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Psychopathy's Influence on the Coupling between Hypothalamic-Pituitary-Adrenal and – Gonadal Axes among Incarcerated Adolescents

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Abstract

Conduct disorder (CD) is a heterogeneous diagnosis, leading researchers to initiate research into the neurobiological mechanisms underlying this disorder. One specifier of CD currently considered for inclusion in the DSM-V is callous-unemotional (CU) traits. CU traits are thought to have neuroendocrine underpinnings, yet little is known about Hypothalamic-Pituitary-Adrenal (HPA) and –Gonadal (HPG) hormones in the context of psychopathic traits. The current study sought to identify daily coupling patterns between HPA and HPG hormones in order to clarify distinct neurobiological underpinning associated with psychopathic/CU traits. Fifty incarcerated adolescent males who met criteria for CD were recruited and provided 10 saliva samples across two days. Participants completed the Psychopathy Checklist Youth Version (PCL:YV) and Inventory of Callous Unemotional Traits (ICU) on a third day. Diurnal cortisol, testosterone, and DHEA functioning was modeled via hierarchical linear modeling. Psychopathy subscales from the measures administered were used as predictors of daily coupling patterns between these hormones. Results indicated that all three hormones were tightly coupled. Further, higher PCL-YV interpersonal scores related to greater coupling between all three hormones, whereas higher ICU callousness scores related to greater uncoupling of testosterone with cortisol and DHEA. The current study is novel in its emphasis on testing the coupling of HPA and HPG hormones among incarcerated adolescent males. Results suggest that affective and interpersonal psychopathic traits are marked by unique HPA- and HPG- coupling.

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Keywords

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Introduction

Individuals with Conduct Disorder (CD) vary considerably in symptom presentation, which has led leaders to pursue symptom heterogeneity as indicative of multiple causal pathways and underlying mechanisms (Frick & Ellis, 1999). One specifier of this disorder currently being considered for inclusion in the Diagnostic and Statistical Manual of Mental Disorders V (DSM-V) are callous unemotional (CU) traits (Pardini, Frick, & Moffit, 2010). CU traits refer to a subset of symptoms from "Factor 1" of the adult form of psychopathy, including affective traits such as low empathy, lack of guilt, and manipulation of others for personal gain (Frick & Ellis, 1999). These traits are often combined with "Factor 2" which include antisocial behavior and aggression (Hare, 2003). The importance of CU traits has been consistently demonstrated (e.g., Frick & White, 2008). In children with conduct problems, CU trait expression has been associated with a host of problems, including emotional and interpersonal relationship disruptions (Fontaine, McCrory, Moivin, Moffitt, & Viding, 2011) and more virulent conduct problems that are stable across time (e.g., higher levels of aggression, police contacts; Frick, Cornell, Barry, Bodin, & Dane, 2003; Frick, Stickle, Dandreaux, Farrell, & Kimonis, 2005; Kimonis, Frick, & Barry, 2004). Thus, empirical support indicates that CU traits delineate a pathway to conduct disorder, and its presence indicates a serious form of CD.

Emerging research highlights CU traits are specific and distinct, demonstrating clear neurobiological mechanisms or pathways (Shirtcliff, 2009). In response to the new priorities espoused in the National Institute of Mental Health strategic plan (Health, 2008) calling for the development of new ways of classifying psychopathology based on associated neurobiological underpinnings, the current project seeks to define the hormonal coupling associated with different clusters of psychopathic traits among a severely antisocial adolescent sample meeting criteria for CD. Investigating underlying mechanisms or underpinnings related to the components of psychopathy, especially CU traits, will enhance our understanding of risk factors related to the initiation or persistence of antisocial behavior.

Given this new emphasis on neurobiological mechanisms, research is needed to understand the purported causal processes underlying psychopathy, CD symptoms, and indicators of persistence and severity, such as CU traits. The present study examines the dimensional contribution by focusing on hormonal coupling between hormonal end-products of the hypothalamic-pituitary-adrenal (HPA) and –gonadal (HPG) axes because these stress and sex hormones likely have long term effects, contributing to both initiation and maintenance of psychopathology (Shirtcliff et al., 2009). Neuroendocrine measures serve as potent biomarkers in CD as these hormones have direct effects on central neurocircuitry implicated in CD (e.g., prefrontal cortex, amygdala, hippocampus; (Phan, Wager, Taylor, & Liberzon,

2002; Pruessner et al., 2010). We examine the neuroendocrine measures of cortisol, dehydroepiandrosterone (DHEA) and testosterone as potential underlying mechanisms for CD in extremely antisocial youth in the hopes that these measures will provide a window into the etiology that could lead these youth to be psychopathic.

Two major hypotheses implicate neuroendocrine processes in the development of psychopathy that can contribute to the understanding of how CU traits might develop in children with CD, converging on the notion that investigating biomarkers of the stress system will lend insights into the etiology of CD (e.g., van Goozen, Fairchild, & Harold, 2008). First, psychopathy (and presumably CU predecessors in children) may originate from aberrant fear conditioning that disrupts socialization of conscience (Lykken, 1995). Second, we have focused on HPA hypo- arousal to explain lack of empathy or callous/unemotional traits. The HPA-axis is extensively connected to the limbic system, the affect- or emotion-related parts of the brain responsible for initiating the stress response that culminates in cortisol release from the adrenal gland. Low cortisol functioning has been linked to elevated levels of affective and interpersonal psychopathy traits (Factor 1) in non-referred (O'Leary, Taylor, & Eckel, 2010) and prison samples (Holi, Auvinen-Lintunen, Lindberg, Tani, & Virkkunen, 2006). Similarly, children referred for disruptive behavior disorders such as CD and attention deficit/hyperactivity disorder with co-occurring CU traits have been shown to have lower cortisol functioning (e.g., McBurnett, Lahey, Rathouz, & Loeber, 2000). Meta-analyses have highlighted that the link between aggression and cortisol functioning (basal and stress reactive) in children and adolescents is somewhat equivocal, with some studies documenting an association between low cortisol functioning and aggressive behavior, while others document an opposite pattern (Alink et al., 2007; van Goozen, Fairchild, Snoek, & Harold, 2007). However, overall both meta-analyses found a small negative correlation between aggression/disruptive behavior problems and resting cortisol functioning across studies. It remains unclear whether psychopathy symptoms (affective, interpersonal, or both) parallel this deficit .

In addition to cortisol, other steroid hormones have potential as neurobiological mechanisms underlying CD or psychopathy. In 1959, Phoenix and colleagues proposed the organizational-activational hypothesis of sex-differentiation (Phoenix, Goy, Gerall, & Young, 1959) to suggest that hormones which originally trigger males to differentiate *in utero* will do so again at adolescence, and this sexual differentiation extends to behaviors in which males and females reliably differ (Schulz, Molenda-Figueira, & Sisk, 2009; Shirtcliff and Ruttle, 2010). Most individuals meeting criteria for CD and psychopathy are male (Hartung & Widiger, 1998; Rutherford, Alterman, Cacciola, & McKay, 1998), implicating sex hormones as potential biomarkers of interest in association with antisocial behavior. In males, testosterone is primarily secreted by the gonads as an end-product of the HPG axis which has masculinizing, androgenic properties. Testosterone has been linked to aggression and dominance (Mazur & Booth, 1998), and thus theoretically is related to behavioral aspects of CD and psychopathy. Despite frequent speculation, however, only one study (that we know of) has linked testosterone with the conduct problems in a forensic sample (Stalenheim, Eriksson, van Knorring, & Wide, 1998); other studies have not replicated a direct association between testosterone and psychopathy in community samples (e.g., Glenn, Raine, Schug, Gao, & Granger, 2011). Other literature has indicated a lack of direct

relationship between testosterone and CD in children and adolescents (e.g., van Goozen, Matthys, Cohen-Kettenis, Thijssen, & van Engeland, 1998), though testosterone may be linked to specific aspects, such as social dominance (Schaal, Tremblay, Soussignan, & Susman, 1996) and aggression (McBurnett et al., 2000).

Like cortisol, DHEA is a major secretory end-product of the adrenal cortex, is the most widely circulating hormone in the body (Parker, 1999; Wolf & Kirschbaum, 1999), and is released in response to stress or ACTH administration. However, like testosterone, DHEA operates as a sex hormone that exerts masculinizing physiological effects. To date, little has been done to examine the relationship between DHEA and psychopathy, though elevated DHEA has been associated with CD (van Goozen et al., 2008). This is surprising given that most endocrine correlates of CD have centered on hypo-aroused stress hormone functioning or hyper-aroused sex hormone functioning. DHEA, with its distinguished properties as an adrenal androgen, could clarify whether the physiological mechanism is of adrenal or gonadal origin (Shirtcliff, Zhan-Waxler, Klimes-Dougan, & Slattery, 2007).

Historically, researchers and clinicians have described the HPA and HPG axes as reciprocally-related, such that activation of one axis would inhibit the other. The relationship can be more complex, with the level of cross-communication between these two axes permitting cooperation or co-activation (Viau, 2002) rather than operating as discrete, contextually isolated agents (Hastings et al., 2011). Only one study has examined the ratio of hormones (cortisol to testosterone) in relationship to psychopathy facets, and this study demonstrated an increased ratio of baseline testosterone to cortisol reactivity (Glenn et al., 2011). Studies indexing hormones in relationship to CD in particular usually only find relationships to low cortisol (McBurnett et al., 2000) but not testosterone (van Goozen et al., 1998). No studies have examined incarcerated adolescents, who are known to have high psychopathy symptoms (Caputo, Frick, & Brodsky, 1999).

Despite theoretical promise and considerable speculation, empirical studies have not yet identified clear biomarkers of severe and persistent antisocial behavior. Clearer insights may be garnered by accounting for conceptual and methodological limitations. First, studies investigating these hormones in concert are rare; however, given the tight linkage between the HPA and HPG axes, a broader perspective of coupling between sex and stress hormones utilizing advance statistical techniques is expected to clarify how they operate together with one another and in relation to facets of psychopathy and antisocial behavior. Second, given that CD is heterogeneous and psychopathy is multifaceted, we attempted to clarify which facets of psychopathy are differentially related to neuroendocrine coupling by utilizing a multi-method (i.e., interview and self-report measure) approach to assessment. Further, utilizing a sample of adolescent boys is a benefit to the study as this age period is characterized by both potential emergence of behavior problems (Kaufman, Martin, King, & Charney, 2001), and maturational alterations in sex and stress hormones (Walker, Walder, & Reynolds, 2001)., Finally, we examined antisocial males incarcerated at a juvenile treatment facility due to the higher rate of antisocial/psychopathic symptoms in males, and to overcome obstacles presented by restricted symptom range of psychopathic traits present in community samples.. By investigating clusters of symptoms associated with CD and psychopathy in adolescents, this study informs extant literature regarding the

neurobiological patterns associated with CD. Increasing our understanding of these neurobiological endophenotypes in concert with dimensionally contextual behavioral phenotypes could offer promise for early identification and improved intervention strategies.

Methods

Participants

Participants included 50 male incarcerated adolescents (M age=16.08, SD=1.06, range 14–18 yrs) from Mendota Juvenile Treatment Center (MJTC), an intense hybrid facility that combines correctional and treatment elements. MJTC receives youth who are transferred from other maximum security corrections facilities for extreme behavior problems from the entire state of Wisconsin. This provides for an enriched sampling of adolescents meeting full criteria for CD. Participants were predominantly of African-American ethnicity (60%), with a large minority (for an incarcerated sample) of Caucasian (26%), Hispanic (12%), and Other (2%) ethnic groups. All participants were diagnosed with conduct disorder by a licensed clinical psychologist, though there was a large range of symptom severity. Furthermore, psychiatric difficulties were highly prevalent, with 62% meeting criteria for Attention Deficit/Hyperactivity Disorder, 84% meeting criteria for a mood disorder, 32% meeting criteria for Post-Traumatic Stress Disorder, and 16% meeting criteria for a psychotic disorder. Smoking, caffeine, and illicit drugs were outlawed and not consumed due to correctional facility rules and constant monitoring. All youth were incarcerated at other maximum security prison settings prior to admission to MJTC, and therefore did not have the opportunity to use alcohol and drugs for an extended period of time and were familiar with the experience of being incarcerated. To manage behavior and/or symptoms of mental disorders, 38 participants were administered one or more medications. The impacts of these medications were statistically assessed.

Procedure

Informed assent were obtained from each participant before testing. Saliva collections were conducted between 1–2 weeks after admission to MJTC from a different (typically maximum security) prison environment to allow for acclimation to the facility and establish normal sleep or meal schedules, but preclude treatment effects. Testing occurred over 3 days, including two days for collecting saliva samples and one for conducting the Psychopathy Checklist Youth Version (PCL-YV) interview and self-report measures of CU traits and demographic information.

Measures

Saliva Collection—Saliva was collected by research staff on two days with five samples each day to permit examination of multiple measurements across the entire day. Saliva was collected (a) upon waking (*M*=7:07am, *SD*=11min, range=6:10–7:53am); (b) 45 minutes later to capture the response to awakening (*M*=7:46am, *SD*=15min, 7:10–8:25am) (Wust et al., 2000); (c) before lunch to minimize the influences of mealtimes (*M*=11:31am, *SD*=5min, 11:19–11:47am); (d) before dinner (*M*=5:33pm, *SD*=9min, 5:10–6:38pm); and (e) immediately before bedtime to capture the entire rhythm (*M*=10:00pm, *SD*=16min,

9:30–11:55pm). Saliva was collected following published protocols (Schwartz, Granger, Susman, Gunnar, & Laird, 1998) and frozen immediately (−80°C).

On the day of assay, each saliva sample was thawed and assayed with 24 hrs for cortisol, testosterone, and DHEA in duplicate using well-established highly sensitive enzyme immunoassay kits (www.salimetrics.com) by Middleton Research (www.middletonresearch.com). All samples from an individual were assayed on the same kit to minimize measurement error. Mean intra-assay coefficients of variation (CVs) were less than 3.8%, 6.7% and 5.8% for cortisol, testosterone and DHEA, respectively. Mean inter-assay CVs were less than 7.4%, 14% and 8.5% for cortisol, testosterone and DHEA, respectively. For each hormone, the sample was reanalyzed if the CV for the duplicate measurements were ≤15%. To normalize distributions, raw hormones were log-transformed and extreme values were winsorized.

The Daily Diary saliva information sheet measured time of awakening, time of collection, medication use, mood, sleep, and daily hassles or uplifts and other control variables for salivary hormones (Shirtcliff, Granger, Booth, & Johnson, 2005). Medication usage was coded as medication usage may influence hormone functioning (Shirtcliff et al., 2012). The percentage of the sample taking each medication was as follows: (1) Psychostimulants, 2.1% (2) Mood Stabilizers 2.4% (3) Antidepressants, 2.1% (4) Neuroleptics, 7.5% (5) Other Meds, 4.5%. Pubertal status and timing was assessed through confidential self-report (Petersen et al., 1988).

Psychopathic Traits—Psychopathy Checklist-Youth Version (PCL-YV). Interviewers administered the semi-structured (PCL-YV, Forth, Kosson, & Hare, 2003), which was adapted for use with adolescents from the adult version. Associations between adolescent psychopathy and antisocial/violent behavior are well-documented (Edens, Campbell, & Weir, 2007). The total score was used, but research on the construct of psychopathy has also noted specific sub-factors of psychopathy to be related to distinct neurocognitive deficits and genetic heritability (e.g., Blair, 2001; Viding, Larsson, & Jones, 2008). The four facets of the PCL-YV were also analyzed, which include the Interpersonal facet (e.g., grandiose sense of self, manipulation), Affective facet (e.g., lack of remorse, callous lack of empathy), Behavioral facet (e.g, stimulation seeking, irresponsibility), and Antisocial facet (poor anger control, criminal versatility). Interviewers went through a rigorous training program that involved full day training on the PCL-YV and conducted multiple “test cases” to practice administration and scoring. The full scale was highly reliable in the current study (α=.91).

Inventory of Callous Unemotional traits (ICU). Subscales of the (ICU, Kimonis et al., 2008) were examined. While affective and interpersonal facets of the PCL-YV tap some symptoms involved in the CU trait specifier, the ICU is an alternative self-report instrument that measures CU traits specifically (Frick, 2004). The ICU has been linked to higher rates of delinquency and aggression (Kimonis et al., 2008). Factor analysis of the ICU indicated three major subscales, including callousness, uncaring, and unemotional. Again, each subscale may have different neurobiological correlates. Reliability for the full scale was excellent (α=.83).

Analytic Strategy

Data were cleaned using SPSS v18.0. Missing data were minimal: out of 500 total possible, 443 samples (89%) were obtained in sufficient quantity for assay. Analyses were conducted using Hierarchical Linear Modeling (HLM v6.05) (Raudenbush, 2004) to account for the inherent nesting of samples collected within the individual (level-1) across 50 individuals (level-2). HLM is advantageous as it allows for the simultaneous modeling of hormone levels and the dynamic changes in coupling between hormones across the day. Three sets of analyses were conducted. For the first two sets of analyses, cortisol levels were the outcome of interest ($Y_{cort,}$). At level-1, four additional predictors captured the change in cortisol across the day. The best fitting model captured cortisol functioning included a CAR dummy variable indexing cortisol increase 45 minutes post- awakening (β_{1CAR}), diurnal slope captured by time since waking (β_{2TSW}), and two dummy variables representing the pre-lunch and the pre-bedtime collections to account for nonlinear declines in cortisol across the later portion of the day. We also included the sex hormone into the model to capture the intra-individual coupling of sex hormones with the stress hormone cortisol ($\beta_{3sex\ hormone}$). As level-1 variables, the interpretation is these hormones are coupled within an individual at the moment of sample collection.

Once a level-1 or within-individual equation is established, level-1 predictors can become outcomes-of-interest at level-2 (between individual level). Cross-level interactions capture how individual difference factors impact level-1 associations, specifically coupling between hormones. Present analyses focused on psychopathy as an individual difference factor capable of impacting hormone coupling.

Level-1 Model

$$Y_{CORT} = \beta_0 + \beta_{1CAR} + \beta_{2TSW} + \beta_{3sex\ hormone} + \beta_{4after\text{-}lunch} + \beta_{5Tpre\text{-}dinner} + R$$

Level-2 Model

$$\beta_0 = \gamma_{00} + \gamma_{01(Psychopathy)} + U_0$$

$$\beta_{1CAR} = \gamma_{10} + \gamma_{11(Psychopathy)}$$

$$\beta_{2TSW} = \gamma_{20} + \gamma_{21(Psychopathy)} + U_1$$

$$\beta_{2DHEA\ or\ Testo} = \gamma_{30} + \gamma_{31(Psychopathy)} + U_2$$

$$\beta_{3after\text{-}lunch} = \gamma_{40} + \gamma_{41(Psychopathy)}$$

$$\beta_{4pre\text{-}dinner} = \gamma_{50} + \gamma_{51(Psychopathy)}$$

The third set of analyses focused on modeling DHEA as the outcome of interest ($Y_{DHEA)}$ as DHEA can, like cortisol, operate like a stress hormone. After controlling for the diurnal rhythm (β_{2TSW}), we examined if DHEA and testosterone levels were coupled within the individual at the moment of sample collection. For these analyses, the following base model was used.

Level-1 Model

$$Y_{DHEA} = \beta_0 + \beta_{1TSW} + \beta_{2Testo} + R$$

Level-2 Model

$$\beta_0 = \gamma_{00} + \gamma 0_{1(\text{Psychopathy})} + U_0$$

$$\beta_{1TSW} = \gamma_{10} + \gamma_{11(\text{Psychopathy})}$$

$$\beta_{2Testo} = \gamma_{20} + \gamma_{21(\text{Psychopathy})}$$

Age, pubertal status, pubertal timing, body mass index (BMI), race, and social economic status (SES) were examined first to assess their impact on hormone functioning. Table 1 indicates none of these had significant effects on hormone outcomes with the exception of BMI on wakening DHEA levels. BMI was then entered as a covariate into DHEA analyses, but it did not significantly alter the results. Potential effects of medications were assessed by adding each category as a level-1 predictor (see Table 2). No significant interactions emerged for any medication category.

Results

The two-level HLM showed substantial within-person variability in cortisol, DHEA, and testosterone levels (63%, 49%, and 52% of total variability, respectively), as well as substantial stability in these hormones within an individual (37%, 51%, and 48% of the total variability for cortisol, DHEA and testosterone, respectively, was due to between-person effects).

Analyses set 1: How is DHEA release coupled with cortisol?

Beyond cortisol level upon awakening, (*B*=.57, *p*=.18), cortisol sharply rose according to the CAR by 45 minutes after waking (*B*=.59, *p*<.001). Thereafter, cortisol's diurnal slope indicated gradual decrease across the day (*B*=−.09, *p*<.001). Lunch-time cortisol did not alter cortisol functioning (*B*=−.05, *p*=.51), but cortisol was higher before dinner than predicted by the rhythm (*B*=.70, *p*<.001). Beyond these effects, DHEA was tightly coupled with cortisol (*B*=.53, *p*<.001), such that at moments in which a participant had elevated DHEA, they also had elevated cortisol levels. Psychopathy facets were distinctly related to aspects of cortisol functioning and coupling of DHEA with cortisol. Individuals with higher PCL interpersonal facet scores had lower cortisol upon awakening (*B*=−.27, p=.05), a steeper CAR rise (*B*=.06, *p*<.01), and somewhat tighter coupling of DHEA with cortisol (*B*=.04, *p*=.08). Individuals with higher PCL-YV antisocial facet scores had a trend for a steeper CAR rise, (*B*=.06, *p*=.07) and greater coupling of DHEA with cortisol across the ten saliva assessments (*B*=.01, *p*<.05). Conversely, individuals with higher PCL-YV behavioral facet scores had somewhat lower waking cortisol (*B*=−.294, *p*=.08), a steeper CAR rise (*B*=.081, *p*<.01). PCL-YV affective facet scores were unrelated to coupling between DHEA and cortisol, as were the callous, uncaring, and emotional scales of the ICU.

Analyses set 2: How is testosterone release coupled cortisol?

The base model cortisol with testosterone coupling showed similar functioning of cortisol's diurnal rhythm. Beyond this base model, testosterone levels were coupled with cortisol functioning in incarcerated adolescent males (*B*=.61, *p*<.001), such that at moments in which individuals had higher testosterone, they also had higher cortisol.

Individuals with higher PCL-YV interpersonal facet scores had lower cortisol upon awakening (B=−.31, p<.05), steeper CAR rise (B=.08, p<.001), and even tighter coupling of testosterone with cortisol (B=.05, p<.05). PCL-YV affective facet scores (B=.05, p<.05), antisocial facet scores (B=.07, p<.05), behavioral facet scores were all related to steeper CAR (B=.095, p=.001), but no subscales were related to other aspects of cortisol functioning or hormone coupling. Thus, the PCL-YV interpersonal facet is distinguished as the psychopathy facet relating to tighter coupling of testosterone with cortisol.

Among the ICU facets, individuals with higher ICU callousness scores showed de-coupling of testosterone with their cortisol, (B=−.03, p<.05), such that individuals with high ICU typically had low cortisol at the moments in which their testosterone was elevated. Interestingly, individuals with higher ICU scores often had higher cortisol levels (B=.13, p<.05). No other associations were found using this measure, suggestive of a typical pattern of high testosterone coupled with low cortisol.

Analyses set 3: How is testosterone release coupled with DHEA?

Because the analyses in which the stress hormone cortisol was the outcome indicated that the psychopathy facets were differentially related to a coupling of stress and sex hormones, we then examined if DHEA (which sometimes operates as a stress hormone) was coupled with testosterone levels within an individual. This base model illustrated that DHEA levels were high upon awakening (B=.998, p=.001), and then decreased throughout the course of the day (B=−.01, p=.001). Further, testosterone was tightly coupled with DHEA (B=.95, p<.001) such that at moments in which a participant had elevated testosterone, they also had elevated DHEA levels. PCL-YV facets again indicated differential relationships to coupling between testosterone and DHEA. Individuals with higher PCL-YV interpersonal facet scores had lower DHEA upon awakening (B=−.39, p<.001), steeper DHEA diurnal slope (B=.04, p<.05) and even tighter coupling of testosterone with DHEA (B=.08, p<.001), such that DHEA is typically elevated within individuals when testosterone is also elevated, but even more so if that individual has high interpersonal symptoms. Similarly, PCL-YV affective facet scores were related to lower DHEA upon awakening (B=−.32, p<.01), steeper DHEA slope (B=.005, p< 01), and greater coupling between testosterone and DHEA (B=.06, p<.05). PCL-YV antisocial facet scores and behavioral facet scores were unrelated to DHEA as an outcome.

When specifically examining the ICU as an index of the CU specifier, the callousness facet was related to de-coupling of testosterone with DHEA (B=−.01, p<.05) such that at moments when individuals had high testosterone, males high on CU traits had low DHEA. No other associations were observed. BMI was significantly related to DHEA (B=.92, p<.01) but follow up analyses including it as a covariate indicated no change in the pattern of results.

Discussion

First, the present study reveals novel findings of coupling between cortisol, testosterone, and DHEA. This index of hormone functioning could be a new, innovative way to address the global question of how these hormones mechanistically operate together as integrative,

within-person processes. Most research on HPA and HPG axes presupposes an inverse relationship between the axes, citing the inhibitory effects of stress exerted by the HPA-axis on the reproductive system, specifically decreased release of gonadal hormones such as testosterone (Tilbrook, Turner, & Clark, 2000). Similarly, some components of the HPG-axis that are affected by stress-released hormones exert an inhibitory impact on HPA functioning (Viau, 2002). The current results with incarcerated adolescent males seem contradictory to the prominent belief that if there is an increase in HPA or HPG, there must be a decrease in the opposing system. Our findings are in line with other research indicating that these systems do indeed have commonalities, mainly that all three hormones are stress-responsive, can ebb and flow in the same direction, and that adolescence may be a unique activational stage for both axes (Shirtcliff & Ruttle, 2010). Thus, tighter coupling amongst these hormones may indicate that, at least within adolescence, sex and stress hormones are not operating in a mutually exclusive manner, but may be aiding one another in the day-to-day struggles of adolescent life.

Second, the present findings regarding psychopathic or CU symptoms illustrate sex and stress hormone coupling may be physiologically meaningful, capturing the balance of sex and stress hormones or shift from catabolic toward anabolic/androgenergic processes within an individual (Shirtcliff & Ruttle, 2010). Although previous research has documented psychopathic and CD symptoms to be related to aberrant hormone functioning, it remained unclear which specific traits were relating to hormone abnormalities (McBurnett et al., 2000; O'Leary et al., 2010), and integrative mechanisms linking HPA with HPG hormones has scarcely been tested. Most other researchers have looked at correlations or ratios between hormones at single points in time (e.g., Glenn et al., 2011; Goodyer, Herbert, & Altham, 1998; Matchock, Dorn, & Susman, 2007). While this method was useful given the nascent nature of this type of research, the more comprehensive assessment method utilized here across several repeated hormone measurements provides an understanding of the moment-by-moment time course and dynamic balance amongst fluctuating cortisol, testosterone, and DHEA. From a clinical standpoint, understanding how all three differentially operate in concert in the presence of psychopathic or CU symptomatology has revealed information about a biologically meaningful mechanism that may potentiate destructive behavior; these insights could prove useful to the creation of effective treatment targets in the future.

Adult psychopathy is typically delineated into Factor 1- affective and interpersonal traits, and Factor 2 – antisocial behavior. The present findings challenge previous models that group affective and interpersonal traits into one factor, as these traits appear to have very different hormone coupling. Higher PCL Interpersonal scores are related to tighter coupling between all three hormones. Similarly, higher PCL-YV Antisocial facet scores were related to greater coupling between cortisol and testosterone. Given testosterone's relationship to social dominance (Schaal, et al., 1996) it could be that the HPG-axis is one driving force in individuals with high social dominance and manipulative traits. Specifically, when testosterone is high in individuals with high interpersonal scores, HPG-axis functioning could be so powerful that it recruits the HPA-axis (in which DHEA and cortisol are typically used for stress response) to operate in an androgenergic manner. The linkage between high interpersonal scores, higher cortisol awakening response, and flatter diurnal slope indicates that these individuals have the biological potential to be especially attentive or engaged with

social encounters in their environment. We can speculate that the observed biological profile may promote these individuals to be well equipped to manipulate/dominate in a manner advantageous to them. In accord with this interpretation, it is notable that most PCL-YV facets were related to steeper CAR, indicating that the HPA-axes are preparing them for the anticipated challenges of an imprisoned environment.

Interestingly, the ICU callousness subscale was related to greater uncoupling of testosterone with cortisol and DHEA. The callous attitude measured by the callousness subscale has be viewed as the "core" of CU traits – cold-heartedness, not caring about harming others or about how others feel, and lacking remorse – which remains more specific and delineated than global assessments of CU traits indexed by the PCL-affective and ICU-total scales (Frick et al., 1994). In line with these unique behavioral properties of the CU-specifier, our results revealed unique biological properties of individuals with greater callous scores. DHEA can operate both as a sex and stress hormone; in the context of high callous scores, the results indicate that DHEA is operating more as a stress hormone within the most callous antisocial males, such that when high levels of testosterone are observed, lower than expected DHEA and cortisol (stress) complements HPG-axis functioning. This could be a particularly hazardous combination (Glenn et al., 2011) insofar as high testosterone is associated with dominant or aggressive behavior and low stress hormones (both cortisol and DHEA) are associated with insensitivity to signals of distress or pain in others (Shirtcliff et al., 2009). Within a high callous individual, both components are likely to operate in concert given that a high testosterone moment is likely to be coupled with lower overall cortisol and DHEA. This is consistent with other research indicating high rates of aggression *and* lack of remorse among children and adolescents who meet criteria for CD with high CU traits (Munoz, Frick, Kimonis, & Aucoin, 2008) and extends these behavioral observations to a unique combination of underlying neurobiological mechanisms for this subtype of CD and potentially the persistence of antisocial behaviors across time.

While this investigation yielded valuable information about the hormonal patterns associated within a severe sample of antisocial adolescents demonstrating variation in targeted risk factors (CU-traits, psychopathy), the current findings must be interpreted in light of the following limitations. First, as is common with incarcerated populations, one notable limitation of this study is the lack of a control group matched in their psychopathy symptoms or their living situations. Future studies should attempt to collect hormone data from adolescents residing in comparable temporary living situations (e.g., a sports team or school retreat) to assess how these adolescents' hormone coupling patterns differ from incarcerated conduct disordered youth. Second, it was beyond the scope of this research study to test the interaction of specific comorbidities (e.g., depression, anxiety) with psychopathy on hormone functioning, but testing such interactions with larger sample sizes could lead to more fine grained results regarding the coupling of HPA and HPG axes in the face of such psychopathology. Third, the study is limited to adolescent males, but examining these hormones in incarcerated adolescent females would be valuable in future studies.

In conclusion, a burgeoning field has highlighted neurobiological mechanisms, including hormone functioning, to be specifically related to CD and individual differences in antisocial behavior (CU traits, psychopathy). The current study is novel in its emphasis on testing the

co-regulation or coupling of hormones released by the HPA and HPG axes among incarcerated adolescent males with severe antisocial behavior. This has allowed us to ascertain a broad perspective in the role hormone synchrony plays in relationship to these phenotypes. Furthermore, a sophisticated analytical strategy permitted close examination of individual differences in momentary fluctuations in cortisol, testosterone, and DHEA. The results highlight the differences in hormonal patterns in relationship to conduct disordered youth and psychopathy facets. Future studies should continue to take this broader perspective when assessing hormonal mechanisms underlying antisocial phenotypes, especially as they are related to severe and persistent antisocial behavior.

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Table 1

Potential covariates in prediction of each component of each model.

	Cortisol as Outcome				Cortisol as Outcome				DHEA as Outcome		
	level[a]	CAR	Slope	DHEA	level[a]	CAR	Slope	Testo	level[a]	Slope	Testo
Race	1.24	−.179	−.019	−.137	.208	−.188	−.011	.085	.275	−.012	−.009
Age	.077	.047	.011	−.028	−.282	.061	.014+	.028	−.240	.000	.042
Pub.Stat.	.614	−.131	−.012	−.078	−.324	−.080	−.003	.089	−.115	−.004	.025
Pub.Time	.476	−.123+	−.013+	.054	−.196	−.086	−.007	.068	−.060	−.003	.015
BMI	−.010	.003	.000	.002	.003	.004	−.000	−.000	.016*	.000	−.001
SES	.130	.127	.009	−.048	−.111	.099	.010	−.005	−.191	.001	.043

+ p<.10;

* p<.05;

** p<.01;

*** p<.001.

Note:

[a] level=basal cortisol level represented by the intercept upon awakening

Table 2

Descriptive information and correlations between psychopathy subscales.

	Subscales (Mean, SD)	1	2	3	4	5	6	7	8	9	10
PCL	1. Interpersonal (4.85, 2.35)	***									
	2. Affective (5.19, 2.14)	.72***	***								
	3. Antisocial (7.81, 2.09)	.53***	.59***	***							
	4. Behavioral (6.88, 2.38)	.66***	.61***	.65***	***						
	5. Total (27.02, 8.41)	.88***	.85***	.79***	.85***	***					
ICU	6. Callous (7.54, 4.38)	.35*	.25+	.13	.17	.27+	***				
	7. Uncaring (10.97, 4.98)	.26+	.12	.13	.20	.13	.50***	***			
	8.Emotional (8.08, 3.22)	.15	.12	.05	.10	.05	.17	.15	***		
	9. Total (29.27, 9.85)	.36**	.22	.15	.22	.15	.83***	.82***	.49***	***	

+ p<.10;

* p<.05;

** p<.01;

*** p<.001.

Note:

[a] level=basal cortisol level represented by the intercept upon awakening

Table 3

HLM model coefficients loading psychopathy subscales onto each component of the model.

		Cortisol as Outcome				Cortisol as Outcome				DHEA as Outcome		
		level[a]	**CAR**	**Slope**	**DHEA**	**level[a]**	**CAR**	**Slope**	**Testo**	**level[a]**	**Slope**	**Testo**
PCL	Interpersonal	−.27^{+}	.06**	–	.04^{+}	−.31*	.08***	–	.05*	−.39***	.00*	.08**
	Affective	−.11	–	−.01^{+}	.02	–	.05*	–	–	−.32**	.00**	.06*
	Antisocial	–	.06^{+}	–	.01*	–	.07*	−.00	.01	.09	.00	.02
	Lifestyle	−.294^{+}	.081**	.001	.046	−.237	.095**	.001	.041	–	–	.005
	Total	−.10*	.02**	–	.02*	−.09*	.03**	–	.02^{+}	−.09**	.00*	.02**
ICU	Callous	–	–	.00	.00	.13^{+}	–	.00	−.03*	–	.00	−.01*
	Uncaring	−.10	–	.00	.02	–	–	–	.00	–	.00	.00
	Emotional	.12	–	–	−.02	.17	–	.00	−.03	–	–	.00
	Total	–	−.00	–	.00	.03	.00	−.00	−.00	–	−.00	−.00*
IRI	Total	–	–	–	−.00*	–	–	–	−.00*	–	–	.00^{+}

$^{+}$p<.10;

*p<.05;

**p<.01;

***p<.001.

Note:

[a]level=basal cortisol level represented by the intercept upon awakening