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# Dehydroepiandrosterone (DHEA) and its ratio to cortisol moderate associations between maltreatment and psychopathology in male juvenile offenders

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ABSTRACT

This study examined whether DHEA and its ratio to cortisol moderated risk for psychopathology among incarcerated youth exposed to childhood maltreatment. Resistance to stress-related psychopathology under adversity was also examined in relation to callous-unemotional (CU) traits, a personality construct characterized by resistance to pathological anxiety and blunted reactivity to threatening stimuli. Participants were 201 ethnically heterogeneous (41.8% White, 35.3% Black, 17.2% Hispanic) adolescent boys ($M$ age = 16.75, $SD$ = 1.15 years) incarcerated in a juvenile detention facility in the South Eastern United States who provided four afternoon saliva samples (later assayed for DHEA and cortisol) and completed self-report questionnaires. Results indicated that childhood maltreatment was associated with greater internalizing problems at lower DHEA concentrations and at higher cortisol-to-DHEA ratios. Conversely, higher DHEA levels and lower cortisol-to-DHEA ratios were associated with greater CU traits, irrespective of maltreatment exposure. CU traits did not attenuate levels of psychopathology in maltreated youth. Findings inform biosocial models of how exposure to parental maltreatment in early life contributes to risk and resilience through mechanisms associated with adaptive environmentally sensitive biological systems and processes.

## 1. Dehydroepiandrosterone (DHEA) and its ratio to cortisol moderate associations between maltreatment and psychopathology in male juvenile offenders

Individuals respond to stress and adversity in early life in diverse ways, from healthy adaptation to psychiatric illness. For example, chronic stress common to exposure to childhood maltreatment is associated with poor physical and mental health outcomes, and has numerous detrimental effects on biobehavioral health (Kuhlman et al., 2017). These associations are likely the result of alterations to environmentally sensitive physiological systems, such as the hypothalamic-pituitary-adrenal (HPA) axis. In the short term, physiological reactivity to stress and challenge is adaptive, but when these responses are experienced on a chronic basis they result in allostatic load and overload (McEwen and Wingfield, 2003). Cortisol, a glucocorticoid, is the primary adrenal product of HPA axis activation, and cortisol is a well established mediator of allostasis. Surprisingly, though, studies investigating the role of cortisol in stress induced psychiatric illnesses yield inconsistent findings. Recent reviews and meta-analyses reveal the association between cortisol and psychopathology involves multiple components of the stress response system working in coordination (e.g., Alink et al., 2008; Bernard et al., 2017). That is, empirical attention is now focused on determining how patterns of interacting changes in the main components of the psychobiology of the stress response relate to the expression of atypical behavior and symptoms of psychiatric illness.

When the HPA axis is activated under stress, the adrenal gland also produces dehydroepiandrosterone (DHEA), an androgen (from the zona reticularis). DHEA has opposing effects to cortisol. Studies suggest that DHEA is an anxiolytic, can enhance learning and memory, and potentiates immune responsiveness (Majewska, 1995). DHEA may also be

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associated with resilience to stress, and low susceptibility to stress-related psychopathology (Rasmusson et al., 2003; Russo et al., 2012). For example, highly resilient maltreated youth showed greater DHEA concentrations than their less resilient counterparts (Cicchetti and Rogosch, 2007; Haglund et al., 2007). Conversely, DHEA hyposecretion is associated with internalizing problems (Goodyer et al., 1996). Contemporary theorists speculate that higher DHEA levels, and the ratio of cortisol to DHEA, may have utility as a biomarker for resilience (Russo et al., 2012).

The mechanism of action by which DHEA promotes risk and resilience to psychopathology under conditions of extreme stress is not fully understood; however, current evidence implicates multiple mechanisms. Under chronic stress, effective coping requires the HPA system to continually maintain a high cortisol level, which comes at the cost of overstimulating and producing structural and functional abnormalities in brain areas implicated in emotion regulation and fear conditioning (e.g., prefrontal cortex, hippocampus and amygdala; see Kamin and Kertes, 2017). With its anti-glucocorticoid properties, DHEA lessens cortisol's physiological potency by antagonizing its neurotoxic effects, thus mitigating stress-induced neural degeneration and providing neuroprotection (Maninger et al., 2009). With long term chronic stress exposure, pregnenolone metabolism may shift to favor corticosteroid pathways over androgens, resulting in attenuated DHEA production (Beishuizen et al., 2002; Strelzyk et al., 2012). With continued frequent HPA axis activation, down-regulation of DHEA is later followed by down-regulation of cortisol due to adrenal fatigue (Kamin and Kertes, 2017).

A pattern of adrenocortical activity characterized by increased production of cortisol over DHEA, whereby the effect of cortisol is unopposed, is implicated in the initiation and progression of stress-related mental and physical health problems (Granger and Kivlighan, 2003). From adolescence on, an imbalanced high cortisol-to-DHEA ratio is thought to reflect HPA dysfunction associated with chronic stress (i.e., low levels of DHEA are unable to counteract the negative effects of high cortisol levels), and is associated with increased risk for psychopathology with the most robust findings for internalizing disorders (e.g., Goodyer et al., 1996, 2003). For example, elevated cortisol-to-DHEA ratios were associated with childhood maltreatment (van Voorhees et al., 2014), PTSD, and internalizing problems (Goodyer et al., 1998; Young et al., 2002). Conversely, lower cortisol-to-DHEA ratios and higher DHEA levels among healthy subjects undergoing military survival training were associated with superior performance and fewer psychological symptoms (Rasmusson et al., 2003). Thus, high and low cortisol-to-DHEA ratios may represent biomarkers for risk and resilience to psychopathology, respectively.

Setting aside hormones momentarily, resistance to anxiety and atypically blunted emotional/stress reactivity characterizes individuals with psychopathic personality traits; however, paradoxically, psychopathic traits are robustly positively associated with childhood maltreatment (Graham et al., 2012; Weiler and Widom, 1996). This unusual pattern of low stress-related psychopathology paired with adverse exposure might reflect a resistant hormone profile in which production of DHEA is favored over cortisol. This possibility is supported by preliminary research by Kimonis et al. (2017a) finding the highest DHEA levels among incarcerated boys with low internalizing symptoms and high callous-unemotional (CU) traits, the putative childhood antecedent to psychopathy. Although the chronic and aggressive antisocial presentations of CU individuals run counter to traditional concepts of 'resilience'—defined as the capacity to avoid social, psychological, and biological consequences of extraordinary stress and trauma and maintain normal psychological and physical functioning (Russo et al., 2012)—resilience is a multidimensional construct manifested as competence in some domains and maladaptation in others (Masten et al., 2006). Within the aversive and threatening environments associated with chronic childhood maltreatment, this CU phenotype may represent a functional adaptation to interpersonal stress (Mealey, 1995). Crucially, it is unknown whether the CU phenotype or its underlying resilient hormone patterns (i.e., high DHEA, low cortisol-to-DHEA ratio), or both, explain the resistance to psychopathology.

Incarcerated youth are an ideal population for examining this question because of their higher than average rates of childhood maltreatment, psychopathology, and CU traits. Indeed, in comparison to the general population, incarcerated youth have far higher rates of childhood maltreatment (Coleman and Stewart, 2010) and psychiatric disorders (Teplin et al., 2002). Apart from Kimonis et al. (2017a), the few published studies to examine DHEA in incarcerated youth draw from a single sample (N = 50) and focus on diurnal coupling of hormones in association with life adversity (Dismukes et al., 2015) and psychopathic traits (Johnson et al., 2014, 2018). While they have enhanced understanding of individual differences in the co-fluctuation of HPA and hypothalamic-pituitary-gonadal (HPG) axes, additional research using larger samples is needed to understand whether hormones modify risk for a broader range of psychopathologies linked with chronic stress among individuals exposed to life adversity.

The purpose of the present study was to examine in incarcerated boys whether DHEA concentrations and their ratio to cortisol moderated associations between childhood maltreatment exposure and a range of stress-related psychopathology. It was hypothesized that maltreatment would be associated with greater anxiety, depression, and PTSD symptoms at lower DHEA concentrations and at higher cortisol-to-DHEA ratios. A second study aim was to examine whether CU traits, as a "resistant" personality trait, moderated associations between maltreatment and stress-related psychopathology, controlling for hormone levels. It was hypothesized that maltreated boys high on CU traits would show fewer anxiety, depression, and PTSD symptoms than those low on CU. Investigating psychobiological mechanisms underlying resilient and psychopathological functioning holds promise for advancing developmental models of psychopathology and informing intervention efforts with at-risk individuals.

## 2. Methods

### 2.1. Participants

Participants included 232 male juvenile offenders housed in a secure confinement facility in the southeastern United States. Youth between the ages of 14 and 18 years (*M* age = 16.75, *SD* = 1.15) were eligible to enroll in the study if they were not diagnosed with an intellectual disability or psychotic disorder, nor taking any disqualifying medications that may affect neuroendocrine measures (e.g., immunosuppressive agents, glucocorticoids, or beta-blockers) (Granger et al., 2009). On obtaining youth assent, parents of participants under the age of 18 years were contacted via telephone to obtain informed consent. Ninety-seven youth self-identified as White (41.8%), 82 as Black (35.3%), 40 as Hispanic (17.2%), 3 as Native American (1.3%), and 10 as mixed race/ethnicity (4.3%), an ethnic composition that is representative of youth incarcerated in this region of the US. The majority of youth were charged with nonviolent index offenses (78.6%) with 37.7% charged with a violent offense and 1.9% with a sexual offense. The average number of criminal charges prior to entering the facility was 17.93 (SD = 11.27, Range = 0–70) and violent charges was 1.03 (SD = 1.43, Range = 0–7), with an average age at first offense of 13.92 (SD = 1.75, Range = 7.12–17.89) years for the 203 boys for whom criminal history data were available from the State's Department of Juvenile Justice.

### 2.2. Procedure

All study procedures were approved by a University Institutional Review Board (IRB) and the Florida Department of Juvenile Justice. The majority (89%) of parents/guardians contacted consented to their child's participation in the study; the youth assent rate was 88%. Youth

completed a one to two-hour set of study questionnaires via laptop computer and were asked to donate four separate saliva samples. Samples were collected at 30-minute intervals between 1400 and 1630 h. Following recommendations by Granger et al. (2012) participants were instructed to donate whole saliva by passive drool within five minutes, samples were immediately secured on ice, then transported to a facility for storage at −80 °F. Participants were compensated $10 for their participation in the session.

### 2.3. Measures

#### 2.3.1. Demographic information

Participants self-reported demographic information including their age and race/ethnicity.

#### 2.3.2. Childhood maltreatment

The Childhood Trauma Questionnaire (CTQ; Bernstein and Fink, 1998) is a 28-item self-report measure assessing different types of childhood trauma, producing five clinical subscales each comprising five items: Physical Abuse, Sexual Abuse, Emotional Abuse, Physical Neglect, and Emotional Neglect scales. CTQ items are rated on a five-point scale from 'Never True' to 'Very Often True'. in past research, CTQ total scores were internally consistent with alpha coefficients ranging from .80 to .97 (Krischer and Sevecke, 2008), demonstrated a test-retest correlation of .88, and convergence with the Childhood Trauma Interview (Bernstein and Fink, 1998). Internal consistency of CTQ total scores was good (α = .87) in the present study. Using Walker et al.'s (1999) thresholds for determining whether individuals have been exposed to a clinically meaningful degree of childhood maltreatment, 43.1% of the sample were physically abused, 43.1% physically neglected, 41.8% emotionally abused, 15.1% emotionally neglected, and 7.3% sexually abused. The average number of types of maltreatment experienced was 1.5 (*SD* = 1.31, Range: 0–5) and 27% of boys experienced no maltreatment.

#### 2.3.3. Callous-unemotional traits

The 24-item Inventory of Callous-Unemotional Traits (ICU; Kimonis et al., 2008) provides one of the most comprehensive assessments of CU traits currently available. ICU total scores are internally consistent and manifest expected associations with relevant criterion constructs in diverse samples of youth (Kimonis et al., 2008). Consistent with these prior studies, items 2 and 10 were removed due to low item-to-total correlations, and internal consistency of this 22-item ICU total score was good (α = .82). According to Docherty et al. (2017), 52.6% of boys scored at or above the ICU cut-off score of 28.

#### 2.3.4. Anxiety

The Revised Children's Manifest Anxiety Scale (RCMAS; Reynolds and Richmond, 1990) is a standardized measure designed to assess anxiety in 6 to 19-year-old youth. It includes 37 items to which youth respond with a "Yes" or "No" answer, and is divided into four scales: Physiological Anxiety (10 items; e.g., "Often I feel sick in my stomach," α = .64), Worry/Oversensitivity (11 items; e.g., "I worry about what is going to happen," α = .76), Social Concerns/ Concentration (7 items; e.g., "A lot of people are against me," α = .68), and a Lie Scale (9 items; e.g., "I never get angry"). RCMAS total scores were used in the present study and were internally consistent (α = .88). Thirty five percent of boys reported clinically significant anxiety symptoms (T-score ≥ 60).

#### 2.3.5. Depression

Depressive symptoms were assessed using the Center for Epidemiological Studies-Depression Scale (CES-D; Radloff, 1977). The CES-D has been widely used with adolescents and is composed of 20 items (e.g., "I felt sad", "I felt that everything I did was an effort"). CES-D total scores demonstrated good internal consistency (α = .86) in the present study. Using Weissman et al.'s (1980) cut-off score of 15, 69.8% of the incarcerated boys reported clinically significant symptoms of depression.

#### 2.3.6. PTSD symptoms

The UCLA PTSD Index (Rodriguez et al., 1999) is a 22-item self-report instrument assessing DSM-IV PTSD symptomatology. Items are rated on a 5-point frequency scale and can be summed to form a severity score or scored categorically, yielding a likely diagnostic grouping. The instrument demonstrates strong convergent validity and high internal consistency (.90). The total PTSD symptom count demonstrated excellent internal consistency (α = .91) in the present study. Ten percent of boys reported symptoms consistent with a PTSD diagnosis (Rodriguez et al., 1999). Considered together, 32.8% of boys scored above clinical cut-offs for both anxiety and depression, while 6.5% of boys scored above cut-offs for all three stress-related disorders (anxiety, depression, and PTSD).

#### 2.3.7. Determination of salivary biomarkers

On the day of assay, all samples were thawed and centrifuged to remove mucins. Cortisol assays were performed at an earlier date and involved individual testing of each of the four individual samples and averaging values across samples to obtain a mean measurement. At a later time, an equal volume (50 µl) from each of the four individual samples was physically pooled and DHEA assays were performed. Salivary cortisol (in micrograms/deciliter, µg/dl) and DHEA (in picograms/milliliter, pg/ml) were assayed using commercially available enzyme immunoassay kits without modification to the manufacturer's (Salimetrics, State College, PA) recommended protocol. All samples were tested in duplicate. The cortisol assay used 25 µl of saliva and has a lower limit of sensitivity of 0.007 µg/dl, and the DHEA test used 50 µl of saliva and has a minimum detection limit of 10.0 pg/ml. Average intra- and inter-assay coefficients of variation were less than 10 and 15%, respectively. Fifteen participants were excluded from hormone analyses due to the presence of blood in their sample according to discoloration ratings (Kivlighan et al., 2004), leaving 201 participants. For ease of interpretation, cortisol values in µg/dl and DHEA values in pg/ml were transformed into nanomoles/liter (nmol/l) values (conversion factors are x 27.59 and x 3.47, respectively) prior to computing cortisol-to-DHEA ratios, as per guidelines provided by Sollberger and Ehlert (2016). Since they were non-normally distributed, cortisol and DHEA averaged values were Winsorized ($5^{th}$/$95^{th}$ percentile) and log transformed for analyses. Descriptives for raw DHEA values and cortisol-to-DHEA ratios (in nmol/l) were *M* = .74, *SD* = 1.40, skewness = 8.80, kurtosis = 90.67, and *M* = 25.35, *SD* = 135.73, skewness = 14.19, kurtosis = 209.29, respectively. Descriptives for transformed and Winsorized values were *M* = .60, *SD* = .46, skewness = 1.09, kurtosis = .11 for DHEA, and *M* = .15, *SD* = .34, skewness = -.20, kurtosis = -.63 for ratios.

### 2.4. Planned analyses

Descriptive statistics and zero-order correlations were used to examine mean levels and associations between main study variables. To test the primary study aim that salivary hormone concentrations moderate associations between childhood maltreatment and psychopathological outcomes, a series of hierarchical regression analyses were conducted. Analyses controlled for age given its positive correlation with DHEA levels (Shirtcliff et al., 2007), and findings of tighter coupling of cortisol and DHEA in older versus younger adolescents (Marceau et al., 2014). Age was entered into the first step of the model, CTQ maltreatment and salivary concentrations into the second step, and their interaction terms computed using mean centered values was entered into the third step. Analyses were conducted separately for DHEA and cortisol-to-DHEA concentrations, and were repeated for each outcome measure; anxiety, depression, PTSD symptoms, and CU traits.

To address the second study aim investigating CU traits as a

moderating variable, regression analyses were repeated including ICU scores in the second step and the interaction between maltreatment and ICU in the third step of the model. Significant interaction effects were probed using simple slopes analyses with the PROCESS macro for SPSS (Hayes, 2017), and followed up with the Johnson-Neyman technique to identify regions of significance. A simple slope is defined as the regression of the outcome on the predictor at a specific value of the moderator. PROCESS models the relationship between varying levels of the predictor and criterion variable, at three levels of the moderator (-1SD, mean, +1SD). Regions of significance refer to the range of moderator values for which there is a significant association between independent and dependent variables (see Roisman et al., 2012).

## 3. Results

### 3.1. Descriptives

Descriptive statistics and correlations among main study variables are presented in Table 1. Maltreatment scores were moderately positively correlated with all forms of psychopathology, but uncorrelated with hormone measures. CU scores were not significantly correlated with other forms of psychopathology. Cortisol-to-DHEA concentrations were negatively correlated with CU traits ($r$ = -.165, $p$ = .019) and marginally positively correlated with anxiety ($r$ = .135, $p$ = .055)[1].

### 3.2. Moderation analyses

Table 2 presents results of hierarchical regression analyses testing DHEA as moderator of the association between maltreatment and psychopathological outcomes. Maltreatment significantly predicted all outcomes with moderate effect size. The interaction between maltreatment and DHEA was significant in predicting depression and anxiety but not PTSD symptoms or CU traits. As depicted in Fig. 1, results of PROCESS analyses to probe the form of significant interaction using simple slopes analyses revealed that the association between maltreatment and depression was significant at low (B = .30, p < .001, 95% CI[.17,.44]) and average (B = .21, p < .001, 95% CI[.11,.31]), but not high DHEA concentrations. The Johnson-Neyman test indicated that the association between maltreatment and depression was significant from the lowest DHEA concentrations through to .85 *SD*s above the mean. For anxiety, the association with maltreatment was also significant at low (B = .19, p < .001, 95% CI[.10,.28]) and average (B = .12, p = .0005, 95% CI[.05,.18]) but not high DHEA concentrations, with the Johnson-Neyman significance region falling under .56 SDs above the mean. The form of the interaction was similar to that depicted for depression in Fig. 1.[2]

Table 3 presents results of hierarchical regression analyses testing cortisol-to-DHEA ratio as moderator of the association between maltreatment and psychopathological outcomes. There was a significant main effect of ratio for anxiety and CU traits, with marginal effects for depression ($p$ = .07) and PTSD ($p$ = .09). Anxiety was the only outcome for which there was a significant maltreatment X ratio interaction. As depicted in Fig. 2, PROCESS results revealed that the association between maltreatment and anxiety was significant at high (B = .21, $p$ < .001, 95% CI[.11,.30]) and average (B = .13, $p$ = .0001, 95% CI[.07,.20]) ratios, but not low ratios. The Johnson-Neyman test showed that the association between maltreatment and anxiety was significant from the highest ratio value through to .72 *SD*s below the mean.

Table 4 presents results of hierarchical regression analyses testing CU traits as moderator of the association between maltreatment and psychopathological outcomes controlling for DHEA concentrations and cortisol-to-DHEA ratio. The maltreatment X CU interaction was significant for PTSD symptoms ($p$ = .037) but not depression or anxiety. As depicted in Fig. 3, PTSD symptoms increased as levels of CU traits *increased* among maltreated boys. PROCESS results revealed that the association between maltreatment and PTSD was significant at high (B = .12, $p$ < .001, 95% CI[.06,.18]) and average (B = .08, $p$ = .001, 95% CI[.03,.12]), but not low, levels of CU traits. The Johnson-Neyman test showed that the association between maltreatment and PTSD was significant at CU scores .58 *SD*s below the mean and higher.

## 4. Discussion

In an ethnically heterogeneous sample of incarcerated boys, we examined whether cortisol, DHEA, and the cortisol-to-DHEA ratio moderated levels of psychopathology among those exposed to childhood maltreatment. Consistent with predictions, maltreated boys with low DHEA concentrations and with high cortisol-to-DHEA ratios showed the highest levels of internalizing problems. The opposite pattern of high DHEA concentrations and low cortisol-to-DHEA ratios characterized boys with CU traits, irrespective of maltreatment exposure. Contrary to predictions, the CU phenotype did not confer resilience against stress-related psychopathology under maltreatment conditions but instead predicted *greater* PTSD symptoms relative to low CU traits.

While we found evidence that low DHEA concentrations and high cortisol-to-DHEA ratios increased internalizing symptoms for incarcerated boys exposed to childhood maltreatment, Cicchetti and Rogosch (2007) failed to find this relationship among 6-12-year-old low-income youth (55% male). One likely explanation for this inconsistency is that DHEA, unlike cortisol, shows dramatic differences across development; detectable concentrations decline after the first year of life, remaining low until adrenarche (i.e., 6–7 years in girls, 8–9 years old in boys), after which levels continually increase to peak at 25–30 years old (Granger and Kivlighan, 2003; Havelock et al., 2004; Shirtcliff et al., 2007). Thus, the cortisol-to-DHEA ratio is skewed in favor of cortisol for much of childhood. This raises interesting questions that future prospective longitudinal studies may address about whether DHEA has less of a buffering effect on cortisol prior to adrenarche than post-adrenarche, and whether rising levels increase this capacity, which may have important implications for the timing of interventions involving DHEA. However, safeguarding itself during this period of relative vulnerability, the body's cortisol response to stress is attenuated between about two and seven years old, limiting neurotoxic effects on the brain in the absence of DHEA's protective anti-glucocorticoid effects (Jansen et al., 2010).

Our findings highlight the importance of considering relevant contextual factors when examining associations between salivary analytes and psychopathology, and may explain further inconsistencies with prior literature (Mouthaan et al., 2014; Rasmusson et al., 2004; van Voorhees et al., 2014). That is, low DHEA concentrations and high cortisol-to-DHEA ratios may only increase anxiety, and low DHEA

[1] The CTQ total score and CES-D total score were significantly positively skewed, these scores were square root transformed and analyses were repeated, all results remained largely unchanged.

[2] Analyses were repeated including main and interaction effects with race/ethnicity and revealed no change to significant results. There was no main effect of race/ethnicity in these models, except greater PTSD symptoms were endorsed by boys identifying as Native American or mixed race/ethnicity ("Other") in the DHEA model (B = .16, p = .019, 95% CI[.43,4.77], $R^2$ = .036, $p$ = .082), and by Black and "Other" boys, relative to White boys, in the Ratio and CU moderator models (Black B = .15, p = .053, 95% CI[-.02,2.38]; Other: B = .17, p = .019, 95% CI[.45,4.83], $R^2$ = .048, $p$ = .045). For interaction effects, there was a significant race/ethnicity (Hispanic = 1, White = 0 reference group) *X* maltreatment *X* DHEA effect in predicting depression (B = .20, p = .017, 95% CI[.12,1.16], $\Delta R^2$ = .027, $p$ = .082) and anxiety scores (B = .17, p = .036, 95% CI[.02,.71], $\Delta R^2$ = .019, $p$ = .215), although omnibus tests were not significant. The form of these interactions was probed using PROCESS simple slopes analyses and is presented for anxiety scores in Fig. 4. Full analytic details available upon request.

**Table 1**
Descriptive Statistics and Correlations among Main Study Variables.

| | 1 | 2 | 3 | 4 | 5 | 6 | 7 |
|---|---|---|---|---|---|---|---|
| 1. Maltreatment | 1 | | | | | | |
| 2. Depression | .26*** | 1 | | | | | |
| 3. Anxiety | .23** | .66*** | 1 | | | | |
| 4. PTSD Symptoms | .26*** | .45*** | .45*** | 1 | | | |
| 5. CU Traits | .28*** | .11 | .03 | .11 | 1 | | |
| 6. DHEA | .03 | −.11 | −.12 | −.11 | .16* | 1 | |
| 7. Cortisol/DHEA ratio | −.07 | .10 | .14[a] | .10 | −.17* | −.86*** | |
| *Descriptives* | | | | | | | |
| *M* | 40.64 | 20.69 | 11.03 | 3.87 | 28.33 | .60 | .15 |
| *SD* | 11.43 | 9.02 | 5.86 | 3.76 | 8.07 | .46 | .34 |
| Range | 25-75 | 2-54 | 0-26 | 0-18 | 5-54 | .14-1.72 | −.80 - .81 |
| *α* | .87 | .86 | .87 | .91 | .84 | – | – |

*Note.* *** $p < .001$; ** $p < .01$; * $p < .05$; [a]$p = .055$. Pearson zero-order correlations with transformed hormone variables are reported.

**Table 2**
Hierarchical regression analyses testing DHEA as a moderator between maltreatment and psychopathological outcomes.

| | Variable | Std. Beta | Sig. | 95% CI | $R^2/\Delta R^2$ |
|---|---|---|---|---|---|
| Depression | | | | | |
| Model 1 | Age | 0.022 | .742 | [-.85,1.18] | |
| | | | | | 0.000 |
| Model 2 | CTQ | 0.264 | .000 | [.11, .31] | |
| | DHEA | −0.933 | .352 | [-3.65, 1.20] | |
| | | | | | .073*** |
| Model 3 | CTQxDHEA | −0.126 | .048 | [-.41,-.002] | |
| | | | | | .016* |
| Anxiety | | | | | |
| Model 1 | Age | 0.039 | .558 | [-.46,.86] | |
| | | | | | 0.001 |
| Model 2 | CTQ | 0.225 | .001 | [.05,.18] | |
| | DHEA | −0.032 | .624 | [-2.03,1.22] | |
| | | | | | .053** |
| Model 3 | CTQxDHEA | −0.153 | .017 | [-.30,-.03] | |
| | | | | | .077* |
| PTSD | | | | | |
| Model 1 | Age | −0.07 | .290 | [-.65,.20] | |
| | | | | | 0.005 |
| Model 2 | CTQ | 0.257 | .000 | [.04,.13] | |
| | DHEA | −0.082 | .202 | [-1.70,.36] | |
| | | | | | .073*** |
| Model 3 | CTQxDHEA | −0.052 | .412 | [-.12,.05] | |
| | | | | | 0.003 |
| CU Traits | | | | | |
| Model 1 | Age | −0.027 | .705 | [-1.13,.76] | |
| | | | | | 0.001 |
| Model 2 | CTQ | 0.241 | .000 | [.08,.26] | |
| | DHEA | 0.163 | .018 | [.50,5.32] | |
| | | | | | .086*** |
| Model 3 | CTQxDHEA | 0.036 | .599 | [-.14,.25] | |
| | | | | | 0.001 |

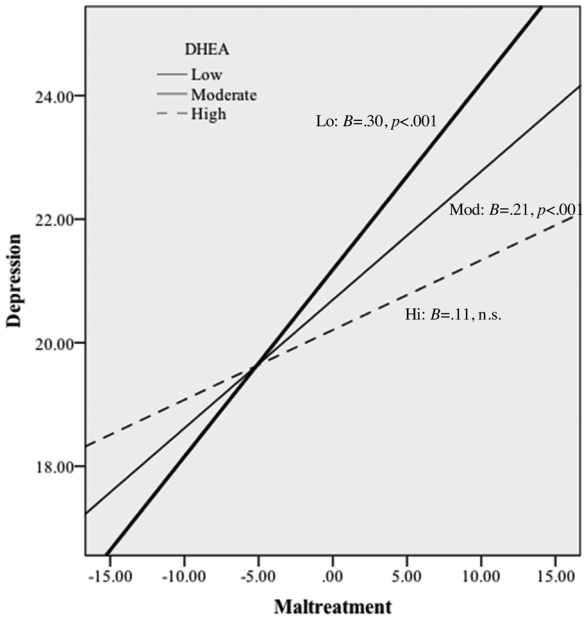


**Fig. 1.** DHEA moderates association between maltreatment and depression.

increase depression, within stressful contexts. These findings are consistent with explanatory accounts suggesting that the ratio of cortisol-to-DHEA indexes degree of buffering against the negative effects of extreme stress, and high DHEA concentrations index greater recovery from such stress (Haglund et al., 2007). Mechanistically, DHEA's protective function comes from its anti-glucocorticoid effect, which buffers the stress response system from the neurotoxic effects of prolonged cortisol exposure and aids in its return to homeostasis (Granger and Kivlighan, 2003; Maninger et al., 2009). Relevant to anxiety in particular, DHEA is thought to offset the actions of glucocorticoids by inhibiting long-term potentiation and contextual-fear conditioning (Fleshner et al., 1997), and via its effects on neurotransmission involving NMDA—a neurotransmitter implicated in emotion and cognition (Barkus et al., 2010).

Youth with the distinct protective hormone pattern characterized by higher DHEA concentrations and lower cortisol-to-DHEA ratios had greater CU trait scores, raising some interesting questions regarding the association of CU traits and internalizing psychopathology. The ability to increase DHEA in response to extreme stress is thought to predict more competent adaptation and greater ability to cope with exposure-related demands (Cicchetti and Rogosch, 2007). This resilient hormone profile may explain our finding that CU traits were unassociated with depression, anxiety, and PTSD symptomatology, despite their positive association with maltreatment at a magnitude comparable to these other psychopathologies. Several related personality constructs similarly serve protective functions for maltreated children, e.g., higher self-esteem, ego resilience (Cicchetti et al., 1993).

An unexpected finding was that maltreated boys most vulnerable to PTSD were those scoring *highest* on CU traits, irrespective of hormone levels. While contrary to hypotheses, this finding aligns with the growing literature on a secondary developmental pathway to CU traits that involves childhood exposure to adverse life events. Kerig et al. proposed that some youth exposed to interpersonal traumas cope by adopting posttraumatic *over*modulation (i.e., excessive repression or control of negative emotions via emotional avoidance, numbing, or dissociation) that places them at risk for developing CU traits (Bennett and Kerig, 2014; Mozley et al., 2018). Youth with secondary CU traits, most often distinguished from primary variants on either a history of

**Table 3**
Hierarchical regression analyses testing cortisol-to-DHEA ratio as a moderator between maltreatment and psychopathological outcomes.

| | Variable | Std. Beta | Sig. | 95% CI | $R^2/\Delta R^2$ |
|---|---|---|---|---|---|
| Depression | | | | | |
| Model 1 | Age | 0.006 | .932 | [-1.03,1.13] | |
| | | | | | 0.000 |
| Model 2 | CTQ | 0.283 | .000 | [.12,.33] | |
| | Ratio | 0.123 | .073 | [-.32,6.97] | |
| | | | | | .090*** |
| Model 3 | CTQxRatio | 0.107 | .121 | [-.09,.55] | |
| | | | | | 0.009 |
| Anxiety | | | | | |
| Model 1 | Age | 0.044 | .534 | [-.47,.89] | |
| | | | | | 0.002 |
| Model 2 | CTQ | 0.269 | .000 | [.07,.20] | |
| | Ratio | 0.16 | .023 | [.38,4.96] | |
| | | | | | .091*** |
| Model 3 | CTQxRatio | 0.143 | .037 | [.01,.41] | |
| | | | | | .020* |
| PTSD | | | | | |
| Model 1 | Age | −0.073 | .306 | [-.68,.21] | |
| | | | | | 0.005 |
| Model 2 | CTQ | 0.258 | .000 | [.04,.13] | |
| | Ratio | 0.116 | .093 | [-.22,2.81] | |
| | | | | | .076*** |
| Model 3 | CTQxRatio | 0.041 | .556 | [-.09,.17] | |
| | | | | | 0.002 |
| CU Traits | | | | | |
| Model 1 | Age | −0.027 | .705 | [-1.13,.76] | |
| | | | | | 0.001 |
| Model 2 | CTQ | 0.235 | .001 | [.07,.26] | |
| | Ratio | −0.151 | .029 | [-6.78,-.37] | |
| | | | | | .083*** |
| Model 3 | CTQxRatio | −0.077 | .269 | [-.44,.12] | |
| | | | | | 0.006 |

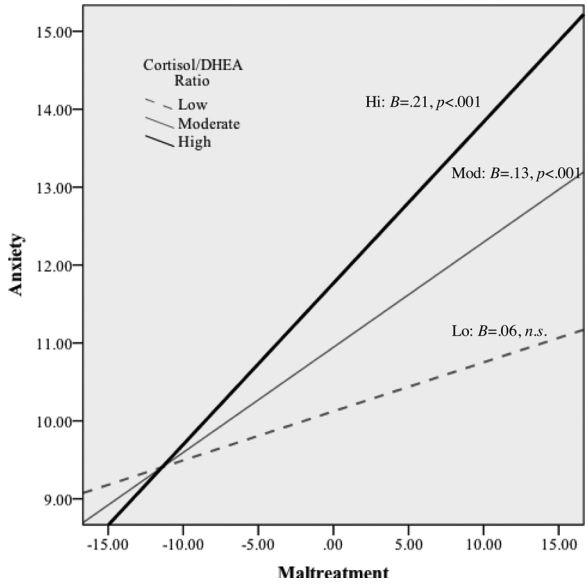


**Fig. 2.** Cortisol-to-DHEA ratio moderates association between maltreatment and anxiety.

maltreatment and/or concurrent high levels of anxiety, reported elevated PTSD symptomatology (Sharf et al., 2014) and failed to show emotional deficits observed in primary variants that are considered core to psychopathy, supportive of distinct causal factors involved in their development (Kimonis et al., 2012). For example, Meffert et al. (2018) found that prior maltreatment moderated the relationship between right amygdala responses to fearful facial expressions and CU traits;

**Table 4**
Hierarchical regression analyses testing CU traits as a moderator between maltreatment and psychopathological outcomes covarying hormone levels.

| | Variable | Std. Beta | Sig. | 95% CI | $R^2/\Delta R^2$ |
|---|---|---|---|---|---|
| Depression | | | | | |
| Model 1 | Age | 0.006 | .932 | [-1.03,1.13] | |
| | | | | | .000 |
| Model 2 | CTQ | 0.261 | .000 | [.10, .32] | |
| | DHEA | −0.075 | .572 | [-6.88, 3.81] | |
| | Ratio | 0.072 | .589 | [-5.14,9.01] | |
| | CU Traits | 0.087 | .223 | [-.06,.26] | |
| | | | | | .098*** |
| Model 3 | CTQxCU | −0.014 | .843 | [-.01,.01] | |
| | | | | | .843 |
| Anxiety | | | | | |
| Model 1 | Age | 0.044 | .534 | [-.47,.89] | |
| | | | | | .002 |
| Model 2 | CTQ | 0.270 | .000 | [.07,.21] | |
| | DHEA | −0.003 | .981 | [-3.42,3.34] | |
| | Ratio | 0.154 | .249 | [-1.85,7.09] | |
| | CU Traits | −0.003 | .972 | [-.10,.10] | |
| | | | | | .091** |
| Model 3 | CTQxCU | −0.028 | .694 | [-.01,.01] | |
| | | | | | .001 |
| PTSD | | | | | |
| Model 1 | Age | −0.073 | .306 | [-.68,.21] | |
| | | | | | .005 |
| Model 2 | CTQ | 0.249 | .001 | [.04,.13] | |
| | DHEA | −0.054 | .69 | [-2.68,1.78] | |
| | Ratio | 0.075 | .577 | [-2.11,3.78] | |
| | CU Traits | 0.031 | .663 | [-.05,.08] | |
| | | | | | .077** |
| Model 3 | CTQxCU | 0.147 | .037 | [.00,.01] | |
| | | | | | .02* |

high CU scores predicted heightened brain responses when maltreatment was high but attenuated responses when maltreatment was low. Importantly, prior research with this dataset also found that boys with secondary CU traits showed the lowest afternoon DHEA concentrations and the highest cortisol-to-DHEA ratios (Kimonis et al., 2017b).

In contrast to internalizing disorders, hormonal patterns did not influence risk for PTSD symptoms under abusive home conditions, consistent with the possibility that different subtypes of childhood adversity show distinct physiological pathways to psychopathology (Kuhlman et al., 2017). An interesting finding was that maltreatment was not associated with PTSD symptoms at low levels of CU traits. This raises intriguing questions around whether CU traits represent a vulnerability factor for PTSD, and their absence a protective factor under conditions of adversity. Drawing from the broader PTSD literature, shortly after a traumatic event those victims who displayed emotional numbing, dissociation, and escape or avoidance of trauma reminders—a pattern termed experiential avoidance (Hayes et al., 1996)—were more likely to subsequently develop PTSD than those who did not (Foa et al., 1995). It is conceivable that this emotionally avoidant process may explain the callous and unemotional presentations of some individuals with CU traits. Consistent with this possibility, Kimonis et al. (2018) found that young men scoring high on meanness (similar construct to CU traits) and disinhibition were faster to disengage from threatening images on a dot-probe task than those scoring low. Future longitudinal research is needed to test whether the presence of CU traits prior to a traumatic event increases risk for later development of PTSD.

Our findings must be considered within the context of several limitations. First, for feasibility's sake within this institutional setting, only single snapshot afternoon saliva measures were taken to assess hormone levels. We specifically selected this period since cortisol and DHEA would be changing less dramatically due to the diurnal rhythm, producing a more stable ratio across multiple measurements made

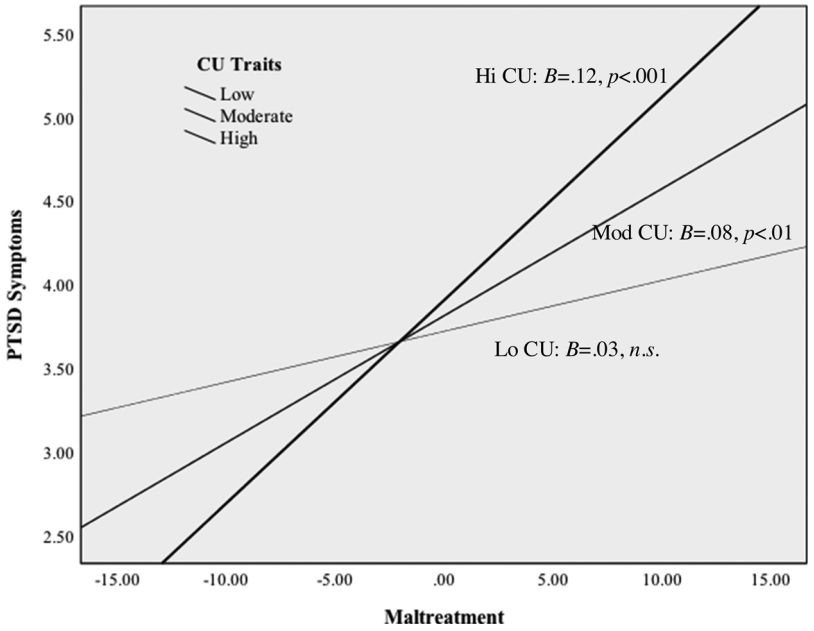


**Fig. 3.** CU traits moderate association between maltreatment and PTSD covarying hormone levels.

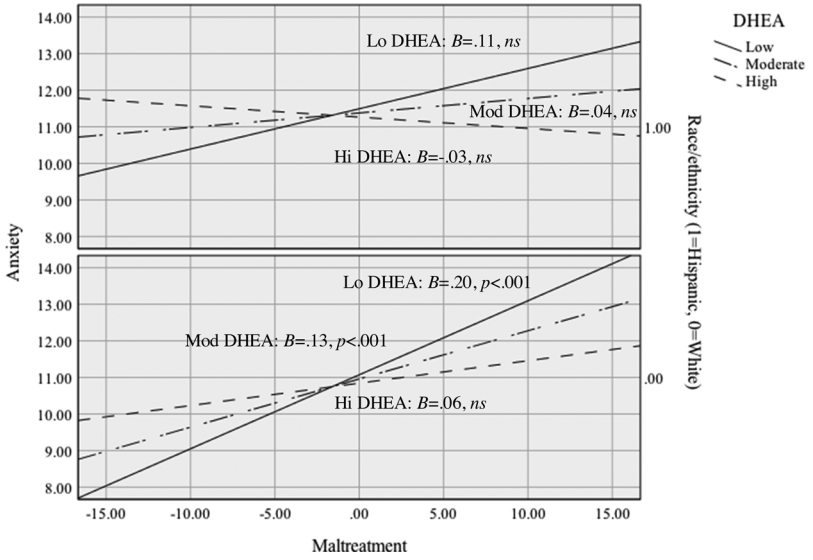


**Fig. 4.** Graphic representation of maltreatment *X* DHEA *X* Race/ethnicity interaction effect in statistically predicting anxiety scores. Race/ethnicity was dummy coded (1 = Hispanic; White is reference group (0)). This pattern was similar for depression except that the interaction effect for White boys was marginally significant at high DHEA levels ($p$ = .057).

during this period relative to the morning when the ratio would be much less stable. Future research should explore diurnal and reactive measures to further elucidate endocrine patterns associated with risk and resistance to psychopathology. Second, future research should additionally examine testosterone since DHEA is a potent testosterone antagonist, testosterone is produced downstream of DHEA via androstenedione within the hormone metabolic pathway, and is associated with psychopathy (Glenn et al., 2011; Johnson et al., 2014). Third, while our focus on understudied, ethnically heterogenous incarcerated boys was a strength and beneficial to sampling variables of interest, findings may not generalize to community settings, non-maltreated populations, or to girls, especially given sex differences in DHEA levels and stress responses (Shirtcliff et al., 2007). Our novel finding that the moderating effect of DHEA was not significant for Hispanic boys requires replication as it may reflect a lack of power since they represented a small proportion of our sample. While future research should examine generalizability to other developmental periods, adolescence is an optimal period for studying neuroendocrine patterns given important maturational changes in HPA and HPG axes (Gunnar and Quevedo, 2007). Finally, due to the cross-sectional design, no definitive causal conclusions regarding hormone levels and psychopathology can be drawn.

In conclusion, this study demonstrates that examining the effects of *multiple* hormones together and in consideration of the individual's context may be key for elucidating the role of endocrine functioning in the context of development and psychopathology. With increasing interest in DHEA supplementation to improve mental health (Peixoto et al., 2014) and preliminary evidence that stress and sex hormones are highly receptive to intervention among incarcerated adolescents (Johnson et al., 2018), continued research into endocrine markers has great potential to inform intervention efforts aimed at high-risk individuals.

## Author notes

Eva R. Kimonis was previously at the University of South Florida, Tampa, Florida.

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## Conflict of interest

In the interest of full disclosure, Douglas A. Granger is founder and chief scientific and strategy advisor at salimetrics LLC and SalivaBio LLC. The nature of these relationships is managed by the policies of the committees on conflict of interest at Johns Hopkins University School of Medicine and the University of California at Irvine. All other authors report no financial interests or potential conflicts of interest.

## CRediT authorship contribution statement

**Eva R. Kimonis:** Conceptualization, Methodology, Formal analysis, Writing - original draft. **Georgette E. Fleming:** Writing - review & editing. **Rhonda R. Wilbur:** Formal analysis. **Maureen W. Groer:** Funding acquisition, Methodology. **Douglas A. Granger:** Writing - review & editing.

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