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Maternal cocaine use and mother–toddler aggression

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ABSTRACT

This study examined the direct and indirect associations between maternal cocaine use during pregnancy and mother–toddler aggression in an interactive context at 2 years of child age. We hypothesized that in addition to direct effects of cocaine exposure on maternal and child aggression, the association between maternal cocaine use and mother–toddler aggression may be indirect via higher maternal psychiatric symptoms, negative affect, or poor infant autonomic regulation at 13 months. Participants consisted of 220 (119 cocaine exposed, 101 non-cocaine exposed) mother–toddler dyads participating in an ongoing longitudinal study of prenatal cocaine exposure. Results indicated that mothers who used cocaine during pregnancy displayed higher levels of aggression toward their toddlers compared to mothers in the control group. Results from model testing indicated significant indirect associations between maternal cocaine use and maternal aggression via higher maternal negative affect as well as lower infant autonomic regulation at 13 months. Although there were no direct associations between cocaine exposure and toddler aggression, there was a significant indirect effect via lower infant autonomic regulation at 13 months. Results highlight the importance of including maternal aggression in predictive models of prenatal cocaine exposure examining child aggression. Results also emphasize the important role of infant regulation as a mechanism partially explaining associations between cocaine exposure and mother–toddler aggression.

Maternal cocaine use during pregnancy is associated with higher levels of aggression in both the mother and the child. However, the majority of studies focusing on maternal aggression have used animal models. In contrast, a number of animal and human studies report higher levels of child aggression among prenatally cocaine exposed compared to non-exposed children. The majority of human studies are restricted to school aged children. For instance, Bendersky et al. (2006) reported high levels of child aggression as measured by caregiver, teacher, and child reports among cocaine exposed children at age 5. The association between cocaine exposure and high levels of child aggression remained for cocaine exposed boys in the same sample at 10.5 years of age (Bennett et al., 2007). Others have reported high levels of aggression among cocaine exposed girls without prenatal alcohol exposure at 6–7 years of age (Sood et al., 2005), and for cocaine exposed children in foster care at age 6 (Linares et al., 2006). Animal studies are supportive of these results indicating higher aggression in cocaine exposed compared to non-exposed rats (Johns et al., 1994; Wood and Spear, 1998), and higher frequency and duration of aggression among cocaine exposed male rats (Johns and Noonan, 1995). Thus, maternal cocaine use is likely to be associated with high levels of child aggression. However, none of the studies examining child aggression among cocaine exposed children has included levels of maternal aggression toward the child in their predictive models.

A number of animal studies have reported increases in maternal aggression following gestational cocaine treatment (Heyser et al., 1992; McMurray et al., 2008). These results seem to vary by chronic vs. acute cocaine treatment and by the number of postpartum days at time of assessment and has been attributed to the effect of cocaine on oxytocin levels in the postpartum period (Heyser et al., 1992; Johns et al., 1995; McMurray et al., 2008). In spite of the accumulation of animal studies indicating consistent associations between gestational cocaine treatment and maternal aggression, few human studies have addressed this issue directly. However, a number of studies have reported higher levels of aggression among cocaine dependent adults (Davis, 1996; Licata et al., 1993; Murray et al., 2008). For instance, in a study of substance dependent men and women in treatment, Murray et al. (2008) reported that cocaine use was significantly associated with physical and psychological aggression toward people other than intimate partners. Others have reported increases in aggression after onset of cocaine use and associations between cocaine use and laboratory measures of aggression (Licata et al., 1993).

In addition to the potential for direct effects of cocaine use itself on maternal aggression, maternal cocaine use could also be considered as a marker variable for a number of associated risk factors that are not only associated with cocaine use, but are also known to be consistent

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predictors of maternal and child aggression. These include children's autonomic regulation, maternal psychopathology, and maternal parenting behavior. These indirect paths are explicated below.

There has been accumulating evidence that prenatal cocaine and other substance exposure may be associated with poor autonomic regulation from the neonatal period to later infancy (Bard et al., 2000; Mehta et al., 1993; Schuetze and Eiden, 2006; Schuetze et al., 2009a, 2009b; Silvestri et al., 1991). Similarly, cocaine and other substance using mothers generally report more psychiatric symptoms compared to non-cocaine-using mothers (Bendersky et al., 1996; Eiden et al., 2007; Singer et al., 1995; Woods et al., 1993). Evidence from both animal and human models indicates that cocaine use may be associated with alterations in maternal behavior during interactions with offspring (Johns et al., 1995; Molitor et al., 2003; Tronick et al., 2005). Other variables such as child gender have been primarily conceptualized as a moderator of risk.

One physiological system that supports infant social behaviors and provides a guide for maternal behavior is the parasympathetic branch of the infant autonomic system. This system allows for quick changes in metabolic inputs and outputs from the heart and facilitates behaviors necessary for social exchanges and can be indexed by RSA which is a measure of the variability in heart rate that occurs at the frequency of respiration. Two commonly used measures of parasympathetic regulation are vagal tone or respiratory sinus arrhythmia (RSA) during rest, and vagal reactivity indexed by change in RSA in response to challenge (Porges, 1991, 2007). In response to challenge, the vagus acts as a brake to accelerate cardiac and metabolic output and this may be indexed by a decrease in RSA (Bornstein and Suess, 2000; Porges, 1996, 2007). These changes in RSA in response to challenge reflect an ability to respond to rapidly changing environmental inputs, changes in social signals that underlie interpersonal interactions (Beauchaine, 2001) and the initiation of coping strategies to manage affective and behavioral arousal (Calkins, 1997).

There is emerging evidence that prenatal cocaine exposure may be associated with poor autonomic regulation, although with a few exceptions, the majority of these studies have been limited to the neonatal period. For instance, studies have reported lower heart rates (Silvestri et al., 1991) greater high-frequency power as a portion of total spectral power (Mehta et al., 1993) and greater overall heart rate variability (Regalado et al., 1996, 2001) in cocaine-exposed compared to non-cocaine-exposed neonates. These studies suggest increased parasympathetic activity during rest among cocaine-exposed neonates. Beyond the neonatal period, a small number of studies indicate that cocaine exposed infants exhibited lower parasympathetic regulation during sleep at 4–8 weeks of age (Schuetze and Eiden, 2006) and an increase in RSA from rest to challenge instead of the more adaptive decrease in RSA at 7 and 13 months of infant age (Schuetze et al., 2009a, 2009b).

RSA measures in infancy may be predictive of both maternal behavior and child outcomes. For instance, infant RSA is predictive of mother–infant affect synchrony (Feldman, 2006), maternal affiliation, and affectionate touch (Feldman, 2007), and lack of RSA decrement in response to challenge is associated with higher maternal negative and controlling behaviors (Calkins et al., 1998). Similarly, low RSA decrement in infancy is associated with higher rates of mother reported child aggression and internalizing problems in the preschool period (Porges, et al., 1996), and concurrently within the elementary school years under conditions of risk (El-Sheikh et al., 2009). A decrement in RSA in response to challenge is associated with more adaptive functioning (Calkins and Dedmon, 2000; El-Sheikh et al., 2001; El-Sheikh and Whitson, 2006). Thus, RSA change may be a critical predictor of both maternal and child aggression.

Several studies have demonstrated associations between maternal psychiatric symptoms such as depression and child behavior problems including aggressive behavior (Downey and Coyne, 1990; Elgar et al., 2003; Goodman and Gotlib, 1999). Studies have demonstrated that indices of maternal mood such as depression have concurrent, bi-directional, and prospective associations with child aggression across a wide age range (Elgar et al., 2003). The role of maternal psychiatric symptoms may be particularly relevant among substance using mothers given the comorbidity of maternal substance use and psychiatric symptoms (Bendersky et al., 1996; Eiden et al., 2007; Singer et al., 1995; Woods et al., 1993). Maternal psychiatric symptoms may also be conceptualized as a mediator of risk such that cocaine using mothers and their children may experience higher levels of psychiatric symptoms and this in turn may increase the risk for higher maternal and child aggression.

Cocaine-exposed children also experience greater risk for poor parenting. Although parenting behavior has not often been examined as a predictor or mediator of outcome in cocaine exposed samples (see Bennett et al., 2002, for an exception), it is associated with maternal substance use and is a consistent and significant predictor of children's aggression in other samples (Conger et al., 2003; Kim et al., 2003). Cocaine-using mothers have been reported to display higher negative affect toward their infants compared to non-using mothers (Burns et al., 1997; Eiden et al., 2009). High levels of maternal negative affect have been consistently associated with high levels of maternal and child aggression across a number of studies (e.g., Conger et al., 2003; Kim et al., 2003; Rubin et al., 2003, 1998). Thus, in addition to infant autonomic regulation, maternal psychiatric symptoms, and environmental risk, maternal negative affect toward the child during infancy may serve as a mediator of the association between prenatal cocaine exposure and child aggression in the toddler period.

To add to this complexity, the majority of cocaine using mothers also use other substances such as alcohol, cigarettes, and marijuana. Results from several studies, both animal and human, indicate that prenatal alcohol and cigarette exposure may have significant effects on children's aggression and may be associated with high levels of maternal aggression (see Dixon et al., 2008 review; Wakschlag and Hans, 2002). Thus, the association between prenatal cocaine exposure and mother–toddler aggression can only be examined in the context of comorbid substance use.

Based on this literature, we hypothesized that prenatal cocaine and/or other substance exposure would be associated with maternal and toddler aggression at 24 months of child age. These associations may be direct, or indirect via infant autonomic regulation, maternal psychiatric symptoms, and maternal negative affect measured at 13 months. Thus, we tested an a priori model that included these variables as intervening variables between prenatal substance exposure and toddler behavior problems. Given the literature on sex differences in child aggression and some empirical evidence indicating that the association between prenatal substance exposure and child aggression may be moderated by child gender (Nordstrom Bailey et al., 2005; Delaney-Black et al., 2004), we examined child gender as a moderator of risk.

1. Method

1.1. Participants

The sample consisted of 220 mother–infant dyads participating in an ongoing longitudinal study of prenatal cocaine exposure (119 cocaine exposed, 101 not cocaine exposed). 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 220 children, 108 (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 gender. 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 interviews and infant assessments were conducted at 4–8 weeks, 7 and 13 months of infant age, and mother–child interactions in a number of different observational contexts were videotaped at 24 months of age. By 24 months of toddler age, 23 toddlers in the cocaine group had been removed from parental care and placed in non-parental care. Of these 23 infants, 67% were placed in non-kin care, with the remainder being cared for by a grandmother or maternal aunt. 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 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 4800 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. Mothers who participated were also more likely to be in the cocaine group (with a participation rate of 91% among cocaine group eligible) 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 (g), 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 Psychemedics 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 in. 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 in.), 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).

Approximately 32% of mothers in the study (55% of the mothers in the cocaine group) had positive urine toxicologies at delivery, and 25% of mothers (79% of the mothers in the cocaine 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 h).

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. Average number of cigarettes per week, number of standard drinks per week, and number of joints per week were used as measured indicators of the latent construct reflecting maternal substance use other than cocaine. Confirmatory factor analysis with these three indicators (cigarettes, alcohol, and marijuana) indicated that average number of joints per week had a poor factor loading. Average number of joints per week was also not associated with cocaine group status (see below), or with the mediators or outcomes examined in this study. Thus, this variable was dropped from model testing. Average number of cigarettes per week and number of standard drinks per week loaded onto one latent factor in model testing, with factor loadings of .50 (drinks per week) and .74 (cigarettes per week) in the context of the larger model.

1.5. Maternal psychiatric symptoms and maternal negative affect

Maternal psychiatric symptomatology was assessed using the Brief Symptom Inventory (BSI; Derogatis, 1993) at 13 months. This scale is a brief form of Symptom Checklist 90-R, and is a widely used mental health screening measure in a variety of clinical and research settings. The measure consists of 53 items rated on a five-point scale. The items are grouped into nine scales of Anxiety, Hostility, Somatization, Obsessive–Compulsive, Interpersonal Sensitivity, Depression, Phobic Anxiety, Paranoid Ideation, and Psychoticism. A positive symptom distress index was computed by summing the items for all the subscales and dividing by the number of items endorsed with a positive response. The BSI subscales have high internal consistency and the measure has been used in a large number of studies, including studies of maternal cocaine use (e.g., Eiden et al., 2007; Singer et al., 2002). Higher scores indicate higher psychiatric symptoms.

Maternal negative affect was assessed using behavioral observations during a Free Play task at 13 months. Mothers were asked to interact with their infants as they normally would at home for 10 min in a room filled with toys. These interactions were coded using a collection of global 5-point rating scales developed by (Clark et al., 1980), with higher scores indicating more positive affect or behavior. The scale for maternal negative affect consisted of items such as angry, hostile tone of voice; expressed negative affect; angry, hostile mood; and displeasure or disapproval or criticism. The maternal negative affect scale had high internal consistency with Cronbach's alpha of .94. Two coders rated maternal behavior. Both coders were trained on the Clark scales by the first author and were unaware of group membership. Inter-rater reliability was conducted on a random selection of 14% ($n = 24$) of the tapes and was fairly high ($r = .90$). Higher scores indicate higher maternal negative affect.

1.6. Infant autonomic regulation

At the 13 month assessment, the physiological assessment of reactivity and regulation was recorded during a 3-minute baseline period, a 2-minute puppet show, a 3-minute inter-task interval and the two arm restraint trials (2 min) by examiners blind to infant group status. Infants were tested while seated in a high-chair. Recording of the physiological data began once the infant was observed to be in a stable, quiet, alert state. A resting state was induced by having the infant watch a three minute segment of a neutral videotape "Baby Einstein" (see Calkins, 1997) for similar procedures for inducing rest. Although this condition was not a true baseline because infant attention was engaged, it served to keep the infant seated quietly without eliciting affect, thereby minimizing movement artifact. All physiological data 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. Disposable electrodes were triangulated on the infant's chest. A respiration bellows was placed at the bottom of the sternum (zyphoid process) 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. 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 (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, for the puppet show, and for each arm restraint trial. The arm restraint paradigm is a widely-used, well-validated measure of anger/frustration used to assess infant regulation and reactivity (Goldsmith and Rothbart, 1988; Stifter and Braungart, 1995). In this episode, the child was allowed to play with an attractive toy for 30 s, until the child was engaged with the toy. The caregiver was asked to stand behind the child, place her hands on the child's forearms, move them to the child's sides, and hold them there for 30 s, while maintaining a neutral expression. After the first trial, the caregiver was again asked to play with the child for 30 s followed by the second trial. The session was stopped at the caregiver's request or if the child reached a maximum distress code, defined as the child reaching the highest intensity of negative affect of a full cry. The child was allowed to play with the toy at the end of the two trials. Because there were no significant differences in RSA between the two trials, we created mean RSA for the two arm restraint trials. To assess autonomic regulation, we calculated a change score for RSA from baseline to arm restraint. Negative scores indicate a decrease in RSA and are reflective of more optimal parasympathetic regulation.

1.7. Maternal and child aggression

Maternal and child aggression were coded during specific segments of the 24 month observational assessments. These included a 10-minute mother–child free play paradigm, a 10 minute clean-up, 8-minute structured play, 10-minute eating a snack, and 5-minute emotion regulation paradigm. Following previous studies (Keenan and Shaw, 1994), this allowed for coding of maternal and child aggression across varying levels of stress, from none (e.g., during free play), to moderate (clean up), to higher levels of stress (emotion regulation paradigm). For free play, mothers were asked to spend some time with their children as they normally would at home in a room with age appropriate toys. This was followed by the clean up paradigm. Mothers were asked to have their children clean up the toys, with the primary responsibility for toy clean up being the child's. During snack, mother–child dyads were presented with a choice of snacks and drinks and spent time eating, and looking at books if they finished eating before 10 min. The structured play situation consisted of a series of goal oriented tasks (e.g., puzzles, sorting, etc.). Mothers

were asked to have the child complete each task. During the 5-minute emotion regulation paradigm, mother–child dyads were left in the room with no toys or activities to interest the child. Mothers were asked to sit at a table and complete questionnaires. This situation is generally stressful for both mothers and reflective of naturalistic situations where they may have competing demands on their attention (Newby and Campbell, 1999).

Aggression was coded on the basis of codes developed in previous studies (Cummings et al., 1989; Keenan and Shaw, 1994). This included physical aggression (hitting, kicking, biting, and pushing) directed toward a person (e.g., to mother or examiner from child and to child from mothers); physical aggression directed toward an object (e.g., banging, throwing, and pounding toys); verbal aggression that consists of cursing (use of obscene language or gestures); and verbal aggression that consists of threats (words used to attack a person or threats of harm). Event coding of each aggressive episode was triggered by the mother or the child displaying any of these behaviors. Each aggressive episode was coded for duration or length of time that episode lasted, and the highest rating of aggression during that episode ranging from 1 = none to 4 = highly aggressive. An overall rating of intensity of maternal and intensity of child aggression was also coded along a 4-point scale ranging from 1 = no aggression to 4 = severely aggressive. For children, average intensity of verbal aggression (average of cursing and threat) ranged from 1 to 1.33 (mean = 1.02, SD = .05), and average intensity of physical aggression (toward mother or object) ranged from 1 to 2.38 (mean = 1.62, SD = .29). Approximately 86% of children displayed no verbal aggression and 12% of children displayed no physical aggression. Average duration of verbal or physical aggression was 204 s (SD = 210.75). For mothers, average intensity of verbal aggression (average or cursing and threat) ranged from 1 to 2 (mean = 1.374, SD = .26). Average intensity of physical aggression ranged from 1 to 2.25 (mean = 1.37, SD = .28). Average duration of verbal or physical aggression was 69.21 s (SD = 96.72). Approximately 21% of mothers displayed no verbal aggression and 21% displayed no physical aggression. However, for both mothers and children, the overall intensity of verbal or physical aggression was low. Thus, the final variables for maternal and child aggression measures consisted of sums and averages across the different types of aggression, with higher scores indicating higher levels of aggression. Three measures of aggression for mothers, and three measures for children were derived from this coding: total duration of aggression during the entire interaction, number of aggressive episodes, and overall intensity of aggression. Confirmatory factor analysis indicated that the three measures of maternal aggression loaded on one factor, with factor loadings ranging from .81 to .93. The three measures of child aggression also loaded on one factor, with factor loadings ranging from .86 to .94.

Two coders blind to group status rated mother and toddler aggression. They were trained by the first author until inter-rater reliability criterion was reached (agreement of 90% or above). Subsequently inter-rater reliability was established on 20% of the tapes. Inter-rater reliability on the six aggression measures (three each for mother and toddler aggression) ranged from intra-class correlations of .81 to .92.

1.8. Data analytic strategy

Group differences in demographics, perinatal risk characteristics, maternal substance use variables, and maternal and child aggression 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. MANOVAs were used to examine group by gender interaction on maternal and child aggression to examine the hypothesis that child gender may moderate the association between cocaine exposure and aggression. Demographic or perinatal risk variables that were associated with both the predictors and outcomes at $p<.10$ were used as covariates in subsequent analyses. Structural equation modeling (SEM) was used to test the hypothesized model with maternal psychiatric symptoms, infant autonomic regulation, and maternal negative affect as intervening variables between maternal substance use and child behavior problems. SEM analyses were conducted using Mplus, Version 5.2 software (Muthén and Muthén, 1998–2004) using full-information maximum likelihood estimation procedures (Arbuckle, 1996). Indirect effects were tested using the bias-corrected bootstrap method. This method has been found to provide a more accurate balance between Type 1 and Type 2 errors compared with other methods used to test indirect effects (MacKinnon et al., 2004). Five hundred bootstrap samples and the 95% bias-corrected confidence intervals (CIs) were used to test significance of indirect effects.

1.9. Missing data

As expected in any longitudinal study, there were some incomplete data for some of the participants at one or more of the four assessment points included in this study. Of the 220 mother–infant dyads who completed the 4- to 8-week laboratory visit, 189 completed the 13 month visit, and 177 completed the 24 month assessment. There were no significant differences between families with complete vs. missing data at 24 months on any demographic or substance use variable. As noted earlier, full-information maximum likelihood was used to estimate model parameters.

2. Results

2.1. Demographics and perinatal risk

Results from MANOVA with the demographic variables as the dependent measures and cocaine group status yielded a significant multivariate effect of group status, $F(4, 215) = 6.51$, $p<.01$. Results from univariate analyses indicated that control group mothers were younger, had lower parity, and higher occupation compared to those in the cocaine group (see Table 1). Correlational analyses with the demographic variables and mediators and aggression variables in the model indicated significant associations between maternal education and maternal psychiatric symptoms ($r = -.20$, $p<.01$), RSA change ($r = -.25$, $p<.01$), and all three indicators of maternal aggression (correlations ranged from $-.20$ to $-.25$, $p<.01$). High levels of maternal

Table 1
Group differences in demographic variables, birth outcomes, and substance use.

Exposure group	Non-cocaine		Cocaine		*F* value	Partial η^2
	M	SD	M	SD		
Demographics						
BM age	27.77	5.60	30.82	6.11	14.57**	.06
BM parity	3.22	1.70	4.15	2.39	10.75**	.05
Years of education	12.02	1.86	11.59	1.84	2.92	.01
Maternal occupation	2.09	1.40	2.55	1.98	4.02*	.02
Birth outcomes						
Gestational age (weeks)	39.34	1.24	38.59	1.85	11.97**	.05
Birth weight (g)	3328.84	504.41	2916.55	538.31	33.95**	.14
Birth length (cm)	49.94	2.91	48.12	3.11	19.38**	.08
Head circumference (cm)	33.60	1.39	33.07	2.10	4.61*	.02
OCS	100.69	17.43	86.24	15.18	42.21**	.17
Cigarettes/week	12.77	25.75	36.99	43.32	24.16**	.10
Drinks/week	.19	.82	3.92	11.47	10.63**	.05
Joints/week	1.45	7.32	1.27	4.15	.05	.00
Days cocaine/week	0	0	.94	1.58	35.42**	.14

Note: BM: biological mother; OCS: obstetrical complications scale score, high scores are more optimal.
** $p<.01$.
* $p<.05$.

education were associated with low levels of psychiatric symptoms, a decrease in RSA from baseline to arm restraint, and low duration, episodes, and intensity of maternal aggression. Low levels of maternal education were also associated with high levels of cigarette and alcohol use during pregnancy (r = −.24 and −.22 respectively, p<.01). Thus, maternal education was used as a covariate in model testing. None of the other demographic variables was associated with the variables in the model (p>.10).

Univariate ANOVA with perinatal outcomes and obstetrical complications indicated that cocaine exposed infants had lower gestational age, birth weight, birth length, and cocaine using mothers had higher scores on the obstetrical complications scale compared to those in the control group (see Table 1). 11% of cocaine exposed infants (ranged from 33 to 41 weeks) and 3% of the control group infants (ranged from 36 to 42 weeks) were preterm (<37 weeks gestational age). Cocaine exposed infants were significantly more likely to have been preterm than control infants, Pearson chi-square = 7.76, p<.01. All testing was conducted after age correction for prematurity. Infants ranged from 1531 to 5072 g at birth (M = 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 mediators or aggression variables used in the model (p>.10). MANOVA with child sex as the independent variable and the three maternal aggression variables as the dependent measures indicated a significant multivariate effect of child gender, F(3, 166) = 3.65, p = .01. Univariate analyses indicated that mothers displayed higher duration (means = 7.65 and 5.17, SD = 5.46 and 4.93), episodes (means = 7.44 and 5.05, SD = 5.35 and 5.10), and intensity (means = 2.18 and 1.57, SD = 1.25 and 1.16) of aggression toward boys compared to girls. Thus, child gender was included in model testing as a covariate.

2.2. Maternal substance use and other variables

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, 215) = 11.46, p<.001. As expected, mothers in the cocaine group were heavier users of cigarettes, alcohol, and cocaine during pregnancy (see Table 1). There was no group difference in marijuana use. These results remained unchanged when the 23 foster care mothers were excluded from the analyses. All 23 of these children were in the cocaine group. There were no significant differences between biological care vs. foster care on maternal or child aggression for the sample as a whole. However, among cocaine exposed children, those in foster care had lower number of aggressive episodes (means = 3.57 and 5.60, SD = 3.04 and 3.74) and lower intensity of aggression (means = 1.48 vs. 1.94, SD = .98 vs. .86) compared to cocaine exposed children who were in the care of their biological parent. Similarly, foster care mothers of cocaine exposed children displayed lower intensity of aggression (means = 1.45 vs. 2.28, SD = 1.37 and 1.26). Thus, foster care status was used as a covariate in model testing.

2.3. Group differences in maternal or child aggression

MANOVA with the three maternal aggression variables as the dependent measures and maternal cocaine group status as the independent variable yielded a significant multivariate effect of maternal cocaine use on maternal aggression, F (3, 166) = 2.93, p<.05. Univariate analyses indicated that mothers who used cocaine during pregnancy had higher duration of aggression, displayed more aggressive episodes, and higher intensity of aggression compared to control group mothers (see Table 2). These analyses were repeated with maternal education and other substance use as covariates. There were no group differences on intensity of aggression. Results remained unchanged with regard to duration of aggression and number of aggressive episodes. MANOVA with the three child aggression variables as the dependent measures indicated no significant multivariate or univariate effects of cocaine group status on child aggression. Results remained unchanged with maternal education and other maternal substance use variables as covariates.[1]

Table 2
Group differences in maternal and child aggression.

Exposure group	Non-cocaine		Cocaine		F value	Partial η^2
	M	SD	M	SD		
Maternal aggression						
Duration (in seconds)	47.74	75.44	89.20	109.70	7.86**	.05
# of episodes	5.04	4.19	7.34	6.05	8.23**	.05
Intensity	1.63	1.09	2.09	1.34	5.90**	.03
Child aggression						
Duration (in seconds)	59.76	78.72	48.87	60.94	.94	.006
# of episodes	5.54	4.01	5.10	3.65	.51	.00
Intensity	1.99	.95	1.82	.92	1.20	.008
Maternal psychiatric S	130.95	26.02	132.06	29.06	.08	.00
Maternal NA	4.66	.54	4.36	.80	7.84**	.05
RSA change	−.01	.02	.01	.03	17.85**	.11

Note: S: symptoms; NA: negative affect, RSA: respiratory sinus arrhythmia.
** p<.01.

2.4. Model testing

Correlations among variables in the model are depicted in Table 3. At the bivariate level, mothers who smoked more cigarettes during pregnancy displayed higher duration and intensity of aggression during interactions with their toddlers. Maternal alcohol use was marginally associated with higher maternal aggression. Higher maternal negative affect at 13 months was associated with higher maternal aggression at 24 months, perhaps reflecting stability in negative affect/aggression across time. Lower infant autonomic regulation was associated with higher maternal and child aggression at 24 months.

The hypothesized model tested included maternal psychiatric symptoms, maternal negative affect, and infant autonomic regulation as potential mediators or intervening variables between maternal substance use and mother–child aggression. The model also included covariances among the residuals of intervening variables, between maternal substance use and cocaine group status, and between maternal and child aggression at 24 months. Maternal education and foster care status were used as covariates in the model. Goodness of fit indices indicated that the structure of our hypothesized model provided a good fit to the data (χ^2(65) = 76.89, p = .15, comparative fit index = .99, root mean square error of approximation = .03 (.00, .05)). This indirect effects model was contrasted with a model that included direct paths from maternal cocaine use to maternal and child aggression. Results indicated that the addition of these direct paths did not improve the fit of the model, $\Delta\chi^2(2) = 3.61$, p = NS. Thus, the final model displayed in Fig. 1 did not include these direct paths. The latent variable for maternal cigarette and alcohol exposure was associated with cocaine group status. The residuals of maternal and child aggression were associated with each other. Maternal education

[1] We examined bivariate association between postnatal cocaine and other substance use and maternal and child aggression. At the bivariate level, number of days used cocaine postnatally was significantly correlated with number of maternal aggressive episodes (r = .19, p<.05) and intensity of maternal aggression (r = .19, p<.05). Number of cigarettes per day was also correlated with number of maternal aggressive episodes (r = .15, p<.05) and intensity of maternal aggression (r = .23, p<.01). However, when these postnatal variables were included in the model, neither of these variables accounted for unique variance on maternal or child aggression and thus, the final model did not include these variables.

Table 3
Correlations among study variables.

	1	2	3	4	5	6	7	8	9	10	11	12
1. Cigs/week: Preg.												
2. AA/week: Preg.	**.34**											
3. Group status	**.32**	**.22**										
4. Foster care status	.16*	.09	**.37**									
5. Maternal PS 13 months	**.20**	−.01	.02	**−.21**								
6. Maternal NA: 13 months	−.02	.02	**.21**	−.03	−.06							
7. RSA change 13 months	.10	.19*	**.33**	.11	−.05	.10						
Maternal aggression												
8. Duration	.16*	.11	**.21**	−.06	.11	**.33**	**.23**					
9. # of episodes	.13	.14	**.22**	−.06	.01	**.31**	**.27**	**.86**				
10. Intensity	.15*	.13	.18*	−.13	.11	**.33**	**.22**	**.87**	**.86**			
Child aggression												
11. Duration	−.01	−.00	−.08	−.10	−.01	.05	.17*	**.42**	**.39**	**.41**		
12. # of episodes	.02	.10	.01	−.14*	−.01	.04	**.23**	**.46**	**.46**	**.43**	**.74**	
13. Intensity	.02	.02	.01	−.12	.03	.01	.15*	**.46**	**.45**	**.51**	**.64**	**.81**

*p<.05, p<.01 in bold face. Cigs: cigarettes, Preg.: pregnancy, AA: average # of standard drinks, PS: psychiatric symptoms, NA: negative affect.

was negatively associated with the residual of RSA change, and foster care mothers had lower psychiatric symptoms.

The structural paths indicated that mothers in the cocaine group had higher levels of negative affect during play interactions with their 13 month old infants and these infants had poorer autonomic regulation at 13 months above and beyond other drug use. High levels of maternal cigarette and alcohol use during pregnancy were associated with high levels of maternal psychiatric symptoms at 13 months, but maternal psychiatric symptoms did not predict maternal or child aggression. Maternal negative affect during play interactions with infants at 13 months was associated with high levels of maternal aggression during mother–child interactions at 24 months, perhaps reflecting stability in maternal negative behavior during interactions from infancy to the toddler period. Poorer autonomic regulation at 13 months was associated with high levels of maternal and child aggression at 24 months. Mothers of boys displayed higher aggression compared to mothers of girls, and boys were more aggressive compared to girls. Children in foster care had lower aggression at 24 months, and mothers with higher education had lower aggression at 24 months.

Our model included hypotheses about several indirect effects. The association between maternal cocaine use and maternal aggression via higher maternal negative affect in infancy was statistically significant (B = .36, 95% CI: .1–1.89), as was the indirect via infant autonomic regulation (B = −.56, 95% CI: .045–1.61). Similarly, the indirect association between maternal cocaine use and child aggression via autonomic regulation in infancy was significant (B = −.37, 95% CI: .09–1.09).

2.5. Moderation by child gender

We examined moderation by child gender using MANCOVA, as sample size limitations did not permit full multiple group SEM analyses. MANCOVA with maternal aggression variables as the dependent measures, child gender and cocaine group status as the independent variables, and other substance use and maternal education as covariates indicated no significant group by gender multivariate or univariate interaction effects on maternal aggression (p>.10). Similarly, MANCOVA with child aggression variables as the dependent measures, child gender and cocaine group status as the independent variables and other substance use and maternal education as covariates indicated no significant group by gender multivariate or univariate interaction effects on child aggression (p>.10). Thus, child gender did not moderate the association between prenatal cocaine exposure and maternal or child aggression.

3. Discussion

The purpose of this study was to examine if prenatal cocaine and other substance exposure was associated with higher maternal and

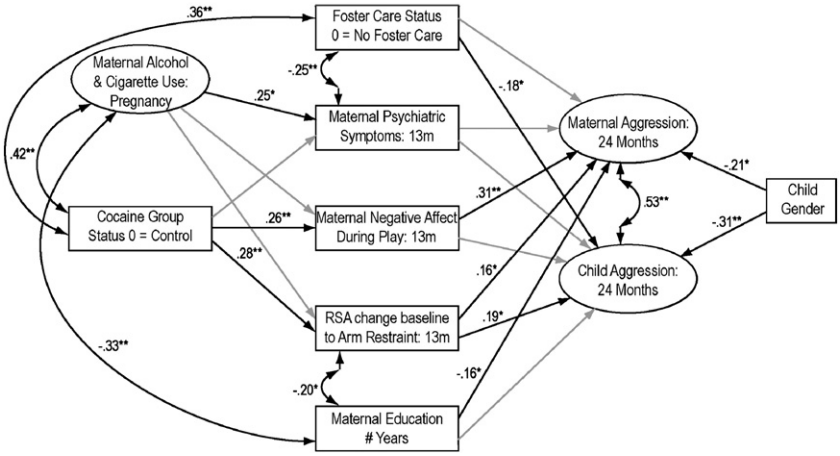

Fig. 1. Results of structural equation modeling. The numbers represent standardized path coefficients. Non-significant paths included in the model are in grey. The model included covariances among the residuals of mediators, maternal education, and foster care status, but only the significant covariances are presented in the figure for ease of presentation. The R^2 for maternal aggression was .24 and for child aggression was .16.

child aggression during observations at 24 months, and if these associations were mediated by maternal psychiatric symptoms, negative affect, or infant autonomic regulation. As expected, mothers in the cocaine group displayed greater duration, number of episodes, and intensity of aggression compared to mothers in the control group. These results are supportive of previous studies using animal models indicating that gestational cocaine treatment increases maternal aggression (Heyser et al., 1992; McMurray et al., 2008), and that the effects of chronic gestational cocaine treatment on maternal behavior persist beyond the lactation period (Johns et al., 2005). Although it is possible that it is cocaine use itself and not cocaine use during pregnancy that is predictive of higher aggression, continued postnatal cocaine use from birth to 24 months measured with the TLFB interview was not predictive of maternal or child aggression in the context of model testing despite significant associations at the bivariate level. It should be noted that about a quarter of the children in the cocaine group were in foster care, and thus the results regarding the lack of associations with postnatal used may be somewhat biased. However, we note that when children in foster care were excluded from analyses, our findings did not change. Given prior findings regarding prospective associations between the onset of cocaine use and increased physical and psychological aggression among adults (Licata et al., 1993), it is possible that there may be acute or chronic effects of cocaine on aggression that are not reflected in these data.

Results from model testing indicated that aggression displayed by mothers in the cocaine group was mediated by higher maternal negative affect toward the infant during play interactions as well as lower infant autonomic regulation. The mediated effect via maternal negative affect could reflect stability in aggressive behavior over time since the dimension of maternal negative affect included items such as expressions of displeasure and criticism, expressed negative affect, as well angry/hostile tone of voice. Although few human studies of maternal cocaine use during pregnancy have examined maternal aggression per se, several have examined maternal behaviors related to maternal negative affect. For instance, cocaine using mothers have been reported to display higher negative engagement with their child during the still-face paradigm in infancy (Tronick et al., 2005), less emotional engagement in the infant to toddler period (Gottwald and Thurman, 1994; Molitor et al., 2003), fewer positive reinforcements and more threats of physical discipline in the toddler/preschool period (Bauman and Dougherty, 1983), and more hostile and intrusive behaviors in a structured teaching situation at 3 years of age (Johnson et al., 2002). Thus, the current results are supportive of this body of literature indicating a cascading effect whereby prenatal cocaine use predicts maternal negative affect during infancy, which subsequently predicts maternal aggression in the toddler period.

Fewer studies have examined the role of infant parasympathetic regulation in predicting maternal behavior in general, and maternal aggression in particular. However, Feldman and Eidelman (2007) reported that more adaptive parasympathetic regulation in infancy was predictive of maternal behaviors such as affectionate touch and affiliative behaviors, as well as mother–infant affect synchrony (Feldman, 2006). Similarly, Calkins et al. (1998) reported lower vagal suppression or RSA change from baseline to an affect arousing procedures to be associated with higher maternal negative and controlling behaviors at 24 months of child age. The current results are supportive of these studies indicated that poor parasympathetic regulation in infancy is associated with higher maternal aggression toward the child in the toddler period, controlling for concurrent or within time associations between infant parasympathetic regulation and maternal negative affect. If maternal aggression reflects lack of regulation of maternal emotions in response to challenging interactions with the infant, these results indicate that poor parasympathetic regulation in infancy elicits less regulated behavior from mothers and this is reflected in higher maternal aggression toward the child.

Contrary to expectations, there were no group differences in child aggression, or associations between other substance use and child aggression. This lack of direct association could be a function of child age. Aggression tends to peak between 2 and 3 years of age and exhibit a rapid decline between 3 and 4 years of age (Campbell, 1995; Edwards et al., 2006; Nagin and Tremblay, 1999; Tremblay, 2000). It is possible that the effect of exposure on aggression becomes more apparent with increasing age as the normative and non-normative trajectories for aggression may begin to diverge beyond this age (Edwards et al., 2006). To date, there have been four human studies on the association between prenatal cocaine exposure and aggression, all at older child ages. Bendersky et al. (2006) reported an association between prenatal cocaine exposure and higher child aggression at 5 years of age. These associations remained significant for boys, but not girls at 10.5 years of age (Bennett et al., 2007). Linares et al. (2006) reported that cocaine exposed children in foster care had higher rates of aggression according to maternal report compared to those in maternal care or the control group at 6 years of age. Sood et al. (2005) reported a significant association between prenatal cocaine exposure and higher aggression among girls who did not have concomitant alcohol exposure. Thus, it is possible that aggression for cocaine exposed children may not decline after ages 2–3 as is normative, making group differences larger after this age period.

Although there were no direct associations between prenatal cocaine or other substance exposure and child aggression, there was an indirect association via autonomic regulation in infancy. Cocaine exposed infants had lower RSA change in response to challenge and lower RSA change was associated with higher child aggression during interactions at 24 months of age. These results are supportive of previous studies indicating significant associations between parasympathetic regulation and children's externalizing behaviors more generally (e.g., Porges et al., 1996), and aggression in particular (Lorber, 2004). However, this literature is complex with different patterns of associations with different measures of parasympathetic regulation (resting RSA vs. RSA change). We chose to use the measure of RSA change reflecting vagal reactivity in this study because RSA change may better reflect the ability to respond to environmental demands necessary during social interactions (Beauchaine, 2001). Future studies with measures of both sympathetic (e.g., skin conductance, pre-ejection period) and parasympathetic activity in infancy may well examine the role of both in predicting aggressive behavior during social interchanges in dyadic contexts.

Overall, our pattern of results was supportive of the hypothesized model, indicating good fit to observed data. However, it is possible that some of the variables considered as covariates in our model (e.g., foster care status) may have been better conceptualized as moderators. The current results indicated that unlike previous studies (e.g., Linares et al., 2006), cocaine exposed foster care children had lower levels of aggression compared to cocaine exposed children in biological care, but were not significantly different from the control group children. It is possible that this indicates in part a teratological effect of cocaine that may be buffered by the caregiving environment. However, due to limits of sample size, we were unable to examine if pattern of associations tested in this model was the same for children in foster care vs. biological care. Future studies with larger sample sizes or pooled samples may be better able to examine this issue.

As would be expected, both maternal and child aggression were significantly and moderately associated with each other. Higher levels of maternal aggression were associated with higher levels of child aggression. Future studies measuring maternal and child aggression and multiple time points could examine direction of influence. Some studies have noted that in the early childhood years, the direction of influence during parent–child interactions may be from parent to child. In this case, perhaps the higher levels of child aggression among cocaine exposed children noted in previous studies is a function of higher maternal aggression among cocaine using mothers.

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. The second limitation is that the measure of maternal negative affect was brief, and limited to a single play session. A more representative measure of maternal negative affect may have been predictive of child aggression in addition to maternal aggression. However, this was an objective measure of parenting, as opposed to parent reports of their own parenting behavior and was associated with maternal aggression in theoretically expected ways. The third and important caveat of this study is that both maternal and child aggression were measured in an interactive context, and can only be generalized to this context. Thus, multiple methods of measuring child aggression outside of the interactive context would be more reflective of aggression beyond this context.

In spite of these limitations, the study fills an important gap in the literature on maternal cocaine use in the examination of both maternal and child aggression as outcome variables. An additional strength is the consideration of multiple mediators that included both maternal characteristics and infant regulation. The results highlight the role of infant autonomic regulation as a significant mediator of both maternal and child behavior. The results also suggest the need for caution in interpreting the effects of prenatal cocaine exposure on child aggression without accounting for variations in maternal aggression.

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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