ABSTRACT

Title of dissertation: PRESCHOOL PSYCHOPATHOLOGY & PSYCHOSOCIAL FUNCTIONING: PHYSIOLOGICAL AND BEHAVIORAL SUSCEPTIBLITY TO THE EARLY ENVIRONMENT

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The aim of this investigation was to examine how physiological (cortisol reactivity) and behavioral (negative and positive emotionality) markers of susceptibility moderate the relations between a wide range of early environmental experiences (parental depression, parenting, and family stress) and preschool psychopathology, psychosocial functioning, and social competence using a multi-method approach. One hundred and fifty-six preschool-age children (ages 3-5) and their biological parents were recruited from the Washington, DC metropolitan area. Stress reactivity was assessed by collecting five salivary cortisol samples from children, which included one pre-task and four post-task samples. Observational assessments were used to assess children's temperamental emotionality and parenting behavior. Children and parents' psychopathology and psychosocial functioning were assessed using psychiatric clinical interviews. Primary caregivers reported on children's social competence. Overall, we found evidence consistent with diathesis-stress models of psychopathology. Specifically, we found that the combination of a blunted pattern of HPA axis reactivity *and* environments

characterized by family stress, including recent stressful life events and harsh parenting, was related to higher levels of children's externalizing symptoms and lower psychosocial functioning. Additionally, we found that children with high levels of negative emotionality *and* who are exposed to mothers with depression had the lowest social competence. In contrast to differential susceptibility theory, we did not find evidence that children's stress reactivity and temperament rendered them more sensitive to the effects of supportive parenting. The distinct patterns of findings observed for children's stress reactivity and temperament suggest that children's physiological and behavioral reactivity reflect separate pathways of risk to environmental influences rather than indices of a shared, common system of sensitivity. Taken together, our findings highlight the critical role of the early environment, particularly for children with identified risk factors (e.g., blunted cortisol reactivity, high negative emotionality), and add to our understanding of mechanisms and pathways involved in risk for early emerging, clinically significant psychopathology and functional impairment.

PRESCHOOL PSYCHOPATHOLOGY & PSYCHOSOCIAL FUNCTIONING: PHYSIOLOGICAL AND BEHAVIORAL SUSCEPTIBLITY TO THE EARLY ENVIRONMENT

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Chapter 1: Introduction

Psychiatric disorders in children and adolescents are highly prevalent and impose lasting consequences on affected youth. Children's emotional and behavioral problems were ranked among the top five causes of impairment among chronic conditions in the United States (Slomski, 2012). While much of the developmental psychopathology literature has examined psychiatric disorders among school-age children and adolescents, emotional and behavioral problems have their roots early in life. Rates of psychopathology among preschool-age children are similar to those observed in older youth (Egger & Angold, 2006). Additionally, recent evidence has documented the continuity (Bufferd, Dougherty, Carlson, Rose, & Klein, 2012) and impairment (Bufferd, Dougherty, Carlson, & Klein, 2011) associated with early emotional and behavioral disorders, revealing that psychiatric diagnoses in young children are not simply transient, developmental phases but rather can be chronic and clinically significant conditions (Bufferd et al., 2011; 2012). Given the high degree of neuroplasticity during early childhood (Nelson, de Haan, & Thomas, 2006), there is a growing need to identify and understand the underlying processes and mechanisms that explain who is at greatest risk for psychopathology.

Biological and Environmental Influences on Risk & Resilience

Exposure to adverse life experiences (e.g., maltreatment, harsh parenting) has repeatedly been linked to increased risk for emotional and behavioral problems in youth (Cicchetti & Toth, 2005; McLeod, Weisz, & Wood, 2007). However, these experiences do not result in increased rates of psychopathology universally. Consequently, several theoretical frameworks have been proposed to explain differential risk for

psychopathology. One widely studied theory is the diathesis-stress model (Monroe & Simons, 1991; Zuckerman, 1999), which posits that person-level characteristics, or diatheses/vulnerabilities, increase certain individuals' risk for maladaptation when those individuals are exposed to environmental adversity. To date, temperament dimensions (e.g., negative emotionality), endophenotypes (e.g., biological stress reactivity), and genetic variants (e.g., 5-HTT) have been identified as possible risk factors that when coupled with exposure to various stressors result in heightened risk for maladaptation. Support for the diathesis-stress model has emerged for several forms of psychopathology, including depression (Caspi et al., 2003), anxiety (Degnan, Almas, & Fox, 2010), and antisocial behavior (Caspi et al., 2002). For instance, Caspi and colleagues (2003) found that individuals who were homozygous for the short-repeat allele on the serotonin transporter promoter gene (5-HTT) *and* who experienced high levels of life stress had higher rates of depressive symptoms than those with only one copy of the short-repeat allele. Additionally, under the diathesis-stress model, res*ilient* individuals, those who have been exposed to adversity but do not exhibit maladaptive outcomes, have also been studied to identify protective developmental factors and processes, which include sensitive and authoritative parenting, parental monitoring, a supportive relationship with a teacher or mentor, higher intellectual functioning, and feelings of self-efficacy (Luthar & Cicchetti, 2000; Luthar & Zigler, 1991; Masten, 2001).

Differential Susceptibility: For Better or Worse

While the diathesis-stress theory has made a significant contribution toward understanding the interplay between biological and environmental risk factors for psychopathology, this literature has primarily focused on identifying characteristics that

place individuals at heightened risk for negative outcomes in the context of stressful environments. Thus, this framework does not address how identified diatheses or risk factors may function in supportive and enriched contexts. Two theories, Biological Sensitivity to Context (BSC; Boyce & Ellis, 2005) and Differential Susceptibility (DS; Belsky, 1997a; 1997b; 2005), have attempted to address this gap in the developmental psychopathology literature. Both theories posit that certain endogenous characteristics render individuals more sensitive or susceptible to positive and/or negative environmental experiences in a "for better or worse" manner. BSC and DS developed simultaneously from two research groups, who proposed different views on the mechanisms explaining individual differences in susceptibility (Ellis, Boyce, Belsky, Bakermans-Kranenburg, & van Ijzendoorn, 2011). We will briefly review each theory and then discuss their shared implications for developmental psychopathology research.

Biological Sensitivity to Context Theory. Boyce and Ellis (2005) proposed that individual differences in biological stress reactivity function as a mechanism through which contextual influences exert differing levels of impact on developmental outcomes. In contrast to the traditional view that genetic risk and environmental adversity result in hyperactivity of the stress response, ultimately increasing risk for psychopathology and physical disease, Boyce and colleagues (1995) conducted a seminal study in which they found that a highly reactive phenotype increased individuals' sensitivity to context for better or worse. Specifically, consistent with the diathesis-stress framework, preschool-age children who were highly reactive (as defined as high cardiovascular and immunologic reactivity) had elevated rates of respiratory illness when raised in stressful rearing environments compared to those who were less reactive and raised in similar

environments. However, highly reactive children who were raised under conditions of low stress had the lowest rates of respiratory illness across all children in the sample, including those who were less reactive and raised in low stress environments (Boyce et al., 1995). Thus, these findings suggest that individuals with a highly reactive phenotype were more susceptible to both the positive *and* negative influences of the environment.

BSC theory is rooted in evolutionary psychology and proposes that developmental mechanisms have evolved over time, which monitor characteristics of the environment (e.g., level of support or stress) to inform the calibration of the stress response system (Boyce & Ellis, 2005). This process of conditional adaptation is assumed to have been preserved via natural selection with the aim of increasing individuals' reproductive fitness across a variety of contexts. Within the BSC framework, genes are hypothesized to regulate the range or extent to which the susceptibility phenotype may be expressed (Ellis et al., 2011). In support of the theorized integrated role of genetic and contextual influences on stress reactivity, evidence from rodent models, non-human primates, and human children and adults suggest that both genetic and early environmental experiences contribute to the calibration of individuals' stress response (Boyce & Ellis, 2005). Boyce and Ellis (2005) made three hypotheses regarding the distribution of reactive phenotypes across different types of early environments. First, individuals raised in highly stressful environments were expected to exhibit a highly reactive stress response given their need to be biologically prepared for frequent high levels of threat. Second, individuals raised in supportive, enriched environments also were expected to exhibit a highly reactive stress response to reap the benefits of their positive contexts. Lastly, the majority of children were hypothesized to exhibit a less reactive profile, given the body's need to

buffer itself from chronic levels of moderate stress, which is characteristic of most typical rearing environments. Thus, according to BSC theory, individuals with highly reactive phenotypes will be most prevalent in highly stressful *and* highly supportive contexts. In support of these hypotheses, Ellis and colleagues (2005) found that individuals with the highest stress reactivity were from either highly supportive or stressful environments, consistent with the theory's proposed u-shaped curve of individual differences of sensitivity to context.

Differential Susceptibility. While Boyce and colleagues were developing the BSC theory, Belsky and colleagues were considering how certain characteristics render children more or less susceptible to environmental processes, with a focus on caregiving (Belsky, 2005). Consequently, Belsky (1997a) proposed Differential Susceptibility (DS) theory, which argues that children maintain individual differences in their degree of "plasticity" to positive and negative parenting to promote reproductive fitness, the passing of one's genes onto future generations (Pluess & Belsky, 2010). Given that over the course of evolution, parents are uncertain about the types of caregiving that will best prepare their offspring to thrive in subsequent environments, Belsky posited that it is adaptive for parents to "hedge their bets" and ensure that children within a family vary in their susceptibility to caregiving to increase the probability of reproductive success (Ellis et al., 2011). As such, Belsky (2005) argued that individual differences in susceptibility to parenting are based on genotypic variability and manifested through differences in children's temperament. This hypothesis was based on Belsky's observation that children who are highly emotionally reactive (e.g. those characterized by a difficult temperament)

appeared to be more susceptible to environmental influences, possibly because of increased nervous system sensitivity.

Integrated Differential Susceptibility Framework. The main difference between BSC and DS is in their theoretical explanation of the origins of individual differences in susceptibility (Ellis et al., 2011). Namely, BSC posits that individual differences in susceptibility result primarily via conditional adaptation, or the calibration of the stress response system based on early exposure to stressful and/or supportive environments. In contrast, DS hypothesizes that individual differences in susceptibility result primarily from genotypic variability. However, both theories acknowledge that individual differences in susceptibility likely involve some combination or interaction of genetic and environmental influences. Additionally, both theories make key assumptions that lay the foundation for an integrated differential susceptibility theory (Ellis et al., 2011). First, BSC and DS assert that sensitivity or susceptibility to the environment results from neurobiological processes. Second, both theories posit that individual differences in neurobiological susceptibility to the environment persist across development. However, less work to date has examined how susceptibility changes across the lifespan (Ellis et al., 2011). Lastly, both theories are rooted in evolutionary psychology and argue that over the course of evolution it has been adaptive to maintain individual differences in neurobiological susceptibility to various environmental contexts (Belsky & Pluess, 2009). Taken together, Boyce and colleagues and Belsky and colleagues argue that neurobiological differential susceptibility moderates the relation between environmental experiences and psychosocial functioning and physical health. Importantly, both theories extend the diathesis-stress vulnerability model, through the assumption that susceptible

individuals are more reactive to environmental experiences and thus are at-risk in adverse environments, but are also the most likely to "flourish" in enriched environments.

Empirical Evidence for Proposed Susceptibility Markers

Physiological Markers. Much of the work examining physiological susceptibility to context has focused on the construct of stress reactivity. When humans are faced with stress, an integrated complex system of neurobiological processes is activated starting with the "fight-or-flight" response (Gunnar & Quevedo, 2007). Under the regulation of the autonomic nervous system, the "fight-or-flight" response triggers rapid changes in the body including, accelerated heart rate and increased blood pressure, which promote responsiveness to signs of threat (Ulrich-Lai & Herman, 2009). The sympathetic branch of the autonomic nervous system activates the increase in the body's response to stress, while the parasympthatic branch regulates the body's recovery to stressors. Additionally, the hypothalamic-pituitary-adrenal (HPA) axis is stimulated by the signal of perceived threat or stress. Activation of the HPA axis involves a cascade of neurobiological events resulting in the synthesis and release of glucocorticoids from the adrenal cortex, including cortisol, the primary stress hormone in humans (Gunnar & Vazquez, 2006; Meaney, 2001; Thase, 2009). The HPA axis regulates several key systems in the body, including metabolism, immune system functioning, and the cardiovascular system (Dickerson & Kemeny, 2004) and has been associated with internalizing and externalizing psychopathology (Gunnar & Vasquez, 2006). In addition to cross-sectional associations, hyperactivity of the HPA axis, as indexed via basal cortisol samples (Essex, Klein, Cho, & Kalin, 2002; Halligan, Herbert, Goodyer, & Murray, 2007) and the cortisol awakening response (Adam et al., 2010; Adam et al., 2014), prospectively predicted

elevated internalizing and externalizing symptoms, depressive symptoms, onset of anxiety disorders, as well as onset and recurrence of major depressive disorder. It has been hypothesized that individuals' responsivity or *reactivity* to stressors, in particular, may underlie vulnerability to developing stress-related forms of psychopathology under adverse contextual influences (Gunnar & Vazquez, 2006).

To date, multiple indicators of physiological reactivity to stress including, autonomic reactivity: respiratory sinus arrhythmia (RSA; Eisenberg et al., 2012; El-Sheikh, Harger, & Whitson, 2001; Obradovic, Bush, Stamperdahl, Adler, & Boyce, 2010), mean arterial pressure (MAP; Boyce et al. 1999; Essex, Armstrong, Burk, Goldsmith, & Boyce 2011), and skin conductance (Cummings, El Sheikh, Kouros, & Keller, 2007; El-Sheikh, Keller, & Erath, 2007), as well as adrenocortical reactivity: HPA axis response (Obradovic et al., 2010), have been found to moderate the relation between children's contextual influences and developmental outcomes. For instance, Obradovic and colleagues (2010) found that among a sample of 338 kindergarten children, high RSA was related to increased rates of externalizing symptoms, and decreased school engagement and prosocial behavior for children exposed to high levels of family adversity. In contrast, for children exposed to low levels of adversity, high RSA was related to decreased rates of externalizing symptoms, and increased school engagement and prosocial behavior. Additionally, Obradovic and colleagues (2010) found that children with high cortisol reactivity, an indicator of the HPA axis response, were reported to exhibit significantly less prosocial behavior when exposed to high family adversity but more prosocial behavior when exposed to low family adversity. In addition to stress reactivity, genetic variants of the serotonin transporter gene (5-HTT) and

dopamine receptor gene (DRD4) have been found to interact with adverse and supportive environments in predicting positive and negative developmental outcomes, including children's prosocial behavior (Bakermans-Kraneburg & Ijzendoorn, 2011; Knafo, Israel, & Ebstein, 2011), levels of positive affect (Hankin et al., 2011), externalizing behavior (Bakermans-Kranenburg & van IJzendoorn, 2007), and substance use (Brody, Chen, & Beach, 2013), highlighting genetic evidence for markers of susceptibility.

Differential Susceptibility Research and the HPA Axis. While a growing body of literature suggests that biological reactivity to stress is a marker of susceptibility to the environment, the majority of this work has focused on indices of autonomic reactivity and genetic variants with fewer studies examining HPA axis reactivity. Recent reports have begun to examine HPA axis activity as a moderator on the relations between environmental influence and youths' externalizing and/or internalizing symptoms (Badanes, Watamura, & Hankin, 2011; Boyce et al., 2006; Hastings et al., 2011; Klitzing et al., 2012; Laurent et al., 2013; Obradovic et al., 2010; Rudolph, Troop-Gordon, & Granger, 2011; Saxbe, Margolin, Spies Shapiro, & Baucom, 2012). Boyce and colleagues (2006), in a sample of 120 7 year-old children, found that fathers' involvement during infancy interacted with children's adrenocortical reactivity (anticipatory cortisol response to researchers arriving at the child's house) to predict mental health symptom severity, such that children with low father involvement and high adrenocortical reactivity had higher symptom severity in comparison to children with high father involvement and low adrenocortical reactivity. Additionally, Saxbe and colleagues (2012) found that in a sample of 54 adolescents, cortisol reactivity moderated the relations between cumulative family aggression and adolescents' self-reported post-traumatic stress symptoms and

antisocial behavior. For adolescents whose cortisol increased following a family discussion task, family aggression was related to higher post-traumatic stress symptoms and antisocial behavior, whereas for adolescents whose cortisol did not increase following the stressor, family aggression was not significantly related to adolescents' symptoms and behavior. Additionally, Rudolph and colleagues (2011) found that among a sample of 132 pre-pubescent children, self-reported peer victimization interacted with children's cortisol levels in anticipation of a social stressor. Specifically, for children exposed to high victimization, those with higher cortisol had higher depressive symptoms than children with lower cortisol, and for children exposed to low victimization, those with dampened anticipatory cortisol had higher depressive symptoms than those with higher cortisol. While the aforementioned studies found that the combination of elevated cortisol and environmental stress was related to increased mental health problems, Badanes and colleagues (2011) found that among a sample of third, sixth, and ninth grade children, increases in youths' depressive symptoms over time were observed only among children with greater stress exposure and a blunted cortisol response across a laboratory visit Thus, elevated and/or blunted HPA axis reactivity may serve as susceptibility markers to the early environment.

To date, four studies have examined whether HPA axis functioning moderated the relations between young children's environment and emotional or behavioral problems. As described above, Obradovic and colleagues (2010) found that cortisol reactivity moderated the relation between kindergartners' exposure to family adversity (a composite of influences including financial burden, harsh parenting, and maternal depression) and prosocial behavior. However, they failed to find support for the hypothesized moderating

role of cortisol reactivity on the relation between family adversity and children's externalizing symptoms. Hastings and colleagues (2011) found that across three independent samples of preschoolers, maternal punitive punishment was more strongly related to externalizing behavior among boys with higher cortisol following meeting an unfamiliar adult, in comparison to boys with lower cortisol. Moreover, boys with higher cortisol, whose mothers did not use punitive punishment, had the lowest levels of externalizing behavior. Additionally, Klitzing and colleagues found that young children's cortisol reactivity following a story-completion task differentially moderated the relations between children's family environment, peer victimization experience, and emotional symptoms. Specifically, they found elevated emotional symptoms only among six year-old children who had a negative family environment and whose cortisol increased following the story task. Consistent with differential susceptibility, they also found that children with a high cortisol increase but favorable family environment had the least emotional symptoms. However, they also found that peer victimization of children at age five predicted an increase in emotional symptoms at age six only among children who exhibited a blunted cortisol response to the story completion task. Lastly, Laurent and colleagues (2013) examined whether young children's basal cortisol moderated the relation between adoptive parents' depressive symptoms and children's internalizing and externalizing symptoms among 210 children in a longitudinal design. Consistent with differential susceptibility, Laurent and colleagues (2013) observed a positive relation between adoptive fathers' depressive symptoms and children's internalizing symptoms over time only among children with high evening cortisol. Additionally, mothers and

fathers' overall depressive symptoms were positively related to children's externalizing symptoms among children with high evening cortisol.

Other developmental outcomes outside of children's mental health symptoms have also been examined in work studying HPA axis activity as marker of differential susceptibility. For instance, in an experimental design, Quas, Bauer, and Boyce (2004) manipulated 4- to 6-year-old children's support received during a mildly stressful task and assessed how children's stress reactivity (autonomic and HPA axis) influenced the relation between social support and memory. While they found that autonomic reactivity moderated the relation between social support and memory consistent with a differential susceptibility model, the results did not reach significance for cortisol reactivity. Additionally, Ellis, Shirtcliff, Boyce, Deardorff, and Essex (2011) found that early supportive parenting, assessed during the preschool period, predicted slower initial pubertal tempo and later pubertal timing only among 12 year-old children with heightened stress reactivity. Specifically, cortisol reactivity moderated the effect on pubic hair development.

In sum, the work that has examined HPA axis activity as a moderator on the relation between environmental factors and developmental outcomes have yielded inconsistent findings, examined heterogeneous outcomes, studied youth of differing ages, and included methodological limitations that make it difficult to interpret how the *reactivity* of the HPA axis renders children more or less susceptible to early emerging emotional and behavioral problems. For instance, of the five studies that examined how cortisol reactivity influences susceptibility to mental health symptoms, only two studies (Badanes et al., 2011; Saxbe et al., 2012) collected a baseline sample and multiple post-

stressor saliva samples to obtain a more comprehensive assessment of the HPA axis response. Given that salivary cortisol levels tend to reach their peak sometime between 20-40 minutes following the presentation of the laboratory stressor (Dickerson & Kemeny, 2004), using a difference score or residuals between one pre- and one post-stressor (Klitzing et al., 2012; Obradovic et al., 2010) or one anticipatory cortisol value (Boyce et al., 2006; Hastings et al., 2011) limits the ability to assess the full range of the HPA response. Moreover, only three studies (Badanes et al., 2011; Klitzing et al., 2012l Saxbe et al., 2012) implemented a standardized laboratory paradigm, specifically designed with the objective of evaluating cortisol reactivity. Recent reviews in adults and youth highlight the importance of incorporating elements of social evaluative threat and uncontrollability into stressor paradigms to maximize the likelihood of evoking a mean cortisol increase (Dickerson & Kemeny, 2004; Gunnar, Talge, & Herrera, 2009). Lastly, given the delay in the release of glucocorticoids in comparison to the more immediate autonomic measurement indices (Sapolsky, Romero, & Munck, 2000), previous studies designed to assess both autonomic and adrenocortical reactivity may have missed the adrenocortical response and only captured the autonomic response. In sum, further work, particularly during the preschool period when the HPA axis first acquires the more reliable diurnal rhythm observed in adults (Gunnar & Vazquez, 2006), is warranted that addresses these methodological limitations to better understand how HPA axis reactivity moderates the association between children's early environment and emerging psychopathology.

Behavioral Markers. In addition to physiological markers of differential susceptibility, individual differences in children's temperament have been widely studied

as behavioral indicators of sensitivity to context. Temperament includes early emerging, relatively stable patterns of emotional and behavioral reactivity across contexts, which are at least partially rooted in physiology (Rothbart & Bates, 2006). Negative emotionality (NE), one of the primary higher-order temperament dimensions identified in children and adults, reflects a tendency to respond to novel and frustrating situations with sadness, anger, fear, and distress (Rothbart & Bates, 2006). NE has been linked concurrently and prospectively with internalizing and externalizing psychopathology (Eisenberg et al., 2009; Rothbart & Bates, 2006) and has received support as a moderator on the relation between parenting style and children's psychopathology (Belsky, Hsieh, & Crnic, 1998; Paterson & Sanson, 1999; Morris et al., 2002; van Aken, Junger, Verhoeven, van Aken, & Dekovic, 2007). For instance, Belsky and colleagues (1998) found that observed infant NE moderated the relation between maternal negative parenting and externalizing behavior among three-year-old boys, such that negative parenting was more strongly positively related to externalizing behavior in boys who were highly negative. Consistent with Belsky's initial findings, work with toddlers and school-age children also has found that the combination of difficult temperament/negative emotionality and negative parenting (e.g. maternal insensitivity, hostility, overcontrol) is related to increases in children's externalizing (Paterson & Sanson, 1999; Morris et al., 2002; Rubin, Burgess, Dwyer, & Hastings, 2003; van Aken et al., 2007) and internalizing (Morris et al., 2002) behavior problems.

In the studies described above, methodological limitations (e.g. studying only negative parenting styles) prevented analyses from fully examining differential susceptibility theory. However, more recent work has examined NE as a marker of

plasticity or susceptibility to negative *and* positive experiences with respect to youths' psychopathology and adjustment. Consistent with differential susceptibility, children with "difficult" temperaments, characterized by high levels of NE, appear to be more susceptible to negative and positive parenting styles and practices (Bradley & Corwyn, 2008; Dopkins-Stright, Cranley-Gallagher, & Kelley, 2008; Feldman, Greenbaum, & Yirmiya, 1999; Van Zeijl et al., 2007). Several reports from the large-scale, longitudinal NICHD Study of Early Child Care and Youth Development have found that mother-reported infant difficult temperament moderates the relation between quality of care (maternal and/or non-parental childcare) and children's behavior and psychosocial functioning. For instance, Bradley and Corwyn (2008) found that sensitive parenting predicted less teacher-reported externalizing behavior only for children with difficult temperament during infancy, in comparison to children with average or easy infant temperament. Using the same sample, Dopkins-Stright and colleagues (2008) found that supportive parenting across children's first few years of life predicted better academic competence, social skills, and relationships with teachers and peers most strongly among first-grade children rated as having difficult temperament during infancy. In addition to studying parenting influences, Pluess and Belsky (2009) showed that the same children high in NE as infants were also more susceptible to quality of non-parental childcare. Specifically, childcare quality was related to kindergarten children's behavior problems and social functioning "for better or worse" only for children rated high in NE. Moreover, using the same sample, the aforementioned findings supporting differential susceptibility to quality of parental and/or non-parental daycare appeared to continue to exist through middle childhood (Pluess & Belsky, 2010). In an independent sample, Morgan, Shaw,

and Olino (2012) found further evidence for NE as a marker of differential susceptibility to quality of sibling relationship in considering children's risk for later internalizing symptoms. Moreover, specific indices of temperament related to the broader construct of NE, including fear, anxiety, and frustration (e.g., Colder, Lochman, & Wells, 1997; Groeneveld, Vermeer, van IJzendoorn, & Linting, 2012; Kochanska, Aksan, & Joy, 2007; Lengua, 2008) have been observed to moderate relations between environmental influences and children's emotional and behavioral problems. Finally, there is compelling evidence for child NE as a marker of differential susceptibility from experimental studies that highlight "difficult" or irritable children's increased benefit from parenting interventions (Blair, 2002; Cassidy, Woodhouse, Sherman, Stupica, & Lejuez, 2011; Klein Velderman, Bakermans-Kranenburg, Juffer, & van IJzendoorn, 2006; Scott & O'Connor, 2012).

Positive Emotionality & Differential Susceptibility

While NE has been widely studied in relation to parenting and child outcomes, little work has examined whether children's positive emotionality also acts as a marker of susceptibility to the early environment. Positive emotionality (PE) includes individual differences in children's expression of positive affect and enthusiasm (e.g., smiling, laughing), surgency, activity, engagement, and sociability (Rothbart & Bates, 2006; Shiner & Caspi, 2003). PE and NE have been found to be orthogonal dimensions of temperament (Durbin, Klein, Hayden, Buckley, & Moerk, 2005; Lonigan, Hooe, David, & Kistner, 1999), rather than reflecting extremes along a single continuous spectrum. Youth with low PE have been found to be at increased risk for internalizing problems (Anderson & Hope, 2008; Dougherty, Klein, Durbin, Hayden, & Olino, 2010), while

high child PE, more specifically surgency, activity and disinhibition, has been related to risk for externalizing problems (Stringaris, Maughan, & Goodman, 2010). Similar to NE, it is possible that PE may increase or decrease children's susceptibility to positive and negative environmental context. Positive affect has been linked to several health outcomes, and these relationships appear to be independent of negative affect (Steptoe, Dockray, & Wardle, 2009a); thus, it is important for further differential susceptibility work to consider both PE and NE when examining risk for early psychopathology. Interestingly, there is recent evidence that child PE moderates the relation between two previously identified markers of differential susceptibility: child NE and the serotonin transporter promoter polymorphism (5-HTT; Hayden et al., 2010). Specifically, Hayden and colleagues (2010) found that child NE is associated with the short allele of the 5-HTT only for children low in PE. Moreover, in a sample of adults, lower PE was associated with higher cortisol reactivity (Bostock et al., 2011), a hypothesized endophenotype for biological sensitivity to context. In the personality literature, introversion has been linked with greater physiological reactivity and thus it is possible that PE, which includes facets of sociability, may function as another marker of sensitivity to context (Boyce & Ellis, 2005).

To date, two studies (Lengua et al, 2000; Phillips et al., 2012) have examined PE as a moderator on the relations between children's caregiving and adjustment. Lengua and colleagues (2000) found that in a sample of prepubertal children of divorce, parental rejection predicted higher depressive symptoms and conduct problems among children with low PE compared to children with high PE. Conversely, Phillips and colleagues (2012) recently found that temperamentally high reactive (i.e., high positive and/or

negative reactivity to novel stimuli) toddlers were more susceptible to the positive and negative influences of child care quality with respect to their social integration compared to less temperamentally reactive children. Given that Phillips and colleagues (2012) combined children with high negative or positive reactivity, it is unclear whether there are unique differential susceptibility effects for increased or decreased PE. Additionally, in a sample of 64 five-year-old children, Jessee, Mangelsdorf, Shigeto, and Wong (2012) examined how children's positive emotionality moderated the relations between parents' depressive symptoms and children's behavior problems. Jesse et al. (2012) reported an interaction that approached statistical significance such that for children with low positive emotionality, maternal depressive symptoms was related to higher levels of child behavior problems. In sum, little work has examined how youths' PE moderates the relation between the early environment and child adjustment, and only one study with a limited sample size has examined how preschool-age children's PE moderates the relations between the early environment and behavior problems, underscoring the need for further work in this area.

Tests of Diathesis-Stress vs. Differential Susceptibility

Much of the earlier work examining youths' risk for psychopathology used a diathesis-stress model, which focused on adverse contextual influences and maladaptive youth outcomes, limiting the ability to interpret findings from a differential susceptibility framework. As reviewed above, accumulating evidence supports physiological and behavioral markers of susceptibility for moderating the relation between environmental influences and early emotional and behavior problems in a "for better or worse" manner. However, some recent studies examining risk for externalizing problems (Belsky &

Pluess, 2011; Nederhof, Belsky, Ormel, & Oldehinkel, 2012) and academic and social competence (Kochanska, Kim, Barry, & Philibert, 2011) designed to assess whether the data better support a diathesis-stress or differential susceptibility model have yielded evidence in favor of the former. Thus, future work examining factors that contribute to young children's psychopathology and psychosocial functioning should examine whether the data support a diathesis-stress or differential susceptibility framework. It is likely that both theories may be supported across different study designs, and that differences in findings may be due to the vast array and complex nature of individual-level and environmental-level markers of risk and resiliency, as well as the diverse range of measures of functioning.

Examining a Range of Children's Environments

To maximize the likelihood of detecting differential susceptibility effects, Ellis and colleagues (2011) emphasized the importance of examining a range of environments (e.g. stressful and supportive) and developmental outcomes (positive and negative). To date, several adverse environmental exposures, including parental depression, harsh parenting, life stress, marital conflict, and low socioeconomic status, have been associated with increased risk for children's emotional and behavioral problems (e.g., Dougherty, Tolep, Smith, & Rose, 2013; Fihrer, McMahon, & Taylor, 2009; Goodman et al., 2011; McMahon, Grant, Compas, Thurm, & Ey, 2003; McLeod et al., 2007). Conversely, enriched environments, including sensitive and supportive parenting have been linked with children's increased adaptive functioning (e.g., Eisenberg et al., 2005). Notably, associations have been observed between these contextual influences and children's stress response (e.g., Gunnar & Donzella, 2002; Gunnar & Quevedo, 2007)

and temperament (e.g., Lengua & Kovacs, 2005; Rothbart, Ahadi, & Evans, 2000). Many of the studies examining differential susceptibility have focused on the presence or absence of one or two adverse environmental influences, which likely does not adequately assess the influences of supportive or nurturing environments (Ellis et al., 2011). Thus, further work is warranted that examines a comprehensive model of differential susceptibility for early psychopathology and psychosocial functioning, including measures of both stressful and supportive environmental influences.

Multiple Levels of Analysis

In addition to a restricted range of environmental influences, much of the literature examining diathesis-stress and/or differential susceptibility have focused on one level of the hypothesized moderator (e.g., stress reactivity or temperament). This type of design thwarts the opportunity to assess whether different levels of measurement (physiological versus behavioral) are reflecting a common, shared sensitivity to the environment (Ellis et al., 2011). Conversely, it is possible that physiological and behavioral markers of differential susceptibility reflect more specific sensitivities to particular environmental experiences that increase risk and/or adaptation in young children's psychosocial functioning.

Two studies have attempted to address this issue. As discussed above, Boyce and colleagues (2006) found that fathers' involvement during infancy interacted with 7 year-old children's cortisol to predict subsequent mental health symptom severity, such that children with low father involvement and high cortisol had higher symptom severity in comparison to children with high father involvement and low cortisol. Interestingly, this same pattern of results was found for two other measures of sensitivity to context

(temperamental disinhibition and mean arterial pressure). In contrast, Essex and colleagues (2011) found unique patterns of results for children's mean arterial blood pressure and temperamental inhibition/disinhibition moderating the associations between first grade teacher-child relationship and adolescent mental health symptoms. Autonomic reactivity results were consistent with the diathesis-stress framework such that children with high blood pressure had worse mental health symptoms when experiencing poor (high conflict or lack of a closeness) teacher-child relationships but did not evidence lower symptoms when experiencing supportive teacher-child relationships. However, behavioral reactivity results were consistent with differential susceptibility, such that highly reactive children had the most mental health symptoms when having experienced poor teacher-child relationships and the fewest symptoms when experiencing supportive teacher-child relationships. Thus, these initial findings highlight the need for further investigation that includes multiple levels of analysis.

Moreover, individual differences in behavioral markers and physiological markers of risk and resiliency have been linked. For instance, both NE and PE have been related to increased HPA axis functioning in adults (Portella, Harmer, Flint, Cowen, & Goodwin, 2005; Steptoe, Gibson, Hamer, & Wardle, 2007) and children (Dougherty, et al., 2013; Dougherty, Klein, Olino, Dyson, & Rose, 2009; Kagan, Reznick, & Snidman, 1987). Given these observed relations between proposed markers of susceptibility and the complexity of etiological pathways for emotional and behavioral disorders, more work is needed using multiple levels of analysis that examines how measures of physiological and behavioral susceptibility interact with a range of environmental influences to predict young children's adaptation and maladaptation.

Chapter 2: Purpose of the Current Study

Developmental psychopathology research traditionally has attempted to identify factors that place children at risk for maladaptation. With the development and empirical tests of BSC and DS theories, factors often viewed as diatheses, including increased stress reactivity and difficult temperament, have recently received support as markers of susceptibility to the environment in a "for better or worse" manner. To date, little work has examined cortisol reactivity, and no studies have examined how children's PE moderates the relations between early environmental influences and preschoolers' internalizing and externalizing psychopathology and psychosocial functioning. Moreover, there is a need for differential susceptibility work to take a comprehensive approach in studying both physiological and behavioral markers within the same study to assess whether different levels of measurement are assessing a generalized shared sensitivity to the environment or more specialized sensitivities to specific environmental inputs. Lastly, the majority of the work to date, examining differential susceptibility in relation to early forms of psychopathology has utilized parent and/or teacher questionnaires when assessing young children's emotional and behavioral problems. Two studies (Klitzing et al., 2012; Obradovic et al., 2010) incorporated kindergarten children's self-report of emotional and behavioral symptoms via the Berkley Puppet Interview (BPI; Ablow, Measelle, & The MacArthur Working Group on Outcome Assessment, 2003). Given the recent development of reliable and valid measures for assessing and diagnosing preschool psychopathology using semi-structured clinical interviews and the benefits of these diagnostic interviews (e.g., assessing frequency, severity, and duration of symptoms and resulting impairment), future studies using this methodological approach are warranted.

The current study attempted to address these limitations in the literature by examining how proposed physiological and behavioral markers of susceptibility moderate the relations between a wide range of early environmental experiences and preschool psychopathology, psychosocial functioning, and social competence using a multi-method approach. In an attempt to minimize the effects of shared method variance, we used observed assessments of temperament and parenting, physiological markers of stress response, and clinical interviews of parent and child psychopathology and psychosocial functioning. In sum, the proposed study tested three specific aims:

Aim 1: Examine the concurrent associations between proposed physiological and behavioral indices of susceptibility. It has been posited that physiological and behavioral markers of susceptibility may reflect a shared underlying sensitivity to the environment that is often studied separately across different levels of analysis. Thus, in the current study, we examined how children's cortisol reactivity was related to concurrent NE and PE to better understand whether these indices of sensitivity reflect a single integrated system of susceptibility or reflect more distinct processes. Given previously observed relations between HPA axis functioning and temperament (Dougherty, et al., 2013; Dougherty et al., 2009; Kagan et al., 1987; Portella et al., 2005; Steptoe et al., 2007), we hypothesized that children's cortisol reactivity would be positively related to NE and negatively related to PE.

Aim 2: Examine whether physiological reactivity to stress moderated the relation between early contextual influences (parental depression, hostile and supportive

parenting, and family stress) and children's psychopathology, psychosocial functioning, and social competence. Both elevated (Boyce et al., 2006; Hastings et al., 2011; Laurent et al., 2013; Obradovic et al., 2010; Rudolph et al., 2010; Saxbe et al., 2012) and blunted (Badanes et al., 2011; Klitzing et al., 2012) cortisol reactivity have been linked to risk for psychopathology. However, given that the majority of the literature supports increased cortisol reactivity as a marker of susceptibility, consistent with BSC and DS theories, we hypothesized that children with high stress reactivity would have the highest mental health symptoms and lowest psychosocial functioning and social competence under contexts of high stress and the lowest mental health symptoms and greatest psychosocial functioning and social competence under contexts of low stress.

Aim 3: Examine whether behavioral reactivity (NE and PE, respectively) moderated the relation between early contextual influences (parental depression, hostile and supportive parenting, and family stress) and children's psychopathology, psychosocial functioning, and social competence.

a. Consistent with evidence supporting BSC and DS theories (Bradley & Corwyn, 2008; Dopkins-Stright et al., 2008; Feldman et al., 1999; Van Zeijl et al., 2007), we hypothesized that children with high NE would have the highest mental health symptoms and lowest psychosocial functioning and social competence under contexts of high stress and the lowest mental health symptoms and greatest psychosocial functioning and social competence under contexts of low stress.

b. Given that both high and low PE have been associated with HPA axis functioning and psychopathology (Anderson & Hope, 2008; Dougherty et al., 2009; 2010; 2013; Steptoe et al., 2007; Stringaris et al., 2010), we hypothesized that children with high or low PE would have increased susceptibility to the environment. Specifically, we expected that children with high or low PE would have the highest mental health symptoms and lowest psychosocial functioning and social competence under contexts of high stress and the lowest mental health symptoms and greatest psychosocial functioning and social competence under contexts of low stress.

Chapter 3: Methodology

Participants

Participants (N = 175) consisted of a sample of preschool-age children and their biological parents. Potential participants were identified through several methods. Some participants were recruited using a purchased commercial mailing list (http://www.surveysampling.com) (27.0%). The mailing list included a list of phone numbers of families with children aged three to five years who lived within 20 contiguous miles from the University of Maryland, College Park campus. Undergraduate and graduate research assistants called families from this list to recruit for participation in the study. Through print advertisements, participants were also recruited from the Washington, DC metropolitan area (i.e., Maryland, DC, Virginia) (63.8%). Flyers were distributed to local schools, daycares, community centers, and health care providers (medical and specialty clinics, pediatricians). Within the sample, we made an attempt to recruit a group of parents with a lifetime history of depression through the use of flyers specifically focused on this population. Additionally, some participants were referred to the study by a friend or family member (9.2%). Children who: (1) were between the ages of three and five years (36-60 months); (2) never had been diagnosed with mental retardation or a pervasive developmental disorder (PDD); (3) did not have a current physical health condition (including diabetes, cancer, and heart conditions), (4) were not taking corticosteroids; (5) did not have a biological parent who met criteria for psychosis or bipolar disorder as indicated by clinical interviews; and (6) had a biological parent with at least 50% physical custody who consented to participate were eligible.

Of the 175 children participating in the study, one child did not speak English well enough to understand the laboratory tasks and two children had a parent with a lifetime history of bipolar disorder-not otherwise specified and were therefore excluded from the study. Sixteen (9.1%) children did not return for the second laboratory visit that included the clinical interview on child psychopathology. Thus, the total sample for this study resulted in 156 preschool-age children (77 boys and 79 girls).

Table 1 lists demographic characteristics of the sample. Children's mean age was 49.80 months (*SD* = 9.57). Participating families identified themselves as White/European-American (*N* = 74; 48.4%), Black/African-American (*N* = 53; 34.6%), Asian (*N* = 3; 2.0%), or other race (*N* = 23; 15.0%); 26 (17.1%) children were of Hispanic/Latino descent. Over a third of the participating families (34.7%) reported a family income greater than $100,001; 28.7% of families reported a family income ranging from $70,001 to $100,000; 20.7% of families reported a family income ranging from $40,001 to $70,000; 8.7% of families reported a family income ranging from $20,001 to $40,000; and 7.3% of families reported a family income less than $20,000. The majority of the children had at least one parent with a four year-college degree (*N* = 108; 69.2%) and lived in a two-parent household (*N* = 112; 71.8%). Children were of average cognitive ability as measured by the Peabody Picture Vocabulary Test (*M* = 110.29, *SD* = 15.44) (PPVT; Dunn & Dunn, 1997).

Overall Design

This study consisted of two laboratory visits. During the first visit, the child participated in a standardized temperament assessment battery and parent-child interaction tasks. In between laboratory visits, psychiatric clinical interviews were

conducted with mothers and fathers on the telephone. If the biological co-parent did not participate in the telephone interview, mothers provided a history of the fathers' mental health. The second visit to the laboratory assessed children's cortisol reactivity to a developmentally appropriate laboratory paradigm. Additionally, during the cortisol reactivity assessment, primary caregivers (91.0% mothers) completed a psychiatric interview about their child's current emotional and behavioral problems. For a full list of the study's schedule of measures refer to Appendix A. Families were compensated $25 for completion of the first laboratory visit, $25 for parent-report measures, $25 per parental telephone interview, and $50 for completion of the second laboratory visit. Children also received two sets of small prizes for their participation.

Study Implementation

Phone Screening. Trained research assistants conducted a preliminary phone screening. The research assistant verified that the participant met all of the inclusion criteria for the study. The phone screening served as a gross initial screen for parental bipolar disorder and psychosis; however, this was re-visited in the parent psychiatric interview. Parents who met criteria for these disorders were excluded from the study. Additionally, research assistants screened for child gross developmental delays (e.g., mental retardation, autism spectrum disorders) and major health conditions (e.g., cancer, heart disease).

Session One. Upon arrival to the laboratory, a graduate research assistant provided the parent with an overview of the study's purpose and procedures and obtained informed consent. During the initial visit, the child participated in a series of observational tasks designed to assess child temperament and parent-child dyadic

characteristics. At the end of the first laboratory visit, primary caregivers were asked to participate in the second phase of the study. Parents were asked to participate in a telephone interview about their own mental health history.

Session two. During the second laboratory visit, children's cortisol reactivity to a laboratory stressor was assessed. Children participated in a developmentally appropriate, stress-inducing laboratory task. One baseline salivary cortisol sample was collected 30 minutes following the child's arrival to the laboratory prior to the onset of the task followed by four post-stressor salivary cortisol samples. While children were completing this task, parents were interviewed about their child's emotional and behavioral problems during the past three months.

Measures

Demographic information. During the initial visit, parents completed a demographic questionnaire that included information about race/ethnicity, age, yearly household income, marital status, parental education, and child-birth complications/premature status. For the full questionnaire, refer to Appendix B.

Pervasive developmental disorder screener. During the first visit, parents were administered the Social Communication Questionnaire (SCQ; Rutter, Bailey, & Lord, 2003) to screen for pervasive developmental disorders. The SCQ is a parent-report measure of typical autistic behavior in preschool-age children. Recent reports have supported the validity and reliability of the SCQ (Chandler et al., 2007; Charman et al., 2007). No participating children were excluded based on total SCQ score (cut-off score = 15).

Child temperament. All 156 children participated in the laboratory assessment of temperament, during which children interacted with a female experimenter for about an hour in eight standardized tasks selected from the Laboratory Temperament Assessment Battery (Lab-TAB; Goldsmith, Reilly, Lemery, Longley & Prescott, 1995). The eight episodes were selected to elicit a range of emotions and temperament traits, particularly negative and positive emotionality (Durbin et al., 2005; Durbin, Hayden, Klein, & Olino, 2007; Hayden, Klein, Durbin, & Olino, 2006; Hayden et al., 2010; Olino, Klein, Dyson, Rose, & Durbin, 2010). Previous work implementing Lab-TAB has observed relations between indices of children's temperament and children's HPA axis functioning (Dougherty et al., 2009; Dougherty et al., 2012), maternal history of mood disorder (Dougherty et al., 2009; Durbin et al., 2005), and children's psychopathology (Dougherty, Klein, Durbin, Hayden, Olino, 2010; Dougherty et al., 2011) concurrently and over time. Episodes were ordered to prevent carry-over effects. Between episodes the child took brief play breaks with the experimenter to allow for return to a neutral state. Parents were present in the observation room for all episodes, with two exceptions noted below. When present in the room, parents were instructed to remain neutral and redirect the child to task when solicited for help. Episodes are described in the order in which they were conducted. For a full description of the laboratory assessment of temperament refer to Appendix C.

Make that Car Go (positive affect). The child and experimenter raced two remote-controlled cars.

Transparent Box (anger, sadness). The child selected a toy, which the experimenter then locked in a transparent box. The child was then left with a set of

inoperable keys to attempt to open the box. After a few minutes, the experimenter returned to the child and told him/her that she had left the wrong set of keys. The child was then encouraged to use the new keys to open the box and allowed to play with the toy.

Exploring New Objects (fear). The child is presented with the opportunity to explore novel and ambiguous stimuli, including a tent, a small pet carrier, "gooey" toys, a remote-controlled spider, and a plastic head covered with a black cloth.

Pop-up Snakes (positive affect). The experimenter showed the child what appeared to be a can of potato chips, which actually contained coiled spring snakes, without the parent in the observation room. The child was then encouraged to surprise his or her parent with the snakes.

Impossibly Perfect Green Circles (anger, sadness). The experimenter repeatedly asked the child to draw a circle on a large piece of paper. Each attempt was mildly criticized. After approximately two minutes, the experimenter praised the child for his/her efforts.

Popping Bubbles (positive affect). The child and experimenter played together with a bubble-shooting toy.

Snack Delay (positive affect). The child was instructed to wait for the experimenter to ring a bell before eating a small snack. The experimenter implemented a schedule of systematically increasing delays before ringing the bell.

Box Empty (anger, sadness). The child was given a wrapped empty box to open, under the assumption that a prize was inside. After a brief delay in which the child was left alone to discover that the box was empty, the experimenter returned with several

small toys for the child to keep, explaining that she had forgotten to place the toys inside the box.

All episodes were recorded for subsequent coding by thirteen trained undergraduate students and four graduate-student head coders. Students attended weekly coding meetings with head coders to facilitate maintenance of reliability. Coding procedures followed those reported in previous investigations (e.g., Hayden et al., 2010; Olino et al., 2010). Specifically, the coding system considered facial, bodily and vocal indicators of positive affect, fear, sadness and anger. A single rating was made per episode, which was based on all behaviors that were relevant to each affective dimension during that episode. Ratings of positive affect were made with consideration of the qualitative and quantitative displays of joy and enthusiasm. Overall, positive emotionality ratings were computed as the average standardized weighted sum of instances of low, moderate, and high displays of facial, vocal, and bodily positive affect across all episodes. The same procedure was done to create aggregate scores for sadness, anger, and fear. The positive emotionality, sadness, and anger composite variables were calculated using ratings across all eight episodes. The fear composite variable was calculated using ratings based on three episodes only (Exploring New Objects, Pop-up Snakes, and Box Empty). We calculated an aggregate negative emotionality variable, which consisted of averaging ratings of facial, bodily, and vocal anger, sadness, and fear. Internal consistency estimates, as measured by alpha[1], were adequate: positive emotionality (α = .89), negative emotionality (α = .79), sadness (α = .66), anger (α = .76), and fear (α =

[1] Cronbach's alpha is a measure of internal consistency, or how closely related a set of items is as a group, reflecting an underlying construct (Cronbach, 1951).

.80). Interrater reliability, as indexed by the intraclass correlation (ICC)[2] and based on a subsample of 15 cases, was adequate for the composite scales of positive emotionality (*ICC* = .96) and negative emotionality (*ICC* = .83).

Cortisol reactivity assessment. During the second laboratory visit, children engaged in an acute psychological stressor paradigm that was developed by Kryski, Smith, Sheikh, Singh, and Hayden (2011) and based on a modified version of Lewis and Ramsay's (2002) matching task. Kryski and colleagues (2011) demonstrated that this standardized stressor task was effective in eliciting a mean cortisol increase during a home visit with a sample of preschool-age children. As highlighted by Kryski and colleagues (2011), the stressor task incorporates the essential characteristics (uncontrollability, motivated task performance, and social evaluative threat) of laboratory stressor paradigms that have been found to be successful at eliciting a cortisol response in adults (Dickerson & Kemeny, 2004) and children (Gunnar et al., 2009).

The stress assessment first consisted of a 30-minute period of quiet play (e.g., coloring, watching emotionally neutral videos, reading picture books), after which the experimenter collected the first saliva sample (T0 – baseline). After the baseline sample had been obtained, children participated in the structured stressor task. First, children were presented with a desirable and undesirable toy and were told that they could win their preferred prize if they successfully completed a matching game. During the task, children were asked to match colored chips with animal pictures based on a key they were given. Children were told that they had three minutes to complete each trial, and were shown a timer that the experimenter used to track the time. Children were also told

[2] The Intraclass correlation coefficient (ICC) is a measure of interrater reliability, which assesses the degree of consistency between raters on a continuous construct (Shrout & Fleis, 1979).

that most children can finish the trials before the timer goes off. During the explanation of the task, children completed practice turns to ensure understanding of the rules of the game. Following the actual task trials, the experimenter manipulated the timer such that children failed the following three trials. During each of the trials, the experimenter sat with a clipboard and pretended to take notes on the child's performance. Following each of the failed trials, the experimenter said, "Uh oh. You didn't finish in time." At the end of the third failed trial, the experimenter acted confused and said, "Wait a minute! My timer isn't working right! It's been going off after only 2 minutes, not 3 minutes, so you didn't have enough time to finish." After the child was informed that the timer was broken, the experimenter presented the child with the desired prize and worked together to successfully complete the matching game.

Cortisol samples were obtained prior to the start of the task (T0), and then at 20 (T1), 30 (T2), 40 (T3), and 50 (T4) minutes following the completion of the task. Saliva samples were obtained by having children dip a cotton dental roll into 0.025 g of cherry Kool-Aid® mix. The children then placed the cotton roll in their mouths until saturated. The wet cotton was expressed into a vial by the experimenter. After each visit, the vials were kept frozen at -20° Celsius until assayed in duplicate using a time-resolved fluorescence immunoassay with flourometric end-point detection (DELFIA). Salivary cortisol samples were assayed at the Biochemical Laboratory at the University of Trier, Germany. The use of the oral stimulant was carefully monitored across all samples. The procedures employed here have been shown to yield little-to-no effect on cortisol concentrations (Talge, Donzella, Kryzer, Gierens, & Gunnar, 2005). Inter- and intra-

assay coefficients of variation were 7.1%-9.0% and 4.0%-6.7%, respectively. For a full description of the cortisol reactivity task protocol refer to Appendix D.

We collected a total of 5 cortisol samples during the reactivity assessment (baseline, 20, 30, 40 and 50 minutes post-stressor). Of the 156 children, 8 children were excluded from cortisol analyses due to the following reasons: one child did not provide cortisol reactivity samples, four children's cortisol values were extreme (>3 *SD* above the mean; Gunnar & White, 2001), and three children were sick with a fever or currently taking antibiotic medication on the day of the cortisol reactivity assessment. Thus, 148 children's data were used in all cortisol analyses.

To assess children's HPA axis response to the stressor, we examined two indices of cortisol reactivity. First, we calculated the area under the curve (AUC) with respect to increase (AUC_i), derived from the trapezoid formula from the 5 individual cortisol samples (Pruessner, Kirschbaum, Meinlschmid, & Hellhammer, 2003). The AUC_i provides a measure of the total change in cortisol levels across the 5 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., 2011; Dougherty et al., 2013). Additionally, we examined children's peak cortisol level across the laboratory visit. Consistent with previous work studying cortisol, children's peak cortisol values were positively skewed (Gunnar & Talge, 2007), and thus a $\log_{10}$ transformation was applied and used in all analyses. Children's AUC_i was negatively skewed; however, transformations did not improve normality. Given that children's AUC_i was not one of the study's primary dependent variables, its skew does not impact the statistical assumptions for multiple regression tests.

Parental depression. The Structured Clinical Interview for Diagnostic Statistical Manual of Mental Disorders (DSM-IV-TR) (American Psychiatric Association, 2000), Axis I Disorders – non-patient version (SCID-NP; First, Spitzer, Gibbon, & Williams, 1996) was used to assess a lifetime history of depression in parents. The SCID is a widely used diagnostic assessment tool that has been documented to have excellent reliability and validity (Williams et al., 1992). If a father did not complete a SCID, a family history interview was conducted with the co-parent (Andreason, Endicott, Spitzer, & Winokur, 1977). All interviews were conducted by a masters-level clinician who has extensive experience in the administration of these measures. Interviews were conducted on the telephone as several studies have demonstrated that face-to-face and telephone interviews yield similar results with non-patient samples (Rhode, Lewinsohn, & Seeley, 1997; Sobin, Weissman, Goldstein, & Adams, 1993). Interviews took approximately 30-90 minutes, depending on parents' psychiatric history. Based on audiotapes of 16 SCID interviews, the kappa[3] for inter-rater reliability was 1.00 for lifetime depressive disorder.

We had diagnostic information on 154 (98.7%) mothers and 144 (92.3%) fathers. Direct SCID interviews were obtained from all mothers and 77 (53.5%) fathers. Diagnostic information was obtained for 67 (46.5%) fathers using the family history method. Major depressive disorder (MDD) and dysthymic disorder (DD) were collapsed into a single category reflecting depressive disorder. Of the parents, 76 (49.4%) mothers and 38 (26.4%) fathers had a history of MDD or DD. Children were considered to have a family history of depression if either parent had a diagnosis (n = 96; 61.5%). Twenty parents (12.8%) had a current depressive disorder.

[3] Cohen's kappa is a measure of interrater reliability, which measures the degree of agreement between raters on a categorical construct (Cohen, 1960).

If a parent had a lifetime depressive disorder based on the SCID, the onset and offset dates of all episodes were recorded to determine whether the parent had depression during the child's life. A life event calendar approach was used to aid recall (Belli, Shay, & Stafford, 2001). A similar life event calendar approach yielded 92.5 % accurate recall of the timing of depressive episodes in a 1-month test-retest study of 10-year retrospective reporting of psychiatric symptoms (Kim-Cohen, Moffitt, Taylor, Pawlby, & Caspi, 2005). Of the 96 parents with lifetime depression, 62 (64.6 %) parents from 60 families (47 mothers, 15 fathers) had a depressive disorder during the child's life. As only 15 fathers were depressed during the child's life, analyses focusing on cumulative depression exposure were limited to mothers. The total number of months that the child was exposed to maternal depression was summed and divided by the child's age in months to yield the total proportion of offspring exposure across the child's life. Of the 47 children exposed to maternal depression, the average proportion of exposure was 0.49 (*SD* = .36, range: .02-1.00).

Parenting behavior. All 156 children participated with a parent (93.6% mothers) in a series of structured teaching tasks adapted from Egeland et al.'s (1995) Teaching Task Battery. Five tasks were administered that were developmentally age-appropriate but moderately challenging. These tasks included book reading, a guessing game, a maze, a story sequencing task, and a set of puzzles. Each task was designed to elicit parents' involvement. Parents were instructed to provide any type of assistance or support in order for their child to complete the task successfully. During the first task, parents were instructed to tell their child a story using a picture book and to discuss the book with their child. The second task involved a guessing game, during which parents were instructed to

help their child name as many things with *wheels* as he/she could. Next, parents had to help their child complete a maze on an Etch-A-Sketch toy. The fourth task involved parents and children working together to sequence a series of picture cards. Finally, during the fifth task, parents taught their child to use plastic shape pieces to match designs shown on cards. All of the tasks were video-recorded for observational coding by trained undergraduate and graduate research assistants.

For the purposes of this study, we used the parental hostility and parental supportive presence subscales to capture parenting behaviors. Both higher levels of parental hostility and lower levels of parental warmth have been linked to increased risk of children's internalizing (McLeod et al., 2007) and externalizing (Stormshak, Bierman, McMahon, Lengua, Conduct Problems Prevention Research Group, 2000) behavior problems. Coders rated the parent's hostility, based on expression of anger, frustration, and annoyance directed towards the child. Additionally, the parent's supportive presence was coded based on expression of positive regard and emotional support to the child. Both of these subscales were rated on a 5-point scale (higher scores indicating greater hostility and support). An aggregate score of parental hostility was created from the average of the 5 hostility scores across each episode (M = 1.13, SD = 0.27, Range: 1.0-2.6). The same procedure was done to create an aggregate score for parental supportive presence (M = 4.13, SD = 0.74, Range: 1.8-5.0). The parental hostility and supportive presence subscales evidenced acceptable levels of internal consistency (hostility: α = .76; supportive presence: α = .88). The inter-rater reliability for the hostility and supportive presence scales was excellent (ICC = .91 and .96, respectively; n = 38). For a description of the parent-child interaction tasks, refer to Appendix E.

Recent stressors. Recent stressful life events were assessed using the Preschool Age Psychiatric Assessment (PAPA; Version 1.4; Egger, Ascher, & Angold, 1999) interview. Primary caregivers were asked whether 32 major life events (e.g., parental separation or divorce; parental arrest; loss of a loved one) occurred during the child's life, the extent to which the child was affected by the event, and the date of the event. The interviewer determined whether the parent's description matched the defined criteria. For the purposes of this study, we summed the total number of stressful life events that occurred 12 months prior to the PAPA interview (M = 2.38, SD = 1.71; ICC = .95, n = 15).

Composite stress index. Additionally, consistent with prior studies that have examined the cumulative impact of family adversity (e.g., Buss, Davis, & Kiel, 2011; Counts, Nigg, Stawicki, Rappley, & von Eye, 2005; Obradovic & Hipwell, 2010), we calculated a composite stress index. The Demographic Questionnaire was used to obtain information related to family income, number of parents in the home, and level of parental education. As described above, recent stressful life events were assessed using the PAPA. Additionally, parents who completed the SCID provided information about parental depression exposure during the child's life. Family income, number of parents in the household, parental education, recent life stressors, and parental depression exposure were dummy-coded such that 1 point was given for the presence of each of the following: low SES (family income less than $20,000); single-parent household; neither parent with a college education; high occurrence of recent stressors (at least 4 stressors in the past 12 months); and at least one parent with depression occurring during the child's

life. A composite index ranging from 0 to 5 was calculated by taking the sum of the dichotomized environmental adversity variables (M = 1.34, SD = 1.30, Range: 0-5).

Child psychiatric symptoms. Children's current emotional and behavioral symptoms were assessed using a structured psychiatric diagnostic interview with parents, the Preschool Age Psychiatric Assessment (PAPA; Version 1.4; Egger et al., 1999). The PAPA is a parent-reported interview that assesses a comprehensive set of symptoms from the DSM-IV-TR (American Psychiatric Association, 2000) in young children (between the ages of 2 and 6 years) during the past three months. The PAPA follows a required set of questions and probes, but symptoms are only endorsed when they meet the criteria, as outlined in the extensive glossary. Satisfactory test-retest reliability of the PAPA has been reported at levels similar to those found in psychiatric assessments of older children and adults (Egger et al., 2006).

All interviews were conducted by trained graduate students who were unaware of all data on parental psychopathology and parenting. All interviewers met weekly with the Principal Investigator, who has extensive training and expertise in the administration of the PAPA (e.g., see Bufferd et al., 2011; Bufferd et al., 2012; Dougherty et al., 2011), for supervision on all completed interviews. Primary caregivers (142 mothers, 9 fathers, 5 both parents) provided diagnostic information on all 156 children. Dimensional symptom scales for depression (major depressive disorder, dysthymia, 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. For the purposes of this study, we

created aggregate externalizing (*M* = 7.00, *SD* = 5.20) and internalizing (*M* = 16.19, *SD* = 9.38) symptom scales by summing the ADHD and ODD, and depression and anxiety symptoms scales, respectively.

To examine inter-rater reliability, a second rater independently rated audiotapes of 15 PAPA interviews. The interviews were randomly selected, but participants who reported emotional and behavioral concerns were over-sampled to ensure adequate variability. Internal consistency and inter-rater reliability were good for the externalizing (α = .83; *ICC* = .92) and internalizing (α = .83; *ICC* = .96) symptom scales.

Children's psychosocial functioning. Following the completion of the PAPA, the interviewer rated children's overall level of psychosocial functioning using the Children's Global Assessment Scale (CGAS). CGAS scores range from 0 to 100, where 0 reflects the worst functioning and 100 reflects superior functioning (*M* = 72.33, *SD* = 13.95, *ICC* = .78). The CGAS has been documented to display satisfactory psychometric properties as a global index of children's functioning (Bird, Canino, Rubio-Stipec, & Ribera, 1987; Shaffer et al., 1983).

Children's social competence. Children's social competence (α = 0.68, n = 7) was measured using the Ratings of Children's Behaviors Scale (Eisenberg et al., 1993; Spinrad et al., 2006). Parents rated children's general social skills (i.e., "My child finds it hard to make friends" vs. "For my child, it's pretty easy to make friends") on a 4-point response scale, in which they select an option and then indicate if the item was "sort of" or "really" true for their child. Higher scores reflect higher social competence (*M* = 24.02, *SD* = 3.02, Range: 13-28). The validity of the Ratings of Children's Behaviors Scale has been established in samples of preschool-age children (Eisenberg et al., 1993).

Moreover, significant positive associations have been observed between parent and teacher ratings (Eisenberg et al., 2001).

Data Analysis Plan

The current study examined two proposed markers of differential susceptibility: cortisol reactivity and temperament. In all analyses of cortisol reactivity, children's AUC_i and peak cortisol served as independent variables. For analyses of temperament, children's negative emotionality and positive emotionality were examined as independent variables. Additionally, the following early environmental factors were tested as independent variables: lifetime parental depression history, cumulative maternal depression exposure, parental hostility, parental support, recent stressors, and the composite stressor index in separate models. The study has four primary dependent variables: children's psychiatric symptoms (internalizing and externalizing), psychosocial functioning, and social competence.

First, we examined associations between the study's primary variables. We assessed for the presence of any significant bivariate correlations between demographic variables with the study's dependent variables, and significant covariates were controlled for in analyses. To examine associations between proposed markers of susceptibility, we conducted Pearson product-moment correlations between children's AUC_i, peak cortisol, negative emotionality, and positive emotionality. To test our differential susceptibility hypotheses, we performed multiple regression analyses examining the effects of the interactions between early environmental factors (lifetime parental depression history, cumulative maternal depression exposure, parental hostility, parental support, recent stressors, and the composite stress index) and proposed markers of susceptibility

(children's AUC_i, peak cortisol, negative affect, positive affect). Separate models were run for each of the environmental factors and dependent variables (children's internalizing symptoms, externalizing symptoms, psychosocial functioning, and social competence).

Significant interactions first were probed using simple slopes tests according to Aiken and West (1991)'s guidelines. Next, to determine the range of values of the moderator at which the relation between the independent and dependent variable was significantly associated, we employed Hayes and Matthes' guidelines (Hayes & Matthes, 2009) to determine 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 at which the relation between independent and dependent variable is significant ($p < .05$).

Chapter 4: Results

Preliminary analyses

Means, standard deviations, and correlations among all major variables are presented in Table 2. Children's gender was significantly related to children's externalizing symptoms, psychosocial functioning, and social competence. Specifically, boys were reported to have more externalizing symptoms (M = 8.00, SD = 5.90) than girls (M =6.03, SD = 4.22), t(137.45)= 2.40, p = .018; boys were reported to have lower psychosocial functioning (M =69.84, SD = 15.51) than girls (M = 74.75, SD = 11.85), t(142.22)= -2.21, p = .028; and boys were reported to have lower social competence (M =23.23, SD = 3.22) than girls (M = 24.77, SD = 2.63), t(147)= -3.21, p = .002. Additionally, children's age was positively associated with children's social competence (r = .20, p = .014). Thus, children's gender was included as a covariate in analyses including children's externalizing symptoms and psychosocial functioning. Children's gender and age were included as covariates in analyses including children's social competence.

Children's gender also was significantly associated with children's temperament, such that boys exhibited more negative emotionality (M = .13, SD = .78) than girls (M =-.13, SD = .56), t(137.93)= 2.39, p = .018. Children's age was positively associated with children's positive emotionality (r = .29, p < .001) and negatively associated with children's negative emotionality (r = -.17, p = .040).

Children of parents with a history of depression experienced more recent stressors (M = 2.70, SD = 1.75) than children of parents without a history of depression (M = 1.91, SD = 1.54), t(152)= 2.81, p = .006. In addition, children of parents with a history of

depression had higher scores on the composite stress index[4] (M = 1.64, SD = 1.33) than children of parents without a history of depression (M = 0.84, SD = 1.11), $t(152)$= 3.80, p < .001. Parental hostility was negatively associated with and parental support (r = -.54, p < .001). Moreover, cumulative maternal depression exposure was positively associated with the composite stress index (r = .47, p < .001). The composite stress index was also negatively associated with parental support (r = -.38, p < .001) and positively associated with recent stressors (r = .46, p < .001).

Next, we examined the associations among the study's dependent variables. As seen in Table 1, children's internalizing symptoms were significantly associated with children's externalizing symptoms (r = .43, p < .001) and psychosocial functioning (r = -.58, p < .001). Children's externalizing symptoms were significantly associated with children's psychosocial functioning (r = -.68, p < .001) and social competence (r = -.33, p < .001). Lastly, children's psychosocial functioning and child social competence were significantly positively associated (r = .39, p < .001).

Associations between proposed markers of susceptibility & environmental factors

As seen in Table 1, children's temperament was associated with parenting style and the composite stress index. Specifically, children's negative emotionality was positively associated with parental hostility (r = .17, p = .038), and children's positive emotionality was negatively associated with the composite stress index (r = -.17, p = .030). No significant associations were observed between children's cortisol reactivity and environmental factors.

[4] The composite stress index overlaps with associations between parental depression and recent stressors, as these factors were included in the composition of the cumulative index.

Associations between proposed markers of susceptibility and children's psychopathology, psychosocial functioning, and social competence

Next, we examined the associations between proposed markers of susceptibility and children's psychopathology, psychosocial functioning, and social competence. Children's negative emotionality was negatively associated with children's social competence (r = -.17, p = .044). No other significant associations were observed between proposed markers of susceptibility, children's symptomatology, psychosocial functioning, or social competence.

Associations between environmental factors and children's psychopathology, psychosocial functioning, and social competence

We examined whether environmental factors were significantly associated with children's symptomatology, psychosocial functioning, and social competence. Children of parents with a history of depression had more externalizing symptoms (M = 7.76, SD = 5.54), lower psychosocial functioning (M = 70.36, SD = 14.13) and lower social competence (M = 23.63, SD = 3.08), than children of parents without a history of depression, (M = 5.85, SD = 4.42), t(152)= 2.22, p = .028), (M = 75.29, SD = 13.34), t(152)= -2.14, p = .034), (M = 24.65, SD = 2.87), t(146)= -2.03, p = .044, respectively. Additionally, cumulative maternal depression exposure was negatively associated with children's social competence (r = -.18, p = .030). Recent stressors were positively associated with children's internalizing symptoms (r = .29, p < .001) and externalizing symptoms (r = .16, p = .043), and negatively associated with children's psychosocial functioning (r = -.27, p = .001). The composite stress index was negatively associated with children's psychosocial functioning (r = -.18, p = .024).

Associations among proposed markers of susceptibility

To test our first aim, we examined the associations between children's cortisol reactivity and temperament. Children's AUC_i was significantly negatively associated with children's peak cortisol (r = -.19, p = .020). Consistent with previous research, children's negative emotionality and positive emotionality were not significantly correlated (r = -.10, p = .236). Children's AUC_i was not significantly associated with children's negative emotionality (r = -.05, p = .558) or positive emotionality (r = -.02, p = .842). Similarly, children's peak cortisol was not significantly associated with children's negative emotionality (r = .14, p = .083) or positive emotionality (r = -.04, p = .631).

Interactions between proposed markers of susceptibility and environmental factors on children's psychopathology, psychosocial functioning, and social competence

To test our second and third aims, we performed multiple regression analyses examining the effects of the interactions between early environmental factors and proposed markers of susceptibility. Results are presented by dependent variable.

Internalizing symptoms. Table 3 presents the regression models examining the associations between interactions of proposed markers of susceptibility and early environmental factors with children's internalizing symptoms.

Child AUC_i. No significant interactions were observed between children's AUC_i and early environmental factors.

Child peak cortisol. No significant interactions were observed between children's peak cortisol and early environmental factors.

Child negative emotionality. No significant interactions were observed between children's negative emotionality and early environmental factors.

Child positive emotionality. No significant interactions were observed between children's positive emotionality and early environmental factors.

Externalizing symptoms. Table 4 lists the regression models examining the associations between interactions of proposed markers of susceptibility and early environmental factors with children's externalizing symptoms.

Child AUC_i. We observed a significant interaction between children's AUC_i and recent stressors (B = -1.05, SE = .44, p = .019) on children's externalizing symptoms. Figure 1 shows that for children with low levels of AUC_i, there was significant positive association between recent stressors and children's externalizing symptoms (B = 2.05, SE = .63, p = .001), whereas for children with high levels of AUC_i there was no significant association between recent stressors and children's externalizing symptoms (B = -.04, SE = .59, p = .946). To determine the degree of children's AUC_i at which the association between recent stressors and children's externalizing symptoms is statistically significant, Hayes and Matthes (2009)'s guidelines were used for testing regions of significance according to the Johnson-Neyman technique (Johnson & Fay, 1950). We found that at levels of children's AUC_i less than -.52, recent stressors was significantly positively associated with child externalizing symptoms.

As seen in Table 4, we also observed a significant interaction between children's AUC_i and the composite stress index (B = -1.05, SE = .44, p = .019) on children's externalizing symptoms. Figure 2 shows that for children with low levels of AUC_i, there was significant positive association between the composite stress index and children's externalizing symptoms (B = 1.76, SE = .70, p = .013), whereas for children with high levels of AUC_i, there was no significant association between the composite stress index

score and children's externalizing symptoms (*B* = -.15, *SE* = .58, *p* = .792). Regions of significance tests indicated that at levels of children's AUC_i less than -3.49, the composite stress index was significantly positively associated with children's externalizing symptoms.

No other significant interactions were observed between children' AUC_i and early environmental factors on children's externalizing symptoms.

Child peak cortisol. We also observed a significant interaction between children' peak cortisol and parental hostility (*B* = -1.34, *SE* = .57, *p* = .021) on children's externalizing symptoms. Figure 3 shows that for children with low levels of peak cortisol, there was significant positive association between parental hostility and children' externalizing symptoms (*B* = 1.57, *SE* = .77, *p* = .044), whereas for children with high levels of peak cortisol, there was no significant association between parental hostility and children' externalizing symptoms (*B* = -1.10, *SE* = .73, *p* = .136). Regions of significance tests indicated that at levels of children's peak cortisol less than .14, parental hostility was significantly positively associated with children's externalizing symptoms, while at levels of children' peak cortisol greater than 1.00, parental hostility was significantly negatively associated with children's externalizing symptoms. This second region of significance should be interpreted with caution given that there were only 5 children in the sample with peak cortisol values greater than 1.00.

As seen in Table 4, we also observed a significant interaction between children's peak cortisol and the composite stress index (*B* = -1.02, *SE* = .47, *p* = .032) on children's externalizing symptoms. Figure 4 shows that for children with low levels of peak cortisol, there was a significant positive association between the composite stress index and

children's externalizing symptoms (B = 1.71, SE = .66, p = .011), whereas for children with high levels of peak cortisol, there was no significant association between the composite stress index and children's externalizing symptoms (B = -.34, SE = .62, p = .586). Regions of significance tests indicated that at levels of children's peak cortisol less than .36, the composite stress index was significantly positively associated with children's externalizing symptoms.

No other significant interactions were observed between children's peak cortisol and early environmental factors on children's externalizing symptoms.

Child negative emotionality. No significant interactions were observed between children's negative emotionality and early environmental factors.

Child positive emotionality. No significant interactions were observed between children's positive emotionality and early environmental factors.

Child Psychosocial Functioning. Table 5 lists the regression models examining the associations between interactions of proposed markers of susceptibility and early environmental factors with children's psychosocial functioning.

Child AUC_i. We observed a significant interaction between children's AUC_i and recent stressors (B = 2.42, SE = 1.16, p = .039) on children's psychosocial functioning. Figure 5 shows that for children with low levels of AUC_i, there was significant negative association between recent stressors and children's psychosocial functioning (B = -6.39, SE = 1.67, p < .001), whereas for children with high levels of AUC_i, there was no significant association between recent stressors and children's psychosocial functioning (B = -1.55, SE = 1.56, p = .324). Regions of significance tests

indicated that at levels of children's AUC_i less than 4.69, recent stressors was significantly negatively associated with children's psychosocial functioning.

No other significant interactions were observed between children's AUC_i and early environmental factors on children's psychosocial functioning.

Child peak cortisol. As seen in Table 5, we also observed a significant interaction between children's peak cortisol and parental hostility (B = 3.13, SE = 1.54, p = .044) on children's psychosocial functioning. Figure 6 shows that for children with low levels of peak cortisol, there was significant negative association between parental hostility and children's psychosocial functioning (B = -4.26, SE = 2.08, p = .043), whereas for children with high levels of peak cortisol, there was no significant association between parental hostility and children's psychosocial functioning (B = 2.01, SE = 1.98, p = .312). Regions of significance tests indicated that at levels of children's peak cortisol less than .16, parental hostility was significantly negatively associated with children's psychosocial functioning.

No other significant interactions were observed between children's peak cortisol and early environmental factors on children's psychosocial functioning.

Child negative emotionality. No significant interactions were observed between children's negative emotionality and early environmental factors.

Child positive emotionality. No significant interactions were observed between children's positive emotionality and early environmental factors.

Child social competence. Table 6 lists the regression models examining the associations between interactions of proposed markers of susceptibility and early environmental factors with children's social competence.

Child AUC_i. No significant interactions were observed between children's AUC_i and early environmental factors.

Child peak cortisol. No significant interactions were observed between children's peak cortisol and early environmental factors.

Child negative emotionality. We observed a significant interaction between children's negative emotionality and cumulative maternal depression exposure (B = -.61, SE = .28, p = .027) on children's social competence. Figure 7 shows that for children with high levels of negative emotionality, there was a significant negative association between cumulative maternal depression exposure and children's social competence (B = -1.19, SE = .38, p = .002), whereas for children with low levels of negative emotionality, there was no significant association between cumulative maternal depression exposure and children's social competence (B = .03, SE = .34, p = .928). Regions of significance tests indicated that at levels of children's negative emotionality greater than -.12, cumulative maternal depression exposure was significantly negatively associated with children's social competence.

No other significant interactions were observed between children's negative emotionality and early environmental factors on children's social competence.

Child positive emotionality. No significant interactions were observed between children's positive emotionality and early environmental factors.

Supplemental Analyses

We also examined whether proposed markers of susceptibility interacted with parental history of psychopathology and familial loading of parental depression history. Parental lifetime psychopathology was dummy coded (0, 1) for absence or presence of a

lifetime depressive, anxiety (n = 93, 60.8%), or substance-use disorder (n = 59, 38.6%) in at least one parent. One hundred and thirty-two children (85.7%) had at least one parent with a lifetime history of psychopathology. No significant interactions were observed between proposed makers of susceptibility (children's AUC_i, peak cortisol, negative emotionality, positive emotionality) and parental lifetime psychopathology on children's internalizing symptoms, externalizing symptoms, psychosocial functioning, or social competence. Similar procedures were conducted to examine interactions between parental current psychopathology (at least one parent with depressive, anxiety, or substance-use disorder in the past month; n = 66, 43.1%) and proposed markers of susceptibility. No significant interactions were observed between proposed markers of susceptibility and current parental psychopathology.

Next, we examined whether proposed markers of susceptibility interacted with a familial loading of parental depression history. Familial loading of parental depression history ranged from 0 to 2, reflecting children's number of parents with a lifetime history of depression. Fifty-eight children (37.7%) had no family history of depression, 78 (50.6%) children had one parent with a lifetime history of depression, and 18 (11.7%) children had both parents with a lifetime history of depression. Two significant interactions were observed.

First, we observed a significant interaction between children's peak cortisol and familial loading of parental depression (B = -.75, SE = .33, p = .023) on children's social competence. Figure 8 shows that for children with high levels of peak cortisol, there was a significant negative association between familial loading of parental depression and children's social competence (B = -1.23, SE = .42, p = .004), whereas for children with

low levels of peak cortisol, there was no significant association between familial loading of depression and children's social competence (B = .26, SE = .39, p = .497). Regions of significance tests indicated that at levels of children's peak cortisol greater than .41, familial loading of parental depression was significantly negatively associated with children's social competence. Given previous literature that familial loading of depression is a vulnerability marker for offspring's increased risk of psychopathology (Brennan, Hammen, Katz, & Le Brocque, 2002; Nomura, Warner, &Wickramaratne, 2001), we reversed the moderator by exploring the relation between children's peak cortisol and social competence for children with 0, 1, or 2 parents with a history of depression. Figure 9 shows that for children with no parental history of depression, there was a significant positive association between children's peak cortisol and social competence (B = 1.26, SE = .48, p = .009), whereas there was no significant between children's peak cortisol and social competence for children with one parent with a history of depression (B = .12, SE = .29, p = .688) or for children with two parents with a history of depression (B = -1.03, SE = .66, p = .122).

Second, we observed a significant interaction between children's negative emotionality and familial loading of parental depression (B = -.52, SE = .23, p = .027) on children's social competence. Figure 10 shows that for children with high levels of negative emotionality, there was a significant negative association between familial loading of parental depression and children's social competence (B = -.90, SE = .32, p = .005), whereas for children with low levels of negative emotionality, there was no significant association between familial loading of parental depression and children's social competence (B = .13, SE = .34, p = .695). Regions of significance tests indicated

that at levels of children's negative emotionality greater than .11, familial loading of parental depression was significantly negatively associated with children's social competence. Reversing the moderator, we also explored the relation between children's negative emotionality and social competence for children with 0, 1, or 2 parents with a history of depression. Figure 11 shows that for children with no parental history of depression, there was no significant association between children's negative emotionality and social competence (B = .24, SE = .32, p = .452), whereas for children with one parent with a history of depression, there was a significant negative association between children's negative emotionality and social competence (B = -.55, SE = .27, p = .041), and for children with two parents with a history of depression this significant negative association was more pronounced (B = -1.34, SE = .54, p = .014). Thus, there was a significant association between children's negative emotionality and social competence for those with a parent with a history of depression, and this relation was stronger for children with two parents with a history of depression, or a greater parental loading of depression.

Chapter 5: Discussion and Conclusions

The present study examined associations between proposed markers of physiological and behavioral susceptibility, early environmental influences, and young children's symptomatology and functioning. Specifically, we investigated whether children's stress reactivity and temperamental emotionality moderated the relations between environmental experiences and children's psychopathology, psychosocial functioning, and social competence. We considered whether our findings supported differential susceptibility or diathesis-stress theoretical frameworks. Significant findings emerged for children's cortisol reactivity and negative emotionality with respect to moderating the relations between the early environment and children's externalizing symptoms, psychosocial functioning and social competence. No significant findings were observed for children's internalizing symptoms, and no significant findings emerged for children's positive emotionality as a moderator. Overall, our findings are consistent with recent studies that have supported the diathesis-stress model (Belsky & Pluess, 2011; Kochanska et al., 2011; Nederhof et al., 2012). However, our findings with cortisol were in the opposite direction from our hypotheses, which is discussed in greater detail below.

First, we briefly review the significant bivariate associations among the study variables, followed by an in-depth discussion of our significant moderated effects.

For our first study aim, we examined the associations between children's stress reactivity and temperament to better understand whether different levels of measurement (physiological versus behavioral), often examined separately in previous work, reflect a shared sensitivity to the environment or more specific markers or risk/susceptibility. No significant associations were observed between indices of children's cortisol reactivity,

negative emotionality, or positive emotionality. Moreover, distinct patterns of moderation results emerged for cortisol reactivity and temperament. Taken together, our findings suggest that children's physiological and behavioral reactivity reflect separate pathways of risk to environmental influences rather than indices of a shared, common system of sensitivity. Similarly, Essex and colleagues (2011) found different patterns of moderation for autonomic and behavioral indices of reactivity with respect to associations between the child-teacher relationship and children's symptom severity. Given that little work to date has examined multiple levels of analysis of children's physiological and behavioral reactivity within the same study, further work is warranted to tease apart the specific pathways of risk to early emerging psychopathology.

We also observed gender differences among the sample. Consistent with previous literature (Zahn-Waxler, Shirtcliff, & Marceau, 2008), boys were reported to have more externalizing symptoms and lower psychosocial functioning and social competence than girls. Additionally, boys exhibited higher levels of negative emotionality. With respect to age, older children were reported to have higher levels of social competence, and exhibited more positive emotionality and less negative emotionality compared to younger children. We did not have the statistical power to explore possible three-way interactions of markers of sensitivity, the environment, and children's gender and/or age. However, we controlled for these variables in models examining children's externalizing symptoms, psychosocial functioning, and social competence.

As would be expected, several of the adverse environmental experiences were correlated.[5] Consistent with the literature documenting the associations between

[5] We did not discuss associations between the composite stress index and the factors that comprised the index (e.g., parental depression, life stressors).

depression and stressful life events (Kendler, Karkowski, & Prescott, 1999; Monroe, Slavich, & Georgiades, 2009), children of parents with a history of depression were more likely to have experienced more stressful life events in the past 12 months. In addition, the composite stress index was related to less supportive parenting. Moreover, possibly reflecting the bidirectional nature of the parent-child relationship (Bell, 1968), children with higher levels of negative emotionality were more likely to have mothers who engaged in hostile parenting behaviors. Consistent with the findings from a meta-analysis examining the relation between children's temperament and social status (Dougherty, 2004), children with higher levels of negative emotionality had lower social competence. Lastly, providing further evidence for the adverse influence of early family stressors, including parental history of depression, cumulative exposure to maternal depression, recent stressful life events, and composite family stress, on young children's functioning (Dougherty et al., 2013, Fihrer et al., 2009; Goodman et al., 2011; McMahon et al 2003; McLeod et al., 2007), we found that children exposed to early negative environmental factors had more psychiatric symptoms, and worse psychosocial functioning and social competence. Notably, several of these bivariate associations were part of significant interactions models. Thus, next we discuss our findings within the context of the observed significant interactions.

Children's Blunted Cortisol Reactivity: A Risk Factor for Maladaptation in the Context of Early Environmental Stress

Using two indices of children's stress reactivity (AUC_i, peak cortisol), we found similar patterns of moderation in support of the diathesis-stress model. Specifically, we found that for children with lower AUC_i, or total change in cortisol across the reactivity

assessment, more recent life stress was related to children's higher externalizing symptoms and lower psychosocial functioning. Similarly, for children with lower peak cortisol, high parental hostility was related to children's higher externalizing symptoms and lower psychosocial functioning. Notably, both exposure to stressful life events and parental hostility have been linked to risk for children's behavior problems (Campbell, 1995; Grant, Compas, Thurm, McMahon, & Gipson, 2004). Moreover, a recent meta-analysis reported a significant negative association between children's externalizing behavior and basal cortisol, with mixed findings for the relation between externalizing behavior and blunted cortisol reactivity (Alink et al., 2008). We did not observe significant bivariate associations between children's cortisol reactivity and externalizing behavior or psychosocial functioning. However, consistent with diathesis-stress models, we found that environmental stress (more recent life stress and insensitive, hostile parenting) was related to more externalizing symptoms and worse psychosocial functioning, only among children with a blunted pattern of cortisol reactivity to a developmentally appropriate laboratory stressor paradigm. Thus, our findings highlight the critical importance of examining the joint *interactive* effects of blunted HPA axis reactivity and life stress on young children's externalizing behavior.

We observed similar patterns of findings when using a composite stress index, based on family income, number of parents in the home, parental education, and child exposure to recent life stress and parental depression. Specifically, for children with lower AUC_i or lower peak cortisol levels, higher scores on the composite stress index were related to higher externalizing symptoms. It is interesting that the interaction between the composite stress index and children's AUC_i was significantly related only to

children's externalizing symptoms and not psychosocial functioning. Given that our measure of recent life stress was specific to events that were determined to have a significant impact on the child, it is possible that it had a greater effect on children's risk for psychopathology and associated functional impairment. The composite stress index was comprised of more broad family-level factors (e.g., level of parental education, household income), which may have less of a direct impact on children's psychosocial functioning, particularly among children with blunted HPA axis functioning. Nevertheless, taken together, our findings suggest that across different measures of adverse environmental factors, the combination of early environmental stress *and* blunted HPA axis reactivity renders children more vulnerable to early emerging externalizing psychopathology and associated functional impairment.

To date, the previous work examining the HPA axis as a moderator of differential susceptibility has yielded inconsistent findings, examined heterogeneous outcomes, studied youth of differing ages, and included methodological limitations that make it difficult to interpret how the reactivity of the HPA axis renders children more or less susceptible to early emerging emotional and behavioral problems. Although the direction of our cortisol findings (e.g., hypo-reactivity vs. hyper-reactivity) is not consistent with our hypotheses per se, our findings are consistent with two prior studies (Badanes et al., 2011; Klitzing et al., 2012) that supported blunted cortisol as a vulnerability marker of risk in the context of stressful environments. Badanes and colleagues (2011) found that among a sample of third, sixth, and ninth grade children, the combination of children's blunted cortisol reactivity and family stress predicted an increase in depressive symptoms over time. Moreover, Klitzing and colleagues (2012) found that five-year-old children

experienced an increase in emotional symptoms a year later if they exhibited a blunted cortisol response following a story completion task and experienced peer victimization the year prior. Consistent with the patterns observed by Badanes et al. (2011) and Klitzing et al. (2012), we found that children who experienced negative environmental factors and who had blunted cortisol responses had the highest levels of psychiatric symptoms. Moreover, our findings our the first to illustrate that the combination of blunted cortisol reactivity and negative environmental experiences are not only related to higher levels of children's symptomatology but also worse psychosocial functioning, underscoring the clinical significance of the difficulties experienced by children with both HPA axis hypo-activity and stressful early environments.

Importantly, a broader literature has implicated blunted cortisol reactivity to exposure to chronic stress (Badanes et al., 2011; Miller, Chen, & Zhou, 2007; Ronsaville et al., 2006). Notably, the HPA axis is one of several systems in the body, which self-regulates in response to changes in the environment (e.g., allostasis, McEwen, 1998; Sterling & Eyer, 1988). While activation of the HPA axis is adaptive in the context of acute threats, prolonged periods of HPA axis hyperactivity can result in allostatic load, or the negative physiological consequences associated with chronic activation of the stress response (i.e., damage of hippocampal neurons; McEwen & Stellar, 1993; McEwen, 1998). It has been posited that after exposure to chronic sources of stress, the HPA axis down-regulates as an adaptive mechanism to protect the brain and body from the adverse effects of prolonged hyper-activation (Fries, Hesse, Hellhammer, & Hellhammer, 2005). Thus, a blunted pattern of cortisol reactivity in children may be a marker of allostatic load in response to an early stressful environment (Badanes et al., 2011). Interestingly, we did

not find a significant association between exposure to stress and children's cortisol. Rather, our findings suggest that blunted cortisol reactivity renders children more vulnerable to environments characterized by stress rather than being a consequence of stress exposure. Nevertheless, our findings are cross-sectional and do not directly test the directionality of these effects.

Our findings are also somewhat consistent with Del Giudice, Ellis, and Shirtcliff's (2011) Adaptive Calibration Model, an evolutionary framework that extends the tenets of Biological Sensitivity to Context. Within the model, they propose four patterns of stress system functioning and their behavioral correlates. The first three patterns of stress system functioning are consistent with those proposed in Biological Sensitivity to Context theory: a "sensitive", highly reactive stress response observed in individuals raised in enriched, supportive environments; a "buffered" stress response observed in those raised in typical environments characterized by transient stress; and a "vigilant" highly reactive stress response observed in individuals raised in stressful environments. Del Guidice and colleagues further proposed a fourth, "unemotional" pattern, which is assumed to be found predominantly in males who have experienced severe stress in environments characterized by high levels of threat and danger. Notably, individuals with both the "vigilant" and "unemotional" patterns are expected to engage in more externalizing disruptive behavior (Del Guidice et al., 2011).

Thus, our behavioral findings could be interpreted with respect to the Vigilant and Unemotional Profiles as the observed blunted cortisol response in a subgroup of our sample may reflect a temporary down-regulation of HPA axis activity consistent with allostasis. Del Guidice and colleagues noted that children with vigilant profiles may

experience temporary periods of blunted responsivity following exposure to chronic stress, which later revert to a more reactive stress response. However, it is also possible that the children in our study who exhibited decreased patterns of HPA axis reactivity may have developed a more permanent blunted pattern of stress responsivity, characterized by the unemotional profile. It should be emphasized that these interpretations are purely speculative given the cross-sectional nature of our study. Further work is necessary to assess whether this observed pattern of children's blunted stress responsivity will persist across developmental phases. Moreover, it is unclear from our study whether stressful experiences temporally preceded the blunted cortisol response or whether this pattern of responding was the result of a pre-existing genetic vulnerability (Alexander et al., 2011; Steptoe, van Jaarsveld, Semmler, Plomin, & Wardle, 2009b; Wust et al., 2004). Prospective longitudinal work is warranted that investigates the origins and stability of these patterns of stress reactivity and behavioral correlates over time.

Our findings were specific to children's externalizing symptomatology and psychosocial functioning, as no significant associations were observed for children's internalizing symptoms. The specificity of our findings to externalizing symptomatology and psychosocial functioning may be due to developmental and methodological factors. Given that externalizing disorders are more common than several internalizing disorders (e.g., major depressive disorder, generalized anxiety disorder, panic disorder) during the preschool period (Bufferd et al., 2011; Lavigne, LeBailly, Hopkins, Gouze, & Binns, 2009), our lack of significant findings for internalizing symptoms partially may be explained by the varying prevalence of symptoms types during early childhood.

Moreover, externalizing (ODD and ADHD) diagnoses and symptom-scales derived from the use of the PAPA in an independent, large community sample of preschoolers, were more strongly related to preschoolers' level of impairment and treatment use than internalizing diagnoses and symptom-scales (Bufferd et al., 2011). Thus, it is possible that externalizing symptoms may be more intrusive into the daily functioning of preschool-age children and their families (e.g., child noncompliance, temper tantrums, physical aggression with peers), particularly from the parent's perspective, who was the sole informant on psychopathology and psychosocial functioning in the current study.

Although Badanes et al. (2011) and Klitzing et al. (2012) found that youth's blunted cortisol moderated associations between the environment and internalizing symptoms, both studies focused solely on youth's depressive or emotional symptoms rather than externalizing symptoms. Notably, Badanes and colleagues' (2011) sample included children much older than the preschool period. Additionally, Klitzing and colleagues assessed five- and six-year old children's emotional symptoms via a multi-informant approach (parent and teacher questionnaires and youth self-report). The integrated use of several measures for children's internalizing psychopathology, including direct interview with the child, which has been shown to be particularly important for the accurate assessment of internalizing psychopathology in older youth (Angold et al., 1987; Loeber, Green, & Lahey, 1990), may have resulted in different findings. Nevertheless, our findings highlight that children with a blunted pattern of cortisol reactivity, who also have been exposed to stress or insensitive parenting during early childhood are more likely to have clinically significant levels of externalizing symptoms. It is important to note that young children's externalizing behavior problems

have been found to be stable and provide an early salient indicator of later internalizing and externalizing disorders (Campbell 1995; Chronis-Tuscano et al., 2010; Mesman, Bongers, & Koot, 2001). Thus, further work is needed that examines these relations over time across the pre-adolescent and adolescent risk periods for depression and anxiety to test whether these associations are involved in the pathway to later onset of internalizing disorders.

Children's Negative Emotionality: Increasing Risk for Social Impairment with Exposure to Maternal Depression

We also found that children's negative emotionality moderated the relation between cumulative exposure to maternal depression and children's social competence, such that greater exposure to maternal depression across the child's life was related to worse social competence *only* among the children with high levels of negative emotionality. Depression in youth and adults consistently has been linked with social impairment (Segrin, 2000). Thus, it is likely that children who are exposed to significant periods of maternal depression across their first few years of life experience repeated modeling of suboptimal social skills and interactions. Previous work has found that the offspring of depressed parents have more social impairment than the offspring of non-depressed parents (Hammen & Brennan, 2001; Weissman et al., 2006). Moreover, children with high levels of negative emotionality, who are more prone to feelings of sadness, anger, and fear, have been found to have lower social competence and status (Dougherty, 2004; Eisenberg et al., 1993; Eisenberg et al., 1997). The repeated experience of intense and/or prolonged negative emotions likely interferes with young children's ability to initiate and maintain stable peer relations. The significant interaction

we observed between children's negative emotionality and exposure to maternal depression is consistent with diathesis-stress such that high negative emotionality, or a difficult temperament, places children at increased risk for maladaptive outcomes in adverse environments. Notably, our findings build upon previous work examining the separate influences of maternal depression and temperament on children's social functioning, and for the first time highlights the importance of examining the joint, interactive effects of these factors. Taken together, it appears that children who are exposed to mothers with depression *and* who temperamentally are more prone to negative affect and frustration, are at the greatest risk for developing early social impairment.

Social competence and effective social skills are particularly relevant during the preschool period when children often have their first experiences in establishing peer relationships. Early negative peer interactions likely lay the foundation for subsequent deficits in social competence and increase risk for psychopathology, particularly depression. Social competence has been found to predict depression onset, even after controlling for initial levels of depression (Cole, Martin, Powers, & Truglio, 1996). Moreover, Hammen, Shih, Altman, and Brennan (2003) found that chronic social difficulties predicted depression severity more strongly for the depressed adolescent offspring of depressed mothers in comparison to the depressed adolescents of non-depressed mothers. Thus, it is possible that the social impairment we observed in young children, who were high in negative emotionality and exposed to maternal depression, reflects an early vulnerability to depression. However, it is important to note that major depression and negative emotionality/neuroticism share a common genetic liability (Kendler, Neale, Kessler, Heath, & Eaves, 1993), and thus early emerging social

impairment and subsequent depression risk likely is also impacted, at least partly, by familial or shared genetic factors.

Familial Liability to Depression

Given the literature highlighting the increased risk of internalizing and externalizing psychopathology among children with two parents with a history of depression in comparison to those with one parent with a history of depression (Brennan et al., 2002; Nomura et al., 2001), we also explored the interactions between proposed markers of sensitivity and children's parental loading of depression (having zero, one, or two parents with a history of depression). Two significant interactions emerged. First, we found that children's negative emotionality moderated the relation between parental depression loading and children's social competence. Specifically, for children with high negative emotionality, greater parental loading of depression was related to children's lower social competence. We also explored the relation between children's negative emotionality and social competence at each level of parental depression loading (i.e., parental loading as the moderator). For children with no parents with a history of depression, children's negative emotionality was not significantly associated with social competence. However, for children of parents with a history of depression, children's negative emotionality was related to lower social competence, and this relation was most pronounced among children with two parents with a history of depression. Thus, our findings further highlight the negative outcomes associated with increased familial liability to depression, particularly for children prone to strong negative emotions.

Moreover, we found that children's peak cortisol moderated the relation between parental depression loading and children's social competence, such that for children with

higher peak cortisol there was a significant negative association between parental depression loading and children's social competence. Interestingly, we found that higher peak cortisol was significantly related to children's better social competence among children with no parental history of depression. The association between children's peak cortisol and social competence was not significant for children with one or two parents with a history of depression. Thus, the combination of a higher peak cortisol response and no parental liability of depression was related to children's greater adaptive social functioning. In light of our findings highlighting the role of blunted cortisol reactivity in risk for psychopathology and associated impairment, it is possible that children's higher levels of peak cortisol reflect an adaptive response to an acute laboratory stressor paradigm (Gunnar & Vazquez, 2006).

Diathesis-Stress vs. Differential Susceptibility

Overall, our findings supported the diathesis-stress model of risk for psychopathology rather than differential susceptibility. In contrast with our hypotheses, we did not find that children with increased stress reactivity or difficult temperament were more sensitive to the benefits of a supportive environment with respect to level of psychopathology and psychosocial functioning, as proposed by the differential susceptibility hypothesis. To date, the majority of the work supporting physiological differential susceptibility has focused on indices of autonomic stress reactivity (e.g., heart rate, blood pressure) and genetic variants with fewer studies examining adrenocortical reactivity, which was the biological marker examined in this study. To date, findings have been mixed from studies that examined how HPA axis activity moderated the relations between the environment and youth's mental health outcomes, with some

providing evidence consistent with differential susceptibility (e.g., Hastings et al., 2011; Klitzing et al., 2012; Obradovic et al., 2010) and others supporting diathesis-stress (Badanes et al., 2011). Across previous studies, it sometimes was difficult to interpret whether observed moderation results better supported diathesis-stress or differential susceptibility (e.g., lacking measures of positive and negative outcomes, or stressful and supportive environments). We attempted to address these issues by examining children's early psychopathology *and* psychosocial functioning, as well as hostile and supportive parenting. Although we included a measure of observed supportive parenting, it is possible that our study did not adequately assess the truly *enhanced* elements of children's early environments.

Further work testing diathesis-stress and differential susceptibility frameworks with respect to young children's psychopathology and psychosocial functioning is warranted. Particular consideration should be made toward identifying and measuring environmental influences that promote *enriched* development. For instance, researchers may want to consider children's differential susceptibility to the presence of supportive sibling relationships (Morgan et al., 2012), degree of positive relationship with a teacher or mentor figure (Essex et al., 2011), or treatment response to interventions that promote increases in sensitive parenting (e.g., Cassidy et al., 2011; Scott & O'Connor, 2012). Other potential sources of enriched environmental experiences could include measurements of the parent-child relationship in natural contexts, including the quality and amount of time spent with parents, as well as children's engagement in extracurricular activities.

In contrast to previous studies (e.g., Belsky et al., 1998; Bradley & Corwyn, 2008; Van Aken et al., 2007), we did not find that children's negative emotionality, or difficult temperament, moderated the relations between indices of parenting and children's psychopathology and functioning. Interestingly, several of the studies that found support for differential susceptibility, based on children's temperament, utilized ratings or observations made during infancy (Belsky et al., 1998; Bradley & Corwyn, 208; Dopkins-Stright et al., 2008). Thus, it is possible that measurements of temperament across developmental periods provide unique information with respect to sensitivity to the environment. Prospective, longitudinal studies that assess temperament on multiple occasions from infancy through later childhood can best address this issue. Moreover, some studies examined how specific elements of children's temperament, including fear, anxiousness, and frustration (e.g., Colder, Lochman, & Wells, 1997; Groeneveld, Vermeer, van IJzendoorn, & Linting, 2012; Kochanska, Aksan, & Joy, 2007; Lengua, 2008), served as markers of sensitivity or susceptibility to parenting or the early environment. Further work examining composite and specific indices of temperament will help address which elements modulate the impact of parenting on children's development.

Positive Emotionality

We also examined whether children's positive emotionality increased or decreased children's sensitivity to the early environment. However, no significant interactions involving positive emotionality emerged. To date, only two studies (Jessee et al., 2012; Lengua et al., 2000) have examined whether children's positive emotionality moderated the relation between early environmental experiences (e.g., parental

depressive symptoms, parenting) and children's mental health symptoms. Given prior evidence that children's positive emotionality moderated the relation between two other proposed markers of sensitivity: negative emotionality and the serotonin transporter promoter polymorphism (5-HTT; Hayden et al., 2010), further work examining the role of children's positive emotionality in modulating risk for psychopathology is warranted. Future studies of this nature will benefit from comprehensive designs with large samples that afford the opportunity to test complex associations, including the interactive influences of temperament dimensions (e.g., positive emotionality x negative emotionality), and multiple proposed markers of sensitivity with the environment (e.g., positive emotionality x genetic risk variants x parenting).

Study Strengths and Limitations

The present study had several strengths. First, we utilized a multi-method approach, including observational assessments of children's temperamental emotionality and parenting style, a physiological assessment of children's stress reactivity, parent-report of children's social competence, and clinical interviews for assessing parent and child psychopathology and psychosocial functioning. To our knowledge, this is the first study to examine how markers of risk moderated relations between the environment and preschoolers' psychopathology and psychosocial functioning through the use of a semi-structured clinical interview, empirically validated for this age group. Our use of the PAPA allowed for the assessment of frequency, severity, and duration of symptoms, as well as the resulting impairment.

Second, we included measures of children's psychosocial functioning, including a broad global index and measure of social competence, which allowed for a more

comprehensive design in testing differential susceptibility hypotheses (e.g., positive and negative child outcomes). Third, consistent with a recent meta-analysis highlighting the benefits of dimensional approaches to psychopathology (Markon, Chmielewski, & Miller, 2011) and movement toward incorporating this approach into future research consistent with Research Domain Criteria (RDoC) project, we utilized continuous measures of young children's internalizing and externalizing psychopathology.

Fourth, we implemented a developmentally appropriate standardized laboratory stressor paradigm for the assessment of children's stress reactivity. Moreover, we collected five cortisol samples, including four post-stressor samples to better capture individual differences in children's reactivity and recovery responses to the stressor paradigm, which is particularly important given the variability in timing of young children's peak cortisol response (Tolep & Dougherty, 2014). Fifth, we examined proposed physiological and behavioral indices of sensitivity within the same study to examine their unique patterns of response. Sixth, we assessed multiple aspects of the early environment (e.g., parenting style, exposure to parental psychopathology, stressful life events) in an effort to better understand whether children's stress physiology or temperament render them particularly sensitive to specific environmental experiences or more globally to adverse contexts.

This study also had limitations. First, the study was cross-sectional, and thus causal effects cannot be tested. Second, previous work has highlighted the complex relations between children's negative and positive emotionality (Olino, Klein, Dyson, Rose, & Durbin, 2010), and thus it is possible that children's negative and positive emotionality interact with respect to sensitivity to the early environment,

psychopathology, and psychosocial functioning. However, in the present study, we did not have the statistical power to test this three-way interaction. Additionally, we observed gender differences with respect to children's temperament, externalizing symptoms, psychosocial functioning, and social competence. Although we controlled for gender in our analyses, further work with larger samples is needed to examine whether gender moderates the complex associations between children's stress reactivity, temperament, and psychosocial outcomes (Hastings et al., 2011; Gunnar et al., 2010). Fourth, we only included one physiological measure of stress response system functioning in the present study. Further work examining the joint, interactive influences of multiple physiological systems, which together better reflect the integrative processes of allostasis and allostatic load, is warranted (Bauer, Quas, & Boyce, 2002; Lupien et al., 2006). Fifth, primary caregivers were the sole informant for outcome measures on children's psychopathology and psychosocial functioning. It will be important to assess whether our findings replicate using a multi-informant approach, including self-reports from children, particularly with respect to assessing internalizing symptomatology, as well as a teacher ratings of children's behavior and social skills. Sixth, the present study did not examine genetic sources of vulnerability. Prior work has found support for diathesis-stress and differential susceptibility based on genetic variants (e.g., Bakermans-Kranenburg & van IJzendoorn, 2007; van IJzendoorn, Belsky, & Bakermans-Kranenburg, 2012; Nederhof et al., 2012), and thus studies examining how the interactions of genetics, stress physiology, and temperament relate to early emerging psychopathology are warranted. Seventh, even though we made efforts to include fathers in the study, our data on fathers was limited and we assessed current parenting behavior in one parent (typically the mother). This

highlights the need for researchers to augment and expand recruitment efforts targeting fathers' participation. Finally, we did not examine mediational models with this data. For instance, we did not examine whether cortisol reactivity and/or temperament mediates associations between environmental experiences and children's psychosocial outcomes. While these are important questions, mediational models examining developmental pathways should be tested longitudinally, rather than using a cross-sectional design.

Conclusion

Emotional and behavioral problems have their roots early in life. Recent work has highlighted the clinical significance of psychopathology during the preschool period. In an effort to better identify and understand which children are most likely to develop psychiatric disorders, theories of differential risk for psychopathology have been proposed. We found evidence consistent with the diathesis-stress model related to young children's externalizing symptoms, psychosocial functioning, and social competence. It appears that a blunted pattern of HPA axis reactivity renders young children more vulnerable to externalizing behavior problems and their associated impairment in environments characterized by family stress, including recent stressful life events and harsh parenting. Moreover, children who are prone to high levels of negative emotionality and who are exposed to maternal depression appear to be at increased risk for deficits in social functioning, which may result in the later onset of depression. In contrast to differential susceptibility theory, we did not find evidence that children's stress reactivity and temperament also render them more sensitive to the effects of supportive parenting.

Notably, we found that children with identified risk factors (e.g., blunted cortisol reactivity, high negative emotionality) only evidenced increased rates of psychopathology and impairment when also exposed to stressful experiences, highlighting the important role of the early environment in risk for psychopathology. It is important to note that several possible explanations or mechanisms exist for the development of early psychopathology, including genetics, temperament, dysregulated stress responses, insensitive parenting, parental psychopathology, and exposure to life stress. Therefore, the processes involved in these relations are likely complex and further multifactorial investigations into risk for psychopathology are warranted.

Nevertheless, our findings offer several clinical implications. Treatment programs targeting children with blunted cortisol that promote adaptive coping skills for parents experiencing high levels of stress and/or more sensitive parenting strategies may reduce the emergence of early emerging behavior problems in those at highest risk for maladaptation. Moreover, our findings highlight the importance of treatment for depressed mothers of young children, particularly those children exhibiting high levels of negative affect. Interestingly, recent work has found that family interventions targeting parenting and attachment have resulted in changes in children's cortisol (Brotman et al., 2007; Dozier, Peloso, Lewis, Laurenceau, & Levine, 2008), with one study finding evidence that increases in young children's cortisol following an intervention mediated the relation between treatment and children's subsequent decreased aggression (O'Neal et al., 2010). Although these initial studies have been limited to foster and high-risk children, they offer encouraging findings about the potential benefits of early intervention and prevention efforts, particularly for children with physiological and behavioral

markers of risk, during a period of development characterized by a high degree of neuroplasticity.

Table 1. *Demographic characteristics of study sample*

Demographic variable	
Child age, mean (SD), months	49.80 (9.57)
Mother age, mean (SD), years	34.94 (6.15)
Father age, mean (SD), years	37.18 (6.86)
Child sex, male [n (%)]	77 (49.4%)
Child race [n (%)]	
White, European-American	74 (48.4%)
African-American	53 (34.6%)
Asian	3 (2.0%)
Other	23 (15.0%)
Child ethnicity [n (%)]	
Hispanic/Latino descent	26 (17.1%)
Biological parents' marital status [n (%)]	
Married	107 (68.6%)
Living together	5 (3.2%)
Divorced or separated	11 (7.0%)
Never married	33 (21.2%)
Family income [n (%)]	
< $20,000	11 (7.3%)
$20,001 to $40,000	13 (8.7%)
$40,001 to $70,000	31 (20.7%)
$70,001 to $100,000	43 (28.7%)

> $100,000	52 (34.7%)
Parental education: graduated 4-year college [n (%)]	
Mothers	94 (60.3%)
Fathers	86 (58.5%)
PAPA interview respondent [n (%)]	
Mother	142 (91.0%)
Father	9 (5.8%)
Both parents	5 (3.2%)

Note. N = 156. Of the sample, 6 (3.8%) families did not report their yearly income. Nine (5.8%) families did not report paternal education.

Table 2. *Correlations among all study variables*

		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16
1.	Child AUC_i	-															
2.	Child peak cortisol	-.19*	-														
3.	Child positive emotionality	-.02	-.04	-													
4.	Child negative emotionality	-.05	.14	-.10	-												
5.	Parental depressive disorder	.02	-.01	-.13	.02	-											
6.	Maternal. depression exposure	-.04	.09	-.02	-.02	**.39****	-										
7.	Parental hostility	.06	.07	-.04	**.17***	-.01	.14	-									
8.	Parental support	.11	-.07	.09	-.08	-.02	-.09	**-.54****	-								
9.	Recent stressors	.04	.06	-.10	-.03	**.22****	.13	.15	-.10	-							
10.	Composite stress index	.07	.02	**-.17***	.08	**.30****	**.47****	**.38****	**-.38****	**.46****	--						
11.	Child internalizing	-.03	-.07	-.04	-.10	.15	-.03	.04	-.05	**.29****	.13	-					
12.	Child externalizing	-.02	-.10	.01	-.03	**.18***	.15	.03	.09	**.16***	.11	**.43****	-				
13.	Child psychosocial functioning	.02	.06	.02	-.02	**-.17***	-.20	-.07	.03	**-.27****	**-.18***	**-.58****	**-.68****	-			
14.	Child social competence	.03	.08	.09	**-.17***	**-.17***	**-.18***	-.13	-.08	.04	-.04	-.14	**-.33****	**.39****	-		
15.	Child age	-.07	-.09	**.29****	**-.17***	-.15	.04	-.10	.16	.03	-.01	-.08	.01	.02	**.20***	-	
16.	Child gender	-.08	.01	.01	**-.19***	-.04	-.06	-.07	-.07	-.05	-.11	.12	**-.19***	**.18***	**.26****	-.03	-
Mean		-1.50	3.16	-.02	-.01	-	.15	1.13	4.13	2.38	1.34	16.19	7.00	72.33	24.02	49.80	-
(SD)		(10.25)	(3.21)	(.52)	(.69)	-	(.30)	(.27)	(.74)	(1.71)	(1.30)	(9.38)	(5.20)	(13.95)	(3.02)	9.57	-
N		148	148	156	156	154	154	156	156	156	156	156	156	156	149	156	156

Note: AUC_i: Area under the curve with respect to increase; correlation analyses used log10 transformed peak cortisol values; however, means and standard deviations (SD) for peak cortisol levels are reported as raw cortisol levels in nmol/L; Parental depressive disorder: lifetime major depressive disorder or dysthymic order in at least one parent (N = 96) and 0 = no lifetime depression in either parent (N = 58); Maternal cum. depression exposure = proportion of offspring exposure to maternal depressive disorder during the child's life; Recent stressors = number of stressful life events in the past 12 months; Composite stress (range 0-5); Child age reported in months; Child Gender: male = 1 (N = 77) and female = 2 (N = 79); $^{*}p < .05$, $^{**}p < .01$.

Table 3. *Associations between children's proposed markers of susceptibility, environmental influences, and internalizing symptoms*

	B	***b (SE)***	***t***	***p***
Dependent Variable: Internalizing Symptoms				
Moderator: Child AUC$_i$				
Model 1				
Child AUC$_i$	.02	.18 (1.46)	.12	.901
Lifetime Parental Depression	.14	2.77 (1.62)	1.71	.090
AUC$_i$ X Lifetime Parental Depression	-.07	-.92 (1.87)	-.50	.622
Model 2				
Child AUC$_i$	-.01	-.16 (.93)	-.17	.867
Maternal Depression Exposure	-.03	-.26 (.81)	-.33	.746
AUC$_i$ X Maternal Depression Exposure	-.11	-1.24 (.92)	-1.34	.181
Model 3				
Child AUC$_i$	-.04	-.41 (.94)	-.44	.664
Parental Hostility	.04	.41 (.97)	.42	.673
AUC$_i$ X Parental Hostility	.02	.18 (1.09)	.17	.869
Model 4				
Child AUC$_i$	-.09	-.99 (1.13)	-.87	.384
Parental Support	-.05	-.52 (.91)	-.57	.568
AUC$_i$ X Parental Support	-.11	-1.07 (1.00)	-1.07	.287
Model 5				
Child AUC$_i$	-.05	-.53 (.89)	-.60	.547
Recent Stressors	.28	2.73 (.77)	3.54	**.001**
AUC$_i$ X Recent Stressors	-.06	-.61 (.80)	-.76	.446
Model 6				
Child AUC$_i$	-.05	-.52 (.91)	-.57	.572
Composite Stress Index	.15	1.46 (.81)	1.80	.074
AUC$_i$ X Composite Stress Index	-.11	-1.15 (.86)	-1.34	.183
Moderator: Child Peak Cortisol				
Model 1				
Child Peak Cortisol	-.13	-1.44 (1.70)	-.85	.397
Lifetime Parental Depression	.14	2.74 (1.62)	1.69	.093
Peak Cortisol X Lifetime Parental Depression	.07	.88 (1.99)	.44	.658
Model 2				
Child Peak Cortisol	-.08	-.84 (.90)	-.93	.352
Maternal Depression Exposure	-.02	-.21 (.81)	-.26	.795
Peak Cortisol X Maternal Depression Exposure	.05	.54 (.92)	.59	.557

Model 3				
Child Peak Cortisol	-.08	-.84 (.89)	-.94	.349
Parental Hostility	.05	.53 (.92)	.58	.562
Peak Cortisol X Parental Hostility	-.06	-.73 (1.07)	-.69	.492
Model 4				
Child Peak Cortisol	-.08	-.86 (.90)	-.95	.342
Parental Support	-.06	-.66 (.91)	-.73	.465
Peak Cortisol X Parental Support	-.01	-.12 (.92)	-.13	.896
Model 5				
Child Peak Cortisol	-.09	-.97 (.86)	-1.13	.259
Recent Stressors	.28	2.73 (.77)	3.54	**.001**
Peak Cortisol X Recent Stressors	.04	.39 (.88)	.44	.659
Model 6				
Child Peak Cortisol	-.08	-.82 (.89)	-.93	.356
Composite Stress Index	.13	1.25 (.80)	1.57	.119
Peak Cortisol X Composite Stress Index	-.03	-.32 (.88)	-.36	.717
Moderator: Child Positive Emotionality				
Model 1				
Child Positive Emotionality	-.19	-1.85 (1.16)	-1.60	.112
Lifetime Parental Depression	.14	2.79 (1.56)	1.79	.075
Positive Emotionality X Lifetime Parental Depression	.22	2.89 (1.56)	1.85	.066
Model 2				
Child Positive Emotionality	-.04	-.39 (.81)	-.48	.633
Maternal Depression Exposure	-.03	-.26 (.79)	-.33	.740
Positive Emotionality X Maternal Depression Exposure	.02	.26 (.95)	.27	.786
Model 3				
Child Positive Emotionality	-.04	-.37 (.80)	-.47	.643
Parental Hostility	.04	.39 (.89)	.44	.660
Positive Emotionality X Parental Hostility	.01	.18 (1.16)	.15	.879
Model 4				
Child Positive Emotionality	-.04	-.35 (.80)	-.44	.661
Parental Support	-.05	-.47 (.87)	-.54	.588
Positive Emotionality X Parental Support	-.01	-.13 (.98)	-.13	.894
Model 5				
Child Positive Emotionality	-.02	-.18 (.75)	-.24	.812
Recent Stressors	.27	2.54 (.74)	3.45	**.001**

Positive Emotionality X Recent Stressors	-.07	-.72 (.82)	-.88	.381
Model 6				
Child Positive Emotionality	-.03	-.31 (.78)	-.40	.690
Composite Stress Index	.12	1.11 (.75)	1.48	.140
Positive Emotionality X Composite Stress	-.13	-1.21 (.75)	-1.62	.107
Moderator: Child Negative Emotionality				
Model 1				
Child Negative Emotionality	-.14	-1.24 (1.11)	-1.12	.266
Lifetime Parental Depression	.15	2.93 (1.56)	1.88	.062
Negative Emotionality X Lifetime Parental Depression	.04	.55 (1.49)	.37	.715
Model 2				
Child Negative Emotionality	-.10	-.92 (.76)	-1.22	.226
Maternal Depression Exposure	-.03	-.28 (.79)	-.36	.721
Negative Emotionality X Maternal Depression Exposure	.01	-.01 (.90)	-.01	.996
Model 3				
Child Negative Emotionality	-.11	-1.101 (.76)	-1.34	.182
Parental Hostility	.07	.72 (.95)	.76	.451
Negative Emotionality X Parental Hostility	-.03	-.28 (.86)	-.32	.748
Model 4				
Child Negative Emotionality	-.10	-.95 (.75)	-1.27	.205
Parental Support	-.05	-.52 (.85)	-.61	.541
Negative Emotionality X Parental Support	-.05	-.43 (.78)	-.55	.581
Model 5				
Child Negative Emotionality	-.09	-.83 (.72)	-1.17	.246
Recent Stressors	.28	2.62 (.73)	3.60	**<.001**
Negative Emotionality X Recent Stressors	.02	.14 (.71)	.20	.841
Model 6				
Child Negative Emotionality	-.11	-1.04 (.74)	-1.41	.162
Composite Stress	.14	1.26 (.74)	1.71	.089
Negative Emotionality X Composite Stress	-.05	-.42 (.72)	-.58	.562

Note: AUC_i: Area under the curve with respect to increase

Table 4. *Associations between children's proposed markers of susceptibility, environmental influences, and externalizing symptoms*

	B	***b (SE)***	***t***	***p***
Dependent Variable: Externalizing Symptoms				
Moderator: Child AUC_i				
Model 1				
Child Gender	-.15	-1.61 (.86)	-1.86	.065
Child AUC_i	.11	.65 (.80)	.82	.414
Lifetime Parental Depression	.19	2.00 (,88)	2.28	**.024**
AUC_i X Lifetime Parental Depression	-.18	-1.38 (1.02)	-1.35	.178
Model 2				
Child Gender	-.16	-1.70 (.87)	-1.95	.053
Child AUC_i	-.02	-.10 (.51)	-.19	.846
Maternal Depression Exposure	.16	.83 (.44)	1.89	.060
AUC_i X Maternal Depression Exposure	-.03	-.19 (.50)	-.38	.708
Model 3				
Child Gender	-.17	-1.79 (.87)	-2.06	**.041**
Child AUC_i	-.03	-.18 (.52)	-.34	.733
Parental Hostility	.02	.15 (.53)	.28	.784
AUC_i X Parental Hostility	-.01	-.03 (.60)	-.04	.966
Model 4				
Child Gender	-.17	-1.74 (.86)	-2.01	**.046**
Child AUC_i	-.12	-.72 (.62)	-1.16	.247
Parental Support	.09	.51 (.50)	1.03	.305
AUC_i X Parental Support	-.14	-.74 (.54)	-1.37	.172
Model 5				
Child Gender	-.16	-1.64 (.84)	-1.95	.053
Child AUC_i	-.05	-.31 (.49)	-.64	.526
Recent Stressors	.19	1.01 (.43)	2.36	**.020**
AUC_i X Recent Stressors	-.19	-1.05 (.44)	-2.37	**.019**
Model 6				
Child Gender	-.15	-1.61 (.86)	-1.88	.062
Child AUC_i	-.04	-.27 (.49)	-.54	.590
Composite Stress Index	.15	.80 (.44)	1.82	.071
AUC_i X Composite Stress Index	-.17	-.96 (.47)	-2.06	**.042**
Moderator: Child Peak Cortisol				
Model 1				
Child Gender	-.17	-1.78 (.85)	-2.09	**.038**
Child Peak Cortisol	-.24	-1.42 (.92)	-1.55	.123

Lifetime Parental Depression	.18	1.96 (.88)	2.24	**.027**
Peak Cortisol X Lifetime Parental Depression	.16	1.11 (1.08)	1.04	.302
Model 2				
Child Gender	-.17	-1.83 (.86)	-2.11	**.036**
Child Peak Cortisol	-.13	-.76 (.48)	-1.56	.121
Maternal Depression Exposure	.17	.88 (.44)	2.03	**.045**
Peak Cortisol X Maternal Depression Exposure	.08	.50 (.50)	.99	.325
Model 3				
Child Gender	-.17	-1.79 (.85)	-2.11	**.037**
Child Peak Cortisol	-.11	-.64 (.48)	-1.33	.187
Parental Hostility	.04	.23 (.49)	.47	.636
Peak Cortisol X Parental Hostility	-.19	-1.34 (.57)	-2.34	**.021**
Model 4				
Child Gender	-.17	-1.74 (.86)	-2.02	**.045**
Child Peak Cortisol	-.09	-.56 (.49)	-1.14	.256
Parental Support	.07	.43 (.49)	.87	.386
Peak Cortisol X Parental Support	.07	.42 (.50)	.84	.405
Model 5				
Child Gender	-.15	-1.61 (.85)	-1.89	.061
Child Peak Cortisol	-.11	-.68 (.48)	-1.41	.160
Recent Stressors	.18	.97 (.43)	2.25	**.026**
Peak Cortisol X Recent Stressors	.03	.15 (.49)	.31	.760
Model 6				
Child Gender	-.14	-1.44 (.85)	-1.69	.094
Child Peak Cortisol	-.11	-.63 (.48)	-1.32	.189
Composite Stress Index	.13	.69 (.43)	1.60	.113
Peak Cortisol X Composite Stress Index	-.17	-1.02 (.47)	-2.16	**.032**
Moderator: Child Positive Emotionality				
Model 1				
Child Gender	-.20	-2.03 (.83)	-2.46	**.015**
Child Positive Emotionality	-.09	-.48 (.64)	-.76	.451
Lifetime Parental Depression	.17	1.83 (.85)	2.15	**.033**
Positive Emotionality X Lifetime Parental Depression	.16	1.13 (.86)	1.32	.190
Model 2				
Child Gender	-.18	-1.88 (.83)	-2.26	**.025**
Child Positive Emotionality	.01	.04 (.44)	.10	.924
Maternal Depression Exposure	.14	.75 (.43)	1.75	.082

Positive Emotionality X Maternal Depression Exposure	-.01	-.02 (.52)	-.03	.976
Model 3				
Child Gender	-.19	-1.98 (.83)	-2.40	**.018**
Child Positive Emotionality	-.01	-.07 (.44)	-.17	.867
Parental Hostility	.02	.14 (.48)	.29	.774
Positive Emotionality X Parental Hostility	-.09	-.72 (.63)	-1.15	.252
Model 4				
Child Gender	-.19	-1.92 (.83)	2.31	**.022**
Child Positive Emotionality	.01	.01 (.44)	.02	.984
Parental Support	.07	.43 (.48)	.89	.373
Positive Emotionality X Parental Support	-.01	-.05 (.54)	-.08	.934
Model 5				
Child Gender	-.18	-1.90 (.82)	-2.32	**.022**
Child Positive Emotionality	.02	.11 (.42)	.26	.794
Recent Stressors	.16	.81 (.42)	1.94	.055
Positive Emotionality X Recent Stressors	.01	.03 (.46)	.06	.956
Model 6				
Child Gender	-.18	-1.87 (.82)	-2.27	**.024**
Child Positive Emotionality	.01	.07 (.43)	.16	.872
Composite Stress Index	.09	.46 (.41)	1.12	.263
Positive Emotionality X Composite Stress Index	-.12	-.62 (.41)	-1.50	.136
Moderator: Child Negative Emotionality				
Model 1				
Child Gender	-.20	-2.06 (.84)	-2.47	**.015**
Child Negative Emotionality	-.15	-.75 (.61)	-1.21	.227
Lifetime Parental Depression	.17	1.82 (.85)	2.15	**.033**
Negative Emotionality X Lifetime Parental Depression	.11	.72 (.81)	.88	.379
Model 2				
Child Gender	-.18	-1.91 (.84)	-2.26	**.026**
Child Negative Emotionality	-.05	-.25 (.42)	-.59	.555
Maternal Depression Exposure	.15	.80 (.43)	1.87	.063
Negative Emotionality X Maternal Depression Exposure	.08	.51 (.49)	1.04	.299
Model 3				
Child Gender	-.20	-2.09 (.84)	-2.48	**.014**
Child Negative Emotionality	-.07	-.35 (.42)	-.84	.405
Parental Hostility	.03	.16 (.52)	.30	.767

Negative Emotionality X Parental Hostility	.01	.05 (.47)	.10	.919
Model 4				
Child Gender	-.19	-1.98 (.84)	-2.37	**.019**
Child Negative Emotionality	-.05	-.27 (.41)	-.65	.518
Parental Support	.09	.49 (.46)	1.06	.290
Negative Emotionality X Parental Support	-.13	-.71 (.42)	-1.68	.096
Model 5				
Child Gender	-.20	-2.04 (.83)	-2.44	**.016**
Child Negative Emotionality	-.06	-.30 (.41)	-.73	.465
Recent Stressors	.16	.80 (.41)	1.95	.053
Negative Emotionality X Recent Stressors	-.04	-.20 (.40)	-.50	.619
Model 6				
Child Gender	-.20	-2.04 (.84)	-2.42	**.017**
Child Negative Emotionality	-.07	-.37 (.42)	-.90	.370
Composite Stress Index	.10	.48 (.41)	1.19	.238
Negative Emotionality X Composite Stress Index	-.05	-.24 (.40)	-.60	.552

Note: AUC_i: Area under the curve with respect to increase

Table 5. *Associations between children's proposed markers of susceptibility, environmental influences, and psychosocial functioning*

	β	***b (SE)***	***t***	***p***
Dependent Variable: Psychosocial Functioning				
Moderator: Child AUC$_i$				
Model 1				
Child Gender	.15	4.32 (2.34)	1.85	.067
Child AUC$_i$	.03	.43 (2.16)	.20	.842
Lifetime Parental Depression	-.16	-4.53 (2.38)	-1.91	.059
AUC$_i$ X Lifetime Parental Depression	.01	.12 (2.76)	.05	.964
Model 2				
Child Gender	.15	4.12 (2.31)	1.78	.077
Child AUC$_i$	.02	.32 (1.35)	.24	.813
Maternal Depression Exposure	-.19	-2.75 (1.17)	-2.35	**.020**
AUC$_i$ X Maternal Depression Exposure	.01	-.01 (1.34)	-.01	.999
Model 3				
Child Gender	.16	4.45 (2.32)	1.92	.058
Child AUC$_i$	.02	.24 (1.37)	.17	.862
Parental Hostility	-.09	-1.38 (1.41)	-.97	.332
AUC$_i$ X Parental Hostility	.09	1.53 (1.59)	.96	.338
Model 4				
Child Gender	.16	4.52 (2.33)	1.94	.055
Child AUC$_i$	.04	.61 (1.67)	.37	.716
Parental Support	.03	.47 (1.34)	.35	.724
AUC$_i$ X Parental Support	.02	.30 (1.47)	.21	.837
Model 5				
Child Gender	.14	3.84 (2.21)	1.74	.085
Child AUC$_i$	.05	.84 (1.29)	.66	.512
Recent Stressors	-.28	-3.97 (1.12)	-3.54	**.001**
AUC$_i$ X Recent Stressors	.16	2.42 (1.16)	2.08	**.039**
Model 6				
Child Gender	.14	3.83 (2.30)	1.67	.097
Child AUC$_i$	.05	.73 (1.32)	.55	.583
Composite Stress Index	-.18	-2.57 (1.18)	-2.17	**.032**
AUC$_i$ X Composite Stress Index	.14	2.14 (1.25)	1.72	.088
Moderator: Child Peak Cortisol				
Model 1				
Child Gender	.16	4.40 (2.30)	1.91	.058
Child Peak Cortisol	.20	3.13 (2.47)	1.26	.209

Lifetime Parental Depression	-.16	-4.70 (2.36)	-1.98	.050
Peak Cortisol X Lifetime Parental Depression	-.17	-3.10 (2.90)	-1.07	.287
Model 2				
Child Gender	.15	4.16 (2.32)	1.79	.075
Child Peak Cortisol	.08	1.21 (1.30)	.93	.354
Maternal Depression Exposure	-.20	-2.86 (1.17)	-2.44	**.016**
Peak Cortisol X Maternal Depression Exposure	-.02	-.39 (1.34)	-.29	.770
Model 3				
Child Gender	.15	4.34 (2.29)	1.90	.060
Child Peak Cortisol	.06	.97 (1.29)	.75	.453
Parental Hostility	-.07	-1.13 (1.33)	-.85	.398
Peak Cortisol X Parental Hostility	.17	3.13 (1.54)	2.03	**.044**
Model 4				
Child Gender	.16	4.45 (2.33)	1.91	.058
Child Peak Cortisol	.06	.95 (1.32)	.72	.473
Parental Support	.04	.61 (1.33)	.46	.649
Peak Cortisol X Parental Support	.02	.32 (1.36)	.23	.816
Model 5				
Child Gender	.14	3.86 (2.25)	1.72	.088
Child Peak Cortisol	.07	1.13 (1.26)	.90	.372
Recent Stressors	-.27	-3.86 (1.13)	-3.40	**.001**
Peak Cortisol X Recent Stressors	.02	.24 (1.30)	.19	.851
Model 6				
Child Gender	.13	3.62 (2.31)	1.57	.120
Child Peak Cortisol	.06	.92 (1.29)	.72	.476
Composite Stress Index	-.16	-2.23 (1.17)	-1.91	.058
Peak Cortisol X Composite Stress Index	.08	1.24 (1.28)	.97	.334
Moderator: Child Positive Emotionality				
Model 1				
Child Gender	.18	4.96 (2.24)	2.22	**.028**
Child Positive Emotionality	.09	1.33 (1.72)	.78	.440
Lifetime Parental Depression	-.16	-4.68 (2.30)	-2.03	**.044**
Positive Emotionality X Lifetime Parental Depression	-.12	-2.39 (2.32)	-1.03	.305
Model 2				
Child Gender	.16	4.44 (2.21)	2.01	**.046**
Child Positive Emotionality	.03	.46 (1.16)	.40	.692
Maternal Depression Exposure	-.19	-2.69 (1.14)	-2.37	**.019**
Positive Emotionality X Maternal Depression Exposure	.07	1.10 (1.37)	.80	.424

Model 3				
Child Gender	.17	4.81 (2.23)	2.16	**.032**
Child Positive Emotionality	.03	.41 (1.18)	.35	.726
Parental Hostility	-.06	-.97 (1.30)	-.74	.459
Positive Emotionality X Parental Hostility	.05	1.00 (1.70)	.59	.556
Model 4				
Child Gender	.18	4.96 (2.24)	2.22	**.028**
Child Positive Emotionality	.02	.21 (1.18)	.18	.857
Parental Support	.04	.59 (1.28)	.46	.646
Positive Emotionality X Parental Support	.01	.14 (1.45)	.10	.923
Model 5				
Child Gender	.16	4.52 (2.15)	2.10	**.037**
Child Positive Emotionality	-.01	-.05 (1.11)	-.04	.966
Recent Stressors	-.26	-3.62 (1.09)	-3.32	**.001**
Positive Emotionality X Recent Stressors	.04	.57 (1.21)	.48	.635
Model 6				
Child Gender	.16	4.41 (2.18)	2.02	**.045**
Child Positive Emotionality	.01	.06 (1.14)	.06	.956
Composite Stress Index	-.16	-2.18 (1.09)	-2.00	**.048**
Positive Emotionality X Composite Stress Index	.15	2.08 (1.09)	1.90	.059
Moderator: Child Negative Emotionality				
Model 1				
Child Gender	.17	4.84 (2.26)	2.14	**.034**
Child Negative Emotionality	.08	1.06 (1.66)	.64	.524
Lifetime Parental Depression	-.16	-4.73 (2.29)	-2.07	**.041**
Negative Emotionality X Lifetime Parental Depression	-.08	-1.47 (2.20)	-.67	.504
Model 2				
Child Gender	.15	4.23 (2.25)	1.88	.062
Child Negative Emotionality	-.01	-.12 (1.11)	-.11	.912
Maternal Depression Exposure	-.21	-2.96 (1.14)	-2.63	**.010**
Negative Emotionality X Maternal Depression Exposure	-.12	-1.95 (1.30)	-1.50	.136
Model 3				
Child Gender	.18	4.92 (2.27)	2.17	**.032**
Child Negative Emotionality	.02	.33 (1.13)	.29	.772
Parental Hostility	-.06	-.90 (1.41)	-.64	.524
Negative Emotionality X Parental Hostility	-.02	-.25 (1.26)	-.20	.842

Model 4				
Child Gender	.18	5.02 (2.28)	2.21	**.029**
Child Negative Emotionality	.02	.23 (1.13)	.20	.841
Parental Support	.03	.52 (1.27)	.41	.685
Negative Emotionality X Parental Support	.06	.78 (1.15)	.68	.498
Model 5				
Child Gender	.16	4.55 (2.19)	2.08	**.040**
Child Negative Emotionality	.01	.04 (1.08)	.04	.971
Recent Stressors	-.27	-3.69 (1.08)	-3.42	**.001**
Negative Emotionality X Recent Stressors	-.01	-.14 (1.05)	-.13	.897
Model 6				
Child Gender	.17	4.63 (2.25)	2.06	**.041**
Child Negative Emotionality	.03	.38 (1.11)	.35	.730
Composite Stress Index	-.16	-2.25 (1.09)	-2.07	**.040**
Negative Emotionality X Composite Stress Index	.06	.74 (1.06)	.70	.485

Note: AUC_i: Area under the curve with respect to increase

Table 6. *Associations between children's proposed markers of susceptibility, environmental influences, and social competence*

	β	***b (SE)***	***t***	***p***
Dependent Variable: Social Competence				
Moderator: Child AUC$_i$				
Model 1				
Child Age	.21	.64 (.26)	2.51	**.013**
Child Gender	.22	1.34 (.49)	2.72	**.007**
Child AUC$_i$	-.03	-.11 (.45)	-.24	.813
Lifetime Parental Depression	-.12	-.76 (.51)	-1.50	.136
AUC$_i$ X Lifetime Parental Depression	.12	.53 (.58)	.91	.364
Model 2				
Child Age	.22	.70 (.25)	2.79	**.006**
Child Gender	.22	1.34 (.49)	2.74	**.007**
Child AUC$_i$	.05	.19 (.28)	.67	.506
Maternal Depression Exposure	-.17	-.52 (.25)	-2.11	**.037**
AUC$_i$ X Maternal Depression Exposure	.01	.01 (.29)	.02	.985
Model 3				
Child Age	.21	.67 (.26)	2.63	**.010**
Child Gender	.24	1.43 (.49)	2.92	**.004**
Child AUC$_i$	.05	.18 (.29)	.61	.543
Parental Hostility	-.11	-.39 (.30)	-1.30	.196
AUC$_i$ X Parental Hostility	.05	.20 (.33)	.60	.550
Model 4				
Child Age	.22	.70 (.26)	2.74	**.007**
Child Gender	.24	1.42 (.49)	2.89	**.004**
Child AUC$_i$	.15	.53 (.35)	1.50	.135
Parental Support	-.02	-.09 (.29)	-.29	.770
AUC$_i$ X Parental Support	.15	.47 (.31)	1.53	.128
Model 5				
Child Age	.22	.68 (.25)	2.66	**.009**
Child Gender	.24	1.44 (.49)	2.94	**.004**
Child AUC$_i$	.07	.23 (.28)	.83	.410
Recent Stressors	.04	.11 (.25)	.44	.658
AUC$_i$ X Recent Stressors	.11	.33 (.26)	1.30	.195
Model 6				
Child Age	.22	.69 (.26)	2.72	**.007**
Child Gender	.23	1.41 (.49)	2.87	**.005**
Child AUC$_i$	.06	.22 (.28)	.78	.439
Composite Stress Index	-.03	-.08 (.25)	-.33	.740

AUC_i X Composite Stress Index	.07	.23 (.27)	.87	.387
Moderator: Child Peak Cortisol				
Model 1				
Child Age	.23	.71 (.26)	2.76	**.007**
Child Gender	.24	1.44 (.48)	3.00	**.003**
Child Peak Cortisol	.32	1.10 (.52)	2.13	**.035**
Lifetime Parental Depression	-.12	-.73 (.50)	-1.46	.147
Peak Cortisol X Lifetime Parental Depression	-.25	-1.02 (.61)	-1.67	.096
Model 2				
Child Age	.23	.73 (.25)	2.92	**.004**
Child Gender	.22	1.33 (.49)	2.73	**.007**
Child Peak Cortisol	.12	.41 (.27)	1.51	.133
Maternal Depression Exposure	-.18	-.55 (.25)	-2.24	**.027**
Peak Cortisol X Maternal Depression Exposure	.01	.04 (.29)	.12	.903
Model 3				
Child Age	.22	.69 (.25)	2.72	**.007**
Child Gender	.23	1.41 (.48)	2.92	**.004**
Child Peak Cortisol	.12	.40 (.28)	1.44	.152
Parental Hostility	-.11	-.37 (.28)	-1.29	.198
Peak Cortisol X Parental Hostility	.09	.37 (.32)	1.13	.260
Model 4				
Child Age	.23	.73 (.26)	2.84	**.005**
Child Gender	.24	1.42 (.49)	2.90	**.004**
Child Peak Cortisol	.11	.38 (.28)	1.37	.172
Parental Support	-.01	-.01 (.29)	-.05	.961
Peak Cortisol X Parental Support	.02	.07 (.28)	.25	.802
Model 5				
Child Age	.23	.71 (.26)	2.76	**.007**
Child Gender	.23	1.40 (.49)	2.85	**.005**
Child Peak Cortisol	.11	.35 (.28)	1.29	.198
Recent Stressors	.04	.13 (.25)	.52	.602
Peak Cortisol X Recent Stressors	-.07	-..23 (.29)	-.80	.426
Model 6				
Child Age	.23	.73 (.26)	2.86	**.005**
Child Gender	.23	1.41 (.49)	2.86	**.005**
Child Peak Cortisol	.11	.38 (.28)	1.38	.171
Composite Stress Index	-.01	-.04 (.25)	-.16	.876
Peak Cortisol X Composite Stress Index	.03	.11 (.27)	.42	.678

Moderator: Child Positive Emotionality				
Model 1				
Child Age	.19	.58 (.26)	2.26	**.026**
Child Gender	.25	1.49 (.48)	3.10	**.002**
Child Positive Emotionality	-.03	-.10 (.38)	-.26	.798
Lifetime Parental Depression	-.13	-.78 (.50)	-1.57	.118
Positive Emotionality X Lifetime Parental Depression	.07	.28 (.50)	.55	.585
Model 2				
Child Age	.21	.64 (.25)	2.53	**.013**
Child Gender	.25	1.50 (.47)	3.16	**.002**
Child Positive Emotionality	.01	.04 (.26)	.17	.869
Maternal Depression Exposure	-.17	-.52 (.24)	-2.16	**.033**
Positive Emotionality X Maternal Depression Exposure	-.03	-.13 (.29)	-.43	.670
Model 3				
Child Age	.19	.58 (.26)	2.29	**.023**
Child Gender	.25	1.53 (.47)	3.24	**.001**
Child Positive Emotionality	.01	.04 (.27)	.14	.888
Parental Hostility	-.09	-.32 (.28)	-1.16	.250
Positive Emotionality X Parental Hostility	-.06	-.28 (.38)	-.73	.467
Model 4				
Child Age	.20	.62 (.26)	2.41	**.017**
Child Gender	.26	1.54 (.48)	3.21	**.002**
Child Positive Emotionality	.02	.07 (.26)	.26	.799
Parental Support	-.01	-.02 (.28)	-.06	.949
Positive Emotionality X Parental Support	.04	.16 (.31)	.53	.594
Model 5				
Child Age	.19	.59 (.26)	2.30	**.023**
Child Gender	.26	1.57 (.48)	3.31	**.001**
Child Positive Emotionality	.04	.12 (.26)	.48	.632
Recent Stressors	.06	.19 (.24)	.77	.442
Positive Emotionality X Recent Stressors	.06	.19 (.27)	.72	.475
Model 6				
Child Age	.19	.58 (.26)	2.25	**.026**
Child Gender	.26	1.57 (.48)	3.30	**.001**
Child Positive Emotionality	.04	.13 (.26)	.48	.634
Composite Stress Index	-.01	-.02 (.24)	-.09	.930
Positive Emotionality X Composite Stress Index	.08	.25 (.24)	1.03	.304
Moderator: Child Negative Emotionality				
Model 1				

Child Age	.17	.52 (.25)	2.09	**.038**
Child Gender	.24	1.45 (.48)	3.01	**.003**
Child Negative Emotionality	-.01	-.03 (.35)	-.08	.939
Lifetime Parental Depression	-.13	-.79 (.49)	-1.61	.110
Negative Emotionality X Lifetime Parental Depression	-.11	-.44 (.46)	-.94	.348
Model 2				
Child Age	.18	.55 (.24)	2.25	**.026**
Child Gender	.21	1.28 (.47)	2.70	**.008**
Child Negative Emotionality	-.13	-.37 (.24)	-1.59	.114
Maternal Depression Exposure	-.19	-.58 (.24)	-2.44	**.016**
Negative Emotionality X Maternal Depression Exposure	-.18	-.61 (.28)	-2.23	**.027**
Model 3				
Child Age	.18	.57 (.25)	2.29	**.023**
Child Gender	.24	1.45 (.48)	3.01	**.003**
Child Negative Emotionality	-.08	-.23 (.24)	-.95	.343
Parental Hostility	-.08	-.27 (.31)	-.88	.382
Negative Emotionality X Parental Hostility	-.01	-.04 (.27)	-.16	.876
Model 4				
Child Age	.19	.60 (.25)	2.40	**.018**
Child Gender	.24	1.43 (.49)	2.95	**.004**
Child Negative Emotionality	-.09	-.28 (.24)	-1.15	.251
Parental Support	-.03	-.09 (.28)	-.31	.756
Negative Emotionality X Parental Support	.06	.19 (.24)	.79	.432
Model 5				
Child Age	.18	.56 (.25)	2.28	**.024**
Child Gender	.24	1.44 (.48)	2.99	**.003**
Child Negative Emotionality	-.09	-.27 (.24)	-1.15	.252
Recent Stressors	.05	.16 (.24)	.69	.491
Negative Emotionality X Recent Stressors	-.08	-.23 (.23)	-1.02	.311
Model 6				
Child Age	.20	.62 (.25)	2.49	**.014**
Child Gender	.25	1.48 (.49)	3.05	**.003**
Child Negative Emotionality	-.09	-.25 (.24)	-1.04	.300
Composite Stress Index	-.01	-.02 (.23)	-.10	.921
Negative Emotionality X Composite Stress Index	.05	.14 (.23)	.63	.531

Note: AUC*i*: Area under the curve with respect to increase

Figure Captions

Figure 1. Children's externalizing symptoms as a function of children's total change in cortisol and recent stressors. Cortisol change was calculated as area under the curve with respect to increase (AUC_i).

Figure 2. Children's externalizing symptoms as a function of children's total change in cortisol and composite stress index. Cortisol change was calculated as area under the curve with respect to increase (AUC_i).

Figure 3. Children's externalizing symptoms as a function of children's peak cortisol and parental hostility.

Figure 4. Children's externalizing symptoms as a function of children's peak cortisol and composite stress index.

Figure 5. Children's psychosocial functioning as a function of children's total change in cortisol and recent stressors. Cortisol change was calculated as area under the curve with respect to increase (AUC_i).

Figure 6. Children's psychosocial functioning as a function of children's peak cortisol and parental hostility.

Figure 7. Children's social competence as a function of children's negative emotionality and cumulative exposure to maternal depression.

Figure 8. Children's social competence as a function of children's peak cortisol and familial loading of depression.

Figure 9. Children's social competence as a function of familial loading of depression and children's peak cortisol.

Figure 10. Children's social competence as a function of children's negative emotionality and familial loading of depression.

Figure 11. Children's social competence as a function of familial loading of depression and children's negative emotionality.

Figure 1.

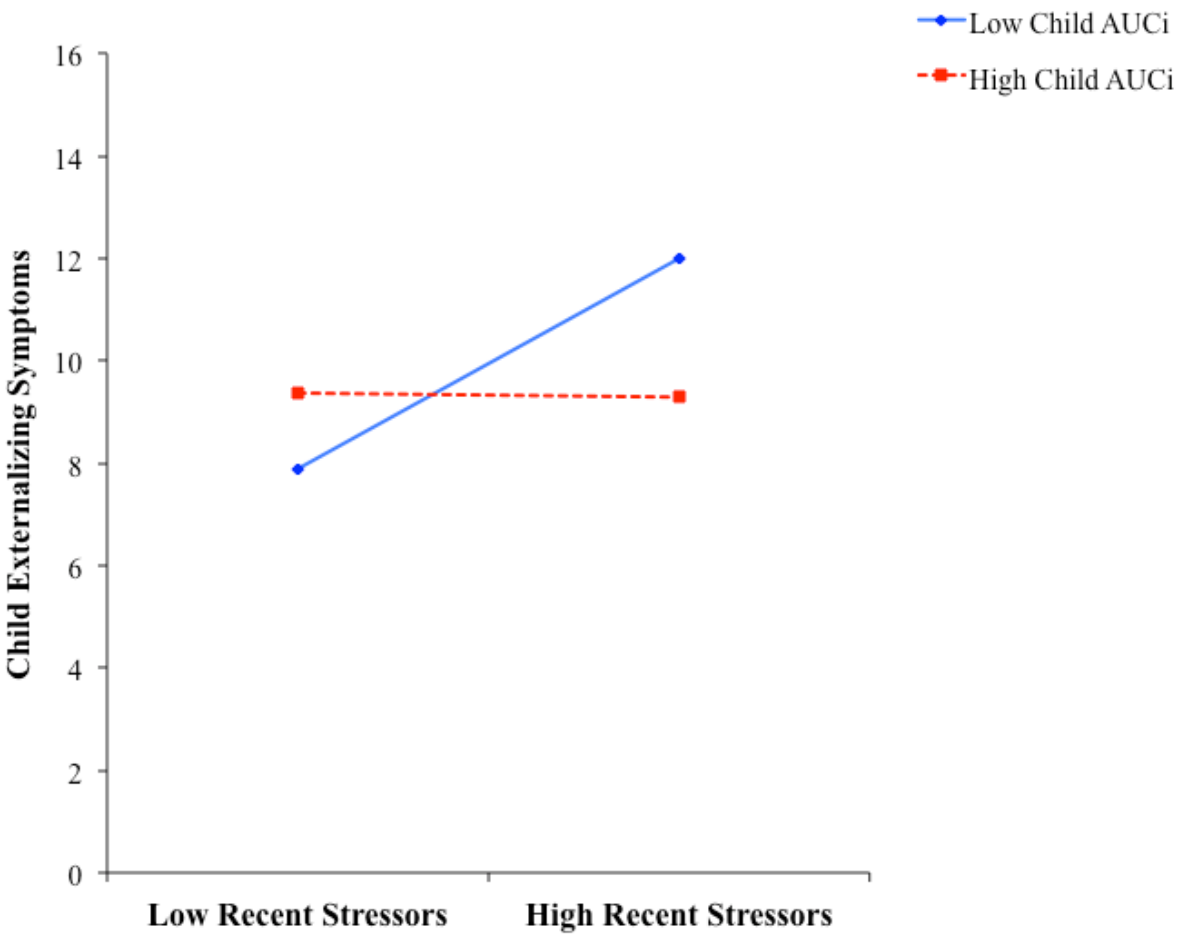

Low Child AUCi
High Child AUCi
Child Externalizing Symptoms
16
14
12
10
8
6
4
2
0
Low Recent Stressors
High Recent Stressors

Figure 2.

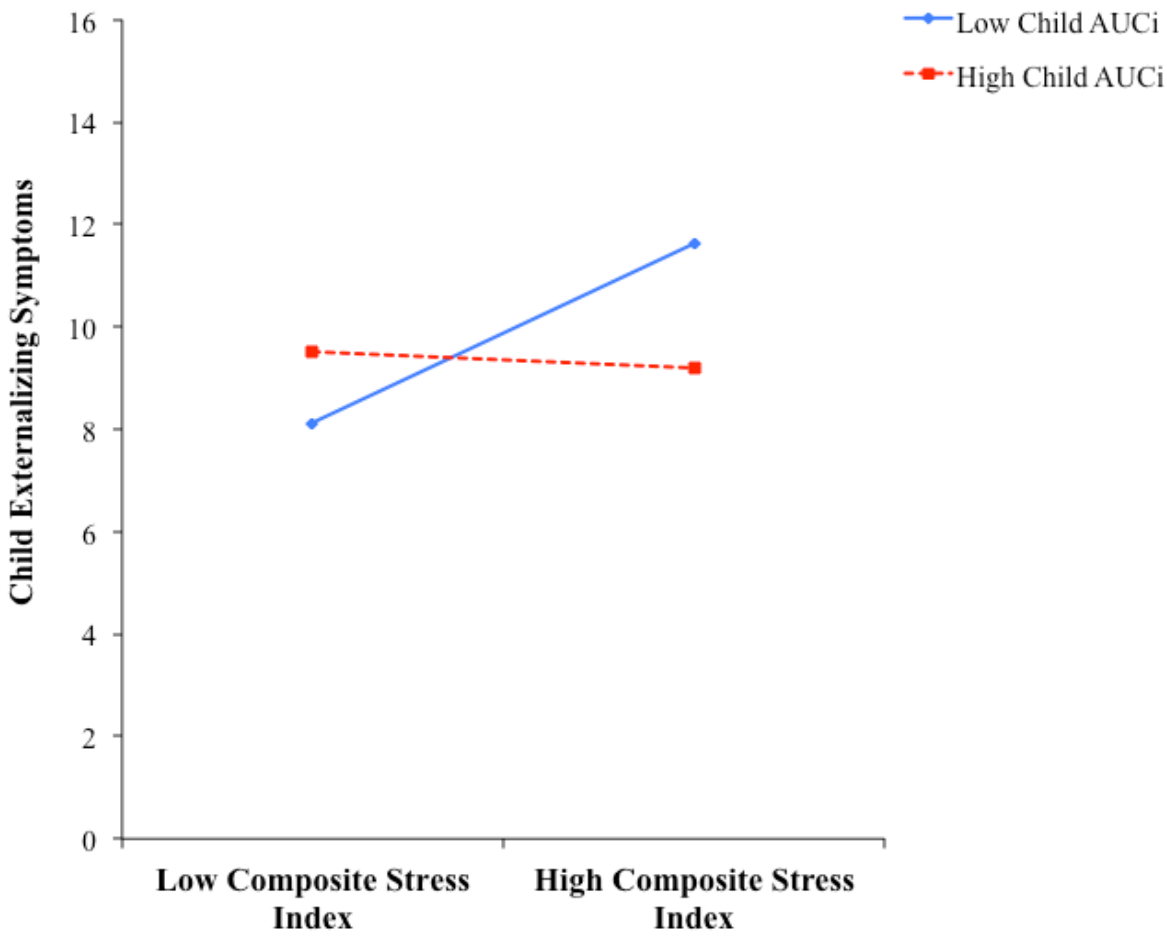

Low Child AUCi
High Child AUCi
Child Externalizing Symptoms
16
14
12
10
8
6
4
2
0
Low Composite Stress Index
High Composite Stress Index

Figure 3.

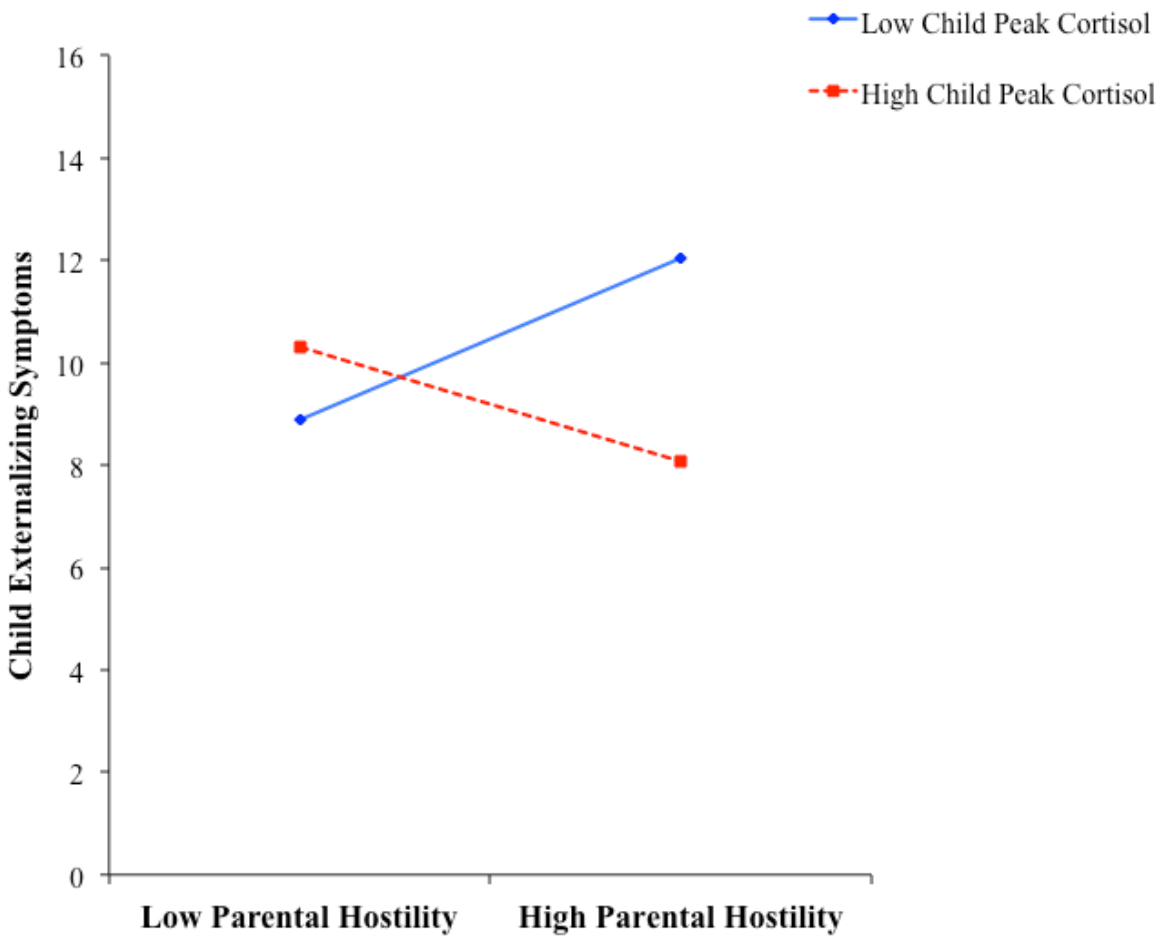

Low Child Peak Cortisol
High Child Peak Cortisol
Child Externalizing Symptoms
16
14
12
10
8
6
4
2
0
Low Parental Hostility
High Parental Hostility

Figure 4.

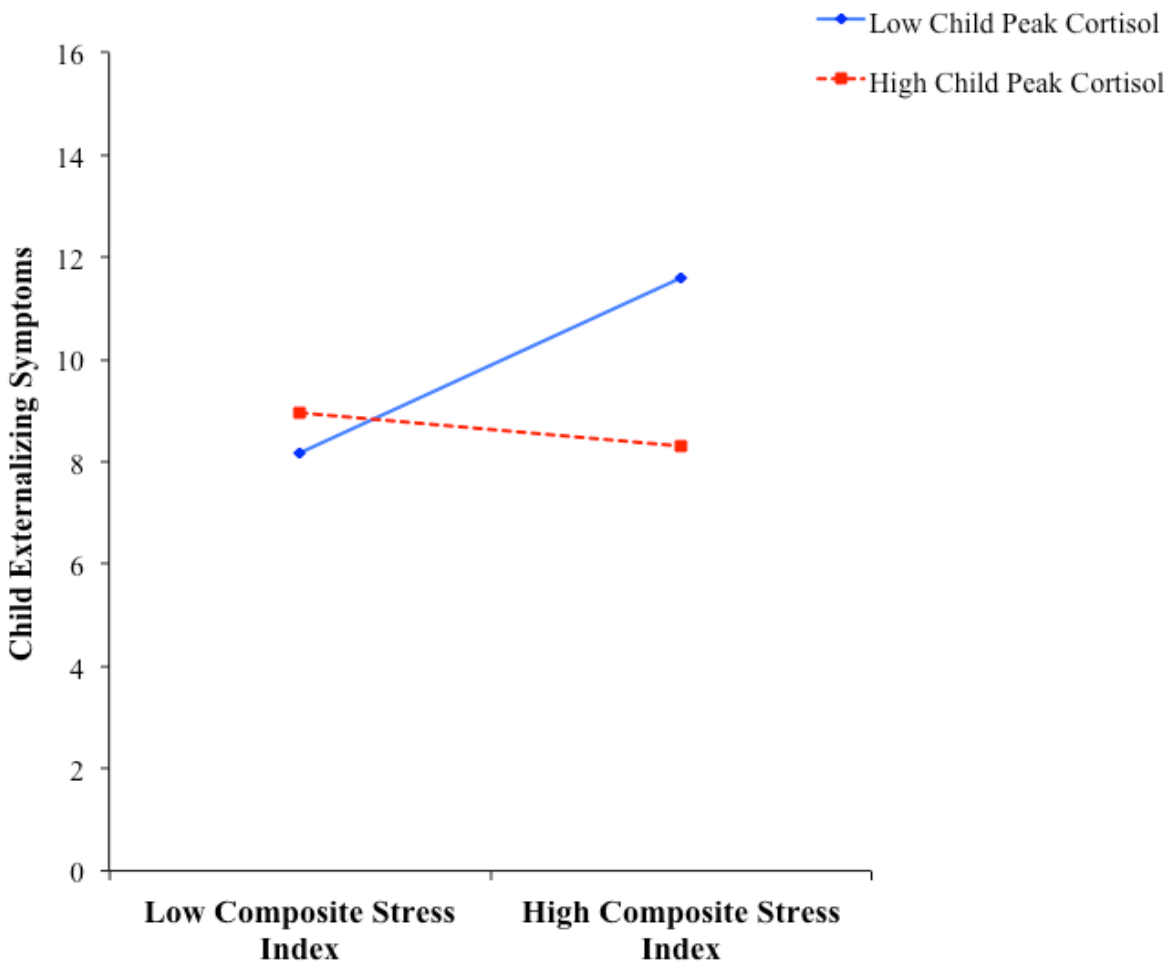

Low Child Peak Cortisol
High Child Peak Cortisol
Child Externalizing Symptoms
16
14
12
10
8
6
4
2
0
Low Composite Stress Index
High Composite Stress Index

Figure 5.

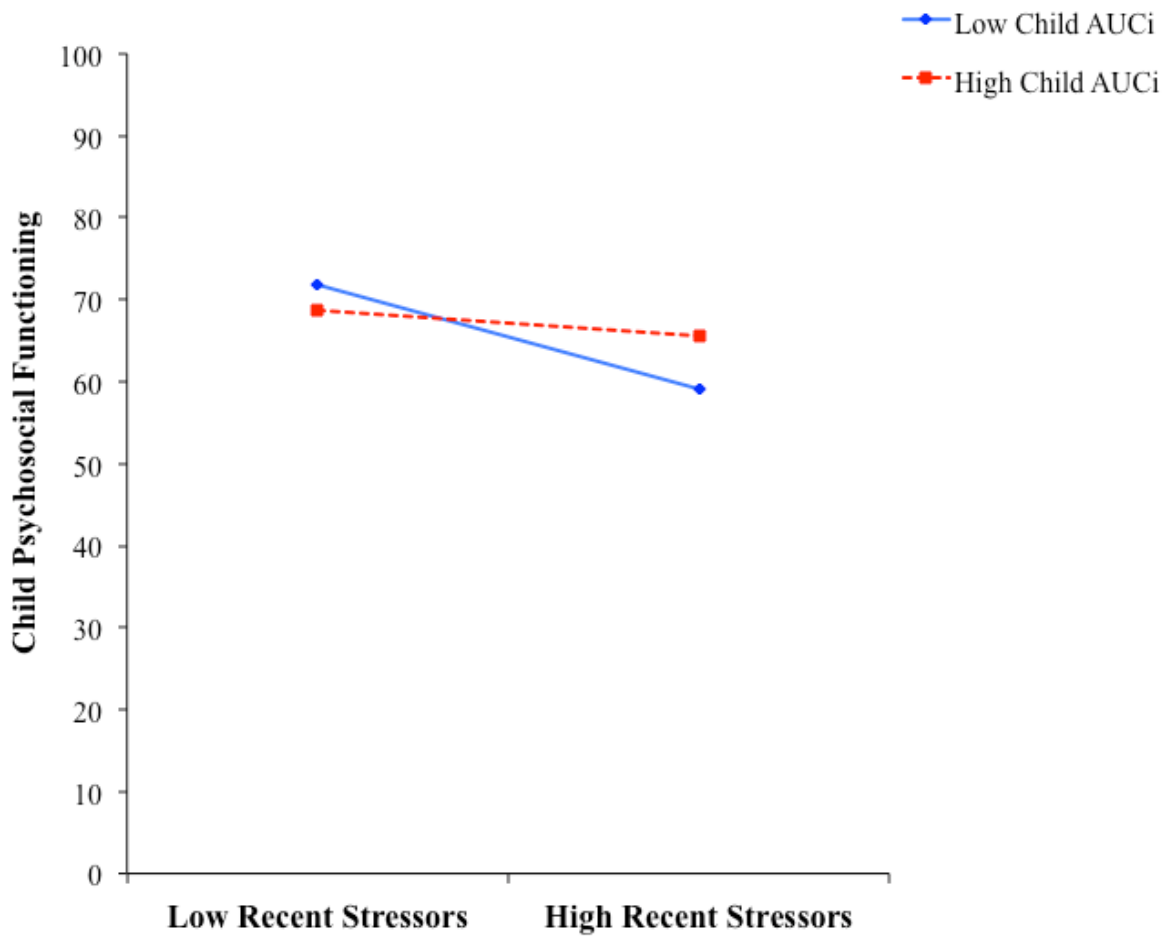

Low Child AUCi
High Child AUCi
Child Psychosocial Functioning
100
90
80
70
60
50
40
30
20
10
0
Low Recent Stressors
High Recent Stressors

Figure 6.

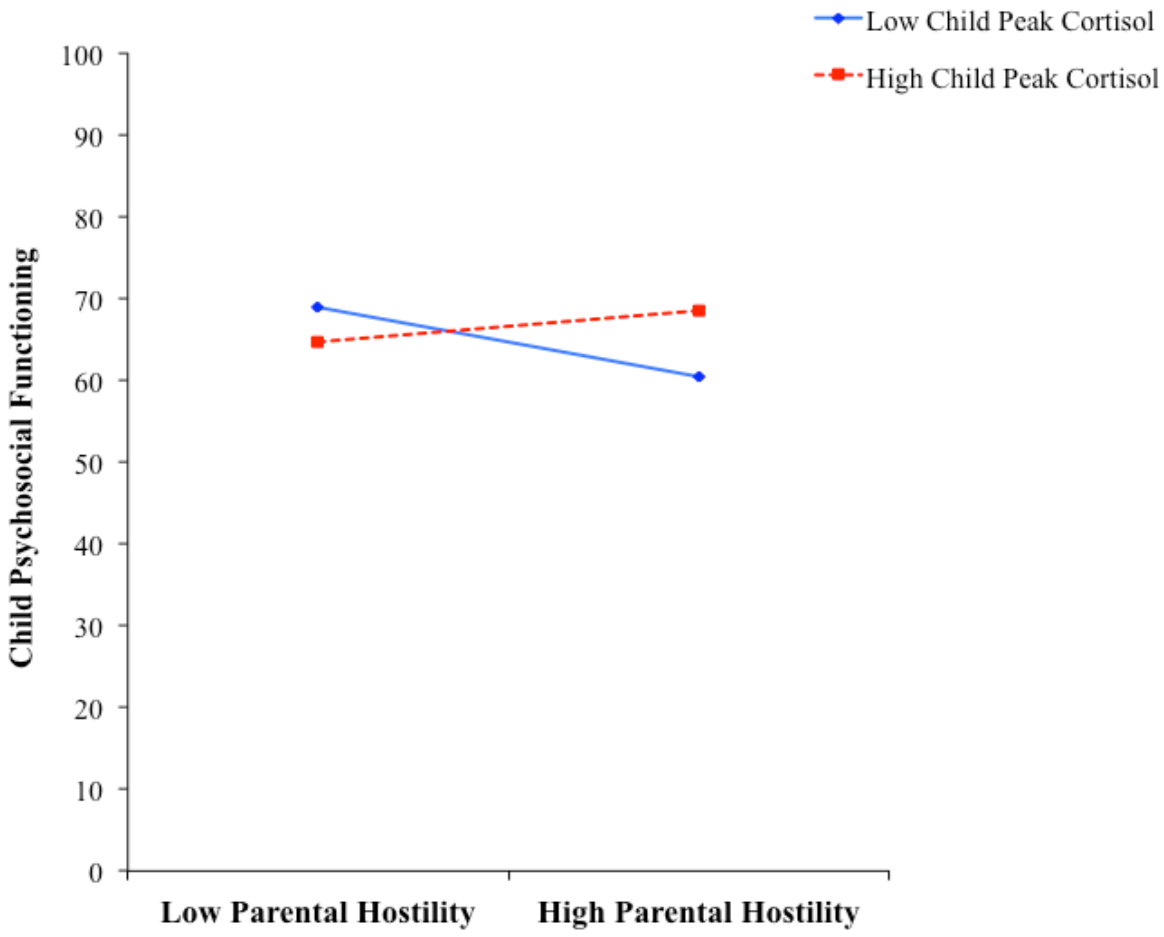

Low Child Peak Cortisol
High Child Peak Cortisol
Child Psychosocial Functioning
100
90
80
70
60
50
40
30
20
10
0
Low Parental Hostility
High Parental Hostility

Figure 7.

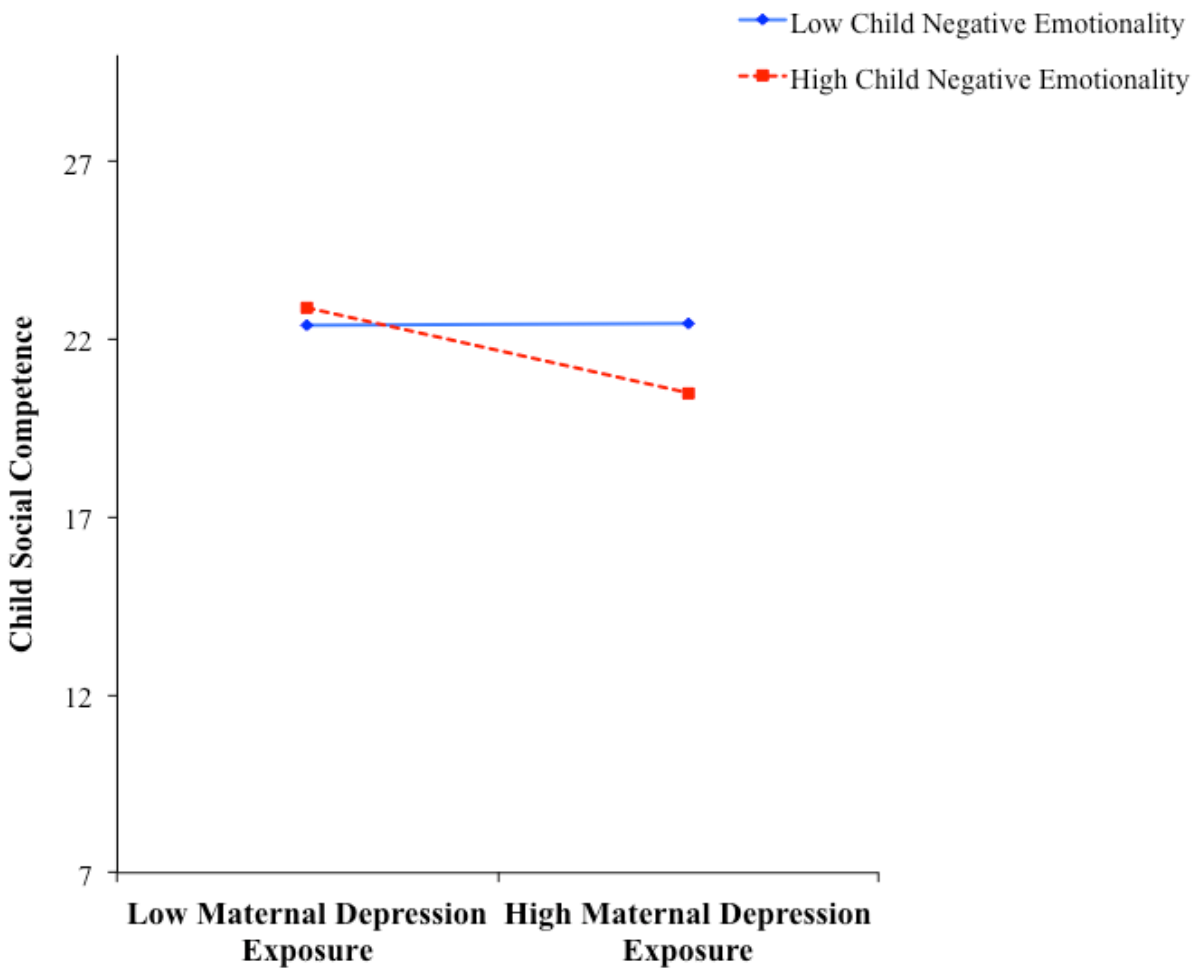

Low Child Negative Emotionality
High Child Negative Emotionality
Child Social Competence
27
22
17
12
7
Low Maternal Depression Exposure
High Maternal Depression Exposure

Figure 8.

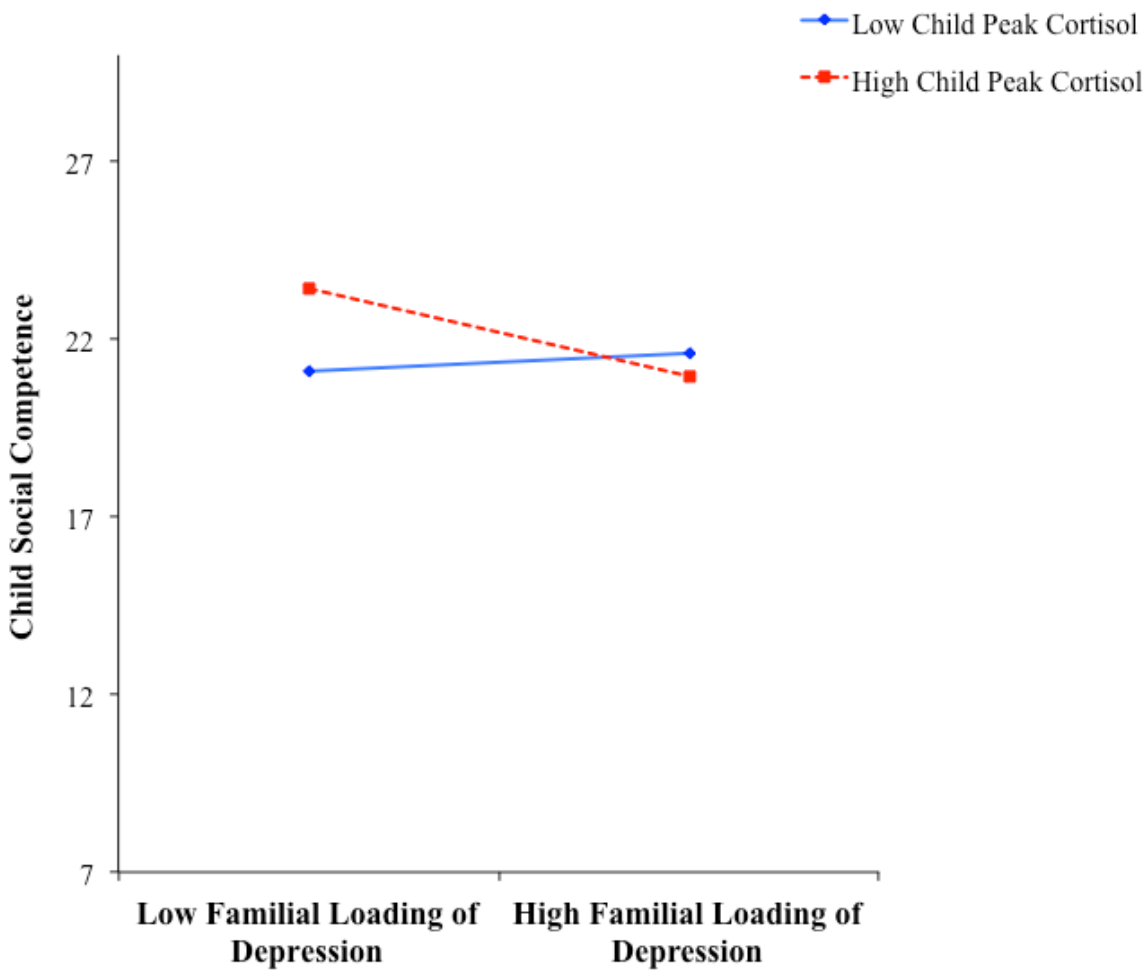

Low Child Peak Cortisol
High Child Peak Cortisol
Child Social Competence
27
22
17
12
7
Low Familial Loading of Depression
High Familial Loading of Depression

Figure 9.

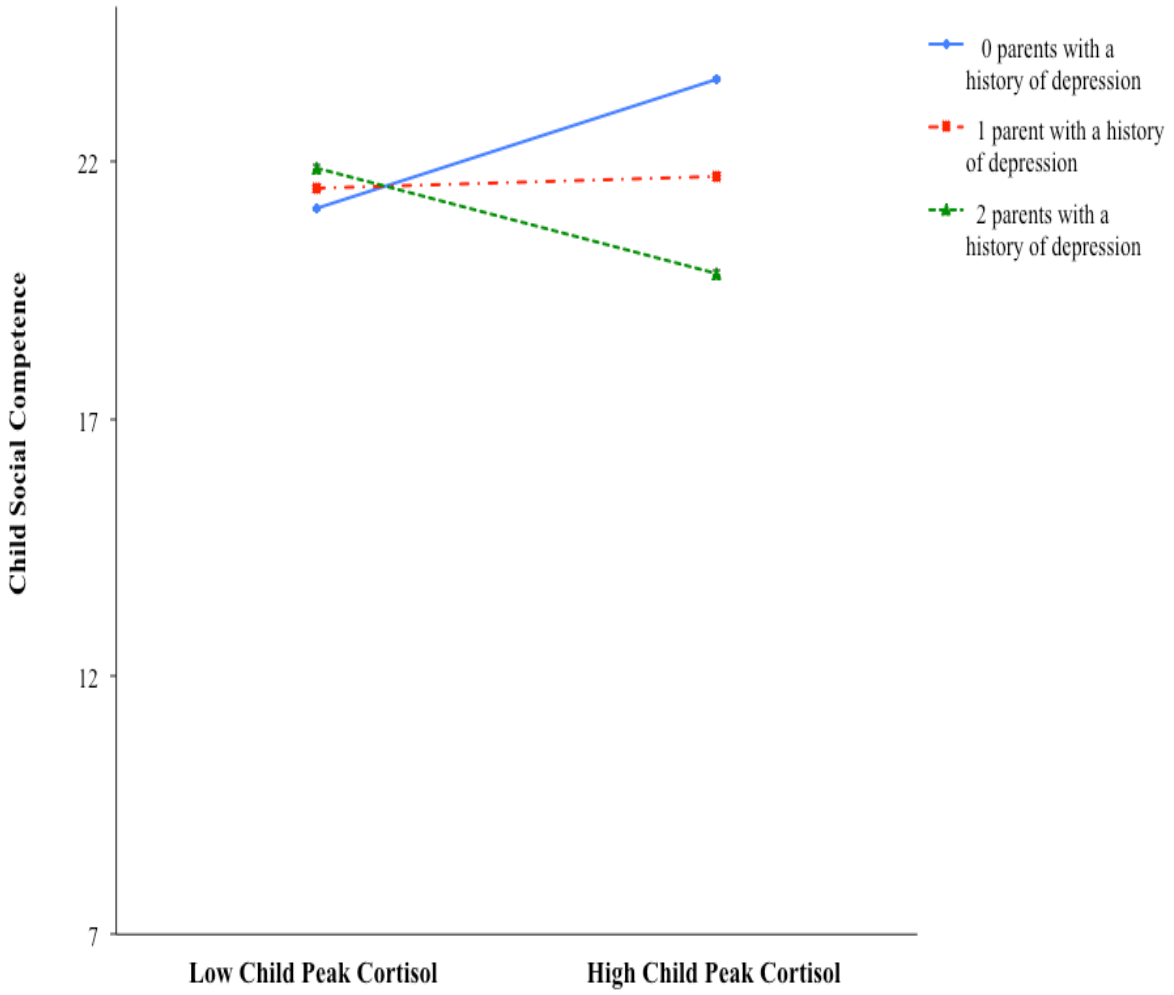

Child Social Competence
22
17
12
7
Low Child Peak Cortisol
High Child Peak Cortisol
0 parents with a history of depression
1 parent with a history of depression
2 parents with a history of depression

Figure 10.

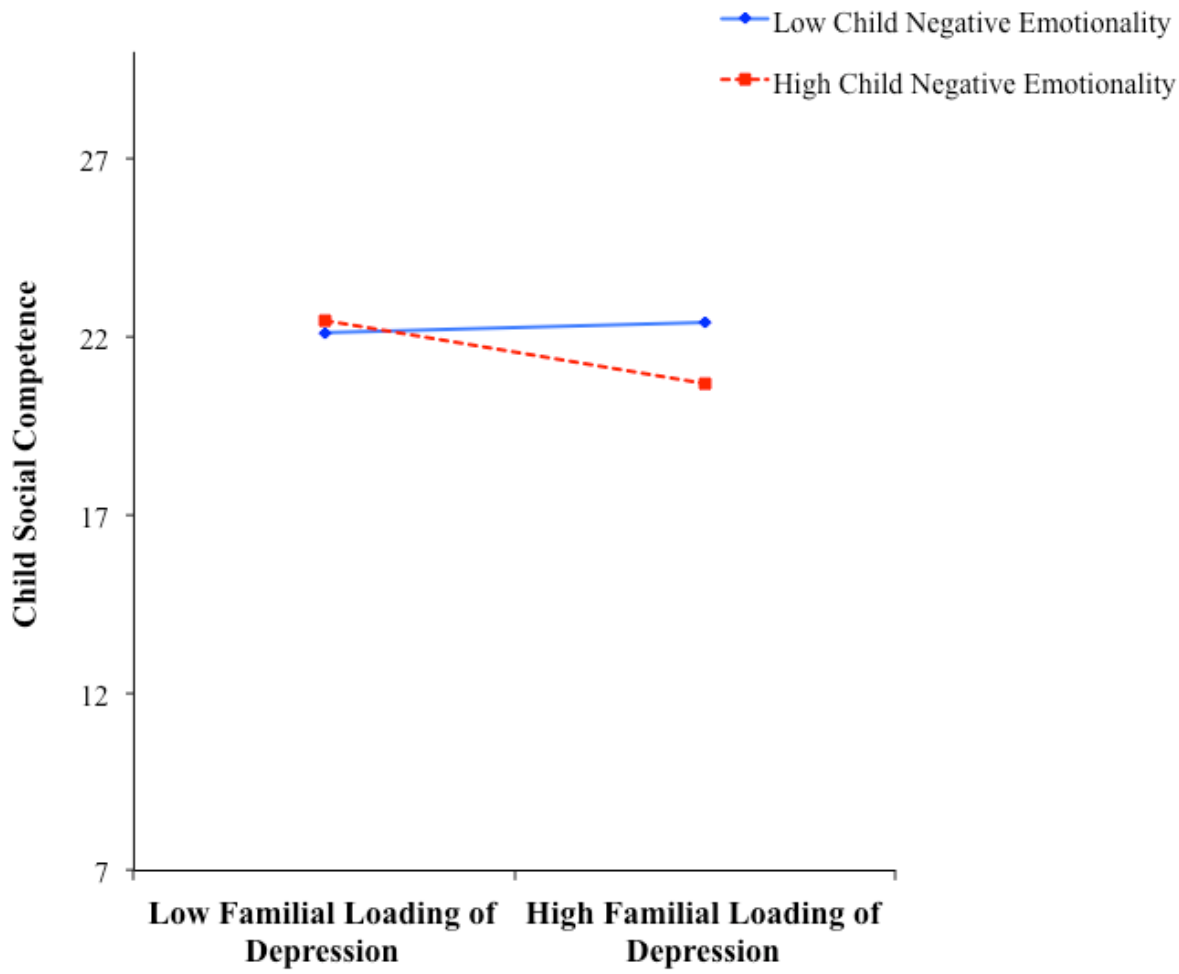
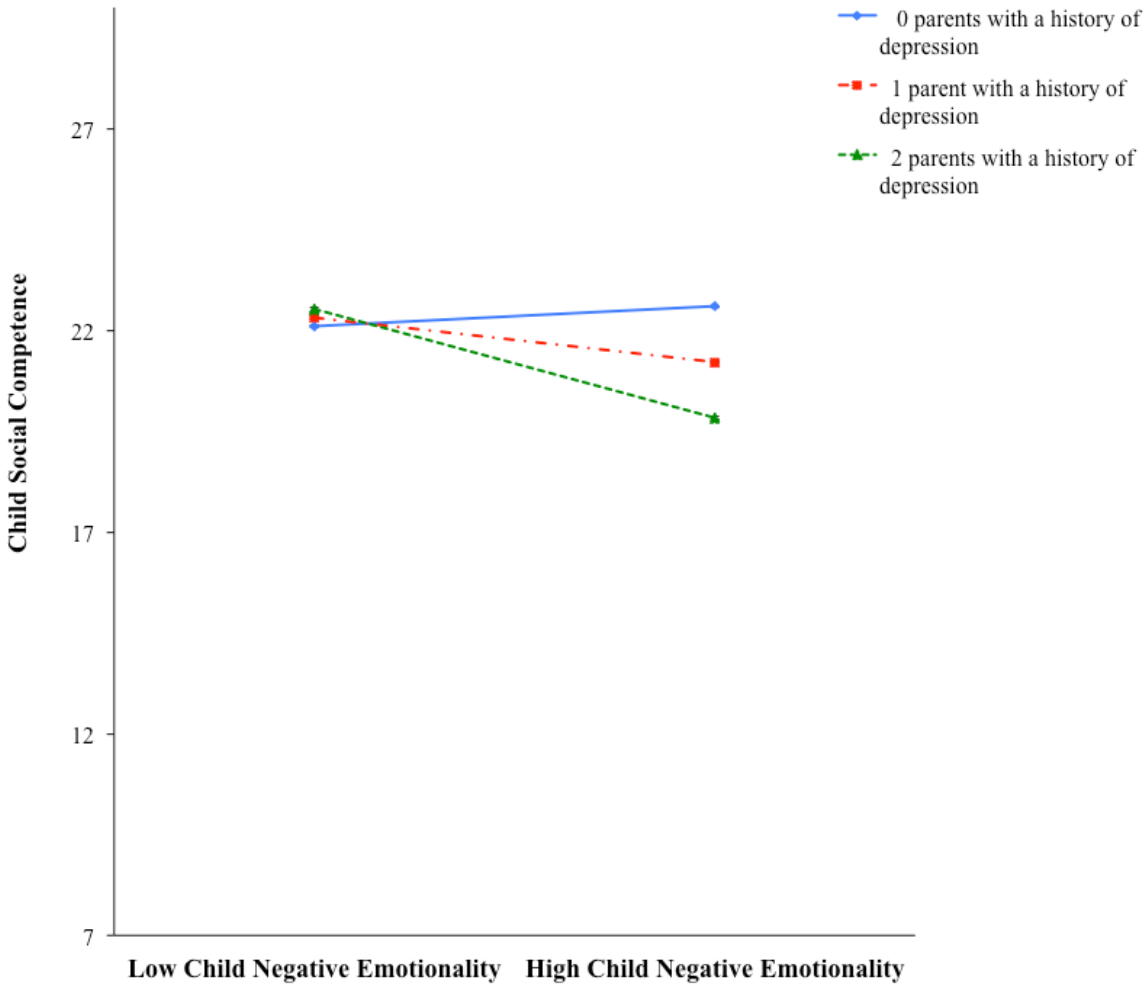

Low Child Negative Emotionality
High Child Negative Emotionality
Child Social Competence
27
22
17
12
7
Low Familial Loading of Depression
High Familial Loading of Depression

Figure 11.


0 parents with a history of depression
1 parent with a history of depression
2 parents with a history of depression
Child Social Competence
27
22
17
12
7
Low Child Negative Emotionality
High Child Negative Emotionality

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