Summer 8-4-2011

Neuroendocrine Function of Female Youth with Callous-Unemotional Traits

Andrew Gostisha
University of New Orleans, agostish@uno.edu

Neuroendocrine Function of Female Youth with Callous-Unemotional Traits

A Thesis

Submitted to the Graduate Faculty of the
University of New Orleans
in partial fulfillment of the
requirements of the degree of

Master of Science
in
Psychology

by

Andrew Gostisha

B.S. University of Wisconsin-Madison

August, 2011

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Abstract

Callous-unemotional (CU) traits have been shown to designate a particular subgroup of antisocial youth that are particularly violent, recidivistic, and more likely to continue offending in adulthood. Disordered neuroendocrine function may be a mechanism for the development of CU traits. We examined whether altered stress responsivity served as a mechanism linking stress exposure and the expression of CU traits. Participants were 15 incarcerated adolescent girls with CU traits. Measures of CU traits, stress exposure, and salivary cortisol were collected. Results revealed girls with CU traits had higher morning levels of cortisol, an intact cortisol awakening response (CAR), and flatter diurnal rhythms. Results indicated the type of stressor being measured and time since stressor onset are crucial to the interpretation of neuroendocrine function. We also found support for a neurobiological model for the development of CU traits drawing on the Adaptive Calibration Model. Implications of the study and directions for further research are discussed.

Key Words: Antisocial Behavior, Callous-Unemotional Traits, Hypoarousal, Cortisol, HPA axis, Stress, Abuse, Neglect

Introduction

The overarching goal of this project is to understand how neurobiological processes influence the development of CU traits. This thesis will review the literature underlying the neurobiological anomalies associated with CU traits, examine the connections between these anomalies and peripheral stress physiology, and propose a neurobiological model for the development of CU traits. Neurobiological measures are emphasized as they can provide information about processes operating within the antisocial individual. This neurobiological model has been applied in a study of incarcerated adolescent females. Due to the dearth of studies examining mechanisms underlying persistent antisocial behavior in females, especially neurobiological mechanisms, the goal of the current study is to examine this model in a parallel group of incarcerated female adolescents. The purpose of this research is to help determine the neurobiology of girls with CU traits to advance our understanding of CU traits in female youth.

Callous-Unemotional Traits

Psychopathy is a pervasive personality aberration in adulthood consisting of a charming, glib interpersonal style, flat affect, a callous disregard for others, and an impulsive and chronically antisocial lifestyle (Hare, 2003). Several authors have called for the downward extension of the construct to youth to identify antecedents to the psychopathy syndrome (Barry et al., 2000; Lynam, 1996; Salekin & Frick, 2005). Callous-Unemotional (CU) traits (i.e. lack of empathy, absence of guilt, manipulation of others) have been one of the core research areas in this downward extension as it may be most relevant to the persistence violent antisocial behavior throughout development into adulthood.

CU traits are a constellation of personality characteristics that designate a particular subgroup of antisocial youth consistently more likely to offend into adulthood, employ violence in their criminal acts, use substances earlier (Frick & White, 2008), and eventually account for a substantially greater portion of youth crime compared to youth without CU traits. Most important, CU traits are highly stable over periods ranging from four through nine years (Frick, Kimonis, Dandreaux, & Farell, 2003; Obradovic, Pardini, Long, & Loeber, 2007), indicating a consistent pattern of problem behavior. Youth with CU traits show deficits in fear learning and emotion recognition (Blair, Budhani, Colledge, & Scott, 2005; Stevens, Charman, & Blair, 2001), passive avoidance (Vitale et al., 2005), impaired attention to the eyes of attachment

figures (Dadds, Jambrak, Pasalich, Hawes, & Brennan, 2010). These findings have led many to conclude CU traits and an associated emotional dysfunction form the stable core of the disorder from youth to adulthood (Blair, Peschardt, Budhani, Mitchell, & Pine, 2006). Indeed, one of the most consistent predictors of violent, persistent criminal offending has been CU traits (Frick, Cornell, Barry, Bodin, & Dane, 2003; Lynam, Caspi, Moffitt, Loeber, & Stouthamer-Loeber, 2007; Pardini, Lochman, & Frick, 2003). Youth with CU traits also display poor orienting responses to distress (Kimonis, Frick, Munoz, & Aucoin, 2007) and under reward-dominant response sets (Frick et al., 2003).

Research on youth with CU traits has yielded positive results in the assessment of persistent antisocial youth (Frick & Hare, 2001; Lynam, 1998) as well as defining the physiological anomalies (Raine, 2002) and personality correlates of youth psychopathy (Lynam et al., 2005). Prediction of aggressive and violent offending in youth has focused on risk factors ranging from impulsivity (Hinshaw, 2003) and delinquent peer affiliation (T.E. Moffitt, 2006) to temperament (Glenn, Raine, Venables, & Mednick, 2007), environmental stress (Del Giudice, Ellis, & Shirtcliff, 2011), child maltreatment (Shields & Cicchetti, 1998) or other psychopathology (Hodgins, Cree, Alderton, & Mak, 2008).

Despite the continuities between youth with CU traits and adults with psychopathy, youth with CU traits differ from adults on several important features. Within youth, CU traits show dissimilar correlates with internalizing symptoms (Lee, Salekin, & Iselin, 2010) and potentially reduced stability compared to adult psychopaths. CU youth appear to be more amenable to intervention than adults with psychopathy (Caldwell, Skeem, Salekin, & Van Rybroek, 2006; Hawes & Dadds, 2005; Salekin, Worley, & Grimes, 2010). Resistance to treatment is a robust finding in adult psychopathy (Rice, Harris, & Cormier, 1992). The dissimilarities between adolescents with CU traits and adult psychopathy and differential response to intervention suggest our knowledge of the development of psychopathy and expression of CU traits can be improved. Examining the mechanisms underlying the development of CU traits from a neurobiological perspective may prove effective in advancing our understanding of the antecedents and processes underlying CU trait expression. The argument delineated here is relevant to male and female youth; however, the current study will focus on females only.

The Association of CU Traits with the Stress Response System

Recent developmental models for CU traits implicates the peripheral stress system and physiology in the development of neural, autonomic, and resulting behavioral endophenotypes that are associated with antisocial behavior, specifically CU traits (Daversa, 2010; Hawes, Brennan, & Dadds, 2009; Shirtcliff et al., 2009). Similar arguments have been made for the role of stress physiology in the development of antisocial behavior more generally (Susman, 2006; S. H. van Goozen, Fairchild, Snoek, & Harold, 2007). These models posit that peripheral physiological arousal and accompanying activation of emotion- and stress-related neural circuits are crucial to the development of empathy and, conversely, the development of callousness and CU trait expression. Investigations into the neurobiology of psychopathic traits in adults have found abnormal function and structure in limbic structures like the amygdala and hippocampus (Kiehl et al., 2001; Marsh et al., 2008) as well as paralimbic structures including the anterior cingulate (ACC) and frontal cortices (Blair, 2007; Kiehl, 2006). These findings have also been corroborated in youth with CU traits (Jones, Laurens, Herba, Barker, & Viding, 2009; Viding, 2004). Activation of limbic and paralimbic circuitry has also been shown to be essential for the activation of empathy and empathy-related emotions (Singer, 2006).

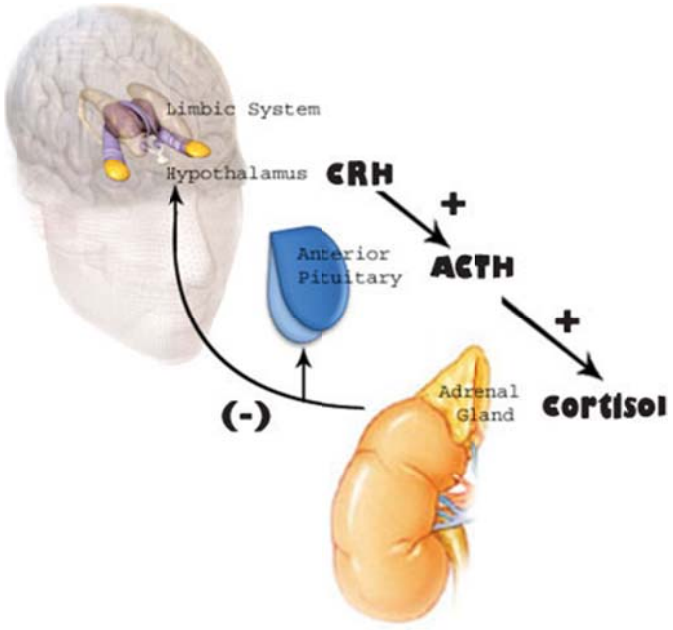
Emotion- and stress-responsivity begins in the limbic system, but the peripheral stress response system (SRS) sustains emotional and stress signals for longer durations. Strong connections between the peripheral SRS and these same limbic areas permit peripheral information from the SRS to feed back to limbic areas and enhance emotional and social information processing. Nelson (2005) emphasized the strong interconnections between social information neural areas and peripheral stress response physiology. While the SRS in general is implicated, Shirtcliff *et al.* (2009) suggest a substantial contribution of the HPA axis to the development of CU traits. The HPA axis is so closely and bidirectionally connected to limbic structures that some have labeled it the limbic-hypothalamic-pituitary-adrenal system (LHPA, Vazquez, 1998). Figure 1 depicts the interconnections between limbic structures and the HPA axis.

CU trait expression is posited to be a product of a transactional cycle of hypoarousal in peripheral stress systems and limbic circuitry. In social contexts in which an emotional- or stress-reaction are appropriate, dysregulation is observed as non-activation of limbic and hypo-activation of SRS functioning. In the absence of strong SRS activation, limbic activation is further coupled by attenuated activation. This decoupling and lack of coincident arousal during

empathic situations fails to facilitate the learning of empathy (Eisenberg, 2007), and this emerges, over development, as a pathway toward CU traits.

The application of stress physiology to the development of CU traits (and ultimately the development of psychopathy) still remains to be sufficiently explored. Applying Shirtcliff and colleagues' (2009) model to the development of empathy and CU traits requires an understanding of the inputs, outputs and experience-based calibration of the SRS, specifically the HPA axis.

Figure 1. The L-HPA Axis



The HPA Axis as an Index of Hypoaroused Stress Response System Function

An understanding of the hypoactivity of the SRS, and its component, the HPA axis, requires an explanation of its basic functioning. The stress response system begins when the threat detection areas such as limbic and paralimbic brain structures provide an error signal to activate the parasympathetic (PNS) and sympathetic (SNS) nervous systems to handle mild to medium threats. Should the threat be severe enough, a stronger error signal is sent to the hypothalamus indicating the body requires additional resources to deal with the current stressor. In response to this error signal, the hypothalamus secretes corticotropin-releasing hormone (CRH) through the hypophyseal portal system to the anterior pituitary. This hormonal cascade continues as the anterior pituitary releases adrenocorticotropin hormone (ACTH) into the bloodstream where it thereafter binds to receptors in the adrenal gland (see Figure 1). The

adrenal gland then releases glucocorticoids to increase energy mobilization, glucose metabolism and immune function throughout the body. Within humans, the main glucocorticoid is cortisol. This cascade is adaptive in the face of stressors, helping the individual cope with the social context (Del Giudice, et al., 2011). In the long-term, insufficient mobilization of resources reduces the stress response system's ability to monitor and encode environmental threats and leaves the organism vulnerable to further physiological insults in the face of future stressors without coping resources (Miller et al, 2007; Weems & Carrion, 2007).

After release by the adrenal gland, cortisol feeds back to the brain where this negative feedback signal eventually inhibits further activation of the HPA axis. This feedback occurs most strongly in limbic areas, primarily the hippocampus and amygdala but also the prefrontal cortex. The amygdala is critically involved in threat processing (Blair, 2006), the hippocampus is essential to learning and memory, especially emotional memory (Sterzer, Stadler, Krebs, Kleinschmidt, & Poustka, 2005), and the prefrontal cortex is involved in the top-down coordination and flexibility of the emotional response (Derryberry & Tucker, 1992). Taken together, these structures are implicated during social information processing in general, and emotion-laden processing more specifically. HPA axis feedback to limbic and prefrontal neurons has both short and long-term effects depending on where it binds on the neuron. Cortisol binds to mineralcorticoid (MR) and glucocorticoid (GR) receptors on the cell membranes and nuclei respectively. MR receptors exert their effects for minutes to hours because binding at the membrane modulates excitability, in turn modulating synaptic transmission. GR cortisol binding occurs in the nucleus can exert effects that last for months or years by affecting gene transcription (Tasker, Di, & Malcher-Lopes, 2006). This genomic action has been repeatedly cited as one mechanism whereby stressful early life experiences can distally shape HPA axis activity (Del Giudice, et al., 2011; McEwen, 2000).Through the powerful and long-lasting effects of cortisol, the HPA axis can have profound effects on social and emotional information processing in addition to terminating the SRS activation.

Deviation from typical negative feedback can result in a host of problematic effects. Negative early life experiences can have profound effects in derailing development of HPA axis arousal and potentiate the cyclic top-down and bottom-up feedback process that can result in a high arousal threshold, reduced limbic activity, and a hypoaroused HPA diurnal rhythm. Poor feedback has been documented in populations undergoing significant stress and trauma including

combat, child abuse and PTSD survivors (Carrion et al., 2002; De Bellis et al., 1999; Golier & Yehuda, 1998; Heim, Ehlert, Hanker, & Hellhammer, 1998; Johnson, Delahanty, & Pinna, 2008; Liberzon et al., 2007). Evidence from the dexamethasone suppression test, a measure of an individual's HPA axis feedback sensitivity, indicates those with poor negative feedback are also likely to have a higher threshold for activation of the HPA axis (Maes, Meltzer, D'Hondt, Cosyns, & Blockx, 1995). The HPA axis can influence the development of hypoarousal through top-down processes through reduced limbic activation or a high stress threshold that fails to activate the HPA axis. Relatedly, bottom-up processes are also implicated as reduced feedback to these brain areas can result in a failure to prime the SRS and HPA axis for future arousal. Dysregulation in both top-down and bottom-up pathways may leave limbic circuitry and the SRS especially vulnerable to disturbance via environmental stressors.

While some studies of HPA function in antisocial behavior focus on acute stress reactivity of CU individuals (O'Leary, Loney, & Eckel, 2007), the axis' overall dysregulation is implicated in the development of CU traits. Stress regulation encompasses many components of HPA functioning (Siever & Davis, 1985), including flexibility and rhythmicity (Dallman, 2003). Inflexibility, or signs of non-response to a changing environment, may enhance the probability of a stress response in the short-term and yet increase dysregulation risk in the long-term (Skinner, in press). Measuring cortisol throughout the day provides information about both tonic activation in the morning and variability in the axis later in the day, thereby capturing components of both flexibility and rhythmicity. The diurnal rhythm provides different information depending on the part of the day cortisol is sampled. This is an important methodological issue as cortisol research in antisocial behavior is often viewed in terms of cortisol simply being "low" and broadly associated with antisocial behavior with little respect for what low cortisol means relative to the diurnal rhythm.

Having "high" or "low" cortisol is not good or bad in an absolute sense. Rather, cortisol levels relative to the time of day and context are critical to the interpretation of whether HPA function at that time is adaptive or detrimental. The diurnal rhythm consists of an initial morning level, a cortisol response to awakening, a subsequent decrease and leveling off during midday, followed by a gradual decline in the afternoon and evening hours. Upon waking, cortisol levels begin to increase for 30-45 minutes in what is known as the cortisol awakening response (CAR). This portion of the diurnal rhythm is primarily controlled by the anterior pituitary, is under

strong genetic influence and is thought to be relatively immune from environmental disturbance (Van Hulle, in preparation). The initial morning (basal) level and the CAR represent tonic HPA function which is a product of genetic influences on tonic activation and the cumulative effect of longitudinal stressor exposures. After the CAR, the diurnal rhythm becomes more responsive to environmental stimuli and concurrent stressor exposure. The latter portion of the diurnal rhythm is a strong measure of the flexibility of the HPA axis; flexibility allows an individual to respond to a rapidly changing environment in an adaptive way. Dysregulated diurnal HPA activity is a likely area of research to further the model of hypoarousal as a mechanism for the development of CU traits. The types of inputs that appear to dysregulate the HPA axis will be examined next.

Stress: Inputs for the Stress Response System

Though the term stress is commonly used, it is just as frequently misused or over-used to describe a nebulous negatively-valenced concept. Understanding the variations in defining the input to the stress response system is critical to proper interpretation of its outputs. Various definitions of stress emphasize stress type (perceived vs. objective), timecourse (acute vs. chronic), and mechanism of action (genomic vs. non-genomic).

Perceived vs. Objective Stress. Stress has been commonly characterized as the psychological interpretation or appraisal of negative life events (S. Cohen, Kamarck, T., & Mermelstein, R., 1983; van Eck, Berkhof, Nicolson, & Sulon, 1996). Accordingly, perceived stress has been shown to affect susceptibility to infectious agents (S. Cohen, Tyrrell, & Smith, 1993) and is an essential measure in stress physiology research on work-related burnout (Pruessner, Hellhammer, & Kirschbaum, 1999). From a neurobiological perspective, perceived stress necessitates a stress signal that includes, at minimum, activation in neural circuitry involved in the perception and appraisal of stress in the central nervous system, especially limbic and frontal circuitry. Perceived stressors that are more severe should thereafter more consistently activate peripheral stress physiology in addition to changing short-term cortical activity. Nevertheless, perceived stress is an emotion-laden construct, highly related to negative affect (S. Cohen, et al., 1993), and often confused with anxious or depressive affect (Kendzor et al., 2009). Perceived stress is unique from other definitions of stress in that it requires a subjective interpretation of life events. Perceived stress measures are subject to the informant's cognitive, emotional, perceptual, and psychopathological biases. Catastrophizing and learned helplessness may be readily measured on a perceived stress scale without a corresponding peripheral stress

response to affect CNS functioning, thereby enhancing error variance of perceived stress measures. While important to models of burnout and internalizing, this conceptualization of stress is less applicable to a model of hypoarousal as youth with CU traits have been consistently shown to be low on traits that enhance perceived stress, such as anxiety and neuroticism (Frick & White, 2008; Johansson, Andershed, Kerr, & Levander, 2002).

Supporting a definition emphasizing physiological changes, Cohen and colleagues (1993) found subjective and objective measures of stress were mediated by different biological pathways and perceived stress was not necessary for negative life events to affect risk for disease. Objective stress, on the other hand, relies on external validation of an event as a stressor. There are three main criticisms of objective stress measures. First, they often rely on the perception of the experimenter to define an event as a stressor, and such definitions are subject to debate (Gunnar, Talge, & Herrera, 2009). For example, several studies have utilized exposure to emotional stimuli or facial expressions as a stressor without demonstrating that such stimuli is, indeed, stressful. Such criticism can be countered by validation of a stressor's impact, rating of an event by a team rather than a single individual, or validation by an external stressor indicator (such as a SRS response). Second, objective stress measures such as life event checklists fail to account for the individualized contextual forces which modify a stressor or the very real impact of perception on a stressor's impact. Third, objective stress may miss events which are putatively stressful for some individuals, but not others, potentially glossing over important sources of individual differences in favor of capturing the reliable, "tip of the iceburg" of stressors. Such measures often focus on severe or intense stressors, such as experience of neglect, physical and/or sexual abuse, combat, witnessing death, neighborhood disorganization (Pynoos, 1998). More severe stressors are, by definition, more likely to have a profound effect on a diverse range of physiological systems, beyond the minor alterations in limbic activity necessitated by perceived stress. The final criticism of objective stress measures is that their physiological impact is not clearly delineated. Childhood abuse does not unidirectionally impact HPA functioning (Cicchetti & Rogosch, 2001a, 2001b), and paradoxes abound (Lupien, McEwen, Gunnar, & Heim, 2009). One reason for this is that the SRS is a regulatory system; as such, its purpose is to keep functioning within an adaptive range. The impact of extreme objective stress may be to, eventually, pull functioning back within a normal range at high cost to the individual.

Timecourse of Stress (acute vs. chronic). Stressor duration is another method of defining stress and can yield decidedly different effects on HPA function. Miller *et al*.'s (2007) meta-analysis found increased HPA activity in the short-term after a stressor but HPA hypoarousal as the stressor becomes more distal. Acute stress is commonly associated with increased HPA activity. This form of stress is typically studied through laboratory paradigms like the Trier Social Stress Test (Gunnar, et al., 2009; Kirschbaum, Pirke, & Hellhammer, 1993). Chronic stress on the other hand is characterized by repeated instances of acute stressors or general negative experiences across a range of domains (Rudolph & Hammen, 1999). Though seemingly contradictory to the effects of acute stress, chronic stress is associated with decreased HPA activity, especially in maltreated children (Cicchetti & Rogosch, 2001a; Tarullo & Gunnar, 2006) and those with chronic PTSD symptoms (Weems & Carrion, 2007; Yehuda, 2001). Duration of stress and elapsed time since that stress is crucial to interpreting HPA axis function.

Mechanism of Action (genomic vs. non-genomic). Another method of defining stress is by mechanism of action, which emphasizes the interplay of stressful experiences, physiological responsivity, and biological outcomes. When the stress hormone cortisol binds to MR receptors in the cell membrane, these receptors exert relatively more immediate and short-lived effects; stress is indexed according to measurement of these short-lived effects. Alternatively, when cortisol binds to GR receptors in the cell nucleus, it affects gene transcription which can exert long-term effects that may persist for hours to years or may even be permanent. This genomic action is best indexed by the early portion of cortisol's diurnal rhythm (M. Bartels, de Geus, Kirschbaum, Sluyter, & Boomsma, 2003; Schreiber et al., 2006) more so than the latter portion because the rhythm is under strong pituitary control and not as subject to environmental influences at this time (Shirtcliff et al., under review). Supporting the mechanism of action perspective are findings that show acute or momentary stress is generally associated with action at MR receptors while GR receptor action is more often associated with chronic stress like neighborhood disorganization and chronic child maltreatment (De Kloet, 2004). Ultimately, the mechanism of action perspective may reach the same conclusions as the timecourse perspective, though biological processes are emphasized.

Stress vs. Stressor. An implicit distinction in the literature above is that of stress and stressor. The folk use of the term "stress" implies that stress is an external event or experience. An alternate, though not converse, definition of stress came from Selye's (1950) original model

which described stress not in terms of the interpretation of environmental events, but rather emphasized the strain or impact of stimuli on physiological and cellular processes. Much like the mechanism-of-action perspective, an individual is 'under stress' when the body instantiates that strain through physiological changes. Downstream effects in the brain and body also constitute stress. A process of "biological embedding" of stress occurs, where the environment can be instantiated in physical body systems and brain areas (Hertzman, 1999). The event which triggered the physiological changes is defined as a "stressor" if the stimuli had produced a physiological change in the body (i.e., stress). This somewhat circular interplay between stress and stressor underscores the ability of the stress system to adapt to changes in physiological processes that manifest the impact of environmental events.

Summary of Stress Definitions. The above literature review is not meant to imply that a single definition of stress is optimal or all-inclusive. Rather, the review emphasizes there are multiple definitions of stress, each of which has its relative strengths and weaknesses, and that stressors and stress are distinct but interrelated. The current study emphasized objective stress as it is most likely to modify peripheral SRS functioning in addition to changes in CNS activation. Furthermore, these changes are expected to be a function of time since stressor with recent stress likely creating HPA hyperactivity while distal stressors should be related to HPA hypoactivity. As noted above, the prediction is not necessarily that greater stress exposure will lead to higher cortisol or SRS responsivity. Rather, our prediction is that greater objective stress exposure will necessitate greater need to physiologically adapt to that environment and culminate in greater evidence of stress dysregulation. Severe objective stressors, those most likely to disrupt HPA axis functioning, are critical to a neurobiological model of the development of CU traits where there are documented structural and functional abnormalities in brain areas with strong connections to the periphery. The main implication is that each form of stress may have distinct neurobiological underpinnings. The HPA axis is more or less implicated in each form of stress exposure, and (as reviewed below) the expected direction of the effect of stress exposure on HPA functioning may be different, even oppositional, depending on how stress is defined.

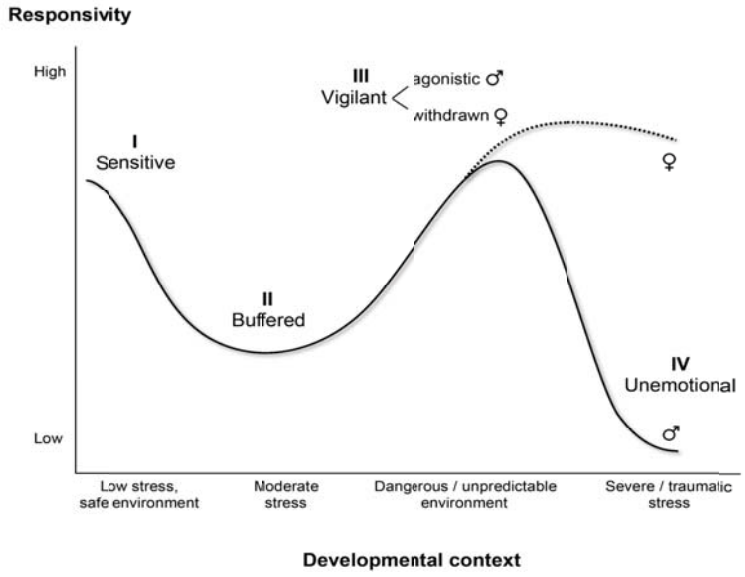
The Stress Response System in the Development of CU Traits

Hypoarousal may have a variety of origins, but there is some evidence that extreme environmental stressor exposure contributes to the development of hypo-arousal over time. That is, as environmental stress chronically activates peripheral stress physiology, the threshold for

future stress system activation is increased. Consequently, the emotion-related neurocircuitry it innervates receives less peripheral activation and becomes less easily activated.

The Adaptive Calibration Model of Stress Responsivity (ACM; see Figure 2) is a recent integrative theory which attempts to describe how these different forms of stress exposure may be predictive of highly divergent SRS profiles and behavioral outcomes. The ACM describes four stress responsivity profiles that result from a reciprocal process of modifying the responsiveness of the SRS in the presence of varying degrees of contextual or environmental danger (Del Giudice, et al., 2011). Importantly, this model describes how stress exposure might, paradoxically, lead to low or hypo-arousal of the HPA axis, rather than a straightforward prediction that the stress hormone cortisol would be positively associated with stressor exposure. As the review above illustrates, stressors of different types, intensity, duration or mechanism of action can yield dramatically different impacts on HPA functioning. These associations are complex, yet predictable.

Figure 2. Stress Responsivity Patterns in the Adaptive Calibration Model



According to the ACM, the openness of the SRS is shifted, or calibrated, according to the organism's contextual environment to maximize the organism's physiological and energetic fitness to that context. This calibration often involves a trade-off between immediate and long-term benefits that is referred to as a life history strategy. For example, in a high stress context, a fast life history strategy, which generally favors the short-term, would facilitate early pubertal development to speed up the potential for immediate reproductive success in a high stress

context. This type of strategy is characterized by lower parental investment and therefore has a smaller likelihood associated with it that one's offspring will be successful. However the above short-term strategy contrasts with a slower reproductive strategy characterized by later pubertal onset and more parental investment, a strategy much more likely to be taken in a lower stress context where immediate survival is not a salient daily task. Thus stressful contexts force an individual to adopt fast life history strategies at the expense of long-term offspring success.

Trade-offs in life history strategy also extend to stress responsivity or non-responsivity in the ACM. In a low stress environment, high responsivity is adaptive (the Sensitive profile) whereas in a high stress context, low responsivity helps to buffer the organism from the harmful effects of SRS overactivation (Buffered profile). In extremely unpredictable or dangerous environments where HPA responses are common, a hyperresponsive phenotype is expected to emerge (Vigilant profile) as well as a virtually unresponsive prototype (Unemotional profile). In the ACM, exposure to environmental danger and unpredictability downregulates SRS activity to preserve the overall health and survival of the organism. For better and for worse, this calibration of the organism's physiology helps the individual adapt to the environmental context, though sometimes at the expense of social relationships or societal norms. Indeed, "adopting an exploitative/antisocial interpersonal style requires one to be shielded from social rejection, disapproval, and feelings of shame (all amplified by heightened HPA responsivity)" (p. 17, Del Giudice *et al*. 2011). The tradeoff for short-term adaptation comes at the expense of social information processing and empathic responding.

Adaptation at the expense of survival in a high-stress context dovetails with the model put forth by Shirtcliff *et al*. (2009) which emphasizes the connections between peripheral stress physiology and limbic and paralimbic structures as key to the suppression of empathy learning and critical to the development of callousness. Evidence indicates HPA function has a modulatory role in social behavior (S. Taylor et al., 2000) and, as part of the SRS, is responsible for creating the optimal level of arousal to facilitate empathy development (Eisenberg, 2007). Marked interconnections of the SRS with social information and empathy processing areas facilitate the association of arousal with situations that call for an empathic response. For example, when seeing another in pain, pairing your own arousal with the social information relevant to the situation comprises the empathy learning process (P.D. Hastings, Zahn-Waxler, & McShane, 2006; P. D. Hastings, Zahn-Waxler, Robinson, Usher, & Bridges, 2000). With an

underaroused or non-responsive SRS, empathic and social learning cannot effectively take place because the stress-arousal levels are not matched or attuned across individuals (P. L. Ruttle, Serbin, L.A., Stack, D.M., Shirtcliff, E.A., Schwartzman, A.E., under review). Youth with CU traits are able to "talk the talk" of empathy (cognitive understanding of when one should feel empathy) but are unable to "walk the walk" (the emotional and physiological arousal to another's distress) (Dadds et al., 2009).

Taken together, the models put forth by Shirtcliff and colleagues (2009) and Del Giudice and colleagues (2011) propose a detailed model for the development of CU traits in youth. A child raised in an unpredictable, dangerous, and high stress environment (objective stress again being defined as intense enough to activate a peripheral stress response) is expected to experience multiple HPA axis responses to deal with these stressors acutely. As the youth's HPA axis is activated in the face of extreme stressors, HPA functioning becomes decoupled from limbic and paralimbic structures and it is this decoupling that may instantiate CU traits in this neurocircuitry (Shirtcliff et al, 2009). Over time and after repeated exposure, it becomes beneficial for him or her to biologically "tune out" less intense environmental stimuli to preserve overall physiological function. This may, at first, allow a youth to confront the more intense environmental stimuli, yet the canalization of hypoarousal makes these adjustments more and more difficult over time (Gottlieb, 1991; Turkheimer & Gottesman, 1991). Over time, in a stressful, dangerous, or unpredictable environment, chronic activation of the HPA axis is likely to yield a pattern of low HPA axis activity as the youth's SRS no longer perceives and/or responds to environmental threats and cues with the same degree of activation it initially did. While this maximizes the fitness of the youth in terms of their ability to cope with stressors in the near-term, an underaroused or nonresponsive SRS compromises the empathy learning process. Underarousal of the SRS, including the HPA axis, becomes a major contributing factor to the failure or suppression of empathy development and potentially concurrent development of CU traits.

Gender Differences in CU Traits and the Stress Response System

Gender Differences in CU traits. Gender differences are predicted by the ACM, and fall neatly in line with many of the documented differences in CU traits and antisocial behavior. The ACM predicts a male predominance of the Unemotional profile, and this maps onto the preponderance of high CU-low anxiety males compared to females (Frick, Lilienfeld, Ellis,

Loney, & Silverthorn, 1999). Dadds and colleagues (2009) found gender differences in empathy development in callous-unemotional youth with males displaying deficits in affective empathy ("walking the walk") across all ages while no such deficit was found for females. Both sexes displayed deficits in cognitive empathy ("talking the talk") in childhood. Males, but not females, overcame the deficit in cognitive empathy during the pubertal transition. A similar dissociation between affective and cognitive empathy was found for youth with conduct problems and CU traits, such that youth with conduct problems and CU traits showed a deficit only in affective perspective-taking whereas youth with conduct problems but few CU traits had deficits in both affective and cognitive perspective-taking (Anastassiou-Hadjicharalambous & Warden, 2008).

Such gender differences are expressed within antisocial behavior expression as well. One of the most replicated gender differences in antisocial behavior is the increased severity, frequency, and violence of antisocial males compared to females (Tracy, Kempf-Leonard, & Abramoske-James, 2009). Males tend to comprise a greater proportion of violent crime committed (Tracy, et al., 2009), and show an earlier age of onset of criminal activity (Kjelsberg & Friestad, 2009) while females tend to show a delayed onset of criminal activity (Silverthorn & Frick, 1999; Silverthorn, Frick, & Reynolds, 2001). These differences may point to a decidedly different etiology underlying the development of antisocial behavior and CU traits. While we have previously sampled from the most severe antisocial male youth, matching according to this sample is difficult as antisocial female youth are both few in frequency and differ in forms of antisocial behavior compared to males. Whereas males with CU traits are likely to exhibit both overt and covert aggression, females tend to show predominantly covert aggression, though generally no more than boys (Card, Stucky, Sawalani, & Little, 2008).

Gender Differences in the SRS. Males and females show different patterns of stress responsivity in general and in the context of youth with antisocial behavior. Among community populations, men have been shown to have stronger responses to social stressors compared to women (Kirschbaum, Kudielka, Gaab, Schommer, & Hellhammer, 1999; Wolf, Schommer, Hellhammer, McEwen, & Kirschbaum, 2001). In cortisol challenge tests, young adult men show stronger responses whereas in older adults, females show stronger responses to challenge (Seeman, Singer, Wilkinson, & McEwen, 2001). Boys with externalizing problems have been found to have low trait-like (basal) cortisol while girls did not show this inverse relationship (Shirtcliff, Granger, Booth, & Johnson, 2005). Similar gender differences exist in HPA axis

functioning of antisocial and psychopathic individuals. O'Leary and colleagues (2007) found male college students high on psychopathic traits exhibited reduced cortisol response to a stressor while non-psychopathic male participants showed a traditional stress response. Females showed no differences in stress response as a function of psychopathic traits. While psychopathic traits are not interchangeable with CU traits, they share a common core of deficient affective responding (Frick, Bodin, & Barry, 2000; Hawes, et al., 2009). Kobak, Zajak, and Levine (2009) found antisocial boys displayed a similar pattern of non-response to a stressor while antisocial girls showed a typical stress response to a laboratory stressor. Antisocial males and females displayed lower pre-task cortisol than controls providing further evidence for a hypoarousal model of antisocial behavior. While Loney *et al*.'s (2006) low cortisol results for high-CU youth supported a hypoarousal model, no hormone effects were found in females. These documented gender differences in HPA axis function in antisocial youth emphasize the need for detailed investigation of the development of CU traits and disordered SRS function in both sexes, with a notable relative lack of research on corollary groups of antisocial females.

Gender Differences in the ACM Unemotional Profile. The observed gender differences in CU traits and SRS functioning by implication suggest there are gender differences in the Unemotional profile of the ACM. The ACM posits the observed gender differences in phenotypic antisocial behavior is a product of differences in the underlying neurobiological functioning of boys and girls and the life history strategies each gender employs responding to stress. While environmental stress cues facilitate faster life history strategies like earlier pubertal transition and a greater emphasis on reproduction for both genders (Belsky, Steinberg, & Draper, 1991), the early pubertal transition can manifest antisocial behavior differently in males and females and this may be due in large part to the different life history strategies each employs.

Fast life history strategies help male youth maximize their reproductive success by achieving reproductive eligibility earlier and gaining social status, even at the expense of long-term development. Around early childhood, as social competition increases and the occurrence of risk-taking becomes more common, males in high stress environments are expected to shift from a Vigilant pattern of responsivity to a more Unemotional pattern. The demands of a more high-risk environment can force youth to "block out" the salience of the danger associated with their social competition and risk-taking. From a life history perspective, due to the importance of gaining social status in male reproduction, responding to a stressful environment with risk-taking

can be adaptive and may therefore pull boys with an otherwise Vigilant pattern of responsivity toward an Unemotional pattern. Furthermore, the "fight or flight" nature of male stress responsivity may increase males' probability of responding to a chaotic context with aggression. Indeed, this pattern of aggression has been found in both rats (Haller & Kruk, 2006) and humans with hypoaroused HPA function (S. Van Goozen, Matthys, W., Cohen-Kettenis, P.T., Buitelaar, J., & Van Engeland, H., 2000). Life history strategy helps explain why males are expected to shift toward and Unemotional pattern of responsivity generally, while the architecture of their stress response system retains their tendency to respond to short-term stress with aggression.

Alternatively, as the transition from the Vigilant to Unemotional profile unfolds, girls are expected to remain relatively similar to the Vigilant profile as they employ a different life strategy and favor an alternate system to respond to stress that helps accomplish this. Females employ life history strategies centering on social relationships and cooperation rather than social competition (Brumbach, Figueredo, & Ellis, 2009). Therefore, additional stress or trauma during this period for girls is expected to reduce the quality of social relationships and reduce her parental investment in any offspring (Hrdy, 1999). To navigate an immediate stressful context, it is also advantageous for girls to keep a higher level of responsivity so as to maximize the utility of their affiliative response system to stress (S. E. Taylor, 2006; S. E. Taylor, Dickerson, & Klein, 2002). While aggression in males has been has been associated with a combination of hypoaroused HPA function and high levels of androgens (Popma et al., 2007), the importance of androgens in the female response to stress pales in comparison. Rather, the response to stress in females is more likely to involve the hormone oxytocin and vasopressin, known facilitators of attachment and bonding (A. Bartels & Zeki, 2004).

The above comparisons of life history strategies and stress responsivity between boys and girls help illustrate why there is a dissociation of gender-specific phenotypic behavior in the ACM model. In a high stress context, employing a faster life history strategy, early pubertal onset, facilitates social competition and risk-taking in boys, but reduced cooperativeness and quality of social relationships in girls. In boys the early pubertal strategy is associated with rule-breaking and attention problems, however in girls it is associated with relational aggression (Susman et al., 2007).

The gender differences in the Unemotional profile also center on differences in the onset of antisocial behavior. These differences are generally supported by the types and onset of

delinquent behavior that have been hypothesized. Two types of youth offenders, adolescent-limited and life-course-persistent, have been characterized. As the label implies, adolescent-onset offenders manifest their offending alongside puberty in the "relatively roleless years between their biological maturation and their access to mature privileges and responsibilities, a period called the 'maturity gap'" (p. 351,T. E. Moffitt & Caspi, 2001). As such, their offending desists as they enter adulthood. On the other hand, life-course-persistent (LCP) offending is generally associated with an early onset of problem behavior in childhood that continues throughout adulthood even as adolescent onset offenders desist (T.E Moffitt, 1993). LCP offenders often have high levels of CU traits (Viding, Blair, Moffitt, & Plomin, 2005) and are therefore expected to predominate Unemotional profile in the ACM. While boys have been thought to predominate in the childhood onset LCP offender type (Eme, 2007), some have posited that a persistent group of female offenders may emerge in adolescence and continue offending into adulthood (Silverthorn & Frick, 1999; Silverthorn, et al., 2001). This latter adolescent onset pathway for girls has been recently supported with empirical data (Kaufman, 2007), emphasizing the need to examine the neurobiological functioning of girls making the adolescent transition.

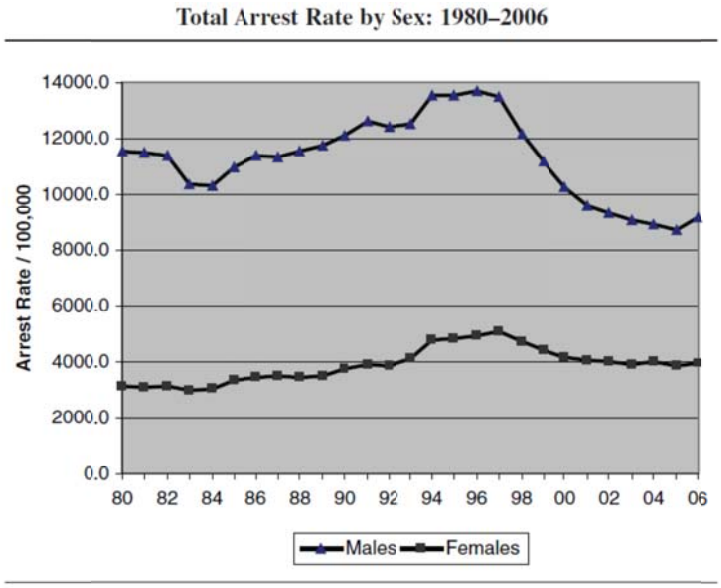
Need for the Application of HPA Models to Antisocial Girls

While the ACM provides clear theoretical motivations for examining HPA functioning in females, there are also reasons to examine from applied clinical work. As reviewed earlier, CU traits seem to designate a specific subgroup of persistent antisocial youth. While CU traits have most often been studied in male youth, new trends in crime data and empirical research indicate there is still a need to explore the role of CU traits in antisocial females. While the application of the psychopathy construct to females has been questioned, Schrum and Salekin (2006) found that the facets of psychopathy that most discriminated psychopathic girls from other offenders were those most closely captured by CU traits and most clearly implicated in HPA-related models (callous/lack of empathy, conning and manipulation, and grandiose sense of self-worth).

Additionally, the gender gap in youth crime has been narrowing in recent years because total male crime has decreased much more rapidly than female crime (-23% vs. -13.5%). Across various violent and nonviolent offenses, female crime is actually *increasing* while those same crimes are decreasing in boys (Tracy, et al., 2009). For example, assault is increasing in females greater than males (+10.1% vs. -4.4%) as is murder and manslaughter (+51.3% vs. +0.3%). The

differential crime trajectories over the past decade highlight how mechanisms underlying reductions in ASB in boys have not operated the same way in girls (see Figure 3).

Figure 3. Recent Crime Trends for Juvenile Boys and Girls.



Source: National Center for Juvenile Justice (2007).

The differential crime trajectories over the past decade highlight the possibility that mechanisms underlying reductions in antisocial behavior in boys have not operated in the same way in girls. Intense intervention with the most-severe antisocial adolescent male offenders has been shown to greatly reduce violent crime compared to those receiving regular correctional center intervention (Caldwell, et al., 2006). Broadening the research focus to girls and the mechanisms behind their antisocial behavior may yield similar results.

While female crimes are highly detrimental to society, antisocial behavior in girls is particularly detrimental to the offender herself. Incarcerated girls have significant comorbid mental health problems that persist throughout their lives even after the incarceration period (Schnittker & John, 2007). This is especially problematic for incarcerated antisocial girls as they have high rates of anxiety disorders (55%), substance dependence (82%), affective disorders (41%), and conduct/disruptive disorders (91%) (Karnik et al., 2009). Antisocial girls are prone to dysfunctional relationships later in life (Pajer, 1998) and poor physical health outcomes such as infectious diseases, reproductive problems, and suicide (Messina & Grella, 2006). Antisocial girls also engender serious risk for antisocial behavior in their offspring with maternal behaviors comprising 4 of 6 top risk factors for aggression in their offspring (Maughan, Taylor, Caspi, &

Moffitt, 2004). Chronically antisocial females thus perpetuate a cycle of violence that, with focused research and efforts at understanding female ASB, could be significantly reduced, reducing the deleterious effects of female ASB to both society and the offender herself.

The differences in recent crime trends provides further evidence from the applied areas of antisocial behavior to bolster the theoretical motivations for exploring HPA function in girls with CU traits as described by the ACM. While the neurobiological functioning of boys with CU traits has recently been described (Gostisha, in preparation), there remains a gap in the literature characterizing HPA axis functioning in girls with CU traits. The above review emphasizes the need for application of the ACM model to a sample of incarcerated girls due to differences in the underlying neurobiological systems that boys and girls use to respond to stress, the sex-specific life history strategies each tend toward when under stress, the disparate patterns of onset of antisocial behavior, and the recent divergent trends in youth crime between boys and girls.

Present Study

The present study will explore whether CU traits and stress exposure affect HPA axis function. Three main hypotheses will be explored:

1.) **Cortisol levels will be linked to CU traits.** The literature reviewed above lends to a prediction of a hypoaroused HPA function in individuals with CU traits. We expected to extend this association of low cortisol levels and a dysregulated diurnal rhythm to antisocial girls with CU traits. While some literature lends toward hypotheses for gender differences, the dearth of investigations into the role of HPA function in the development of CU traits in antisocial girls renders gender differences as purely exploratory.

2.) **Cortisol levels will be linked to elapsed time since stressor.** We hypothesized that greater objective stressor exposure would predict HPA functioning, though time since stressor may be an important factor in predicting HPA hyperactivity or hypoactivity. Specifically, we expected stress exposure in the past year (proximal stress) to be associated with high cortisol levels and a reactive diurnal rhythm while more distal or life stressors (greater than 1 year ago) should be related to low cortisol levels and a non-reactive diurnal rhythm.

3.) **CU traits and stress will interact to affect cortisol levels.** Finally, we expected an interaction between CU traits and stress such that those who experienced the most life

stress and have the greatest levels of CU traits to have low cortisol levels and a non-reactive or flat diurnal rhythm.

Method

Participants

Participants included 15 female incarcerated adolescents recruited from Southern Oaks Girls School (SOGS), a correctional facility in Wisconsin. Participants were split between African-American (40%) and Caucasian (46%) girls with Hispanic girls making up lower proportion of the sample (13%). Participants ranged in age from 15 to 18 (*M*=16.82, *SD*=.69).

Procedure

Informed consent and assent were first obtained from one parent and the participant. Testing occurred over the course of 3 days, including two days for collecting saliva samples and one for conducting the PCL-YV, interviews, demographic information, and the self-report measures of CU traits.

Measures

Salivary Cortisol Collection. Salivary cortisol was collected by A.G. on two days of five samples each day to permit examination of the stability of cortisol's diurnal rhythm (Shirtcliff & Essex, 2008). Saliva was collected (a) upon waking (range=6:05am to 7:49am, *M*=6:31am, *SD*=21 min); (b) 45 minutes later to capture the response to awakening (6:30am to 7:56am, *M*=7:10am, *SD*=21 min) (Wust, Federenko, Hellhammer, & Kirschbaum, 2000); (c) at before lunch to minimize the influences of mealtimes (range=11:31am to 12:35am, *M*=11:58am, *SD*=23 min); (d) before dinner (range 4:01pm to 5:09pm, *M*=4:37pm, *SD*=23 minutes); and (e) immediately before bedtime to capture the entire rhythm (range=6:34pm to 9:25pm, *M*=7:53pm, *SD*=45 min). Saliva was collected following published protocols (Schwartz, Granger, Susman, Gunnar, & Laird, 1998) and frozen immediately (-80^{o}C).

The Daily Diary saliva information sheet measured time of awakening, time of collection, medication use, mood, and daily hassles or uplifts (Shirtcliff, et al., 2005). The Pittsburgh Sleep Questionnaire was administered at each morning collection to account for changes in the diurnal rhythm due to sleep quality and duration (Buysse, Reynolds, Monk, Berman, & Kupfer, 1989).

Pubertal development stage was assessed through a confidential self-report measure (Petersen, Crockett, Richards, & Boxer, 1988).

Saliva was assayed for cortisol in duplicate using a well-established highly sensitive enzyme immunoassay kit (www.salimetrics.com) by Madison Biodiagnostics (Madison WI). Mean intra-assay and inter-assay coefficients of variation (CVs) were 3.8% and 7.4%, respectively. Samples were reanalyzed if the CV for the duplicate measurements were $\leq$20%. To normalize distributions, raw cortisol was log-transformed (with a constant of 5 added) and extreme values were winsorized.

Callous-Unemotional Traits. Participants were given the Antisocial Process Screening Device (APSD, Frick & Hare, 2001) and the Inventory of Callous Unemotional Traits (ICU, Kimonis et al., 2008). The Callous subscales of these measures were analyzed as they are most likely to form the core of the hypothesized hypoarousal model described above. Given increased reliability of multiple indices across methods and raters, we also administered the semi-structured Psychopathy Checklist-Youth Version interview (PCL-YV, Forth, Kosson, & Hare, 2003). Interviewers were trained on multiple practice cases and went through a "check-out" interview to maximize standardization. The Affective dimension of the PCL-YV was examined as it is most related to CU traits (Vincent, Vitacco, Grisso, & Corrado, 2003).

Child abuse. Two measures of physical abuse exposure, the Childhood Trauma Questionnaire (CTQ, Bernstein, Ahluvalia, Pogge, & Handelsman, 1997) and the Conflict Tactics Scale (CTS, Straus, 1998) were administered. The physical abuse subscales (r=.51, p=.052) were Z-scored and averaged to form a physical abuse composite that balances the more subjective CTQ with the more objective CTS measure. Reliabilities of this composite and the other scales can be found in Table 1.

Table 1. Intercorrelations and Descriptive Statistics of CU and Stress Measures.

Measure	1	2	3	4	5	6	7	8
1. APSD Callous	-							
2. ICU Callous	.69**	-						
3. PCL-YV Affective	.29	.37	-					
4. LSI Lifetime Ranking	-.09	.16	.43	-				
5. LSI Past-Year Stress	.01	-.19	.32	-.07	-			
6. Perceived Stress Scale	.14	.17	.42	.22	.33	-		
7. Neglect Composite	-.11	.08	.27	.20	.11	.60*	-	
8. Physical Abuse Composite (Z-scored)	-.14	.14	.39	.28	.32	.75**	.77**	-
Mean	23.40	32.47	22.73	6.90	1.035	32.87	5.33	0.00
Standard Deviation	4.93	7.46	8.71	1.04	.41	5.53	4.98	.87
Chronbach's α	.19	.78	.85	-[+]	-[++]	.69	.85	.68
Predicted Low Score	7	5.4	1.4	5.7	.5	28	-1.3	-1.05
Predicted High Score[+++]	10.8	19	8	8.2	1.52	39	10.6	.9

*p<.05, **p<.01, [+] ranking only comprises one item, [++] Past-year stress composite made up of generally independent stress domains (e.g. academic, family stress) so consistency statistics were inappropriate. [+++]Predicted scores were based on 15th and 85th percentiles for each measure.

Neglect. The emotional neglect and physical neglect subscales (r=.69, p<.001) of the CTS were Z-scored and averaged to form a neglect composite that more accurately captures the full construct of child neglect.

Life Stress. The Life Stress Interview (LSI, Adrian & Hammen, 1993) was administered to capture subtle individual variation in stressor exposure with a clearly delineated timecourse. The LSI measures stressor exposure in the past year by tapping several salient domains including academic, peer, relationship, and family stress. The LSI incorporates the context of life events while remaining objective about the impact of stressors. Interviewers were trained through multiple practice interviews and had to pass a "check-out" interview to maximize standardization across interviewers. After the interview, past-year stressors are then presented to an independent team of 3-7 trained raters, none of whom had met the participant. Language that conveys emotional responses that tap subjective experience of stress is removed prior to rating. Stressors are rated on a scale of 1 (not at all stressful) through 5 (very severely stressful). Reliability scores

could not be obtained on the single sample of girls in the present study, however the LSI has shown strong reliabilities between .82 and .97 (Rudolph & Hammen, 1999).

At the end of the study, LSI lifetime stressors were aggregated for each girl who was then ranked on a 10-point scale by the trained raters. This scale was previously created using a sample of 50 incarcerated males of similar age and backgrounds to aid in the matching of life stress histories across genders. The time-course of lifetime stressor exposure ranges from as early as the prenatal period (e.g. teratogen exposure) up until the past year so that it does not overlap with the past-year LSI domains.

Past-Year Stress. The Life Stress Interview also obtains indices of past-year stress across several domains including academic, behavioral, peer, cross-gender platonic, romantic, family, and marital stress. The behavioral stress domain was not included in analyses due to the preponderance of high scores on this domain as all girls were incarcerated with behavior problems. Additionally, the marital stress domain was not included as this domain was not applicable to a majority of girls either due to separation from parents greater than one year or there was not a relationship between the parent(s) in the past year.

Perceived Stress. The Perceived Stress Scale (PSS, S. Cohen, Kamarck, T., & Mermelstein, R., 1983) was administered to capture perceived stress over the past week. The PSS was developed to examine the non-specific role of stress appraisal in the etiology of psychopathology. As reviewed above, perceived stress is different from objective stress and may have a different relationship to HPA functioning characterized by hyperarousal. Its use as a measure of stress over the past week also provides further exploration of the potential effect time since stressor exposure can have on HPA functioning. The PSS total score is derived by summing all regular and reverse-coded items.

Analytic Strategy

Data were cleaned using SPSS v18.0. Due to the regularity of the daily schedule at SOGS, hormone sample and questionnaire missingness were minimal. Out of 150 total possible samples, 149 samples (99.3%) were obtained in sufficient quantity to be assayed. Analyses were run using the Hierarchical Linear Modeling (HLM) program (Raudenbush, 2004). Scores for the stress and CU traits measures were centered at each variable's mean before being entered into the HLM program models. Cortisol's diurnal rhythm was modeled in HLM as a function of time since waking (TSW). HLM allows for the simultaneous modeling of cortisol levels, the cortisol

awakening response, and diurnal slope. Cortisol models were set up such that within-individual variation in cortisol constitutes the first level of analysis while between-individual differences in cortisol, CU traits, life stress, and their interaction comprised the second level of analysis.

Results

Hierarchical Linear Model Development

Cortisol quantity was the outcome of interest in all analyses (Y_{cort}). In Level 1 analyses, the intercept was a significant predictor of cortisol (β_0= 3.72, p<.001), so that in Level 2, the intercept captures trait-like predicted cortisol levels. Analyses indicated 83.38% (ICC=.833) of the variance in cortisol was attributable to Level 1 within-individual variation. Additionally, 16.62% (ICC=.166) of the variance in cortisol was attributable to between-individual variation in HPA axis activity at Level 2. The intercept's unique variance was not significant (χ^2= 16.48, p=.284) meaning that individual differences in cortisol levels between the 15 girls was not yet large. Nevertheless, an ICC of .166 is consistent with other work on cortisol's trait-like variance. Given that variance tests are traditionally underpowered, the intercept was allowed to vary in keeping with prior literature. The CAR dummy variable indicated that cortisol levels were significantly higher when collected 45 minutes after awakening (β_{CAR}= 0.43, p=.002). The CAR's unique variance was not significant (χ^2= 22.66, p=.066) meaning between individual differences in the CAR were not yet substantial. Thereafter, cortisol displayed a significant diurnal rhythm, with cortisol declining linearly across the day (β_{TSW}= -0.12, p<.001). The unique variance for the slope was significant (χ^2=41.89, p<.001) meaning that the 15 girls had different or unique diurnal rhythms.

Once these predictors of cortisol level were modeled at Level 1 (within individual variation), they could become an outcome of interest at Level 2 (between individual variation). Analyses thereafter focused on Level 2 effects for cortisol level (intercept) and cross-level interactions (cortisol's CAR and diurnal slope) with individual differences in CU traits, life stress, and CU*life stress. Pubertal status, body mass index (BMI), and age were all examined as control variables. Puberty status and age did not significantly predict cortisol. BMI significantly influenced the CAR (β_{CAR}= 0.05, *p*=.002) such that youth with greater BMI scores had greater cortisol awakening responses. Therefore only BMI was included in subsequent models as illustrated below:

Level-1 Model

$Y_{CORT} = \beta_0 + \beta_{CAR} + \beta_{TSW} + R$

Level-2 Model

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

$\beta_{CAR} = \gamma_{10} + \gamma_{11}*(BMI) + \gamma_{11}*(CU) + U1$

$\beta_{TSW} = \gamma_{20} + \gamma_{21}*(Stress) + \gamma_{22}*(CU) + \gamma_{23}*(Interaction) + U_2$

<u>Are CU Traits Associated with Hypoaroused HPA Functioning?</u>

We examined whether there was a main effect of CU traits on HPA functioning. Girls with high scores on the callous subscale of the APSD exhibited a trend for steeper diurnal rhythms (β_0=-0.016, p=.066). Girls with high scores on the callous subscale of the APSD showed a trend for steeper diurnal slopes (β_{TSW} =-0.02, p=.083) compared to low callous girls. Girls with high scores on the callous subscale of the ICU had significantly higher morning levels (β_0=0.03, p<.001) than girls low in CU traits however this was only after a non-significant main effect for the ICU was included in the slope term. Girls scoring high on the Affective dimension showed a trend for having higher morning levels (β_0=.07, p=.142) and a significantly lower CAR (β_{CAR}=-0.07, p=.041) compared to girls with low Affective scores.

Results from main effects models indicated girls with CU traits had higher morning cortisol levels than girls low in CU traits. These results did not support a model of hypoarousal of HPA axis function.

Does Elapsed Time Since Stressor Predict HPA Functioning?

We examined whether there were differential associations between stressor experience and HPA activity as a function of time elapsed since stressor. Proximal stress exposure was measured through past-year stress exposure across multiple domains of functioning in the LSI interview. Additionally, the PSS measured perceived stress over the past week prior to participation in the study. Distal stressor exposure (greater than 12 months prior to testing) was measured through the neglect and abuse composites as well as the life stress ranking of the LSI.

Proximal Stressor Exposure. Girls with greater stress exposure in the past year were found to have a reduced CAR (β_{CAR}=-0.42, p=.004) and flatter diurnal slope (β_{TSW} =0.07, p<.001) compared to girls with less past-year stress. Girls who reported greater perceived stress over the week prior to study participation had a reduced CAR (β_{CAR}=-0.02, p=.054) compared to girls who reported less perceived stress over the past week.

Distal Stressor Exposure. Girls who experienced emotional and physical neglect in childhood, as measured by the CTQ, had a reduced CAR (β_{CAR}=-0.03, p=.027) compared to non-neglected girls. Girls who were physically abused in childhood, as measured by the physical abuse scales of the CTS and CTQ, had greater initial morning cortisol levels (β_0= 0.02, p=.007) and a lower cortisol awakening response (β_{CAR}=-0.42, p=.004) compared to girls who were not physically abused. Girls with greater intensity of life stress, as measured by the LSI lifetime ranking, showed a trend for having greater morning cortisol levels (β_0= 0.13, p=.075) compared to girls with less life stress. Further differences between proximal and distal stressor exposure can be found in the interaction analyses below.

Results indicated that stressor exposure was generally associated with higher morning cortisol levels and a blunted CAR.

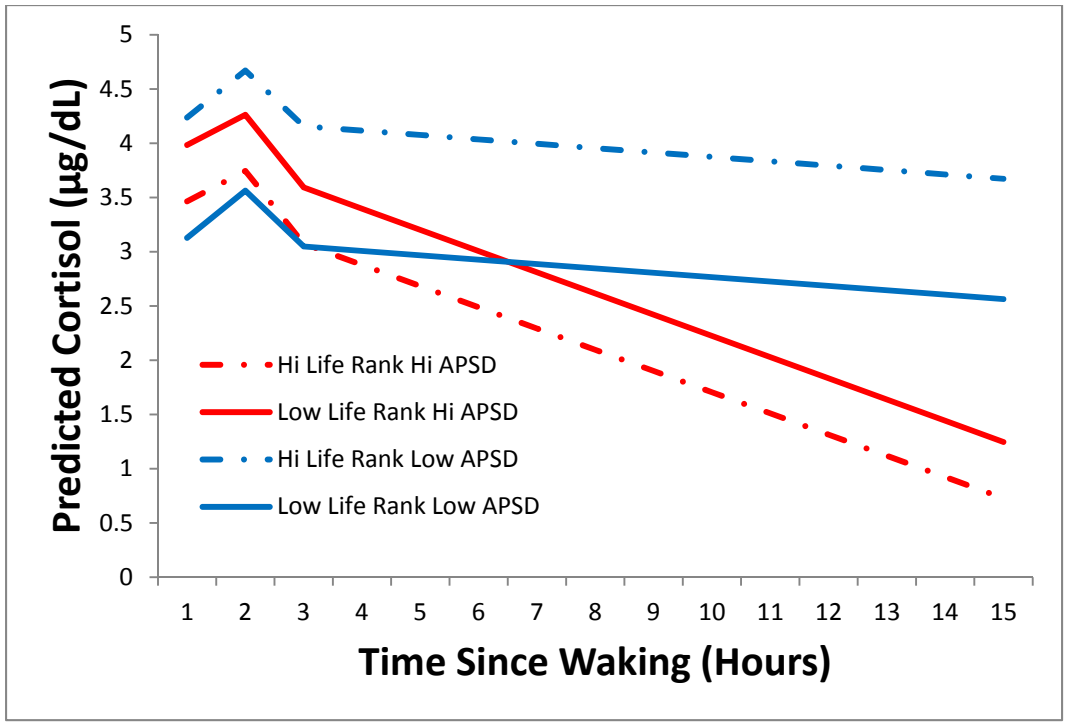
Do CU Traits and Stress Interact to Affect HPA Functioning?

Based on the ACM model and Shirtcliff *et al*. (2009), we posited that CU traits and stress exposure would interact to affect HPA axis activity. Specifically, we expected their interaction to predict hypoaroused HPA activity defined by low morning levels and a flat diurnal rhythm. Interactions were conducted between stress measures (PSS, LSI Lifetime Stress, LSI past-year stress, abuse, and neglect) and measures of CU traits (APSD Callous score, ICU Callous score and PCL-YV Affective scores). Analyses are organized firstly by measure of CU traits and

secondarily by stress measure (proximal vs. distal) to further illustrate how time since stressor can affect HPA functioning.

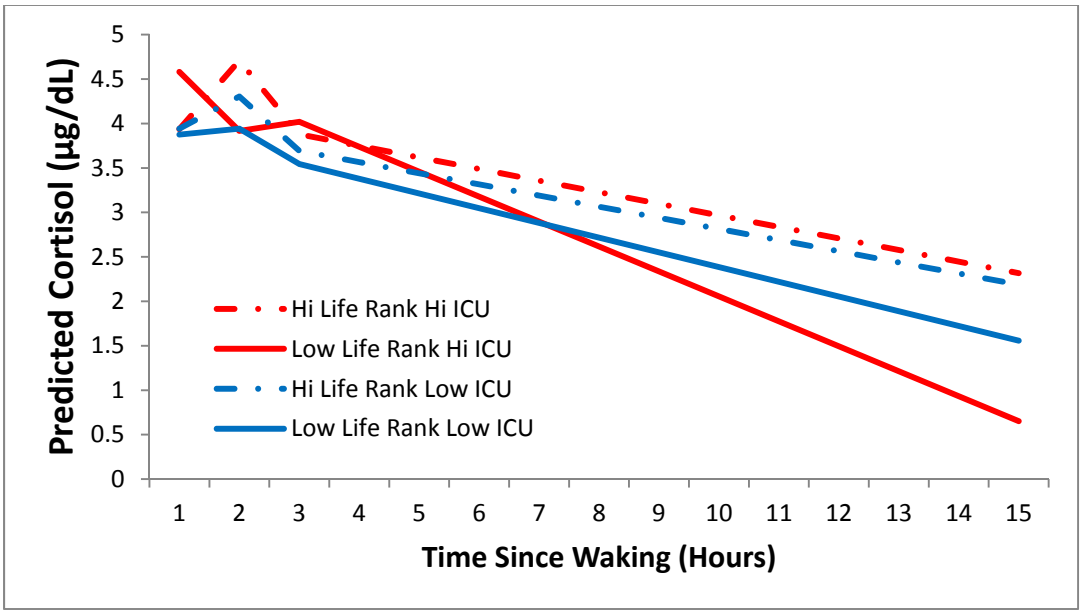
APSD Callous Score. The APSD Callous score interacted only with the lifetime stress ranking to predict cortisol's morning level (β_0=-0.081, p=.091). Girls high in CU traits with more severe lifetime stress were most distinguished by a higher CAR and a flatter slope across the day compared to CU girls with lower lifetime stress. Conversely, girls low in CU traits with less severe lifetime stress had lower morning levels and a flatter diurnal rhythm than low CU girls with severe lifetime stress (see Figure 4). The APSD did not interact with any other stress measures in predicting cortisol activity.

Figure 4. Model of Cortisol's Diurnal Rhythm as a Function of APSD Callous and Life Stress.



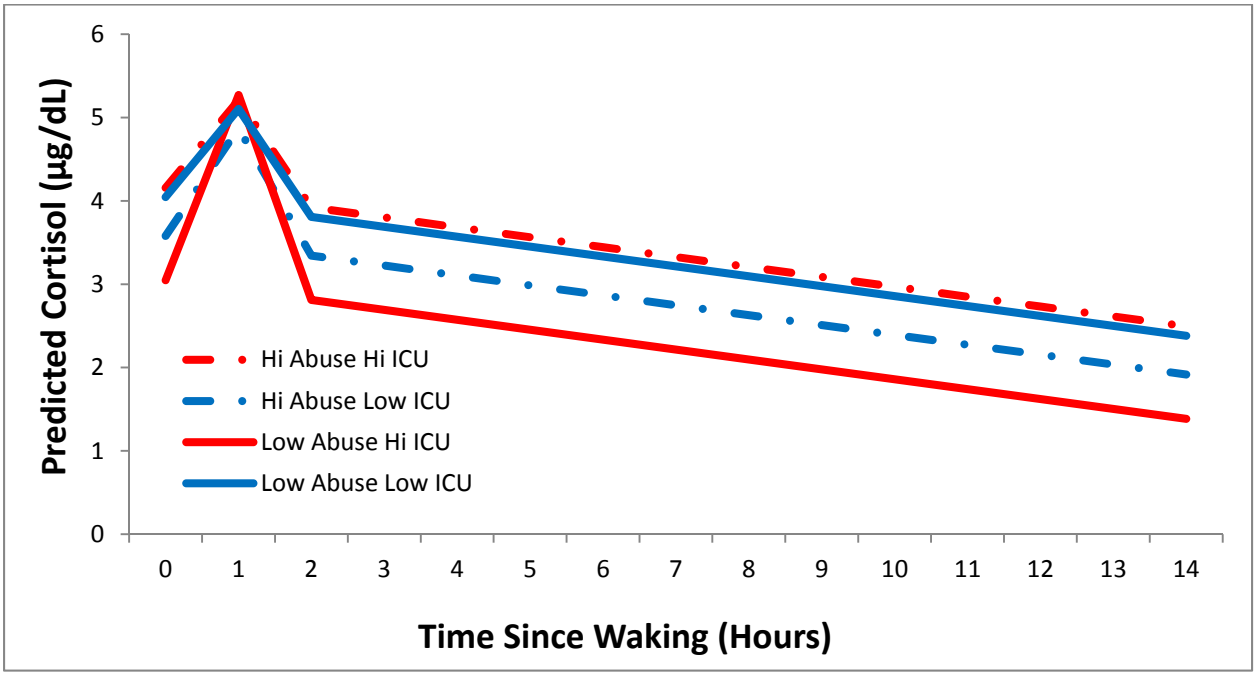
ICU Callous Score. There was an interaction between the ICU Callous subscale score and the lifetime stress predicting cortisol's morning level (β_0=-0.01, p=.041), awakening response (β_{CAR}=0.03, p=.008), and diurnal slope (β_{TSW}=0.004, p=.001). Among girls high in CU traits, those who had experienced greater lifetime stress had lower morning levels, a higher CAR, and flatter diurnal slopes compared to girls high in CU traits with less lifetime stress. Among girls low in CU traits, those with high lifetime stress had slightly higher morning levels, a higher CAR, and flatter slopes compared to girls with less lifetime stress (see Figure 5).

Figure 5. Model of Cortisol's Diurnal Rhythm as a Function of ICU Callous Score and Lifetime Stress.



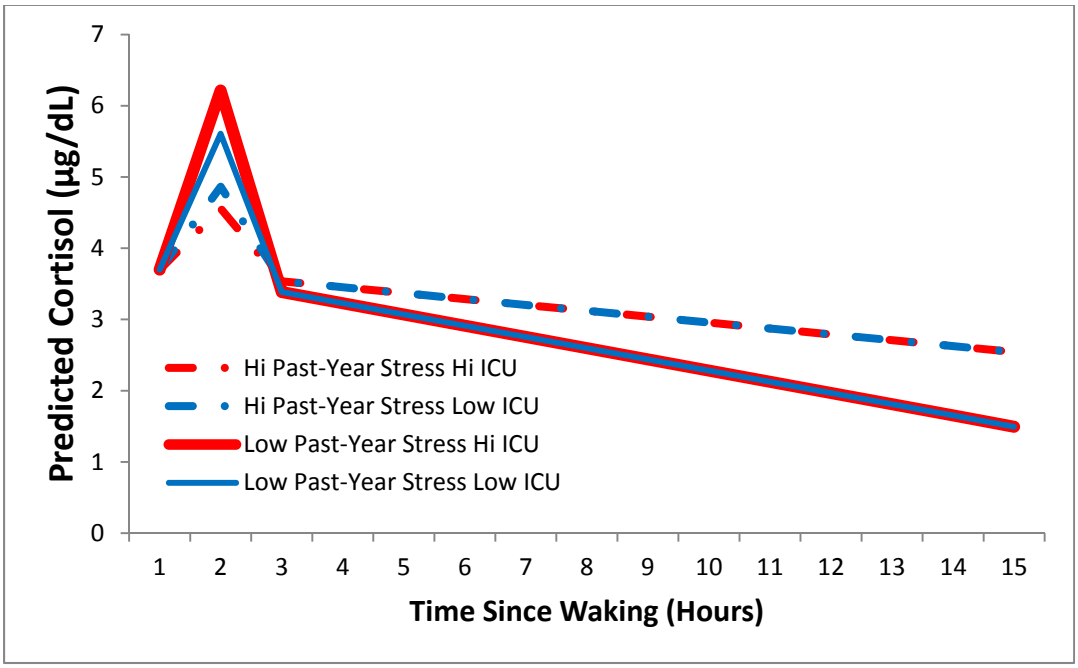
There was an interaction between the ICU callous score and the abuse composite predicting cortisol's morning level (β_0=0.05, p=.013) and awakening response (β_{CAR}=-0.05, p<.001). Among girls high in CU traits, extremely abused girls had lower morning levels and awakening responses than CU girls who were not extremely abused. Among girls low in CU traits, extremely abused girls had higher morning cortisol levels than girls who were not extremely abused (see Figure 6).

Figure 6. Model of Cortisol's Diurnal Rhythm as a Function of ICU Callous Score and Abuse



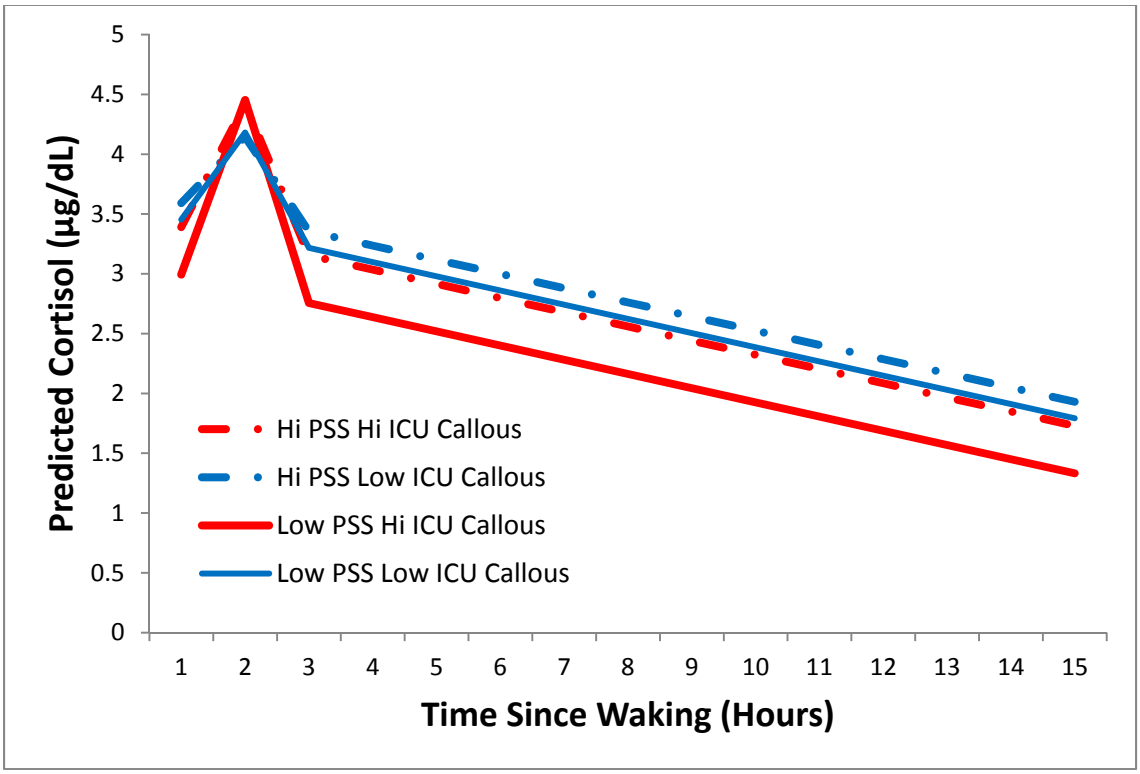
There was also an interaction between the ICU Callous score and past-year stress predicting cortisol's awakening response (β_{CAR}=-0.07, p=.008). Among girls high in CU traits, those who had experienced greater past year stress had a much lower CAR than girls experiencing less past-year stress. Among girls low in CU traits, the difference in awakening responses as a function of past-year stress was much smaller. Low CU girls with high past year stress had greater awakening responses compared to girls with less past-year stress (see Figure 7).

Figure 7. Model of Cortisol's Diurnal Rhythm as a Function of ICU Callous Score and Past-Year Stress.



The ICU Callous scale interacted with the Perceived Stress Scale to predict cortisol's morning level (β_0=0.01, p=.016) and awakening response (β_{CAR}=-0.01, p<.001). Among girls high in CU traits, those who reported more stress over the past week had higher morning levels and a greater awakening response than CU girls reporting less stress over the past week (though this effect was largely driven by lower levels). Among girls low in CU traits, those reporting higher stress over the past week had higher morning levels than girls reporting less stress in the past week (see Figure 8).

Figure 8. Model of Cortisol's Diurnal Rhythm as a Function of ICU Callous Score and Perceived Past-Week Stress.

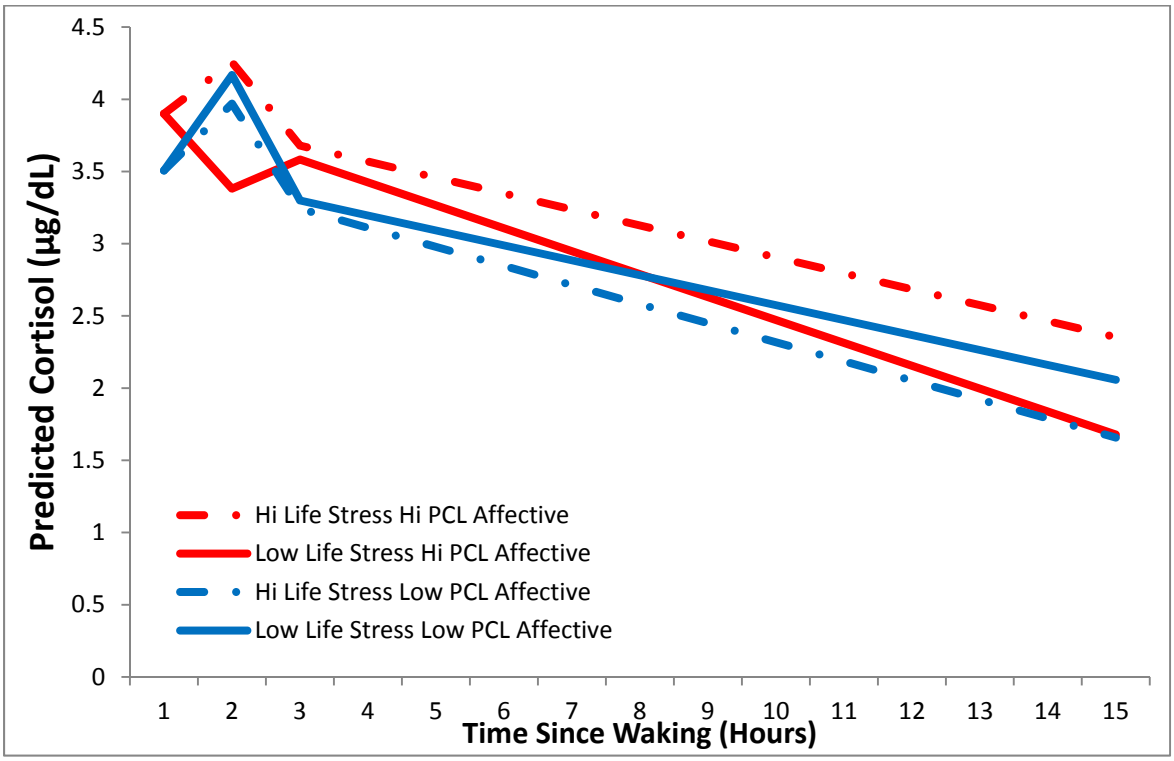


The ICU Callous scale did not interact with the neglect composite. Overall, the ICU Callous score interacted slightly differently with each measure of stress whether it was proximal, distal, perceived, or objective stress.

PCL Affective Score. In line with previous analyses on a corollary sample of incarcerated males and due to its overlap with CU traits, interactions analyses were conducted for the Affective dimension of the PCL-YV. The PCL Affective score interacted with lifetime stress

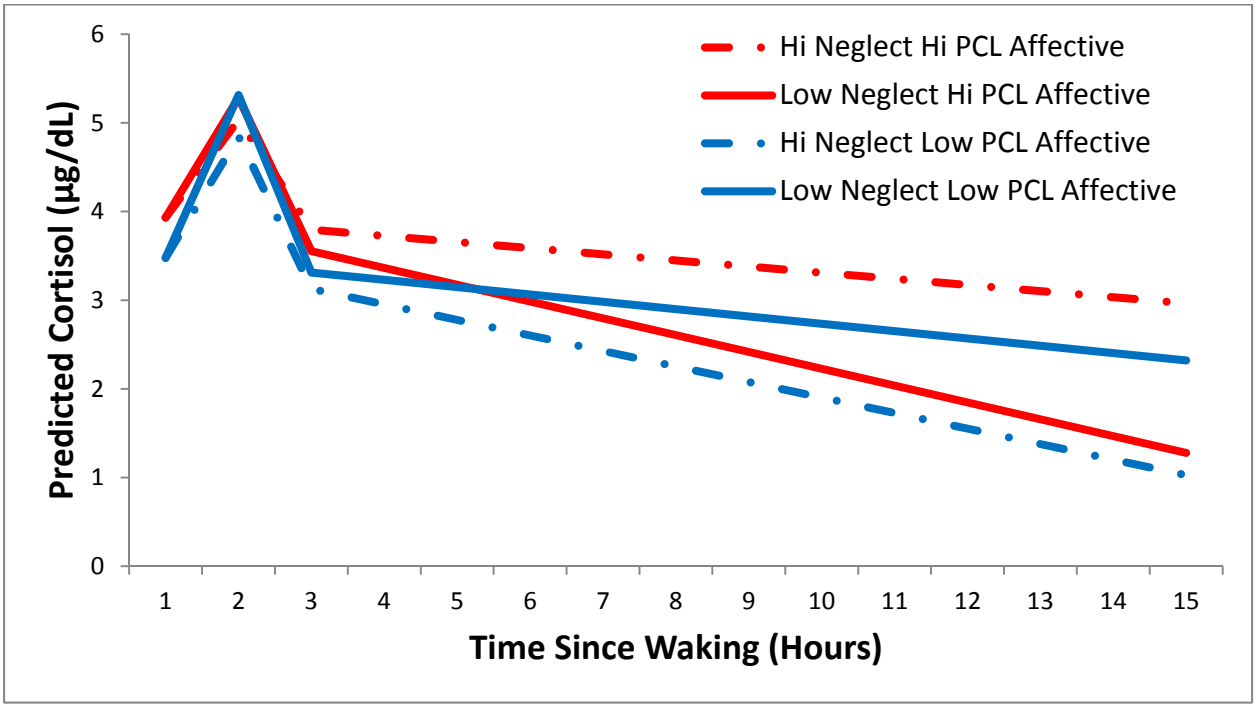
ranking (β_{CAR}=0.10, p<.001) such that girls with high Affective scores stood out by having a reduced CAR if they experienced lower lifetime stress. Meanwhile, high PCL girls with severe lifetime stress and low PCL girls (regardless of lifetime stress severity) had higher awakening responses. In addition to the fact that girls with high Affective scores had higher morning cortisol (β_0=0.08, p=.021), these girls also had steeper diurnal rhythms if they had severe lifetime stress; if their life stress was not as severe, these girls had high morning cortisol and relatively flat diurnal rhythms. For girls with low Affective scores, their morning cortisol levels were lower and had steeper diurnal rhythms if they had severe lifetime stress; if their life stress was not as severe, these girls had flatter diurnal rhythms. Further, among girls with less severe lifetime stress, girls with high Affective scores had steeper diurnal rhythms than girls with low Affective scores. Among girls with severe lifetime stress, girls with high Affective scores had flatter diurnal rhythms compared to girls with low Affective scores (see Figure 9).

Figure 9. Model of Cortisol's Diurnal Rhythm as a Function of PCL-YV Affective Score and Lifetime Stress Ranking.



There was an interaction between the Affective dimension and childhood neglect predicting cortisol's awakening response (β_{CAR}=0.03, p=.004) and diurnal slope (β_{TSW} =0.002, p=.065). Non-neglected girls had higher awakening responses regardless of PCL score, however among neglected girls, girls who scored high on the Affective dimension had a higher CAR compared to girls with low scores on the Affective dimension (see Figure 10).

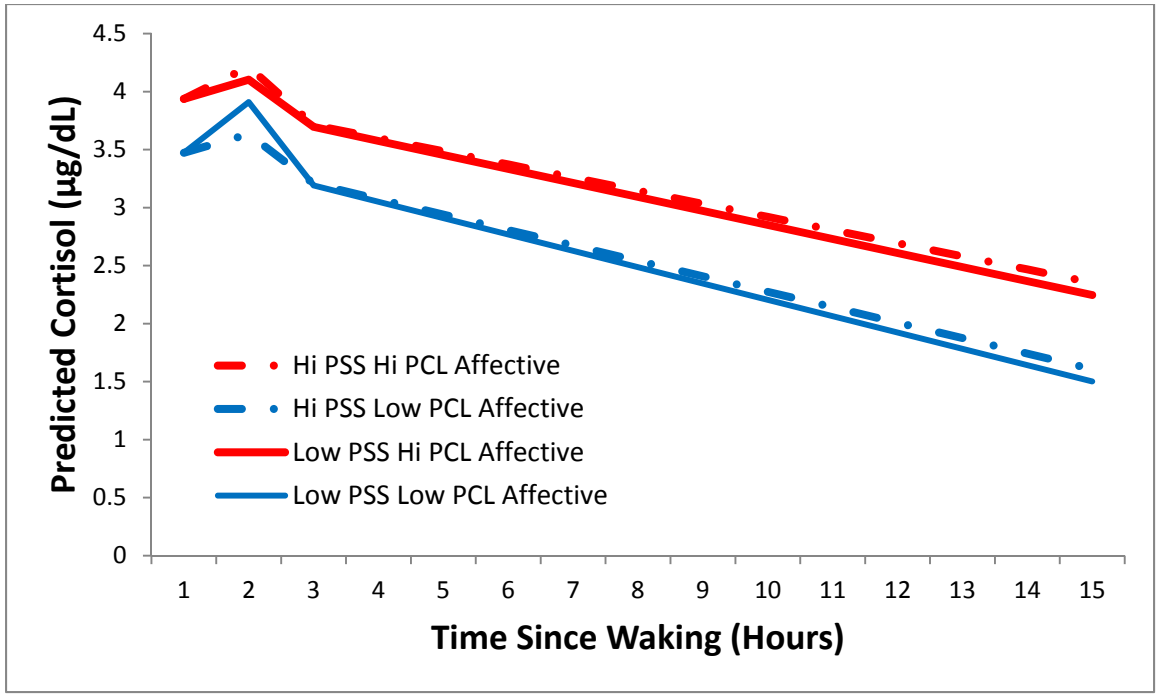
Figure 10. Model of Cortisol's Diurnal Rhythm as a Function of PCL-YV Affective Score and Neglect.



There was an interaction between the Affective dimension and physical abuse predicting cortisol's awakening response (β_{CAR}=0.13, p<.001) and diurnal rhythm (β_{TSW} =0.01, p=.003). Results nearly mirrored those obtained in the interaction between neglect and the PCL Affective scores, with the only exception being a reduced CAR among extremely abused girls with low Affective scores compared to all other girls. The Affective dimension also interacted with the Perceived Stress Scale predicting cortisol's awakening response (β_{CAR}= 0.01, p<.001) and diurnal rhythm (β_{TSW} = 0.002 p=.002). There was also a main effect of Affective scores predicting higher morning levels (β_0=0.08, p=.021) such that girls with low Affective scores had

lower morning cortisol, and greater awakening responses than girls with high Affective scores (see Figure 11). There was no interaction between past-year stress and the Affective dimension.

Figure 11. Model of Cortisol's Diurnal Rhythm as a Function of PCL-YV Affective Score and Perceived Stress Scale Total Score.



Overall, the PCL-YV Affective dimension interacted with the various stress measures such that girls high in CU traits had higher levels and steeper diurnal rhythms compared to low CU girls. Findings for the role of CU traits in predicting the CAR varied based on the type of stress (proximal, distal, perceived, or objective) being measured.

Discussion

Results supported a biopsychosocial model in which CU traits and life stress exposure impact HPA functioning in incarcerated girls. Main effects and interaction models indicated girls with CU traits had higher morning cortisol levels than girls low in CU traits. These results did not support a simple model of hypoarousal of HPA axis function. Similarly, results for stress exposure were not straightforward. We found that stressor exposure was generally associated with higher morning cortisol levels and a blunted CAR. Furthermore, CU traits and stressor

exposure generally interacted to predict the diurnal rhythm of the HPA axis. Specifically, among girls high in CU traits, those with low stress had steeper slopes while CU girls who experienced high stress had flatter slopes. Among girls low in CU traits, girls with low stress had flatter slopes, while low CU girls with high stress had steeper slopes.

Are CU Traits Associated with Hypoaroused HPA Functioning?

Although results of the current study provided preliminary support for a model linking environmental stressors to CU traits via HPA axis functioning, the expected direction of this relationship was not supported. Girls high in CU traits were found to have higher morning levels of cortisol and a higher cortisol awakening response. This pattern ran counter to our expectations of a hypoaroused HPA axis.

The bulk of literature on the stress response system in callous-unemotional traits males suggests HPA hypoarousal. The ACM model predicts this Unemotional profile as well, but only for males. The ACM also predicts gender differences in the Unemotional profile although this prediction was largely hypothetical given the dearth of investigations on such antisocial girls. Specifically, females are more likely to exhibit a Vigilant pattern of SRS and HPA activity even after the environmental stressors advance from dangerous/unpredictable to traumatic (see dotted line, Figure 2). As opposed to the hypo-aroused Unemotional profile in males, the present findings antisocial girls matched the predicted pattern of increased HPA activity in line with predictions of a Vigilant ACM profile in our sample. This finding fits with several other findings in antisocial girls that suggest the Vigilant profile is more characteristic of girls at the high end of the stress exposure continuum. Different systems employed by males and females in response to stress may account for the preserved responsivity in girls with CU traits. The "tend and befriend" response to stress is largely subserved by the hormone oxytocin and increases the likelihood of affiliative or social orienting responses to stress rather than an aggressive or escape strategy typically expressed by males (S. E. Taylor, 2006). Yet in a dangerous and traumatic environment (Shields & Cicchetti, 1998), such affiliation is not likely to be expressed in a prosocial manner even if oxytocin levels are elevated (Seltzer & Pollak, under review), nor is it likely to be reducing interpersonal anxiety (Marazziti et al., 2006). Instead, the endocrine system may be enhancing social behavior, but toward reactive or relational aggressive behavior and increased social anxiety. In sum, the hypoarousal model was not supported in girls with CU traits, but supported the predicted pattern of responsivity in girls.

Does Elapsed Time Since Stressor Predict HPA Functioning?

Results also provided some support for the importance of time since stressor as a meaningful variable in interpreting HPA axis activity. We expected proximal stress (past-year stress and perceived past-week stress) to be related to HPA hyperactivity while distal stress (lifetime stress, physical abuse, and neglect) would predict HPA hypoactivity. We found that both proximal and distal stress were related to a reduced CAR. Past-year stress also predicted a flatter diurnal slope while greater distal stress (physical abuse) predicted high morning levels of cortisol. Broadly speaking, it appears as though the different components of the HPA axis may be calibrated more or less closely by the chronicity and recency of stressors. Results support findings presented by Miller (2007) that increased HPA activity in the short-term following a stressor is succeeded by reduced HPA activity as months passed since experiencing the stressor. These findings have been replicated in PTSD survivors (Yehuda, 2003).

Additional support for the importance of time since stressor onset in predicting HPA activity came from interaction analyses. This was best evidenced by variations in the diurnal rhythm (Figures 7 & 11). While proximal stress (perceived stress and past-year stress) exhibited relatively straightforward effects, distal stressors (lifetime stress, abuse, and neglect) were associated with much more intricate diurnal rhythms that interacted with measures of CU traits. This is in keeping with previous work on incarcerated antisocial boys (Gostisha, in preparation) finding a substantial contribution of time since stressor as part of understanding an individual's context to properly interpret their HPA axis activity. Findings similar to these were also present in a sample of youth with internalizing and externalizing problems (P. L. Ruttle et al., 2010). Specifically, that study found youth with internalizing problems had higher morning levels while youth with externalizing problems had flatter diurnal rhythms.

Which Components of the Diurnal Rhythm Were Associated with CU traits and Stress?

Morning Basal Levels. As reviewed above, the three main components of cortisol's circadian rhythm (basal level, CAR, and diurnal rhythm) have specialized functionality and each measure is distinct. Cortisol levels have generally been viewed as a measure of basal activity of the HPA axis (Shirtcliff, et al., 2005). This perspective coincides with the general finding that externalizing and CU traits more specifically are related to hypoarousal of the SRS and HPA axis. While the robustness of this relationship has been questioned (Alink et al., 2008), hypoarousal as it pertains to the HPA axis theoretically focuses on low basal (morning) cortisol.

The present findings contradict the traditional model of hypoarousal as girls with CU traits had high morning cortisol levels. This hyperarousal maps onto the Vigilant profile in the ACM framework, and is hypothesized to be characterized by low PNS activity and high SNS and HPA activity with the present results supporting the HPA expectations. Hyperarousal of the SRS can result in a phenotype that is quickly aroused and may be especially manifest in a high-stress situation or context. High morning levels may be an indicator of a stress response system that is "primed" for a response and therefore may strongly underlie reactive forms of aggression (Lopez-Duran, Olson, Hajal, Felt, & Vazquez, 2009).

Cortisol Awakening Response. A second component to the diurnal rhythm is the cortisol awakening response. The CAR has received some recent attention though its full set of functions is still being explored rendering strong conclusions about the CAR tentative. Some have presented evidence for its role in anticipation of the upcoming day (Fries, Dettenborn, & Kirschbaum, 2009), regulating cognitive and immune functioning as well as recovery from inertia (A. Clow, Hucklebridge, F., Thorn, L., 2010), or physiological preparing or readying the body as a kind of "jump start" (A. Clow, Hucklebridge, Stalder, Evans, & Thorn, 2010). Blunted CARs are often found in individuals who are currently under stress (Kunz-Ebrecht, Kirschbaum, Marmot, & Steptoe, 2004; Wessa, Rohleder, Kirschbaum, & Flor, 2006). The results from this study are the first to our knowledge documenting an intact CAR among incarcerated adolescent girls with CU traits. It appears that girls with CU traits are readying themselves for the day; an important function in a stressful setting of incarceration. This is in keeping with parallel results of an intact CAR among incarcerated boys (Gostisha, in preparation). Conversely, those experiencing recent chronic stress have been found to have a blunted CAR (Kunz-Ebrecht, et al., 2004). While the intact CAR of youth with CU traits may be a sign they are readying themselves to take on the strain of incarceration, a blunted CAR in youth without CU traits may be signal an inability to cope with the chronic stress of incarceration. The similar findings of an intact CAR for boys and girls will be further discussed below. Despite similar CAR findings in both incarcerated boys and girls, caution must be exercised when interpreting the CAR as a biomarker of illness or psychopathology until the process is better understood in normal populations.

Diurnal Rhythm. A third component of HPA axis activity, the diurnal rhythm, has recently been posited to be a measure of environmental openness (P. L. Ruttle, et al., 2010) and the ability of the HPA axis to rhythmically match its changes with the environment (Skinner,

2011). Viewing the diurnal rhythm in this manner means that the more responsive the rhythm is (i.e. more closely follows the natural or steep circadian decline), the more opportunity exists for the axis to adjust to proximal environmental demands as the individual's natural rhythm accentuates high cortisol levels when biological forces promote high cortisol and to attenuate cortisol levels later in the day on a daily cycle. Flat rhythms therefore, are indicative of less environmental openness as greater physiological resources are expended to reduce rhythmicity in the morning and overcome environmental threats later in the day when cortisol levels should be low. As such, flat rhythms have been found to be previously posited as a direct index of stress dysregulation (P. L. Ruttle, et al., 2010; Shirtcliff & Essex, 2008).

Flat rhythms were evident in a number of interactions between CU traits and stress exposure. There were significant interactions between the ICU Callous score and 4 of the stress measures as well as between the PCL-YV total score and 2 of the stress measures (see Figures 4-11). There was also a significant interaction between the APSD Callous score and lifetime stress. In general, we found girls with CU traits and low stress had steeper diurnal rhythms than CU youth with high stress. It seems that CU girls with low stress may be buffered from the context of incarceration and are therefore able to have an HPA axis more open to environmental cues. CU trait expression, in the context of recent incarceration and a high accumulation of lifetime stress exposure, however, may overwhelm girls' physiological resources and a blunted diurnal rhythm may result. Among girls low in CU traits, those with low stress had flatter diurnal rhythms while those with high stress had steeper rhythms. Girls low on both CU traits and life stress may be overwhelmed by the new, unfamiliar stressors of being recently incarcerated. Taking the girls' context into consideration, we see that CU girls with high stress and low CU girls with high stress had the most dysregulated diurnal slopes.

To the extent that hypoarousal can be defined as less environmental openness, the flat rhythms observed in youth with CU traits and high stress support a variation on the traditional model of hypoarousal in severely antisocial youth. The presence of both hyper- and hypoarousal in our sample (high levels and flat rhythms respectively) was not expected. However, given the three components of the diurnal rhythm can each add unique information, the lack of hypoarousal at each component highlights the importance of specifying which part of cortisol's rhythm one is testing. Results of this study emphasize the dynamic nature of HPA axis activity

and the need to tightly define the type of stress being measured (i.e. proximal, distal, objective, subjective).

Implications

The present study contributes to several areas. First, the present findings expand our knowledge of the components of cortisol's diurnal rhythm. While cortisol has been looked at using a multitude of methodologies, the present findings highlight the importance of capturing the full diurnal rhythm and viewing its various components in light of the unique information each has to offer. Secondly, findings suggest researchers must take youth's traumatization history and context into consideration when interpreting cortisol data. To the extent that neuroendocrine measures may someday become a clinically-relevant assessment tool, the present findings suggest clinicians should also keep in mind a youth's stress history when using biomarkers as part of a case conceptualization. Third, the findings provide preliminary support for a mechanistic model by which stress exposure can instantiate CU traits in the stress response system. Results from this study illustrate the synergistic utility of applying biopsychological methods to developmental psychopathology research. The present study also paves the way for additional research on neuroendocrine function in antisocial youth. Additional research on the nature of the CAR in antisocial youth may prove it to be an important biomarker for CU traits and/or may inform treatment selection. Indeed, correctly identifying youth with CU traits for treatment placement may be increasingly important as effective interventions these youth become more common (Caldwell, et al., 2006; Caldwell & Van Rybroek, 2005).

Limitations

The present study did not measure genetic influences on CU trait expression so we do not know how much findings are driven by genetic vs. environmental effects. The model presented for the dysregulation of the HPA axis in CU traits does not argue for an exclusively environmentally-mediated pathway to CU traits, but leaves room for genetic and epigenetic effects to produce a CU phenotype. Indeed, the different components of the HPA axis are under differential genetic influences (Van Hulle, in preparation). Likely genetic influences may lie in genes controlling the initial level and range of environmental openness of the SRS a youth begins life with. Blair (2006) proposes a model whereby psychopathy develops largely due to genetic factors underlying development of the amygdala and orbitofrontal cortex. The present study underlined the importance of stressor type and the specific component of cortisol's diurnal

rhythm for interpreting HPA axis function. Future studies of the neurobiological function of antisocial girls should focus not on genetic *or* environmental influences, but rather on what genetic- *and* environmentally-mediated parts of the diurnal rhythm HPA activity is dysregulated.

Examination of the importance of context and time since stressor was hampered by the confluence of perceived and objective measures of stress. The PSS confounds past-week stress (proximal) with perceived stress and is therefore not a one-to-one comparison with our measures of distal stressor exposure. While this highlighted the importance of objective vs. subjective measures of stress, (objective past-year stress predicted a low CAR, subjective stress over the past year predicted a high CAR), it remains necessary to have a past-week measure of objective stress to fully examine the role of time since stressor onset. Furthermore, all girls in this study were incarcerated and could be assumed to all be experiencing some level of concurrent stress. A future study of antisocial girls who are not incarcerated could eliminate concurrent stress (i.e., recent incarceration) as a confound, but will still have to manage the varying individual differences in concurrent stress exposure.

Another limitation stemmed from discontinuous distributions in a small sample size. For BMI and some interaction models, there were scores at the high ends of the distributions. While in the normal range expected for the measures, with such a small sample size, statistical models may have unduly been influenced by one or two girls. In accordance, some betas returned somewhat anomalous results (e.g. negative CAR for girls with high Affective scores and low lifetime stress, see Figure 9) precluding firm conclusions from being drawn until the final sample of 50 girls is reached. Additional participants will fill in these distributions resulting in more normal distributions and robust statistical models.

Conclusion

The present study provided support for an interactive model of environmental stressors and CU traits to aid the development of the neuroendocrine and neural circuitry anomalies found in youth with CU traits and adult psychopaths. Detailed understanding of girls' stress histories, including time since stressor onset, and the specific components of the diurnal should be accounted for in future studies. Characterizing the stress histories of antisocial females can help us better understand their neurobiological functioning that might inform gender-specific intervention strategies. While purely speculative, it may be that interventions that emphasize consistency and routine may stabilize the high morning levels, intact cortisol awakening

responses, and flat diurnal rhythms exhibited in callous boys and girls. The present investigation largely focused on cortisol activity throughout the day whereas the reactivity of the HPA axis in a stressor paradigm remains a largely unstudied phenomenon in antisocial youth. Further study of both diurnal activity as well as acute stress reactivity can help better characterize the multiple functions of the HPA axis in youth with CU traits.

Recommendations for future research center on extending further examination of the neurobiological processes in callous males and females. The present results are in line with previous findings from a study of incarcerated adolescent boys high in CU traits (Gostisha *et al*., in preparation). High morning levels were a robust finding among the boys of that study as was the case with the girls of the present study. Also common to the HPA axis functioning of callous youth of both genders was an intact CAR. Finally, flat diurnal rhythms were associated with high levels of CU traits among both genders (though the presence of high or lower levels of stress modulated the degree of flatness in some findings). Thus the girls with extremely high CU traits in the present study had remarkably similar HPA components to corollary CU boys when these three HPA components are considered. The ACM framework predicts gender differences in the responsivity of males and females in the Unemotional profile and it may be that methodological differences between the two studies account for some of the lack of hyporesponsivity of morning levels on the part of callous boys, and a less responsive diurnal rhythm among callous girls. The similar findings in both genders highlight the importance of continued research on neuroendocrine function as a potential biomarker for CU traits as well as the role of stress exposure in the development of these similar neuroendocrine patterns.

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Vita

The author was born in Wausau, WI. He obtained his Bachelor's degree in Psychology from the University of Wisconsin-Madison in 2008. He joined the University of New Orleans Applied Biopsychology graduate program in 2009. Under the mentorship of Dr. Elizabeth Shirtcliff, he pursued the present research project and others in the field of developmental psychopathology with special emphasis on stress physiology in antisocial youth.