Published in final edited form as:

Neurotoxicol Teratol. 2014 ; 42: 1–8. doi:10.1016/j.ntt.2014.01.003.

Empathic Responsivity at 3 Years of Age in a Sample of Cocaine-exposed Children

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Abstract

This study examined the association between prenatal exposure to cocaine and behavioral and physiological responsiveness during an empathy task at three years of age. Participants were 216 mother-infant dyads (116 cocaine exposed-CE, 100 nonexposed-NCE) recruited at birth. Measures of heart rate (HR) and respiratory sinus arrhythmia (RSA) were obtained during baseline and during a task designed to elicit empathy (exposure to infant crying). When the effects of prenatal cocaine use were examined in the context of polydrug use, results of model testing indicated that lower gestational age, prenatal exposure to cocaine and postnatal exposure to alcohol were each associated with a reduced suppression of RSA during the empathy task. These findings provide additional support for an association between prenatal cocaine exposure and dysregulation during early childhood during affect-eliciting environmental challenges.

Keywords

prenatal cocaine exposure; empathy; regulation; respiratory sinus arrhythmia; heart rate

Prenatal exposure to cocaine (PCE) has increasingly been linked to a risk of dysregulation beginning in infancy and continuing into childhood. A number of human studies have consistently reported significant associations between prenatal cocaine exposure and some aspects of the regulatory system including both behavioral (Karmel and Gardner, 1996; Bendersky and Lewis, 1998; Mayes et al., 1998) and autonomic regulation (Silvestri et al., 1991; Bard et al., 2000; Schuetze and Eiden, 2006; Schuetze et al., 2009). Animal models also indicate that prenatal cocaine alters offspring attention and arousal regulation (Gendle

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Conflict of interest statement

There is no conflict of interest. The study was funded by a grant from the National Institute on Drug Abuse.

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et al., 2004), disrupts emotionality and social behaviors in juvenile and adult offspring (Wood et al., 1994; 1995; Johns and Noonan, 1995; Johns et al., 1998; Wood & Spear, 1998; Overstreet et al., 2000) and increases sensitivity to environmental stressors (Sobrian et al., 1990; Spear et al., 1998). Taken together, both the human literature and studies using animal models suggest that prenatal cocaine exposure has the potential to significantly alter the regulatory system.

An increasing number of studies have found that cocaine-exposed children have particular difficulty regulating their arousal during emotional-eliciting tasks. To date, most studies with cocaine-exposed children have focused on emotional responsivity during tasks designed to elicit frustration. For instance, cocaine-exposed infants and children display higher negative affect (Bendersky and Lewis, 1998; Mayes et al., 1996), more anger (Alessandri et al., 1993), higher frustration and more disruptive behavior (Dennis, Bendersky, Ramsay and Lewis, 2006) and disrupted patterns of physiological regulation (Eiden, Granger and Veira, 2009; Magnano, Gardner and Karmel, 1992; Schuetze, Eiden, and Danielewicz, 2009; Schuetze, Eiden and Coles, 2007). Fewer studies have examined responsivity during other types of emotional challenges. One exception found cocaine-exposed 3- to 6-year-old children showed fewer empathic reactions and had greater right frontal EEG asymmetry, a pattern related to greater negative affect, when exposed to infant crying (Jones, Field, Davalos, Hart, 2004).

One aspect of emotion regulation that has not received much attention to date in cocaine-exposed children is empathic responsiveness. Empathy has been defined as an affective response resulting from either the apprehension or comprehension of another's affective state (Eisenberg and Fabes, 1998; Mehrabian and Epstein, 1972) and is conceptualized as leading to either sympathy (i.e., concern for another; Eisenberg et al., 1991) or personal distress (i.e., self-focused, aversive emotional reactions; Batson, 1991). Eisenberg and colleagues have demonstrated that individual differences in self-regulation are associated with empathy (Eisenberg et al., 1994; Eisenberg et al., 2007). Individuals who have difficulty regulating arousal in response to empathy-eliciting situations are more likely to experience personal distress. Specifically, young children who experience high levels of arousal in response to the personal distress of others may focus on self-comforting behaviors rather than on prosocial behaviors directed towards others (Gill and Calkins, 2003). Thus, children who are prone to increased reactivity are expected to show less regulation in empathy-eliciting situations. More moderate and optimal arousal responses, on the other hand, are associated with sympathy. Thus, children who have the capacity to regulate emotionality are more likely to experience sympathy. Taken together, these data suggest that cocaine-exposed children may have difficulty regulating their emotional responses during empathy-eliciting situations.

One physiological regulatory system that supports self-regulation is the parasympathetic branch of the autonomic system. This system allows for quick changes in metabolic inputs and outputs from the heart and facilitates behaviors necessary for self-regulation and social exchanges. One commonly used measure of physiological responsivity to affect-eliciting tasks is respiratory sinus arrhythmia (RSA) reactivity, indexed by change in RSA in response to challenge. Change in RSA as a response to challenge reflects an ability to respond to rapidly changing environmental inputs, i.e., changes in social signals that underlie interpersonal interactions (Beauchaine, 2001) and the initiation of coping strategies to manage affective and behavioral arousal (Calkins, 1997). Among normative developmental populations, RSA change is associated with aspects of self-regulation such as executive control (Marcovitch et al., 2010) and empathy (Eisenberg et al., 1994; Fabes, Eisenberg and Eisenbud, 1993; Fabes et al., 1994), with a decrease in RSA indicating more

adaptive regulatory functioning. More specifically, as children focus their attention on this external event, RSA is expected to decrease (Calkins and Dedmon, 2000).

The purpose of the present study was to examine behavioral and physiological indices of empathy in a sample of 36-month-old cocaine exposed children. We chose to examine reactions to empathy at 36 months of age because previous research suggests that empathic responding undergoes significant development during the second year of life (Young, Fox, and Zahn-Waxler, 1999). During this time, children begin to respond to distress in others with concern, focused attention and prosocial interventions. Thus, by 36-months of age, we expect to see empathic responses in children when exposed to a distressing event involving others. Based on existing studies, however, we hypothesized that prenatal exposure to cocaine would be associated with reduced behavioral and physiological responsiveness to infant crying. Specifically, we hypothesize that cocaine-exposed children would display less anxiety, an index of personal distress, and would have reduced rates of concerned verbal attention, indicating reduced sympathy, relative to nonexposed children. Furthermore, we hypothesized that exposed children would have smaller changes in RSA in response to an empathy task, indicating reduced physiological regulation, than nonexposed children.

1. Method

1.1 Participants

The sample consisted of 216 mother-child dyads participating in an ongoing longitudinal study of prenatal cocaine exposure (116 cocaine exposed or CE, 100 not cocaine exposed or NCE). An outreach worker on the project staff recruited all participants after delivery from two local area hospitals. Mothers ranged in age from 18 to 42 years ($M=29.78$; $SD=5.46$). The majority of mothers were African American (74%), were receiving Temporary Assistance for Needy Families (71%) at the time of their first laboratory visit (Years 2001–2004), and were single (60%). Of the 216 children, 106 (49%) were male. All families were recruited from two hospitals serving a predominantly low-income population and the two groups were matched on maternal education, maternal race/ethnicity, and infant sex. The study received approval from the institutional review boards of the hospitals as well as the primary institution at which the study was conducted. Informed written consent was obtained from all recruited participants. Participants were compensated for their time in the form of gift certificates, checks, and infant toys at each assessment, with the amount increasing over time. All assessments were conducted at age corrected for prematurity.

Maternal and child assessments were conducted at 4–8 weeks, 7, 13, 24, and 36 months of child age. Measures obtained at 4–8 weeks, 24 months and 36 months were included in the current analyses. By 36 months of child age, 46 children in the cocaine group and 4 children in the control group had been removed from parental care and placed in non-parental care. All assessments were conducted with the primary caregiver of the child at that time, although for ease of presentation the terms mother and maternal are used throughout the manuscript when referring to the primary caregiver. The primary caregiver was identified as the adult who had legal guardianship of the child and accompanied the child at all appointments.

1.2 Procedure

All mothers were screened after delivery for initial eligibility and matching criteria. Interested and eligible mothers were given detailed information about the study and asked to sign consent forms. About 2 weeks after delivery, mothers were contacted and scheduled for their first laboratory visit, which took place at the time that their infant was approximately 4–8 weeks old. Additional visits were scheduled when the infant was 7, 13, 18, and 24

months old. All visits (with the exception of the 18 month visit consisting of maternal interview only) consisted of a combination of maternal interviews, observations of mother-infant interactions, and infant assessments. In the circumstance of a change in custody arrangements, the person who had legal guardianship of the child was contacted and asked to participate. Biological mothers were interviewed at the 4–8 week assessment in addition to the foster mother in order to obtain accurate information about prenatal substance use.

Once a family was recruited into the cocaine group, the closest matching non-cocaine group family was recruited. However, a significantly higher proportion of mothers in the non-cocaine group declined participation or withdrew before formal enrollment, resulting in a smaller number of families in the control group. Of the 4,800 women screened at delivery, 340 were eligible for participation in either group. Of these 340 women, 35% either declined participation or were not enrolled in the study because they expressed initial interest but later withdrew, resulting in a final sample of 220 mother-infant dyads. Mothers who participated were more likely to be between 18 and 25 years of age, ($p < .001$), and were more likely to have a high school or below high school education ($p < .001$), compared to those who were eligible but not enrolled. The participation rate was higher among eligible mothers who used cocaine (91%) than for eligible mothers who did not use cocaine during pregnancy (68%). Mothers who participated were also more likely to be in the cocaine group (with a participation rate of 91% among cocaine group eligibles) compared to those who were eligible but not enrolled. The majority of mothers in the cocaine group who were eligible but not enrolled in the study had children who were placed in non-maternal care. There were no other differences on any demographic variables between those who participated and those who were eligible but not enrolled or between mothers in the cocaine group who participated compared to those who did not.

1.3 Assessment of growth and risk status

Three measures of growth were used in this study: birth weight (gm), birth length (cm), and head circumference (cm). All measurements were taken by obstetrical nurses in the delivery room and recorded in the infant's medical chart. Research staff recorded this information from the charts after recruiting the mother-infant dyad. Medical chart review at the time of recruitment also was used to complete the Obstetrical Complications Scale (OCS; Littman and Parmelee, 1978), a scale designed to assess the number of perinatal risk factors experienced by the infant. Higher numbers on this scale indicate a more optimal obstetric score. Gestational age was calculated by dates and extracted from medical records.

1.4 Identification of Substance Use

Cocaine status was determined by a combination of maternal report, chart review, and maternal hair analysis. Urine toxicologies were routinely conducted at the first prenatal visit on maternal urine and/or at delivery (for those mothers who tested positive prenatally, obtained prenatal care elsewhere, or did not receive any prenatal care) on infant and maternal urine by participating hospitals. Mothers were included in the cocaine group if self-reports were positive, regardless of urine toxicology or hair-sample results. Similarly, mothers who reported that they did not use cocaine but had positive urine toxicology or hair samples were included in the cocaine group.

Urine toxicologies consisted of standard urine screening for drug level or metabolites of cocaine, opiates, benzodiazepines, and tetrahydrocannabinol. Urine was rated positive if the quantity of drug or metabolite was >300 g/ ml. Hair samples were collected from the mothers at the first laboratory visit and sent to the Psychomedics Corporation for Radioimmunoanalyses (RIAH). Hair samples were screened for cocaine followed by a gas chromatography/mass spectrometry (GC/MS) confirmation for positive cocaine screens.

Drugs and their metabolites are absorbed into the hair and can be extracted and measured. As hair grows at an average rate of 1/2 inch per month, it can record a pattern of drug consumption related to the amount and frequency of use (see Baumgartner et al., 1989). Thus, a 2-inch length of hair could contain a record of approximately 4 months of use, and given adequate hair length (i.e., about 4–5 inches), use per trimester may be recorded. Drugs become detectable in hair about 3 to 4 days after use, a time when cocaine is rendered undetectable by urinalysis. RIAH is the most well-established hair-analysis technique and has been replicated by independent laboratories across the world (see Magura et al., 1992). GC/MS confirmations of RIAH have not revealed any false positives because of testing errors (Magura et al., 1992). Special washing techniques and data pertaining to kinetics of washing were used to distinguish external contamination from intentional use. These methods have been verified by independent investigators to distinguish between passive and active exposure (see Mieczkowski and Newel, 1997).

Approximately 32% of mothers in the study (55% of the mothers in the cocaine group, 0% in the control group) had positive urine toxicologies at delivery, and 25% of mothers (79% of the mothers in the cocaine group; 0% in the control group) had hair samples that tested positive for cocaine during pregnancy. There were 23 mothers in the cocaine group who did not have a positive toxicology result on any biomarker of cocaine, but all of these mothers admitted to having used cocaine in the brief self-report screening instrument administered after delivery. Mothers in the comparison group reported not having used any illicit substances other than marijuana. They also tested negative for cocaine or illicit substances other than marijuana based on urine and hair analysis results. Additional exclusionary criteria for all mothers were (a) maternal age younger than 18 years, (b) use of illicit substances other than cocaine or marijuana, and (c) significant medical problems for the infant (e.g., genetic disorders, major perinatal complications, baby in critical care for over 48 hours).

The Timeline Follow-Back Interview (TLFB; Sobell et al., 1986) was used to assess maternal substance use during pregnancy. Participants were provided a calendar and asked to identify events of personal interest (i.e., holidays, birthdays, vacations, etc.) as anchor points to aid recall. This method has been established as a reliable and valid method of obtaining longitudinal data on substance-use patterns, has good test-retest reliability, and is highly correlated with other intensive self-report measures [Brown et al., 1998]. The TLFB yielded data about the average number of days of cocaine use per week, average number of joints smoked per week, average number of cigarettes smoked per week, and average number of standard drinks per week during pregnancy. These variables were quite skewed and were transformed using square root transformations before further analyses. Postnatal substance use was computed by taking the average number of days used cocaine, number of cigarettes per week, number of standard drinks per week, and number of joints per week from the 4–8 week, 24 and 36 months assessments. Average number of joints per week during and after pregnancy and average amount number of days of cocaine use per week after pregnancy were not associated with cocaine group status (see below), or with the outcomes examined in this study. Thus, these variables were dropped from model testing.

1.5 Child Empathy: Crying Tape

Behavioral and physiological measures of empathic responsiveness were obtained at the 36 month assessment during a task modified from Martin and Clark (1982) and used by Gill and Calkins (2003) with preschool-aged children. First, disposable electrodes were triangulated on the child's chest. A respiration bellows was placed at the bottom of the sternum to measure inspiration and expiration. IBI Analysis software (James Long Company, Caroga Lake, NY) was used to process the HR data and to calculate RSA. Children were then seated at a table and given a neutral video to watch for three minutes

while baseline physiological measures were obtained. Although this procedure does not get true resting data because the child is attending to an external stimulus, it has been used successfully in previous studies by Calkins and colleagues (e.g., Gill and Calkins, 2003) to keep preschool-aged children sitting quietly, thereby minimizing lost data due to movement artifact. After obtaining the baseline data, the video tape was turned off and child was given picture books at which to look. The child then heard an audiotape of an infant crying over an intercom for a 2-minute period of time. If the child referred to the crying in any way, the experimenter responded by saying "It's a baby. Somebody will take care of it." The entire procedure was videotaped and later coded for behavioral measures of empathy.

1.6 Physiological Measures of Empathy

All physiological data during the baseline period and empathy task were recorded continuously on-line directly into a data acquisition computer. A five-channel Bioamp (James Long Company, Caroga Lake, NY) recorded respiration and electrocardiograph (ECG) data. Heart rate (HR) samples, which were collected every 10 ms, were used to calculate mean HR per one-second period. A level detector was triggered at the peak of each R-wave. The interval between sequential R-waves was calculated to the nearest millisecond. Data files of R-wave intervals were later manually edited to remove incorrect detection of the R-wave or movement artifacts. The software computes RSA using respiration and interbeat interval (IBI) data as suggested by Grossman (1983). The difference between maximum IBI during expiration and the minimum IBI during inspiration was calculated. The difference, which is measured in seconds, is considered to be a measure of RSA, and is measured twice for each respiration cycle (once for each inspiration and once for each expiration). The time for inspirations and expirations is assigned as the midpoint for each. The time for each arrhythmia sample is assigned as the midpoint between an inspiration time and an expiration time. The software synchronizes with respiration and is, thus, relatively insensitive to arrhythmia due to tonic shifts in heart rate, thermoregulation, and baroreceptor. Average RSA was calculated for the 3-minute baseline period (BRSA) and for the empathy task. To assess autonomic regulation, we calculated a change score for RSA from baseline to empathy. Negative scores indicate a decrease in RSA and are reflective of more optimal parasympathetic regulation.

1.7 Behavioral Measures of Empathy

Behavioral coding of empathy tasks included two measures, personal distress as indicated by anxiety or arousal behaviors and verbal concern or sympathy. These measures were coded every 30-seconds using a 5-point scale with 1 = no arousal/anxiety or no verbal concern to 5 = strong anxiety/arousal or strong display of concern. These codes were taken from previous codings of empathy paradigms at this age (Hastings, Zahn-Waxler, Robinson, Usher, and Bridges, 2000; Young, Fox, and Zahn-Waxler, 1999; Zahn-Waxler, Robinson, and Emde, 1992). These codings follow previous work that has conceptualized empathy as consisting of both personal distress and concern/sympathy (Bateson, 1991). The codes of anxiety/arousal reflecting personal distress and the codes for verbal concern were composited for the final measures by taking the maximum code across the four 30-second periods. Two coders blind to group status coded the empathy tapes. Of the 129 videotapes, 10% were coded jointly for training and initial reliability. Following training, 12% of the tapes were coded independently by the two coders. Inter-rater reliability coefficients were $r = .82$ for arousal/anxiety and $r = .92$ for verbal concern.

2. Results

2.1 Data Analytic Strategy

Group differences in demographics, perinatal risk characteristics, maternal substance use variables, and the exogenous variables included in the model were examined first using ANOVAs or MANOVAs in order to provide descriptive data and guide selection of potential covariates. MANOVAs were used when multiple theoretically associated constructs were the dependent measures in order to control for high Type I error rate. Because previous studies have found sex differences in empathy, we conducted MANOVAs to examine sex differences in empathy. Demographic or perinatal risk variables that were associated with both the exogenous variables and indices of empathy at $p < .10$ were used as covariates in subsequent analyses.

All SEM analyses were conducted using AMOS 7.0 software (Arbuckle, 1997). Full estimation procedures were employed and standardized estimates are presented. Model fit was assessed using the comparative fit index (CFI) and the root-mean-square error of approximation (RMSEA). The CFI varies between 0 and 1, where values of .90 or greater indicate inadequate adequate fit (Hu and Bentler, 1995). The RMSEA is bounded by 0 and will take on that value when a model exactly reproduces a set of observed data. A value of .05–.06 is indicative of close fit, a value of .08 is indicative of marginal fit, and values greater than .08 are indicative of poor fit (Browne and Cudeck, 1994).

2.2 Missing Data

As expected in any longitudinal study, there was some incomplete data for some of the participants at one or more of the three assessment points included in this study. Of the 216 child-mother dyads in the final sample, 165 completed the 36 month assessment. Behavioral data were collected on 129 and complete valid RSA data were collected on 107 of these. Families with missing data had mothers with less education, $F(1, 213) = 4.24, p = .04$, and who smoked marginally more cigarettes during pregnancy, $F(1, 213) = 3.76, p = .054$. Data were thus determined to fit criteria for missing at random (MAR), but not missing completely at random (MCAR). As noted earlier, full-information maximum likelihood was used to estimate model parameters for SEM. Variables that were significantly different for families with missing vs. complete data (maternal education, and number of cigarettes used per day) were included in model testing as exogenous variables.

2.3 Group Differences for Demographics and Perinatal Risk

Table 1 displays descriptive statistics for the cocaine and for the control group. Results from MANOVA with the demographic variables as the dependent measures and CE group status yielded a significant multivariate effect of group status, $F(3, 98) = 3.79, p = .013$. Results from univariate analyses indicated that control group mothers were younger and had lower parity compared to those in the CE group (see Table 1). MANOVA with perinatal outcomes and obstetrical complications as the dependent measures yielded a significant multivariate effect of group status, $F(5, 90) = 8.67, p < .001$. Univariate analyses indicated that CE children had lower gestational age, birth weight, birth length, and cocaine using mothers had lower scores on the obstetrical complications scale compared to those in the control group (see Table 1). All testing was conducted after age correction for prematurity. Infants ranged from 1531 to 5072 grams at birth ($Means = 3142.01, SD = 567.33$). When these analyses were repeated after using gestational age as covariate, the differences in birth weight and length remained significant ($p < .01$). However, there were no significant associations between any of the perinatal risk variables and the other variables in the model. Finally, we conducted a MANOVA with the behavioral and physiological measures of empathy as the dependent variables and child sex and group status as the independent variables to explore

the possibility of child sex by group status interactions. The findings of this MANOVA indicated that child sex did not moderate the association between PCE and empathic responsiveness, $F(4, 96) = 1.12, p = 0.37$.

2.4 Maternal Substance Use

Results from MANOVA with prenatal substance use variables as the dependent measures and group status as the independent variable yielded a significant multivariate effect of group status, $F(4, 96) = 7.05, p < .001$. As expected, mothers in the CE group were heavier users of cigarettes, alcohol, and cocaine during pregnancy (see Table 1). There was no group difference in marijuana use.

2.5 Sex and Foster Care Differences

MANOVAs with child sex as the independent variable and the two behavioral and two physiological empathy variables as the dependent measures indicated no significant sex differences in empathic responsiveness, $F(4, 91) = 1.2, p = .32$. Thus, child sex was not included in as a covariate in the testing of the overall model.

MANOVA with foster care status as the independent variable and the two behavioral and two physiological empathy variables as the dependent measures yielded a significant multivariate effect for foster care status, $F(4, 91) = 2.60, p = .041$. Children in foster care had an increase in RSA during the empathy task whereas children who were not in foster care showed the expected decrease in RSA during the empathy task (Means = .014 and -.01, Standard Deviations = .03, .04, respectively). Thus, foster care status was used as a covariate in model testing.

2.6 Model Testing

Correlations among variables in the model are depicted in Table 2. As noted in Table 2, prenatal alcohol exposure, prenatal cigarette exposure and gestational age were each marginally associated with change in RSA. In addition, prenatal cocaine exposure, maternal postnatal alcohol consumption and foster care status were each significantly associated with change in RSA. None of the exogenous variables were associated with either of the behavioral measures of empathy.

MANOVA with cocaine group status as the independent variable and the two behavioral and two physiological empathy variables as the dependent measures indicated no significant group differences in behavioral empathic responsiveness (see Table 3). However, cocaine-exposed children had significantly smaller increases in HR and significantly smaller decreases in RSA during the empathy task than nonexposed children.

The hypothesized model tested the association between maternal cocaine use during pregnancy and physiological and behavioral responsivity during an empathy-eliciting task at three years of age. The model also included the within time covariance between physiological and behavioral responsivity during the empathy task. Foster care status, gestational age, prenatal exposure to cigarettes and alcohol, maternal education and postnatal maternal alcohol consumption were included as covariates in the model (see Figure 1). Goodness of fit indices indicated that this hypothesized model fit the data well, ($\chi^2(1) = 1.84, p = .18$, comparative fit index = 0.99, root mean square error of approximation = .06 (.00, .21). The structural paths indicated that children who were prenatally exposed to cocaine and cigarettes, and children with lower gestational age, had lower RSA reactivity. However, prenatal substance exposure was not associated with behavioral responsivity during empathy. In addition, mothers who consumed more alcohol, postnatally, had children with greater RSA reactivity and lower behavioral responsivity.

2.7 Within-group Associations between Behavioral and Physiological Measures of Empathy

We then conducted correlational analyses to further explore the association between behavioral and physiological responsivity within exposed and nonexposed children. Among exposed children, change in RSA during the empathy task was not associated with personal distress, $r = .03$, $p = .85$, or sympathy, $r = -.04$, $p = .76$. However, among nonexposed children, change in RSA was significantly associated with personal distress, $r = -.42$, $p = .005$, but no sympathy, $r = .02$, $p = .89$. Thus, nonexposed children who have higher levels of personal distress show higher levels of physiological regulation as indicated by greater decreases in RSA. However, there is no association between personal distress and physiological regulation among exposed children.

3. Discussion

We hypothesized that maternal cocaine use during pregnancy would be associated with lower behavioral and physiological responsivity during an empathy task at three years of age. As hypothesized, cocaine-exposed children had less RSA suppression during the empathy task than nonexposed children. This finding is similar to previous work that has shown biological differences in empathic responsivity between exposed and nonexposed children. Specifically, Jones and colleagues (2004) found that cocaine-exposed children had greater right frontal EEG asymmetry in response to infant crying, indicating increased negative affect (Jones et al., 2004), than nonexposed children. However, EEG is a measure of central nervous system responsivity rather than a measure of autonomic functioning. Thus, our findings are the first to suggest that there are differences in autonomic regulation during an empathy task between exposed and nonexposed children during early childhood.

Decreases in RSA are believed to indicate an attempt to regulate arousal as attention becomes more focused on environmental events (Calkins, 1997; Calkins and Dedmon, 2000). Thus, one possible explanation for the failure of the cocaine-exposed children to suppress RSA is that the empathy task did not increase their arousal enough to require physiological regulation. This explanation is supported by the finding that heart rate increased significantly less during the empathy task among cocaine-exposed children than it did among nonexposed children. However, there were behavioral responses for both the exposed and nonexposed children during the empathy task. Although there were no group differences in the magnitude of their responses, both exposed and nonexposed children displayed signs of personal distress during the empathy task. Thus, children in both groups were impacted enough by the empathy task to respond behaviorally. However, only the nonexposed children showed signs of physiological regulation.

Previous work has suggested that children who are unable to regulate themselves physiologically in response to their increased arousal to the distress of others may be more concerned with self-comforting than with the reactions of the individuals in distress (Gill & Calkins, 2003). Overarousal that persists as the result of failure to regulate is one process that may interfere with the ability to display concern for others (Young, Fox, & Zahn-Waxler, 1999). This has important implications for the development of prosocial behaviors (Eisenberg et al., 1996).

Empathy is widely believed to contribute to the quality of social relationships and social competence (Davis, 2004). Furthermore, reduced concern towards others is an indicator of externalizing behavior problems in children (APA, 2013). Children with higher levels of externalizing behaviors such as aggression have been found to have poorer physiological regulation during environmental challenge (Calkins & Dedmon, 2000). Thus, indicators of

the ability to regulate should be considered in future studies examining the development of both prosocial behaviors and externalizing behavior problems among exposed children.

Closer examination of the pattern of behavioral and physiological responses within groups indicated that personal distress was associated with physiological regulation for the nonexposed children but not for the exposed children. This lack of concordance between behavior and physiology may be one indicator of dysregulation, especially under stressful contexts. In fact, asynchrony between behavioral and physiological responses to environmental challenge have been found in other high-risk samples including children born very low birthweight (Erickson, MacLean, & Lowe, 2013) and at lower gestational ages (Jansen et al., 2010). This asynchrony may be one process or mechanism linking substance exposure to developmental risk. Future studies may well examine if this index of dysregulation is predictive of clinical outcomes among high risk children.

Importantly, higher postnatal maternal alcohol consumption was associated with less RSA suppression during the empathy task. Recent research indicates that there are developmental changes in the parasympathetic nervous system after birth. The autonomic responses of young children to challenge are believed to be influenced by ongoing exposure to stressors as well as the way in which their caregivers respond to and cope with these stressors (Alkon et al., 2006). Since maternal alcohol consumption is associated with a range of nonoptimal developmental influences, including more negative mother-infant interactions (Lowe, Handmaker and Aragon, 2006), the association between higher maternal postnatal alcohol consumption and reduced RSA suppression in this sample may reflect the impact of a chronic stressor on parasympathetic nervous system development.

The findings of this study as well as those of previous studies also suggest that gestational age is one factor that may impact RSA. According to Porges (1996), the neural regulation of autonomic functioning is sensitive to a range of perinatal factors that may disrupt the development of self-regulatory skills. This is particularly true for reactivity responses which do not demonstrate the stability of resting physiological states (Bornstein and Suess, 2000). For example, several studies have found that RSA responses of nonexposed preterm infants during attention tasks differ from those of full-term infants (Richards, 1994; Stroganova, Posikera, Pisarevski, and Testlin, 2006). Similarly, in samples of cigarette-exposed (Schuetze, Eiden, Colder, Gray and Heustis, 2011) and alcohol-exposed infants (Oberlander, Jacobson, Weinberg, Grunau, Molteno and Jacobson, 2010) gestational age has been associated with differences in RSA suppression during environmental challenge. Thus, these findings lend support to a growing body of evidence suggesting that perinatal experiences are associated with change in RSA during exogenous stimulation.

This study has several limitations, in addition to those mentioned previously. First, accurate assessment of substance use both prenatally and postnatally is difficult. Pregnant and postpartum women are often hesitant to divulge substance use information, particularly illicit substances such as cocaine. One strength of this study is the use of multiple methods to ascertain prenatal substance use which partially mitigated this limitation even though the urine toxicology information was abstracted from medical records. However, measures of prenatal use were retrospective. This has some advantages as well as limitations. One advantage is that cocaine using women are less likely to present for prenatal care and may be missed in prenatal recruitment (Brady et al., 2003). Another advantage is that some women are more likely to acknowledge drug use postnatally after a successful delivery than in the prenatal period (Pickett et al., 2009). There are disadvantages as well, with the primary disadvantage being retrospective recall of drug use data. We attempted to address this by including well validated measures for retrospective recall such as the timeline follow-back and use of hair samples that reflects drug use over at least the last trimester for

most women, and longer given adequate hair length. A second limitation is that the measure of empathic responsivity was brief, involving only the auditory sense and was limited to a single task. A different measure of empathy that was presented to multiple sensory modalities may have been more effective at eliciting empathy-related behavior and physiological responding. However, this procedure was effective in eliciting physiological responsivity in the nonexposed children. Thus, future studies using multiple tasks to elicit empathy should explore the possibility that cocaine-exposed children have lower physiological responsivity even in the face of similar behavior responsivity, and that this may be a particularly important mechanism to later social risk behaviors.

In spite of these limitations, the study fills an important gap in the literature in the examination of responsivity during nonfrustrative emotional challenges. These results highlight the differences in autonomic regulation among cocaine-exposed children relative to nonexposed children and provide support for the idea that physiological, but not behavioral regulation is altered for a range of emotional experiences. This mismatch between physiology and behavior may be a salient marker of dysregulation that needs further attention.

Acknowledgments

The authors thank parents and children who participated in this study and the research staff who were responsible for conducting numerous assessments with these families. Special thanks to Drs. Amol Lele and Luther Robinson for collaboration on data collection at Women and Children's Hospital of Buffalo, and to Dr. Michael Ray for his collaboration on data collection at Sisters of Charity Hospital of Buffalo. This study was made possible by a grant from NIDA (R01 DA 013190).

Abbreviations

RSA	Respiratory Sinus Arrhythmia
BRSA	Baseline Respiratory Sinus Arrhythmia
HR	Heart Rate
PCE	Prenatal Cocaine Exposure
CE	cocaine exposed
NCE	noncocaine exposed
TLFB	Timeline Followback Interview
IBI	Interbeat Interval

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Highlights

- Empathic responsivity and prenatal cocaine exposure (PCE) at 3 years of age.
- Respiratory sinus arrhythmia (RSA) obtained during exposure to infant crying.
- PCE, postnatal alcohol, gestational age associated with physiological responsivity
- Only postnatal alcohol exposure was associated with behavioral responsivity.

Figure 1.
Final Model

Table 1

Group Differences in Demographic Variables and Birth Outcomes

Exposure Group:	Non-Cocaine		Cocaine		F value	η^2
	<u>M</u>	<u>SD</u>	<u>M</u>	<u>SD</u>		
Demographics:						
BM age	28.22	5.20	31.46	5.74	8.66**	.08
BM parity	3.12	1.73	4.23	2.67	5.02*	.05
Years education	12.24	1.76	11.75	1.57	2.20	.02
Birth outcomes:						
Gestational age (weeks)	39.53	1.08	38.74	1.88	6.12*	.06
Birth weight (gms)	3458.38	559.07	2982.91	526.26	8.32**	.16
Birth length (cm)	50.73	2.24	48.41	3.03	17.73**	.16
Head circumference (cm)	33.71	1.43	33.16	1.47	3.35+	.03
OCS	101.95	17.08	83.58	14.9	31.62**	.25
Prenatal substance use:						
Cigarettes/week	6.23	14.76	31.87	36.55	19.54**	.17
Drinks/week	.07	.16	4.71	13.67	5.18*	.05
Joints/week	1.53	7.8	1.07	3.24	.17	.00
Days cocaine/week	0	0	.98	1.56	17.62**	.15
Postnatal substance use:						
Cigarettes/day	1.68	3.26	5.49	6.75	12.05**	.14
Drinks/day	2.15	1.97	2.35	3.18	.15	.00
Joints/day	1.06	2.89	.62	1.02	1.15	.01
Days cocaine	0	0	19.49	74.25	3.10+	.03
Foster Care	4% (n=4)		40% (n=46)			

Note. BM: biological mother; OCS: Obstetrical complications scale score; high scores are more optimal.

+ $p < .10$

* $p < .05$

$10^3 > d$
**

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Table 2

Correlations among variables

	1	2	3	4	5	6	7	8	9
1. Cocaine Group Status									
2. # Cigarettes/week Pregnancy	0.41**								
3. # Drinks/week Pregnancy	0.22*	0.39**							
4. Years education	-0.11	-0.34**	-0.31**						
5. Foster Care Status	0.43**	0.26**	0.09	.004					
6. Gestational Age	-.25*	-0.15	0.08	-.13	-.29**				
7. # Drinks/week Postnatal	-0.001	0.09	0.03	0.03	-0.11	0.24*			
8. RSA Change/Empathy	0.28**	.19+	0.19+	0.02	0.28**	-.19+	.24*		
9. Personal Distress	-0.02	.07	0.04	0.02	0.08	-0.08	0.04	0.14	
10. Concern/Sympathy	0.04	0.05	0.06	-0.03	0.15	0.01	0.20+	0.01	0.43**

Notes: RSA = respiratory sinus arrhythmia;

+ $p < .10$ * $p < .05$ ** $p < .01$

Table 3

Group Differences in Empathic Responsivity

Exposure Group:	Non-Cocaine	Cocaine		F value	η^2
	<u>M</u>	<u>SD</u>	<u>M</u>		
Behavioral Responses:					
Personal Distress	3.22	0.96	3.30	0.97	.00
Sympathy	2.01	1.16	2.16	1.33	.43
Physiological Responses:					
Change in HR	4.23	4.69	1.36	3.73	12.39**
Change in RSA	-.033	.03	-.01	.04	4.03*

Notes. HR: heart rate, RSA: respiratory sinus arrhythmia. Change variables are from baseline to empathy task.

+ $p < .10$

* $p < .05$

** $p < .01$