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Biological Correlates of Conduct Disorder and Callous-Unemotional Traits

Abstract

Callous-unemotional (CU) traits have been proposed to identify a unique subgroup of children with conduct disorder (CD). Little is known, however, about the biological correlates of these traits. In addition, research into the biological correlates of CD has been mixed. This dissertation tested the hypothesis that CU traits moderate the relationship between CD and biological indicators of activity in the central nervous system, the autonomic nervous system, and the hypothalamic-pituitary-adrenal (HPA) axis. Specifically, CU traits were expected to be associated with decreased arousal at rest and in response to stress, whereas it was predicted that symptoms of CD would be associated with decreased arousal at rest and increased arousal in response to stress. These hypotheses were tested in a community sample of 11-12 year old children (N = 446). Symptoms of CD were assessed using child- and caregiver-report, and both the child and the caregiver reported on levels of CU traits using the Antisocial Process Screening Device (APSD). Section 1 focused on electroencephalography (EEG) recorded during an eyes-open rest period. CU traits were associated with a marginally significant increase in theta power in African American participants. In participants of other races, CU traits predicted significantly decreased theta, alpha, and beta power. CD was not significantly associated with EEG in any frequency band. Section 2 examined heart rate (HR) and skin conductance level (SCL) at rest and in response to a modified version of the Trier Social Stress Test (TSST). Heart rate was negatively associated with CU traits, but it was not significantly associated with symptoms of CD. CD symptoms and CU traits interacted to predict SCL such that CD was negatively associated with SCL, but only in the context of low levels of CU traits. Section 3 investigated cortisol response to the TSST. Results indicated that CD was positively associated with total cortisol production (as measured by area under the curve with respect to ground [AUCG]), whereas CU traits were negatively associated with AUCG at a trend level. Overall, these results suggest that the biological correlates of CU traits differ from those of CD as a whole, with CU traits being associated with hypoarousal and CD symptoms being associated with a pattern indicating impulsivity. These divergent results for CD and CU may imply that children with CD who are high in CU traits have different treatment needs compared to children with CD who are low in CU traits.

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BIOLOGICAL CORRELATES OF CONDUCT DISORDER AND CALLOUS-
UNEMOTIONAL TRAITS

Anna S. Rudo-Hutt

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ABSTRACT

BIOLOGICAL CORRELATES OF CONDUCT DISORDER AND CALLOUS- UNEMOTIONAL TRAITS

Anna S. Rudo-Hutt, M.A.

Adrian Raine, D.Phil.

Callous-unemotional (CU) traits have been proposed to identify a unique subgroup of children with conduct disorder (CD). Little is known, however, about the biological correlates of these traits. In addition, research into the biological correlates of CD has been mixed. This dissertation tested the hypothesis that CU traits moderate the relationship between CD and biological indicators of activity in the central nervous system, the autonomic nervous system, and the hypothalamic-pituitary-adrenal (HPA) axis. Specifically, CU traits were expected to be associated with decreased arousal at rest and in response to stress, whereas it was predicted that symptoms of CD would be associated with decreased arousal at rest and increased arousal in response to stress. These hypotheses were tested in a community sample of 11-12 year old children (N = 446). Symptoms of CD were assessed using child- and caregiver-report, and both the child and the caregiver reported on levels of CU traits using the Antisocial Process Screening Device (APSD). Section 1 focused on electroencephalography (EEG) recorded during an eyes-open rest period. CU traits were associated with a marginally significant increase in theta power in African American participants. In participants of other races, CU traits predicted significantly decreased theta, alpha, and beta power. CD was not significantly associated with EEG in any frequency band. Section 2 examined heart rate

(HR) and skin conductance level (SCL) at rest and in response to a modified version of the Trier Social Stress Test (TSST). Heart rate was negatively associated with CU traits, but it was not significantly associated with symptoms of CD. CD symptoms and CU traits interacted to predict SCL such that CD was negatively associated with SCL, but only in the context of low levels of CU traits. Section 3 investigated cortisol response to the TSST. Results indicated that CD was positively associated with total cortisol production (as measured by area under the curve with respect to ground [AUC_G]), whereas CU traits were negatively associated with AUC_G at a trend level. Overall, these results suggest that the biological correlates of CU traits differ from those of CD as a whole, with CU traits being associated with hypoarousal and CD symptoms being associated with a pattern indicating impulsivity. These divergent results for CD and CU may imply that children with CD who are high in CU traits have different treatment needs compared to children with CD who are low in CU traits.

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GENERAL INTRODUCTION

Conduct Disorder: A Heterogeneous Construct

Conduct disorder (CD) is a disruptive behavior disorder characterized by violation of societal rules and the rights of others. It is a costly disorder, both for the affected individual and society. Not only is a diagnosis of CD associated with concurrent impairment such as substance use and failure to complete high school, it also predicts lifelong criminal and antisocial behavior, psychopathology, poverty, and other poor life outcomes (Loeber et al., 2000; Odgers et al., 2008). Scott, Knapp, Henderson, and Maughan (2001) calculated that the cost to society of children with CD is at least ten times that of children without behavioral problems. Thus, prevention and treatment of CD has been a priority of both clinical psychologists and criminologists.

Complicating the matter of treating CD is the observation that CD encompasses a heterogeneous population of disordered children. As laid out by the American Psychiatric Association's (APA) Diagnostic and Statistical Manual of Mental Disorders (DSM-5), the symptoms of CD fall into four clusters: aggression to people and animals (e.g., fighting, using a weapon, cruelty to animals); destruction of property (e.g., fire setting); deceitfulness or theft (e.g., conning others, shoplifting); and serious violations of rules (e.g., truancy, running away from home; APA, 2013). Given that a diagnosis of CD only requires that three of 15 symptoms be present in the past 12 months, it is clear that children and adolescents with CD can vary greatly from one another. For instance, it is possible for a child with purely aggressive symptoms to be diagnosed with CD, whereas another child may only engage in status violations (i.e., staying out past curfew, truancy, and running away). The causal factors, behavioral profiles, and treatment options are

likely to differ significantly between these two children. This hypothetical scenario reflects what has been found in studies of children with CD. Analyses of the structure of CD symptoms suggest that they cluster into at least two groups, aggressive versus rule-breaking (Bezdjian et al., 2011).

Subtypes of Conduct Disorder

In order to better characterize the features of CD, and thus improve diagnostic accuracy and treatment planning, several different subtyping schemes have been proposed over the years for inclusion in the DSM. One such scheme, meant to differentiate between children who display psychopathic-like symptoms (“undersocialized”) and those who do not (“socialized”), was incorporated into DSM-III (APA, 1980). Unfortunately, this early attempt at identifying psychopathic features was hindered by confusion over the core features by which undersocialized CD should be identified (Frick & Moffitt, 2010), and this subtyping scheme was not included in the DSM-IV criteria for CD. In DSM-IV, the subtypes of childhood-onset (i.e., symptoms present before age 10) and adolescent-onset were added to the criteria for CD. There is evidence that childhood-onset CD is more severe and more persistent than adolescent-onset CD, and different risk factors have been associated with each subtype (Frick, 2006). These subtypes appear to be useful in treatment planning, with some evidence that addressing neuropsychological deficits is more helpful for childhood-onset CD, whereas improving parent supervision and reducing contact with deviant peers may be more efficacious for adolescent-onset CD (Barry, Golmaryami, Rivera-Hudson, & Rick, 2013).

These subtypes do not capture the observation that psychopathic traits may be present in some children with CD, however. Recently, an accumulation of research

evidence has resulted in the addition of callous-unemotional (CU) traits (labeled as “with limited prosocial emotions”) as a specifier for CD in the DSM-5 (APA, 2013). Unlike the undersocialized subtype of CD in DSM-III, CU traits represent a more direct extension of the affective/interpersonal component of psychopathy, usually only identified in adults, to child and adolescent populations. According to DSM-5 criteria for the specifier, CU traits are indicated by the presence of at least two of the following symptoms: lack of remorse or guilt, callous-lack of empathy, unconcerned about performance, and shallow or deficient affect (APA, 2013).

A number of findings support the incremental validity of CU traits. First, these traits appear to identify a particularly severe and violent form of CD. For instance, CU traits predict greater self-reported delinquency and police contacts (Frick, Stickle, Dandreaux, Farrell, & Kimonis, 2005), a relationship that remains significant even after controlling for initial severity of CD symptoms (Rowe et al., 2010). Another study found that, when adolescent offenders were compared, violent sex offenders had higher levels of CU traits compared to violent non-sex offenders and non-violent (property or drug) offenders (Caputo, Frick, & Brodsky, 1999). Second, youths with CD who are high in CU traits (callous CD) show greater stability of CD symptoms over time, as shown by studies which measured CD symptoms over three-year (Moran et al., 2009; Rowe et al., 2010) and four-year periods (Frick et al., 2005). Third, the findings cited above appear to hold, albeit in a weaker form, in youths who are high in CU traits but who do not have a diagnosis of CD (callous-only). For example, Frick and colleagues (2005) found that a callous-only group of youths consistently reported higher levels of drug and property delinquency than youths who met criteria for CD but who did not have CU traits (CD-

only) at all time-points, and Rowe et al. (2010) reported that callous-only children had higher rates of mental disorders and police contact than healthy control children three years after their initial screening. Thus, not only do CU traits appear to predict more severe and long-lasting problems in youths with CD, they may also lead to poorer long-term functioning in children without CD.

Despite these suggestive results, it is not yet clear whether CU traits identify a qualitatively different group of CD youths. Indeed, an alternate interpretation of these findings could be that CU traits simply describe a more severe form of CD. Furthermore, some evidence suggests that CU traits are more common among individuals with childhood-onset CD (Frick & Ellis, 1999; Rowe et al., 2010), which begs the question of whether CU traits provide any additional information. Therefore, evidence other than severity and chronicity of symptoms would be helpful in clarifying the utility of the CU specifier.

Biological Correlates of CD and CU Traits

One source of clarification regarding the relationship between CD and CU traits is the biological correlates of each. If CU traits identify a subset of children with CD who are in some way distinct from other children with CD, it seems that this distinction could be present in the biological correlates of CU traits, especially given that researchers have long argued that psychopathy reflects different developmental precursors and pathways than antisocial behavior in general (Blair, Peschardt, Budhani, Mitchell, & Pine, 2006; Frick, 2006). Blair (2008) has articulated an emotional deficit model of psychopathy, wherein dysfunctions in the amygdala and ventromedial prefrontal cortex cause impairment in emotional learning and responding to expressions of fear and sadness.

Evidence for this model includes reduced autonomic arousal to distress cues and poor conditioning of autonomic responses to aversive stimuli in psychopathic samples (Blair, 2008; Flor et al., 2002).

There is evidence for reduced psychophysiological arousal in children with CD without regard to CU traits. However, the literature on psychophysiological reactivity to noxious stimuli is varied, with some authors reporting increased reactivity (e.g., Crozier et al., 2008) and others reporting decreased reactivity (e.g., De Wied et al., 2009) compared to controls. The variability in these results may reflect the unaccounted influence of CU traits on psychophysiological responding. If CU traits were found to moderate the relationship between CD and physiological reactivity to negative stimuli, the case for CU traits as a specifier for CD would be bolstered.

This Dissertation

This dissertation presents the results of a series of investigations into the biological correlates of CD and CU traits in a sample of 11-year-old children. Three major biological systems are surveyed in these studies, including the central nervous system (via electroencephalography) and the two stress response systems, the autonomic nervous system (via heart rate and skin conductance level) and the hypothalamic-pituitary-adrenal (HPA) axis (via cortisol). The goal of each of these studies was to examine whether there is evidence for the contention that CU traits identify a group of children who are qualitatively distinct from children with CD who do not have CU traits.

SECTION 1: ELECTROCORTICAL ACTIVITY IN CONDUCT DISORDER AND CALLOUS-UNEMOTIONAL TRAITS

Abstract

Previous studies have found an association between decreased cortical arousal (as measured by electroencephalography [EEG]) and antisocial behavior, including conduct disorder (CD). A recent meta-analysis suggests that significant heterogeneity exists in the current literature that cannot be completely accounted for by previously measured factors. The present study tested the hypothesis that the association between cortical arousal and symptoms of CD would be moderated by the presence of callous-unemotional (CU) traits in a sample of community-residing children. EEG was recorded in 11-12 year old children (N=446) during an eyes-open resting baseline. Symptoms of CD were assessed using child- and caregiver-report, and both the child and the caregiver reported on levels of CU traits using the Antisocial Process Screening Device (APSD). CU traits were associated with a marginally significant increase in theta power in African American participants. In participants of other races, CU traits predicted significantly decreased theta, alpha, and beta power. By contrast, symptoms of CD were not significantly associated with EEG in any frequency band. Results are interpreted in relation to the hypoarousal theory of antisocial behavior.

Electrocortical Activity in Conduct Disorder and Callous-Unemotional Traits

Introduction

Electroencephalography (EEG), a measure of electrical potential on the scalp that is produced by neuronal activity, has been investigated as a potential marker of abnormal brain activity in aggressive and delinquent populations. Electrocortical activity changes with age, level of arousal, and attentional processes, among other things, and thus may provide insight into what biological processes are associated with antisocial behavior. The EEG waveform can be classified according to activity within several frequency bands, which can be broadly categorized as slow-wave (delta [generally below 4 Hz] and theta [4-8 Hz]) or fast-wave (alpha [8-12 Hz], beta [12-30 Hz] and gamma [above 30 Hz]) activity. The different frequency bands have been shown to be associated with different mental and physiological states: delta waves are predominant during deep sleep; theta waves are associated with intake of sensory information and spatial memory; alpha waves are common during wakeful relaxation and are thought to be related to decreased cortical activity; beta waves are indicative of increased activation and arousal; and gamma waves correlate with alertness and often occur after sensory stimulation (Colgin, 2013; Hugdahl, 2001; Hughes, 2008).

Studies examining EEG activity in children with conduct problems have found increased slow-wave (delta and theta) activity (Coble et al., 1984; Knyazev, Slobodskaya, Aftanas, & Savina, 2002; Knyazev et al., 2003; Raine, Venables, & Williams, 1990) and decreased activity in higher frequency bands (alpha, beta, and gamma; Gilmore, Malone, & Iacono, 2010; Knyazev et al., 2002; Knyazev et al., 2003; Rudo-Hutt, 2008; Surface, 1995). In a recent meta-analysis, externalizing disorders in general (including CD,

oppositional defiant disorder, attention deficit/hyperactivity disorder, antisocial personality disorder, psychopathy, and criminal behavior in adults or children) were found to be associated with increased slow-wave (delta and theta) and decreased fast-wave (alpha and beta) EEG activity at rest (Rudo-Hutt, under review). However, heterogeneity within studies of EEG in externalizing disorders was high, and none of the moderators tested (including sex, age, and attention problems vs. other externalizing problems) could fully account for this heterogeneity.

Hypotheses regarding the interpretation of these differences in EEG activity seen in externalizing populations may shed some light on the source of this heterogeneity. Historically, these findings with EEG and other findings involving decreased autonomic nervous system arousal (e.g., low heart rate) have been interpreted as indicating low physiological arousal. According to the hypoarousal theory, chronically low arousal may predispose to stimulation-seeking via aggressive and antisocial behavior (Quay, 1965) or fearlessness in the face of dangerous and criminal activities (Raine, 2002). An alternative explanation for alterations in electrocortical activity has also been proposed: that increased slow-wave and decreased fast-wave EEG reflects cortical immaturity or delayed maturation. This hypothesis arises from the observation that EEG activity shifts toward higher frequencies with age (Banaschewski & Brandeis, 2007; Barry & Clarke, 2009). At present it is unclear which of these hypotheses fully account for the data.

Electrocortical Activity and Callous-Unemotional Traits

While it remains unclear whether hypoarousal or delayed maturation accounts for the EEG findings in antisocial populations, there is a possible explanation for the heterogeneity in effects seen across the studies included in the aforementioned meta-

analysis (Rudo-Hutt, under review). This possibility is that low overall physiological arousal, as captured by increased delta and theta power, may be more common in those with CD or aggressive behavior alone, but that psychopathic or callous-unemotional (CU) traits would be associated with low fear or emotional insensitivity, as shown by decreased beta activity. This hypothesis draws from the work of Christopher Patrick and colleagues, who have argued that “meanness,” or callousness, is a phenotypic expression of underlying, genotypic fearlessness (Patrick, Fowles, & Krueger, 2009), and that the difference between psychopathy and antisocial personality disorder in adults is the presence of fearlessness in the former, in addition to the impulse control difficulties seen in both disorders (Drislane, Vaidyanathan, & Patrick, 2013). Therefore, the heterogeneity seen in the EEG activity across studies of children with CD may be at least partially accounted for by the level of CU traits found in the participants of these studies.

At present, there are little data available to illuminate this possibility. There appear to be no published studies of EEG power in children or adolescents with CU traits, and there are very few studies of EEG and psychopathic traits in adults. In contrast to the data reviewed above for externalizing disorders in general, two studies from the 1970s suggest a decrease, rather than an increase, in slow-wave power in psychopathic adults (Blackburn, 1979; Syndulko, Parker, Jens, Maltzman, & Ziskind, 1975). These findings in adults would support the hypothesis that psychopathy, and therefore CU traits, may not follow the same pattern of increased slow-wave activity seen in most forms of externalizing behavior.

The only study of psychopathic traits in children and EEG that could be located measured alpha asymmetry (the difference in alpha activity between the right and left

hemispheres of the brain) and found that boys who were high in externalizing symptoms and psychopathic traits had greater relative right frontal alpha activity and greater relative left parietal alpha activity than controls (Crowley, 2004). This study also included a group of boys with conduct problems who were low in psychopathic traits, and the author found that these boys showed this same pattern (i.e., greater right hemisphere alpha power) at frontal leads but did not differ from controls on parietal alpha asymmetry. Crowley (2004) interpreted the frontal alpha asymmetry in both of these groups as reflecting increased approach motivation, and he noted that high left parietal alpha power, as seen in the boys with psychopathic traits, has been associated with anxious arousal. It is important to emphasize that the measure of electrocortical activity used in this study (alpha asymmetry) is distinct from the measures of total EEG power in each frequency bands and is thus not directly comparable to the literature cited above. Overall, however, the studies conducted to date would suggest that, unlike other forms of antisocial behavior, psychopathic traits may be associated with increased, rather than decreased, arousal.

Rationale and Hypotheses for the Current Study

The relative dearth of studies on EEG activity in CD as well as the unexplained heterogeneity in the results of the studies that have been conducted suggests that research into distinctions among children with CD may be helpful. Furthermore, participants in previous studies of CD have been mostly male, and thus it is unclear whether this research generalizes to females. In addition, aside from one study of alpha asymmetry in children, there appear to be no studies analyzing the relationship between EEG activity and CU or psychopathic traits in children. This study tests the hypothesis that the

unaccounted presence of CU traits in CD samples has contributed to inconsistencies in the psychophysiological literature and interfered with appropriate interpretation of the data. Specifically, the hypotheses for the current study were that, during rest, symptoms of CD would be associated with increased delta and theta activity (i.e., decreased arousal) and CU traits would be associated with decreased beta activity (i.e., decreased emotional sensitivity/fear).

Method

Participants

Participants were recruited as part of a larger study of the biopsychosocial bases of childhood aggression. An effort was made to recruit participants from five counties in Southeast Pennsylvania which include a range of neighborhood characteristics (e.g., urban, suburban, rural; socioeconomic status; school systems; community resources; racial/ethnic groups; family structures). Census data were used to define communities at the zip code level for the catchment area. From this population of communities, a subset of zip code areas was randomly selected such that those randomly selected zip code communities were likely to represent the larger population of communities. We saturated schools, churches, health care providers, and other community organizations within these selected areas with fliers to solicit enrollment of parents who identified their children as prone to conduct problems. Additionally, advertisements inviting parents of 11-year-old children to participate in the study were placed in local newspapers and public transportation vehicles. Eligible child participants were fluent speakers of English, could provide informed assent, and had a caregiver who would participate along with the youth and who was able to give informed consent. Exclusion criteria included: 1) a diagnosed

psychotic disorder; 2) mental retardation; 3) a pervasive developmental disorder; 4) current treatment with psychiatric medication; 5) current treatment with a medication which alters hormone levels. Further details of recruitment and study procedures can be found in Liu et al. (2013) and Richmond, Cheney, Soyfer, Kimmel, and Raine (2013).

The final sample of participants included 446 11-year-old children (220 girls), of whom there were 358 African American, 53 European American, 22 multiracial, and 9 other race participants, as well as 4 children of Hispanic ethnicity. See Table 1 for further characteristics of the sample.

Measures

Conduct and Oppositional Defiant Disorder Questionnaire. Symptoms of CD were assessed using the Conduct and Oppositional Defiant Disorder questionnaire (COD; Raine, 2008), administered separately to the caregiver and child. The COD is a 26-item, paper-pencil questionnaire developed by the principal investigator on the study (A. Raine) to assess DSM-IV symptoms of disruptive behavior disorders (a copy of the questionnaire is available upon request). Each item on the CD portion of the COD asks how frequently each symptom of CD would describe the target child (rated as “never,” “sometimes,” or “often”). Following the recommendations for combining parent and child data for other diagnostic measures (Piacentini, Cohen, & Cohen, 1992; Shaffer, Fisher, Lucas, Dulcan, & Schwab-Stone, 2000), and because children may report behaviors of which their caregivers are unaware (Molina et al., 2007), children were considered to have a symptom of CD if either the child or the caregiver endorsed the symptom, and the higher score for each item (given by either the child or the parent) was used for each child. In this sample, parent and child ratings for the CD items of the COD

were moderately correlated ($r = .34, p < .001$), which is commensurate with cross-informant agreement for other measures of child psychopathology (see, e.g., Althoff, Rettew, Ayer, & Hudziak, 2010; Youngstrom, Loeber, & Stouthamer-Loeber, 2000). The score from each CD item of the COD was added to create a total CD COD score for each child. Note that a diagnosis of CD requires the presence of at least three symptoms of CD (APA, 2013), and that a COD score of 6 would correspond to the child or parent reporting that the child displays at least three symptoms of CD “often” or up to six symptoms of CD “sometimes.” Approximately one-third (33.9%) of the participants included in this analysis scored 6 or higher on the COD.¹

Antisocial Process Screening Device. Callous-unemotional traits were assessed using the parent and self-report versions of the Antisocial Process Screening Device (APSD; Frick & Hare, 2001). The APSD was used to develop draft criteria for the DSM-5 CU specifier for CD (Frick & Moffitt, 2010). It is intended for use with children ages 6 to 13 years and can be completed by a parent, teacher, or child. Each item of the APSD asks the rater whether a given trait is “not at all true,” “sometimes true,” or “definitely true” of the target child. As recommended by the authors, parent and child scores were combined by using the higher score from either report for each item (Frick, Cornell, Bodin, Dane, Barry, & Loney, 2003). In this sample, parent and child ratings on the APSD were moderately correlated ($r = .26, p < .001$). The total score used in the analysis was the sum of the scores from each of the six items comprising the Callous-Unemotional (CU) dimension of the APSD. Although there are no strict guidelines as to when a child might be considered to have a high score on the APSD, a cluster-analysis performed on a

¹ Caregivers also reported symptoms of CD on the Diagnostic Interview Schedule for Children (DISC; see below) but the COD was used in these analyses in order to include information from both caregivers and children. On the DISC, 10.6% of the children in this sample met full criteria for CD in the past year.

community sample of third to seventh grade children by Frick, Bodin, and Barry (2000) identified approximately 14% of these children as belonging to a “high psychopathy” group. This group had a mean score of 7.9 on the CU dimension of the APSD. Of the participants included in this study, 17.8% scored an 8 or higher on the CU dimension of the APSD.

Diagnostic Interview Schedule for Children. Attention-deficit/hyperactivity disorder (ADHD) is frequently comorbid with CD (Waschbusch, 2002) and has previously been shown to be associated with increased theta power and decreased beta power (Arns, Conners, & Kraemer, 2012; Boutros, Fraenkel, & Feingold, 2005). Therefore, ADHD was included as a potential covariate in the current study. Symptoms of ADHD were assessed using the National Institute of Mental Health Diagnostic Interview Schedule for Children – Version IV (NIMH DISC – IV; Shaffer et al., 2000). The DISC is a structured interview designed to diagnose common DSM-IV mental disorders in children and adolescents. The interview can be administered by lay interviewers who have had brief training in use of the DISC, and it has parallel parent and child versions. The current study used parent report only. One year test-retest reliability of DISC diagnoses of ADHD based on parent report has been estimated to be high ($\kappa = 0.79$; Shaffer et al., 2000). On the DISC, 15.9% of the children in this sample met full criteria for ADHD (any type) in the past year.

Child Behavior Checklist/Youth Self-Report. Internalizing psychopathology was included as a covariate due to reports that internalizing symptoms are associated with altered EEG activity, as shown by increased beta power (Begić, Hotujac, & Jokić-Begić, 2001; Cornelius, Schulz, Brenner, Soloff, & Ulrich, 1988; Jokić-Begić & Begić, 2003).

Children and their caregivers reported on emotional and behavioral problems via the Youth Self-Report (YSR) and the Child Behavior Checklist (CBCL), respectively (Achenbach & Rescorla, 2001). The YSR is a paper-pencil measure that can be completed by children ages 11-16 years. It consists of 112 items describing problem behaviors, which can be rated as “not true,” “somewhat or sometimes true,” or “very true or often true” of the child. The CBCL is a paper-pencil measure designed to be completed by parents or guardians of children ages 6-18 years. It includes 113 items with the same rating scale as the YSR. Several scales and subscales can be calculated from the YSR and CBCL, including internalizing, externalizing, eight empirically-derived symptom subscales, and six scales corresponding roughly to disorders defined in the DSM. Only the internalizing scale was used in the current study. The CBCL and YSR are widely used in the literature and have been found to have good reliability and validity (Ang et al., 2012; Achenbach, Dumenci, & Rescorla, 2002; Stanger, McConaughy, & Achenbach, 1992). For the current analyses, CBCL/YSR internalizing T-scores were combined by taking the maximum value reported by either parent or child. Individual item scores were not readily available from the CBCL/YSR scoring software for combination.

Procedure and Psychophysiology Recording

Children and their caregivers arrived at the laboratory at approximately 9:00 am on the day of testing. Tasks in the morning included a blood draw (child), fMRI scan (child), and completion of questionnaires (child and caregiver). At approximately 11:30 am, children were prepared for a psychophysiology assessment. Electroencephalographic activity was recorded during an eyes-open resting period during which participants were asked to remain as still as possible and fix their eyes on a point on the computer screen in

front of them for two minutes. The laboratory was sound-proofed and air-conditioned to 72° F in order to ensure consistent psychophysiology recording.

The EEG data were collected as part of a larger psychophysiological battery in which electrocardiography and skin conductance were also measured. All psychophysiological data were acquired using a Biopac MP150 with *AcqKnowledge* version 4.1 software (Biopac Systems, Inc.). Electroencephalographic activity was recorded using an Electro-Cap (Electro-Cap International [ECI]) with tin (Sn) electrodes at the following sites, placed in accordance with the International 10-20 system: FP1, FP2, F3, F4, F7, F8, P3, P4, T3, T4, O1, and O2. Each electrode was amplified using a single-channel EEG100C biopotential module (Biopac Systems, Inc.). The EEG signal was referenced to linked earlobes (via 9 mm Sn cup electrodes) and grounded via 8 mm diameter silver/silver chloride (Ag/AgCl) electrodes attached to the distal phalanges of the first and second fingers of the non-dominant hand (which were also used to record skin conductance). In addition, an electrooculograph (EOG) channel monitored vertical eye movement via 4 mm diameter Ag/AgCl electrodes placed above and below the supra- and infra-orbital ridges of the left eye. A Q-tip stick was used to abrade the scalp electrode sites. Skin on the earlobes and around the left eye was prepared using NuPrep abrasive skin prepping paste. Biopac isotonic recording gel was used as the electrolyte medium for EOG, and Electro-gel was used for the earlobes and scalp. Impedance was monitored using a UFI Checktrode impedance meter (Morro Bay, CA). Impedance for EEG was kept below 10 k Ω and was under 5 k Ω for most participants, while impedance for EOG and ear electrodes was kept below 20 k Ω . Data from EEG channels were recorded using a bandpass of 0.01-35 Hz, 60 Hz notch filter, 500 Hz sampling rate, and

gain set to 5000. Data from the EOG channel were recording using a bandpass of 0.05-35 Hz, 60 Hz notch filter, 500 Hz sampling rate, and gain set to 1000.

Data from each EEG channel were visually inspected in *AcqKnowledge* in order to identify data that were artifactual due to equipment failure; these data were removed from further analysis. Processing of the EEG data was done in MATLAB (MathWorks) using custom scripts. Remaining artifacts were removed by rejecting EEG epochs that exceeded $\pm 80 \mu\text{V}$, and a fast-Fourier transform was used to average power into frequency bands for each electrode site as follows: delta, 0.5-4 Hz; theta, 4-8 Hz; alpha, 8-13 Hz; beta, 13-30 Hz; gamma, 36-44 Hz. Power in each frequency band was averaged over the entire resting period.

Data Reduction and Statistical Analysis

As is often the case with EEG data, the EEG power values were positively skewed, so a natural logarithm transformation was applied prior to statistical analysis. In order to reduce collinearity, the variables for CD symptoms, CU traits, ADHD symptoms, and internalizing were mean-centered. Participant age, sex, and race were included as covariates in the analysis. Due to the fact that African American participants comprised approximately 80% of the participants and no other racial/ethnic group made up more than 12% of the sample, race was dichotomized into African American versus other race. For the purposes of the present analysis, EEG power for the twelve electrodes was averaged into two regions, anterior (FP1, FP2, F3, F4, F7, and F8) and posterior (P3, P4, T3, T4, O1, and O2), in order to reduce the need to correct for multiple comparisons. EEG activity was analyzed with multilevel modeling using linear mixed models in SPSS (IBM, version 20.0). Multilevel modeling was chosen for this analysis due to its ability to

include participants with incomplete data and to account for the possibility of correlated residuals, a significant concern when analyzing data such as EEG which is correlated within region and frequency band.

Potential outliers were handled using a series of steps recommended by Aguinis, Gottredson, and Joo (2013). First, boxplots were visually inspected to identify possible error outliers, and any errors were fixed by referencing raw data. Next, cases with EEG data > 2.24 SD away from the mean for each frequency band were flagged as potential outliers². These potential outliers were then tested for their influence on the multilevel models by removing each potential outlier, one-by-one, and examining whether they significantly impacted model fit. In addition, potential outliers which did not impact model fit were tested further to see if they were prediction outliers by calculating their DFFITS, Cook's distance, and DFBETAS values in a regression of the model predictors on HR and/or SCL. Values were considered prediction outliers if one of the following criteria was met: 1) $DFFITS > +/- 2\sqrt{\left(\frac{k+1}{n}\right)}$, where k = number of predictors and n = number of observations; 2) Cook's distance significant under the F distribution with $df = (k+1, n - k - 1)$ and $\alpha = .50$; or 3) $DFBETAS > +/- 2\sqrt{n}$. Results are presented for the multilevel models without model fit and prediction outliers; results with the outliers are available upon request. A total of 18 data points, from 16 participants, were identified as outliers.

² Aguinis et al. (2013) recommend using a cutoff of 2.24 SD because this criterion identifies observations in the top and bottom 2.5% of a normal distribution, which they consider sufficiently unlikely to warrant further investigation as potential outliers.

After discarding data compromised by excessive participant movement and/or equipment failure, EEG data were available for 410 children³ (i.e., approximately 8.1% of the EEG data were discarded). Children with EEG data available did not differ from the total sample on age, sex, race, CD symptoms, CU traits, internalizing, or ADHD symptoms (all $ps > .34$).

Participant was included as a level 1 predictor of EEG power, with region (anterior, posterior) and frequency band (delta, theta, alpha, beta, gamma) repeated within participants. Level 2 predictors (CD symptoms, CU traits, ADHD symptoms, internalizing score, age, sex, and race) were added to the model sequentially as fixed effects (main effects and interactions). The covariates added in Level 2 were chosen based on their significant bivariate correlations with EEG activity. As recommended by Field (2009), these predictors were retained in the model if they significantly improved model fit, and each of the predictors was added as a random effect if it significantly improved model fit, as measured by the change in the $-2 \times \log$ likelihood of the model. The $-2 \times \log$ likelihood has the same distribution as χ^2 and can be tested for significance using the critical values for χ^2 with degrees of freedom = $df_{\text{model 2}} - df_{\text{model 1}}$.

After the final model was fit to the data, statistically significant ($p < .05$) and trend-level ($p < .10$) interactions were broken down by conducting separate multilevel models for each level of the categorical variable involved in each interaction. For example, in cases where frequency band interacted with one of the other terms in the model, separate multilevel models were run for each frequency band, where the model in each case was the same as the main model except that frequency band was removed as a

³ This includes the 16 children who had outlying data, as they had some data points (i.e., from the other region/frequency bands) that were not outliers.

main effect and interaction term. For the final model, the pseudo- R^2 statistic was calculated as a measure of global effect size. More commonly used effect size statistics, such as Cohen's d or R^2 , are not appropriate for multilevel models (Peugh, 2010). Following Peugh (2010), pseudo- R^2 was calculated by using the regression coefficients produced by the final model to obtain predicted EEG values for each participant, correlating these predicted values with observed values, and squaring the result. The pseudo- R^2 can be interpreted as the proportion of variance in EEG power that can be accounted for by the predictor variables in the final model (Peugh, 2010).

Results

Zero-Order Correlations

As expected, there were strong positive correlations among CD symptoms, CU traits, and ADHD (see Table 2). There was also a strong positive correlation between CD symptoms and internalizing, and there was a weaker but still significant positive correlation between CU traits and internalizing. When symptoms of CD were controlled, however, the partial correlation between CU traits and internalizing fell to non-significance, $r(418) = .02, p = .683$. In contrast, controlling for CU traits, sex, age, race, and ADHD symptoms did not greatly diminish the significant positive correlation between CD and internalizing, $r(405) = .29, p < .001$. Therefore, it is clear that the apparent positive relationship between CU traits and internalizing is accounted for by their shared relationship with CD symptoms. The measures of EEG power in each frequency band were strongly and positively correlated with each other, although the correlation of gamma power with the other frequency bands was somewhat weaker.

Multilevel Model Predicting EEG

The final model included region, frequency band, CD symptoms, CU traits, ADHD symptoms, internalizing, sex, CD symptoms \times CU traits, age \times frequency band \times region, sex \times frequency band \times region, and CU traits \times race \times frequency band as fixed effect predictors of EEG power (see Table 3 for parameter estimates). The pseudo- R^2 statistic indicated that the predictors included in the final model accounted for 69.6% of the variance in EEG power.

Conduct Disorder Symptoms

As a main effect, symptoms of CD did not significantly predict EEG in the full model, $F(1, 378.29) = 0.05, p = .945$. Furthermore, symptoms of CD did not significantly predict EEG power in any frequency band: for delta, $b = -0.003, t(361.48) = -0.47, p = .636$; theta, $b = -0.004, t(375.59) = -0.51, p = .608$; alpha, $b = -0.0004, t(375.53) = -0.04, p = .966$; beta, $b = -0.001, t(382.56) = -0.09, p = .924$; gamma, $b = 0.01, t(378.11) = 0.68, p = .495$.

Callous-Unemotional Traits

The interaction of CU traits, race, and frequency band significantly predicted EEG power, $F(1, 658.08) = 9.18, p = .003$. This interaction was broken down by first conducting separate multilevel models for each frequency band. These analyses showed that the interaction of CU traits and race was a significant predictor of theta ($F[1, 375.15] = 12.35, p < .001$), alpha ($F[1, 375.13] = 12.85, p < .001$), and beta power ($F[1, 380.20] = 8.87, p = 0.003$). The interaction of CU traits and race was also a marginally significant predictor of delta power ($F[1, 360.50] = 3.57, p = 0.060$). Neither CU traits alone nor the interaction of CU and race were significant predictors of gamma power, $F(1, 380.73) = 0.65, p = .419$, and $F(1, 379.05) = 1.84, p = .175$, respectively.

These interactions were broken down further by performing separate analyses for African American versus other race participants. The relationship between delta power and CU traits was not significant in African American participants ($b = 0.0001$, $t[286.20] = 0.01$, $p = .993$), but there was a marginally significant decrease in delta power in association with CU traits for other race participants ($b = -0.05$, $t[75.55] = -1.83$, $p = .071$). For theta power in African American participants, CU traits were associated with a marginally significant increase in theta power ($b = 0.03$, $t[299.82] = 1.84$, $p = .067$), but, in other race participants, CU traits predicted decreased theta power ($b = -0.08$, $t[75.88] = -2.34$, $p = .022$). The relationship between CU traits and alpha power was positive but not statistically significant for African American participants ($b = 0.02$, $t[300.04] = 1.20$, $p = .231$), but the relationship in other race participants was negative and significant ($b = -0.13$, $t[75.40] = -2.97$, $p = .004$). Beta power was not significantly associated with CU traits in African American participants ($b = -0.003$, $t[304.66] = -0.20$, $p = .843$), but there was a negative association in other race participants ($b = -0.08$, $t[77.39] = -2.50$, $p = .015$). See Figures 1 to 4.

Conduct Disorder × Callous-Unemotional Traits

The interaction between CD symptoms and CU traits was not a significant predictor of EEG, $F(1, 380.76) = 0.44$, $p = .505$. Nor was the interaction between CD symptoms and CU traits a significant predictor in any frequency band: for delta, $F(1, 359.88) = 0.30$, $p = .583$; theta, $F(1, 374.99) = 0.93$, $p = .335$; alpha, $F(1, 375.98) = 2.48$, $p = .116$; beta, $F(1, 379.05) = 0.09$, $p = .762$; gamma, $F(1, 374.62) = 0.10$, $p = .751$.

Covariates

ADHD symptoms did not significantly predict EEG power, $F(1, 376.36) = 1.26, p = .262$, nor did internalizing, $F(1, 382.42) = 0.63, p = .427$. Among the other covariates included in the model, frequency band ($F[1, 1053.26] = 8773.59, p < .001$), region ($F[1, 746.91] = 361.98, p < .001$), and age \times frequency band \times region ($F[1, 857.32] = 142.71, p < .001$) were significant predictors of EEG power. There was more total EEG power in the lower frequency bands ($b = -1.71, t[1053.26] = -93.67, p < .001$) and at anterior electrodes ($b = -0.55, t[746.91] = -19.03, p < .001$). Breaking down the interaction between age, frequency band, and region revealed that increased age was associated with decreased posterior delta power ($b = -0.08, t[338.00] = -1.97, p = .050$).

Discussion

Overall, EEG activity was more strongly linked to level of CU traits than to symptoms of CD. However, the relationship between CU traits and EEG activity varied greatly by race. That is, in African American participants, CU traits were marginally associated with increased theta power and a tendency toward higher alpha power, whereas in other race participants, CU traits predicted lower levels of delta, theta, alpha, and beta power. These results suggest that the unaccounted presence of both CU traits and race have contributed to the significant heterogeneity seen in the literature on EEG and antisocial behavior.

The trend toward increased theta power seen in African American participants who were high in CU traits suggests that these children are experiencing lower levels of arousal compared to their peers, given that theta waves are associated with drowsiness and low arousal at rest (Hugdahl, 2001). The pattern of increased theta activity found in African American children with high levels of CU traits is striking in its similarity to the

pattern long thought to be associated with ADHD (i.e., increased theta in comparison to beta; Barry & Clarke, 2009). The ratio of theta to beta power has long been a subject of interest in ADHD research, and an elevated theta/beta ratio at rest has been suggested as a marker of attention difficulties (see, e.g., Mann, Lubar, Zimmerman, Miller, & Muenchen, 1992). In fact, increased theta (slow-wave) activity has been proposed as a diagnostic test for ADHD (Boutros, Fraenkel, & Feingold, 2005), and the U.S. Food and Drug Administration recently approved the marketing of a device that purports to diagnose ADHD based on the theta/beta ratio (U.S. Food and Drug Administration, 2013). The results of the current study suggest that this movement is premature, given that CU traits may at least partially account for the findings in children with ADHD. There is evidence to suggest that CU traits may be increased in children with ADHD in comparison to typically-developing controls (Brammer & Lee, 2012; DeLisi et al., 2011; Haas et al., 2011), and some researchers have noted heterogeneity in the electrocortical activity seen in children with ADHD (see, e.g., Clarke et al., 2011). Indeed, as seen in Table 2, ADHD symptoms and CU traits were significantly and positively correlated in the current sample. It is therefore possible that previous studies identifying an increased theta/beta ratio as a biomarker for ADHD may have overlooked the role of CU traits in those findings.

In contrast, the findings of the current study for non-African American participants suggested a very different pattern of EEG activity in association with CU traits. The pattern of decreased delta, theta, alpha, and beta activity along with typical levels of gamma activity in non-African American children with CU traits may provide insight into what differentiates these children from their low callous counterparts. Delta

power increases during sleep, theta waves are associated with drowsiness and low arousal, alpha is more common when participants are resting with eyes-closed or during suppression of non-task-relevant brain activity, and beta waves increase during active cognitive processing and anxiety (Cooper, Croft, Dominey, Burgess, & Gruzelier, 2003; Hugdahl, 2001; Sokhadze, 2007). Thus, overall, these children may be experiencing increased arousal without feeling particularly anxious. These findings are similar to the reports of decreased slow-wave activity in adult psychopaths (Blackburn, 1979; Syndulko, Parker, Jens, Maltzman, & Ziskind, 1975).

It is unclear why the pattern of EEG activity associated with CU traits was so different for African American versus other race participants in this study. However, one possible reason for these differing patterns by race may be related to the fact that the African American participants were rated as having significantly more CU traits and symptoms of CD than the other race participants. It is therefore possible that the results among the African American participants may reflect the EEG patterns typical of more symptomatic children. However, Blackburn's (1979) study points to a different possibility. Blackburn (1979) found that primary psychopaths (i.e., those with low levels of anxiety) were characterized by decreased theta and alpha activity, whereas secondary psychopaths (i.e., those who have high levels of anxiety) produced increased levels of theta and alpha activity. In this sample, when looking at children in the top 50% on CU traits, African American participants were reported to have significantly lower levels of internalizing than participants of other races, which is counter to what would be expected based on Blackburn's (1979) results. However, the distinction between primary and secondary psychopathy highlights the importance of examining how CU traits are

measured and whether they are truly capturing what researchers mean to capture in a measure of callousness and unemotionality.

Limitations

There are some limitations to the present study that must be considered. First, the sample used in this study was a community sample and, as such, likely includes children whose symptoms are less severe than would be seen in a clinical sample. Second, as noted above, ratings of CU traits were significantly higher in African American than in other race participants. Given that different electrocortical correlates were associated with CU traits in African American versus other race participants, it is possible that the measurement of CU traits by the APSD may not be tapping equivalent processes in African American and non-African American participants. One study that addressed this possibility did not find that race moderated the relationship between CU traits and a variety of antisocial outcomes (McMahon, Witkiewitz, & Kotler, 2010), although this finding could reflect insufficient power to detect an interaction. It is also important to note that the sample of African American participants in the current study was much larger than the sample of non-African American children, thus making it difficult to compare across the two groups.

These limitations notwithstanding, the present study adds to the current literature in several ways. First, few studies of EEG in CD have been conducted and none appear to have investigated the EEG in the context of a potential interaction of CD with CU traits. In addition, many studies of CD include a majority or completely male sample, and this sample was evenly divided between boys and girls. Furthermore, the present study made

use of both parent and child report of CD symptoms and CU traits, which may provide a more accurate diagnostic picture of the child participants than using parent report alone.

Conclusions

In sum, the results of the current study provide mixed support for the hypoarousal theory of antisocial behavior. The theory received some support in that marginally increased theta activity was associated with higher levels of CU traits in African American participants, and these participants appear to represent children with more severe CU traits. However, CU traits predicted lower delta and theta activity in non-African American participants, which suggests increased, rather than decreased, arousal in these children. Furthermore, symptoms of CD were not significantly associated with EEG activity in any frequency band. Overall, these results suggest that some of the heterogeneity in past research may have arisen from the failure to consider CU traits and race as important predictors of electrocortical activity. Given that EEG activity is seen as having the potential to inform understanding of etiological pathways and prediction of treatment response (Banaschewski & Brandeis, 2007), it will be important for future investigations to consider the role of CU traits and race in antisocial behavior.

SECTION 2: AUTONOMIC NERVOUS SYSTEM ACTIVITY IN CONDUCT DISORDER AND CALLOUS-UNEMOTIONAL TRAITS

Abstract

Studies of autonomic nervous system (ANS) activity and reactivity in children with conduct disorder (CD) have produced mixed results. It is possible that these inconsistent results may be due to the unaccounted presence of callous-unemotional (CU) traits within the population of children with CD. The goal of the current study was to examine the relationships among CU traits, CD symptoms, and ANS activity in children. Heart rate (HR) and skin conductance level (SCL) were measured at rest and during a modified version of the Trier Social Stress Test (TSST) in a community sample of 11-year-old children (N = 446; 220 female). Symptoms of CD were assessed using child- and caregiver-report, and both the child and the caregiver reported on levels of CU traits using the Antisocial Process Screening Device (APSD). Heart rate was negatively associated with CU traits across tasks, but it was not significantly associated with symptoms of CD. Symptoms of CD and CU traits interacted to predict SCL such that CD was negatively associated with SCL, but only in the context of low levels of CU traits. Results are interpreted in relation to the hypoarousal theory of antisocial behavior and polyvagal theory.

Autonomic Nervous System Activity in Conduct Disorder and Callous-Unemotional Traits

Introduction

Decreased physiological arousal to stress, as measured by indicators of sympathetic nervous system activity, has frequently been associated with antisocial behavior. According to the hypoarousal theory of antisocial behavior, low physiological arousal leads to stimulation-seeking or fearlessness in the face of dangerous situations, thus encouraging involvement in rule-breaking and aggression (Quay, 1965; Raine, 2002). Some questions about the nature of this association remain, however. These questions are exemplified by the results of an extensive meta-analysis of heart rate (HR) and skin conductance level (SCL) in antisocial behavior conducted by Lorber (2004). In this meta-analysis, Lorber (2004) presented evidence for decreased resting HR and SCL, with some evidence for decreased HR and SCL during tasks. Results varied widely, however, depending on the specific measure of antisocial behavior, age of the sample, and stimulus valence (i.e., whether participants performed a task intended to induce negative affect). For instance, aggression in adolescents and adults was found to be associated with a trend toward overall *increased* HR reactivity (Cohen's $d = 0.10$), but effect sizes indicated significant heterogeneity across studies that was partially accounted for by stimulus valence. Specifically, aggression was associated with increased HR reactivity to negative stimuli ($d = 0.31$) but with decreased HR reactivity to nonnegative stimuli ($d = -0.34$).

Nonetheless, the moderators tested by Lorber (2004) did not account for all of the heterogeneity. For example, there was significant heterogeneity in resting SCL among

studies of children with conduct problems, with effect sizes ranging from $d = -1.02$ to 0.89 ; therefore, age of the sample and type of behavior did not fully account for the heterogeneity in this measure⁴. Heterogeneity was also present across studies of resting HR in aggressive children, HR reactivity to negative stimuli in samples with aggression and conduct problems, and SCL reactivity in psychopathic adults (Lorber, 2004). These results suggest that, while there is a trend toward decreased sympathetic nervous system activity in antisocial populations, there exists significant heterogeneity which has not yet been accounted for. It is possible that the heterogeneity in the studies of children may be at least partially accounted for by psychopathic traits in children, as there were too few studies of psychopathic traits in children at that time to permit a meta-analysis. The aim of the current study is to examine whether psychopathic traits, as measured by callous-unemotional (CU) traits, moderate the relationship between conduct disorder (CD) and autonomic nervous system activity and reactivity to stress, as measured by HR and SCL.

Autonomic Nervous System Activity and the Stress Response

The two branches of the autonomic nervous system (ANS) are well-known for their opposing roles: the sympathetic branch is associated with the “fight-or-flight” response, whereas the parasympathetic branch has been dubbed the “rest-and-digest” system. At rest, the parasympathetic branch dominates. When a stressor is encountered, stress responses follow two paths: one through the sympathetic branch of the ANS (sympathetic nervous system, [SNS]) which is fast and short-term, and another slower, longer-term response through the hypothalamic-pituitary-adrenal (HPA) axis (Shirtcliff et al., 2009). The SNS is activated by the release of adrenaline/epinephrine from the adrenal

⁴ Stimulus valence is not relevant in this case because SCL was measured at rest, i.e., there was no stimulus.

gland as well as the withdrawal of the inhibiting actions of the parasympathetic nervous system (PNS; Shirtcliff et al., 2009). This inhibiting role of the PNS highlights the importance of both branches of the ANS in the response to stress: although the stress response is mediated by the SNS, activity of the PNS can reduce the stress response, leading some researchers to interpret SNS activity as an index of inhibition and PNS activity as an indicator of emotion regulation (Beauchaine, Gatzke-Kopp, & Mead, 2007).

Changes in HR and SCL have long been measured as indicators of SNS activity, as they both typically increase when the SNS is activated. Specifically, eccrine sweat glands, from which measures of electrodermal activity arise, are innervated entirely by the SNS and therefore increase output when SNS activity increases (Sokolov, Shabadash, & Zelinkina, 1980). Cardiac output (i.e., HR), in contrast, is modulated by both the SNS and the PNS. The PNS input to the heart arises from activity of the vagus nerve, which typically acts as a “brake” on HR, whereas SNS input to the heart involves changes in the force with which the left ventricle of the heart contracts (Beauchaine, Katkin, Strassberg, & Snarr, 2001). In the presence of danger, vagal input to the heart withdraws and SNS activation of the left ventricle grows, leading to increased HR that prepares the organism to fight or flee (Beauchaine et al., 2007). Thus, SCL can be interpreted as a relatively “pure” indicator of SNS activity, whereas HR reflects both SNS and PNS activity.

Polyvagal Theory and Antisocial Behavior

In order to explain the impact of ANS function on social behavior, Porges (2001) has proposed the “polyvagal theory.” In contrast to the univariate arousal view of ANS activity, as is implied in hypoarousal theory, the polyvagal theory argues for a more

nuanced view of ANS activity, given that multiple physiological systems interact with the ANS to promote homeostasis both at rest and during times of challenge (Porges, 2001). Porges (2001) argues that the ANS functions as a social engagement system, regulating social behavior through a series of evolutionarily adapted pathways. Specifically, Porges (2001) posits that the ANS regulates social behavior in a hierarchical manner via three subsystems: the ventral vagal complex (VVC), consisting of the myelinated fibers of the vagus nerve and the nucleus ambiguus of the vagus; the SNS; and the dorsal vagal complex (DVC), consisting of the unmyelinated fibers of the vagus nerve and the dorsal motor nucleus of the vagus.

Based on phylogenetic studies of these three subsystems, Porges (2001) contends that the VVC is the most recently evolved of these three subsystems and the DVC is the oldest, and he proposes that newer structures are activated first in any social encounter whereas older structures are only activated if the newer structures fail to deal with the environmental challenge in a way that will ensure survival of the organism. As put forth by Porges (2001), the VVC promotes communication, the SNS supports fight or flight behaviors, and DVC activation leads to immobilization. Thus, when encountering another animal, the initial activation of the VVC should lead mammals⁵ to attempt to defuse the situation through visual displays and vocalizations; if that fails, SNS activation would lead to aggression or fleeing from the situation; and, if fight/flight is not an option, DVC activation would cause the mammal to “freeze” and reduce physiological functioning so that it appears dead. Porges (2001) notes that the older subsystems are more costly, both physiologically and behaviorally (e.g., deactivation of the VVC in favor of SNS activity can lead to hypertension and irritability).

⁵ The VVC is not present in other vertebrates.

Beauchaine and colleagues have applied polyvagal theory to explain the relationship between externalizing behavior and ANS activity. In particular, they maintain that the VVC allows control of emotions and that deficiencies of the VVC, as shown by decreased PNS activity, should be associated with emotional dysregulation and psychopathology (Beauchaine et al., 2007). They further argue that low SNS activity results in impulsivity and disinhibition (Beauchaine et al., 2007). Therefore, they have proposed that CD results from a combination of disinhibition/impulsivity and emotional dysregulation (Beauchaine, 2012; Beauchaine et al., 2007); that is, decreased SNS and PNS activity. Psychopathic traits, in contrast, are theorized under this model to arise from disinhibition in the context of very low trait anxiety, and thus would not necessarily be linked to emotion dysregulation (Beauchaine, Neuhaus, Brenner, & Gatzke-Kopp, 2008), and so psychopathy may be linked to decreased SNS activity but normal PNS function. In terms of HR and SCL in CD and CU traits, this theory would predict that:

1. CD symptoms would be associated with decreased SCL (low SNS function) and normal HR at rest (low SNS and PNS function balance each other out).
2. CD symptoms would be associated with decreased SCL (low SNS function) and increased HR during stress (PNS function now lower than SNS function due to deficiencies in the VVC responding to stress, leading to a withdrawal of the vagal brake on HR).
3. CU traits would be associated with decreased SCL (low SNS function) and decreased HR both at rest and during stress (low SNS function and normal PNS function, leading to vagal inhibition of HR).

Autonomic Nervous System Activity and Conduct Problems

Both the hypoarousal theory and polyvagal theory have been bolstered by reports of low resting SCL among a variety of antisocial populations, including among children with conduct problems, although the low resting HR seen in many samples is more consistent with the hypoarousal theory. Low resting HR has been found across children and adolescents with conduct problems (Lorber, 2004) and has been called the “best-replicated biological correlate to date of antisocial behavior in children and adolescents” (Ortiz & Raine, 2004). Similarly, Lorber’s (2004) meta-analysis found evidence for decreased resting SCL in children with conduct problems, compared to controls, although this effect was not found for adolescents. However, as noted above, the findings for resting SCL contained significant unexplained heterogeneity across samples.

As for physiological reactivity to stress, the hypoarousal theory would predict decreased HR and SCL reactivity in antisocial populations, whereas the polyvagal theory would predict decreased SCL but increased HR in these samples. There are further reasons to predict both increased and decreased reactivity to stress in children with conduct problems. Researchers have noted that a tendency to interpret ambiguous social situations with hostility (i.e., the hostile attribution bias) or simply a greater tendency to experience anger, as is common in children with disruptive behavior disorders, may be associated with a more intense psychophysiological reactivity to these situations (Crozier et al., 2008; van Goozen et al., 1998). At the same time, it has also been suggested that fearlessness and low sensitivity to punishment (Popma et al., 2006) or perhaps greater lifetime exposure to stress and thus an attenuation of the stress response (van Goozen, Matthys, Cohen-Kettenis, Buitelaar, & van Engeland, 2000) should lead to decreased reactivity to stress.

The mixed nature of the literature supports this divide in hypotheses. Lorber's (2004) meta-analysis reported a small effect of increased HR reactivity in youths with conduct problems across different types of tasks (negative or nonnegative), and HR during tasks (i.e., not taking into account the change from baseline) did not differ between groups. When looking specifically at HR during a stressor, Ortiz and Raine's (2004) meta-analysis found a medium effect for antisocial youths which suggested an overall decrease or less change in response to a stressor in antisocial youths compared to controls. Articles published more recently support Ortiz and Raine's (2004) findings of decreased HR reactivity to stressors in children with CD compared to controls (Fairchild et al., 2008) and in children with early-onset, but not late-onset, CD (Bimmel, van IJzendoorn, Bakermans-Kranenburg, Juffer, & De Gues, 2008).

There is less information about SCL reactivity in children with conduct problems. Lorber's (2004) meta-analysis found evidence for decreased task SCL in children with conduct problems, but there were no studies of SCL reactivity in children with conduct problems at that time. Some more recent studies have begun to fill that gap. A study of four-year-olds found that SCL reactivity to an exciting film was lower in the aggressive children compared to the non-aggressive children (Posthumus, Böcker, Raaijmakers, van Engeland, & Matthys, 2009). However, Popma and colleagues (2006) found no difference in SCL reactivity to a public speaking task between delinquent adolescent boys and controls. Therefore, the evidence for increased or decreased ANS reactivity in children with conduct problems appears to be equivocal at this time.

Autonomic Nervous System Activity and Callous-Unemotional Traits

One possible explanation for these inconsistencies in the literature is the unaccounted effect of psychopathic or CU traits. The prediction of hyporeactivity due to fearlessness or low sensitivity to punishment fits in particularly well with theories of psychopathy as well as with the predictions from polyvagal theory. Patrick, Fowles, and Krueger (2009) have proposed that fearlessness is central to the development of psychopathy. They theorize that the “meanness” component of psychopathy, which corresponds well to CU traits, arises from decreased capacity for fear combined with disregard for the wellbeing of others (Patrick et al., 2009). Given that polyvagal theory predicts normal baseline HR and increased HR reactivity for CD but decreased HR at rest and during stress for psychopathic traits, it is possible that CU traits account for the finding of decreased baseline HR and reactivity, whereas conduct problems in the absence of CU traits may be associated with increased HR reactivity alone.

Some research does, in fact, suggest that psychopathy or CU traits may be associated with low HR at rest and during tasks, although there is some inconsistency in results. Lorber (2004) reported no relationship between adult psychopathy and HR at rest or HR reactivity; however, there were no studies of HR and psychopathic traits in children at that time. More recently, Baker and colleagues (2009) found a negative relationship between resting HR and psychopathic traits in a community sample of children, and another study of children recruited from clinical settings found decreased resting HR in callous CD children compared to CD-only and control children, with no difference between CD-only and control children (Anastassiou-Hadjicharalambous & Warden, 2008). In contrast, de Wied, van Boxtel, Matthys, and Meeus (2012) found no difference in resting HR between adolescent boys with disruptive behavior disorders who

were high versus low in CU traits. Notably, the two studies which found significant effects for psychopathic traits included a younger sample (7 to 11 years) and also included girls, in comparison to de Wied and colleagues (2012), whose participants were boys aged 12 to 15 years. It is possible that studies of the biological correlates of antisocial behavior in adolescence may be complicated by the addition of adolescent-onset offenders to the pool of participants, given that adolescent-onset CD appears to have different risk factors compared to childhood-onset CD (Frick, 2006).

Studies of HR reactivity and psychopathic traits in children provide some more consistent results. Barhight (2011) divided fourth and fifth grade children into two groups based on their HR reactivity to videos of bullying episodes and found that those whose HR decreased during the videos scored higher on a measure of CU traits. When shown a video evoking sadness, the adolescent boys who were high in CU traits in de Wied et al.'s (2012) sample experienced less HR deceleration compared to boys with disruptive behavior disorders who were low in CU traits. Given that HR deceleration is the typical response to displays of sadness, de Wied and colleagues (2012) interpreted this decrease in HR deceleration as indicating less empathy. Additionally, callous CD children were found to have lower HR while viewing a film meant to evoke fear compared to CD-only and control children (Anastassiou-Hadjicharalambous & Warden, 2008). One study that breaks this trend found that psychopathic traits in children were positively correlated with HR acceleration in anticipation of an aversive event (a loud noise; Wang, Baker, Gao, Raine, Lozano, 2012). It is important to note that, unlike the studies mentioned above, this study used a countdown task and measured anticipatory HR rather than HR reactivity to the actual aversive stimulus. Wang et al. (2012) reported that previous studies of

psychopathic adults have found increased HR acceleration during the anticipatory phase of the countdown task compared to controls, but that HR acceleration returned to normal levels at the end of the countdown task. Wang et al. (2012) interpreted this increased anticipatory acceleration as reflecting a reduced threshold for aggressive responding.

Overall, it seems that psychopathic traits may account for the unexplained heterogeneity in HR found in earlier studies of conduct problems in children. However, only one study of HR reactivity in children with psychopathic traits used a stress-inducing task (Wang et al., 2012), while the others used empathy tasks, and this study did not test the effect of psychopathic traits separate from the effect of conduct problems (i.e., they did not control for level of conduct problems). Additionally, Wang et al. (2012) focused on psychopathic traits as a whole, rather than CU traits, which is important given the central role CU traits are thought to play in the predisposition to violent and criminal behavior (Patrick et al., 2009).

Polyvagal theory predicts that decreased SCL should be associated with both CD and psychopathic traits, so the relationship of resting SCL and CU traits should be expected to be minimal when controlling for conduct problems. Lorber (2004) was unable to examine psychopathic traits in children, although he did report significantly decreased resting SCL and SCL reactivity in adults with psychopathy. Studies in children with significant conduct problems, however, have found little evidence for a link between resting SCL and psychopathic or CU traits. No significant difference in resting SCL has been found in: 8- to 17-year-old boys with high versus low levels of psychopathic traits who were institutionalized for emotional or behavioral difficulties (Blair, 1999); adolescent boys at risk for delinquency who were high versus low in psychopathic traits

(Fung et al., 2005); and adolescent boys housed in a juvenile detention facility who were high versus low in CU traits (Muñoz, Frick, Kimonis, & Aucoin, 2008b). Another study found no difference in SCL between community-residing 9-year-old children with psychopathic traits and those without during an initial rest period but did find a significant decrease in the male psychopathic group during a second rest period (Ward, 2005). It seems that, at least among samples with high levels of conduct problems, CU or psychopathic traits are not uniquely associated with resting SCL.

The literature on SC reactivity and psychopathic traits in children and adolescents is somewhat more promising. Muñoz and colleagues found that high levels of CU traits in boys with both high and low levels of aggression were associated with decreased SCL reactivity to minor taunting during a competitive reaction time task (Muñoz et al., 2008a). They further found decreased SCL reactivity to more intense provocations among boys with high CU traits and relatively higher verbal ability (Muñoz et al., 2008b). Changes in skin conductance responses (SCRs, increases in SCL $> 0.05 \mu\text{S}$) have also been examined in children with psychopathic traits. Wang et al. (2012) found that psychopathic traits were associated with decreased numbers of SCRs during the countdown period, although, as noted earlier, they did not control for level of conduct problems. Similarly, Fung and colleagues (2005) found that boys who were high in psychopathic traits were more likely to be “non-responders” to a noise blast and during signaled anticipatory periods; that is, more boys in the high psychopathy group had no skin conductance responses (SCRs, changes in) during these periods than controls. It is important to note, however, that when Fung and colleagues (2005) examined only boys who were high in delinquency in both groups, there was no difference in non-responder status. In contrast, Isen and colleagues

(2010) found that psychopathic traits were associated with decreased SCR amplitude to an orienting task (including sounds such as baby cries, bird song, and tones) in community-residing 9-year-old boys (but not girls), even after controlling for symptoms of CD and externalizing. Thus, while there are some indications that CU traits in children may predict decreased SCL reactivity, the possibility remains that, in children, decreased SCL reactivity is associated with antisocial behavior more generally, and not psychopathic traits specifically.

The Current Study

Given the heterogeneity present in the literature on ANS activity and conduct problems in children, along with the largely unexamined role of CU traits in this relationship, the current study aimed to examine the relationship between CD, CU traits, and ANS activity at baseline and in response to a social-evaluative stressor. This study adds to the literature in the following ways: by using a community sample of both boys and girls who were recruited with the goal of oversampling aggressive and antisocial children; by using a social stress task that may be more ecologically valid than stressors involving loud or aversive noises; and by examining the roles of both conduct problems and CU traits, as well as their interaction.

The hypotheses of the current study are based on the predictions of polyvagal theory articulated above. An additional hypothesis was added concerning the interaction of CD and CU traits, due to the fact that these are positively correlated. Thus, the current study tested the following hypotheses:

1. CD symptoms would be associated with decreased SCL and normal HR at rest.

2. CD symptoms would be associated with decreased SCL and increased HR during stress.
3. CU traits would be associated with decreased SCL and decreased HR both at rest and during stress.
4. CD symptoms and CU traits would interact such that, among children high in CU traits the pattern of ANS activity proposed in hypothesis 3 would be present, regardless of level of CD symptoms. In contrast, children low in CU traits were expected to follow the pattern of ANS activity outlined in hypotheses 1 and 2.

Method

Participants

See Section 1 for details.

Measures

Conduct and Oppositional Defiant Disorder Questionnaire. See Section 1 for details.

Antisocial Process Screening Device. See Section 1 for details.

Diagnostic Interview Schedule for Children. Some research has suggested that ADHD may be associated with decreased SCL (Barry, Clarke, Johnstone, McCarthy, & Selikowitz, 2009; Dupuy, Clarke, Barry, Selikowitz, & McCarthy, 2014) and increased HR (Imeraj et al., 2011). Therefore, ADHD was included as a potential covariate in the current study. See Section 1 for details.

Child Behavior Checklist/Youth Self-Report. Internalizing psychopathology was included as a covariate due to reports that internalizing symptoms are associated with altered ANS activity, as shown by increased HR (Baker, Baibazarova, Ktistaki, Shelton,

& van Goozen, 2012; Hastings et al., 2011) and SCL reactivity (Keller & El-Sheikh, 2011). See Section 1 for details.

Procedure

Children and their caregivers arrived at the laboratory at approximately 9:00 am on the day of testing. Tasks in the morning included a blood draw (child), fMRI scan (child), and completion of questionnaires (child and caregiver). At approximately 11:30 am, children were prepared for a psychophysiology assessment. During this assessment, children performed a series of tasks, three of which were the focus of the present analyses: an initial rest task, a stress task, and a final rest task. For the initial and final rest tasks, participants were asked to sit as still as possible and fix their eyes on a point on the computer screen in front of them for two minutes.

The stress task was a modified version of the Trier Social Stress Test for Children (TSST-C; Buske-Kirschbaum et al., 1997; modified version, McBurnett et al., 2005). In a meta-analysis Dickerson and Kemeny (2004) found the greatest stress response can be elicited via uncontrollability (performing under time constraints, hurry up prompts, a sense of failing) and social-evaluative elements (critical feedback, video recording). The modified TSST-C involved both of these components. First, children were asked to think of the worst or most stressful thing that has ever happened to them. They were given two minutes to prepare and then two minutes to describe the event while being videotaped. If the child stopped speaking before two minutes elapsed, the experimenter probed for more detail about the child's reactions to and feelings about the stressful event. Immediately after this speech, children were asked to count backward from the number 758 by sevens for two minutes. At 30-second intervals, the experimenter prompted the children to count

more quickly or, if they have made a mistake, to return to the beginning and start over. For both parts of the stress paradigm, a countdown timer showing the time remaining was displayed on a computer screen in front of the child. Because speaking can cause alterations in HR and SCL due to increased respiration, only data from the thinking part of the speech task was used for the current analyses.

Psychophysiology Equipment and Software

The HR and SCL data were collected as part of a larger psychophysiological battery in which EEG was also measured. All psychophysiological data were acquired using a Biopac MP150 with AcqKnowledge version 4.1 software (Biopac Systems, Inc.). Initial processing of heart rate and skin conductance data was completed in AcqKnowledge, and further processing was completed in MATLAB (MathWorks) using custom scripts. Impedance was monitored using a UFI Checktrode impedance meter (Morro Bay, CA). The laboratory was sound-proofed and was air-conditioned to 72° F in order to ensure consistent psychophysiology recording.

Heart Rate. Electrocardiograph (ECG) was recorded axially on the left and right ribs at the level of the heart (to avoid movement artifact) using silver/silver chloride (Ag/AgCl) adhesive disposable electrodes. Prior to attaching electrodes, skin was prepared using NuPrep abrasive skin prepping paste. Biopac isotonic recording gel was used as the electrolyte medium. Impedance for ECG was kept below 10 k Ω . Data were recorded using a bandpass of 0.5-35 Hz and a 60 Hz notch filter, and the recording was digitized at 1000 Hz. ECG data were cleaned for artifacts manually after using AcqKnowledge analytic tools to identify unusually large changes in HR. HR was then quantified using AcqKnowledge analytic tools, and custom scripts in MATLAB were

used to calculate HR during periods of interest. For each task included in the present analyses, HR was averaged over four 30-second epochs, for a total of 12 epochs across the three tasks.

Skin Conductance. Skin conductance (SC) was recorded using 8 mm diameter Ag/AgCl electrodes attached to the distal phalanges of the first and second fingers of the non-dominant hand. Double-sided adhesive collars were used to secure the electrodes on the fingers, and Biopac isotonic recording gel was used as the electrolyte medium. Data were recorded using a low pass filter of 1 Hz with a gain of 10 $\mu\text{S}/\text{V}$, digitized at 62.5 Hz. Potential artifacts were identified using a custom script in MATLAB, and were then visually inspected and removed by interpolating the SC level (SCL) over the artifact period using the data immediately prior to and after the artifact. Artifacts were removed in this way from $M = 33.03$ seconds of data (median = 14.60 seconds) for 268 of the participants included in the current analyses. In addition, any SCL data which fell below 0 μS were rejected as artifactual. As with HR, for each task included in the present analyses, SCL was averaged over four 30-second epochs, for a total of 12 epochs (360 seconds) across the three tasks.

Data Reduction and Statistical Analysis

Due to moderate skewness and kurtosis, HR data were natural-log-transformed and SCL data were square root-transformed. In order to reduce collinearity, the variables for CD symptoms, CU traits, ADHD symptoms, and internalizing were mean-centered. In two separate sets of analyses, HR and SCL were analyzed with multilevel modeling using linear mixed models in SPSS (IBM, version 20.0). Multilevel modeling was chosen for this analysis due to its ability to include participants with incomplete data and to account

for the possibility of correlated residuals, a significant concern when analyzing repeated measures data. Potential outliers were handled as in section 1. Results are presented for the multilevel models without model fit and prediction outliers; results with the outliers are available upon request.

After discarding data compromised by excessive participant movement and/or equipment failure, HR data were available for 415 children and SCL data were available for 345 children. Children with HR data available did not differ from the total sample on age, sex, race, CD symptoms, CU traits, internalizing, or ADHD symptoms (see Table 4). Children with SCL data available did not differ from the total sample on age, race, CD symptoms, CU traits, or ADHD symptoms; however, there was a trend for fewer boys and lower internalizing symptoms in the group (see Table 4). Removing outliers following the procedure detailed above resulted in a sample of 386 children for the HR analysis and 327 children for the SCL analysis.

Time and time^2 were included as level 1 predictors of HR and SCL, with values for HR and SCL repeated over the 12 epochs. Time^2 was included because a quadratic relationship between time and HR/SCL was expected (i.e., HR/SCL was expected to be higher during the stress task than during the initial and final rest tasks). Level 2 predictors (sex, age, race, ADHD symptoms, internalizing score, CD symptoms, CU traits, and $\text{CD} \times \text{CU}$) and cross-level interactions ($\text{CD} \times \text{time}$, $\text{CU} \times \text{time}$, $\text{CD} \times \text{CU} \times \text{time}$, $\text{CD} \times \text{time}^2$, $\text{CU} \times \text{time}^2$, $\text{CD} \times \text{CU} \times \text{time}^2$) were added to the model sequentially as fixed effects. As recommended by Field (2009), covariate predictors (i.e., those other than CD, CU, and $\text{CD} \times \text{CU}$) were retained in the model if they significantly improved model fit, and each of the predictors was added as a random effect if it significantly improved model fit, as

measured by the change in the $-2 \times \log$ likelihood of the model. The $-2 \times \log$ likelihood has the same distribution as χ^2 and can be tested for significance using the critical values for χ^2 with degrees of freedom = $df_{\text{model 2}} - df_{\text{model 1}}$.

After the final model was fit to the data, statistically-significant ($p < .05$) and trend-level ($p < .10$) interactions were broken down by conducting separate multilevel models for each level of the categorical variable involved in each interaction. The global effect size for the full model, pseudo- R^2 , was calculated as in section 1.

Results

Manipulation Check

Average HR across all participants increased significantly from the baseline resting task ($M = 81.60$ bpm, $SD = 10.12$) to the stress task ($M = 83.13$ bpm, $SD = 10.82$), $t(422) = -5.14$, $p < .001$, $d = 0.15$. Average SCL across all participants also increased significantly from the baseline resting task ($M = 7.78$ μS , $SD = 3.72$) to the stress task ($M = 8.43$ μS , $SD = 3.79$), $t(315) = -7.14$, $p < .001$, $d = 0.17$. These results suggest that the portion of the stress task used in this analysis (i.e., the thinking portion of the speech task) was successful in increasing stress levels in this sample, albeit with a small effect size.

Zero-Order Correlations

Table 5 presents correlations among predictor and outcome variables. Notably, HR and SCL were generally not significantly correlated, although there was a small, significant positive correlation between HR and SCL during the stress task.

Heart Rate

The final multilevel model included time, time², sex, age, CD symptoms, CU traits, and the interaction between CD symptoms and CU traits as fixed effects predictors of HR. Adding cross-level interactions between CD symptoms, CU traits, and time did not significantly improve model fit, all $ps > .57$, nor did adding race, ADHD symptoms, or internalizing score, all $ps > .26$. The pseudo- R^2 statistic indicated that the predictors included in the final model accounted for 4.6% of the variance in HR.

The final model indicated that symptoms of CD did not significantly predict HR, $F(1, 386.03) = 0.67, p = .413$, nor did the interaction between CD symptoms and CU traits, $F(1, 385.25) = 0.56, p = .453$. CU traits significantly predicted lower HR, $F(1, 387.13) = 6.43, p = .012$ (see Figure 5). Effects for the covariates included in the model were as follows: male sex predicted lower HR, $F(1, 386.78) = 5.80, p = .016$; older age predicted lower HR, $F(1, 387.08) = 6.50, p = .011$; and HR demonstrated a negative quadratic shape over the course of the three tasks (i.e. HR was higher during the stress task than during the rest tasks), $F(1, 368.54) = 80.96, p < .001$ (see Table 6).

Skin Conductance Level

The final multilevel model included time, time², sex, age, race, CD symptoms, CU traits, the interaction between CD symptoms and CU traits, and the interaction between time and CD symptoms as fixed effects predictors of SCL. Adding further cross-level interactions between CD symptoms, CU traits, and time did not significantly improve model fit, all $ps > .15$, nor did adding ADHD symptoms or internalizing score, both $ps > .99$. The pseudo- R^2 statistic indicated that the predictors included in the final model accounted for 8.5% of the variance in SCL.

In the final model, symptoms of CD did not significantly predict SCL, $F(1, 347.79) = 1.12, p = .291$, nor did CU traits, $F(1, 323.30) = 2.02, p = .156$, or the interaction of time and CD symptoms, $F(1, 301.45) = 0.26, p = .608$. However, the interaction between CD symptoms and CU traits significantly predicted SCL, $F(1, 318.75) = 4.91, p = .027$ (see Table 7). To interpret the interaction between CD symptoms and CU traits, participants were divided into three groups of roughly equal size based on level of CU traits (low = score of 0-4 on the APSD CU dimension; medium = score of 5-6; high = score of 7-12) and the multilevel model was rerun, without outliers and without including CU traits as a predictor. The results indicated that, among children who were low in CU traits, symptoms of CD predicted significantly lower SCL, $F(1, 93.86) = 5.03, p = .027$ (see Figure 6). Among children with medium or high levels of CU traits, however, CD was not a significant predictor of SCL, $F(1, 117.88) = 1.37, p = .244$, and $F(1, 110.67) = 1.68, p = .197$, respectively.

Effects for the covariates included in the model were as follows: male sex predicted a trend toward higher SCL, $F(1, 320.42) = 2.65, p = .105$; older age predicted higher SCL, $F(1, 319.30) = 7.86, p = .005$; African American race predicted lower SCL, $F(1, 316.83) = 16.94, p < .001$; and SCL demonstrated a positive quadratic shape over the course of the three tasks (i.e., SCL was higher overall during stress than during rest, and within each task, SCL was higher at the beginning than at the end of the task), $F(1, 301.89) = 33.14, p < .001$.

Discussion

As predicted, CU traits were associated with decreased HR at rest and during stress, and symptoms of CD were associated with decreased SCL at rest and during

stress, but only among children who were low in CU traits. These effects remained even when controlling for sex, age, and symptoms of other forms of psychopathology. Also in line with predictions, CD symptoms were not significantly associated with HR at rest. However, in contradiction to the hypotheses, CD symptoms did not predict increased HR during stress, and CU traits were not associated with decreased SCL during rest or stress. These findings provide mixed support for the hypothesis that the unaccounted presence of CU traits has resulted in heterogeneity in the previous literature.

Heart Rate, Conduct Disorder, and Callous-Unemotional Traits

Although symptoms of CD were negatively correlated with HR across tasks, symptoms of CD did not predict HR in the multilevel model. In contrast, CU traits predicted significantly lower HR across tasks. These results suggest that CU or psychopathic traits may in fact account for the negative relationship between HR and antisocial behavior observed in numerous studies. However, none of the cross-level interactions between CD symptoms, CU traits, and time were significant in predicting HR. That is, the relationship between CD symptoms, CU traits, and HR was constant across the three tasks. Given that CU traits were predicted to be associated with decreased HR at rest and during stress, it is not surprising that the interaction of CU with time did not significantly predict HR. An interaction between CD symptoms and time was expected, however, due to the predicted positive relationship between CD symptoms and HR during stress. Although the stress task in this study did lead to an overall average increase in HR in this sample, it is possible that children with high levels of CD may not have been sufficiently stressed by the portion of the stress task used in the current analysis (i.e., the two-minute preparation time before giving a speech). Alternatively, the

predicted decrease in PNS activity in children with CD may not outweigh the decrease in SNS activity. Future studies may explore this issue by using more direct measures of PNS activity, such as respiratory sinus arrhythmia, which is thought to tap PNS activity more accurately (Porges, 2001).

Skin Conductance Level, Conduct Disorder, and Callous-Unemotional Traits

Unlike the results for HR, CU traits did not significantly predict SCL when other variables were controlled, whereas CD symptoms did. In fact, as seen in the significant interaction between CD symptoms and CU traits, the relationship between CD and SCL was only statistically significant in the context of low levels of CU traits. These results would seem to suggest that CU traits do not account for the negative relationship between SCL and antisocial behavior, and that, at least in children, low SCL may in fact be a marker for conduct problems in the absence of CU traits. This possibility suggests that CU traits may be responsible for some of the heterogeneity seen in past research, given that conduct problems and CU traits tend to be positively correlated.

When interpreting the results of this interaction, it is important to note that the range of CD symptoms included in each group varied significantly: for the low CU group, COD CD symptom scores ranged from 0 to 11; for the medium CU group, CD symptom scores ranged from 0 to 16; and for the high CU group, CD symptom scores ranged from 0 to 27. When level of CD symptoms in the CU groups were compared using one-way ANOVA, the groups were found to differ significantly, $F(2, 424) = 32.04$, $p < .001$. Post-hoc tests revealed that all three CU groups differed significantly from each other on CD symptoms, in the expected direction (i.e., higher CU = higher CD symptoms). Although it is not unexpected to find that the low CU group encompasses

children with milder levels of CD symptoms than the other groups, interpretation of the significant effect of CD symptoms on SCL found only in the low CU group must take into account the fact that this effect only extends over a limited range of CD symptoms.

The use of CU traits specifically, rather than psychopathic traits as a whole, may account for the unexpected finding that CU traits did not predict SCL. The hypothesis of low SNS activity, and therefore low SCL, was based on Beauchaine et al.'s (2008) conceptualization of psychopathy as developing from disinhibition in the context of low trait anxiety. Although disinhibition is considered to play a central role in the development of psychopathy, it has also been found to fall on a different dimension or factor from CU traits in various measures of psychopathy (Frick et al., 2000; Patrick et al., 2009). Thus, it may be that the impulsivity dimension of psychopathy may be more strongly linked with low SNS activity than are CU traits.

As with HR, none of the cross-level interactions between CD symptoms, CU traits, and time were significant in predicting SCL. That is, the relationship between CD symptoms, CU traits, and SCL was constant across the three tasks. Although $CD \times time$ was included in the final model because it improved model fit, it did not reach statistical significance. These results are consistent with the hypothesis that the low SNS function associated with impulsivity should not vary across tasks for children with CD.

Theoretical Implications

The results appear to support the contention of the hypoarousal theory of antisocial behavior that decreased arousal is associated with rule-breaking, which is consistent with the idea that fearlessness may underlie these behaviors. In addition, they are consistent with the prediction, based on the polyvagal theory, that the source of this

hypoarousal (i.e., SNS or PNS function) varies according to the specific form of antisocial behavior at question. That is, as suggested by Beauchaine et al. (Beauchaine, 2012; Beauchaine et al., 2007), symptoms of CD by themselves appear to be associated with decreased SNS and PNS function, at least at rest. The results for CU traits are somewhat more complicated, in that it is not clear whether the decreased HR seen in relationship with CU traits is due to a combination of slightly decreased SNS activity and slightly increased PNS activity, or if it is solely driven by an increase in PNS activity. The lack of a significant relationship between CU traits and SCL suggests that the decrease in HR is not solely due to a decrease in SNS function. Alternatively, there is some evidence suggesting interactions between the ANS and the HPA axis via cortisol secretion (Porges, 2001). Therefore, it is possible that the relationship between decreased HR and CU traits at least partially reflects decreased HPA axis activity. This possibility will be explored further in section 3.

These results suggest that CU traits do, in fact, contribute to the heterogeneity of results seen in previous studies of ANS activity and conduct problems in children. Moreover, they suggest that children who are high in CU traits and CD symptoms may differ in the biological processes related to their behavior from children who have CD but who lack CU traits. Beauchaine et al. (2007) have hypothesized that the low SNS activity seen in disinhibited and impulsive children may reflect a deficit in reward responsiveness due to low dopamine levels in the brain's reward circuit, which explains the efficacy of stimulant medications for these symptoms. Additionally, Beauchaine and colleagues (2007) proposed that, because children with CD suffer from emotional dysregulation, as seen in deficits in PNS activity, environmental changes (e.g., reducing negative

reinforcement of dysfunctional emotion regulation strategies through parent training) may be particularly helpful for these children.

If children with CD and CU traits do not experience the same deficits, however, it is unlikely that the same interventions would be effective for these children. Indeed, a growing literature exists showing that children with CU traits tend not to respond as well to traditional interventions for CD as those low in CU traits. In a recent review, Frick, Ray, Thornton, and Kahn (2014) reported that 90% of the studies they reviewed reported poorer outcomes for children and adolescents with CU traits, including less engagement in treatment and higher post-treatment reoffense rates. However, they did note that some researchers had reported success in using an intensive approach focused on reward and appealing to the self-interests of the children. If CU traits are in fact associated with increased PNS activity, children with these traits would be less likely to experience negative emotions, which may contribute to their insensitivity to punishment. This insensitivity to punishment may account for the relative success of reward-oriented treatments for this population. Although it is unclear at this time whether ANS activity relates to treatment efficacy in children with CU traits, this possibility highlights the importance of understanding the unique pattern of ANS activity in these children.

Limitations

While these results are suggestive, several limitations must be taken into account. First, as noted above, the result of decreased HR seen in children high in CU traits is difficult to interpret due to the combined influences of the PNS and SNS on cardiac output. Future research may explore the relationship of CU traits to respiratory sinus arrhythmia, a measure of HR variability, as this is a more accurate indicator of PNS

activity (Porges, 2001). Second, although a fair number of the children in this study had high levels of CU traits and CD symptoms, there were fewer with opposing levels of CU traits and CD symptoms (i.e., high CU and low CD or low CU and high CD). The relative dearth of participants in these groups made it difficult to interpret the interaction of CD and CU in predicting SCL, as the children in the low CU group had a much narrower range of CD symptoms than the children in the other CU groups. Finally, it is important to note that low physiological arousal, as indicated by low HR, is not a feature unique to antisocial populations and is in fact associated with some positive attributes (e.g., cardiovascular fitness; Saxena et al., 2013). It is possible, however, that awareness of this low physiological arousal may contribute to whether it becomes associated with antisocial behavior. Gao, Raine, and Schug (2012) reported that psychopathic traits in adults were associated with “somatic aphasia,” or the mismatch of reported sensations of arousal with recorded physiological arousal. Thus, both level of arousal and cognitive appraisal or awareness of that arousal may need to be taken into account when predicting who will engage in antisocial behavior.

Conclusions

In sum, the current study provides evidence for a split in the type of hypoarousal which is associated with CD versus CU traits. That is, while low SNS activity alone appears to be associated with CD, CU traits seem to reflect an imbalance in the activity of the SNS and PNS, leading to low overall arousal. This divide may help to explain the relatively intractable nature of CU traits as well as the heterogeneity that exists in the literature on autonomic arousal in antisocial populations. Future research should address

the exact nature of the ANS imbalance seen in children high in CU traits and examine whether these results extend to adolescents and adults.

SECTION 3: CORTISOL IN CONDUCT DISORDER AND CALLOUS- UNEMOTIONAL TRAITS

Abstract

Cortisol, a product of the hypothalamic-pituitary-adrenal (HPA) axis, has been measured in children with conduct disorder (CD) due to its role in the potentiation of fear and sensitivity to punishment. A recent meta-analysis of cortisol stress reactivity in children with conduct problems found equivocal results, possibly due to the significant heterogeneity among the studies analyzed. The goal of the current study was to examine whether CU traits account for some of the heterogeneity in the relationship between salivary cortisol reactivity and symptoms of CD. Saliva was collected from 11-12 year old community-residing children (N=446) at baseline and five, 20, and 40 minutes after the end of a stressor. The stress task was comprised of a modified version of the Trier Social Stress Test (TSST) followed by a math task. Symptoms of CD were assessed using child- and caregiver-report, and both the child and the caregiver reported on levels of CU traits using the Antisocial Process Screening Device (APSD). Results indicated that CD symptoms were positively associated with total cortisol production (as measured by area under the curve with respect to ground [AUC_G]), whereas CU traits were negatively associated with cortisol production at a trend level. These findings support the contention that CD symptoms and CU traits are associated with different patterns of stress reactivity.

Cortisol in Conduct Disorder and Callous-Unemotional Traits

Introduction

Cortisol has been a target of investigation in youths with conduct problems due to its role in the potentiation of fear and sensitivity to punishment (Schulkin, Gold, & McEwen, 1998; van Goozen, Fairchild, Snoek, & Harold, 2007). Studies of cortisol at rest and in response to stress have suggested that children with conduct problems exhibit low basal cortisol and may exhibit an attenuated stress response in the face of a strong stressor, compared to children without conduct problems (Alink et al., 2008; van Goozen et al., 2007). It is unclear, however, whether this finding applies equally across children with different forms of conduct problems. In particular, there is reason to believe that cortisol hypo(re)activity may be associated with callous-unemotional (CU) traits rather than with conduct problems per se (Hawes, Brennan, & Dadds, 2009). The purpose of the current study is to explore this possibility.

Cortisol and the Stress Response

Cortisol is the end product of the hypothalamic-pituitary-adrenal (HPA) axis, which is a major driver of the stress response. In the presence of a stressor, the sympathetic branch of the autonomic nervous system produces an immediate and acute response, whereas the HPA axis produces a slower and longer-lasting reaction (Shirtcliff et al., 2009). Exposure to stress, especially uncontrollable and social-evaluative stressors, activates the structures of the limbic system, which begins the cascade of hormones that are released by the HPA axis (Dickerson & Kemeny, 2004). First, the paraventricular nucleus of the hypothalamus produces corticotropin-releasing hormone (CRH); next, CRH causes the release of adrenocorticotrophic hormone (ACTH) from the pituitary

gland; and, finally, ACTH activates cortisol production from the adrenal gland. This acute hormonal cascade is gradually slowed when cortisol levels are high enough to cross the blood-brain barrier and bind to glucocorticoid receptors in the brain, thereby inhibiting further release of CRH, ACTH, and cortisol (Alink et al., 2008; Myers, McKlveen, & Herman, 2012).

As both the end product of and source of negative feedback on the HPA axis, cortisol is not only influenced by limbic system activity but also modulates the limbic system itself. That is, the level of activity in the emotional circuitry of the brain (primarily located in the limbic system) directly influences the activity of the HPA axis. For example, if the amygdala is lesioned, HPA axis activity decreases (Schulkin et al., 1998), while increased activity in the amygdala leads to increased HPA axis activation (Myers et al., 2012). In turn, the presence of glucocorticoid receptors in the amygdala, hippocampus, and other limbic structures means that cortisol affects the functioning of these structures. For instance, Schulkin and colleagues (1998) proposed that cortisol secretion increases CRH gene expression in the amygdala, and thereby increases the likelihood of responding to events with fear and anticipatory anxiety.

As a result of these interactions with the limbic system, cortisol has been implicated in social information processing, bonding, and emotional learning. In particular, cortisol has been found to potentiate fear conditioning, or the association of a previously neutral stimulus with an aversive stimulus. Experiments in rats have found that administration of corticosterone (the rat equivalent of cortisol) increases conditioned fear-induced freezing, whereas blocking corticosterone reduces learning of context-dependent fear responses (Schulkin et al., 1998). Similar results have been found in

humans. For example, a recent fMRI study of fear conditioning in adults found that cortisol secretion was positively associated with amygdala activity during the fear conditioning task (Merz, Stark, Vaitl, Tabbert, & Wolf, 2013). In addition, Root and colleagues (2009) found that cortisol was positively correlated with amygdala and hippocampus activity during exposure to threatening images. The association of cortisol with fear conditioning has led to investigations into its role in antisocial behavior.

Cortisol and Conduct Disorder

Conduct disorder (CD) has been proposed to be the result of impulsivity combined with deficits in emotion regulation (Beauchaine et al., 2007; Cappadocia, Desrocher, Pepler, & Schroeder, 2009). The hypoarousal theory of antisocial behavior would suggest that children with CD should be expected to have a reduced basal cortisol and reduced cortisol reactivity to stress. However, research in this area is mixed. A recent meta-analysis of basal cortisol in children with conduct problems found increased cortisol levels in early childhood ($r = .09$), decreased cortisol in middle childhood ($r = -.14$), and null effects for adolescence ($r = -.01$; Alink et al., 2008). The authors proposed that stressful environments early in life may initially cause increased cortisol activity as well as externalizing behavior, but that long-term hypercortisolemia may lead to downregulation of the HPA axis in school-age children with conduct problems. Finally, they suggest that brain reorganization during adolescence may overwhelm any physiological differences in cortisol production (Alink et al., 2008). These hypotheses suggest that measuring psychophysiology before adolescence may be crucial to finding differences in these systems.

Alink and colleagues' (2008) meta-analysis of externalizing behavior and cortisol reactivity found that, although the effect was in the hypothesized direction, the total effect size was not statistically significant ($r = -.04$). Notably, the authors reported a statistically significant effect among studies which log-transformed their cortisol data (which is frequently skewed; $r = -.07$). In addition, the effect of $r = -.18$ was significant for the four studies of disruptive behavior disorders (CD or oppositional defiant disorder). Therefore it is possible that the analysis of overly broad behavior categories and/or improper statistical techniques has distorted the effect. Furthermore, only one study included in Alink et al.'s (2008) meta-analysis appears to have examined the role of psychopathic or CU traits in the relationship between cortisol and externalizing, so it is possible that the unaccounted presence of CU traits may have affected their results.

Cortisol and Callous-Unemotional Traits

There is reason to believe that cortisol reactivity may play a crucial role not just in antisocial behavior in general, but specifically in the case of psychopathic traits. Blair (2008) proposed that the central impairment in psychopathy revolves around deficits in emotional learning, especially aversive or fear conditioning. As noted above, cortisol, through its interactions with the limbic system, is implicated in fear conditioning. The theory is that, through low reactivity to situations that would usually cause fear or anxiety, children with CU traits may not learn from punishment and therefore resist attempts at socialization (Blair, Peschardt, Budhani, Mitchell, & Pine, 2006). Therefore, children with CU traits would be expected to show a decrease in cortisol reactivity in response to stress.

Very few studies have examined cortisol in relation to CU traits, but there is some evidence that HPA axis activity differentiates CD and CU traits. In one of the first studies on this topic, Loney, Butler, Lima, Counts, and Eckel (2006) found low baseline cortisol levels in adolescent boys high in CU traits (measured via parent report on the Antisocial Process Screening Device), both with and without accompanying conduct problems, compared to boys without conduct problems or CU traits. Interestingly, in this study the CU-only group of boys (high CU traits without conduct problems) had lower cortisol than conduct problem-only boys, but the combined group did not differ from the conduct problem-only group. Notably, this effect was not seen in the girls in this sample. Additional evidence for low basal cortisol in CU traits comes from a prospective study. Burke, Loeber, and Lahey (2007) found that basal cortisol in late childhood or early adolescence was negatively associated with psychopathy (assessed by trained interviewers using the revised Psychopathy Checklist) at ages 18 and 19. These studies provide some early indications that CU traits may be associated with low basal cortisol.

Other studies have not supported a relationship between basal cortisol and CU traits. In a study attempting to validate the Inventory of Callous and Unemotional Traits (ICU), a measure of CU traits incorporating three dimensions (callous, uncaring, and unemotional), self-reported CU traits were not found to have a significant relationship with basal cortisol in adolescents (Berg et al., 2013). However, in this study, self-reported CU traits were not correlated with other indicators as expected; for example, self-reported CU traits as measured by the ICU had a strong positive correlation with anxiety, depression, and loneliness, even after controlling for externalizing symptoms. In contrast, caregiver-reported scores on the ICU were not significantly correlated with most

measures of internalizing symptoms in this study, and the relationship between caregiver-reported CU traits and cortisol was not reported. Therefore, it is possible that Berg et al.'s (2013) results indicate that some children may interpret their own internalizing symptoms as reflecting CU traits. Some of the items of the ICU may also overlap with internalizing constructs. For example, one item on the uncaring dimension is "I always try my best" (reverse-coded), and an item included on the unemotional dimension is "I do not show my emotions to others." These issues highlight the importance of further research into the validity of measures of CU traits.

One other study has reported null findings for CU traits and cortisol. Poustka and colleagues (2010) reported a negative association between cortisol and aggression, but no significant effect for CU traits, as measured by parent report on the Psychopathy Screening Device, in a community sample of German adolescents. It is important to note that this study measured plasma cortisol, or cortisol levels in the blood, whereas most studies use salivary cortisol. Salivary cortisol represents the level of "free" cortisol, or the amount available to bind to receptors, whereas plasma cortisol measures "total" cortisol, including bound and unbound cortisol. It has been argued that "free" cortisol is of more interest because it indexes the portion of the cortisol that can bind to receptors in the brain (Alink et al., 2008). Thus, although the results reported in Berg et al. (2013) and Poustka et al. (2010) may contradict earlier findings, they suffer from substantial weaknesses.

In terms of cortisol reactivity, there appears to be only one published study of CU traits and cortisol reactivity in children. Stadler and colleagues (2011) examined the impact of CU traits (measured via parent-report on the ICU) on cortisol reactivity within

a group of children with attention-deficit/hyperactivity disorder (ADHD) and disruptive behavior. The authors found that the group of children with ADHD who were high in CU traits had a blunted cortisol response to the TSST compared to ADHD-only children. While these results are in the expected direction, there is clearly a large gap in the literature given that cortisol reactivity does not appear to have been measured in children high in CU traits without ADHD.

The Current Study

The current study aims to test the hypothesis that CU traits, and not CD, are associated with decreased cortisol reactivity. As noted by Blair (2008), deficits in emotional reactivity of the kind that are associated with decreased HPA axis activity are thought to be particular to psychopathy rather than to antisocial behavior as a whole. Therefore, the mixed findings cited by Alink and colleagues (2008) may have arisen from the unaccounted presence of CU traits. The present study addresses this hypothesis in a community sample of pre-adolescent boys and girls. As noted by Shirtcliff, Granger, Booth, and Johnson (2005), children between the ages of 6 and 16 may be particularly good targets for research on hormone-behavior relationships because behavior problems often develop within this age range and because the HPA axis undergoes significant developmental changes during puberty. Furthermore, much of the previous literature has focused solely on boys, whose hormone-behavior relationships may differ from girls (see, e.g., Loney et al., 2006). Thus, the current study is well-positioned to fill several gaps in the literature.

Method

Participants

See Section 1 for details.

Measures

Conduct and Oppositional Defiant Disorder Questionnaire. See Section 1 for details. *Antisocial Process Screening Device.* See Section 1 for details.

Diagnostic Interview Schedule for Children. Attention-deficit/hyperactivity disorder (ADHD) has previously been shown to be associated with alterations in HPA axis activity (Imeraj et al., 2012; McCarthy et al., 2011; Pesonen et al., 2011); therefore, ADHD was included as a potential covariate in the current study. See Section 1 for details.

Child Behavior Checklist/Youth Self-Report. Internalizing psychopathology was included as a covariate due to reports that internalizing symptoms are associated with altered HPA axis activity (Hartman, Hermanns, de Jong, & Ormel, 2013; Pervanidou et al., 2013; Tyrka et al., 2012). See Section 1 for details.

Tanner Stage. Puberty has been associated with changes in HPA axis activity; specifically, greater pubertal development predicts increased cortisol and a blunted circadian rhythm in cortisol production (Shirtcliff et al., 2012). Therefore, puberty was included as a covariate in the current study. Pubertal development was assessed via self-report using the measure developed by Morris and Udry (1980) based on Tanner's (1962) descriptions of puberty. The measure consists of a set of drawings that represent five stages of development of breasts (for girls) or penis/testes (for boys) and pubic hair (for girls and boys). The drawings are accompanied by a description of each stage. Children were instructed to choose the picture that is closest to their stage of development. Although some children over- or under-estimate pubertal development, self-reported

Tanner stage is considered to be an adequate estimate of pubertal development when exact pubertal stage is not necessary (Dorn & Biro, 2011). Furthermore, most children report a Tanner stage within one stage of physician-assessed pubertal development. For instance, Schmitz and colleagues (2004) reported correlations of $r = .79$ to $r = .88$ for agreement between self-reported and physician-assessed Tanner stage. For the current analyses, set 1 (breast/male genitalia development) and set 2 (pubic hair growth) were entered as separate predictors of cortisol activity.

Procedure

Children and their caregivers arrived at the laboratory at approximately 9:00 am on the day of testing. Tasks in the morning included a blood draw (child), fMRI scan (child), and completion of questionnaires (child and caregiver). At approximately 11:30 am, children were prepared for a psychophysiology assessment. During this assessment, children performed a series of tasks, one of which was a stress task. See section 2 for details.

Saliva Collection and Analysis

Saliva samples were collected at the following times during the day: 1) three samples collected in the morning starting at 9:00 am, 15 minutes apart; 2) at the beginning of the psychophysiology assessment (approximately 12:00 pm); 3) five minutes after the end of the stress task (approximately 12:30 pm); 4) 20 minutes after the end of the stress task (approximately 12:45 pm); and 5) 40 minutes after the end of the stress task (approximately 1:05 pm). Only samples 2-5 were included in the present analysis. Peak levels of cortisol are expected to occur 20 minutes after the stress task (Granger et al., 2007). Participants were instructed to refrain from eating or drinking

(except water) prior to sample collection (Granger et al., 2012). As recommended by Granger and colleagues (2007), whole, unstimulated saliva was collected by passive drool. Samples were frozen immediately after collection at -80° F until assay.

Saliva samples were analyzed in the laboratory using commercially available enzyme immunoassay kits from Salimetrics (State College, PA). Samples were assayed in duplicate, using two 25- μ L samples of saliva, and the average of the tests was used. Sample plates were read at 450 nm using a plate reader and accompanying software was used to obtain standard curves and sample values. Intra-assay and inter-assay coefficients of variation were calculated to test for reliability. Assay performance characteristics for cortisol kits have been previously shown to be very good. Average recovery across saliva samples with known cortisol concentrations is 100.8%, inter-assay precision is 6.4% for low cortisol and 3.8% for high cortisol samples, and sensitivity of the cortisol kit is 0.003 μ g/dL (Salimetrics, 2006).

Data Reduction and Statistical Analysis

The area under the curve (AUC) is a measure often used to quantify total cortisol production over repeated measurements as well as cortisol reactivity. It uses a trapezoidal formula to calculate the area contained by the shape that is produced when the cortisol values are plotted on a graph. The AUC is preferred for use with cortisol because the length of time between saliva samples is usually not equally spaced, whereas an analysis such as repeated-measures ANOVA cannot account for variable spacing of measures (Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003). In the present analysis, I calculated both the AUC with respect to ground (AUC_G), which gives a measure of total cortisol output and is more closely linked with basal cortisol, and the AUC with respect

to increase (AUC_I), which provides more information about cortisol reactivity. The formulae used are as follows:

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

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

In these formulae, m represents each measurement and t represents the time elapsed between each measurement. Although t ideally would be identical for every participant, this was not the case with these data due to complications with the psychophysiology equipment, which necessitated a pause in the experiment protocol at times. Therefore, the average time elapsed was used to calculate AUC_G and AUC_I. Additionally, in order to explore the possible effect of these differences in timing, adjusted values of both AUC_G and AUC_I were calculated. For the adjusted values, the formulae were the same as above, with two exceptions. The first was that, in this case, rather than representing the mean time elapsed, t represents the time elapsed for each individual participant (i.e., the formula for each participant used his or her own elapsed time to calculate the AUC). Second, these values were then divided by the total time elapsed for that participant in order to account for the fact that larger values for t in the original formulae would produce larger AUCs. Therefore, the adjusted values were calculated as follows:

$$\text{adjusted } AUC_G = \frac{AUC_G'}{\sum_{i=1}^{n-1} t_{i+1} - t_i}$$

$$\text{adjusted } AUC_I = \frac{AUC_I'}{\sum_{i=1}^{n-1} t_{i+1} - t_i}$$

As is often the case with cortisol data, the AUC values were positively skewed, so a natural logarithm transformation was applied prior to statistical analysis. Outliers for each AUC measure as well as for time of day and total time elapsed were defined as values more than three standard deviations away from mean and were removed. In order to reduce collinearity, the variables for CD symptoms, CU traits, internalizing symptoms, and ADHD symptoms were mean-centered. The analyses consisted of a series of linear regressions predicting each AUC measure. The predictors entered into each model were CD symptoms, CU traits, the interaction between CD symptoms and CU traits, Tanner stage (set 1 and set 2), sex, race (coded as African American versus other race), internalizing symptoms, and ADHD symptoms. In order to improve model fit, covariates were dropped from the model if they were non-significant.

Results

Table 8 presents correlations among predictor and outcome variables and Table 9 presents parameter estimates and significance tests.

AUC_G. The final model predicting *AUC_G* included as predictors Tanner stage set 2 (pubic hair growth), internalizing, CD symptoms, CU traits, and CD symptoms × CU traits. The final model was significant, with the predictors accounting for approximately 6% of the variance in *AUC_G*. Symptoms of CD predicted significantly higher *AUC_G*, whereas CU traits were associated (at a trend level) with decreased *AUC_G* (see Figures 7 and 8). The interaction between CD symptoms and CU traits did not significantly predict

AUC_G. Unexpectedly, internalizing symptoms predicted decreased AUC_G, whereas pubic hair growth predicted increased AUC_G.

Adjusted AUC_G. When AUC_G was adjusted for individual variations in the length of time between saliva samples, the results were fairly similar. The final model predicting adjusted AUC_G included the same predictors as for AUC_G: Tanner stage set 2, internalizing, CD symptoms, CU traits, and CD symptoms × CU traits. The model was significant, with the predictors account for approximately 4% of the variance in adjusted AUC_G. As before, symptoms of CD predicted higher adjusted AUC_G, but only at a trend level, and CU traits again showed a trend toward predicting lower adjusted AUC_G. The interaction between CD symptoms and CU traits did not significantly predict adjusted AUC_G. Although the effect was not as strong as for AUC_G, internalizing symptoms was a significant predictor of decreased adjusted AUC_G, and pubic hair growth predicted increased adjusted AUC_G.

AUC_I. The final model predicting AUC_I was not statistically significant. Symptoms of CD and CU traits, either as main effects or in interaction, did not predict AUC_I. Tanner stage set 1 (breast/genitalia development) was positively associated with AUC_I, and non-African American participants had slightly higher values of AUC_I than African American participants.

Adjusted AUC_I. The final model predicting adjusted AUC_I was not statistically significant. Symptoms of CD and CU traits, either as main effects or in interaction, did not predict adjusted AUC_I. Non-African American race was associated with higher values of adjusted AUC_I.

Discussion

Conduct Disorder, Callous-Unemotional Traits, and Cortisol

As predicted, CU traits, rather than symptoms of CD, were found to be associated with a trend toward lower cortisol reactivity to stress, as measured by AUC_G . In fact, for unadjusted AUC_G , symptoms of CD were associated with *increased* cortisol reactivity when CU traits were included in the model. These results were significant (for CD), or marginally so (for CU traits), for AUC_G but not for AUC_I . These two measures of cortisol production vary in their interpretation. Given that AUC_G includes the differences between each cortisol measure as well as the distance of these measures from zero, it can be interpreted as representing the sensitivity and the overall intensity of the cortisol response (Francis, Granger, & Susman, 2013). The AUC_I , in contrast, does not incorporate the distance from zero and thus only indexes changes in cortisol output compared to the baseline set by the first sample (Francis et al., 2013). Therefore, these results suggest that higher levels of CU traits tend to be associated with lower intensity of cortisol response; that is, lower overall absolute level of cortisol production over the four samples. Symptoms of CD, in contrast, appear to be associated with higher intensity of cortisol response.

The marginally significant negative association between CU traits and cortisol reactivity provides some evidence for the hypothesis that CU traits reflect an underlying deficit in emotional responses (Blair, 2008). This deficit, reflected in hypoarousal to a stressor, may simultaneously lead children high in CU traits to engage in antisocial behavior out of a desire for stimulation (Quay, 1965) or fearlessness (Raine, 2002) while also reducing the effectiveness of punishment for these behaviors (Blair et al., 2006). In contrast, the positive association between symptoms of CD and cortisol reactivity

suggests that children with CD (in the absence of CU traits) may actually experience hyperarousal to a stressor, rather hypoarousal. This finding is not unique in the literature. McBurnett and colleagues (2005) noted that studies in community samples frequently report positive associations between cortisol reactivity and conduct problems, whereas clinic-based samples more often report negative associations. The authors suggest that this difference may reflect higher levels of psychopathic traits among clinic-referred samples, and they note that “hostile-reactive” aggression may be expected to be positively associated with HPA axis activity (McBurnett et al., 2005). While Alink and colleagues’ (2008) meta-analysis did not support a moderating role of clinic versus community samples, the authors did suggest that reactive aggression might be associated with increased cortisol activity, whereas proactive aggression may predict decreased cortisol. Given the evidence that CU traits appear to be more strongly linked than CD symptoms to proactive aggression (Blader et al., 2013; Kimonis et al., 2014; Thornton, Frick, Crapanzano, & Terranova, 2013), the current results are consistent with Alink and colleagues’ (2008) proposal.

Internalizing Symptoms and Cortisol

In the current study, internalizing symptoms were found to predict decreased AUC_G, indicating that higher levels of internalizing symptoms were associated with a less intense cortisol response to stress. This result is surprising, given that increased HPA axis activity would be expected in response to the symptoms associated with internalizing (e.g., anxiety, withdrawal). Furthermore, previous studies have associated internalizing in childhood with enhanced cortisol reactivity (Davies, Sturge-Apple, & Cicchetti, 2011; Hartman et al., 2013; Hastings et al., 2011). However, there have been indications that

different forms of internalizing may be associated with different patterns of HPA activity. A meta-analysis found that depression in childhood and adolescence was associated with increased cortisol reactivity (Lopez-Duran, Kovacs, & George, 2009), while another meta-analysis of posttraumatic stress disorder (including studies of both children and adults) found evidence for blunted cortisol reactivity (Morris, Compas, & Garber, 2012). Thus, the negative relationship between internalizing and cortisol reactivity in the current study may reflect the type of internalizing symptoms expressed by the children.

Limitations

The results of the current study should be interpreted within the context of several possible limitations. First, cortisol in this study was measured without adjusting for menstrual phase of the female participants because these data were not collected from the participants. Although many of the participants in this study may not have passed menarche, there is evidence that menstrual phase is associated with cortisol reactivity to stress in adult women (Duchesne & Pruessner, 2013; Espin et al., 2013). Second, it is possible that the stress task in the present study was not strong enough to elicit a robust stress response. As noted in section 2, the stress task did elicit an increase in HR and SCL. However, most participants exhibited declining cortisol levels over the course of the saliva samples collected after the stressor. Diurnal patterns in cortisol secretion dictate that cortisol does decline from a peak in the morning (Matchock, Dorn, & Susman, 2007), and thus this rhythm may have overshadowed the cortisol response in our sample. However, the flattening of the slope across samples 2 to 4 may reflect the influence of a stress-driven delay in the decrease of cortisol. Third, although the models predicting AUC_G and adjusted AUC_G were statistically significant, they represented very

small effect sizes. These results are in line with previous research, but they highlight the need for caution in interpreting the practical significance of these effects.

Conclusions

These limitations notwithstanding, the current study adds to the extant literature in several regards. For one, it appears to be the first study to examine differences in cortisol reactivity to stress based on CU traits in children. In addition, the use of a community sample in the current study suggests that findings of differences in cortisol production are generalizable to non-clinical populations of children with CD symptoms. Finally, this study included both boys and girls, in contrast to the heavy reliance on male samples in research on CD.

The finding of increased cortisol reactivity in association with CD symptoms and a trend toward decreased reactivity in CU traits adds to the growing literature suggesting that CU traits are accompanied by a unique neurobiological profile (Blair et al., 2006; Frick & Viding, 2009). With further research examining cortisol reactivity in children who have not yet been diagnosed with CD, this measure may be helpful in identifying children at risk for developing CD and/or CU traits. Additionally, further examination of HPA axis activity may deepen our understanding of the biological risk and protective factors involved in producing antisocial behavior.

GENERAL DISCUSSION

Across these three studies, significant evidence has emerged suggesting that the biological correlates of CU traits differ from those of CD as a whole. In fact, while there were some significant relationships between CD and the biological indicators, for the most part CU traits accounted for more of the variation in these indicators than did symptoms of CD. These results suggest that CU traits do, in fact, identify a qualitatively distinct subset of children with CD. Specifically, CU traits in this sample appeared to identify children who were generally underaroused and who had a blunted response to stress, even after controlling for symptoms of CD. In contrast, when controlling for CU traits, CD symptoms were not associated with general hypoarousal but were linked to a mixture of decreased SNS activity and increased HPA axis activity, possibly reflecting both disinhibition and hyperreactivity to stress. The biological profile of hypoarousal and hyporesponsivity to stress in children with CU traits paints a picture very much in line with Blair's (2008) contention that psychopathy develops from a poverty of emotion, whereas the decreased SNS activity and increased cortisol reactivity to stress seen in relationship with CD symptoms supports Beauchaine and et al.'s (2007) view that CD results from a combination of impulsivity and emotion dysregulation.

These findings have several implications for the study of antisocial behavior, especially for biological research. As noted in the literature review for each study, meta-analyses of the relationship between antisocial behavior and various biological measures have, without fail, uncovered substantial heterogeneity in effect sizes across studies. Although this in and of itself is not unusual, it is striking that, despite substantial evidence that children with CD encompass a heterogeneous group, most studies included

in these meta-analyses did not attempt to address this heterogeneity. The results reported here suggest that inconsistencies in the literature may be due at least in part to the presence of psychopathic or CU traits in these studies, and future research would benefit from accounting for these traits.

Additionally, these findings highlight some areas in need of further research. One such area is the question of how to conceptualize children who are high in CU traits but low in CD symptoms. On the one hand, it is possible that these children are not impaired by their CU traits. Alternatively, past research indicates that, in comparison to typical controls, these children self-report higher levels of delinquency, are more likely to be later diagnosed with CD, ADHD, oppositional defiant disorder, or an anxiety disorder, and are more likely to have contact with police (Frick et al., 2005; Rowe et al., 2010). Given that CU traits were related to biological correlates independent of CD in the studies reported here, children high in CU traits without CD likely experience similar biological risk factors for antisocial behavior to those with CD. These children may, therefore, benefit from prevention efforts.

A further question that arises from this work pertains to the relationship between CU traits and anxiety. As noted earlier, the positive correlation between CU traits and internalizing seen in this sample was accounted for by their shared relationship with CD. However, although their relationship was no longer significant once CD symptoms were controlled, their correlation does indicate that there are some children who are both high in CU traits and internalizing symptoms. Berg and colleagues (2013) noted a similar finding in their attempt to validate the Inventory of Callous and Unemotional Traits (ICU). They found that self-reported ICU scores (but not caregiver-reported scores) were

strongly and positively correlated with anxiety, depression, and loneliness. These findings contradict the idea that psychopathy in children reflects an underlying emotional deficit and insensitivity to punishment. In noting the possible existence of a group of callous children who are high in anxiety, Lahey (2014) speculated that such a group may be similar to secondary psychopathy in adults. Studies of primary versus secondary psychopathy have found that the former tend to be low in anxiety and commit more violent offenses, whereas the latter score high on measures of internalizing symptoms and disinhibition (Drislane et al., 2014). The presence of high levels of anxiety in some samples with psychopathic traits suggests either that measurement of psychopathic traits may need to be refined to exclude this group, or that biological theories of psychopathy may need to be reconceptualized in order to account for this group.

A third question that arises concerns the incremental utility of each of the biological measures used in this dissertation. Although each measure taps into different physiological systems, the systems do interact and it is unclear whether EEG, HR, SCL, and cortisol each provide unique data about the biological underpinnings of CD and CU traits. Additionally, it is unclear whether these measures can be used together to predict CD symptoms and/or levels of CU traits. One potential future direction for this research would be to use latent class analysis to group children by CD symptoms and CU traits and then examine the ability of EEG, HR, SCL, and cortisol together to predict class membership in a logistic regression.

In sum, the results of this dissertation support the contention that CU traits do provide useful information about children with CD. Future research exploring the precursors to and outcomes of CU traits in children will help provide a greater

understanding of how these traits develop and, in turn, influence the development of antisocial behavior in children and adolescents.

TABLES

Table 1: Characteristics of Participants, Total Sample and by Race

	Total (N = 446) Mean (SD)	African American (N = 358) Mean (SD)	Other Race (N = 88) Mean (SD)	F/χ^2	p
Age (years)	11.91 (0.60)	11.94 (0.60)	11.84 (0.56)	1.74	.188
Sex (% male)	50.67%	50.28%	52.27%	0.11	.738
COD score	4.64 (4.31)	4.93 (4.44)	3.43 (3.48)	8.32	.004
APSD CU score	5.73 (2.08)	5.95 (2.03)	4.84 (2.02)	20.81	<.001
ADHD symptoms	4.52 (4.96)	4.64 (5.02)	4.07 (4.75)	0.91	.341
CBCL/YSR Internalizing (<i>T</i> -score)	59.00 (9.18)	59.28 (9.18)	58.04 (9.08)	1.31	.254

Note. Significance tests indicate difference between African American and other race participants. COD = Conduct and Oppositional Defiant Disorder Questionnaire; APSD CU = Antisocial Process Screening Device, Callous-Unemotional Traits dimension; CBCL = Child Behavior Checklist; YSR = Youth Self-Report; ADHD = attention-deficit/hyperactivity disorder.

Table 2: Correlations Among Predictor and Outcome Variables, EEG

	1	2	3	4	5	6	7	8	9	10	11
1. Sex	–										
2. Age	.01	–									
3. Race	-.02	-.06	–								
4. CU Traits	-.09 [†]	-.02	-.21***	–							
5. CD symptoms	-.15**	-.005	-.14**	.37***	–						
6. ADHD symptoms	-.25***	-.03	-.05	.31***	.40***	–					
7. Internalizing	-.14**	-.03	-.06	.15**	.37***	.25***	–				
8. Delta power	-.12*	-.10 [†]	.06	-.06	-.03	.11*	.03	–			
9. Theta power	-.03	-.16**	.11*	.02	.02	.10 [†]	.09 [†]	.74***	–		
10. Alpha power	-.03	-.03	.09 [†]	-.03	-.02	.02	.06	.56***	.76***	–	
11. Beta power	-.06	.01	.14**	-.09	.001	.04	.05	.56***	.58***	.64***	–
12. Gamma power	-.09 [†]	.02	.07	-.05	.05	.10 [†]	.01	.23***	.13*	.11*	.62***

Note. Sex coded as male = 1, female = 2. Race coded as African American = 0, other race = 1. SCL and HR values averaged over the four time points recorded for each task. CU = callous-unemotional; CD = conduct disorder; ADHD = attention-deficit/hyperactivity disorder

[†] $p < .10$, * $p < .05$, ** $p < .01$, *** $p < .001$

Table 3: Parameter Estimates for Multilevel Model Predicting EEG

Parameter	Estimate (SD)	<i>t</i> (df)	<i>p</i>
Intercept	1.47 (0.11)	13.78 (1077.00)	< .001
Level 1 (within)			
Frequency band	-1.71 (0.02)	-93.67 (1053.26)	< .001
Region	-0.55 (0.03)	-19.03 (746.91)	< .001
Level 2 (between)			
CD symptoms	0.0004 (0.01)	0.07 (378.29)	.945
CU traits	0.001 (0.01)	0.06 (413.01)	.955
CD symptoms × CU traits	-0.002 (0.002)	-0.67 (380.76)	.505
ADHD symptoms	0.006 (0.005)	1.12 (376.36)	.262
Internalizing	0.002 (0.002)	0.79 (382.42)	.427
Cross-level			
CU × race × band	-0.02 (0.007)	-3.03 (658.08)	.003
Age × band × region	0.01 (0.001)	11.95 (857.32)	< .001
Sex × band × region	-0.006 (0.008)	-0.82 (635.31)	.415

Note. CU = callous-unemotional; CD = conduct disorder; ADHD = attention-deficit/hyperactivity disorder. Sex coded as male = 1, female = 2. Race coded as African American = 0, other race = 1.

Table 4: Characteristics of Participants, Total Sample and by HR and SCL Data

Available

	Total (N = 446) Mean (SD)	HR Available (N = 415) Mean (SD)	SCL Available (N = 345) Mean (SD)
Age (years)	11.91 (0.60)	11.92 (0.59)	11.91 (0.60)
Sex (% male)	50.67%	50.9%	48.7% [†]
Race (% African American)	80.3%	80.8%	79.7%
COD score	4.64 (4.31)	4.59 (4.27)	4.64 (4.41)
APSD CU score	5.73 (2.08)	5.71 (2.10)	5.69 (2.10)
CBCL/YSR Internalizing (<i>T</i> -score)	59.00 (9.18)	58.95 (9.30)	58.56 (9.11) [†]
ADHD symptoms	4.52 (4.96)	4.50 (4.93)	4.49 (4.92)

Note. Significance symbols indicate difference from total sample. HR = heart rate; SCL = skin conductance level; COD = Conduct and Oppositional Defiant Disorder Questionnaire; APSD CU = Antisocial Process Screening Device, Callous-Unemotional Traits dimension; CBCL = Child Behavior Checklist; YSR = Youth Self-Report; ADHD = attention-deficit/hyperactivity disorder.

[†] $p < .10$

Table 5: Correlations Among Predictor and Outcome Variables, SCL and HR

	1	2	3	4	5	6	7	8	9	10	11	12
1. Sex	–											
2. Age	.01	–										
3. Race	-.02	-.06	–									
4. CU Traits	-.09 [†]	-.02	-.21***	–								
5. CD symptoms	-.15**	-.005	-.14**	.37***	–							
6. ADHD symptoms	-.25***	-.03	-.05	.31***	.40***	–						
7. Internalizing	-.14**	-.03	-.06	.15**	.37***	.25***	–					
8. SCL rest	-.05	.13*	.34***	-.17**	-.15**	-.09 [†]	-.16**	–				
9. SCL speech	-.09	.13*	.32***	-.14*	-.18**	-.10 [†]	-.16**	.91***	–			
10. SCL final	-.13*	.10 [†]	.32***	-.14*	-.17**	-.06	-.17**	.88***	.95***	–		
11. HR rest	.13**	-.15**	.02	-.08 [†]	-.10*	-.07	-.03	.08	.08	.03	–	
12. HR speech	.15**	-.09 [†]	.11*	-.16**	-.12*	-.13**	-.06	.10 [†]	.12*	.06	.84***	–
13. HR final	.12*	-.12*	.03	-.08	-.13**	-.07	-.03	.04	.07	.03	.86***	.89***

Note. Sex coded as male = 1, female = 2. Race coded as African American = 0, other race = 1. SCL and HR values averaged over the four time points recorded for each task. CU = callous-unemotional; CD = conduct disorder; ADHD = attention-deficit/hyperactivity disorder; SCL = skin conductance level; HR = heart rate.

[†] $p < .10$, * $p < .05$, ** $p < .01$, *** $p < .001$

Table 6: Parameter Estimates for Multilevel Model Predicting Heart Rate

Parameter	Estimate (SD)	<i>t</i> (df)	<i>p</i>
Intercept	4.63 (0.10)	48.63 (387.81)	< .001
Level 1 (within)			
Time	0.01 (0.001)	10.85 (375.88)	< .001
Time ²	-0.001 (0.0001)	-9.00 (368.54)	< .001
Level 2 (between)			
CD symptoms	-0.001 (0.001)	-0.82 (386.03)	.413
CU traits	-0.01 (0.002)	-2.53 (387.13)	.012
CD symptoms × CU traits	-0.0003 (0.001)	-0.75 (385.25)	.453
Sex	-0.02 (0.01)	-2.41 (386.78)	.016
Age	-0.02 (0.01)	-2.55 (387.08)	.011

Note. CU = callous-unemotional; CD = conduct disorder. Sex coded as male = 1, female = 2.

Table 7: Parameter Estimates for Multilevel Model Predicting Skin Conductance Level

Parameter	Estimate (SD)	<i>t</i> (df)	<i>p</i>
Intercept	1.59 (0.53)	3.00 (320.46)	.003
Level 1 (within)			
Time	-0.03 (0.003)	-9.03 (310.76)	< .001
Time ²	0.001 (0.0002)	5.76 (301.89)	< .001
Level 2 (between)			
CD symptoms	-0.01 (0.01)	-1.06 (347.79)	.291
CU traits	-0.02 (0.01)	-1.42 (323.30)	.156
CD symptoms × CU traits	0.01 (0.003)	2.22 (318.75)	.027
Sex	0.09 (0.05)	1.63 (320.42)	.105
Age	0.13 (0.04)	2.80 (319.30)	.005
Race	-0.28 (0.07)	-4.12 (316.83)	< .001
Cross-level			
CD symptoms × Time	0.0002 (0.0003)	0.51 (301.45)	.608

Note. CU = callous-unemotional; CD = conduct disorder. Sex coded as male = 1, female = 2. Race coded as African American = 0, other race = 1.

Table 8: Correlations Among Predictor and Outcome Variables, Cortisol

	1	2	3	4	5	6	7	8	9	10	11	12
1. Sex	–											
2. Age	.01	–										
3. Race	-.02	-.06	–									
4. CU Traits	-.09 [†]	-.02	-.21***	–								
5. CD symptoms	-.15**	-.005	-.14**	.37***	–							
6. Tanner stage, set 1	.20***	.37***	-.28***	.09 [†]	.01	–						
7. Tanner stage, set 2	.18***	.32***	-.28***	-.01	-.03	.73***	–					
8. ADHD symptoms	-.25***	-.03	-.05	.31***	.40***	-.15**	-.17***	–				
9. Internalizing	-.14**	-.03	-.06	.15**	.37***	-.05	-.01	.25***	–			
10. AUC _G	.02	.06	-.002	-.09 [†]	-.04	.10 [†]	.17**	-.14**	-.10*	–		
11. AUC _I	-.06	-.02	-.01	.01	.002	-.01	-.01	-.01	-.04	-.06	–	
12. Adjusted AUC _G	.02	.06	-.003	-.10 [†]	-.04	.10 [†]	.17**	-.14**	-.10*	1.00***	-.05	–
13. Adjusted AUC _I	-.05	-.06	.02	.03	.04	-.08 [†]	-.09 [†]	.06	.01	-.45***	.79***	-.45***

Note. Tanner stage set refers to genitalia (set 1) or pubic hair (set 2). CU = callous-unemotional; CD = conduct disorder; ADHD = attention-deficit/hyperactivity disorder; AUC_G = area under the curve with respect to ground; AUC_I = area under the curve with respect to increase.

[†] $p < .10$, * $p < .05$, ** $p < .01$, *** $p < .001$

Table 9: Regression Coefficients and Significance Tests, By Outcome, Cortisol

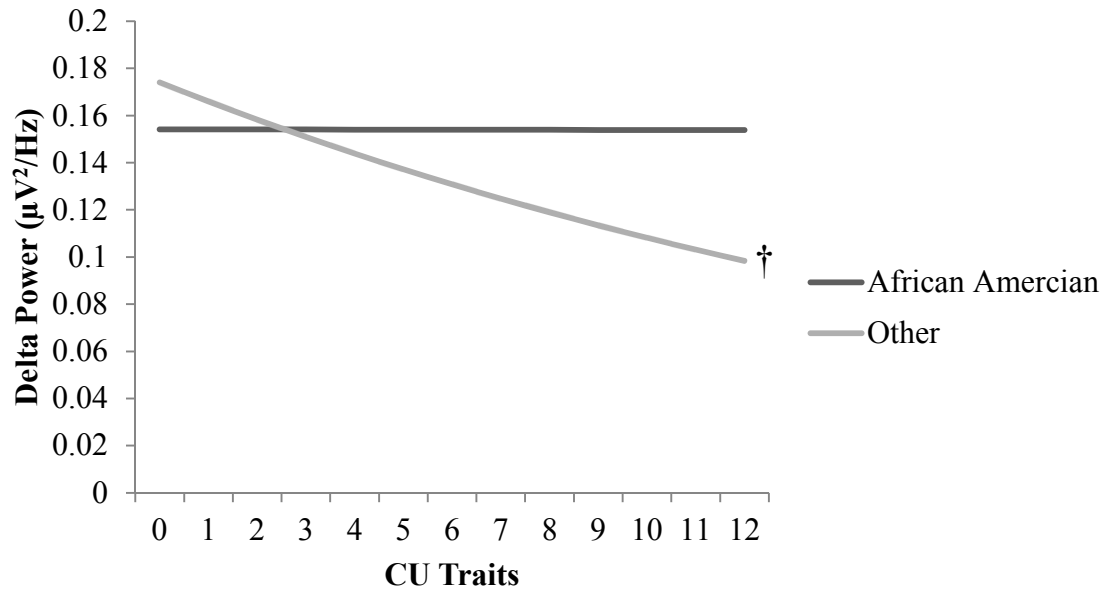
Outcome	Predictor	β^a	t	p	Full Model		
					R^2	F	p
AUC _G	Constant	2.00	30.63	<.001	0.06	4.19	.001
	Tanner Stage (set 2)	0.16	3.06	.002			
	Internalizing	-0.16	-2.88	.004			
	CD	0.13	1.98	.048			
	CU	-0.10	-1.83	.068			
	CDxCU	-0.04	-0.80	.426			
Adjusted AUC _G	Constant	-6.52	-97.98	<.001	0.04	3.31	.006
	Tanner Stage (set 2)	0.13	2.60	.010			
	Internalizing	-0.13	-2.44	.015			
	CD	0.10	1.63	.103			
	CU	-0.11	-1.95	.052			
	CDxCU	-0.03	-0.63	.529			
AUC _I	Constant	4.46	653.82	<.001	0.02	1.53	.180
	Tanner Stage (set 1)	0.12	2.19	.029			
	Race	0.12	2.04	.042			
	CD	-0.002	-0.04	.968			
	CU	-0.001	-0.01	.990			
	CDxCU	0.03	0.55	.579			
Adjusted AUC _I	Constant	1.06	1037.56	<.001	0.02	1.86	.117
	Race	0.11	1.99	.047			
	CD	0.03	0.55	.582			
	CU	0.10	1.81	.071			
	CDxCU	-0.02	-0.30	.766			

Note. AUC_G = area under the curve with respect to ground; AUC_I = area under the curve with respect to increase; CD = conduct disorder; CU = callous-unemotional traits. Tanner stage set refers to genitalia (set 1) or pubic hair (set 2).

^aBetas are in standardized form, except for the constant.

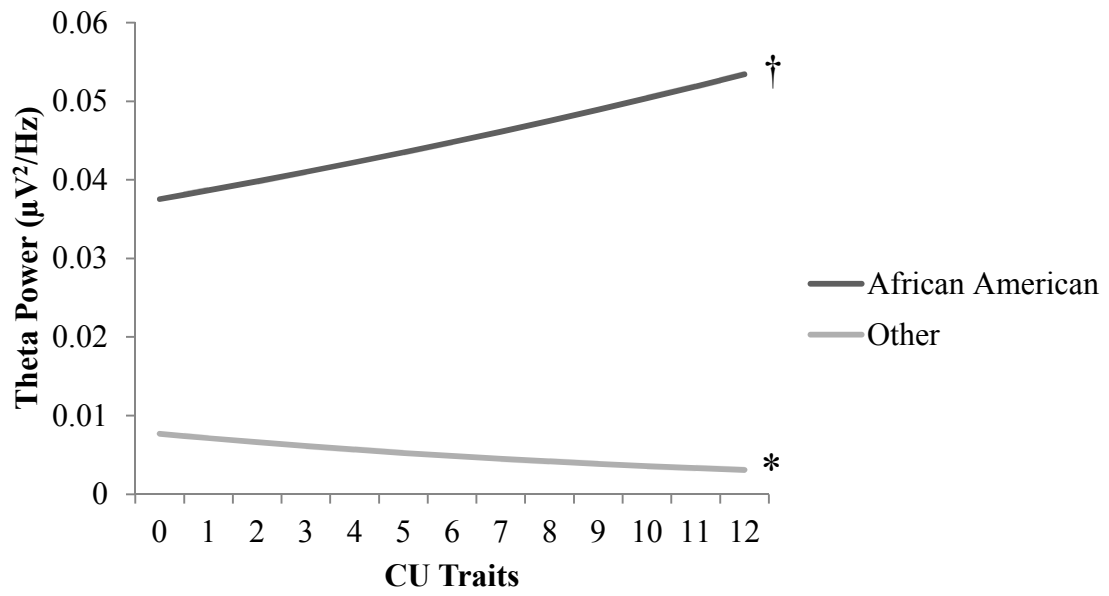
FIGURES

Figure 1: Modeled interaction between callous-unemotional traits and race, delta



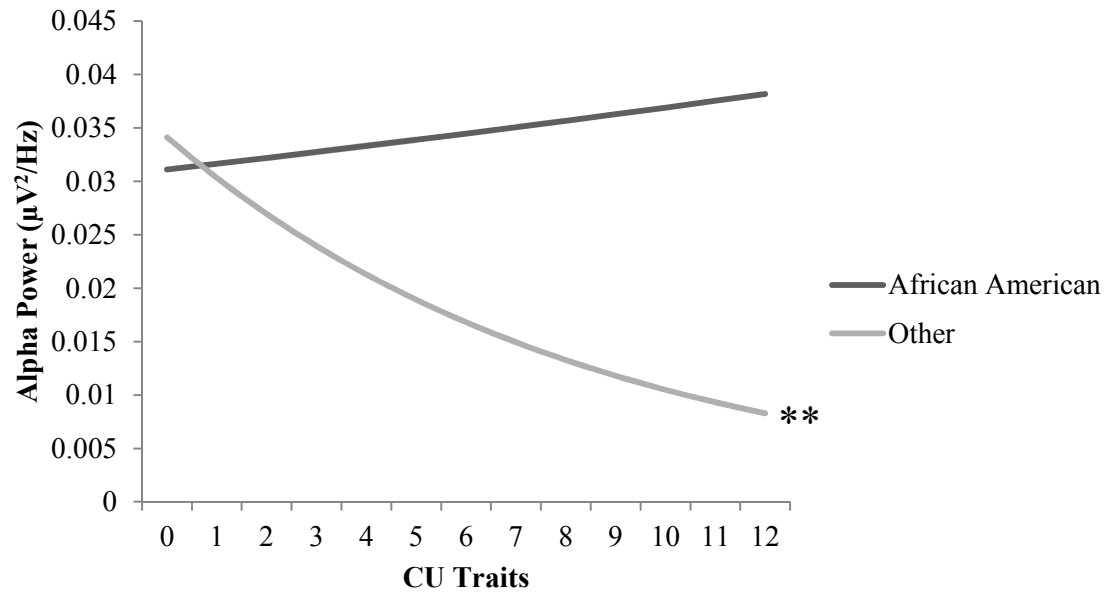
† $p < .10$

Figure 2: Modeled interaction between callous-unemotional traits and race, theta



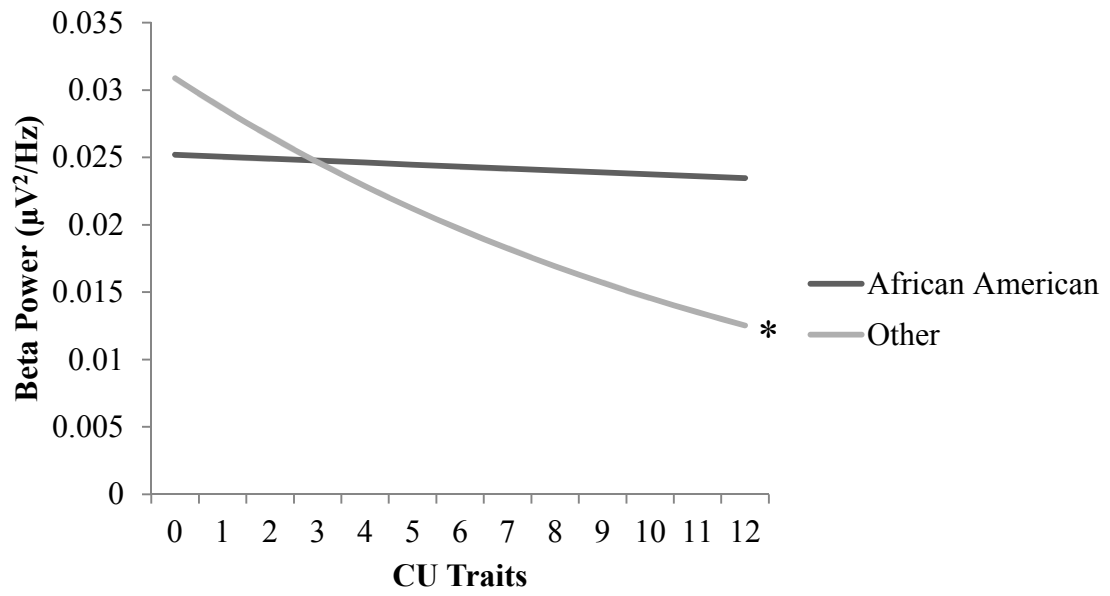
† $p < .10$
* $p < .05$

Figure 3: Modeled interaction between callous-unemotional traits and race, alpha



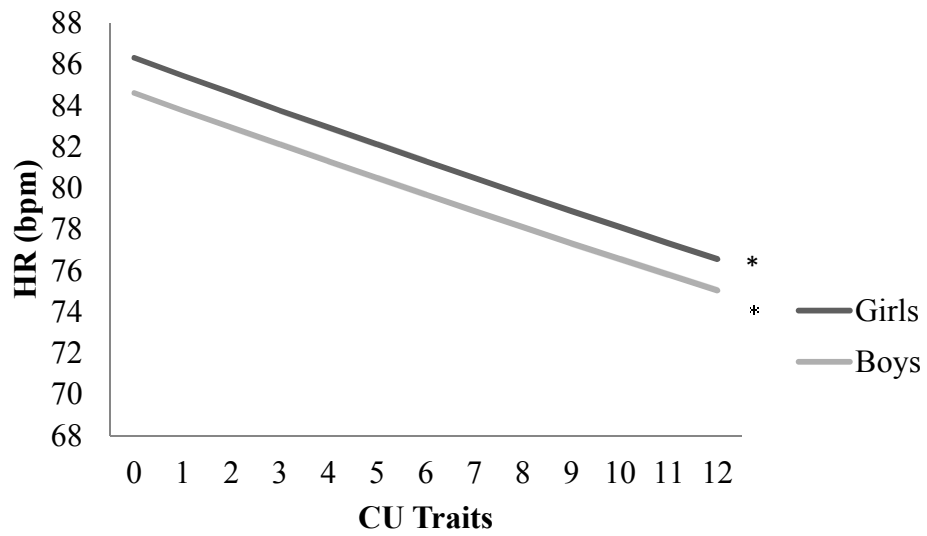
** $p < .01$

Figure 4: Modeled interaction between callous-unemotional traits and race, beta



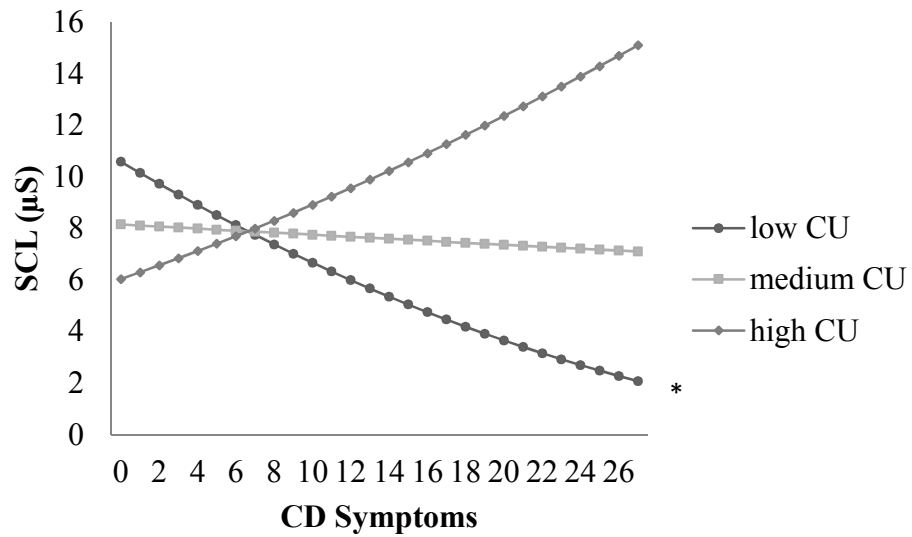
* $p < .05$

Figure 5: Modeled relationship between heart rate and callous-unemotional traits for a child of average age, with no symptoms of conduct disorder, at rest, by sex.



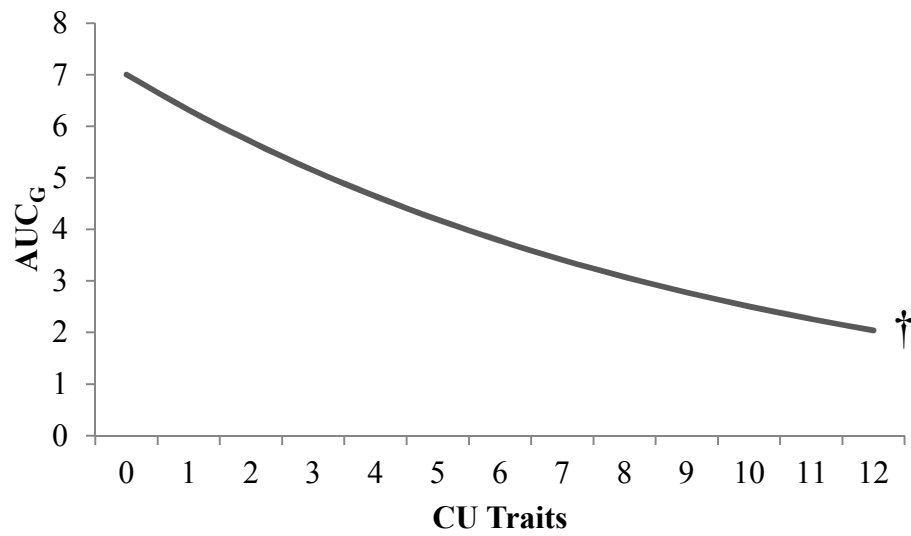
* $p < .05$

Figure 6: Modeled relationship between skin conductance level and conduct disorder score for a child of average age, African American race, and female sex, at rest. Low CU = score of 0 on the Antisocial Process Screening Device; medium CU = score of 6 on the APSD; high CU = score of 12 on the APSD.



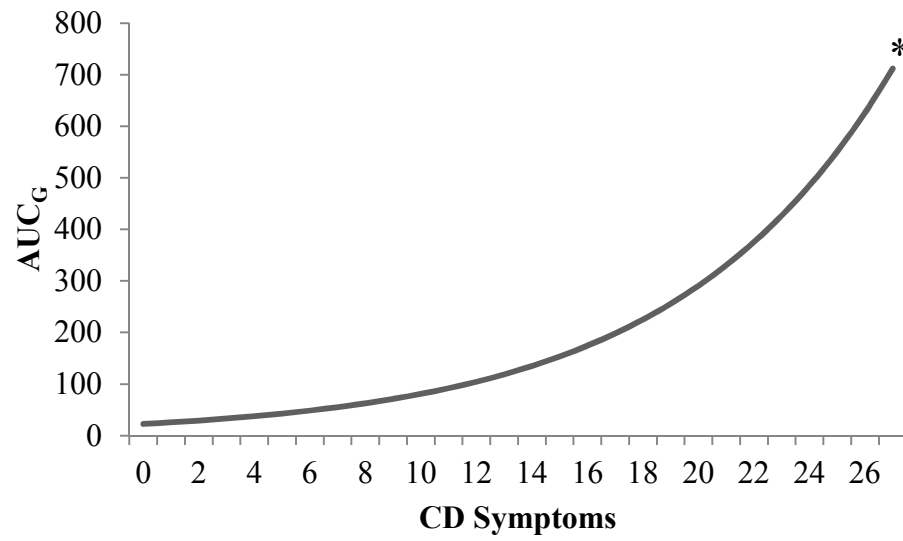
* $p < .05$

Figure 7: Modeled relationship between AUC_G and callous-unemotional traits for a child of average level of conduct disorder symptoms, internalizing, and pubertal development.



† $p < .10$

Figure 8: Modeled relationship between AUC_G and conduct disorder score for a child of average level of callous-unemotional traits, internalizing, and pubertal development.



* $p < .05$

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