stressor. Dev Psychobiol. 2010; 52(6):598–602. [PubMed: 20806333]

Highlights

- We simultaneously measure alpha-amylase and cortisol as indicators of two stress response systems – the autonomic nervous system and the HPA axis.
- Adult males scoring higher on a measure of psychopathic traits demonstrate modest reductions in alpha-amylase reactivity to a psychosocial stressor.
- Interactions between the baseline alpha-amylase and cortisol were observed, but no interactions between reactivity of the two stress response systems were observed.

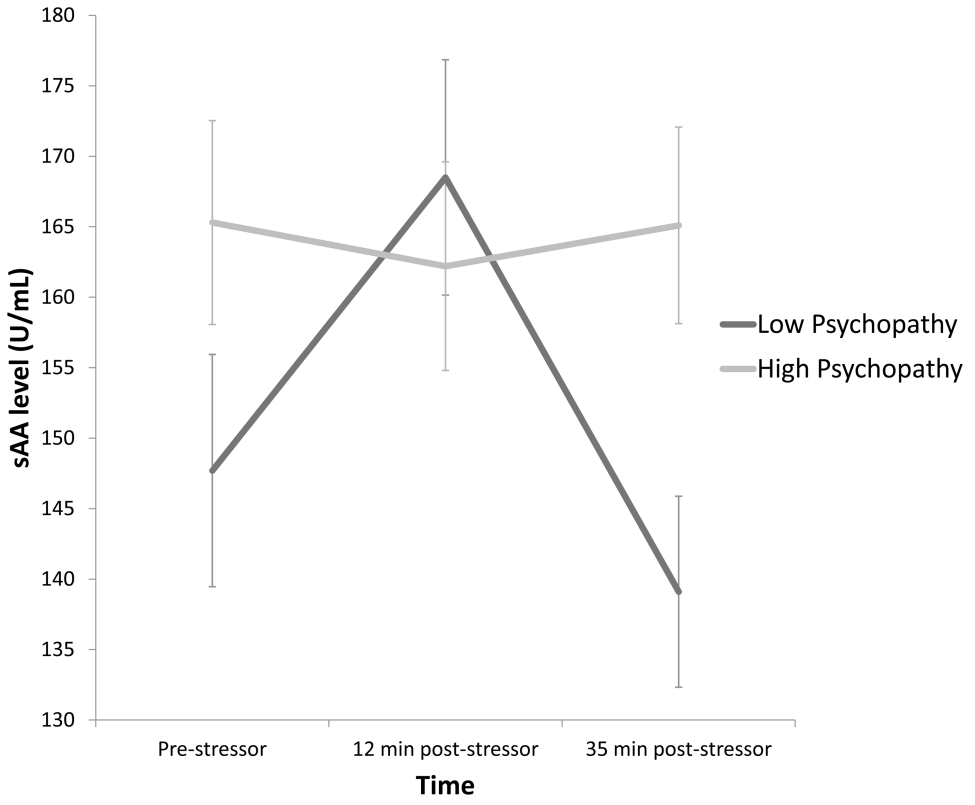

Figure 1.

Males scoring low in psychopathy (PCL-R < 14) demonstrated a significant increase in sAA levels following the social stress task whereas individuals scoring high in psychopathy (PCL-R > 23) did not. Pre-stressor levels of sAA were not significant between the two groups (t = .80, p = .43). Error bars represent standard error.

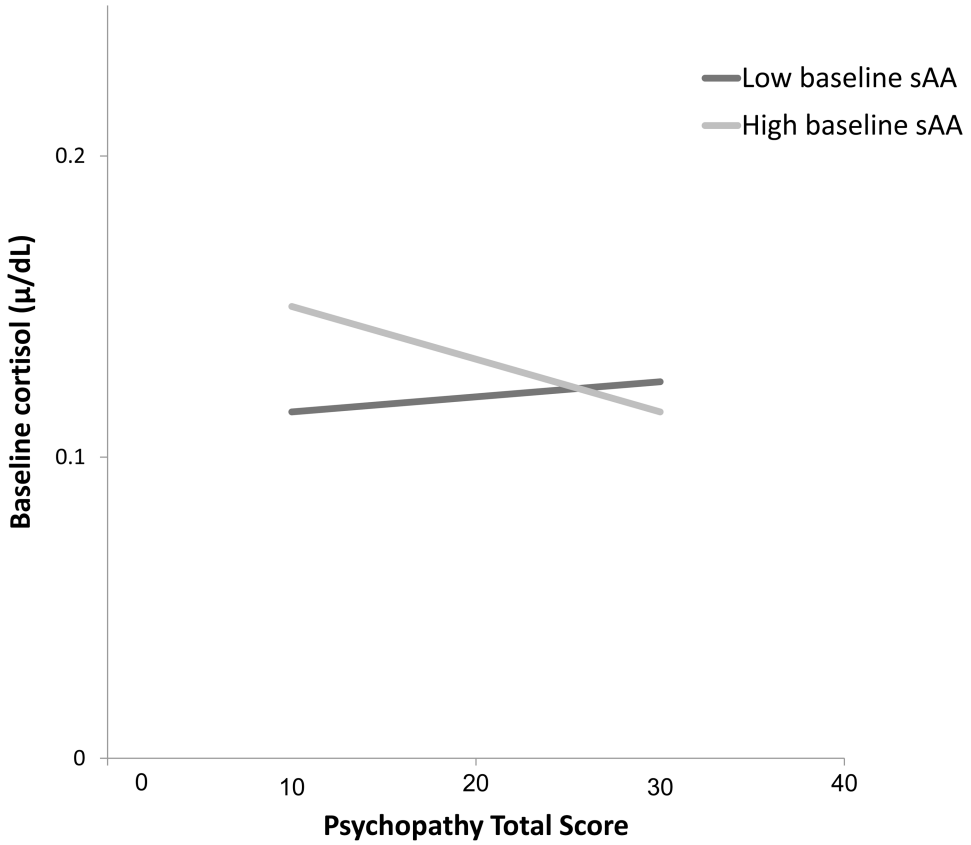

Figure 2.
Relation between baseline cortisol and psychopathy for males scoring above and below the median on baseline sAA.

Table 1

Descriptive Statistics

Variable	Mean (SD)
Age (years)	36.81 (8.57)
PCL-R Total	19.12 (9.19)
sAA sample 1 (U/mL)	162.76 (100.69)
sAA sample 2 (U/mL)	165.12 (100.23)
sAA sample 3 (U/mL)	152.94 (93.22)
Cortisol sample 1 (μg/dL)	.126 (.069)
Cortisol sample 2 (μg/dL)	.121 (.078)
Cortisol sample 3 (μg/dL)	.109 (.071)
Sample 1 collection time (minutes)	844.38 (40.97)
Sample 2 collection time (minutes)	865.34 (40.08)
Sampe 3 collection time (minutes)	888.53 (40.74)

Table 2

Correlations between Study Variables (Males)

	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
1. Age	1																
2. AA sample 1	.176	1															
3. AA sample 2	.074	.874**	1														
4. AA sample 3	.114	.823**	.839**	1													
5. Cortisol sample 1	-.128	.163	.194*	.141	1												
6. Cortisol sample 2	-.124	.218*	.298**	.250**	.789**	1											
7. Cortisol sample 3	-.129	.147	.159	.147	.543**	.687**	1										
8. sAA AUCg	.039	.914**	.937**	.884**	.169	.248*	.163	1									
9. Cortisol AUCg	-.158	.208*	.263*	.176	.838**	.942**	.710**	.260*	1								
10. sAA AUCi	-.199*	-.343**	.140	.122	.059	.140	.042	-.023	.048	1							
11. Cortisol AUCi	.110	-.012	.061	.064	-.384**	.219*	.272**	.024	.095	.169	1						
12. Psychopathy	-.072	.055	-.055	.085	-.058	-.048	-.047	-.016	-.191	-.111	-.117	1					
13. Factor 1	-.092	.060	-.027	.105	-.024	.005	.006	.005	-.168	-.059	-.091	.921**	1				
14. Factor 2	-.074	.040	-.067	.068	-.103	-.091	-.080	-.028	-.193	-.127	-.114	.945**	.766**	1			
15. Facet 1	-.076	.082	.010	.106	-.032	.006	-.003	.040	-.133	-.037	-.079	.830**	.923**	.672**	1		
16. Facet 2	-.084	.023	-.074	.070	-.019	.000	.018	-.054	-.167	-.089	-.079	.888**	.942**	.751**	.759**	1	
17. Facet 3	-.031	.108	.002	.138	-.079	-.083	-.071	.037	-.156	-.120	-.096	.867**	.715**	.910**	.621**	.711**	1
18. Facet 4	-.083	-.044	-.121	-.032	-.085	-.034	-.042	-.093	-.145	-.095	-.057	.780**	.604**	.837**	.533**	.596**	.566**

* $p < .05$

** $p < .01$