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Parental sensitivity mediates the sustained effect of Attachment and Biobehavioral Catch-up on cortisol in middle childhood: A randomized clinical trial

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ABSTRACT

Importance: Parenting interventions have been found to normalize cortisol regulation among high-risk children early in development; it is important to investigate the sustainability of these effects and their mechanisms, given the maladaptive outcomes associated with cortisol dysregulation.
Objective: To determine whether the Attachment and Biobehavioral Catch-up (ABC) intervention, implemented in infancy, predicts cortisol regulation in middle childhood via changes in early parental sensitivity.
Design: Double blind randomized clinical trial design; started January 2006, the follow-up for this project concluded March 2016.
Setting: Parents of children under age 2 referred from child protective services agencies in a large, mid-Atlantic city.
Participants: 103 parent-child dyads (45.6% female children) with histories of child protective services involvement, randomly assigned to receive ABC (n = 45) or a control intervention (n = 58); in infancy, the children's ages ranged from 1.60 to 25.30 months (M = 9.87 months); at the middle childhood follow-up, they ranged from 8.0 to 11.0 years old (M = 8.52 years).
Interventions: Both conditions included 10-week, in-home, manualized interventions. The experimental condition, ABC, has 3 primary targets for parents: increasing nurturance to child distress, increasing following the child's lead, and decreasing frightening behavior. The control intervention, Developmental Education for Families (DEF), is an adaptation of a program focused on enhancing cognitive and language development.
Main outcomes and measures: Parental sensitivity was coded from a semi-structured interaction task between the parent and child in early childhood. Middle childhood diurnal cortisol slopes were modeled by collecting salivary cortisol samples from children at wake-up and bedtime over the course of 3 consecutive days.
Results: ABC participation in infancy was associated with increased parental sensitivity post-intervention, $\beta = 0.28$, $p = .004$, and this increased sensitivity predicted steeper decline across the day in children's cortisol concentration in middle childhood, $\beta = -.53$, $p = .002$. The indirect effect of ABC on cortisol regulation via sensitivity was significant, $\beta = -0.15$, $p = .038$.
Conclusions and relevance: ABC has an indirect effect on middle childhood diurnal cortisol regulation via parental sensitivity; future research should seek to determine how this enhanced neurobiological regulation relates to children's behavioral, socioemotional, and psychological outcomes.
Trial registration: clinicaltrials.gov Identifier: NCT02093052.

1. Introduction

Children facing early life adversity, such as child maltreatment, are vulnerable to dysregulation of the hypothalamic pituitary adrenal (HPA) axis (Dozier et al., 2006a; Bernard et al., 2010). This dysregulation can take the form of atypical diurnal patterns in the body's production of cortisol, an end product of the HPA axis. However, there is evidence that high quality parenting can contribute to adaptive HPA axis functioning (Pendry and Adam, 2007; Roisman et al., 2009). Interventions, such as Attachment and Biobehavioral Catch-up (ABC),

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have been developed to facilitate sensitive caregiving in an effort to support positive development in children following experiences of maltreatment. ABC, which is implemented in infancy or toddlerhood, has been found to have lasting effects on children's diurnal cortisol rhythm into early childhood (Bernard et al., 2015a). The present study explores the enduring impact of ABC on HPA axis regulation into middle childhood.

1.1. The impact of maltreatment on the regulation of the HPA axis

The HPA axis has several important and orthogonal functions, among them mounting a stress response and maintaining a diurnal pattern of cortisol production. These processes involve the hypothalamus, which releases corticotrophin releasing factor (CRH), a hormone that targets the anterior portion of the pituitary gland. In response, the anterior pituitary gland releases adrenocorticotropic hormone (ACTH), which targets the cortex of the adrenal glands. This initiates the release of glucocorticoids (i.e., cortisol in humans). The diurnal pattern of cortisol is characterized by a rise in values prior to waking, with a peak at 30 minutes after wake-up, followed by a steep decline, then a gradual decrease in concentration across the day to its nadir at bedtime. In young children, this pattern typically emerges by three months of age (Larson et al., 1998; Price et al., 1983) and mirrors that of adults by age two (Gunnar and Donzella, 2002). Thus, the first two years of life may be a sensitive period for the development of healthy diurnal cortisol regulation.

Risk factors, such as extreme poverty (Doom et al., 2018), institutional care (Koss et al., 2014), and child maltreatment (Bruce et al., 2009), can create a context of stress that leads to diurnal cortisol dysregulation. For children who have experienced maltreatment, this perturbation often takes the form of low morning cortisol values which translate to blunted, or flattened, rates of decline over the course of the day (Dozier et al., 2006a; Bernard et al., 2010). Child maltreatment has been shown to have negative effects on HPA axis regulation into adolescence (Trickett et al., 2010) and adulthood (Heim et al., 2001). The diurnal rhythm of cortisol is integral to the regulation of the immune system response, metabolic systems, and cardiovascular functioning, which may explain why dysregulation of this system has been associated with a host of negative physical outcomes across the life span (Adam et al., 2017). In addition, cortisol dysregulation is associated with maladaptive behavioral (Bernard et al., 2015b; Martin et al., 2014), social-emotional (Alink et al., 2012), and psychological (Ruttle et al., 2011) outcomes for children.

1.2. Intervening to regulate HPA axis functioning

Although child maltreatment has been shown to relate to dysregulation of HPA axis functioning, there is evidence that high quality, sensitive parenting can serve as a buffer against environmental adversity. Parental sensitivity, which is characterized by timely and appropriate responses to a child's social signals (Ainsworth, 1969; Ainsworth et al., 1978), has been found to have positive benefits for children's cortisol regulation. In a cross-sectional study with a non-maltreated sample, higher quality parenting was found to predict a steeper diurnal cortisol slope than lower quality parenting in both young children and adolescents (Pendry and Adam, 2007). Furthermore, prospective studies have found that parental sensitivity experienced in early childhood is predictive of later cortisol regulation, such that children with more sensitive caregivers in early childhood exhibited more normative cortisol production when they were adolescents (Roisman et al., 2009). Taken together, these findings highlight that enhancing early parental sensitivity could have positive effects on cortisol production through adolescence, which suggests that parental sensitivity may be an important target for interventions to improve child outcomes.

Intervening to enhance the caregiving environment of high-risk children has been shown to promote adaptive regulation of the HPA axis in children (Bernard et al., 2015a; Bernard et al., 2015c; Slopen et al., 2014). Bernard and colleagues (Bernard et al., 2010) found that children placed in foster care showed more normative cortisol levels than children who remained with neglecting birth parents following Child Protective Services (CPS) involvement. Although this study is limited by its cross-sectional and correlational design, findings may suggest that a positive shift in caregiving environment is associated with improvements in cortisol regulation. Experimental evidence from randomized clinical trials further support the association between enhanced caregiving and cortisol regulation. Fisher and colleagues (Fisher et al., 2007) investigated the effects of a family-based therapeutic intervention, the Multidimensional Treatment Foster Care for Preschoolers (MTFC-P), which trains foster parents to respond in contingent, predictable ways to children's behavior. They found that the cortisol profiles of preschool-aged children whose foster parents received the intervention resembled those of non-maltreated controls, with higher morning values and a steeper decline in cortisol across the day than children in standard foster care placement (Fisher et al., 2007).

Interventions that enhance parenting behavior among CPS-involved birth parents have also been found to enhance children's regulation of cortisol. Cicchetti et al. (2011) investigated the impact of parental and relational interventions on cortisol regulation in a sample of maltreated toddlers living with their birth parents. Following the interventions, children who experienced maltreatment were found to have cortisol profiles that were comparable to those of non-maltreated controls, whereas the children who were maltreated and received no intervention exhibited increased dysregulation of cortisol (Cicchetti et al., 2011). This effect held one year post-intervention, as maltreated children whose parents were randomized to an intervention continued to have more normative cortisol regulation than children with a history of maltreatment whose parents did not receive an intervention (Cicchetti et al., 2011). In a randomized clinical trial investigating the efficacy of Attachment and Biobehavioral Catch-up (ABC), CPS-involved children whose parents received ABC exhibited more normalized cortisol production, characterized by higher wake-up values and a steeper slope from wake-up to bedtime, than children participating in a control intervention (Bernard et al., 2015c). Similar to Cicchetti et al. (2011) who found sustained effects one year post-intervention, ABC has also been found to have lasting effects on children's HPA axis functioning in high-risk children three years post-intervention (Bernard et al., 2015a). Specifically, in a follow-up study of the same sample, ABC children continued to exhibit more normative cortisol production in early childhood than children in the control intervention (Bernard et al., 2015a).

1.3. Present study

Exposure to chronic early life adversity, such as child maltreatment, is associated with the down-regulation of HPA axis activity, often in the form of blunted diurnal cortisol slopes (Dozier et al., 2006a; Bernard et al., 2010). High quality parenting has been associated with healthy cortisol regulation among children (Pendry and Adam, 2007; Roisman et al., 2009) and interventions that target parental sensitivity in infancy, such as ABC, have been shown to have lasting effects on normalizing HPA axis activity of high-risk children into early childhood (Bernard et al., 2015a; Cicchetti et al., 2011). What is unclear is the extent to which these positive effects on HPA axis function are sustained into later developmental periods, and the mechanisms that account for the association between ABC intervention participation and HPA axis regulation. The present study sought to investigate the enduring effects of ABC participation on cortisol regulation into middle childhood, as well as examine whether parental sensitivity serves as a mediator of the association between ABC and HPA axis regulation.

Table 1
Sample Demographic Characteristics. SD: standard deviation.

Characteristic	ABC Intervention $n = 45$	DEF Control Intervention $n = 58$
Child Gender, n (%)		
Male	26 (57.8)	30 (51.7)
Female	19 (42.2)	28 (48.3)
Child Ethnicity, n (%)		
White	3 (6.7)	6 (10.3)
African-American	27 (60.0)	38 (65.5)
Hispanic	3 (6.7)	10 (17.2)
Biracial	12 (26.7)	4 (6.9)
Child Age, mean (SD)		
Pre-Intervention (*months*)	10.32 (5.42)	9.55 (6.18)
Range	2.5 – 24.1	1.6 – 25.3
Post-Intervention (*months*)	20.62 (5.10)	20.70 (5.39)
Range	9.05 – 32.80	11.80 – 33.00
Middle childhood (*years*)	8.6 (0.81)	8.45 (.55)
Range	8.00 – 11.00	8.00 – 10.00
Parent Income, mean (SD)	24, 731 (16,362)	23, 502 (23,974)
Parent Education, years, mean (SD)	10.73 (2.63)	11.43 (2.15)
Parental Sensitivity, mean (SD)		
Pre-intervention	2.13 (0.88)	2.20 (1.10)
Range	1.00 – 4.00	1.00 – 5.00
Post-intervention	2.48 (1.09)	1.95 (0.77)
Range	1.00 – 5.00	1.00 – 4.00

2. Methods

2.1. Participants

The current sample included 103 parent-child dyads who were involved with CPS when the children were infants due to risk for child neglect. At the start of the intervention, the children's ages ranged from 1.60 to 25.30 months (M = 9.87 [5.86] months) and at the time of the middle childhood measure of cortisol regulation, children's ages ranged from 8.0 to 11.0 years old (M = 8.52 [0.67] years). Demographic information for the sample is provided in Table 1. Written informed consent was obtained from parents and verbal assent was obtained from children in middle childhood. The study was approved by the University of Delaware Institutional Review Board.

2.2. Procedure

Starting in January 2006, parents of children between birth and 2 years of age were referred to the study by CPS caseworkers as part of a city-level program in a large mid-Atlantic city that was designed to divert children from entering foster care. The only inclusion criteria for referral to the study were that the target child was under the age of 2 and living with their birth parents. Children were excluded if they had serious medical conditions that interfered with locomotion, such as cerebral palsy. Study access to formal CPS records was restricted; however, based on parent report and agency referral sources, the conditions that most frequently led to participation in the diversion program were homelessness, domestic violence, maltreatment of other children, and parental substance abuse. Following referral, a project coordinator contacted families for recruitment, obtained consent from interested parents during an initial home visit, and randomly assigned families to the experimental or control group using a randomly generated sequence of numbers. Parents and research staff were blind to experimental condition. Families completed research visits before and after their intervention, and annually thereafter until children were 4 years old. The CONSORT flow diagram is displayed in Fig. 1. Of the families that were randomized, 183 (86.3 %) participated in at least one post-intervention follow-up visit during this initial study period of early childhood, which concluded in July 2012. The present study also includes data collected during the study's second phase, which followed children into middle childhood. Families were contacted around the target child's 8th birthday and completed middle childhood follow-up lab visits at the University of Delaware. This portion of the follow-up project ran from June 2014 and concluded in March 2016. Of the original sample, 128 participants (60.3 %) were retained at the middle childhood follow-up. This sub-sample did not differ significantly in terms of race/ethnicity ($\chi^2(3, N = 201) = 4.76$, $p = .190$), child sex ($\chi^2(1, N = 206) = .028$, $p = .867$), income ($t(101) = -.403$, $p = .688$), or parental education ($t(176) = -.455$, $p = .664$) from the sample that did not participate in the middle childhood follow-up. Saliva samples were collected from 103 children (described below) for analyses of cortisol concentration, while the remaining children (n = 25) lacked cortisol data because the families did not return the samples.

2.3. Interventions

Both the experimental and control treatments consisted of 10 weekly sessions and were implemented by trained parent coaches in the families' homes.

2.3.1. Experimental intervention: Attachment and Biobehavioral Catch-up

The ABC intervention has three primary targets: increasing parental nurturing behavior when children are distressed (parental nurturance to distress), increasing parental following the lead when children are not distressed (parental sensitivity), and decreasing frightening, harsh, and intrusive parent behavior. These targets were selected based on parental behaviors that are theoretically and empirically linked with child attachment as well as biological and behavioral regulation. Specifically, the importance of nurturance was included as a target because we found that children who were placed into foster care were especially likely to develop disorganized attachments unless their foster parents were nurturing (Dozier et al., 2001). We reasoned that nurturance was critical for children who had experienced adversity if they were to develop organized attachments. The second target, following the lead, was included in response to our finding that children living with neglecting parents showed flat diurnal patterns of cortisol production (Bernard et al., 2010). Although we could not find experimental evidence, correlational evidence suggested that the children of sensitive, responsive parents developed better self-regulatory capabilities than children of unresponsive parents (Raver, 1996). Third, we observed anecdotally in parents' homes that some parents were frightening and intrusive in their interactions. We were aware of the evidence that frightening behavior would undermine children's self-regulation and their ability to rely on parents (Schuengel et al., 1999) – even if parents were nurturing and responsive. In addition to the delivery of the manualized content about the rationale for each intervention target, parents were provided with specific feedback about their behaviors that relate to intervention targets during the sessions via in-the-moment commenting and the use of video-recordings. In studies that have examined the effectiveness of ABC, in-the-moment commenting has been found to be a key component of the intervention (Caron et al., 2016). ABC has been shown to increase parental sensitivity (Bick and Dozier, 2013; Bernard et al., 2015d), as well as enhance attachment quality (Bernard et al., 2012), and help regulate behavior (Dozier et al., 2006b), affect (Lind et al., 2014), and HPA axis function (Bernard et al., 2015a; Bernard et al., 2015c) in children.

2.3.2. Control intervention: Developmental Education for Families (DEF)

The Developmental Education for Families (DEF) intervention is an adaptation of a home visiting program focused on educating parents regarding their child's cognitive, motor, and language development (Brooks-Gunn et al., 1993; Ramey et al., 1984; Ramey et al., 1982). The parent coaches engage in a range of activities with parents and children that support development in these domains.

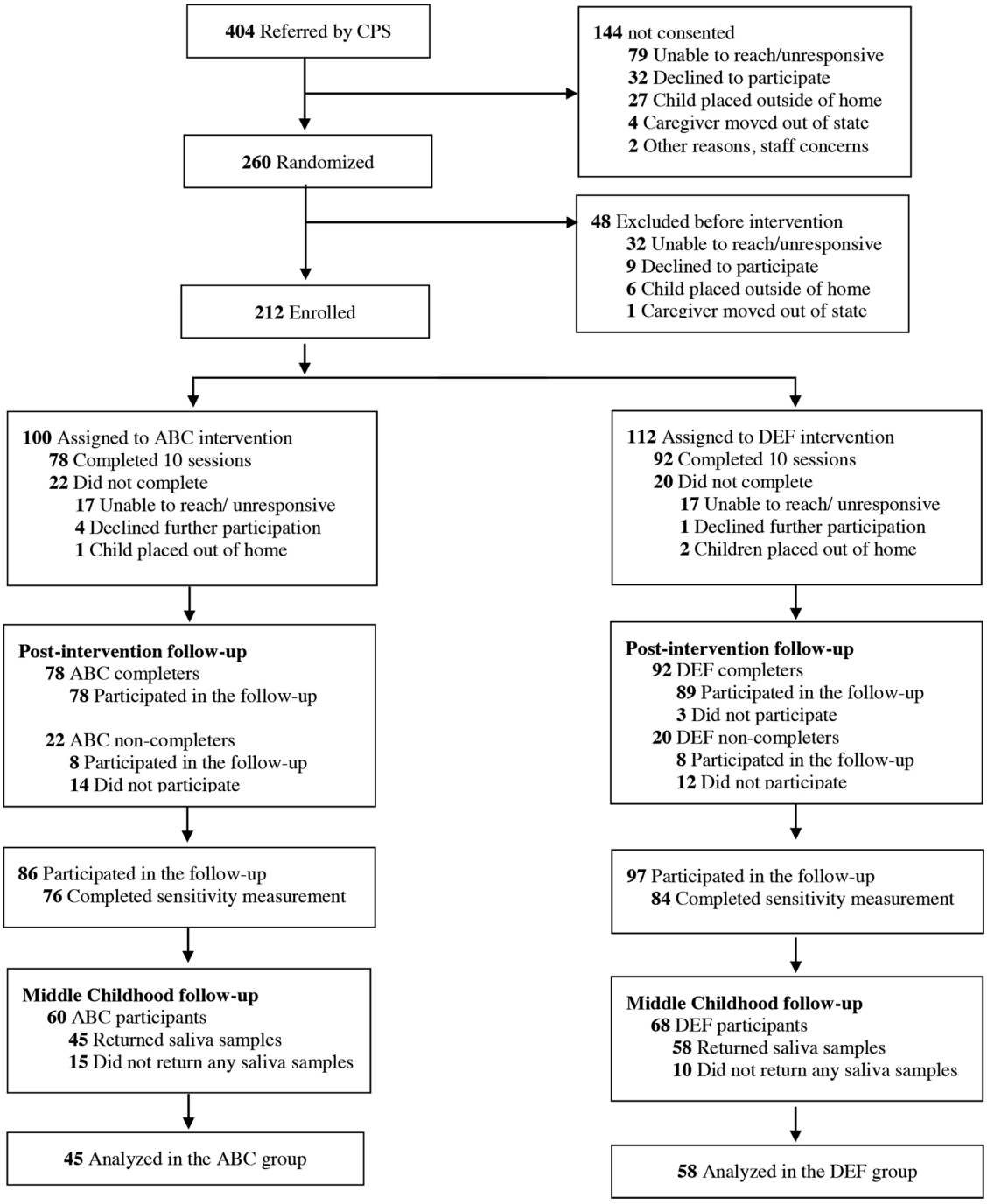

Fig. 1. Consort flow diagram. CPS: Child Protective Services; ABC: Attachment and Biobehavioral Catch-up; DEF: Developmental Education for Families.

2.4. Measures

2.4.1. Parental sensitivity

To assess for parental sensitivity, parents and children were video-recorded completing a semi-structured interaction task pre-intervention, approximately 1-month post-intervention, and when children were 1 and 2 years old; if children were between 1 to 2 years old at the time of the post-intervention visit, this annual age-based visit was combined with the 1-month post visit. Parent behaviors were coded for sensitivity to non-distress using established protocols (Bick and Dozier, 2013; Bernard et al., 2015d). Of the videos, 40 % were double coded (ICC = .70) and scores were averaged across coders. For children who had multiple assessments of parental sensitivity after the intervention, scores were averaged for analyses.

2.4.2. Saliva sampling and assay

At the middle childhood follow-up visit, research staff trained parents to collect and store saliva samples in their homes. For three consecutive days, parents helped their child collect saliva samples via passive drool into pre-labeled vials within 30 minutes of the child waking up and immediately before bedtime. Parents also completed a daily diary to provide information on saliva sampling date and time, child health status, medication usage, and whether the child had eaten prior to collecting the sample. Parents were also instructed to not collect samples while their child was sick. Table 2 provides the descriptive statistics for the saliva samples. Samples were collected from the parents and stored in a −20 °C freezer prior to being assayed in duplicate using a high-sensitivity salivary cortisol enzyme immunoassay kit (Salimetrics, LLC). The duplicate samples were assayed on the same

Table 2
Saliva sampling descriptive statistics (*to convert cortisol values from micrograms per deciliter to nanomoles per liter, multiply by 27.59). ABC: Attachment and Biobehavioral Catch-up; DEF: Developmental Education for Families; SD: standard deviation.

Intervention	*n*	Mean (SD) [Range]		
		Time of Sample	Cortisol (μg/dL)	Log transformed Cortisol (μg/dL*)
ABC intervention				
Waking				
Day 1	40	7:48 (1:47) [12:00 – 10:40]	0.14 (0.12) [0.004 – 0.46]	−1.08 (0.56) [−2.40 to −.34]
Day 2	43	7:59 (1:26) [5:30 – 1:14]	0.14 (0.13) [0.004 – 0.55]	−1.0 (0.56) [−2.40 to −.26]
Day 3	43	8:03 (1:23) [5:30 – 1:16]	0.15 (0.12) [0.004 – 0.53]	−1.10 (0.65) [−2.70 to −.28]
Bedtime				
Day 1	38	9:02 (1:02) [7:00 – 11:18]	0.07 (0.08) [0.002 – 0.27]	−1.50 (0.64) [−2.70 to −.57]
Day 2	40	9:16 (1:03) [7:00 – 11:47]	0.08 (0.10) [0.004 – 0.32]	−1.50 (0.64) [−2.40 to −.50]
Day 3	45	9:18 (1:01) [7:00 – 11:27]	0.13 (0.15) [0.004 – 0.52]	−1.31 (0.72) [−2.40 to −.28]
DEF control intervention				
Waking				
Day 1	55	8:18 (1:17) [6:00 – 11:34]	0.12 (0.12) [0.001 – 0.54]	−1.24 (0.66) [−3.00 to −.27]
Day 2	56	8:00 (1:10) [5:50 – 11:40]	0.11 (0.11) [0.003 – 0.51]	−1.23 (0.62) [−2.52 to −.29]
Day 3	54	8:05 (1:41) [12:30a–11:30]	0.12 (0.13) [0.003 – 0.65]	−1.16 (0.55) [−2.52 to −.19]
Bedtime				
Day 1	53	8:25 (2:56) [6:00 – 11:30]	0.06 (0.06) [0.003 – 0.25]	−1.56 (0.59) [−2.52 to −.60]
Day 2	57	8:33 (2:58) [12:00a–11:30]	0.06 (0.07) [0.001 – 0.31]	−1.57 (0.58) [−3.00 to −.51]
Day 3	54	8:55 (1:04) [4:46 – 10:57]	0.06 (0.10) [0.001 – 0.43]	−1.59 (0.68) [−3.00 to −.36]

plate to minimize variability. The intra-assay and inter-assay coefficients of variation were below 7% and 11 %, respectively.

2.4.2.1. Cortisol data preparation. As indicated above, each child could have provided as many as six saliva samples, for a total of 618 possible samples. Of the total, 578 samples (93.53 %) were included in analyses, with 24 (3.88 %) either not collected by the family or removed due to insufficient saliva volume and 16 (2.59 %) removed as outliers. Outliers were removed from analyses using established procedures (Bernard et al., 2015c); biologically implausible values (those > 2.0 μg/dL: 4 values) and values > 3 SDs above the mean (12 values) were excluded. In addition, 14 % of samples had cortisol concentration below the detectable limit, so their values were replaced with .004 μg/dL. To normalize the positively skewed distribution of the cortisol values, the values were log transformed. Table 2 displays the descriptive statistics of the cortisol values.

2.5. Analytic approach

Intervention groups were compared on key demographic variables. We estimated power for the direct effect of ABC on cortisol using data from an earlier study demonstrating that ABC had a medium effect on diurnal cortisol ($d = -.43$) at a preschool follow-up time point (Bernard et al., 2015a). To detect a within-between interaction effect of this magnitude using a repeated measures ANOVA (using an alpha error probability of .05 and a correlation between wake-up and bedtime cortisol of $r = .58$), our sample size of N = 103 afforded > .80 power. Primary analyses were conducted in MPlus 8.0 (Muthén and Muthén, 2017). Wake-up (AM) and bedtime (PM) cortisol values were defined as latent factors, each with three indicators (i.e., log-transformed cortisol values from three samples). Child diurnal cortisol slope was specified as a latent change score (Bernard et al., 2015b; Kertes et al., 2008; McArdle and Hamagami, 2001), representing the change in cortisol from wake-up to bedtime (i.e., PM cort – AM cort); a more negative latent change score reflected a steeper (i.e., more normative) decline in cortisol across the day. Sample time was included as a time-varying covariate by regressing each cortisol indicator on the standardized time of sample collection. To determine whether parental sensitivity mediated the association between intervention group and children's diurnal cortisol slope, a series of regression pathways was modeled (See Fig. 2): the outcome (i.e., latent change score for cortisol) was regressed on the predictor (i.e., intervention group) and on the mediator (post-intervention sensitivity); post-intervention sensitivity was regressed on intervention group and pre-intervention sensitivity. In order to test for mediation, we estimated the indirect effect of intervention group on middle childhood cortisol via post-intervention sensitivity. Child sex and racial/ethnic minority status were included as covariates. The model was estimated using maximum likelihood estimation and absolute model fit was assessed with the chi-square test of model fit, the root mean square error of approximation (RMSEA), and the comparative fit index (CFI).

3. Results

ABC and DEF groups did not differ with regard to children's sex, minority status, parental education, or income. For primary analyses, the model fit statistics demonstrated good fit to the data. The chi-square test of model fit was non-significant, $\chi^2(85) = 103.63$, $p = .082$, which indicates acceptable model fit (Byrne, 1989; Carmines and McIver, 1981). Similarly, the RMSEA = .05 and CFI = 0.92 met criteria for

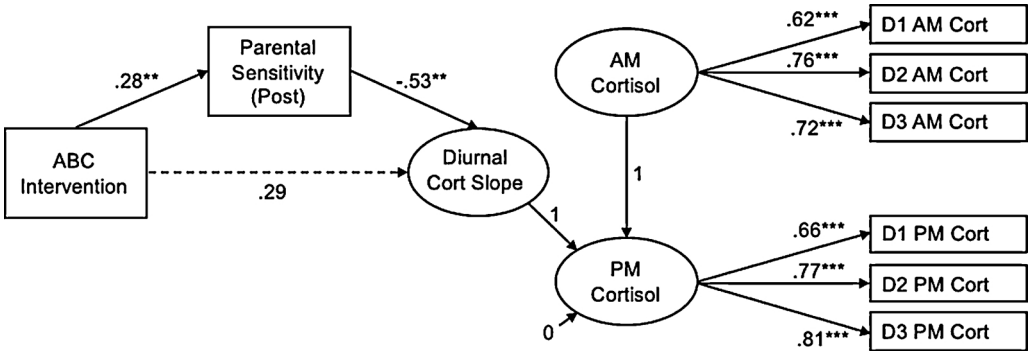

Fig. 2. Path diagram with standardized coefficients for full model of ABC assignment predicting children's diurnal cortisol slope via parental sensitivity. D1 AM Cort-D3 AM Cort and D1 PM Cort-D3 PM Cort represent log-transformed wake-up cortisol indicators and bedtime cortisol indicators for Days 1 through 3, respectively. Covariates (pre-intervention sensitivity, child sex, racial/ethnic minority status, and sampling time) were included in the model, but are not depicted for simplicity. Model fit statistics indicated good fit: $\chi2(85) = 103.63$, $p = .082$, RMSEA = .05, CFI = 0.92. **$p < .01$, *** $p < .001$. ABC: Attachment and Biobehavioral Catch-up.

Table 3
Model estimated parameters for the full model. C.I.: 95 % confidence interval; SE: standard error; est.: standardized estimate; ABC: Attachment and Biobehavioral Catch-up.

Effect	Standardized Estimate, β [C.I.]	SE	Est./SE	p
Measurement model factor loadings				
AM cortisol				
Day 1 wake-up	0.62 [0.49, 0.75]	0.07	9.03	0.000
Day 2 wake-up	0.76 [0.64, 0.89]	0.06	12.24	0.000
Day 3 wake-up	0.72 [0.59, 0.86]	0.07	10.54	0.000
PM cortisol				
Day 1 bedtime	0.66 [0.54, 0.78]	0.06	10.88	0.000
Day 2 bedtime	0.77 [0.64, 0.89]	0.06	12.21	0.000
Day 3 bedtime	0.81 [0.70, 0.91]	0.05	15.03	0.000
Path model: Direct effects				
Diurnal cortisol slope regressed ON				
Post-intervention sensitivity	−0.53 [−0.87, −0.19]	0.17	−3.04	0.002
ABC intervention	0.29 [−0.01, 0.60]	0.16	1.87	0.061
Child female sex	0.02 [−0.29, 0.32]	0.16	0.11	0.916
Racial/ethnic minority status	0.06 [−.023, 0.36]	0.15	0.43	0.668
Post-intervention sensitivity ON				
ABC intervention	0.28 [0.09, 0.47]	0.10	2.90	0.004
Pre-intervention sensitivity	0.23 [−0.05, 0.51]	0.14	1.61	0.108
Child female sex	0.20 [0.01, 0.40]	0.10	2.02	0.043
Racial/ethnic minority status	−0.09 [−0.29, 0.11]	0.10	−0.86	0.391
Path model: Indirect effects				
ABC intervention to cortisol slope, via sensitivity	−0.15 [−0.29, −0.01]	0.07	−2.08	0.038

good fit between the estimated model and observed data, based on respective cutoffs of ≤ .08 and ≥ .90 (Browne and Cudeck, 1993; Chen et al., 2005). Fig. 1 shows the model with standardized coefficients and significance levels, with detailed information about estimated parameters presented in Table 3.

Controlling for parental sensitivity at pre-intervention, assignment to ABC was associated with parental sensitivity at post-intervention, $\beta = 0.28$, $p = .004$, 95 % CI [0.09, 0.47]. Parents who were assigned to ABC had higher ratings of parental sensitivity ($M = 2.48$, $SD = 1.09$) at post-intervention than parents in the control condition ($M = 1.95$, $SD = 0.77$). In addition, there was a significant association between parental sensitivity at post-intervention and children's diurnal cortisol slope in middle childhood, controlling for pre-intervention sensitivity, child sex, and child minority status, $\beta = -0.53$, $p = .002$, 95 % CI [−0.87, −0.19]. Children with more sensitive parents had steeper declines in their cortisol from wake-up to bedtime than children with less sensitive parents. Further, the indirect effect of ABC participation on children's diurnal cortisol slope via post-intervention sensitivity was significant, $\beta = -0.15$, $p = .038$, 95 % CI [−0.29, −0.01]. This indicated that parental sensitivity mediated the association between ABC participation on children's diurnal cortisol slope. ABC participation did not have a significant direct effect on children's diurnal cortisol slope before ($\beta = 0.29$, $p = .061$, 95 % CI [−0.01, 0.60]) or after ($\beta = -0.14$, $p = .36$, 95 % CI [−0.17, 0.45]) including parental sensitivity in the model as a mediator.

4. Discussion

The present study examined the enduring effects of the ABC intervention on child cortisol regulation in middle childhood and explored the role of early parental sensitivity as a potential mediator of this association. Parents assigned to ABC when their children were infants exhibited higher levels of post-intervention parental sensitivity than parents assigned to a control intervention. Higher post-intervention levels of parental sensitivity during infancy predicted a greater decline in cortisol concentration across the day in middle childhood, as evidenced by steeper diurnal cortisol slopes, than lower levels of sensitivity. Although ABC did not have a significant direct effect on middle childhood diurnal cortisol regulation, post-intervention sensitivity mediated the association between ABC and middle childhood diurnal cortisol slopes. This study emphasizes the importance of early interventions to support long term benefits for children's regulatory abilities following experiences of maltreatment.

ABC targets several aspects of parenting behavior, including nurturance to distress, following the lead, and frightening behavior; the decision to specifically test parental sensitivity (i.e., following the lead) as a mediator of intervention effects on cortisol regulation was influenced by previous literature. Past research has suggested that sensitive parenting that involves contingent responsiveness to children's cues supports children's regulatory capacities generally (Raver, 1996) and cortisol regulation (Roisman et al., 2009; DePasquale et al., 2018), in particular. Consistent with these correlational studies, the present study offers experimental evidence that following the lead serves as one mechanism by which ABC influences children's cortisol regulation. Nevertheless, it will be important to explore the extent to which improvements in the other parenting dimensions (i.e., nurturance, frightening behavior) also explain intervention effects on HPA axis functioning, as well as whether each parenting target predicts distinct outcomes from the others. Such evidence of unique effects of each target on outcomes may inform the development of new interventions, as well as inform approaches for personalizing existing interventions for different parents.

Given that our findings demonstrated that increased parental sensitivity during infancy led to more normative cortisol regulation in middle childhood, it is important to consider processes involved in sustaining these effects over time. Although diurnal cortisol slopes are dynamic and susceptible to contextual factors, there is evidence that this metric of cortisol regulation also exhibits trait-like stability across childhood (Shirtcliff et al., 2012). Altered profiles of HPA axis regulation following early life stress have been found to be sustained over time (Essex et al., 2011). Given that ABC has been found to predict more normative cortisol regulation than the control condition immediately after (Bernard et al., 2015c) and 3 years post-intervention (Bernard et al., 2015a), it is plausible that this experience with more sensitive parenting early in life may have helped set a trajectory for normative cortisol regulation across childhood. Although early caregiving experiences have been found to be more predictive of later cortisol regulation than concurrent measures of caregiving (Roisman et al., 2009), it is also possible that sustained changes in caregiving quality may have supported sustained changes in cortisol regulation for children. Future studies should examine the trajectory of post-intervention parenting behavior over time and its subsequent influence on child diurnal cortisol regulation over time. It will also be important to investigate whether the neurobiogical benefits associated with the enhanced parental sensitivity early in life extend beyond middle childhood, into adolescence and adulthood.

The findings of the present study have important implications, given that cortisol dysregulation has been associated with increased instances of mental and physical health disorders across the lifespan (Adam et al., 2017). Moreover, HPA axis dysregulation has been identified as a candidate mechanism by which early adverse experiences confer risk for psychopathology (Koss and Gunnar, 2018) and physical health outcomes (Berens et al., 2017). Therefore, regulation of cortisol following experiences of maltreatment is key to aid in the prevention and possible amelioration of negative health outcomes for children in high-risk environments. Given the importance of cortisol regulation to subsequent health outcomes, it will be critical to examine whether the enhanced diurnal cortisol regulation associated with increased parental sensitivity impacts future mental and physical health for children.

The present study had a number of methodological strengths, including its randomized design and use of a control intervention with the same structure and duration as ABC. The longitudinal nature of the study allowed for the examination of prospective associations between ABC assignment in infancy, parental sensitivity in early childhood, and children's diurnal cortisol regulation in middle childhood. In addition, observing parental sensitivity at multiple time-points allowed us to account for normative within-person fluctuations in sensitivity. Despite these strengths, the study also had limitations. In particular, access to participant CPS records was limited; thus, information on the specific types, duration, and severity of maltreatment experienced by the children in the sample was not available to the researchers. The collection of only wake-up and bedtime samples of cortisol is a limitation to the findings; the sampling of multiple timepoints may have provided a more robust picture of the regulation of cortisol across the day. Another limitation of this study was the reliance on parents to accurately collect saliva samples immediately following wake-up and prior to bedtime, as well as accurately record the sampling times. Although this was a limitation of the present study, it should be noted that with proper training and resampling, maltreating families exhibit saliva sampling adherence comparable to demographically similar non-maltreating families (Valentino et al., 2017). In addition, we did not control for all variables that can influence cortisol levels, such as quality and quantity of sleep, daily experiences with acute stress, and contextual risk factors, such as neighborhood quality, home environment, and parent/child psychopathology. Despite these limitations, the present study provides additional support for the utility of ABC as a change agent in the quality of parental behavior in infancy, which subsequently enhances children's ability to regulate neurobiology over time.

4.1. Conclusion

In conclusion, the present study provides experimental evidence of the sustained effect of ABC on middle childhood diurnal cortisol regulation via early childhood parental sensitivity. This finding emphasizes the importance of an early intervention in supporting children's regulatory abilities following experiences of maltreatment. Future research should seek to determine the enduring impact of ABC participation beyond this developmental period, as well as examine how this enhanced neurobiological regulation relates to children's behavioral, psychological, and physical health outcomes.

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CRediT authorship contribution statement

Mallory Garnett: Formal analysis, Writing - original draft, Writing - review & editing. **Kristin Bernard:** Formal analysis, Project administration, Writing - review & editing. **Julie Hoye:** Investigation, Project administration, Writing - review & editing. **Lindsay Zajac:** Project administration, Writing - review & editing. **Mary Dozier:** Conceptualization, Funding acquisition, Methodology, Writing - review & editing.

Declaration of Competing Interest

None.

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