Published in final edited form as:

J Exp Child Psychol. 2015 September ; 137: 12–29. doi:10.1016/j.jecp.2015.02.007.

Prenatal Substance Exposure and Child Self-Regulation: Pathways to Risk and Protection

Rina D. Eiden,

State University of New York at Buffalo, 1021 Main Street, Buffalo, NY 14203

Stephanie Godleski,

State University of New York at Buffalo, 1021 Main Street, Buffalo, NY 14203

Pamela Schuetze, and

Buffalo State College, 1300 Elmwood Avenue, Buffalo NY 14222

Craig R. Colder

State University of New York at Buffalo, 1021 Main Street, Buffalo, NY 14203

Abstract

A conceptual model of the association between prenatal cocaine exposure (PCE) and child self-regulation via maternal harshness and language development was examined. Specifically, the model tested whether PCE was associated with self-regulation either directly or indirectly via high maternal harshness and poor language development. The role of child sex, autonomic reactivity, and cumulative environmental risk as potential moderators was also explored. The sample was 216 mother-child dyads recruited at birth and assessed at 2, 7, 13, 24, 36, and 48 months of child ages. Participating mothers were primarily African American (72%). Results indicated a significant indirect association between PCE and child effortful control at 36 months via higher maternal harshness. Autonomic reactivity moderated the association between maternal harshness and self-regulation, such that among children with poor autonomic reactivity, high maternal harshness was associated with lower conscience at 3 years. Child sex and environmental risk did not moderate the association between PCE and self-regulation. Thus, the quality of caregiving experience played a significant role in the development of self-regulation among PCE children, especially those at higher autonomic risk. In particular, PCE children who also exhibit poor autonomic reactivity may be particularly susceptible to environmental influences such as parenting.

© 2015 Published by Elsevier Inc.

Corresponding author: Rina D. Eiden, Research Institute on Addictions, State University of New York at Buffalo, 1021 Main Street, Buffalo, NY 14203. eiden@ria.buffalo.edu, Phone: (716)887-3350, Fax: (716)887-2510.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

Keywords

Maternal Harshness; Emotion Regulation; Autonomic Reactivity; Cocaine Exposure; Effortful Control

Prenatal Cocaine and Child Regulation

Although initial reports of highly impaired “crack babies” have not been borne out by systematic research on the effects of prenatal cocaine exposure (PCE), well controlled prospective studies indicate significant effects of cocaine on the arousal/attention regulatory system (Lester & Padbury, 2009). Indeed, this is one of the most consistent findings in the cocaine literature across multiple stages of development ranging from the neonatal period to adolescence including diverse methods such as parent reports, behavioral measures, and autonomic reactivity (e.g., Bendersky & Lewis, 1998; Carmody, Bennett, & Lewis, 2011; Coles, Bard, Platzman, & Lynch, 1999; Karmel & Gardner, 1996; Li et al., 2009; Schuetze & Eiden, 2006; Schuetze, Eiden, & Danielewicz, 2009). Recent brain imaging studies have indicated potential mechanisms explaining these associations such as reduction of amygdala response to emotional stimuli during a task demanding high cognitive load among control children, but not among PCE children (Li et al., 2009) and lower ventral prefrontal cortex activation in response to increased cognitive load during this task among PCE children (Li et al., 2013). Animal models are supportive of this literature indicating that prenatal exposure to cocaine results in alterations in attention and arousal regulation among offspring (Gendle et al., 2004) and increases susceptibility to stresses in the environment (Spear, Campbell, Snyder, Silveri, & Katovic, 1998). Thus, both the human and animal literature suggests that PCE has the potential to significantly alter the regulatory system. However, few human studies of PCE have examine specific aspects of self-regulation such as effortful control (see Carmody et al., 2011 for an exception) and conscience nor included mediators or moderators of risk. The purpose of this study was to examine if PCE was associated with two specific aspects of self-regulation, effortful control and conscience, either directly, or indirectly via high maternal harshness and poor language development. A second goal was to examine the role of child sex, autonomic reactivity, and cumulative environmental risk as potential moderators (see Figure 1).

Self-Regulation

As children enter the preschool period, they increasingly use effortful forms of regulation developed through interactions with the caregiving environment (Posner & Rothbart, 2007). Effortful control has been theorized to be an aspect of temperament, with roots in both biological processes (Posner & Rothbart, 2007) and the quality of parent-child interactions (Kim & Kochanska, 2012). It has been defined as actively suppressing a predominant response and performing a subdominant response given environmental demands. It is an aspect of self-regulation that emerges over the second and third years of life and denotes active processes of effortful or willful control of impulses (Rothbart & Ahadi, 1994), and is an important dimension of self-regulation predictive of disruptive and antisocial behaviors in later years (Kooijmans, Scheres, & Oosterlaan, 2000; Rothbart, Posner, & Kieras, 2006).

While effortful control represents the temperamental aspect of self-regulation (Eisenberg, Smith, & Spinrad, 2011), internalization of rules of conduct or development of conscience reflects self-regulated behavior in the absence of surveillance and is an ultimate goal of socialization (Kochanska & Aksan, 1995). In the toddler-to-preschool period, there is a marked shift from external monitoring of child behavior to more self-regulated child behavior in the absence of close supervision. This shift occurs gradually, and parents increasingly monitor their children at a distance as opposed to the close supervision of earlier years. This normative change culminates in children internalizing rules of conduct and following these rules even in the absence of adult supervision. Theories of temperament (Rothbart, 1989) suggest that effortful control plays an important role in the development of conscience. Children who are able to control their own emotions and impulses in response to environmental demands may also be more likely to internalize rules of conduct. Although empirical evidence is supportive of this hypothesis (Kochanska & Knaack, 2003; Kochanska, Murray, & Coy, 1997), few studies have examined bidirectional associations between these two aspects of self-regulation in prospective analyses, controlling for within time associations. Moreover, few have been conducted with high risk samples characterized by poverty, minority group status, and/or prenatal substance exposure.

Predictors of Self-Regulation

Conceptual frameworks of the development of self-regulation (Calkins & Hill, 2007; Eisenberg et al., 2011) suggest that both intrinsic, child driven factors as well as extrinsic factors such as caregiver behavior are important influences on self-regulation. Among child driven factors, individual differences in children's language abilities may play an important role in the development of self-regulation, especially in the preschool years (e.g., Cole, Armstrong, & Pemberton, 2010). Indeed, one optimal strategy for regulating affect and behavior for young children is by communicating needs and using language to regulate negative emotions (Cole et al., 2010). Empirical evidence is supportive of this hypothesis indicating significant associations between language ability and effortful control in early childhood (Allan & Lonigan, 2011; Wolfe & Bell, 2004). The role of language may be especially important among substance exposed children. Several studies of cocaine exposed children have reported deficits in receptive and expressive language and more subtle problems in specific aspects of language development such as phonological processing, semantics, and syntax (Bandstra et al., 2002; Beeghly et al., 2006; Delaney-Black et al., 2000; Lewis et al., 2011). Thus, individual differences in language acquisition may be predictive of both effortful control and conscience, and may be an important intervening variable for the association between PCE and child self-regulation.

Parenting behavior is a potential indirect pathway through which PCE and child self-regulation are associated. The role of parenting behavior in the development of self-regulation has been discussed extensively in the broader developmental literature (e.g., Calkins & Hill, 2007; Eisenberg et al., 2011; Kochanska & Aksan, 1995). A number of parenting dimensions have been implicated as being critical for the development of optimal self-regulation. However, one of the most critical aspects of parenting that has long been known to have a detrimental impact on self-regulation is maternal power assertion, negativity, or harshness in the context of mother-child interactions (Kochanska & Knaack,

2003). This aspect of parenting may be of special relevance among children at risk due to maternal substance use and associated environmental stress. For instance, cocaine-using mothers display higher harshness or negative affect toward their infants compared to non-using mothers (Burns, Chethik, Burns, & Clark, 1997; Eiden, Schuetze, Colder, & Veira, 2011), and exhibit more negative affect and intrusiveness during a structured teaching situation at three years of age (Johnson et al., 2002). The animal literature lends support to these findings indicating dose-dependent associations between cocaine treatment during gestation and disruptions in maternal caretaking behavior in the immediate post-partum (e.g., Johns et al., 2005; Nelson, Ayers, Meter, Walker, & Johns, 1998). Thus, PCE may have indirect associations with preschool self-regulation via maternal harshness in the infant/toddler years.

Moderators

In addition to potential direct and indirect associations between PCE and child self-regulation in the preschool years, we also examined three moderators of these associations: environmental risk, autonomic reactivity in infancy, and child sex. While mediators elucidate pathways to risk or resilience, moderators test whether specific variables exacerbate or ameliorate risk or resilience. Our inclusion of specific mediators was guided by theoretical frameworks of self-regulation indicating the importance of specific child and caregiver factors that play an etiological role in the development of self-regulation (Calkins & Hill, 2007; Cole et al., 2010). Our consideration of moderators was guided by empirical evidence from the PCE literature emphasizing the role of these variables in predicting aspects of child behaviors linked to self-regulation. For instance, studies of PCE highlight the importance of the postnatal environment in predicting child outcomes (Brown, Bakeman, Coles, Platzman, & Lynch, 2004). Several aspects of the postnatal environment are specific to children of substance using women such as frequent separations from the primary caregiver, changes in caregivers, changes in living situations, and lack of male caregivers, leading to higher levels of caregiving instability (Brown et al., 2004). Children experiencing prenatal substance exposure also often live in contexts that are at high risk for violence (Bada et al., 2011; Conners-Burrow, Johnson, & Whiteside-Mansell, 2009). In addition to these risks associated with the broader caregiving context, substance using mothers experience higher psychiatric symptoms and these have significant implications for developmental outcomes related to self-regulation (Eiden, Foote, & Schuetze, 2007). These aspects of environmental risks often co-occur (Rutter, 1987; Seifer, 1995). Given the nested nature of these risk characteristics, the total number of environmental risk factors may be more predictive of child outcomes and may be more representative of the actual caregiving context than examining associations with specific risk conditions (Seifer, 1995). Moreover, not all PCE children experience the same adverse environmental risk conditions (Brown et al., 2004; Eiden et al., 2007), and given this heterogeneity, environmental risk may moderate the association between PCE and self-regulation.

In addition to risks associated with the caregiving context, individual differences in autonomic reactivity in infancy may be a significant moderator of the association between PCE and self-regulation via harshness or language ability. One particular index of autonomic reactivity that is widely discussed in the developmental literature is respiratory

sinus arrhythmia (RSA). RSA is a measure of variability in heart rate that occurs at the frequency of respiration and is believed to provide an index of parasympathetic influence on cardiac output. This index is assessed most commonly during sleep or non-arousing tasks, often termed baseline RSA (BRSA) as well as during environmental demands (RSA regulation; Bornstein & Suess, 2000; Calkins, 1997). BRSA provides a measure of the infant's ability to maintain homeostasis during periods of minimal external stimulation. During challenges to homeostasis, as a result of exogenous stimulation, the myelinated vagal system optimally responds by inhibiting the effect of the parasympathetic nervous system on cardiac output (Porges, Doussard-Roosevelt, Portales, & Greenspan, 1996) and decreasing RSA (withdrawal). RSA withdrawal during periods of environmental challenges is believed to reflect one's ability to appropriately engage or disengage with the environment (Bornstein & Suess, 2000; Porges, et al., 1996). Thus, the measurement of change in RSA from baseline to challenge is an important index of autonomic reactivity.

Theories of biological sensitivity to context and differential-susceptibility (Ellis, Boyce, Belsky, Bakermans-Kranenburg, & Van Ijzendoorn, 2011) suggest that children who are highly reactive may be particularly susceptible to the adverse parenting experiences. This may be particularly true in high risk samples where parenting problems such as harshness and intrusive control may be more common (Fox & Calkins, 1993). This is bolstered by empirical evidence indicating that low RSA suppression is predictive of behavior problems in the context of parents' alcohol problems and marital conflict (El-Sheikh, Harger, & Whitson, 2001). However, little is known about the interactive effects of autonomic reactivity indexed by RSA withdrawal and harsh parenting on self-regulatory outcomes among substance exposed children. Thus, there may be greater variations in autonomic reactivity among samples characterized by biological vulnerability due to maternal substance use, and high autonomic reactivity in infancy combined with harsh parenting in infancy may lead to lower self-regulation in the preschool years.

Gender may also moderate the association between PCE and self-regulation. Results from both animal and human studies indicate that boys may be more vulnerable to PCE effects compared to girls for regulatory outcomes such as attention, affective reactivity, and behavior problems (Beaudin, 2012; Delaney-Black et al., 2004). However, others have noted no such associations, or associations with aspects of regulation such as behavior problems only for girls (Minnes et al., 2010). Thus, child sex may be an important moderator of the association between PCE and self-regulation, although the direction of this association may not be clear.

Finally, it is important to note that maternal cocaine use is a poly-drug issue. Cocaine using mothers commonly use other substances such as marijuana, cigarettes, and alcohol (Lester et al., 2012). Both alcohol and cigarettes are well known teratogens that have significant effects on development of self-regulation (Irner, 2012). Thus, the potential effects of cocaine use can only be examined in the context of other substance use during pregnancy.

In summary, we examined a conceptual model for development of self-regulation in the preschool years for PCE and demographically similar non-exposed children. In addition to potential direct associations between PCE and self-regulation, this model included maternal

harshness in the infant/toddler years and language development as two indirect pathways. The model included two aspects of self-regulation, effortful control and conscience. We examined both within-time and prospective associations between effortful control and conscience from 3 to 4 years. We examined the role of environmental risk, autonomic reactivity in infancy, and child sex as potential moderators. We hypothesized that the association between PCE and self-regulation would be stronger under conditions of high environmental risk. We also hypothesized that the pathway from PCE to self-regulation via maternal harshness would be stronger among children with high autonomic reactivity. Given the mixed results in prior literature, we did not hypothesize a direction of effect with regard to moderation by child sex, but examined if the association between PCE and self-regulation variables were different for boys and girls.

Materials and Methods

Participants—The sample consisted of 216 mother-infant dyads participating in an ongoing longitudinal study of CE (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 ($M=29.53$; $SD=6.06$). The majority of caregivers in both groups were primarily African-American, with 64% and 78% (72% overall) African-American in the NCE and CE groups respectively. Most caregivers were receiving Temporary Assistance for Needy Families (76%) at the time of their first laboratory visit (Years 2001–2004), and were single (66%). Of the 216 children, 106 (49%) were male, with 50% and 48% male children in the NCE and CE groups respectively. 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 children and youth institutional review board of the University at Buffalo. Informed written consent was obtained from all recruited participants and they were compensated for their time.

Maternal and child assessments were conducted at 4–8 weeks, 7, 13, 24, 36, and 48 months of child ages with phone interviews at 18, 30, and 42 months. Children born at or before 37 weeks gestation were scheduled for their appointments at chronological age corrected for prematurity until the 24 month assessment. By the 36 month assessment, 44 children in the CE group (38%) and 4 children in the NCE group (4%) had been or $\chi^2(1) = 38.38, p = .00$. All assessments were conducted with the primary currently were in non-parental care, 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. 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. The primary caregiver was identified as the adult who had legal guardianship of the child and accompanied the child at all appointments.

Procedure—All mothers were screened after delivery for initial eligibility and matching criteria (see below) and maternal use of alcohol, cigarettes, and illicit substances in pregnancy using a 3-point scale (never, sometimes, often). Exclusionary criteria based on

screening and medical record review of all mothers were (a) maternal age younger than 18 years, (b) use of illicit substances other than cocaine or marijuana or use of antipsychotic/seizure medication, (c) significant medical problems for the mother or infant (e.g., genetic disorders, major perinatal complications, baby in critical care for over 48 hours), (d) maternal hospitalization due to mental illness, (e) mother not English speaking or lived too far away. Once a family was recruited into the cocaine group, the closest matching NCE group family was recruited (based on maternal education, race/ethnicity, age, infant sex). Mothers in the NCE 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. Urine toxicologies were routinely conducted by participating hospitals at the first prenatal visit and/or at delivery and hair samples were collected from mothers at the first laboratory visit at infant age of 4 to 8 weeks old. Of the 4800 potential participants, 380 were less than 18 years of age, 126 acknowledged using illicit substances other than cocaine or marijuana, 149 infants had major medical problems, 66 used antipsychotic/seizure medications, 29 had been hospitalized for major mental illness, 193 were not English speaking, 184 had major medical problems (HIV+, gestational diabetes, syphilis), 209 did not have transportation and lived more than an hour drive away, 112 refused screening, and 3,012 were non-users who did not match a CE woman in education, race/ethnicity, age, and infant sex. The remaining 340 (7%) were eligible for participation in either group.

Of these 340 women, 199 were eligible for the NCE group and 141 were eligible for the CE group. Among the 199 initially eligible NCE group women based on being the closest match to a CE group participant, 22 refused participation, 56 did not keep their first appointment within the narrow window (4–8 weeks of infant age), we were unable to locate 21 participants, and 17 were recruited into the cocaine group because their hair analysis was positive for cocaine. The remaining 100 were recruited into the control group. Among the 141 initially eligible CE group women, 21 were not recruited because they did not keep their first appointment or there was a change in custody and we could not locate the child, resulting in a sample of 220 mother-infant dyads. Of these 220 mother-infant dyads, 4 were excluded from analyses (two infants were later diagnosed with fetal alcohol syndrome, one was later diagnosed with shaken baby syndrome, and one infant was severely delayed), resulting in a final sample of 216 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 majority of mothers in the CE group who were eligible but not enrolled ($N = 21$) 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 CE group who participated compared to those who did not. 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. All visits consisted of a combination of maternal interviews, observations of mother-infant interactions, and infant assessments.

Measures

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 & Parmelee, 1978), a scale designed to assess the number of perinatal risk factors experienced by the infant. Higher numbers on this scale indicate lower obstetrical risk. Gestational age was calculated by dates and extracted from medical records.

Identification of Substance Use—Cocaine status was determined by a combination of maternal report, chart review that included urine toxicologies, and maternal hair analysis. Urine toxicology results were available for 90% of the families in the NCE group and 92% of the families in the CE group and hair samples were collected from all mothers. Mothers who were positive for cocaine based on any of these methods were recruited into 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 screened for cocaine followed by a gas chromatography/mass spectrometry (GC/MS) confirmation for positive cocaine screens. The Timeline Follow-Back Interview (TLFB; (Sobell, Sobell, Klajmer, Pavan, & Basian, 1986) was used to assess maternal substance use during pregnancy and postnatally. Participants were provided a pregnancy and past month calendar at the first laboratory assessment, and over the time period since the last assessment for the other postnatal assessments (e.g., 6 month period at the 7 month assessment, and one year period at the 48 month assessment) 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 per trimester and during the entire pregnancy. Preliminary analyses were conducted with trimester specific information and pregnancy averages. These data were quite skewed and were transformed using square root transformations. Average number of days per week of cocaine use during pregnancy based on the TLFB ranged from 0 to 6.63 days. Self-reported cocaine use decreased substantially over the duration of pregnant from approximately once a week in the first trimester to once a month in the third trimester, although only 5 women reported use only in the first trimester. The remainder of women in the CE group reported use throughout pregnancy. The majority of women in the CE group used crack cocaine. Postnatal substance use was computed by taking the average of number of days used cocaine, number of cigarettes per week, number of standard drinks per week, and number of joints per week at each assessment from 7 to 36 months.

Autonomic Reactivity—Autonomic reactivity in response to a frustration task was assessed at 13 months of infant age. Infants were tested while seated in a high-chair. Recording of the autonomic data began once the infant was observed to be in a stable, quiet, alert state which was induced by having the infant watch a 3-minute segment of a neutral videotape “Baby Einstein” (Calkins, 1997). The frustration paradigm consisted of a gentle arm restraint episode which is a widely-used, well-validated measure of anger/frustration used to assess infant regulation and reactivity (Goldsmith, Reilly, Lemery, Longley, & Prescott, 1999; Stifter & Braungart, 1995).

A five-channel Bioamp (James Long Company, Caroga Lake, NY) recorded respiration and electrocardiograph (ECG) data. Average RSA was calculated for the 3-minute baseline period and for the frustration task. The final measure was a change score from baseline to the frustration task. Negative scores indicated a decrease in RSA and were reflective of more optimal parasympathetic regulation. Infants with an adaptive decrease in RSA from baseline to frustration were categorized in the optimal RSA group, and infants with no change or an increase in RSA were categorized in the non-optimal RSA group for multiple group analyses.

Maternal Harshness—Intensity of maternal harshness was coded during free play at 7, 13, and 24 months. Mothers were asked to interact with their infants as they normally would at home for 10 minutes in a room filled with toys at 7 and 13 months. These interactions were coded using a collection of global 5-point rating scales (Clark, Musick, Scott, & Klehr, 1980), with higher scores indicating more positive affect or behavior. The scale for maternal harshness consisted of items such as angry, hostile tone of voice; expressed harshness; angry, hostile mood; and displeasure or disapproval or criticism. The maternal harshness scale had high internal consistency with Cronbach’s alpha of .96 at 7 months and .94 at 13 and 24 months. Two coders blind to group status rated maternal harshness at different ages. Both coders were trained on the Clark scales by the first author until inter-rater reliability criterion was reached (agreement of 90% or above). Subsequently inter-rater reliability was established on a random selection of 14% of the tapes. Inter-rater reliabilities were intra-class correlation coefficients of .96, .82, and .98 at 7, 13, and 24 months, respectively. Confirmatory factor analysis indicated that the measures of maternal harshness across the infant-toddler period at the three ages loaded on one factor reflecting high maternal harshness with standardized factor loadings of .54, .54, and .65 at 7, 13, and 24 months respectively.

Effortful Control—The effortful control measures at 36 and 48 months consisted of two tasks, snack delay and prize delay. These were taken from a battery of tasks developed by (Kochanska & Knaack, 2003). These measures have been used extensively in developmental studies, have high internal consistency, and high construct and predictive validity (see Kochanska et al., 2003). The scores for prize delay and snack delay were standardized and the average of these five standard scores was used as the composite measure for effortful control at each age. Higher scores indicated higher effortful control.

Conscience—Observations of child conscience were conducted according to the paradigm developed by Kochanska and her colleagues (Kochanska & Aksan, 1995) at 36 and 48

months. Mothers were instructed to show their children a shelf with attractive objects when they entered the observation room, to instruct their children to not touch those objects, and to keep their child from touching these prohibited objects during the hour-long session that followed (consisting of free play, structured play, clean-up, reading, etc.). This was followed by a 12-minute internalization paradigm consisting of 3-minutes during which the child was left alone in front of the shelf with a boring task (sorting cutlery), a stranger who came and played with the prohibited objects with obvious enjoyment for the next minute, and an additional 8-minutes of sorting cutlery. Children's behavior was coded for every 15 second interval using 6-point rating scales with 0 = playing with prohibited objects in a "wholehearted", unrestrained manner to 6 = sorting cutlery. The final composite score for conscience was computed by taking the average rating across the intervals and was then standardized. Conscience was coded by two independent coders blind to group status and inter-rater reliability was computed for 15% of the sample at 36 months and 10% of the sample at 48 months. Inter-rater reliability for conscience was high (intra-class correlation coefficient of .99 at 36 and 48 months).

Child Language—Receptive and expressive language was assessed using the Mullen Scales of Early Learning (MSEL, Mullen, 1992). These scales were administered by trained research assistants who were blind to group status. Receptive Language scale consists of auditory organization, sequencing, and memory, discriminating between different objects or pictures, and following a sequence of instructions. The Expressive Language scale consists of the noting spontaneous use of words and sentences during the test administration as well as responses to naming tasks. Raw scores on the two subscales were converted to t-scores. The MSEL has good reliability and validity and has been used extensively with high and low risk children ranging in age from birth to 68 months (Mullen, 1992).

Environmental Risk—A composite caregiving environmental risk was computed from the following measures. Maternal psychopathology was assessed using the Brief Symptom Inventory (BSI; (Derogatis, 1993) at 1, 7, 13, 24, 36 and 48 months. The measure consists of 53 items rated on a five-point scale. A positive symptom distress index was summing all items and dividing by number of items endorsed with a positive response. The BSI has 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 maternal psychopathology. Maternal exposure to violence was assessed at 1, 7, 13, 18, 24, 30, 36, 42, and 48 months using the Timeline Followback Interview (TLFB, Sobell & Sobell, 1996). Although the original interview was a calendar based method to assess substance use, it has also been used to measure episodes of intimate partner violence in various studies (e.g., Mignone, Klostermann, & Chen, 2009). Women were asked about their exposure to violence using a daily calendar at each assessment point. The total number of days women witnessed, experienced, or perpetrated violence were summed within each time point. Given the apparent bimodal distributions at each time point, exposure to violence was dummy-coded (i.e., 0, 1) at each time point and then a count variable was created from each of the dummy-coded time points to reflect exposure to violence across time. Caregiving Instability was assessed at 1, 7, 13, 24, and 36 months using a structured caregiver interview (Platzman, Coles, Lynch, Bard, & Brown, 2001). The Structured

Clinical Interview (SCI) was developed for use with high risk infants from 6 months to 24 months and was administered to the child's caregiver by a trained examiner. Following Platzman et al. (2001), individual items from the SCI were summed into a cluster called caregiving instability. The five items included in this scale were as follows: no male adult in the household, baby separated from primary caregiver for more than 48 hours, baby is fed and sleeps significantly less than average, there are custody changes, or baby does not see biological mother regularly. Thus, the total score on caregiving instability was based on the presence or absence of the 5 specific risk characteristics described above (see Platzman et al., 2001 for details regarding scale development). The caregiving instability scores ranged from 0 to 4 in the current study with the majority of the children in the sample having a score of 0 or 1. Thus, caregiver instability was dummy-coded at each time point and a count variable was created from each of the dummy-coded time points reflecting caregiver instability across the time periods. The cumulative environmental risk variable was created by computing a count variable which included the BSI, exposure to violence, and caregiving instability for each time point that each variable was assessed based on scores in the upper quartile. BSI was assessed at six time points (i.e., 1, 7, 13, 24, 36 and 48 months), exposure to violence was assessed at ten time points (i.e., 1, 7, 13, 18, 24, 30, 36, 42, and 48 months), and caregiving instability was assessed at five time points (i.e., 1, 7, 13, 24, and 36 months). Thus, scores for cumulative caregiving environmental risk could theoretically range from 0 to 20. The scores for cumulative caregiving environmental risk ranged from 0 to 14 in this sample, with a median score of 4. Children with 4 or higher number of cumulative risks were grouped into the high environmental risk group and the remainder were classified as low environmental risk.

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. MANOVAs were used to examine sex differences in externalizing behaviors. Demographic or perinatal risk variables that were associated with both the exogenous variables and indices of externalizing behavior problems at $p < .10$ were used as covariates in subsequent analyses. Structural equations modeling (SEM) was used to test the hypothesized model with maternal harshness as an intervening variable between maternal substance use and the two indices of self-regulation, effortful control and conscience. Child language scores were included in the model as a covariate, with receptive and expressive scales as the measured indicators of a latent variable reflecting overall language, to account for within and across time associations with effortful control and conscience. Multiple group analyses were used to examine moderation by sex, environmental risk, and autonomic reactivity. The multiple group analysis by child sex and environmental risk examined if the potential direct associations between maternal substance use and self-regulation differed for boys and girls and for children experiencing high and low environmental risk. Maternal harshness was not included in this model. The multiple group analysis by autonomic reactivity included the full model, but composite variables (for maternal harshness and child language) were used instead of latent variables to simplify the model given concerns about

model complexity. These models were tested by comparing models with constrained and unconstrained path coefficients. The χ^2 was used as an omnibus test of differences across child sex and autonomic reactivity. SEM analyses were conducted using Mplus, Version 5.2 software (Muthen & Muthen, 2006) 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, Lockwood, & Williams, 2004). Five thousand bootstrap samples and the 95% bias-corrected confidence intervals (CIs) were used to test significance of indirect effects.

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 216 mother-infant dyads who completed the 4- to 8- week laboratory visit, 177 completed the 24 month assessment, 165 completed the 36 month assessment, and 162 completed the 48 month assessment. Of these, observational measures of effortful control and conscience could be coded for 156 children at 3 years and 158 children at 4 years, and autonomic data were available for 150 infants at 13 months. There were no significant differences between families with complete vs. missing on any of the variables included in this study and demographics at any age. Data were thus determined to fit criteria for missing at random (MAR). As noted earlier, full-information maximum likelihood was used to estimate model parameters for SEM.

Results

Consideration of Covariates and Descriptive Data

Group differences in demographic and perinatal risk variables are presented in Table 1 for descriptive purposes. Correlations among variables included in model testing are presented in Table 2. As noted in Table 2, there were no direct associations between PCE and the two aspects of self-regulation: effortful control and conscience. Additional analyses revealed no differences between light (less than two days per week of cocaine use) vs. heavy (two or more days of cocaine use per week) vs. control group children on self-regulation variables and no associations by trimester of use. Among demographic variables, maternal education was associated with maternal substance use (cigarettes and alcohol), with maternal harshness at 24 months, with child language scores, and with effortful control at 36 months. Accordingly, maternal education was included as an exogenous variable in the model. There were no significant associations between any of the perinatal risk variables and the other variables in the model. ANOVA with child sex as the independent variable and the self-regulation variables at each age as the dependent variables indicated a significant sex difference on effortful control at 4 years, $F(1, 156) = 8.35, p < .01$, on conscience at 3 years, $F(1, 154) = 6.00, p < .01$, and on conscience at 4 years $F(1, 156) = 8.49, p < .01$. Boys had lower effortful control and conscience scores compared to girls. Means (with standard deviations in parentheses) for effortful control at 4 years, conscience at 3 years and 4 years were $-.20 (.92)$, $3.81 (1.46)$, $4.56 (1.18)$ for boys, and $.19 (.73)$, $4.40 (1.55)$, $5.04 (.91)$, for girls respectively. Thus, child sex was included as a covariate in testing the overall model. There were no associations between foster care status and the self-regulation variables, but

there was a significant difference between foster and biological mothers on maternal harshness at 7 months, $F(1, 162) = 6.22, p < .05$, with biological mothers displaying lower harshness ($M = 1.25, SD = .45$) during free-play compared to foster mothers ($M = 1.53, SD = .83$). Thus, foster care status was included as a covariate in testing of the overall model. There were no significant associations between age of entry into foster care, number of care changes, and kin vs. non-kin care on child language or self-regulation variables.

Model Testing—Average number of joints per week during pregnancy was not associated with CE group status, or with the mediators or outcomes examined in this study. Thus, this variable was dropped from model testing. Similarly, initial analyses with per trimester substance use data suggested no significant associations between cocaine, cigarettes, marijuana, or alcohol use per trimester based on maternal self-reports and the self-regulation variables. Thus, model testing was conducted with the average number of alcohol and average number of cigarettes per week for the entire pregnancy, and cocaine group status ascertained using multiple methods as noted above. Addition of postnatal substance use variables did not account for additional variance in self-regulation once prenatal substance use variables were in the model. Thus, these variables were not included in the final model.

The hypothesized model tested included maternal harshness as a potential mediator or intervening variable between maternal substance use during pregnancy and effortful control and conscience at 3 years, and these in turn were associated with effortful control and conscience at 4 years. The model included the measured indicators of maternal years of education, child ever been in foster care between birth and 36 months, cocaine group status, average number of standard drinks per week during pregnancy, and the average number of cigarettes per week during pregnancy as exogenous variables. Child sex was included as a covariate with directional paths to effortful control and internalization. Based on bivariate associations (see Table 2) the model included a directional path from maternal education to the latent variable for child language, a path from maternal harshness to child language, and a path from child language latent variable to effortful control and conscience at 3 and 4 years. The model also included the within time covariance between effortful control and conscience at 3 years and between effortful control and conscience at 4 years. Goodness of fit indices indicated that this hypothesized model fit the data well, ($\chi^2(64) = 79.24, p = .10$, CFI = .97, RMSEA = .03, 95% CI [.00, .05]). The structural paths indicated that mothers in the CE group displayed higher harshness during interactions across the infant-toddler period, as did those with lower years of education (see Figure 2). Maternal harshness during play interactions in the infant/toddler period was associated with lower effortful control and lower conscience at 3 years. Lower conscience at 3 years was prospectively predictive of lower effortful control at 4 years. However, effortful control at 3 years was not associated with conscience at 4 years. Higher maternal education was associated with higher child language scores, and this in turn was associated with higher effortful control at 3 and 4 years, and higher conscience at 3 years (Figure 2).

Figure 2. The indirect effects model for the association between prenatal cocaine exposure (CE) and child self-regulation via maternal harshness and child language. Non-significant paths and residuals are not depicted in the model for ease of presentation. An alternate model with maternal warmth/sensitivity (WS) instead of harshness was also examined. CE

was not associated with WS from 7 to 24 months. Maternal WS accounted for unique variance in child effortful control at 3 years ($\beta = .30, p = .04$), but not in child conscience at 3 years. Thus maternal WS could not be considered at an intervening variable for examining the potential indirect association between CE and child self-regulation. The associations among the exogenous variables are depicted in Table 2. Child sex: 0 = male. The numbers are standardized path coefficients. * $p < .05$, ** $p < .01$.

Our model included hypotheses about indirect effects, and the pattern of path coefficients provided evidence for two potential paths from CE to effortful control at 3 years via higher maternal harshness and the other from CE to conscience at 3 years via higher maternal harshness. The association between maternal cocaine use and effortful control at 3 years via higher maternal harshness was statistically significant, $B = -.24$, 95% CI $[-.52, -.01]$. The indirect association between maternal cocaine use and conscience at 3 years via higher maternal harshness was not statistically significant, $B = -.22$, 95% CI $[-.62, .005]$. Maternal substance use during pregnancy was not associated with child language scores, although language development was a significant predictor of both effortful control and conscience.

Moderation by Child Sex—We examined moderation by child sex using multiple group analyses in SEM. This model only included the exogenous variables (cocaine group status, alcohol/cigarette use, maternal education, foster care status) and effortful control and conscience variables at 3 and 4 years. We first examined fit indices for a fully unconstrained model for boys and girls and compared this unconstrained model with a fully constrained model. The chi-square change between these two models was significantly different ($\chi^2(14) = 26.30, p < .05$), suggesting that the model was not equivalent for boys and girls. Examination of the individual path coefficients indicated that the path from number of cigarettes per week during pregnancy to conscience at 3 years was significantly different for boys and girls, $\chi^2(1) = 8.28, p < .01$. For boys, higher cigarette exposure was associated with lower conscience ($\beta = -.30, p < .05$) but for girls, higher cigarette exposure was associated with higher conscience ($\beta = .25, p < .05$). The stability coefficient for effortful control from 3 to 4 years was also different for boys and girls, $\chi^2(1) = 5.46, p < .05$, with boys displaying moderate stability in effortful control ($\beta = .41, p < .01$) and girls displaying no stability from 3 to 4 years ($\beta = .03, p > .05$).

Moderation by Environmental Risk—Multiple group analyses were also used to examine if the association between prenatal substance exposure and self-regulation variables may be moderated by environmental risk. As with child sex, this model only included the exogenous variables (cocaine group status, alcohol/cigarette use, maternal education, foster care status) and effortful control and internalization variables at 3 and 4 years. The chi-square change between the constrained and unconstrained models was not significantly different ($\chi^2(14) = 23.43, p > .05$), suggesting that the model was equivalent for high and low environmental risk groups.

Moderation by Autonomic Reactivity—Due to concerns regarding parameter to participant ratio, multiple group models using a composite instead of latent variables for maternal harshness (average of 7 to 24 month harshness) and child language (sum of receptive and expressive scores) were used to test if the associations among variables varied

as a function of autonomic reactivity (baseline RSA and RSA change). Results indicated a significant difference between the fully unconstrained and constrained models for the two RSA change groups (adaptive decrease vs. maladaptive increase/no change, $n = 62, 49$ in the CE group), $\chi^2(21) = 38.35, p < .05$. Examination of the individual path coefficients indicated that the PCE was significantly associated with high maternal harshness for both autonomic reactivity groups, but the path from harshness to conscience ($\chi^2(1) = 3.30, p = .05$), was significantly different for the two groups. Among children displaying a maladaptive increase or no change in RSA in response to frustration, higher maternal harshness was associated with lower conscience at 3 years ($\beta = -.27, p < .05$), while this path was non-significant for children exhibiting an adaptive decrease in RSA from baseline to frustration.

Discussion

The purpose of the present study was to examine if there were direct, indirect, and/or moderated associations between PCE and two aspects of self-regulation, effortful control and conscience at child ages of 3 and 4 years. Our results indicated no significant direct associations between PCE and these two aspects of self-regulation at either age. Only one previous study has examined direct associations between PCE and effortful control (Carmody et al., 2011), with a specific focus on response inhibition during a computerized go-no go task at 6, 9, and 11 years of age. Results indicated that heavily exposed (defined as maternal use of cocaine two or more times per week during pregnancy) boys but not girls exhibited lower overall accuracy in the go-no go paradigm compared to control children. However, cocaine exposure did not account for significant variance in response inhibition, an important aspect of effortful control. Thus, the current results add to this literature indicating that in the preschool period when self-regulation becomes the salient developmental task, there are few direct associations between PCE and effortful control or conscience.

In addition to potential direct associations, we examined if there were indirect associations between PCE and these aspects of self-regulation via maternal harshness and child language development. Results indicated significant indirect association between PCE and effortful control via maternal harshness. Mothers who used cocaine during pregnancy displayed more harshness during interactions with their children across the infant-toddler period compared to control group mothers. Higher maternal harshness in the infant-toddler period was in turn associated with lower effortful control at 3 years of child age. Previous studies have noted that maternal power assertion, a concept similar to maternal harshness, was predictive of effortful control in the toddler to preschool period (Kochanska & Knaack, 2003). Similarly, maternal intrusiveness in the toddler period was prospectively predictive of effortful control a year later (Taylor, Eisenberg, Spinrad, & Widaman, 2013). Researchers have speculated that harsh, punitive, intrusive, and/or controlling parenting may undermine development of effortful control by increasing arousal, undermining the development of appropriate coping, or by modeling poor strategies for regulating arousal or monitoring own behavior (Kochanska & Knaack, 2003; Taylor et al., 2013). Current results are supportive of these findings and indicate that maternal harshness is one pathway to poor self-regulation among cocaine exposed children as well. Previous results from this sample also indicate that

maternal harshness mediated the association between CE and other outcomes associated with self-regulation such as trajectories of externalizing problems from toddler to preschool age (Molnar, Levitt, Schuetze, & Eiden, 2014). Our results indicated that this indirect pathway was important for the development of effortful control in particular, as opposed to conscience. Although maternal harshness in the infant/toddler period was predictive of conscience, the indirect association with PCE was not significant. It is possible that the indirect association between PCE and conscience may occur through other aspects of parenting such as parent-child discourse. Indeed, conscience, defined as internalization of rules in the absence of supervision has been associated with positive parent-child discourse in past research (e.g., Laible & Thompson, 2000). Therefore, it may be important to consider aspects of parent-child discourse in future work investigating the development of conscience.

Contrary to expectations, PCE was not associated with lower language abilities. Thus, there was no indirect pathway from PCE to self-regulation via language scores at 3 years. Language development at 3 years was, however, significantly positively associated with effortful control and conscience at age 3, suggesting that language is an important component for self-regulation (e.g., Cole et al., 2010). Yet, there does not seem to be special significance for this association in children who were exposed to cocaine prenatally as had been hypothesized. This may be because the overall sample is at risk due to poverty and low maternal education, and that influences to language development may be pervasive across the sample.

Our conceptual model included both within-time and prospective associations between effortful control and conscience from 3 to 4 years. Effortful control and conscience were each stable from 3 to 4 years and each were significantly associated with each other within time points. However, only conscience at 3 years of age was prospectively predictive of effortful control at 4 years of age. This is contrary to the expected direction of effect as effortful control is thought to play a role in the development of conscience (Kochanska & Knaack, 2003). However, the possibility of bidirectional prospective associations have seldom been examined, and has never been examined in a high risk sample characterized by low-income, high racial and ethnic minority representation, and prenatal substance exposure. It is possible that the developmental trajectories of effortful control and conscience may follow a different course than anticipated. Future longitudinal studies with diverse samples may examine if the direction of effects are different across samples characterized by different levels of risk. Current results indicate that the degree to which children are able to internalize rules of conduct by 3 years of age is predictive of their performance on effortful control tasks a year later, but not vice versa.

In addition to investigating a conceptual model for indirect associations between PCE and the development of self-regulation, we also examined the role of child sex, environmental risk, and autonomic reactivity in infancy, as potential moderators of these associations. Although we did not hypothesize a direction of effect with regard to moderation by child sex given the mixed results in prior literature, we examined whether the association between PCE and self-regulation variables were different for boys and girls. There were no significant gender differences for this association; however, higher cigarette exposure was

associated with lower conscience for boys and higher conscience for girls at age 3. Further, effortful control was moderately stable for boys from ages 3 to 4, but not for girls. The lack of stability indicates greater changes for girls and based on investigation of mean differences that girls are increasing in effortful control faster than are boys. This is consistent with past research suggesting that girls outperform boys on tasks of effortful control during the early childhood period (e.g., Kochanska, Murray, & Coy, 1997) and that higher cigarette exposure during the prenatal period is associated with regulation and attention based disorders (Linnet et al., 2003). Further, it has been suggested that there is a greater effect for boys in regards to regulation and attention based disorders when considering prenatal exposure to cigarettes (for review see Coles, Kable, & Lynch, 2012). However, that cigarette exposure is associated with higher conscience for girls is puzzling. One possibility is that this is a sample specific effect that needs replication. This finding regarding cigarette exposure also highlights the importance of investigating PCE as a poly-drug issue (Lester et al., 2003).

In regards to environmental risk, we hypothesized that the association between PCE and self-regulation would be stronger under conditions of high environmental risk. However, the model was equivalent for high and low environmental risk groups. Given that the entire sample is arguably at high risk due to poverty and low maternal education, the examined risk factors may be salient for the entire group and even low risk may still be a substantial level of exposure to environmental risk. One of the strengths of the current study is considering the impact of cumulative environmental risk given that children are subject to a variety of nested risk factors and are not exposed to risk factors individually. However, results with other aspects of child behavior associated with self-regulation such as trajectories of externalizing problems do indicate moderation by environmental risk (Molnar et al., 2014).

We also investigated the role of potential moderation by autonomic reactivity in infancy. It was hypothesized that the pathway from PCE to self-regulation via maternal harshness would be stronger among children with high autonomic reactivity. This hypothesis was supported, as higher maternal harshness was associated with lower conscience at 3 years for children who displayed a maladaptive decrease or no change in RSA in response to frustration. The path was non-significant for children exhibiting an adaptive decrease in RSA from baseline to frustration. Thus, the combination of high biological vulnerability due to poor autonomic reactivity and the experience of poor parenting was associated with low conscience. These results are supportive of diathesis stress models indicating the experience of harsh parenting is particularly significant for the development of conscience among children who experience greater diathesis posed by poor autonomic reactivity. Results are also supportive of models of biological sensitivity to context (e.g., Boyce & Ellis, 2005) and differential susceptibility to environmental influences (Belsky & Pluess, 2009) indicating that some individuals may be particularly susceptible to good or bad environmental influences. Our results indicate that children with poor autonomic reactivity may be particularly sensitive to high maternal harshness associated with PCE.

This study presents many strengths, such as a diverse and at risk sample, investigating PCE within the context of poly-drug use and environmental risk, including important covariates such as foster care and maternal education, laboratory assessments of key constructs, as well

as considering important indirect and moderated pathways to risk and resilience. However, there are limitations as well. To begin, accurate pre- and post-natal substance use data can be difficult to obtain given that parents may be reticent to disclose this information or may experience potential recall bias in retrospective self-reports of substance use; however, in order to address this potential concern the present study employed a variety of methods in order to determine substance use. Second, the measure of parenting was focused mainly on maternal harshness given the strong theoretical and empirical associations between harsh, punitive parenting and development of self-regulation as well as associations between PCE and harshness. However, others aspects of parenting such as the role of parent-child discourse may be important to examine as well. Third, aspects of child temperament such as fearfulness and attentional abilities may be other important predictors of self-regulation (Kochanska & Knaack, 2003). These may also be associated with PCE in theoretically predictable ways. Future studies may incorporate these aspects of temperament in more complex models. Fourth, maternal IQ may have been an important covariate to include in analyses, but we did not have measures of maternal IQ. Finally, in this conceptual model, we hypothesized that maternal harshness in the infant/toddler period would predict children's self-regulation at 3 and 4 years. It is possible that children who had lower self-regulation were more likely to elicit higher harsh parenting during interactions. Future studies may well examine this possibility of such bidirectional associations.

In conclusion, the results indicate that the quality of caregiving experience plays a significant role in the development of self-regulation among children who are more biologically vulnerable in infancy, as indicated by the interaction of poor autonomic regulation and high maternal harshness. Results also suggest that in addition prevention of maternal substance use during pregnancy, secondary preventive interventions should also focus on reducing maternal harshness and promoting strategies for fostering self-regulation in the infant/toddler period.

Acknowledgments

The authors thank the families who participated in this study and the research staff responsible for data collection and coding of observational assessments. Special thanks to Dr. Claire Coles for collaboration on the larger study, Dr. Amol Lele for collaboration on data collection at the Women and Children's Hospital of Buffalo, and Dr. Michael Ray for his collaboration on data collection at Sisters of Charity Hospital of Buffalo. Research reported in this paper was supported by the National Institute on Drug Abuse of the National Institutes of Health under award number R01DA013190.

References

- Allan NP, Lonigan CJ. Examining the dimensionality of effortful control in preschool children and its relation to academic and socioemotional indicators. *Developmental Psychology*. 2011; 47(4):905–915.10.1037/a0023748 [PubMed: 21553957]
- Arbuckle, JL. Full information estimation in the presence of incomplete data. In: Marcoulides, GA.; Schumacker, RE., editors. *Advanced Structural Equation Modeling: Issues and Techniques*. Mahwah, NJ: Lawrence Erlbaum Associates; 1996. p. 243-277.
- Bada HS, Bann CM, Bauer CR, Shankaran S, Lester B, LaGasse L, Higgins R. Preadolescent behavior problems after prenatal cocaine exposure: relationship between teacher and caretaker ratings (Maternal Lifestyle Study). *Neurotoxicology & Teratology*. 2011; 33:78–87.10.1016/j.ntt.2010.06.005 [PubMed: 20600844]

- Bandstra ES, Morrow CE, Vogel AL, Fifer RC, Ofir AY, Dausa AT, Anthony JC. Longitudinal influence of prenatal cocaine exposure on child language functioning. *Neurotoxicology & Teratology*. 2002; 24:297–308. [PubMed: 12009485]
- Bard KA, Coles CD, Platzman KA, Lynch M. The effects of prenatal drug exposure, term status, and caregiving on arousal and arousal modulation in 8-week-old infants. *Developmental Psychobiology*. 2000; 36(3):194–212. [PubMed: 10737865]
- Beaudin, SA.; Gendle, MH.; Strupp, BJ. Gender influences on the cognitive and emotional effects of prenatal cocaine exposure: Insights from an animal model. In: Lewis, ML.; Kestler, L., editors. *Gender differences in prenatal substance exposure*. Washington, DC: American Psychology Association; 2012. p. 77-96.
- Belsky J, Pluess M. Beyond diathesis stress: differential susceptibility to environmental influences. *Psychol Bull*. 2009; 135(6):885–908.10.1037/a0017376 [PubMed: 19883141]
- Bendersky M, Lewis M. Arousal modulation in cocaine-exposed infants. *Developmental Psychology*. 1998; 34:555–564. [PubMed: 9597364]
- Bornstein MH, Suess PE. Physiological self-regulation and information processing in infancy: cardiac vagal tone and habituation. *Child Development*. 2000; 71:273–287. [PubMed: 10834463]
- Brown JV, Bakeman R, Coles DC, Platzman KA, Lynch ME. Prenatal cocaine exposure: a comparison of 2-year-old children in parental and nonparental care. *Child Development*. 2004; 75:1282–1295. [PubMed: 15260878]
- Brown RA, Burgess ES, Sales SD, Whiteley JA, Evans DM, Miller IW. Reliability and validity of a smoking timeline follow-back interview. *Psychology of Addictive Behaviors*. 1998; 12:101–112.
- Burns KA, Chethik L, Burns WJ, Clark R. The early relationship of drug abusing mothers and their infants: An assessment at eight to twelve months of age. *Journal of Clinical Psychology*. 1997; 53:279–287. [PubMed: 9075056]
- Calkins SD. Cardiac vagal tone indices of temperamental reactivity and behavioral regulation in young children. *Developmental Psychobiology*. 1997; 31:125–135. [PubMed: 9298638]
- Calkins, SD.; Hill, Ashley. Caregiver Influences on Emerging Emotion Regulation: Biological and Environmental Transactions in Early Development. In: Gross, James J., editor. *Handbook of emotion regulation*. New York, NY US: Guilford Press; 2007. p. 229-248.
- Carmody DP, Bennett DS, Lewis M. The effects of prenatal cocaine exposure and gender on inhibitory control and attention. *Neurotoxicol Teratol*. 2011; 33:61–68.10.1016/j.ntt.2010.07.004 [PubMed: 21256425]
- Clark, R.; Musick, J.; Scott, F.; Klehr, K. The mothers' project rating scale of mother-child interaction. 1980.
- Cole, PM.; Armstrong, LM.; Pemberton, CK. The role of language in the development of emotion regulation. In: Calkins, SD.; Bell, MA., editors. *Child development at the intersection of emotion and cognition*. Washington, DC US: American Psychological Association; 2010. p. 59-77.
- Coles CD, Bard KA, Platzman KA, Lynch M. Attentional response at 8 weeks in prenatally drug-exposed and preterm infants. *Neurotoxicology & Teratology*. 1999; 21:527–537. [PubMed: 10492387]
- Conners-Burrow NA, Johnson B, Whiteside-Mansell L. Maternal substance abuse and children's exposure to violence. *Journal of Pediatric Nursing*. 2009; 24(5):360–368.10.1016/j.pedn.2008.03.006 [PubMed: 19782894]
- Delaney-Black V, Covington C, Nordstrom B, Ager J, Janisse J, Hannigan JH, Sokol RJ. Prenatal cocaine: Quantity of exposure and gender moderation. *Developmental & Behavioral Pediatrics*. 2004; 25(4):254–263.
- Derogatis, LR. The Brief Symptom Inventory (BSI) administration, scoring, and procedures manual. Minneapolis, MN: National Computer Systems; 1993.
- Eiden RD. Exposure to violence and behavior problems during early childhood. *Journal of Interpersonal Violence*. 1999; 14(12):1299–1313.
- Eiden RD, Foote A, Schuetze P. Maternal cocaine use and caregiving status: Group differences in caregiver and infant risk variables. *Addictive Behaviors*. 2007; 32:465–476. [PubMed: 16837139]
- Eiden RD, Peterson M, Coleman T. Maternal cocaine use and the caregiving environment during early childhood. *Psychology of Addictive Behaviors*. 1999; 13(4):293–302.

- Eiden RD, Schuetze P, Colder CR, Veira Y. Maternal cocaine use and mother–toddler aggression. *Neurotoxicol Teratol.* 2011; 33(3):360–369.10.1016/j.ntt.2011.03.001 [PubMed: 21396441]
- Eisenberg, N.; Smith, CL.; Spinrad, TL. Effortful control: Relations with emotion regulation, adjustment, and socialization in childhood. In: Vohs, KD.; Baumeister, RF., editors. *Handbook of self-regulation: Research, theory, and applications.* 2. New York, NY US: Guilford Press; 2011. p. 263–283.
- El-Sheikh M, Harger J, Whitson SM. Exposure to interparental conflict and children's adjustment and physical health: the moderating role of vagal tone. *Child Development.* 2001; 72:1617–1636. [PubMed: 11768136]
- Ellis BJ, Boyce TW, Belsky J, Bakermans-Kranenburg MJ, Van Ijzendoorn MH. Differential susceptibility to the environment: An evolutionary–neurodevelopmental theory. *Development and Psychopathology.* 2011; 23(1):7–28.10.1017/S0954579410000611 [PubMed: 21262036]
- Fox, NA.; Calkins, SD. Multiple-measure approaches to the study of infant emotion. In: Lewis, M.; Haviland, JM., editors. *Handbook of emotions.* New York: Guilford Press; 1993. p. 167–184.
- Gendle MH, White TL, Strawderman M, Mactutus CF, Booze RM, Levitsky DA, Strupp BJ. Enduring effects of prenatal cocaine exposure on selective attention and reactivity to errors: Evidence from an animal model. *Behavioral Neuroscience.* 2004; 118:290–297. [PubMed: 15113253]
- Goldsmith, HH.; Reilly, J.; Lemery, KS.; Longley, S.; Prescott, A. The Laboratory Temperament Assessment Battery Preschool Version: Description of Procedures. Madison, WI: University of Wisconsin, Department of Psychology; 1999. p. 1–139.
- Imer TB. Substance exposure in utero and developmental consequences in adolescence: A systematic review. *Child Neuropsychology.* 2012; 18(6):521–549.10.1080/09297049.2011.628309 [PubMed: 22114955]
- Johns JM, Elliott DL, Hofler VE, Joyner PW, McMurray MS, Jarrett TM, Walker CH. Cocaine treatment and prenatal environment interact to disrupt intergenerational maternal behavior in rats. *Behavioral Neuroscience.* 2005; 119:1605–1618.10.1037/0735-7044.119.6.1605 [PubMed: 16420163]
- Johnson AL, Morrow C, Accornero VH, Xue L, Anthony JC, Bandstra ES. Maternal cocaine use: Estimated effects on mother-child play interactions in the preschool period. *Journal of Developmental & Behavioral Pediatrics.* 2002; 23:191–202. [PubMed: 12177564]
- Karmel BZ, Gardner JM. Prenatal cocaine exposure effects on arousal-modulated attention during the neonatal period. *Developmental Psychobiology.* 1996; 29:463–480. [PubMed: 8809496]
- Kim S, Kochanska G. Child temperament moderates effects of parent-child mutuality on self-regulation: A relationship-based path for emotionally negative infants. *Child Development.* 2012; 83:1275–1289.10.1111/j.1467-8624.2012.01778.x [PubMed: 22670684]
- Kochanska G, Aksan N. Mother-child mutually positive affect, the quality of child compliance to requests and prohibitions, and maternal control as correlates of early internalization. *Child Development.* 1995; 66:236–254.
- Kochanska G, Knaack A. Effortful control as a personality characteristic of young children: Antecedents, correlates, and consequences. *Journal of Personality.* 2003; 71:1087–1112. [PubMed: 14633059]
- Kochanska G, Murray KT, Coy KC. Inhibitory control as a contributor to conscience in childhood: From toddler to early school age. *Child Development.* 1997; 68:263–277. [PubMed: 9180001]
- Kooijmans R, Scheres A, Oosterlaan J. Response inhibition and measures of psychopathology: A dimensional analysis. *Child Neuropsychology.* 2000; 6:175–184. [PubMed: 11402395]
- Lester BM, Lin H, DeGarmo DS, Fisher PA, LaGasse L, Levine TP, Higgins RD. Neurobehavioral disinhibition predicts initiation of substance use in children with prenatal cocaine exposure. *Drug and Alcohol Dependence.* 2012; 126:80–86.10.1016/j.drugalcdep.2012.04.014 [PubMed: 22608010]
- Lester BM, Padbury JF. Third pathophysiology of prenatal cocaine exposure. *Developmental Neuroscience.* 2009; 31:23–35.10.1159/000207491 [PubMed: 19372684]
- Lewis BA, Minnes S, Short EJ, Weishampel P, Satayatham S, Min MO, Singer LT. The effects of prenatal cocaine on language development at 10 years of age. *Neurotoxicology Teratology.* 2011; 33:17–24.10.1016/j.ntt.2010.06.006 [PubMed: 20600843]

- Li Z, Coles CD, Lynch ME, Hamann S, Peltier S, LaConte S, Hu X. Prenatal cocaine exposure alters emotional arousal regulation and its effects on working memory. *Neurotoxicology & Teratology*. 2009; 31:342–348.10.1016/j.ntt.2009.08.005 [PubMed: 19699795]
- MacKinnon DP, Lockwood CM, Williams J. Confidence limits for the indirect effect: Distribution of the product and resampling methods. *Multivariate Behavioral Research*. 2004; 39:99–128. [PubMed: 20157642]
- Mignone T, Klostermann K, Chen R. The Relationship Between Relapse to Alcohol and Relapse to Violence. *Journal of Family Violence*. 2009; 24:497–505.10.1007/s10896-009-9248-1
- Minnes S, Singer LT, Kirchner L, Short E, Lewis B, Satayathum S, Queh D. The effects of prenatal cocaine exposure on problem behavior in children 4–10 years. *Neurotoxicology & Teratology*. 2010; 32:443–451.10.1016/j.ntt.2010.03.005 [PubMed: 20227491]
- Molnar D, Levitt A, Schuetze P, Eiden RD. Prenatal cocaine exposure and trajectories of externalizing behavior problems in early childhood: Examining the role of maternal negative affect. *Development & Psychopathology*. 2014; 26:515–528. [PubMed: 24622033]
- Mullen, EM. Mullen scales of early learning. Cranston, RI: T.O.T.A.L. Child, Inc; 1992.
- Muthen, LK.; Muthen, BO. Mplus User's Guide (1998–2006). Los Angeles, CA: Muthen & Muthen; 2006.
- Nelson C, Ayers A, Meter KE, Walker CH, Johns JM. The effects of multiple doses of chronic gestational cocaine treatment on the onset and maintenance of maternal behavior in Sprague-Dawley rats. *Neurotoxicology & Teratology*. 1998; 20:657–660. [PubMed: 9831128]
- Platzman KA, Coles CD, Lynch ME, Bard KA, Brown JV. Assessment of the caregiving environment and infant functioning in polydrug families: Use of a structured clinical interview. *Infant Mental Health Journal*. 2001; 22:351–373.
- Porges SW, Doussard-Roosevelt JA, Portales AL, Greenspan SI. Infant regulation of the vagal “brake” predicts child behavior problems: a psychobiological model of social behavior. *Developmental Psychobiology*. 1996; 29:697–712. [PubMed: 8958482]
- Posner MI, Rothbart MK. Research on attention networks as a model for the integration of psychological science. *Annu Rev Psychol*. 2007; 58:1–23.10.1146/annurev.psych.58.110405.085516 [PubMed: 17029565]
- Rothbart, MK. Temperament and development. In: Kohnstamm, GA.; Bates, JE., editors. *Temperament in childhood*. Chichester, England: Wiley & Sons; 1989. p. 187-247.
- Rothbart MK, Ahadi SA. Temperament and the development of personality. *Journal of Abnormal Psychology*. 1994; 103:55–66. [PubMed: 8040481]
- Rothbart, MK.; Posner, MI.; Kieras, J. Temperament, attention, and the development of self-regulation. In: McCartney, K.; Phillips, DA.; Malden, MA., editors. *Blackwell handbook of early childhood development*. Oxford: Blackwell; 2006. p. 338-357.
- Rutter M. Psychosocial resilience and protective mechanisms. *American Journal of Orthopsychiatry*. 1987; 57:316–331. [PubMed: 3303954]
- Schuetze P, Eiden RD, Danielewicz S. The association between prenatal cocaine exposure and physiological regulation at 13 months of age. *Journal of Child Psychology & Psychiatry*. 2009; 50:1401–1409.10.1111/j.1469-7610.2009.02165 [PubMed: 19744182]
- Seifer R. Perils and pitfalls of high-risk research. *Developmental Psychology*. 1995; 31:420–424.
- Singer LT, Salvator A, Arendt R, Minnes S, Farkas K, Kliegman R. Effects of cocaine/polydrug exposure and maternal psychological distress on infant birth outcomes. *Neurotoxicology & Teratology*. 2002; 24:127–135. [PubMed: 11943500]
- Sobell MB, Sobell LC, Klajner F, Pavan D, Basian E. The reliability of a timeline method for assessing normal drinker college students' recent drinking history. *Addictive Behaviors*. 1986; 11:149–162. [PubMed: 3739800]
- Spear LP, Campbell J, Snyder K, Silveri M, Katovic N. Animal behavior models. Increased sensitivity to stressors and other environmental experiences after prenatal cocaine exposure. *Annual New York Academy of Sciences*. 1998; 846:76–88.
- Stifter CA, Braungart JM. The regulation of negative reactivity in infancy: Function and development. *Developmental Psychology*. 1995; 31(3):448–455.

- Taylor ZE, Eisenberg N, Spinrad TL, Widaman KF. Longitudinal relations of intrusive parenting and effortful control to ego-resiliency during early childhood. *Child Development*. 2013; 84:1145–1151. [PubMed: 23379965]
- Wolfe CD, Bell MA. Working memory and inhibitory control in early childhood: Contributions from physiology, temperament, and language. *Developmental Psychobiology*. 2004; 44:68–83.10.1002/dev.10152 [PubMed: 14704991]

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Highlights

- Cocaine using mothers exhibited more harshness during interactions with their toddlers.
- Higher maternal harshness was prospectively associated with lower effortful control in the preschool years.
- This association was stronger among children with high autonomic reactivity to frustration in infancy.
- Results highlight the role of caregiving in development of self-regulation among children exposed to cocaine and other substances in utero.

Figure 1.
Conceptual Model

Figure 2.
Structural Equations Model for PCE and Child Self-Regulation

Table 1

Group Differences in Demographic Variables and Birth Outcomes

Exposure Group:	Non-Cocaine <i>n</i> = 100		Cocaine <i>n</i> = 116		<i>F</i> value	η_p^2
	<i>M</i>	<i>SD</i>	<i>M</i>	<i>SD</i>		
Demographics:						
BM age	27.79	5.60	31.03	6.05	16.50**	.07
BM parity	3.17	1.64	4.16	2.42	12.50**	.05
Years education	12.02	1.88	11.64	1.91	2.12	.01
Occupational Status	3.38	1.83	2.78	1.32	7.92**	.04
Birth outcomes:						
Gestational age (weeks)	39.33	1.25	38.62	1.82	10.84**	.05
Birth weight (gms)	3334.45	503.78	2922.72	530.76	33.87**	.14
Birth length (cm)	49.96	2.90	48.13	3.07	20.08**	.09
Head circumference (cm)	33.61	1.38	33.08	2.06	4.77**	.02
OCS	100.81	17.30	85.30	16.34	45.83**	.18
Cigarettes/week T1	16.59	32.50	48.67	55.93	24.78**	.11
Cigarettes/week T2	11.88	26.30	36.80	47.86	20.96**	.09
Cigarettes/week T3	10.77	30.20	29.33	39.47	14.10**	.07
Drinks/week T1	.57	2.53	6.19	16.49	11.35**	.05
Drinks/week T2	.04	.16	4.11	14.81	7.54**	.04
Drinks/week T3	.01	.08	2.23	8.71	6.50*	.03
Joints/week T1	2.81	12.53	1.72	5.44	.65	.00
Joints/week T2	1.55	10.12	1.13	4.19	.15	.00
Joints/week T3	.38	3.17	.66	3.31	.36	.00
Days cocaine/week T1	0	0	1.01	2.06	24.04**	.11
Days cocaine/week T2	0	0	.66	1.70	15.02**	.07
Days cocaine/week T3	0	0	.37	.96	14.61**	.07

Author Manuscript

Author Manuscript

Author Manuscript

Author Manuscript

Note. BM: biological mother; OCS: Obstetrical complications scale score, high scores are more optimal. T1: Trimester 1; T2: Trimester 2; T3: Trimester 3; Peg: Averaged across pregnancy; Occupational status was coded using Hollingshead (1975) scoring system. All of the substance use variables were assessed prenatally.

* $p < .05$
** $p < .01$

Table 2

Correlations among variables.

	1	2	3	4	5	6	7	8	9	10	11	12	13	14
1. Cocaine Group Status														
2. # Cigarettes/week Preg.	.38													
3. # Drinks/week Preg.	.28	.36												
4. Years Education	-.11	-.26	-.23											
5. Foster care status	.41	.27	.08	-.02										
6. Harshness: 7 months	.20	-.02	.05	-.10	.19									
7. Harshness: 13 months	.21	.08	.04	-.13	.03	.29								
8. Harshness: 24 months	.11	.07	.11	-.20	-.06	.37	.33							
9. Expressive language	-.09	-.13	-.05	.18	-.03	-.23	-.02	-.20						
10. Receptive language	-.06	-.08	-.10	.25	-.07	-.18	.04	-.15	.59					
11. EC: 3 years	-.03	-.03	-.06	.21	.07	-.29	-.23	-.38	.27	.35				
12. EC: 4 years	.09	.07	.02	.09	.06	-.12	.10	-.23	.28	.37	.46			
13. Conscience: 3 years	-.04	-.02	-.12	.14	.06	-.16	-.03	-.26	.16	.32	.58	.47		
14. Conscience: 4 years	.13	.08	.02	.01	-.02	.04	.02	-.15	.06	.14	.31	.42	.58	
15. Child sex	.02	-.04	-.17	.02	.02	.14	.00	-.06	.16	.16	.23	.19	.22	

Note. Figures in bold were significant at $p < .05$;

: Number; Preg: Pregnancy; EC: Effortful Control.