

## ABSTRACT

Title of Thesis: THE INTERACTION BETWEEN PARENTING AND CHILDREN'S CORTISOL REACTIVITY AT AGE THREE PREDICTS INCREASES IN INTERNALIZING AND EXTERNALIZING SYMPTOMS AT AGE SIX

Chelsey S. Barrios, Master of Science, 2015

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Little is known about the role of stress reactivity in the emergence of psychopathology across early childhood. In this longitudinal study, we tested the hypothesis that child cortisol reactivity at age three moderates associations between early parenting and children's internalizing and externalizing symptoms from age three to age six. 160 children were assessed at age three and 135 children were reassessed at age six. At age three, we exposed children to stress-inducing laboratory tasks, during which we obtained four salivary cortisol samples, and parental hostility was assessed using an observational parent-child interaction task. At ages three and six, child psychiatric symptoms were assessed using a semi-structured clinical interview with parents. Results indicated that the combination of high child cortisol reactivity and high observed parental hostility at age three was associated with greater

concurrent externalizing symptoms at age three and predicted increases in internalizing and externalizing symptoms from age three to age six. Findings highlight that increased stress reactivity, within the context of hostile parenting, plays a role in the emergence of psychopathology from preschool to school entry.

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REACTIVITY AT AGE THREE PREDICTS INCREASES IN INTERNALIZING  
AND EXTERNALIZING SYMPTOMS AT AGE SIX

by

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## Chapter 1: Introduction

Recent research indicates that psychiatric symptoms and disorders in preschool-aged children constitute a significant public health problem (for reviews see Dougherty et al., 2015a and Egger & Angold, 2006). Preschool psychopathology occurs at similar rates to those observed in older children, is associated with significant impairment, and demonstrates stability over time (Bufferd, Dougherty, Carlson, & Klein, 2011, 2012; Lavigne et al., 1998, 2001; Luby, Gaffrey, Tillman, April, & Belden, 2014; Mesman, Bongers & Koot, 2001; Wichstrom et al., 2012). Preschool mental health problems have also been found to predict psychopathology and impairment across early childhood (Bufferd et al., 2012; Dougherty et al., 2013a; Lavigne et al., 1998; Luby, Si, Belden, Tandon & Spitznagel, 2009), middle childhood (Dougherty et al., 2015b; Lahey et al., 2004) and into adolescence (Chronis-Tuscano et al., 2010; Luby et al., 2014). However, there is a paucity of prospective, longitudinal studies investigating the developmental pathways and mechanisms underlying psychopathology across early childhood to school entry.

The significance of life stress in the development of psychopathology across the lifespan has been well documented (Latimer et al., 2012; Monroe & Reid, 2009). Specifically, stress associated with the early caregiving environment has been found to be a potent predictor of psychiatric disorders across childhood (Humphreys & Zeanah, 2014) and into adulthood (Carr, Martins, Stingel, Lemgruber, & Juruena, 2013). The hypothalamic pituitary adrenal (HPA) axis, one of the body's primary stress response systems, has been hypothesized to play a role in the etiology of numerous forms of psychopathology (Gunnar & Vazquez, 2006). The HPA axis is

activated in the face of perceived threat or stress, resulting in the synthesis and release of the glucocorticoid cortisol, the primary stress hormone in humans. A heightened cortisol response to a psychosocial stressor has been linked concurrently to psychopathology in preschoolers, children, adolescents, and adults (Gunnar & Vazquez, 2006; Murri et al., 2014; Pariante, 2003). However, surprisingly little research has examined whether cortisol reactivity prospectively predicts psychopathology across the lifespan, and there is a particular dearth of studies in children. In a study of adults with depression, increased cortisol reactivity to a relatively minimal psychosocial stressor predicted increases in depressive symptoms six months later (Morris, Rao, & Garber, 2012). In adolescent populations, increased cortisol reactivity predicted increased emotional and/or behavioral problems across six-month (Granger, Weisz, McCracken, Ikeda, & Douglas, 1996) and one-year (Susman, Dorn, Germain, Nottelmann, & Chrousos, 1997) follow-ups.

A growing body of research has focused on vulnerability-stress models, in which dysregulated stress reactivity serves as a vulnerability marker rendering individuals more susceptible to negative outcomes when exposed to adverse environments (Belsky, 2005; Boyce & Ellis, 2005; Monroe & Simons, 1991). It has been proposed that children demonstrating abnormalities in stress reactivity are at increased risk for maladaptive outcomes when they are exposed to adverse environments, including harsh parenting and high levels of family stress. For example, in a sample of adolescents, the combination of increased cortisol reactivity in adolescent youth and greater cumulative childhood family aggression was associated with greater concurrent post-traumatic stress symptoms and antisocial

behavior (Saxbe, Margolin, Spies Shapiro, & Baucom, 2012). Early childhood is a particularly critical developmental period in which to study these effects as children rely heavily on their primary caregiver for most basic needs, and thus the parent-child relationship is a highly influential aspect of young children's environment. A few cross-sectional studies in preschoolers have demonstrated that the combination of increased cortisol reactivity and higher levels of family stress was associated with greater emotional symptoms (von Klitzing et al., 2012), poorer prosocial behavior (Obradović, Bush, Stamperdahl, Adler, & Boyce, 2010), and greater concurrent externalizing symptomatology for boys but not girls (Hastings et al., 2011). In contrast, a recent study reported that the combination of preschoolers' lower cortisol reactivity and greater life stress in the past year was associated with greater externalizing symptoms and poorer psychosocial functioning (Kushner, Barrios, Smith, & Dougherty, in press). Thus, the cross-sectional findings have been somewhat mixed as both higher and lower cortisol reactivity in preschoolers have been found to incur greater vulnerability to the early environment; however, it is unclear what role methodological differences across studies contribute to these different findings.

Very little research has examined these models using longitudinal designs. In a sample of children ages 9 to 15 years old, Badanes, Watamura, and Hankin (2011) reported that children who demonstrated lower cortisol reactivity and high levels of life stress had increased depressive symptoms one-year later after controlling for prior symptoms. In contrast, although cross-sectional findings were observed in two samples of five-year old children (Obradović et al., 2010; von Klitzing et al., 2012),

the interactive effect in these studies did not predict symptoms or functioning across the kindergarten school year. However, the cortisol reactivity assessments used in the early childhood longitudinal studies only collected cortisol samples at two time points (i.e., pre- and post-stressor samples only) (Obradović et al., 2010; von Klitzing et al., 2012). Without multiple post-stressor cortisol samples, the extent to which assessments capture peak cortisol responses and the downregulation of the cortisol response is limited. In addition, the few longitudinal studies have only assessed children's symptoms over relatively short follow-up periods (e.g., one year or less), which may reduce the ability to observe changes in symptoms over time. Furthermore, previous longitudinal studies have not examined outcome measures of children's internalizing and externalizing symptoms in a single study, and these prospective associations may vary across these different dimensions. Internalizing and externalizing psychopathology, though moderately correlated, can be differentiated even in early childhood (Olino et al., 2014; Sterba et al., 2007); nevertheless, models of preschool psychopathology have also supported a single common factor shared by both internalizing and externalizing symptoms (Olino et al., 2014). Thus, it is unknown whether cortisol reactivity represents a vulnerability marker that is specific to one dimension or represents a general shared risk marker for both internalizing and externalizing problems across early childhood.

Using a multi-method assessment, the current study aimed to build upon this research to test the hypothesis that child cortisol reactivity at age three moderates associations between early negative parenting and children's internalizing and externalizing symptoms from age three to age six. Drawn from a larger longitudinal

study ( $N=559$ ), 160 three-year old children were randomly recruited to participate in the early childhood cortisol reactivity assessment (Dougherty, Klein, Rose, & Laptok, 2011b). Of the 160 children, 135 (84.4%) were followed-up three years later at age six. At the age three assessment, children were exposed to stress-inducing laboratory tasks, during which we obtained four salivary cortisol samples, and parental hostility was assessed using an observational parent-child interaction task. We chose to focus on parental hostility because this parenting dimension shows consistent and strong associations with both children's internalizing (McLeod, Weisz, & Wood, 2007) and externalizing (McKee, Colletti, Rakow, Jones, & Forehand, 2008) psychopathology and predicts mental and physical health problems into adulthood (Repetti, Taylor, & Seeman, 2002). In addition, given that research suggests that other family stressors (e.g., socio-economic status) impact the child via parenting (Bradley & Corwyn, 2002), our observational measure of parenting may capture broader environmental family stressors. At the age three and six assessments, child internalizing and externalizing symptoms were assessed using a structured clinical interview with parents. We hypothesized that children at age three who had high levels of cortisol reactivity and were exposed to high levels of parental hostility would demonstrate the highest levels of internalizing and externalizing symptoms concurrently at age three, and the greatest increases in internalizing and externalizing symptoms from age three to six years.

## Chapter 2: Methods

### *Participants*

The sample included 160 children and their primary caregivers recruited from the community as part of a larger longitudinal study ( $N=559$ ) on early temperament and risk for psychopathology (Dougherty et al., 2011a; Olino, Klein, Dyson, Rose, & Durbin, 2010). Children and families were assessed at ages three and six years. At the age three assessment, a random sample of 160 children (80 females) participated in a laboratory-based cortisol reactivity assessment. The mean age of our subsample was 3.58 years ( $SD = .24$ ) at the age three assessment and 6.33 years ( $SD = .34$ ) at the age six assessment. Participants identified themselves as White (95.6%), African-American/Black (1.9%), Asian (1.9%), and other race (.6%). The majority of participants came from two-parent households (98.1%) and was middle-class, as measured by the Four Factor Index of Social Status ( $M = 46.1$ ,  $SD = 10.3$ ; Hollingshead, 1975). Children were of average cognitive ability, as indexed by the Peabody Picture Vocabulary Test ( $M=105.0$ ,  $SD=14.1$ ; Dunn & Dunn, 1997). Of the 160 participants, 135 (84.4%) parents completed the parent-reported clinical interview at the age six assessment. One significant difference emerged comparing the subsample presented in this report to the larger sample: children in the subsample had fewer internalizing symptoms at age three ( $M=8.18$ ,  $SD=6.30$ ) compared to the larger sample ( $M=10.25$ ,  $SD=8.38$ ),  $t(367.66)=3.12$ ,  $p=.002$ .

### *Procedure*

At age three, all children attended a laboratory session approximately 2.5 hours in duration, during which they participated with a female experimenter in 12

standardized tasks selected from the Laboratory Temperament Assessment Battery (Lab-TAB; Goldsmith, Reilly, Lemery, Longley, & Prescott, 1995), and cortisol samples were obtained. The tasks were designed to elicit a range of emotions and behaviors from the child and are described in detail elsewhere (see Dougherty et al., 2011a; Olino et al., 2010). At the age three assessment, parents and children also completed an observational parent-child interaction task to assess parental observed hostility. At both the age three and age six assessments, parents completed a diagnostic clinical interview to assess children's current internalizing and externalizing symptoms.

*Child cortisol sampling procedure.* Salivary cortisol was collected four times during the laboratory assessment. Saliva for cortisol assay was obtained by having the children dip 2-inch-long cotton dental rolls into small cups containing approximately .025 g of cherry Kool-Aid®. Children were then instructed to chew the cotton rolls until they were saturated with saliva. Previous work shows that the use of Kool-Aid® does not compromise the quality of the assays when used sparingly, as it does not significantly alter the pH of the saliva (Talge, Donzella, Kryzer, Gierens, & Gunnar, 2005). The collection of each sample took approximately 1–2 minutes. After each sample was collected, the saliva was expunged from the cotton roll into a micro tube and stored at -20°C until assayed.

The timing of the salivary cortisol samples was determined based on findings that salivary cortisol levels reflect the level of stress experienced in the prior 20–40 min (Dickerson & Kemeny, 2004) and on previous studies using similar stress-inducing paradigms, which have been shown to be sensitive to individual differences

in cortisol reactivity in preschool-aged children (Luby et al., 2003; Talge, Donzella, & Gunnar, 2008). Based on these considerations, the first sample was taken upon arrival to the laboratory after the informed consent process (approximately 20 minutes after arrival). The second sample was collected 30 minutes following the Stranger Approach task of the Lab-TAB, the most stressful episode in the battery, during which the child was separated from his/her parent and a stranger entered the room. The third salivary cortisol sample was taken 30 minutes after Transparent Box, a frustration-inducing task in which the child is unable to unlock a box with a desirable toy inside. The fourth and final sample was collected 20 minutes after completion of all Lab-TAB tasks. To control for non-stress related elevations of cortisol, laboratory assessments were conducted at either 10 am (69% of the assessments) or 2 pm. Families were instructed prior to coming to the laboratory that the child should not eat within one hour before the scheduled lab visit, and that children should avoid caffeine for at least two hours and dairy products for at least 15 minutes prior to arrival. No child was taking corticosteroids at the time of the assessment.

Samples were assayed using a time-resolved fluorescence immunoassay with fluorometric end point detection (DELFLIA). All samples were assayed in duplicate. Samples yielding values above 44 nanomoles per liter (nmol/L) were excluded, which applied to four laboratory samples from four different individuals. The inter- and intra- assay coefficients of variation were between 7.1% and 9.0% and 4.0% and 6.7%, respectively.



To quantify cortisol reactivity, we calculated the area under the curve (AUC) with respect to increase ( $AUC_i$ ), derived from the trapezoid formula from the four individual cortisol samples (Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003). The  $AUC_i$  provides a measure of the total change in cortisol levels across the four time points, and has been used widely in the literature as an index of HPA axis response (e.g. Booji, Bouma, de Jonge, Ormel, & Oldehinkel, 2013; Brennan et al., 2008; Dougherty et al., 2011b; Dougherty, Tolep, Smith, & Rose, 2013b).  $AUC_i$  was positively skewed and was log10 transformed. The standardized z-score of the log10 transformed  $AUC_i$  variable was used in all analyses.

*Observed parental hostility.* At age three, 149 of the 160 children participated in a laboratory-based parent-child interaction task with one parent (96% mothers). The observational assessment was based on a modified version of the Teaching Tasks Battery and included six standardized tasks (book reading, block building, naming objects with wheels, matching shapes, completing a maze using an etch-a-sketch, and gift presentation) designed to elicit parent and child behaviors (Egeland et al., 1995). Parental hostility, which captures a parent's expression of anger, frustration, and criticism toward the child, was rated on a 5-point scale for each task, and ratings were averaged across tasks ( $M = 1.17$ ,  $SD = 0.27$ , range = 1–3). Coders were unaware of the data on child psychopathology and cortisol reactivity. The internal consistency ( $\alpha = .76$ ) and interrater reliability (intraclass correlation coefficient [ICC] = .83,  $n = 55$ ) of the parental hostility scale were acceptable.

*Child psychopathology.* At the age three and age six assessments, parents were interviewed using the Preschool Age Psychiatric Assessment (PAPA; Egger,

Ascher, & Angold, 1999). The PAPA is a parent-reported structured diagnostic interview designed to assess a range of psychiatric disorders from the Diagnostic and Statistical Manual of Mental Disorders, 4<sup>th</sup> Edition (American Psychiatric Association, 2000) in children ages two to six years old. Interviews were conducted by telephone by advanced graduate students in clinical psychology at the age three assessment and in person by a master's level clinician at the age six assessment. Diagnostic interviews with parents regarding their children have yielded similar results when administered by telephone and face-to-face (Lyneham & Rapee, 2005). For information on the interview's psychometric properties, see Egger et al. (2006).

As described elsewhere (Dougherty et al., 2013a, 2015b), dimensional symptom scales for depression (major depressive disorder, dysthymic disorder, or depression-not otherwise specified [NOS]), anxiety (specific phobia, separation anxiety, social phobia, generalized anxiety disorder, agoraphobia, panic disorder, selective mutism), attention-deficit/hyperactivity disorder (ADHD), and oppositional defiant disorder (ODD) were created by summing items in each diagnostic category. We then created total internalizing and externalizing symptom scales by summing the depression and anxiety symptom scales, and the ADHD and ODD symptom scales, respectively. To examine inter-rater reliability, 21 audiotaped interviews from the age three assessment and 35 audiotaped interviews from the age six assessment were randomly selected and rated by a second interviewer. Inter-rater reliability and internal consistency were good for the age three internalizing ( $ICC = .98$ ;  $\alpha = .84$ ) and externalizing ( $ICC = .81$ ;  $\alpha = .89$ ) symptom scales and for the age six

internalizing (ICC = .73;  $\alpha$  = .86) and externalizing (ICC = .99;  $\alpha$  = .89) symptom scales.

### *Data Analysis Plan*

We examined whether child cortisol reactivity at age three interacted with observed parental hostility at age three to predict internalizing and externalizing symptoms across early childhood. In each model, independent variables included child cortisol reactivity assessed at age three, parental hostility assessed at age three, and the cortisol reactivity X parental hostility interaction term. Dependent variables included internalizing symptoms at age three and age six, and externalizing symptoms at age three and age six. Separate models were run for each of the four dependent variables. For models with age six symptom scales as the dependent variable, we controlled for levels of the same variable at age three. Dependent variables therefore represent residuals; that is, the effects of the predictors on the dependent variables reflect change in that variable from one time point to the next. Child age at baseline and gender were also included as covariates if they were associated with the dependent variable<sup>1</sup>. Significant interactions were probed using simple slopes tests according to Aiken and West (1991). To better examine the pattern of moderation, Hayes and Matthes' guidelines (Hayes & Matthes, 2009) were used to test the regions of significance according to the Johnson-Neyman technique (Johnson & Fay, 1950). This approach uses the asymptotic variances, covariances, and other regression parameters to determine the upper and lower boundaries of the moderator (cortisol reactivity) at which the relation between the independent and dependent variable is

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<sup>1</sup> Child age at the age six assessment was not significantly associated with concurrent symptoms and was not included as a covariate.

significant ( $p < .05$ ).

## Chapter 3: Results

Means, standard deviations, and correlations among study variables are presented in Table 2. Child age at baseline was positively associated with children's externalizing symptoms at age six; thus, child age at baseline was included as a covariate in analyses with age six externalizing symptoms as the dependent variable. Child gender was not significantly associated with children's internalizing or externalizing symptoms at ages three or six. Child cortisol reactivity at age three was significantly positively associated with externalizing symptoms at age three and age six. Observed parental hostility at age three was significantly positively associated with externalizing symptoms at age three and age six. Internalizing and externalizing symptoms demonstrated moderate stability from age three to age six, and internalizing and externalizing symptoms were significantly positively correlated from age three to age six.

### *Early Childhood Cortisol Reactivity, Parental Hostility, and Internalizing Symptoms at Ages Three and Six Years*

Results of the multiple linear regression models for child internalizing symptoms are presented in Table 3. The interaction between cortisol reactivity and parental hostility at age three was associated with age three internalizing symptoms at a trend-level ( $p = .06$ ), and the form of the interaction was consistent with the significant interaction described next. At age six, the interaction between child cortisol reactivity and parental hostility at age three predicted internalizing symptoms at age six after controlling for internalizing symptoms at age three. As seen in Figure 1, for children with high levels of cortisol reactivity at age three, parental hostility at

age three predicted increases in internalizing symptoms at age six ( $b = 2.61$ ,  $SE = 1.06$ ,  $pr = .22$ ,  $p = .02$ ), whereas for children with low levels of cortisol reactivity at age three, there was no significant association between parental hostility at age three and internalizing symptoms at age six ( $b = -3.58$ ,  $SE = 2.18$ ,  $pr = -.15$ ,  $p = .10$ ). Regions of significance testing indicated that for children with cortisol reactivity at levels greater than .80 (standardized z-score), parental hostility at age three predicted increases in internalizing symptoms at age six. Regions of significance tests also demonstrated that this moderated effect was specific to levels of parental hostility greater than 1.07 (standardized z-score).

*Early Childhood Cortisol Reactivity, Parental Hostility, and Externalizing Symptoms at Ages Three and Six Years*

Results of the multiple linear regression models for child externalizing symptoms are presented in Table 4. The interaction between child cortisol reactivity and parental hostility at age three was significantly associated with concurrent externalizing symptoms at age three. For children with high levels of cortisol reactivity at age three, parental hostility at age three was significantly positively associated with externalizing symptoms at age three ( $b = 5.13$ ,  $SE = .92$ ,  $pr = .43$ ,  $p < .001$ ). In contrast, for children with low levels of cortisol reactivity at age three, there was no significant concurrent association between parental hostility at age three and externalizing symptoms at age three ( $b = -2.49$ ,  $SE = 1.80$ ,  $pr = -.12$ ,  $p = .17$ ). Regions of significance tests indicated that for children with cortisol reactivity at levels greater than .15 (standardized z-score), parental hostility at age three was positively associated with externalizing symptoms at age three. Regions of

significance tests also demonstrated that this moderated effect was specific to levels of parental hostility greater than .28 (standardized z-score).

Similarly, the interaction between child cortisol reactivity and parental hostility at age three significantly predicted increases in externalizing symptoms at age six after controlling for externalizing symptoms at age three. As seen in Figure 2, for children with high levels of cortisol reactivity at age three, parental hostility at age three significantly predicted increases in externalizing symptoms at age six ( $b = 3.08$ ,  $SE = .60$ ,  $pr = .42$ ,  $p < .001$ ). In contrast, for children with low levels of cortisol reactivity at age three, parental hostility at age three did not significantly predict externalizing symptoms at age six ( $b = -1.73$ ,  $SE = 1.12$ ,  $pr = -.14$ ,  $p = .13$ ). Regions of significance tests indicated that for children with age three cortisol reactivity at levels greater than .22 (standardized z-score), parental hostility at age three significantly predicted increases in externalizing symptoms at age six. Regions of significance tests also demonstrated that this moderated effect was specific to levels of parental hostility greater than .60 (standardized z-score).

Lastly, we explored whether child gender moderated associations between early child cortisol reactivity and parental hostility and children's psychiatric symptoms. We reran each of the four models described above and added child gender, the two-way interaction terms, child gender X child cortisol reactivity and child gender X parental hostility, and the three-way interaction term, child gender X child cortisol reactivity X parental hostility, as independent variables. No gender differences were observed for any of the four dependent variables.

## Chapter 4: Discussion

The current study tested whether child cortisol reactivity moderated the effects of parental hostility on children's internalizing and externalizing symptoms both concurrently at age three and prospectively at age six after accounting for prior symptoms. We found that preschoolers who exhibited high cortisol reactivity and experienced high levels of parental hostility at age three evidenced greater concurrent externalizing symptoms at age three and increases in both internalizing and externalizing symptoms from age three to age six. Our findings suggest that increased cortisol reactivity in early childhood may render young children more susceptible to negative parenting and increase risk for developing emotional and behavioral problems by school entry. Identifying young children who are at greatest risk for early mental health problems is critical given that early psychopathology impairs young children's functioning and predicts later psychopathology and impairment across development (Bufferd et al., 2012; Dougherty et al., 2013a; 2015b; Mesman et al., 2001).

Our findings are consistent with cross-sectional studies in young children indicating that the combination of dysregulated cortisol reactivity and exposure to negative family contexts is associated with concurrent child internalizing symptoms, externalizing symptoms, and psychosocial difficulties (Hastings et al., 2011; Kushner et al., in press; Obradović et al., 2010; von Klitzing et al., 2012). However, in contrast to our findings, the only other study that observed a significant longitudinal effect found that the combination of low, rather than high, cortisol reactivity and greater family stress predicted greater internalizing symptoms one year later in youth ages 9-



15 (Badanes et al., 2011). Taken together, these findings suggest that dysregulated cortisol reactivity may serve as a vulnerability marker across childhood. However, the risk of high versus low stress reactivity may vary across development, or it may result from prior exposure to earlier chronic stressors. It is important to note that to date, none of the longitudinal studies have considered whether abnormalities in children's cortisol reactivity were present prior to the environmental stressor. It will be important for future research to establish cortisol reactivity as a pre-existing vulnerability marker and to test the temporal or causal associations. Nevertheless, our findings support that these early childhood markers of risk predict psychiatric symptoms three years later, which is the longest follow-up in the literature to date. Moreover, it is especially noteworthy that these effects were evident over and above prior symptoms given the stability of symptoms across the assessments.

We observed significant interactive effects in longitudinal models for both internalizing and externalizing symptoms. In concurrent models, we found a significant interactive effect on age three externalizing symptoms only; however, there was a trend level interactive effect on children's concurrent internalizing symptoms at age three. These findings suggest that cortisol reactivity to environmental stressors may represent a common or shared risk factor for both internalizing and externalizing symptoms across early childhood. It will be important to determine whether this continues to serve as a common vulnerability marker for both internalizing and externalizing problems across development or whether it becomes differentiated and specific to one form of psychopathology over time.

Our findings suggest that child cortisol reactivity may sensitize young

children to negative features of the parent-child relationship. Research suggests that cortisol reactivity is related to emotion regulation abilities (de Veld, Riksen-Walraven, de Weerth, 2012; Lam, Dickerson, Zoccola, & Zaldivar, 2009), as well as other physiological indices of stress sensitivity, including respiratory sinus arrhythmia (Doussard-Roosevelt, Montgomery, & Porges, 2003), neural responses to psychosocial stress (Dedovic, Duchesne, Andrews, Engert, & Pruessner, 2009), and genes involved in the susceptibility to life stress (Dougherty, Klein, Congdon, Canli, & Hayden, 2010). Therefore, children with dysregulated cortisol reactivity may have multiple underlying biological and behavioral markers of stress sensitivity that render them less able to cope with parents' expression of anger, frustration, and criticism. Increased stress sensitivity may also contribute to children's behavioral responses within the parent-child relationship (e.g., greater distress, avoidance, or noncompliance) that evoke or exacerbate negative parenting. It will be important for future research to examine child-level risks across multiple levels of analysis and within the reciprocal context of the parent-child dyad to determine whether they represent common or unique risk markers and how they impact the parent-child relationship and child outcomes.

Although our study focused only on negative aspects of the parenting environment, we must also consider the effects of positive, enriched environments in children with identified vulnerability markers. Recent theoretical models including biological sensitivity to context (Boyce & Ellis, 2005) and differential susceptibility (Belsky & Pluess, 2009) suggest that children with vulnerability markers may respond in a "for better or for worse" manner to the environment, experiencing poor

outcomes when exposed to negative environments but optimal outcomes when exposed to positive environments. Thus, it will be important to examine whether young children with increased cortisol reactivity demonstrate the best adjustment and psychosocial functioning when exposed to more favorable contexts (e.g., Obradović et al., 2010; von Klitzing et al., 2012), including involved and sensitive co-parents or high-quality day care and early education programs. Furthermore, one intervention study with youth ages 8-13 years old demonstrated that children with increased cortisol reactivity at baseline benefited most from treatment (van de Wiel, van Goozen, Matthys, Snoek, & van Engeland, 2004). Other findings also suggest that children's HPA axis functioning mediates the effects of a family intervention on change in children's behavior problems across treatment (O'Neal et al., 2010). Taken together, this work highlights that children's cortisol reactivity may be involved in multiple pathways to child adjustment and holds promise in identifying children who may be most responsive to parent behavior interventions or possibly as a mechanisms of behavioral change.

The current study had several notable strengths. This study included a three-year follow-up assessment, which is the longest follow-up to date examining the interactive effects of cortisol reactivity and negative family influences on child, adolescent and adult outcomes. In addition, we used a multi-method approach, including an observational assessment of early parenting, multiple post-stressor cortisol samplings to capture individual differences in stress responses, and a developmentally-sensitive, parent-reported clinical interview to assess child internalizing and externalizing symptoms from preschool to school entry.

The study also had limitations. First, primary caregivers, typically mothers, were the sole informants regarding children's psychopathology. Future work should incorporate a multi-informant approach, including co-parent and teacher reports. Second, since the combination of child cortisol reactivity and parental hostility was assessed at age three only, we cannot test whether their change across early childhood or whether the continued presence of high cortisol reactivity and parental hostility at age six influence children's symptoms. Third, children in our subsample had significantly fewer internalizing symptoms at age three as compared to the larger sample; this may have decreased our power to detect significant effects, as we found only a trend level interaction effect for children's internalizing symptoms at age three. Fourth, although we did not observe any gender differences in our sample, it is possible that our sample size was too small to detect significant differences. Further work with larger samples is needed to examine whether gender moderates the complex associations between children's stress reactivity, parenting, and child psychopathology (e.g., Hastings et al., 2011). Fifth, our measure of the parenting environment was limited to mostly mothers' observed hostility; thus, we cannot conclude that our pattern of findings extends to fathers' parenting behaviors or measures of family stress that capture the larger family context. Lastly, the sample was largely comprised of White, two-parent, middle class families. Future research should extend this work to more diverse samples.

In summary, we found that children with high levels of cortisol reactivity to a laboratory stressor and who were exposed to high levels of parental hostility at age three demonstrated greater concurrent externalizing symptoms at age three and

increases in internalizing and externalizing symptoms from age three to age six. Our findings suggest that preschoolers with increased cortisol reactivity represent a particularly vulnerable group of children when exposed to adverse parenting contexts, and might be targeted for early intervention to prevent the development of psychopathology. These interventions may be particularly effective during early childhood, a period of development characterized by a high degree of neuroplasticity.

Tables

Table 1.

*Demographic and Clinical Characteristics of the Study Sample*

	<b>Age 3</b>		<b>Age 6</b>	
<i>Demographic Characteristics</i>				
Child mean age: years (SD)	3.58	(.24)	6.33	(.34)
Child sex: female <i>n</i> (%)	80	(50)		
Child race: <i>n</i> (%)				
White	153	(95.6)		
Black/African-American	3	(1.9)		
Asian	3	(1.9)		
Other	1	(.6)		
Child Hispanic/non-Hispanic ethnicity: <i>n</i> (%)	16	(10)		
Biological parents' marital status: <i>n</i> (%)				
Married	150	(93.8)		
Divorced, separated, or widowed	2	(1.3)		
Never married	7	(4.4)		
Parents' education: graduated 4-year college <i>n</i> (%)				
Mother	83	(51.9)		
Father	76	(47.5)		
<i>Mean child symptom scales</i>				
(SD; range)				
Internalizing symptoms	8.18 (6.30)	0-41	14.41 (10.55)	0-51
Externalizing symptoms	14.62 (8.96)	0-65.93	5.60 (6.57)	0-50

Note: Internalizing symptoms included the sum of the depressive and anxiety symptoms on the PAPA; externalizing symptoms included the sum of ADHD and ODD symptoms on the PAPA

Table 2.

*Correlations Among All Study Variables*

	1	2	3	4	5	6	7	8
1. Age 3 child cortisol reactivity	-							
2. Age 3 observed parental hostility	.12	-						
3. Age 3 internalizing symptoms	.08	-.05	-					
4. Age 3 externalizing symptoms	.22**	.34**	.27**	-				
5. Age 6 internalizing symptoms	.12	.11	.50**	.22*	-			
6. Age 6 externalizing symptoms	.23**	.44**	.32**	.64**	.44**	-		
7. Child age at baseline	.09	-.02	.02	.09	.11	.18*	-	
8. Child gender	-.07	-.05	.01	.12	.05	-.05	.01	-
Mean	.05	-.09	8.18	2.40	14.41	5.60	43.01	1.50
(SD)	(.50)	(.79)	(6.30)	(2.67)	(10.55)	(6.57)	(2.83)	(.50)
N	156	149	153	153	135	135	160	160

Note: Internalizing symptoms included the sum of the depressive and anxiety symptoms on the PAPA; externalizing symptoms included the sum of ADHD and ODD symptoms on the PAPA; Child age reported in months at baseline (age three assessment); Child Gender: male = 1 ( $n = 80$ ) and female = 2 ( $n = 80$ ); \* $p < .05$ , \*\* $p < .01$ .

Table 3.

*Early Childhood Cortisol Reactivity, Parental Hostility, and Internalizing Symptoms at Ages Three and Six Years*

	Age 3 Internalizing		Age 6 Internalizing	
	Symptoms		Symptoms	
	<b>b (SE)</b>	<b>B</b>	<b>b (SE)</b>	<b>B</b>
Age 3 Internalizing symptoms	--	--	.77 (.12)	.47***
Age 3 child cortisol reactivity	.39 (1.09)	.03	-.07 (1.53)	.00
Age 3 parental hostility	-1.31 (.84)	-.16	-.48 (1.27)	-.04
Age 3 parental hostility x cortisol reactivity	1.48 (.79)	.20 <sup>†</sup>	3.09 (1.15)	.27**

Note: <sup>†</sup> $p < .10$ ; \* $p < .05$ ; \*\* $p < .01$ ; \*\*\* $p < .001$ .



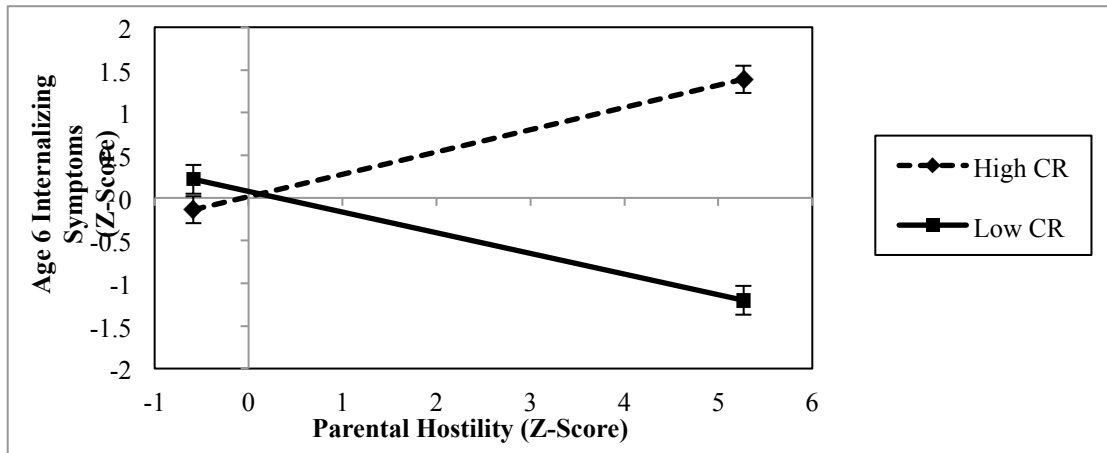
Table 4.

*Early Childhood Cortisol Reactivity, Parental Hostility, and Externalizing Symptoms at Ages Three and Six Years*

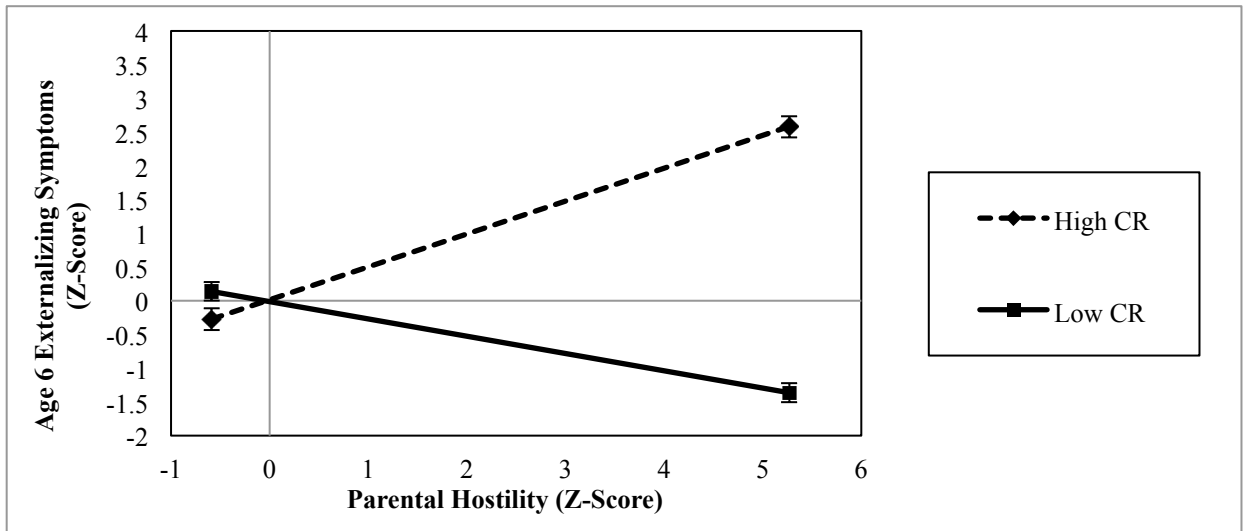
	Age 3 Externalizing		Age 6 Externalizing	
	Symptoms		Symptoms	
	b (SE)	B	b (SE)	B
Age 3 externalizing symptoms	--	--	.32 (.05)	.45***
Age 3 child cortisol reactivity	1.49 (1.34)	.09	-.03 (.79)	.00
Age 3 parental hostility	1.32 (1.04)	.12	.67 (.66)	.08
Age 3 parental hostility x cortisol reactivity	3.81 (.98)	.37***	2.41 (.62)	.34***

Note: \* $p < .05$ ; \*\* $p < .01$ ; \*\*\* $p < .001$ .

## Figures



*Figure 1.* The interaction between child cortisol reactivity and observed parental hostility at age three predicts increases in child internalizing symptoms at age six (error bars included).



*Figure 2.* The interaction between child cortisol reactivity and observed parental hostility at age three predicts increases in child externalizing symptoms at age six (error bars included).

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