Published in final edited form as:

Dev Psychol. 1998 May ; 34(3): 565–573.

Cognitive Functioning in 8- to 18-Month-Old Drug-Exposed Infants

Steven M. Alessandri

Department of Child and Adolescent Psychiatry, Medical College of Pennsylvania and Hahnemann School of Medicine

Margaret Bendersky and Michael Lewis

Institute for the Study of Child Development, University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School.

Abstract

This study examined the cognitive functioning in 236 infants at 8 and 18 months of age. Thirty-seven infants were heavily exposed to cocaine in-utero, 30 were lightly exposed, and 169 were not exposed to cocaine. Cognitive functioning was evaluated with the Bayley Scales of Infant Development (2nd ed.; N. Bayley, 1993) at both ages. Infant information processing was also assessed with an infant-controlled habituation procedure. Results indicated that (a) infants of cocaine-abusing women had higher neonatal medical and environmental risk scores; (b) at 8 months, exposure groups did not differ in Psychomotor Development Index, Mental Development Index (MDI) scores, or recovery to a novel stimulus; and (c) infants heavily exposed to cocaine or high environmental risk had a decrease in MDI scores from 8 to 18 months. These results were obtained when neonatal medical and environmental risk, as well as polydrug exposure, were controlled.

In examining whether prenatal exposure to cocaine impairs later cognitive functioning, research on humans continues to provide equivocal results. The ambiguous nature of outcome findings is due to methodological problems typically associated with behavioral toxicology research. In studies in which researchers are attempting to find relations between prenatal cocaine and some aspect of postnatal development, researchers must contend with a host of methodological problems, including (a) the potential confounding effects of other substances of abuse and poor maternal health and nutrition, (b) sensitive and valid measurement of infant outcome behaviors, and (c) differential effects of the postnatal child-rearing environment (e.g., see Bendersky, Alessandri, Sullivan, & Lewis, 1995; J. L. Jacobson & S. W. Jacobson, 1996).

There are several reasons to hypothesize that prenatal cocaine exposure might lead to early cognitive difficulties. Cocaine influences brain development directly through effects on developing neurotransmitter systems that are critical to neuronal differentiation and brain structure formation and indirectly through effects on blood flow to the developing fetal brain (Gawin & Ellinwood, 1988; Mayes & Bornstein, 1995). Because of the inhibition of monoaminergic neurotransmitter systems, neuro-developmental functioning in infants exposed to cocaine in-utero might be expected to be compromised in areas such as reactivity, arousal modulation, and attentional regulation. In addition, reduction in placental and fetal blood flow might result in impaired overall information-processing and problem-solving ability (Woods, Plessinger, & Clark, 1987).

Correspondence concerning to this article should be addressed to Michael Lewis, Institute for the Study of Child Development, University of Medicine and Dentistry of New Jersey-Robert Wood Johnson Medical School, 97 Paterson Street, New Brunswick, New Jersey 08903-0019. Electronic mail may be sent to lewis@umdnj.edu..

This research was supported by the National Institute of Drug Abuse Grant RO1 DA07109.

Results from animal studies have not as yet yielded clear findings, although it appears that cocaine may differentially affect specific learning systems. Spear et al. (1989) examined the neurobehavioral development of rats who were exposed to cocaine during gestation. The treated pups showed learning and retention difficulties in some tests with appetitive conditioning measures. Heyser, Chen, Miller, Spear, and Spear (1990) reported that the offspring of pregnant rats who were exposed to cocaine failed to exhibit both sensory preconditioning and first-order Pavlovian conditioning. Heyser, Spear, and Spear (1992) reported that gestational exposure to cocaine had no effects on the acquisition of an olfactory conditional discrimination but did retard learning on reversal tasks. However, Riley and Foss (1991) reported no significant differences between rats who were prenatally exposed to cocaine and controls, when tested as either weanlings in a passive avoidance task or when tested as adults in active avoidance and navigational tasks. Although the rodent model of prenatal cocaine exposure appears promising (Spear, 1995), the data are, as yet, sparse and only suggestive.

Research with humans is also mixed concerning a relation between in-utero cocaine exposure and cognitive functioning. In studies with the Brazelton Neonatal Behavioral Assessment Scales (NBAS; Brazelton, 1984), cocaine-exposed neonates showed impairments of orientation, motor, and state regulatory behaviors (Chasnoff & Griffith, 1991; Dixon, Coen, & Crutchfield, 1987). In behavioral and cognitive measures beyond the neonatal period, researchers have used general measures of developmental performance such as the Bayley Scales of Infant Development (BSID; Bayley, 1969). The Bayley Scales appear to be sensitive to detecting the effects of a broad range of toxic substances. These scales have been found to be affected by intrauterine exposure to alcohol (Streissguth, Barr, Martin, & Herman, 1980), lead (Dietrich et al., 1987), and PCBs (Rogan & Gladen, 1991). Studies with cocaine-exposed children have not reported lower scores on the Bayley. Griffith, Chasnoff, and Azuma (1994) reported no mean differences in mental (Mental Development Index, MDI) and motor (Psychomotor Development Index, PDI) scores between drug-exposed and control infants. The researchers concluded, however, that the highly structured tasks on the Bayley may have masked self-regulatory difficulties experienced by drug-exposed children. Mayes, Bornstein, Chawarska, and Granger (1995) found that infants exposed to cocaine obtained lower PDI but not MDI scores on the Bayley Scales at 3 months, relative to nonexposed infants.

Relations between cocaine exposure and discrete cognitive functions have been found when more sensitive and specific process-oriented methods of assessment have been used. Studies examining habituation and operant conditioning in cocaine-exposed infants have suggested deficits in memory, reactivity to novelty, and arousal in infants 3 to 12 months of age. Struthers and Hansen (1992) found impaired recognition memory among cocaine and amphetamine-exposed infants. Alessandri, Sullivan, Imaizumi, and Lewis (1993) reported impaired contingency learning, deficits in arousal, and low levels of emotional responsivity in cocaine-exposed infants. Mayes et al. (1995) found that infants exposed to cocaine were more likely to fail to start the habituation procedure. However, no significant differences were found between cocaine-exposed and nonexposed 3-month-old infants in habituation and in recovery to a novel stimulus. The researchers concluded that impairments in initial reactivity and selectivity toward novel stimuli may exist in a select sub-group of cocaine-exposed infants, such as infants exposed to a high level of cocaine. Findings of S. W. Jacobson, J. L. Jacobson, Sokol, Martier, and Chiodo (1996) supported the hypothesis that heavy but not light cocaine exposure is more likely to have negative consequences. They found that heavy cocaine exposure was related to poorer recognition memory and information processing than was light or no cocaine exposure.

These findings suggest that in studies designed to assess the toxicity of cocaine, researchers consider the types of outcome measures used and the thresholds at which effects might occur.

The goal of the present study was to adopt both an outcome as well as a process approach to the assessment of infant cognitive functioning while examining whether medical or environmental risk factors, or use of other substances and their interactions with cocaine exposure, contribute significantly to cognitive functioning at 8 and 18 months of age. Potentially confounding factors, such as neonatal medical risk, environmental risk, and exposure to other toxic substances, were controlled. Two cognitive outcome measures were used. General cognition was evaluated in drug-exposed infants with the revised Bayley Scales of Infant Development—II (BSID-II; Bayley, 1993). The primary advantage in using the Bayley is its sensitivity to detect a cognitive deficit. Performance on a given item can be affected by deficits in several domains of function (J. L. Jacobson & S. W. Jacobson, 1996). Yet, no information is provided by the Bayley about the type of cognitive deficit.

In contrast, we also measured infant attention and information processing with a habituation paradigm. Attention to environmental stimuli is an indicator of central nervous system (CNS) functioning (Lewis & Taft, 1982). The observable habituation response reflects a complicated interplay between several central neurological processes (Sokolov, 1958/1963). Habituation, as evidenced by a decrease in attention to a repeatedly presented stimulus and recovery of attention to a novel stimulus, reflects the cognitive processes of attention, visual processing, and memory. The capacity to adapt one's behavior in response to meaningful stimuli in the environment is a critical skill related to cognitive development and CNS status. Response decrement to a repeated stimulus and recovery to a novel one have been shown to be cortical functions absent in anencephalic infants and people with disease or destruction of the cortex (Lewis, 1967; Bornstein & Sigman, 1986). Habituation measures increase with advancing age during infancy and discriminate handicapped and high-risk children from normal children (Lewis, 1967). Early habituation measures have been found to have moderate reliability and predictive validity for later cognitive functioning (Colombo, Mitchell, O'Brien, & Horowitz, 1987; Lewis & Brooks-Gunn, 1981; Lewis, Goldberg, & Campbell, 1969).

Some teratogenic effects may manifest only when heavy cocaine exposure is involved. Studies have found that high exposure to toxic substances is more likely to have long-term effects, thus combining all cocaine users into one group might reduce group differences (S. W. Jacobson, J.L. Jacobson, & Sokol, 1994; S. W. Jacobson et al., 1996). We decided, therefore, to examine infants who were exposed to high and low levels of cocaine. Studies have also shown the importance of socioenvironmental influences on cognitive functioning after the 1st year of life (Bradley et al., 1989; McCall, Hogarty, & Hurlburt, 1972). First-year scores on the Bayley are less affected by socioenvironmental influences than are scores on tests administered to older infants. Socioenvironmental influences become more pronounced during the 2nd year of life (Bradley et al., 1989). Information-processing tests are less affected by socioenvironmental influences because they depend less on the infant's ability to interact with the examiner and focus instead on attentional responses that are probably more biologically based (Fagan & Singer, 1983; Haith, Hazan, & Goodman, 1988). Assessment of information-processing measures should allow for the evaluation of the teratogenic effects of cocaine at an age when socioenvironmental influences are less likely to confound or interact with the effects of exposure per se.

We hypothesized that 8-month-old infants exposed to cocaine, especially a high amount, would show less efficient information processing in the habituation procedure and would obtain lower PDI and MDI scores on the BSID-II at 8 months. We hypothesized further that by 18 months, infants exposed to a high level of cocaine would obtain lower cognitive or mental (MDI) scores compared with both nonexposed infants and infants exposed to a low level of cocaine. Moreover, socioenvironmental influences would not be related to infant performance on information-processing measures but would be related to later cognitive performance.

Infants exposed to cocaine are exposed to a number of neonatal risk factors that may contribute to deficits in cognitive functioning. These include prenatal exposure to other toxic substances, including alcohol, nicotine, and marijuana. In addition, mothers who abuse cocaine are more likely to have pregnancies complicated by high life stress and preterm delivery (Bendersky et al., 1995; Mayes, 1992; Woods, Behnke, Eyler, Conlon, & Wobie, 1995). Any of these factors may contribute, along with the effects of in-utero cocaine exposure, to the development of early cognitive functioning. Thus, a final goal of this study was to control for the effects of other substances, medical risk, and environmental risk so that a more thorough assessment of the toxic effects of in-utero cocaine exposure could be determined.

Method

Participants—Infants in this study were part of a larger prospective investigation. The attrition rates were 14% and 20% at 8 and 18 months, respectively, with no differential attrition across cocaine exposure groups. Two hundred and thirty-six infants participated in the study. The cocaine-abusing group was divided into high and low cocaine users on the basis of reported consumption that was assessed by the drug use interview. High cocaine users were women who reported using cocaine two or more times per week, whereas low cocaine users reported using cocaine less than twice per week (above and below median for the sample). Frequency of use during pregnancy rather than amount was used because the purity and dosage of street drugs is so variable. These definitions of high and low exposure have been used in other studies (S. W. Jacobson, J. L. Jacobson, Sokol, Martier, & Anger, 1994; S. W. Jacobson et al., 1996). We determined that 16% (37) of the women were high cocaine users, 13% (30) were low cocaine users, and 72% (169) did not use any cocaine at all.

Infants were recruited from two inner-city hospitals located in Philadelphia and Trenton, New Jersey. Informed consent was obtained from the mother at the time of recruitment. The medical records of the mothers and infants were abstracted for data concerning pregnancy and delivery as well as neonatal outcome, including physical growth. No women reported any serious medical problems during pregnancy. All infants were admitted to the Well-Baby Clinic immediately following delivery. Infants were excluded from the sample if they were born prior to 32 weeks of gestation (4), required special care or oxygen therapy for more than 24 hours (5), exhibited congenital anomalies (3), were exposed to opiates or phencyclidine in-utero (2), or if their mothers were less than 15 years of age or infected with HIV (3). All mothers were inner-city clinic patients and predominantly African American (87%). Ten percent were Caucasian, and the remaining 3% were Hispanic. Participation was voluntary, and incentives were provided in the form of vouchers for exchange at local stores. Only two mothers received no prenatal care. Infants had a mean age of 33.09 weeks ($SD = 2.09$) at the time of the first assessment. All infants lived with their biological mothers.

Maternal Drug Use—Substance use information was obtained through a semistructured interview. Interviews were conducted prenatally (65%), in the mother's room on the maternity ward if she had just delivered (30%), in our laboratories near the hospitals (3%), or in the mother's home within 2 weeks of the infant's birth (2%). They were administered by trained interviewers and substance abuse counselors. The drug use interview contained questions about the frequency of the use of prescription and nonprescription medications and the frequency, amount, and trimester use of cocaine, alcohol, cigarettes, marijuana, opiates, phencyclidine, and other street drugs as well as tranquilizers, amphetamines, and barbiturates. The form of cocaine used, history of substance use, and the level of disruption of substance abuse to the person's life were obtained.

All substance use interview information was confirmed by results of analysis of newborns' meconium. The infants' meconium samples were screened with radioimmunoassay followed

by confirmatory gas chromatography-mass spectrometry for the presence of benzoyl ecgonine (cocaine metabolite), cannabinoids, opiates, amphetamines, and phencyclidine. Seven infants were excluded because their meconium analyses indicated cocaine exposure, but the mothers denied any cocaine use.

Almost all of the women who used cocaine (98%) also admitted use of cigarettes, alcohol, or marijuana during pregnancy. Of the cocaine users, the majority smoked crack (56%), 17% snorted cocaine, and 27% smoked free-base cocaine. The majority used cocaine during all 3 trimesters (56%), whereas 9% said they used only in the first trimester, 6% only during the second trimester, 15% only in the third trimester, whereas the remainder of the group (14%) reported use during some combination of two trimesters.

Neonatal Medical Risk—The infants of substance-abusing women may be at additional risk due to complications of pregnancy and delivery that occur with higher frequency in a low-income, high-risk group of women. To control for the effects on outcome of these early medical complications, prenatal intrapartum and neonatal medical data were abstracted from hospital records by nurses. These data were used to complete a neonatal medical risk scale consisting of 35 possible neonatal complications (Hobel, Hyvarinen, Okada, & Oh, 1973). Variables constituting the neonatal medical risk score were general factors (e.g., a 5-min Apgar less than 5; low birth weight, fetal anomalies), respiratory complications (e.g., congenital pneumonia, apnea, meconium aspiration syndrome), metabolic disorders (e.g., failure to gain weight, hypoglycemia), cardiac problems (e.g., murmur, cyanosis), hematologic problems (e.g., sepsis, anemia), and CNS problems (e.g., CNS depression, seizures). Each variable is weighted by the severity of the condition and summed to derive the risk score.

Environmental Risk—Sameroff, Seifer, Barocas, Zax, and Greenspan (1987) showed that cumulative risk, regardless of the individual constituents, is more predictive of cognitive outcome than is any individual risk factor. Such aggregate variables are more stable than any individual measure, and there is increased power to detect effects of the environment because errors of measurement decrease as scores are summed (Wachs, 1991). We computed a cumulative risk score to control for the effects of a stressful and chaotic environment. Similar cumulative environmental risk measures have been found to account for more variance in child outcome variables than do single factors, including socioeconomic status (Bendersky & Lewis, 1994; McGauhey, Starfield, Alexander, & Ensminger, 1991; Sameroff, Seifer, Baldwin, & Baldwin, 1993). Demographic and lifestyle information was obtained in several ways. Information about the mother's age, living arrangements, educational achievement, sources of income, family history of substance abuse, and information about other children was obtained by a structured interview that was conducted when the infant was 4 months. The amount of maternal life stress and social support was also obtained at this time. Life stress was measured with an adapted version of the Prenatal Social Environment Inventory (Orr, James, & Casper, 1992). This instrument assesses major life events as well as chronic stress from concerns about family, neighborhood, finances, and health that are likely to be especially problematic in a low-income sample. Test-retest reliability equals .73, with high internal consistency. The social support network size was assessed with the Norbeck Social Support Questionnaire (Norbeck, Lindsey, & Carrieri, 1981, 1983). This instrument measures the number of people in a woman's social network, the duration of her relationships, and the frequency of her contact with each member. Test-retest reliability ranged from .85 to .92, with high internal consistency.

An environmental risk score was constructed by using the number of life stressors, social support network size, maternal educational level, use or nonuse of public assistance, minority status, number of supportive adults the mother lived with, number of children in the household, and family history of drug or alcohol use. The standardized scores were combined and scaled to have a mean of 50 and a standard deviation of 10.

BSID-II—The BSID-II (Bayley, 1993) is an individually administered, well-standardized, evaluation that assesses the developmental functioning of infants and children. It consists of the MDI and the PDI. Administration of the BSID-II was performed by trained researchers who were blind with respect to maternal substance use.

Habituation—Participants were placed in a standard infant car seat that was housed in a semiencllosed booth facing a rear-screen projector. A series of color slides was presented, beginning with a warm-up slide of a colorful geometric pattern to attract the child's attention to the screen. The habituation procedure was designed to be infant controlled with a criterion to habituation of at least 50% decrement in visual fixation in two consecutive trials compared with the baseline; the baseline was defined as the mean of the two longest of the three looks following the warm-up slide. The warm-up slide was turned on when the infant looked at the screen and went off when the infant stopped looking for at least 500 ms or did not stop looking for 30 s, whichever came first. This was followed by presentations of a woman's neutral face (habituation stimulus) until the criterion of habituation was met or 15 trials had occurred, whichever came first. Two presentations of the same woman's smiling face (novelty stimulus) and 2 final trials of the same woman's neutral face (rehabilitation) were presented following habituation. Faces have been used successfully as stimuli in several studies during the 1st year of life (Colombo et al., 1987; Fagan, 1974).

The duration of visual fixation of the stimulus by the infant during each slide presentation was recorded by an observer. The observer looked through a peephole in the apparatus and depressed a key connected to a computer as long as a reflection of the stimulus was seen in the infant's cornea. Average fixation time in seconds was calculated during the base-line, habituation, recovery to novelty, and rehabilitation phases. Two additional habituation variables were calculated: the number of trials to habituation and the time to habituation. These measures describe the efficiency of information processing. Observer reliability was obtained from a random sample of the sessions. Observer reliability for determining whether an infant was looking at the stimulus during the session was .94. All variables were checked for normality of distribution prior to analysis and were normalized if indicated by a log transformation.

Results

Descriptive Statistics—Table 1 presents maternal and infant characteristics and neonatal and environmental risk scores for the three groups. Seven additional infants were tested but were excluded from the final sample because of 30 s or more of continuous fussiness during presentation of the habituation procedure. Participant attrition occurred in roughly the same proportion for the three groups (i.e., 2 high cocaine exposed, 2 low cocaine exposed, and 3 nonexposed). There were significant differences in the average daily number of cigarettes and marijuana joints smoked during pregnancy among the three groups, $F(2, 233) = 31.71, p < .001$ and $F(2, 233) = 4.62, p < .05$, respectively. Both high and low cocaine users smoked more cigarettes compared with noncocaine-abusing women ($p < .05$, Tukey Multiple Range Test). There was no significant difference in the amount of cigarette and marijuana consumption between the high and low cocaine-abusing women. High cocaine users consumed significantly more alcohol than low cocaine users, and both high and low cocaine users consumed more alcohol than noncocaine users, $F(2, 233) = 28.44, p < .001$ ($ps < .05$, Tukey Multiple Range Test). Because the cocaine-exposed groups differed in the use of these other substances, group analyses controlled for the average number of cigarettes smoked per day, the average number of alcoholic drinks consumed per day (a drink was defined as 2 oz of hard liquor, 4 oz of wine, or 12 oz of beer), and the average number of marijuana joints smoked per day throughout pregnancy.

With regard to infant characteristics, nonexposed infants had significantly higher birth weights and gestational ages relative to both high and low cocaine-exposed infants, $F(2, 233) = 23.09$, $p < .001$; $F(2, 233) = 19.66$, $p < .001$, respectively; $ps < .05$, Tukey Multiple Range Test. There was no significant difference in birth weight and gestational age between the high and low cocaine-exposed infants. There were no group differences in the proportion of boys to girls.

All risk scores were scaled so that a higher score represents greater risk. There was a significant group difference in the neonatal medical risk score, $F(2, 233) = 11.59$, $p < .001$. High cocaine-exposed infants had significantly higher neonatal medical risk scores relative to nonexposed infants ($p < .05$) but not to low cocaine-exposed infants. There also was a significant group difference in the environmental risk score, $F(2, 233) = 7.16$, $p < .001$. Post hoc analyses indicated that both high and low cocaine-exposed infants had higher environmental risk scores than did nonexposed infants ($ps < .05$, Tukey Multiple Range Test). There was no difference in environmental risk between the high and low cocaine-exposed infants. Because cocaine-exposed infants differed from controls on neonatal and environmental risk variables, all subsequent analyses were controlled simultaneously for these variables.

BSID-II—MDI at 8 and 18 months. A repeated measures multivariate analysis of covariance (MANCOVA) with between-group variables of group (3) and gender (2), covarying simultaneously for neonatal and environmental risk and alcohol, cigarette, and marijuana exposure, was performed on 8- and 18-month MDI scores.¹ There was a significant covariate effect for environmental risk, $t(108) = -3.67$, $p < .001$, such that over both ages, higher environmental risk was associated with lower MDI scores. There were no main effects of gender or group. There was a significant main effect of age, $F(1, 106) = 34.19$, $p < .001$. MDI scores significantly decreased from 8 to 18 months ($M = 92.92$ vs. 84.80), $t(111) = 6.03$, $p < .001$. There was also a significant Group $\times$ Age interaction, $F(2, 106) = 3.66$, $p < .05$. Post hoc analyses with the Tukey test indicated that the nonexposed infants obtained higher MDI scores relative to the high cocaine-exposed infants at 18 months ($p < .05$). Eighteen-month MDI scores of the low cocaine-exposed group were intermediate and did not differ from either the nonexposed or the high exposed group. There were no group differences in MDI scores at 8 months.

PDI at 8 months. To look at the PDI scores at 8 months, a MANCOVA with between-group variables of group (3) and gender (2), covarying simultaneously for neonatal medical and environmental risk and alcohol, cigarette, and marijuana exposure, was performed. There was no significant neonatal medical risk or environmental effect on PDI scores. Results indicated that group also had a nonsignificant effect after adjusting for the covariates.

Habituation and Recovery—Table 2 also presents the means and standard deviations by group for the habituation measures. A repeated measures MANCOVA with between-group variables of group (3) and gender (2), covarying simultaneously for neonatal medical and environmental risk and alcohol, cigarette, and marijuana consumption, was performed on fixation during the four phases of the habituation procedure: baseline, habituation, recovery to novelty, and rehabilitation. Results indicated no significant main effects of group or gender. There was a significant main effect of phase, $F(3, 148) = 19.10$, $p < .001$. As expected, there was a significant decrease in visual fixation from baseline to habituation, a significant increase from habituation to recovery to novelty, and a significant decrease from recovery to rehabilitation. This occurred for all three groups ($ps < .05$). Two additional habituation measures were examined: the number of trials to habituation and the time to habituation. Separate 2 (gender) $\times$ 3 (group) analyses of covariance (ANCOVAs), covarying

¹Birth weight was included in the mean neonatal medical risk score. Analyses that controlled for only birth weight revealed the same pattern of results.

simultaneously for medical and environmental risk and alcohol, cigarette, and marijuana consumption, were conducted. Results indicated no significant main effects or interactions.²

Impact of Neonatal and Environmental Risk Scores on MDI Performance—The previous analysis indicated that environmental risk has an impact on MDI scores. It was removed as a factor to study the effects of cocaine exposure alone. In the following analyses, all of the risk factors were included to determine the amount of variance that they explain in the outcome measures. Four hierarchical regression analyses were conducted to examine the amount of variance explained in the 8- and 18-month MDI scores, the change in MDI scores from 8 to 18 months, and 8-month PDI scores. Cocaine exposure was entered first. The amount of residual variance explained by other substance exposure was examined by adding the amount of alcohol, cigarette, and marijuana use in a second step. The added contribution of medical risk was examined in Step 3, environmental risk in Step 4, and an Exposure Group $\times$ Environmental Risk interactive term was entered last. Beta coefficients and R^2 s are presented in Table 3.

As can be seen, the 8-month MDI score was not significantly predicted from the variables. Group status did not explain any variance. Exposure to other toxic substances, as well as medical and environmental risk, also only explained minimal amounts of variance. Only environmental risk explained a significant amount of variance, $F(6, 105) = 6.60, p < .05$. The Group $\times$ Environmental Risk term explained an additional 2%.

Eighteen-month MDI scores were predicted from these variables, $F(7, 104) = 2.43, p < .05$. Group status predicted a significant amount of the variance, $F(1, 110) = 5.39, p < .05$, although substance use other than cocaine, as well as medical risk, contributed minimal amounts. Environmental risk did explain a significant amount of the variance, $F(6, 105) = 4.25, p < .05$, although the Group $\times$ Environmental Risk interaction did not.

The MDI change score was not predicted by this set of variables, although group status was significantly independently related, $F(1, 110) = 4.17, p < .05$. Substance use other than cocaine, as well as medical and environmental risk, explained a minimal amount of additional variance. Only the Group $\times$ Environmental Risk interaction also accounted for a significant amount of variance, $F(7, 104) = 5.26, p < .05$. Follow-up analyses indicated that for infants highly exposed to cocaine, environmental risk had little impact on the decrease in MDI scores from 8 to 18 months, whereas for lightly exposed and nonexposed infants, higher environmental risk was associated with a greater decline.

Eight-month PDI scores were predicted from these variables, $F(7, 104) = 2.94, p < .01$. Group status was significant when entered in Step 1, $F(1, 110) = 14.24, p < .001$, but was no longer significant after effects of the other predictors were controlled. Substance use other than cocaine, medical risk, environmental risk, and the Group $\times$ Environmental Risk term contributed minimal additional variance. In fact, environmental risk was the only predictor of 8-month MDI scores and explained about the same amount of variance in 18-month MDI scores. The Group $\times$ Environmental Risk interaction indicated a differential impact of environmental risk depending on the level of cocaine exposure.

Discussion

The findings of this study partially support our hypotheses. We observed no differences in cognitive functioning in cocaine-exposed infants at 8 months compared with other infants from similar backgrounds. Young infants exposed to cocaine as opposed to control age-mates

²No significant zero-order correlations were found between the neo-natal medical risk factor or heavy cocaine exposure and the habituation variables, suggesting that these medical risk factors were not mediating a cocaine effect.

showed appropriate information-processing ability and did not differ in MDI scores. These findings add to the results from earlier studies (Hansen, Struthers, & Gospe, 1993; S. W. Jacobson et al., 1996; Mayes et al., 1995; Struthers & Hansen, 1992).

The habituation paradigm provides information about the organization of attention and recognition memory, and it represents an early form of information processing and encoding by the infant (Colombo & Mitchell, 1990; Lewis, 1967). Although Hansen et al. (1993) and Struthers and Hansen (1992) reported information-processing deficits in cocaine-exposed infants, these studies did not adequately control for exposure to other substances. Thus, the information-processing deficits reported occurred when cocaine was combined with alcohol, cigarette, and marijuana use. S. W. Jacobson et al. (1996) did control for other substances and found that heavy cocaine exposure early in pregnancy was related to poorer recognition memory and information processing. Although the present study, along with Mayes et al. (1995), also controlled for the possible effects of other substances, both studies found no differences in information processing indexed by habituation and response to novelty between cocaine-exposed and nonexposed infants.

Another possible explanation for the inconsistency in the literature is that cocaine affects information processing, but the manifestation of such effects depends on the type of measure. Deficiencies in information processing may be detectable when the infant is required to process a greater number and more complicated stimuli within a specified amount of time, commonly found in tests of visual recognition memory (S. W. Jacobson et al., 1996; Struthers & Hansen, 1992) but not in simpler, single stimulus habituation tasks such as the one used in this study and in Mayes et al. (1995).

Studies that have examined cognitive functioning with traditional global methods such as the BSID have reported no relation between cocaine exposure and BSID mental (MDI) performance (Griffith et al., 1994; Graham et al., 1992; Hurt et al., 1995). In this study, no differences were found in cognitive scores for cocaine-exposed infants at 8 months. Mental Development Index scores for infants in all three groups were within the average range and were comparable to those obtained for “at-risk” populations (Bayley, 1993). This lack of a difference is particularly striking because we included a group of heavily cocaine-exposed infants.

This study shows that by 18 months, MDI scores become significantly worse for children exposed to a high level of cocaine and high environmental risk. Although MDI scores decreased across all three groups from 8 to 18 months, infants exposed to high levels of cocaine fared worse. These findings add to the growing evidence that there is a threshold of cocaine exposure for certain outcomes below which problems are not detectable (S. W. Jacobson et al., 1996). These results also suggest that the effects of cocaine are more likely to manifest when more cognitively challenging measures are used. Eighteen-month MDI items cover a wider range of cognitive tasks that require memory, responsivity to environmental cues, and integrated learning. Such skills are not adequately tapped at 8 months (Lewis, Jaskir, & Enright, 1986). The effect seen on infant cognition at 18, but not at 8 months of age parallels effects observed in laboratory animals. That is, in the animal literature, attainment of developmental milestones such as walking and associational learning, items comparable to early MDI items, were relatively unaffected by prenatal cocaine exposure (Dow-Edwards, 1993; Riley & Foss, 1991). However, when more cognitively challenging measures were used requiring integration of behavior in learning and memory tasks, deficits have been found in cocaine-exposed animals (Sobrian et al., 1990; Spear, 1995).

Of particular importance are the findings on environmental risk. Environmental risk was found to be negatively related to MDI scores at both ages. Infants raised in high-risk environments

were more likely to obtain lower MDI scores, even at 8 months of age. Children growing up in environments with multiple risk factors such as multiple caregivers, low maternal education, high caregiver stress, and few familial supports are likely to have reduced cognitive functioning. Many studies have confirmed the impact of the environment on cognitive performance by 18 to 24 months of age (Bendersky & Lewis, 1994; Sameroff et al., 1987, 1993).

Bendersky and Lewis (1994) reported an interaction between the severity of intraventricular hemorrhage (IVH) and environmental risk on MDI scores at 20 months. In that study, for the more biologically compromised group of infants (i.e., those with severe IVH), environmental risk was less important as a predictor of cognitive outcome than for infants with mild or no IVH. That finding parallels those here, that level of exposure interacts with environmental risk as it affects changes in MDI scores. These findings suggest that for infants with severe biological insult, the environment has less impact on the child's development than for those infants with less biological insult. Finally, these results suggest that cocaine-exposed infants should be viewed as a heterogeneous group. Among them, infants exposed to a high level of cocaine are likely to exhibit difficulties in cognitive functioning, especially as they develop more complex skills. However, exposure to low levels of cocaine appears to have little effect.

References

- Alessandri SM, Sullivan MW, Imaizumi S, Lewis M. Learning and emotional responsivity in cocaine-exposed infants. *Developmental Psychology* 1993;29:989–997.
- Bayley, N. Manual for the Bayley Scales of Infant Development. Psychological Corporation; New York: 1969.
- Bayley, N. Bayley Scales of Infant Development. 2nd ed.. Psychological Corporation; San Antonio, TX: 1993.
- Bendersky, M.; Alessandri, SM.; Sullivan, MW.; Lewis, M. Measuring the effects of prenatal cocaine exposure. In: Lewis, M.; Bendersky, M., editors. *Mothers, babies, and cocaine: The role of toxins in development*. Erlbaum; Hillsdale, N J: 1995. p. 163-178.
- Bendersky M, Lewis M. Environmental risk, medical risk, and cognition. *Developmental Psychology* 1994;30:484–494.
- Bornstein MH, Sigman MD. Continuity in mental development from infancy. *Child Development* 1986;57:251–274. [PubMed: 3956312]
- Bradley RH, Caldwell BM, Rock SL, Ramey CT, Barnard KE, Gray C, Hammond MA, Mitchell S, Gottfried AW, Siegel L, Johnson DL. Home environment and cognitive development in the first 3 years of life: A collaborative study involving six sites and three ethnic groups in North America. *Developmental Psychology* 1989;25:217–235.
- Brazelton, TB. Neonatal Behavioral Assessment Scale. 2nd ed.. Lippincott; Philadelphia: 1984.
- Chasnoff, IJ.; Griffith, DR. Maternal cocaine use: Neonatal outcome. In: Fitzgerald, H.; Lester, BM.; Yogman, M., editors. *Theory and research in behavioral pediatrics*. 5. Plenum; New York: 1991. p. 1-17.
- Colombo, J.; Mitchell, DW. Individual differences in early visual attention: Fixation time and information processing. In: Colombo, J.; Fagen, J., editors. *Individual differences in infancy: Reliability, stability, prediction*. Erlbaum; Hillsdale, NJ: 1990. p. 193-227.
- Colombo J, Mitchell DW, O'Brien M, Horowitz ED. The stability of visual habituation during the first year of life. *Child Development* 1987;58:474–487. [PubMed: 3829788]
- Dietrich KN, Krafft KM, Borschein RL, Hammond RB, Berger O, Succop RS, Bier M. Low-lead fetal lead exposure effect on neurobehavioral development in early infancy. *Pediatrics* 1987;80:721–730. [PubMed: 2444921]
- Dixon SD, Coen RW, Crutchfield S. Visual dysfunction in cocaine-exposed infants. *Pediatric Research* 1987;21:359A.

- Dow-Edwards D. The puzzle of cocaine's effects following maternal use during pregnancy: Still unsolved. *Neurotoxicology and Teratology* 1993;15:311–312. [PubMed: 8459786]
- Fagan JF. Infant recognition memory: The effects of length of familiarization and type of discrimination task. *Child Development* 1974;45:351–356. [PubMed: 4837713]
- Fagan, JF.; Singer, LT. Infant recognition memory as a measure of intelligence. In: Lipsitt, LR., editor. *Advances in infant research*. 2. Ablex; Norwood, NJ: 1983. p. 31-72.
- Gawin EH, Ellinwood EH. Cocaine and other stimulants. *New England Journal of Medicine* 1988;318:1173–1182. [PubMed: 3283549]
- Graham K, Feigenbaum A, Pastuzak A, Nulman I, Weksberg R, Einarson T, Goldberg S, Ashby S, Koren G. Pregnancy outcome and infant development following gestational cocaine use by social cocaine users in Toronto, Canada. *Clinical Investigations in Medicine* 1992;15:384–394.
- Griffith DR, Chasnoff IJ, Azuma S. Three-year outcome of children exposed prenatally to drugs: Special section. Cocaine babies. *Journal of the American Academy of Child and Adolescent Psychiatry* 1994;33:20–27. [PubMed: 7511139]
- Haith MM, Hazan C, Goodman GS. Expectation and anticipation of dynamic visual events by 3-5-month-old babies. *Child Development* 1988;59:467–479. [PubMed: 3359865]
- Hansen RL, Struthers JM, Gospe SM. Visual evoked potentials and visual processing in stimulant drug-exposed infants. *Developmental Medicine and Child Neurology* 1993;35:798–805. [PubMed: 8354431]
- Heyser CJ, Chen W, Miller J, Spear N, Spear L. Prenatal cocaine exposure induces deficits in Pavlovian conditioning and sensory preconditioning among infant rat pups. *Behavioral Neuroscience* 1990;104:955–963. [PubMed: 2285493]
- Heyser CJ, Spear N, Spear L. Effects of prenatal exposure to cocaine on conditional discrimination learning in adult rats. *Behavioral Neuroscience* 1992;106:837–845. [PubMed: 1445659]
- Hobel CJ, Hyvarinen MA, Okada DM, Oh W. Prenatal and intrapartum high-risk screening. *American Journal of Obstetrics and Gynecology* 1973;117:1–9. [PubMed: 4722373]
- Hurt H, Brodsky NL, Betancourt L, Braitman LE, Malmud E, Giannetta J. Cocaine-exposed children: Follow up through 30 months. *Journal of Developmental Behavioral Pediatrics* 1995;16:29–35.
- Jacobson JL, Jacobson SW. Methodological considerations in behavioral toxicology in infants and children. *Developmental Psychology* 1996;32:390–403.
- Jacobson SW, Jacobson JL, Sokol RJ. Effects of fetal alcohol exposure on infant reaction time. *Alcohol Clinical Experimental Research* 1994;18:1125–1132.
- Jacobson SW, Jacobson JL, Sokol RJ, Martier SS, Anger JW. Effects of alcohol use, smoking, and illicit drug use on fetal growth in black infants. *Journal of Pediatrics* 1994;124:757–764. [PubMed: 8176567]
- Jacobson SW, Jacobson JL, Sokol RJ, Martier SS, Chiodo LM. New evidence for neurobehavioral effects of in-utero cocaine exposure. *Journal of Pediatrics* 1996;4:581–590. [PubMed: 8859266]
- Lewis M. The meaning of a response or why researchers of infant behavior should be Oriental metaphysicians. *Merrill-Palmer Quarterly* 1967;13:7–18.
- Lewis M, Brooks-Gunn J. Visual attention at three months as a predictor of cognitive functioning at two years of age. *Intelligence* 1981;5:131–140.
- Lewis M, Goldberg S, Campbell H. A developmental study of information processing within the first three years of life: Response decrement to a redundant signal. *Monographs of the Society for Research in Child Development* 1969;34(9, Serial No. 133)
- Lewis M, Jaskir J, Enright M. Development of mental abilities in infants. *Intelligence* 1986;10:331–354.
- Lewis, M.; Taft, L. *Developmental disabilities: Theory, assessment, and intervention*. SP Medical Press; New York: 1982.
- Mayes LC. Prenatal cocaine exposure and young children's development. *American Academy of Political Social Science* 1992;521:11–27.
- Mayes, LC.; Bornstein, MH. Developmental dilemmas for cocaine abusing parents and their children. In: Lewis, M.; Bendersky, M., editors. *Mothers, babies, and cocaine: The role of toxins in development*. Erlbaum; Hillsdale, NJ: 1995. p. 251-272.

- Mayes LC, Bornstein MH, Chawarska K, Granger RH. Information processing and developmental assessments in 3-month-old infants exposed prenatally to cocaine. *Journal of Pediatrics* 1995;95:539–545.
- McCall RB, Hogarty RS, Hurlburt N. Transitions in infant sensorimotor development and the prediction of childhood IQ. *American Psychologist* 1972;27:728–748. [PubMed: 4560389]
- McGauhey P, Starfield B, Alexander C, Ensminger M. Social environment and vulnerability of low birth weight children: A social-epidemiologic perspective. *Pediatrics* 1991;88:943–953. [PubMed: 1945635]
- Norbeck J, Lindsey A, Carrieri V. The development of an instrument to measure social support. *Nursing Research* 1981;30:264–269. [PubMed: 7027185]
- Norbeck J, Lindsey A, Carrieri V. Further development of the Norbeck Social Support Scale Questionnaire. Normative data and validity testing. *Nursing Research* 1983;2:4–9. [PubMed: 6549842]
- Orr S, James S, Casper R. Psychosocial stressors and low birth weight: Development of a questionnaire. *Journal of Developmental and Behavioral Pediatrics* 1992;13:343–347. [PubMed: 1401118]
- Riley EP, Foss JA. The acquisition of passive avoidance, active avoidance, and spatial navigational tasks by animals prenatally exposed to cocaine. *Journal of Neurotoxicology and Teratology* 1991;13:559–564.
- Rogan WJ, Gladen BC. PCBs, DDE, and child development at 18 and 24 months. *Annals of Epidemiology* 1991;1:409–413.
- Sameroff A, Seifer R, Baldwin A, Baldwin C. Stability of intelligence from preschool to adolescence: The influence of social and family risk factors. *Child Development* 1993;64:80–97. [PubMed: 8436039]
- Sameroff A, Seifer R, Barocas R, Zax M, Greenspan S. Intelligent quotient scores of 4-year-old children: Social-environmental risk factors. *Pediatrics* 1987;79:343–350. [PubMed: 3822634]
- Sobrian SK, Burton LE, Robinson NL, Ashe WK, Hutchinson J, Stokes DL, Turner LM. Neurobehavioral and immunological effects of prenatal cocaine exposure in rat. *Pharmacology, Biochemistry & Behavior* 1990;35:617–629.
- Sokolov, YN. Perception and the conditioned reflex. Macmillan; New York: 1963. (S. W. Waydenfeld, Trans)(Original work published 1958)
- Spear, LP. Neurobehavioral consequences of gestational cocaine exposure: A comparative analysis. In: Rovee-Collier, C.; Lipsitt, LP., editors. *Advances in infancy research*. Ablex; Norwood, NJ: 1995. p. 55-105.
- Spear LE, Kirstein CL, Bell J, Yootanasumpun V, Greenbaum R, O'Shea J, Hoffman H, Spear NE. Effects of prenatal cocaine exposure on behavior during the early postnatal period. *Neurotoxicology and Teratology* 1989;15:57–63. [PubMed: 2725442]
- Streissguth AE, Barr HM, Martin DC, Herman CS. Effects of maternal alcohol, nicotine, and caffeine use during pregnancy on infant mental and motor development at 8 months. *Alcoholism: Clinical and Experimental Research* 1980;4:152–164.
- Struthers JM, Hansen RL. Visual recognition memory in drug-exposed infants. *Journal of Developmental and Behavioral Pediatrics* 1992;13:108–111. [PubMed: 1577955]
- Wachs, TD. Environmental considerations in studies with non-extreme groups. In: Wachs, T.; Plomin, R., editors. *Conceptualization and measurement of organism-environment interaction*. American Psychological Association; Washington, DC: 1991. p. 44-67.
- Woods, NS.; Behnke, M.; Eyler, ED.; Conlon, M.; Wobie, K. Cocaine use among pregnant women: Socioeconomic, obstetrical, and psychological issues. In: Lewis, M.; Bendersky, M., editors. *Mothers, babies, and cocaine: The role of toxins in development*. Erlbaum; Hillsdale, NJ: 1995. p. 305-335.
- Woods JR, Plessinger MA, Clark KE. Effect of cocaine on uterine blood flow and fetal oxygenation. *Journal of American Medical Association* 1987;257:957–961.

Table 1
Sample Demographics and Perinatal-Environmental Risk Scores by Group

Demographic characteristic/ risk score	High cocaine (n = 37)		Low cocaine (n = 30)		Nonexposed (n = 169)	
	M	SD	M	SD	M	SD
Mother						
Education (yrs)	11.46	1.32	11.60	1.30	11.21	1.48
Age (yrs)*	28.96	4.67 _a	29.66	4.33 _b	23.34	5.69 _b
Alcohol (no. drinks/day)***	1.25	2.00 _a	0.62	1.18 _b	0.04	0.25 _c
Cigarettes (no./day)***	8.99	8.54 _a	8.37	9.96 _a	1.64	4.46 _b
Marijuana (no. joints/day)**	0.13	0.37 _a	0.14	0.40 _a	0.02	0.17 _b
Infant						
Birth weight (g)***	2673.56	626.55 _a	2871.96	443.87 _a	3266.56	517.27 _b
Gestational age (weeks)	37.68	2.66	38.20	1.63	39.62	1.68
Sex (boys/girls)	19/18		14/16		88/81	
Age (days)	230.33	15.48	226.95	8.83	232.65	14.52
Risk Score						
Neonatal medical risk**	1.73	2.31 _a	0.77	1.15 _b	0.55	1.16 _b
Environmental risk***	53.71	8.24 _a	54.04	11.70 _a	48.47	9.85 _b

Note. Values with different subscripts are significantly different at $p < .05$, Tukey Multiple Range Test.

*
 $p < .05$.

**
 $p < .01$.

 $p < .001$.

Table 2

Bayley Scales of Infant Development-H (BSID-II) and Habituation Adjusted Means and Standard Deviations by Group

Outcome variable	High cocaine		Low cocaine		Nonexposed	
	M	SD	M	SD	M	SD
BSID-II						
MDI (8 months)	94.59	8.91	91.30	7.05	92.48	7.57
MDI (18 months) *	79.05	10.21 _a	86.59	9.76 _b	83.09	13.18 _b
PDI (8 months)	87.33	9.93	89.99	8.70	95.20	12.82
Habituation measures (in s)						
Baseline	4.79	2.12	4.60	1.72	3.92	2.38
Habituation	3.65	1.48	3.50	1.55	3.29	2.02
Recovery to novelty	4.62	4.07	2.90	1.69	4.57	2.82
Rehabituation	2.27	1.26	2.49	1.14	3.44	2.05
Time to habituation	35.57	17.64	33.78	19.60	29.31	18.05
No. of trials to habituation	8.38	3.22	9.57	5.21	8.72	2.75

Note. There were 112 infants with complete Bayley data at both ages: 15 in high cocaine, 19 in low cocaine, 78 in nonexposed groups. There were 156 infants with complete habituation data: 20 in high cocaine, 19 in low cocaine, and 117 in nonexposed groups. MDI = Mental Development Index; PDI = Psychomotor Development Index. Values with different subscripts are significantly different at $p < .05$, Tukey Multiple Range Test.

* $p < .05$.

Table 3

Direct Effects of Determinants of Mental Development Index (MDI) and Psychomotor Development Index (PDI) Scores

Step and variable	8-monthMDI		18-month MDI		AMDI		8-month PDI	
	R ² (Added)	β	R ² (Added)	β	R ² (Added)	β	R ² (Added)	β
Step 1								
Group	.00	0.00	.05 [*]	-0.22 [*]	.04 [*]	-0.19 [*]	.11 ^{***}	-.34 ^{***}
Step 2								
Alcohol		0.06		-0.01		0.03		-0.09
Cigarettes		0.03		-0.01		-0.03		-0.14
Marijuana	.00	0.00	.01	0.08	.01	0.07	.02	-0.07
Step 3								
Medical risk	.00	-0.01	.03	-0.19	.02	-0.16	.00	0.06
Step 4								
Environmental risk	.06 [*]	-0.25 [*]	.04 [*]	-0.20 [*]	.00	-0.04	.02	-0.13
Step 5								
Group × Environmental risk	.02	-0.79	.02	0.88	.04 [*]	1.19 [*]	.01	0.48
Total R ²	.08		.14 [*]		.11		.17 ^{**}	

*
 $p < .05$.

**
 $p < .01$.

 $p < .001$.