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Early Exposure to Parental Depression and Parenting: Associations with Young Offspring's Stress Physiology and Oppositional Behavior

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Abstract Hypothalamic-pituitary-adrenal (HPA) axis reactivity to stress is posited to play a role in the intergenerational transmission of risk for psychopathology and other negative outcomes in the offspring of depressed parents. We tested the hypothesis that the joint, interactive effects of exposure to parental depression during early childhood and parental hostility impact the development of young children's stress physiology and early emerging behavior problems. A sample of 165 preschool-age children (81 boys, 84 girls), of whom 103 had a parent with a history of depression, was exposed to a stress-inducing laboratory task, and five salivary cortisol samples were obtained. Parents completed clinical interviews and an observational parent–child interaction task. We found that the offspring exposed to maternal depression during early childhood and whose parents displayed hostile parenting behaviors during an observational task evidenced high and increasing cortisol levels in response to a laboratory stressor. In addition, the total amount of exposure to maternal depression over the child's life exerted a dose–response effect on the positive relation between parental hostility and child observed oppositional behavior. This study underscores the importance of the early rearing environment on young children's stress physiology and early emerging behavior problems.

Keywords Parental depression · Parenting · Offspring risk · Cortisol · HPA axis · Preschool

The offspring of depressed parents evidence higher rates of psychopathology, including a threefold increased risk of mood and anxiety disorders and a twofold increased risk of substance dependence (Goodman and Gotlib 1999; Weissman et al. 2006). They also experience significant psychosocial impairment and higher rates of medical health problems and earlier mortality than the offspring of non-depressed parents (Weissman et al. 2006). From as early as infancy and the preschool years, children of depressed parents exhibit psychosocial, emotional, and behavioral problems (Hammen 2009). One mechanism proposed to explain the intergenerational transmission of risk for psychopathology and other negative health outcomes in the offspring of depressed parents is dysregulation of the hypothalamic-pituitary-adrenal (HPA) axis, one of the body's major stress response systems (Goodman and Gotlib 1999). Given the robust associations between stress and illness (e.g., Monroe et al. 2009), heightened HPA axis reactivity to environmental stressors has been posited to play a role in the processes linking stress to illness (Holsboer 2000). Furthermore, it has been hypothesized that individual differences in biological reactivity to stressors may predispose some individuals to illness.

Abnormalities in HPA axis *reactivity* to stress have been documented in numerous stress-related disorders, including depression, anxiety disorders, and substance-use disorders (Ehlert et al. 2001; McEwen 2008). Moreover, infants of depressed mothers have been found to exhibit increased cortisol reactivity (Azar et al. 2007; Brennan et al. 2008; Feldman et al. 2009), suggesting that dysregulation of the HPA axis is present in at-risk offspring and may precede and possibly contribute to the development of psychopathology. Investigating the developmental origins of neuroendocrine abnormalities in the high-risk offspring of depressed parents is critical to our understanding of the pathways and mechanisms involved in the intergenerational transmission of risk for negative health outcomes.

Although the origins of individual differences in cortisol reactivity are not fully understood, there is acknowledgement that both genetics and experience play a role in the stress

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response. There is evidence that cortisol reactivity is moderately heritable (Steptoe et al. 2009). In addition, individual differences within the child, such as the child's temperament and behavior, have been linked to cortisol responses to stress (Gunnar and Vazquez 2006). Moreover, animal and human studies provide strong support that early experience, including that encountered in utero, such as stress/adversity and parental psychopathology, influences offspring's HPA-axis reactivity both concurrently and longitudinally (Francis et al. 1999; Gunnar and Vazquez 2006; Talge et al. 2007). There is also evidence that the quality of the family environment moderates relations between early adversity and offspring neuroendocrine functioning (Luecken and Appelhans 2006). Nevertheless, it remains largely unknown whether abnormalities in cortisol function in the offspring of depressed mothers are direct reflections of a familial, possibly genetic, vulnerability for depression, result from exposure to maternal depression and its effects on parenting, or result from their joint effects, as these factors are often confounded.

Consistent with diathesis-stress models that propose individual differences in susceptibility to environmental experiences (Monroe and Simons 1991), and particularly heightened risk in the offspring of depressed parents (Goodman and Gotlib 1999), the present study aimed to test the hypothesis that the joint, interactive effects of exposure to parental depression during early childhood and parental hostility impact the development of young children's stress physiology. Evidence suggests that exposure to parental depression, especially early in a child's development, impacts infants' cortisol reactivity (Brennan et al. 2008) and predicts offspring's emotional and behavioral problems in later childhood and adolescence (Bagner et al. 2010; Hay et al. 2008). In addition, maternal depression has been associated with problematic parenting, specifically, negative, hostile child-rearing behaviors (Lovejoy et al. 2000). Furthermore, parental hostility is the parenting dimension most strongly linked to disturbances in offspring's neuroendocrine functioning (Gunnar and Vazquez 2006).

Surprisingly, little research has investigated the influence of the early parenting context on the relation between parental depression and offspring's stress physiology. In a recent study, we found that the combination of a history of parental depression and current parental hostility was associated with young offspring's increased cortisol reactivity, and this moderating effect of parental hostility was specific to children *exposed* to maternal depression during the first few years of life (Dougherty et al. 2011b). Nevertheless, research in this area remains sparse and critical issues remain unresolved.

First, it is currently unknown whether the moderating effect of parental hostility on the association between exposure to parental depression and offspring cortisol reactivity is dependent on the amount of offspring exposure to parental depression during the early years of the child's life (i.e., the chronicity of exposure). Offspring exposed to chronic maternal depressive symptoms evidence greater child emotional and behavioral problems than offspring exposed to non-chronic maternal depressive symptoms (Brennan et al. 2000). In addition, Essex and colleagues (2011) reported that children exposed to chronic maternal depression and anger expressed in the family environment exhibited dysregulated basal cortisol in childhood and adolescence. Thus, we first aimed to replicate our previous findings in an ethnically diverse sample of high-risk preschoolers exposed to parental depression during early childhood and two groups of comparison children. Comparison groups included children of parents with no history of depression and children of parents with a history of depression occurring only prior to the child's life. We hypothesized that the offspring of parents who were exposed to parental depression during early childhood and who experienced current hostile parenting behaviors would exhibit the highest cortisol reactivity in response to a laboratory stressor. The second aim was to test whether this moderating effect was dependent on the amount of exposure to parental depression the child experienced. We hypothesized that the combination of more chronic exposure to parental depression over the first few years of life and a hostile parenting context would be related to offspring's increased cortisol reactivity.

Second, we examined whether the interactive effect between parental depression exposure and parental hostility extends beyond offspring's stress physiology to children's behavior. Specifically, we aimed to examine whether the combination of offspring exposure to parental depression and hostile parenting is associated with emerging behavior problems in early childhood. The role of children's behavior in these relations is fundamental given the bidirectional associations between children's behavior and parental depression and parenting (Bell and Chapman 1986). We chose to examine children's observed oppositional behavior for several reasons. First, we examined observations of children's oppositional behavior rather than parent reports to minimize bias that may result from depressed parents reporting on their children's behavior (Najman et al. 2000). Second, evidence supports the convergent and predictive validity of observational assessments of preschool oppositional behavior, as they have been found to relate to concurrent preschool psychopathology (Dougherty et al. 2011a) and subsequent disruptive behavior disorders (Wakschlag et al. 2008). Third, while depressive symptoms are relatively rare in preschool-age children, preschool oppositional behavior problems are more common and have been found to be stable and provide an early salient indicator of later internalizing and externalizing disorders (Campbell 1995; Mesman et al. 2001). Moreover, both exposure to parental depression and hostile parenting behaviors

have been independently related to offspring's externalizing behavior problems (Campbell 1995; Hammen 2009). Thus, we hypothesized that the combination of offspring exposure to parental depression and hostile parenting behaviors would be associated with greater observed child oppositional behaviors and this relationship would be dependent on the total amount of offspring exposure to parental depression.

Lastly, we have little understanding of the developmental time course over which early experience shapes biological responses to stress or whether the effects of offspring exposure to parental depression on offspring's cortisol reactivity and behavior are specific to certain sensitive periods during early childhood. Thus, the present study tested whether the interactive effects of offspring's exposure to parental depression and hostile parenting on offspring's stress physiology and behavior vary with respect to the timing of offspring's exposure. We hypothesized that the effects of offspring exposure to parental depression may be specific to earlier (i.e., during the first two years of life), rather than more recent or current exposure to parental depression. Some evidence suggests that earlier exposure to parental depression in the child's development (particularly during the first two years of life) may predominantly impact the child's stress physiology and behavior (Ashman et al. 2002; Bagner et al. 2010; Essex et al. 2002; Halligan et al. 2004). Furthermore, it is well documented that there is significant neuroplasticity during the first 3–5 years of life (Nelson et al. 2006), which may make the brain more vulnerable to contextual risks, including parental depression and maladaptive parenting.

Method

Participants

The sample consisted of 175 children and parents recruited from the Washington, DC metropolitan area. Potential participants were identified using advertisements sent to local schools, daycares, and health care providers (73.1 %) and a commercial mailing list (26.9 %). In our recruitment efforts to obtain a high-risk sample of young offspring of depressed parents, we targeted parents with a history of depression using flyers and advertisements. Our two recruitment methods yielded one significant difference: compared to families who were recruited using the commercial mailing list, families recruited via flyers had mothers who exhibited more hostility during the laboratory task, $t(160.6)=2.98$, $p<0.01$. Families with a child between 3 and 5 years who lived with an English-speaking biological parent, who did not have significant medical conditions or developmental disabilities, and whose biological parents did not have a history of bipolar or psychotic disorder were included. Of the 175 families recruited for the study, seven families without parental diagnostic data, two families in which one parent had a history of bipolar disorder, and one family in which the child did not speak English were excluded from the analyses, leaving a final sample of 165 families. The study was approved by the human subjects review board, and informed consent was obtained from parents.

The mean age of the children was 49.9 months ($SD=9.8$); 81 (49.1 %) were boys and 84 (50.9 %) were girls. On average, mothers were 34.9 years old ($SD=6.2$) and fathers were 37.1 years old ($SD=6.9$). Participating families identified themselves as Caucasian ($N=77$; 47.5 %), African-American ($N=59$; 36.4 %), Asian ($N=3$; 1.9 %), or other race ($N=23$; 14.2 %); 27 (16.8 %) children were of Hispanic/Latino descent. Approximately 61.2 % of the mothers and 57.3 % of the fathers had a 4-year college degree. The majority (71.5 %) of the children lived with both biological parents, and 42.6 % of the mothers worked outside the home part-or full-time. 36.3 % reported a family income greater than $100,001; 28.1 % of families reported a family income ranging from $70,001 to $100,000; 20.6 % of families reported a family income ranging from $40,001 to $70,000; and 15.0 % of families reported a family income less than $40,000. Children were of average cognitive ability as measured by the Peabody Picture Vocabulary Test ($M=109.9$, $SD=15.2$) (PPVT; Dunn and Dunn 1997), and no children met criteria for pervasive developmental disorders based on the Social Communication Questionnaire (SCQ; Rutter et al. 2003). Table 1 details the demographic information for the study sample.

Parental Psychopathology

Children's biological parents were interviewed using the Structured Clinical Interview for DSM-IV, Non-Patient version (SCID-NP; First et al. 1996). Interviews were conducted by telephone, which yields similar results as face-to-face interviews (Rohde et al. 1997), by a master's level rater with extensive training in the SCID. Interviews were conducted following the first laboratory visit and typically prior to the second laboratory visit, which occurred approximately 2 weeks apart. SCIDs were obtained from all 165 mothers and 81 (53.3 %) fathers. If a father did not complete a SCID, a family history interview was conducted with the mother (Andreasen et al. 1977). Diagnoses based on family history data were obtained for 71 fathers. Thus, we had diagnostic information on all 165 biological mothers and 152 biological fathers. Based on audiotapes of 16 SCID interviews, the kappa for inter-rater reliability was 1.00 for lifetime depressive disorder.

Major depressive disorder (MDD) and dysthymic disorder (DD) were collapsed into a single category reflecting

Table 1 Sample offspring characteristics and study variables

	No parental depression (n=62)	Depression before the child's life (n=38)	Depression during the child's life (n=65)
Demographics			
Child sex (% male)	29 (46.8 %)	17 (44.7 %)	35 (53.8 %)
Child mean age, months	51.68 (SD=10.50)	49.29 (SD=7.85)	48.63 (SD=10.01)
Parent graduated from college (n)	43 (69.4 %)	28 (73.7 %)	45 (69.2 %)
Two-parent household (n)	46 (74.2 %)	32 (84.2 %)	40 (61.5 %)
Potential Cortisol Covariates			
Afternoon lab visit (%)	37 (66.1 %)	25 (77.4 %)	45 (81.8 %)
Child mean BMI	15.85 (SD=2.94)	16.76 (SD=4.55)	17.46 (SD=3.82)
Child mean activity	2.62 (SD=0.60)	2.51 (SD=0.75)	2.65 (SD=0.76)
Child mean stress rating	1.34 (SD=0.70)	1.46 (SD=0.70)	1.46 (SD=0.79)
Child ate a meal within hour of visit (n)	24 (42.9 %)	16 (45.7 %)	17 (30.9 %)
Parental Psychopathology			
Maternal depression exposure (n)	–	–	52 (80.0 %)
Paternal depression exposure (n)	–	–	15 (23.1 %)
Mean maternal cumulative depression exposure	–	–	0.50 (SD=0.36)
Mean paternal cumulative depression exposure	–	–	0.57 (SD=0.35)
Observed Parenting			
Mean parental hostility	1.15 (SD=0.32)	1.06 (SD=0.17)	1.23 (SD=0.38)
Observed Child Behavior			
Mean child oppositional behavior	−0.13 (SD=0.22)	−0.13 (SD=0.19)	−0.07 (SD=0.26)
Salivary cortisol indicator			
Mean cortisol level at time 1	2.51 (SD=3.63)	2.06 (SD=1.23)	2.50 (SD=2.54)
Mean cortisol level at time 2	2.11 (SD=1.91)	1.83 (SD=0.88)	2.15 (SD=1.83)
Mean cortisol level at time 3	2.10 (SD=1.91)	1.75 (SD=0.73)	2.21 (SD=2.25)
Mean cortisol level at time 4	2.03 (SD=1.44)	1.80 (SD=0.97)	2.31 (SD=2.74)
Mean cortisol level at time 5	2.22 (SD=2.08)	1.99 (SD=1.40)	2.16 (SD=1.78)
Mean AUC_i	−1.78 (SD=10.47)	−1.08 (SD=4.09)	−1.49 (SD=12.80)
Auc_i positive (n)	19 (33.9 %)	14 (40.0 %)	22 (40.0 %)

Cumulative depression exposure reflects a proportion controlling for children's varying ages. Observed child oppositional behavior reflects a standardized z-score. Cortisol is reported in nmol/L. Area under the curve was measured with respect to increase (AUC_i)

BMI body mass index

depressive disorder. Of the parents, 83 mothers (50.3 %) and 39 fathers (25.7 %) had a lifetime history of MDD or DD. All children with a mother with a lifetime depressive disorder lived with the mother, and 79.5 % of the children with a father with a lifetime depressive disorder lived with the father. Nineteen children had two parents with a lifetime depressive disorder, and 78.9 % of the children with two parents with a lifetime depressive disorder lived with both parents. Children were considered to have a family history of depression if at least one parent had been diagnosed with depression (n=103, 62.4 %). Fifty-one mothers and eight fathers received treatment, and four mothers were hospitalized for their depression. 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 et al. 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 et al. 2005). The total number of months that each parent met criteria for a depressive disorder across each year of the child's life was calculated based on information gathered from the SCID. Separate proportion scores were calculated for mothers and fathers. The total number of months that the child was exposed to parental depression was summed and divided by the child's age in months to yield the total proportion of offspring exposure to maternal and paternal depression during the child's life.

As seen in Table 1, of the 103 parents with lifetime depression, 67 (65 %) parents from 65 families (52 mothers, 15 fathers) had a depressive disorder during the child's life.

Twenty-two parents from 21 families (13.7 %; 12 mothers, 10 fathers) had a current depressive disorder. Two children were exposed to both maternal and paternal depression during the child's life. The proportion of months the child was exposed to maternal depression across each year of the child's life evidenced moderate to high stability (correlation coefficients ranged between 0.46 to 0.90).[1] As only 15 fathers were depressed during the child's life (of whom 13 lived with the child), analyses focusing on exposure were limited to variables capturing exposure to either parent's depression using a categorical variable (present vs. absent) or to maternal depression only using both a categorical variable (present vs. absent) and proportion scores.

Parental Hostility

During the first visit to the laboratory, children participated with the primary caregiver (94.5 % mothers) in an observational parent–child interaction task, in which we measured parental hostility during a modified version of the Teaching Tasks battery (Egeland et al. 1995). This battery included five standardized tasks (e.g., book reading, puzzle task) designed to elicit different parenting and child behaviors. Parental hostility, which captures a parent's expression of anger, frustration, and criticism toward the child, was rated on a 5-point scale for each task, and ratings were averaged across tasks (M=1.16, SD=0.32, range=1.0–2.8). Coders were unaware of the data on parental psychopathology and the cortisol assessment. The internal consistency (α=0.76) and interrater reliability (intraclass correlation coefficient [ICC]=0.89, n=38) of the parental hostility scale were acceptable.

Child Oppositional Behavior

During the parent–child interaction task, ratings of children's compliance and negativity toward the parent were coded. Children's compliance, which assesses the degree to which the child shows willingness to listen to the parent's suggestions and to comply to parental requests, was rated on a 5-point scale for each task, and ratings were averaged across tasks (M=4.73, SD=0.52, range=1.6–5.0). Children's negativity toward the parent, which captures a child's expression of anger, dislike, or hostility toward the parent was also rated on a 5-point scale for each task, and ratings were averaged across tasks (M=1.13, SD=0.32, range=1.0–2.8). The internal consistency and interrater reliability were acceptable for the child compliance (α=0.81; ICC=0.98) and negativity (α=0.75; ICC=0.89) scales. The two scales were strongly negatively correlated (r=−0.70, p<0.01), and we calculated the average of the two standardized z-scores (compliance reverse-scored) to yield a composite measure of child oppositional behavior (M=−0.05, SD=0.88, range=−0.47–4.99). The internal consistency and interrater reliability were acceptable for the oppositional behavior scale (α=0.83; ICC=0.95). Children's oppositional behavior variable was log10 transformed to correct for positive skew.

Laboratory Stressor Paradigm and Cortisol Reactivity

Of the 165 families, 153 (92.7 %) returned for a second laboratory session, in which we assessed children's cortisol reactivity using an acute psychological stressor paradigm that has been demonstrated in a home setting to elicit a mean increase in cortisol in preschoolers (for a complete description of the task see Kryski et al. 2011). The stressor paradigm incorporates elements of stressor tasks that more reliably elicit elevations in cortisol in youth (i.e., negative self-referent emotions) and adults (i.e., uncontrollability) (for a review see Gunnar et al. 2009). The stress assessment first consisted of a 30-min period of quiet play after which the experimenter, who was the same experimenter from the first visit, collected the first saliva sample (T1). After the first sample was obtained, children participated in the stressor paradigm, which consisted of a timed matching task (M=8.1 min, SD=1.8). Children were told that they had 3 min to complete successfully three trials to win a preferred prize. Following each trial, the experimenter manipulated the timer such that children failed the trial. To elicit feelings of social evaluation, the experimenter sat with a clipboard and pretended to take notes on the child's performance. At the end of the third failed trial, the experimenter informed the child that the timer was broken and provided the child with a prize for all of his/her effort. The child and experimenter then played the task together untimed so that the child successfully matched all of the pieces. Seventeen children refused to complete all matching trials; in these cases, the experimenter ended the matching task, explained to the child that the timer was broken, praised the child's efforts, and provided the child with the prize. The child was then given the option to play the game untimed with the experimenter or engage in another activity.

Parents were asked to refrain from feeding their child for 1 h and from giving their child caffeine for 2 h prior to the session, as these factors are known to alter cortisol values (Gunnar and Talge 2008). No children were taking corticosteroids. Of the 153 children who participated in the cortisol assessment, three children were excluded because they were sick with a fever or taking antibiotics, and four children were excluded because they did not provide complete cortisol reactivity samples; thus, 146 children were included in analyses involving cortisol.

[1] Stability of the proportion of months the child was exposed to paternal depression during the child's life is not reported, as few fathers (N=15) experienced depression during the child's life.

Cortisol samples were obtained prior to the start of the task following a 30-min acclimation period to the laboratory (T1, average time between laboratory arrival and T1 sampling=30.0 min, *SD*=0.01, range=26–35 min), and then at 20 (T2; average time between T1 and T2=31.0 min, *SD*=0.02, range=26–41 min), 30 (T3; average time between T2 and T3=10.0 min, *SD*=0.01, range=8–13 min), 40 (T4; average time between T3 and T4=10.0 min, *SD*=0.01, range=8–12 min), and 50 (T5; average time between T4 and T5=10.0 min, *SD*=0.01, range=8–12 min) minutes following the completion of the stressor task. Saliva samples were obtained by having children dip a cotton dental roll into a few grains (0.025 g) of 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. Vials were kept frozen at −20 °C 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 et al. 2005). Inter- and intra-assay coefficients of variation were 7.1 %–9.0 % and 4.0 %–6.7 %, respectively.

To derive a measure of cortisol reactivity, we calculated the area under the curve with respect to the increase (AUC_i) in cortisol using raw cortisol values, which estimates the total change in cortisol across the five cortisol samplings (Pruessner et al. 2003). The AUC_i was treated as the dependent variable in all cortisol analyses.

Data Analysis

We examined whether parental depression exposure, parental hostility, and their interaction were associated with children's cortisol reactivity and oppositional behavior using analysis of covariance (ANCOVA) and multiple linear regression analyses. We examined parental depression exposure both categorically and continuously. Using a categorical approach, we dummy coded parental depression exposure into three groups: no parental depression, parental depression occurring only prior to the birth of the child, and parental depression occurring during the child's life. Additionally, a continuous exposure variable capturing the proportion of time the child was exposed to maternal depression during the child's life was used to examine the main effects of cumulative maternal depression exposure and its interactive effects with parenting on offspring cortisol reactivity and behavior. Significant interactions were probed using procedures outlined by Aiken and West (1991) to conduct simple slopes analyses.

Results

Table 1 shows the means, standard deviations, and N's for characteristics of the sample, potential covariates, and cortisol levels by parental depression history. The three groups did not differ on most variables with two exceptions. Parents who experienced depression during the child's life exhibited greater hostility than those who experienced depression prior to the child's birth, $F(2, 164)=3.61$, $p=0.03$. Children of parents depressed during the child's life were also less likely to live in a two-parent home compared to children of parents who were depressed only prior to the child's birth, $\chi^2(1,103)=5.86$, $p=0.02$. Two-parent household was included as a covariate in all analyses. Cumulative maternal depression exposure was significantly associated with parental hostility ($r=0.20$, $p=0.01$) and observed child oppositional behavior ($r=0.24$, $p<0.01$).

None of the covariates listed in Table 1 were significantly associated with child AUC_i; thus, only two-parent household was included as a covariate in analyses involving cortisol.[2] Child age ($r=-.28$, $p<0.01$) and parental education ($r=-.18$, $p=02$) were negatively associated with child oppositional behavior. In addition, children from two-parent households demonstrated less oppositional behavior than children from one-parent households, $t(163)=-2.69$, $p<0.01$. Thus, child age, parental education and two-parent household were included as covariates in analyses involving child oppositional behavior.

Parental Depression Exposure, Parental Hostility, and Children's Cortisol Reactivity

The main effects of parental depression exposure and parental hostility on children's AUC_i were not significant. No significant differences were observed for child AUC_i among the three groups, $F(2,143)=0.05$, $p=0.95$, and parental hostility was not significantly related to child AUC_i ($B=2.18$, $SE=3.11$, $p=0.48$). As hypothesized, we found a significant interaction between parental depression occurring during the child's life and parental hostility ($B=4.92$, $SE=2.08$, $p=0.02$, $pr=0.20$).[3] The interaction between parental depression prior to the child's life and parental hostility was not significant for child AUC_i ($B=0.50$, $SE=3.55$, $p=0.89$, $pr=0.01$).

As seen in Fig. 1, for children who were exposed to parental depression, parental hostility was significantly associated with

[2] AUC_i was associated at a trend level with the time of the laboratory visit ($r=0.14$, $p=0.08$) and children's difficulty sleeping the night before ($r=-0.15$, $p=0.07$). Results were similar when these variables were included as covariates.

[3] This interaction effect remained significant even controlling for child oppositional behavior ($pr=0.20$, $p=0.02$).

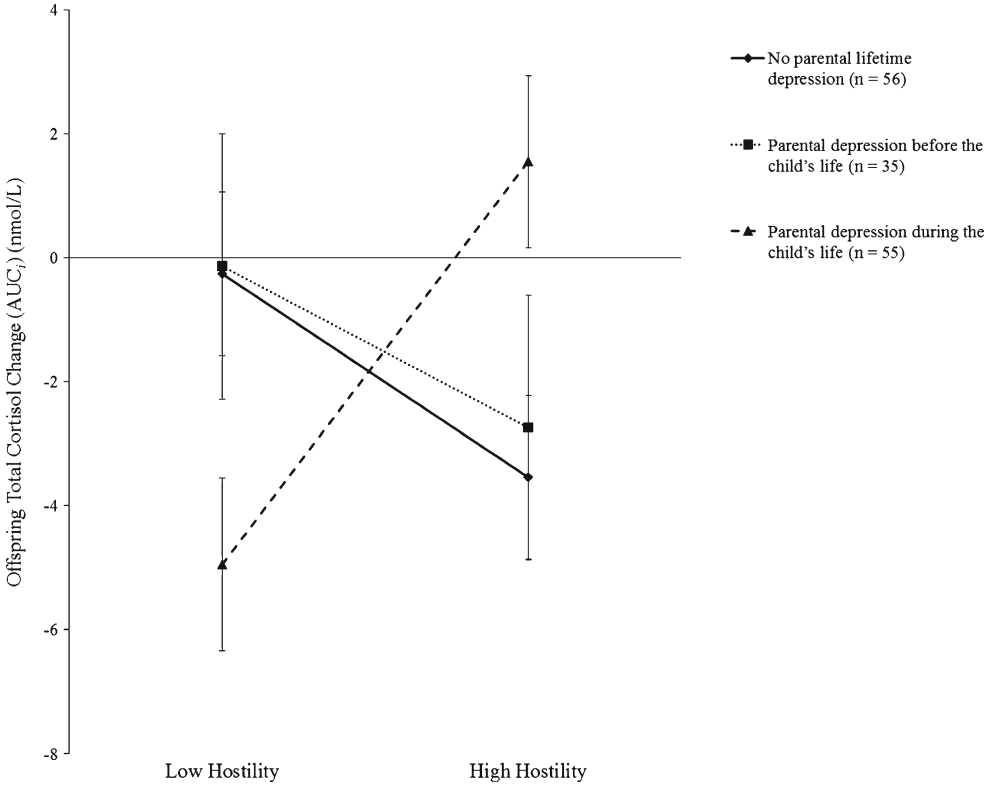

Fig. 1 Offspring's total change in cortisol as function of the timing of parental depression history and parental hostility. Cortisol change was calculated as area under the curve with respect to increase (AUC_i). Bars reflect standard errors of measurement. Positive AUC_i values indicate that cortisol increased following the stressor paradigm and negative AUC_i indicate that cortisol decreased following the stressor paradigm

higher child AUC_i (B=3.25, SE=1.43, p=0.02, pr=0.19). In contrast, there were no significant associations between parental hostility and child AUC_i for children whose parents had no lifetime history of depression (B=−1.67, SE=1.52, p=0.27, pr=−0.09) or for children whose parents had depression prior to the child's life only (B=−1.18, SE=3.21, p=0.71, pr=−0.03). Similar effects were observed for maternal depression exposure only.

To determine the degree of parental hostility at which differences in child AUC_i emerged for offspring of parents with and without depression exposure, Hayes and Matthes (2009)'s guidelines were used for testing regions of significance according to the Johnson-Neyman technique (Johnson and Fay 1950). At levels of parental hostility greater than 1.27 (standardized z-score), offspring who were exposed to parental depression demonstrated significantly higher child AUC_i than offspring without parental depression exposure. The interaction effect was not dependent on the proportion of time the child was exposed to maternal depression (pr=0.04, p=0.64).

Parental Depression Exposure, Parental Hostility, and Child Oppositional Behavior

We examined whether parental depression exposure, parental hostility, and their interaction were associated with observed child oppositional behavior. No main effect of parental depression group on child oppositionality was observed, F (2,159)=0.25, p=0.78. There was a significant main effect of parental hostility on child oppositionality (B=0.09, SE=0.02, p<0.01, pr=0.40). No significant interactions between parental depression occurring during the child's life and parental hostility (B=0.04, SE=0.03, p=0.26, pr=0.09) or between parental depression occurring prior to the child's life and parental hostility (B=0.08, SE=0.07, p=0.23, pr=0.10) were observed for child oppositional behavior. Results were similar using maternal depression only.

Next, we examined whether the interaction was dependent on the total amount of offspring exposure to maternal depression. In the regression model, we observed significant main effects for the total amount of time the child was exposed to maternal depression (B=0.05, SE=0.02, p=0.01, pr=0.16) and parental hostility (B=0.29, SE=0.05, p<0.01, pr=0.40) on child oppositional behavior. As hypothesized, we also observed a significant interaction between total amount of exposure to maternal depression and parental hostility on child oppositional behavior (B=0.04, SE=0.01, p<0.01, pr=24).[4]

[4] Similar to observations of child oppositionality, the interaction between total amount of exposure to maternal depression and parental hostility was significantly associated with the parent-reported Child Behavior Checklist/1.5-5 (Achenbach and Rescorla 2000) oppositional defiant problems DSM scale (pr=0.15, p=0.049).

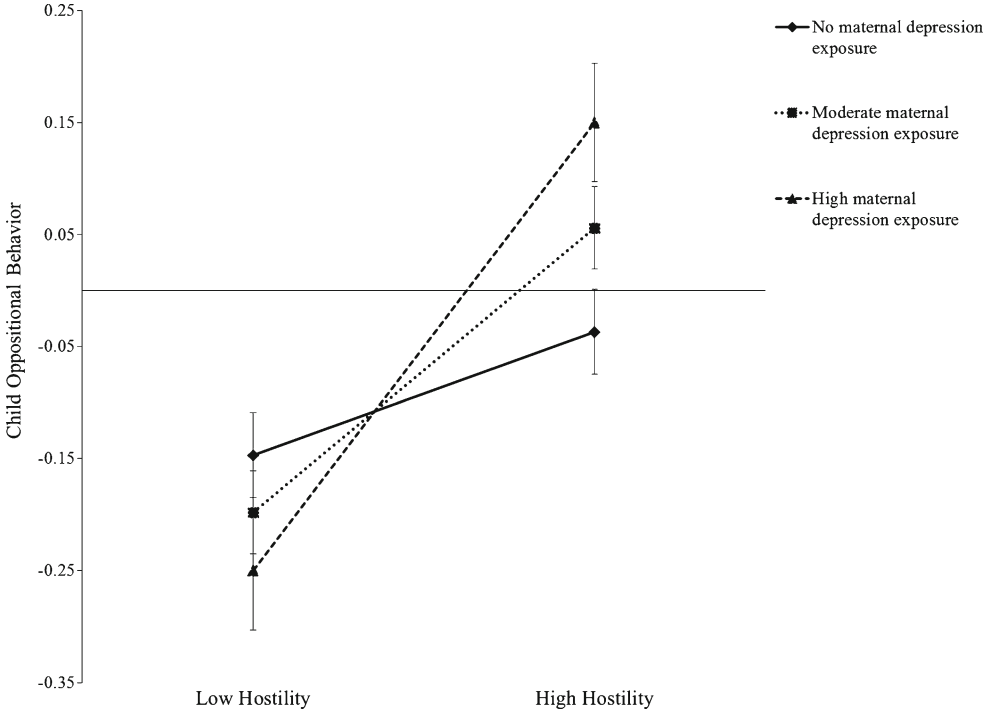

Fig. 2 Children's oppositional behavior as function of cumulative maternal depression exposure and parental hostility. Fifty-two children were exposed to maternal depression. Moderate depression exposure included children who were exposed to maternal depression for at least half of their life. High depression exposure included children who were exposed to maternal depression for their entire life. Bars reflect standard errors of measurement. Observed child oppositional behavior was log10 transformed

To understand the interaction, we conducted simple slopes tests for child oppositional behavior. As seen in Fig. 2, we plotted the relations between estimated levels of offspring's oppositional behavior across estimated levels of high and low parental hostility for offspring who experienced no maternal depression exposure, maternal depression exposure for at least half of the child's life (moderate), and maternal depression exposure for the child's entire life (high). We observed a significant dose–response effect of offspring exposure to maternal depression on the positive relation between parental hostility and child oppositional behavior. The relation between parental hostility and child oppositional behavior increased as offspring exposure to maternal depression increased (no exposure: pr=0.22, p<0.01; moderate exposure: pr=0.38, p<0.01; high exposure: pr=0.45, p<0.01). Using the region of significance test described above, we observed a significant positive association between total maternal depression exposure and child oppositional behavior at levels of parental hostility greater than 0.42 (standardized z-score).

Sensitive Periods of Early Exposure to Maternal Depression

We examined whether the interaction between offspring exposure to maternal depression and parental hostility varied as a function of the timing of the offspring's exposure during his or her life (i.e., maternal depression exposure during the child's first 2 years of life or after the child's first 2 years of life) with respect to child AUC_i and observed child oppositional behavior. Of the 52 children who were exposed to maternal depression, 42 were exposed during the first 2 years of life (11 of whom were exposed only during the first 2 years of life), 41 were exposed after the first 2 years of life (10 of whom were exposed only after the first 2 years of life), and 31 were exposed both during and after the first 2 years of life. Two dummy coded variables were created: exposure to maternal depression during the first 2 years of life (absent or present) and exposure to maternal depression after the child's first 2 years of life (absent or present), which allowed us to retain children who were exposed during both time periods and to maximize power.

We conducted regression models entering the timing of maternal depression exposure (dummy coded exposure during the child's first 2 years of life and dummy coded exposure after the child's first 2 years of life) and hostility in Step 1 and their respective interaction terms with hostility entered at Step 2 for child AUC_i. No main effects for the child's exposure to maternal depression during the first 2 years of life (B=1.29, SE=2.71, p=0.64, pr=0.04) or after the child's first 2 years of life (B=−1.54, SE=2.80, p=0.58, pr=−0.05) were observed for child AUC_i. The interaction between maternal depression occurring during the child's first 2 years of life and parental hostility was not significantly association with child AUC_i (B=−1.89, SE=2.45, p=0.44, pr=−0.07), whereas the interaction between maternal depression occurring after the child's first 2 years of life and parental hostility was significantly associated with child AUC_i (B=6.31, SE=2.66, p=0.02, pr=0.20). For the offspring who were exposed to maternal depression after the first 2 years of life, there was a significant positive association between

parental hostility and child AUC_i (B=4.49, SE=1.95, p=0.02, pr=0.19). In contrast, for children who were not exposed to maternal depression after the first 2 years of life, there was no significant association between parental hostility and child AUC_i (B=−0.55, SE=1.13, p=0.63, pr=−0.04).

We then conducted parallel analyses to explore the effects of the timing of maternal depression exposure and parental hostility on child oppositional behavior. No main effects for the child's exposure to maternal depression during the first 2 years of life (B=0.03, SE=0.05, p=0.57, pr=0.05) or after the child's first 2 years of life (B=0.05, SE=0.05, p=0.34, pr=0.08) were observed for child oppositional behavior. Additionally, no significant interactions between maternal depression occurring during the child's first 2 years of life and parental hostility (B=0.02, SE=0.04, p=0.61, pr=0.03) or between maternal depression exposure after the child's first 2 years of life and parental hostility (B=0.07, SE=0.04, p=0.11, pr=0.13) were observed for child oppositional behavior.

Discussion

This study aimed to test the hypothesis that the joint, interactive effects of exposure to parental depression during early childhood and parental hostility impact the development of young children's stress physiology and early emerging behavior problems. We found that the offspring exposed to parental depression during early childhood and whose parents displayed hostile parenting behaviors during an observational task evidenced high and increasing cortisol levels in response to a laboratory stressor. Moreover, the interaction was specific to offspring exposed to maternal depression, particularly after the child's first 2 years of life. We also found that the combination of offspring exposure to maternal depression and parental hostility was associated with children's observed oppositional behavior. Specifically, the total amount of exposure to maternal depression over the child's life exerted a dose–response effect on the positive relation between parental hostility and child observed oppositional behavior.

We replicated the interactive effect between exposure to maternal depression and parental hostility on offspring's cortisol reactivity observed by Dougherty and colleagues (Dougherty et al. 2011b) using an independent, more ethnically diverse, larger high-risk sample of preschool-age children exposed to parental depression and using a different laboratory stressor, providing further evidence that early exposure to parental depression *and* parental hostility are jointly related to young children's increased stress reactivity. This replication is particularly noteworthy given the paucity of research replicating interaction effects in the literature. This observed pattern of greater cortisol reactivity in our high-risk sample of preschool-age children is consistent with the literature documenting elevated cortisol reactivity in depressed adults (Burke et al. 2005) and youth (Lopez-Duran et al. 2009), as well as offspring of depressed parents (e.g. Brennan et al. 2008). Taken together, it is possible that increased stress sensitivity may render high-risk offspring more vulnerable to the depressogenic effects of stress later in life, suggesting that early dysregulation of the HPA axis may be one mechanism involved in the intergenerational transmission of risk for negative health outcomes in the offspring of depressed parents.

Our findings highlight the critical influence of early environmental experiences, particularly parenting and the mother-child relationship, on the development and functioning of young children's neuroendocrine system. While our study was cross-sectional and cannot test the causality or directionality of the associations observed, our findings are consistent with evidence from the animal literature documenting the significant epigenetic effects of maternal caregiving behavior on offspring's physiological and behavioral responses to stress (Meaney 2001). Maternal caregiving behaviors have also been linked to behavioral and physiological markers of heightened stress reactivity in human offspring (Hane and Fox 2006). Nevertheless, our cross-sectional findings do not rule out passive gene-environment correlations or the effect of shared genes that influence parental depression, parenting behaviors and child functioning, which would be appropriately tested using twin and adoption designs.

The interaction effect between exposure to maternal depression and parental hostility appeared to be specific to exposure occurring after the child's first 2 years of life. While our findings are in contrast to previous work observing main effects of exposure to parental depression during the offspring's first year or 2 years of life on children's stress physiology (Ashman et al. 2002; Essex et al. 2002; Halligan et al. 2004) and behavior (Bagner et al. 2010), our study focused on the influence of timing as it relates to the interaction, or joint, effect of exposure to maternal depression and parental hostility, which has not been previously examined. Additionally, Naicker et al. (2012) recently reported evidence of a sensitive period of exposure to maternal depression during the preschool years that was associated with an increased risk of emotional disorders in offspring during adolescence.

The significant timing effect highlighting exposure occurring after age 2 years and during the preschool period is particularly noteworthy, given the demands of parenting a toddler and preschooler. By age two, children begin to exert their autonomy and challenge parental authority (Campbell 1995). Thus, as toddlers and preschoolers become more oppositional, increasing demands are placed on parents to manage their child's behavior. Oppositional behavior during this developmental period may evoke parental hostility and breakdowns in positive parenting, particularly among parents with depression. Moreover, significant changes in the

brain occur across the entire first 2 years of life, which may result in a greater neurobiological vulnerability to these early stressful experiences and insensitive parenting (Belsky and de Haan 2011). Thus, our findings suggest that the toddler and preschool years may capture a sensitive neurodevelopmental period, and environmental exposures during this period may lead to lasting perturbations on offspring's stress physiology. Nevertheless, it is also possible that this effect reflects more recent exposure to maternal depression, rather than a critical period. In addition, it is just as possible that the child's heightened stress reactivity and oppositionality elicited parental hostility, which could have occurred before the child's second year of life. Replication of our findings is needed and longitudinal work is necessary to determine the directionality of effects and to explore the effects of exposure and parenting beyond the preschool years.

This study also examined whether the joint, interactive effects of exposure to parental depression and parental hostility extend beyond offspring's stress physiology and are associated with offspring's behavior. We found that the total amount of offspring exposure to maternal depression and parental hostility were independently associated with greater observed child oppositional behavior. Moreover, we found that total amount of exposure to maternal depression over the course of the offspring's life evidenced a dose–response effect on the positive relation between parental hostility and children's observed oppositional behavior. The relationship between parental hostility and oppositional behavior increased as offspring exposure to maternal depression increased. Our findings are consistent with prior work that has observed independent main effects of exposure to parental depression and parental hostility on children's externalizing behavior and now extend this literature to examine their joint influences (e.g., Brennan et al. 2000; Campbell 1995; Hammen 2009).

While previous work has highlighted the significance of the chronicity of maternal depressive symptoms on child behavior (Brennan et al. 2008), our study underscores the influence of the parenting context on this relation, particularly given that the total amount of offspring exposure to maternal depression was related to higher levels of observed parental hostility. Consistent with a social-learning perspective, this finding suggests that children's oppositional behavior may emerge as a result of repeated exposure to maladaptive learning experiences, which likely involve a coercive parent–child interaction style (Patterson 1982). The direct effects of child's behavior on parenting behaviors and parental depression likely also play a role (Bell and Chapman 1986). Interestingly, the amount of maternal depression exposure did not influence the interactive effect on offspring's cortisol reactivity, which may suggest that young children's stress physiology may be more sensitive to the mere exposure and timing of both parental depression and parental hostility rather than the total amount of exposure.

The study had a number of strengths. First, we assessed parental psychopathology using clinical interviews and obtained information regarding the course of parental depression, as well as the timing of exposure. Second, we obtained five cortisol samplings in response to a laboratory challenge and observational assessments of parenting and children's oppositional behavior. Lastly, we examined stress reactivity during early childhood, which may be an important developmental period to investigate the stress system and the rearing context, perhaps because of developmental processes that increase neurobiological plasticity in response to environmental influences.

This study also had limitations. First, the study was cross-sectional, and causal effects cannot be tested. Second, similar to other studies in young children, the laboratory paradigm did not evoke increases in cortisol in all children, which poses difficulty in interpreting the results in terms of *cortisol reactivity* (for a review see Gunnar et al. 2009); nevertheless, variability in children's responses was observed, which afforded the examination of individual differences in cortisol responses. Third, we used cotton dental rolls to collect salivary cortisol, which may retain cortisol and reduce the amount of the hormone in the collected saliva. To limit this issue, we collected a minimum of 500 μl of saliva per sample as this problem has been shown to occur particularly in low volume samples. Fourth, we were unable to examine possible genetic or child characteristics, including children's differential susceptibility to environmental influences and biological sensitivity to context, which could underlie these relations (Boyce and Ellis 2005). For instance, future research should investigate whether children's heightened cortisol reactivity moderates associations between early environmental contexts, including both highly stressful and highly protective environments, and child outcomes.

Fifth, the study relied on retrospective parent-reports of the timing of depression. For instance, it is possible that our timing effects may be due to parents' better ability to recall depressive episodes within the past 2 years than for a period in the more remote past; however, using a similar method as employed in this study, the reliability for accurate recall of the timing of depressive episodes was very high (Kim-Cohen et al. 2005). Sixth, even though we made efforts to include fathers with depression 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. Seventh, we did not examine mediational models with this data. For instance, we did not examine whether parenting mediates associations between parental depression and offspring outcomes or whether offspring's stress physiology mediates associations between parental depression, parenting, and offspring behavior. While these are important questions, mediational models examining

developmental pathways should be tested longitudinally, rather than using a cross-sectional design. Lastly, despite being based on previous research (e.g., Ashman et al. 2002), distinguishing offspring who were exposed to maternal depression during the first 2 years of life from offspring exposed to maternal depression after the first 2 years of life was rather arbitrary. Future research should examine alternative ways to investigate the timing of exposure and sensitive developmental periods.

In sum, our findings highlight the importance of early environmental experiences involving parental depression exposure on young children's stress reactivity and behavior. The parenting context appears to play an important role in modulating children's physiological and behavioral outcomes associated with parental depression exposure. Our results have significant clinical implications and underscore the importance of parenting interventions for parents with depressive disorders, particularly for mothers with chronic or recurrent depressive disorders during periods of early childhood and significant neurodevelopmental plasticity.

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Conflict of interest Authors report no conflicts of interest.

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