

Greater fear reactivity and psychophysiological hyperactivity among infants with later conduct problems and callous-unemotional traits

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Background: Approximately one third of children who meet criteria for conduct problems (CP) are also characterized by elevated callous-unemotional (CU) traits. This subgroup is at elevated risk for more pervasive and extreme levels of later antisocial behavior and has been characterized by a fearlessness temperament and blunted stress psychophysiology at older ages. The objective of this study was to examine group differences in fear reactivity and stress psychophysiology in infancy among children classified as having CP with CU (CP + CU), CP without CU (CP only), or no CP in later childhood. **Methods:** A birth cohort study ($n = 1,292$) was followed longitudinally from birth through first grade. Behavioral fear, baseline heart period (HP) and respiratory sinus arrhythmia (RSA), and pretask, 20-min posttask, and 40-min posttask salivary cortisol were assessed at 6 and 15 months of age around a fear challenge task. CP and CU were assessed by maternal report at first grade and children were classified into CP and CU groups if they scored in the upper 10th percentile of these ratings. **Results:** No group differences were observed in children at 6 months of age. However, at 15 months of age children with later CP + CU displayed greater high-intensity fear behavior, higher pretask and overall cortisol levels, and lower levels of HP and RSA compared to children with CP only and children with no CP. **Conclusions:** The discrepancy between the biobehavioral correlates of conduct problems with callous-unemotional traits in infancy and those reported from studies of older children and adults suggests that the etiology of this behavioral phenotype may be more complex than a simple genetic maturation model. **Keywords:** Fearlessness, psychobiology, autonomic, cortisol, conduct problems, callous-unemotional traits.

Introduction

Chronic aggression and violent behavior often follow a life-course trajectory with childhood conduct problems (CP) evidenced early in life (Moffitt & Caspi, 2001). There is also growing evidence that callous-unemotional (CU) traits, considered as a specific dimension of psychopathy, can (a) be extended downward from adolescence into early and middle childhood (Frick & Viding, 2009), (b) account for some of the clinical heterogeneity in children with elevated conduct problems (Rowe et al., 2010), and (c) predict future antisocial behavior (Frick & Viding, 2009). Approximately, one third of all children who meet diagnostic criteria for conduct problems are also characterized by having high callous-unemotional traits, leading to the expectation that approximately 2%–4% of all children meet this joint (CP + CU) criterion (Frick & Viding, 2009). Although understanding the etiology of this subgroup of children clearly has significant clinical and public health

implications, very few prospective studies exist of CP + CU that can examine the very early developmental origins of this behavioral phenotype. Because most of the extant study on this topic is based on clinical samples ranging from preadolescence to adulthood, the developmental and psychobiological models of CP + CU are largely limited to these ages, although an exception to that is a recent prospective study by Gao, Raine, Venables, Dawson, and Mednick (2010) reporting that reduced electrodermal fear conditioning in young children predicted later aggressive behavior at 8 years of age. The current study extends the study of these processes into infancy and is one of the first to examine very early psychophysiological stress functioning and behavioral fear reactivity across children later identified as having CP + CU, CP only, or no CP.

Fear reactivity in early childhood

Longitudinal observations of fear-related behaviors and physiology suggest that an individual's experience of fear is part of a natural continuum for humans, with phenotypic extremes on each end of the distribution for infants and older children

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(Kagan, Snidman, & Arcus, 1998). These studies indicate that fear can be reliably measured (behaviorally and psychophysiological) in infants by the second half of the first year of life (age 6 months and beyond). From this age forward, there is evidence for limited stability in fear reactivity across infancy and increased stability from toddlerhood to early childhood (Lemery, Goldsmith, Klinnert, & Mrazek, 1999). Most psychobiological models of fear processing now include subcortical motivational systems that shape developing representations of experiences, which in turn provide feedback to motivational and attention processes in responses to these experiences (Posner & Rothbart, 2000). Put simply, early differences in fear reactivity are more likely to be the product of underlying individual differences in genetic and neurobiological functioning; however, there also appear to be developmental processes active in the consolidation of individual differences in fear reactivity across time.

Fearlessness and blunted stress psychophysiology in children with CP + CU

Clinical research with older children suggests that children with CP + CU exhibit a temperamental profile that is characterized by fearlessness and a blunted physiological response to stressors (Frick & Morris, 2004), and recent longitudinal research suggests that fearless temperament at 2 years of age predicts both CP and CU in early adolescence above and beyond other familial and contextual risks (Barker, Oliver, Viding, Salekin, & Maughan, 2011). These findings suggest that children with CU represent a distinct biobehavioral phenotype within the broader population of children with CP (Marsh & Blair, 2008). Further support for this characterization comes from neurological studies of older children with CU reporting reduced amygdala activation while processing fearful faces, but not angry or neutral faces as compared to children with ADHD and typical child samples (Marsh et al., 2008). This finding is consistent with previous research with adult samples (Kiehl, Smith, & Hare, 2001) and has since been replicated with older children (Jones et al., 2009).

Research on peripheral nervous system functioning in adults with psychopathy and youth with callous-unemotional traits is largely consistent with the neurological literature. In adult prison inmates, psychopathy levels were negatively correlated with diurnal cortisol levels (Cima, Smeets, & Jelicic, 2008). In youth, high levels of callous-unemotional traits have been associated with low basal cortisol levels in a community sample of 12–18-year-old youths (Loney et al., 2006) and blunted cortisol reactivity in a sample of 8–14-year-old boys with ADHD and disruptive behavior symptoms (Stadler et al., 2011). Low levels of basal cortisol have also been associated with childhood antisocial behavior

(Hawes, Brennan, & Dadds, 2009) and psychopathic personality (Gao, Glenn, Schug, Yang, & Raine, 2009). Similarly, low resting heart rate and reduced skin conductance are predictive of chronic antisocial behavior (Raine, 2002), and children with CP + CU have been observed to display lower magnitude changes in heart rate in response to an emotional evocative film compared to both CP only and typical control in a sample of children 7–11 years of age (Anastassiou-Hadjicharalambous & Warden, 2008). With regard to parasympathetic nervous system functioning, Dietrich et al. (2007) reported that higher resting respiratory sinus (RSA) was associated with more antisocial outcomes among children identified as having behavioral problems in preschool.

As such, relative to CP-only youth, CP + CU youth are thought to follow distinct developmental pathways into conduct problems, one of which involves greater fearlessness (Frick & Morris, 2004). However, there is disagreement in the scientific literature regarding whether fearlessness represents a stable individual difference in the biological basis of CP+CU in children or whether it is a product of developmental processes. There is evidence for moderate to high levels of heritability of temperament (Emde et al., 1992), developmental psychobiology (Inglics et al., 1999), and callous-unemotional traits (Viding, Blair, Moffitt, & Plomin, 2005), suggesting that biobehavioral profiles in children with CP + CU may be genetically determined. Conversely, others propose that fearlessness in children with callous-unemotional traits may be a learned set of cognitive appraisals and behaviors reflecting adaptations to early harsh, atypical, and unpredictable caregiving environments (Dadds & Salmon, 2003), which in turn may lead to later problems encoding emotional stimuli, impairments in the development of empathic concern and perspective taking, and the development of callous and unemotional characteristics over time (Frick, Ray, Thornton, & Kahn, 2014).

The current study

This is one of the first studies to examine individual differences in psychophysiological stress reactivity and observed behavioral fear reactivity in early and late infancy as it relates to CP + CU in middle childhood. Based on a downward extension model of biobehavioral correlates of CP + CU, it was expected that (a) children with CP + CU would display lower basal levels of hypothalamic–pituitary–adrenal (HPA) axis functioning and lower HPA reactivity to challenge, (b) higher tonic levels of RSA and heart period (HP; a measure inversely related to heart rate), and (c) lower levels of behavioral fear reactivity as compared to children with CP only and children without CP.

Methods

Participants

The Family Life Project (FLP) is a birth cohort study of children and families living in two areas of high child poverty in the United States (three counties each in Eastern NC and Central PA). The FLP used a random stratified sampling framework to recruit a representative sample of 1,292 families recruited across a 12-month period from September 2003 through August 2004. Further details on the FLP sample and recruitment procedures can be found in (author reference). Sample sizes for subsamples of children with behavioral fear reactivity, cortisol, and cardiac data across children with CP + CU, CP only, and no CP are presented in Table 1. Informed consent was obtained from each participant in accordance with the Institutional Review Board of the University of North Carolina at Chapel Hill.

Procedures

Children and families were visited for in-home data collection protocols at both the 6- and 15-month home visits, during which primary caregivers (almost exclusively biological mothers) completed demographic questionnaires and children participated in multiple biobehavioral assessment protocols, including the collection of pretask saliva samples prior to the administration of child challenge procedures, including a scary mask task that commonly elicits fear in late infancy and early toddlerhood (Goldsmith & Rothbart, 1990, and postchallenge saliva samples (20-min and 40-min postpeak arousal). Baseline levels of cardiac activity were collected on a subsample of the children ($n = 176$). At first grade, primary caregivers were asked to report on children's levels of conduct problems and callous-unemotional traits.

Measures

Salivary cortisol. Unstimulated whole saliva was collected by using either cotton or hydrocellulose absorbent material and expressing the sample into 2-ml cryogenic storage vials using a needleless syringe (cotton) or by centrifugation (hydrocellulose). All samples were assayed for salivary cortisol with a highly sensitive enzyme immunoassay (Salimetrics, State College, PA) that has been U.S. Food and Drug Administration 510(k) cleared for use as an in vitro diagnostic measure of adrenal function. The test used 25 μ l of saliva (for

singlet determinations), had a range of sensitivity from 0.007 to 1.8 g/dl, and had average intra- and interassay coefficients of variation of <10% and 15%, respectively. All samples were assayed in duplicate. The criterion for repeat testing was variation between duplicates >20%, and the average of the duplicates was used in all analyses. The cortisol distributions were subject to log transformation to correct positive skew. Values >3 *SD* above the mean were removed as outliers. Cortisol reactivity levels were calculated by subtracting the pretask levels from the 20-min postpeak arousal levels. Because of their proximal times of collection, pretask cortisol, 20-min posttask, and 40-min posttask cortisol levels were also averaged to create a trait-like index of cortisol functioning to reflect broader HPA functioning (Taylor et al., 2013).

RSA and HP. Heart Period (HP) is a measure of the average interbeat interval (IBI; the length of time between heart beats) and is used as an index of broad ANS functioning. RSA is measured as the variation in IBIs linked to respiration and is used as a specific index of parasympathetic functioning of the ANS. The experimenter placed three disposable pediatric electrodes in a triangular pattern on the child's chest while seated in caregiver's lap. The electrodes were connected to a preamplifier, the output of which was transmitted to a laptop computer which was equipped with data collection hardware and software (Mindware Technologies, Westerville, OH). Cardiac IBI data were continuously collected for a 4-min period during which the child was stimulated as little as possible to assess baseline RSA and HP. Data files were edited for bodily movements, tugging on electrodes, and physical force. Data files that required editing of more than 10% of the data were not included in the analyses and were considered missing data. The integral of the power in the RSA band (0.24–1.04) was extracted and the natural log of this measure as calculated as an average across 30 s epochs and reported in units of $\ln(\text{ms})^2$.

Observed behavioral fear reactivity. Children's responses to the emotion challenge tasks were video recorded during the mask presentation task, and second-by-second coding of emotional reactivity was accomplished using Better Coding Approach software (Danville, PA). Three levels of negative reactivity were coded: low, moderate, and high negative reactivity (Stifter & Braungart, 1995). Coders were trained to achieve at least 0.75 (Cohen's κ) reliability on the reactivity coding. Subsequent interrater reliability was calculated on 15% of cases using kappa coefficients, resulting in a

Table 1 Criterion variables (mean, *SD*, *n*) for each comparison group^a

	CP + CU	CP only	Comparison
(log)Cortisol ^b			
6 months	-1.82 (0.85), <i>n</i> = 51	-1.77 (0.75), <i>n</i> = 54	-1.82 (0.77), <i>n</i> = 765
15 months	-1.62 (0.86), <i>n</i> = 50	-2.04 (0.84), <i>n</i> = 46	-2.00 (0.82), <i>n</i> = 678
RSA			
6 months	4.02 (0.59), <i>n</i> = 9	3.77 (0.56), <i>n</i> = 9	3.95 (0.90), <i>n</i> = 150
15 months	4.04 (0.52), <i>n</i> = 10	5.08 (0.86), <i>n</i> = 4	4.37 (1.07), <i>n</i> = 161
HP			
6 months	441.48 (22.77), <i>n</i> = 9	420.46 (31.24), <i>n</i> = 9	433.80 (34.04), <i>n</i> = 136
15 months	454.87 (26.62), <i>n</i> = 10	481.58 (37.95), <i>n</i> = 4	473.37 (42.10), <i>n</i> = 150
Moderate-intensity observed fear			
6 months	0.00 (0.00), <i>n</i> = 49	0.00 (0.00), <i>n</i> = 56	0.00 (0.03), <i>n</i> = 709
15 months	0.08 (0.17), <i>n</i> = 45	0.01 (0.04), <i>n</i> = 43	0.03 (0.11), <i>n</i> = 641
High-intensity observed fear			
6 months	0.01 (0.05), <i>n</i> = 49	0.04 (0.14), <i>n</i> = 56	0.07 (0.16), <i>n</i> = 709
15 months	0.23 (0.25), <i>n</i> = 45	0.18 (0.25), <i>n</i> = 43	0.21 (0.125), <i>n</i> = 641

^aMeans and *SD* are estimates controlling for covariates used in analyses.

^bCortisol (μ g/dl) data are normalized using a natural log transformation.

kappa of 0.95 and 0.89 for the masks task at 6 and 15 months, respectively. The current analyses include separate models for the percentages of time children displayed moderate and high levels of negative reactivity during the mask tasks at each age.

Conduct problems and callous-unemotional traits at first grade. Levels of Conduct Problems were rated by caregivers using the Disruptive Behavior Disorder Rating Scale (DBDRS; Pelham, Gnagy, Greenslade, & Milich, 1992), a DSM-IV guided rating scale that includes subscales for assessing conduct problems (including oppositional defiance and conduct disorder behaviors). The validity of the DBDRS has been previously established (Pelletier, Collett, Gimpel, & Crowley, 2006) and the internal consistency for the conduct problem composite for this sample was high ($\alpha = .92$). Callous-unemotional Traits were assessed with the Inventory of Callous-unemotional (ICU; Essau, Sasagawa, & Frick, 2006), a series of 24 items on a 4-point Likert scale developed from other highly established clinical assessments (e.g. APSD, PCL-YV). The ICU total score in the current sample had adequate internal consistency ($\alpha = .71$).

Children were classified as being CP + CU if they were rated in the upper 10% of CP and CU based on the measures above. Children were classified as being CP only if they were in the upper 10% of CP and the lower 90% of CU. Children were classified as having no CP if they were in the lower 90% of both CP and CU.

Data analysis plan

OLS regression analyses in SAS 9.3 (SAS; Cary, NC) were used to examine group differences (CP + CU, CP only, no CP) at 6 and 15 months in (a) pretask cortisol levels, cortisol reactivity to the fear challenge, and overall levels of cortisol, (b) baseline RSA and HP levels, and (c) moderate- and high-intensity behavioral fear reactivity. The CP + CU group was dummy-coded as the reference group to compare this subgroup of children against all others in each analysis, and models were run separately for data collected at the 6- and 15-month assessments. All analyses included multiple child-level controls (sex, race, age, mental development at time of assessment, premature birth status, and birth weight), family income-to-needs ratios, and state of residence. Analyses specific to cortisol also controlled for time-of-day, time-of-day² (to account for nonlinear diurnal rhythms), and child temperature.

Results

Descriptive analyses and missing data

There were no significant differences in the distributions of children with CP + CU, CP only, and comparison children by child race, $\chi^2(2, n = 911) = 4.37, p = .11$, child sex, $\chi^2(2, n = 911) = 0.58, p = .76$, or state of residence, $\chi^2(2, n = 911) = 0.64, p = .73$. Caregivers of children with CP + CU reported lower family incomes than did caregivers of comparison children at 6 months, $t(742) = 4.00, p < .001$, and at 15 months, $t(740) = 3.81, p < .001$. Means, standard deviations, and sample sizes for criterion variables (split by CP + CU, CP only, and no CP groups) are presented in Table 1. Because only a subsample of FLP children participated in cardiac data collection, the numbers of children with CP + CU and CP only with these data are small. Chi-square analyses were used to examine whether there were differences

in rates of missing data for each child psychobiological and behavioral variable across groups and no differences were detected.

Biobehavioral variables observed at 6 months

No group differences in pretask cortisol, reactivity levels of cortisol, or overall levels of cortisol were found at 6 months between children with CP + CU, CP only, and no CP. Similarly, no group differences in baseline RSA and HP, or moderate or high behavioral fear reactivity were found at 6 months.

Biobehavioral variables observed at 15 months

At 15 months, children with CP + CU had significantly higher pretask cortisol levels than children with CP only, $B = 0.41(0.17), t(1, 760) = 2.45, p = .014, Cohen's d = 0.49$, and children with no CP, $B = 0.31(0.12), t(1, 760) = 2.60, p = .011, Cohen's d = 0.44$ (Figure 1). Pretask cortisol levels did not differ between children with CP only and children with no CP. No differences in cortisol reactivity were found between groups 15 months of age. Similar to the pretask cortisol analyses, children with CP + CU also had significantly higher overall cortisol levels than children with CP only, $B = 0.45(0.15), t(1, 811) = 2.99, p = .003, Cohen's d = 0.57$, and children with no CP, $B = 0.29(0.11), t(1, 811) = 2.68, p = .008, Cohen's d = 0.47$. Overall cortisol levels did not differ between children with CP only and children with no CP.

At 15 months, baseline RSA levels were significantly lower for children with CP + CU compared to children with CP only, $B = 1.31(0.65), t(1, 153) = 2.00, p = .047, Cohen's d = 1.44$, and marginally lower compared to children with no CP, $B = 0.61(0.36), t(1, 153) = 1.68, p = .094, Cohen's d = 0.39$ (Figure 2). Baseline RSA levels did not differ between children with CP only and children with no CP. The only between-group difference in baseline HP at 15 months was that children with CP+CU had marginally lower HP as compared to children with no

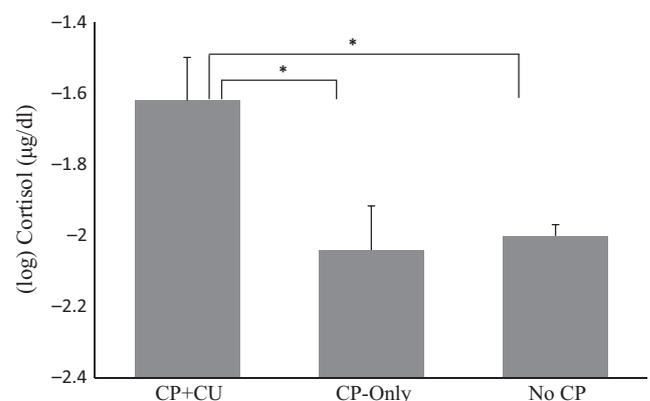


Figure 1 Pretask cortisol at 15 months of age. Error bars represent standard error of the mean (SE). * $p < .05$

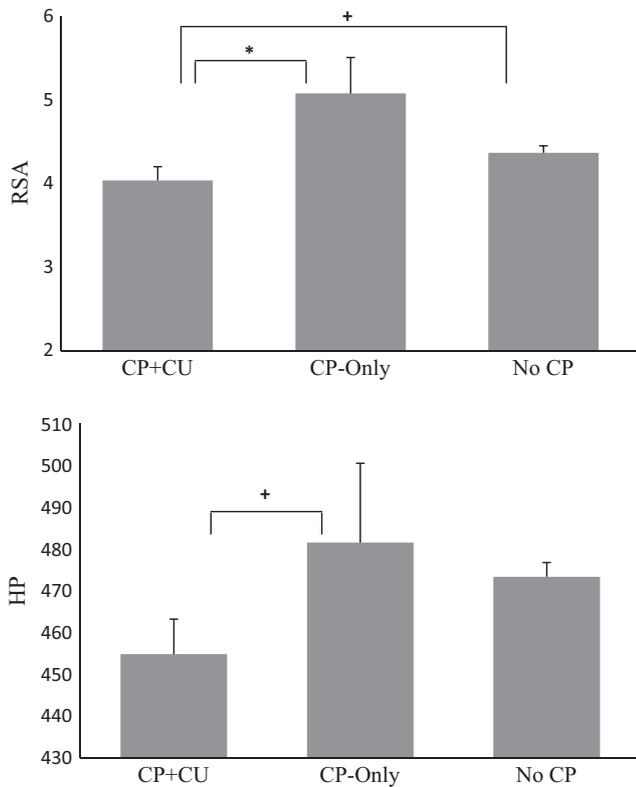


Figure 2 Baseline RSA and HP at 15 months of age. Error bars represent standard error of the mean (SE). * $p < .10$; ** $p < .05$

CP, $B = 24.31(14.49)$, $t(1, 153) = 1.68$, $p = .095$, *Cohen's d* = 0.53.

At 15 months, there were no group differences in displays of moderate-intensity fear reactivity. However, children with CP + CU displayed greater high-intensity fear behavior compared to children with CP only, $B = 0.07 (0.02)$, $t(1, 718) = 2.84$, $p = .005$, *Cohen's d* = 0.60, and children with no CP, $B = 0.04 (0.02)$, $t(1, 718) = 2.52$, $p = .012$, *Cohen's d* = 0.32 (Figure 3). No differences in high-intensity fear were detected between children with CP only and children with either CP + CU or no CP.

Discussion

This study is one of the first birth cohort studies with both longitudinal biobehavioral data and the necessary sample size to examine the early developmental etiology of a behavioral phenotype that, although somewhat rare, incurs high levels of societal cost. Despite initial hypotheses, there was no evidence supporting a downward extension of a biopsychosocial fearlessness model of CP + CU into infancy. Although such a model has been supported in studies of adolescence and preadolescence, the current longitudinal study examining both behavioral and psychobiological measures at 6 and 15 months of age found evidence for *hyperreactivity* of multiple stress response systems instead of *hyporeactivity* in children with CP+CU, as well as *greater fearfulness* instead of fearlessness (although this was only true

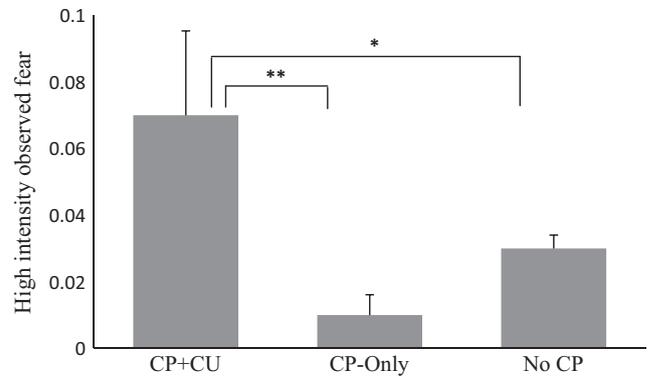


Figure 3 Observed fear reactivity at 15 months of age. Error bars represent standard error of the mean (SE). * $p < .05$; ** $p < .01$

for high-intensity fear which occurred at a lower rate than moderate-intensity fear behavior for all children). Interestingly, there were no group differences at 6 months of age, and when coupled with biobehavioral findings from studies of older children with CP + CU, this suggests that these biobehavioral patterns (a) are emergent during the first 2 years of life as opposed to present at or soon after birth, and (b) somehow transition from hyperactive to hypoactive states over early and middle childhood.

Although these results were not expected based on a downward extension theory of CP + CU, they are consistent with broader research on conduct problems in general. A meta-analysis of the association between baseline cortisol levels and externalizing behavior suggests that greater externalizing behaviors are associated with low basal cortisol levels in elementary school-age children, but among preschool-age children greater externalizing behaviors are associated with high basal cortisol (Alink et al., 2008). Given that CU and CP are positively correlated (Willoughby, Mills-Koonce, Gottfredson, & Wagner, 2014), it is possible that children at the upper end of the externalizing distribution may include children with elevated CP and CU. As such, although it is entirely speculative, the positive association between baseline cortisol and preschool externalizing behaviors may be accounted for by an overrepresentation of children with CP + CU in the upper ranges of externalizing behavior. Thus, although the current findings are not consistent with a downward extension model of CP + CU based on findings with adults and older children, they are not inconsistent within the literature of broadband externalizing behaviors and early childhood psychophysiology.

How then can the current findings be reconciled with the extant literature on fearlessness and blunted psychophysiological stress functioning among older children with CP + CU? One possibility is that hyperreactivity of psychobiological functioning is indicative of enhanced child sensitivity or susceptibility to environmental influences. Both

differential susceptibility (Belsky & Pluess, 2009) and biological sensitivity (Boyce & Ellis, 2005) models posit that children are differentially affected by variations in developmental context, and several studies have identified high fear reactivity as a marker for greater susceptibility or sensitivity to context. For those young children who are particularly sensitive to environmental conditions, harsh and unpredictable environments may lead to severe and chronic emotional and psychophysiological dysregulation. The effects of such an allostatic load (McEwen, 1998) may result in the overall down-regulation of the biobehavioral stress response system and a multisystem transition from hyper- to hypoactivity over time. Children with CP + CU are more likely to be in disorganized attachment relationships (Pasalich, Dadds, Hawes, & Brennan, 2012; Willoughby, Waschbusch, Moore, & Propper, 2011) and in this sample children with CP + CU were in families at greatest sociodemographic risk (as defined by having significantly lower income), so it is possible that children with CP + CU experience more extreme and chronic distal and proximal stress conditions that culminates in a transition of hyperactivity to hypoactivity of stress response over time.

In sum, the current article suggests that children later identified as having conduct problems with callous-unemotional traits are characterized by emerging hyperactivity (as opposed to hypoactivity) of the HPA axis, the ANS, and behavioral fear system in the 2nd year of life. Although these findings are inconsistent with studies that suggest children with CP + CU have low levels of psychophysiological activity (Hawes et al., 2009) and fearless temperaments (Barker et al., 2011), the current study differs methodologically from previous studies in that (a) it examines these systems at a much earlier age than previous studies and (b) it relies on observations of children's acute responses to a fear challenge as opposed to parental report of temperament. Furthermore, it is noteworthy that the pattern of biobehavioral hyperactivity seen in children with CP + CU in the current study is consistent across two physiological systems and a behavioral observation, which strengthens the overall confidence in the current findings.

It should be noted, however, that the greater level of observed fear reactivity was only observed in the form of high-intensity fear (and not for moderate-intensity fear), and that even then the group differences in behavior were only modest in size. In

addition, because saliva was sampled at various times throughout the day, the pretask and overall measures of cortisol should be interpreted with caution until replicated with more rigorous methodologies that assess true baseline HPA functioning. Furthermore, it is important to recognize that, despite these group differences appearing first in toddlerhood, the biological and experiential processes influencing these systems are not necessarily dormant during the prenatal and infancy periods. Future research is needed to both replicate the current results and explicate the developmental timing of these group differences. Understanding the etiology of CP + CU will require the examination of both genetic and experiential processes influencing a potential transition from early biobehavioral hyperactivity to hypoactivity, and may inform more developmentally appropriate models of early risk and intervention to offset negative trajectories for these children.

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Key Points

- Approximately one-third of children who meet criteria for conduct problems are also characterized by elevated callous-unemotional traits.
- This subgroup is at elevated risk for more persistent and pervasive antisocial behavior, but little is known about their early development. This study examines infant and toddler characteristics of children with later conduct problems and callous-unemotional traits.
- At 15 months of age, children with later conduct problems and callous-unemotional traits exhibited more fear and greater psychophysiological activity than children without conduct problems or callous-unemotional traits.
- A downward extension model of behavioral fearlessness and psychophysiological hypoactivity as seen in older children with conduct problems and callous-unemotional traits was not observed, suggesting that developmental processes may underlie the transition from hyper-reactivity to hypo-reactivity between early and later childhood for these children.

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