NEONATAL VISUAL INFORMATION PROCESSING IN COCAINE-EXPOSED AND NON-EXPOSED INFANTS

Lynn T. Singer
Robert Arendt
Joseph Fagan
Sonia Minnes
Ann Salvator
Tina Bolek
Michael Becker
Department of Pediatrics, School of Medicine, and the Department of Psychology
Case Western Reserve University, Cleveland, Ohio

This study investigated early neonatal visual preferences in 267 poly drug exposed neonates (131 cocaine-exposed and 136 non-cocaine exposed) whose drug exposure was documented through interviews and urine and meconium drug screens. Infants were given four visual recognition memory tasks comparing looking time to familiarized stimuli of lattices and rectangular shapes to novel stimuli of a schematic face and curved hourglass and bull's eye forms. Cocaine-exposed infants performed more poorly, after consideration of confounding factors, with a relationship of severity of cocaine exposure to lower novelty score found for both self-report and biologic measures of exposure. Findings support theories which link prenatal cocaine exposure to deficits in information processing entailing attentional and arousal organizational systems. Neonatal visual discrimination and attention tasks should be further explored as potentially sensitive behavioral indicators of teratologic effects.

cocaine neonatal visual attention information processing marijuana alcohol poly drug exposure visual recognition memory

• **Lynn T. Singer,** The Triangle Building, 11400 Euclid Avenue, Suite 250-A, Cleveland, Ohio 44106; Phone: (216) 844-6212; Fax: (216) 844-6233; e-mail: lxs5@po.cwru.edu.

INFANT BEHAVIOR & DEVELOPMENT 22 (1), 1999, pp. 1–15 ISSN 0163-6383

Over the past decade, prenatal cocaine exposure has emerged as a significant public health problem, affecting 5-15% of infants in urban areas of the United States. There is concern and controversy over cocaine's teratogenic potential since cocaine easily crosses the placental barrier during gestation (Woods, Plessinger, & Clark, 1987). This transmission of cocaine may directly and indirectly affect the fetus. Cocaine's stimulant effects on several neurotransmitter systems in adults have been noted (Wise, 1984), as cocaine prevents the re-uptake of catecholamine presynaptically and has been found to affect primarily the cardiovascular, respiratory, and central nervous systems.

There are a number of different mechanisms by which prenatal cocaine exposure could affect fetal development (Volpe, 1992). Alterations in catecholamine levels during gestation may affect the maturation of fetal neurotransmitter systems (Tennyson, Gershon, Budinkas, & Rothman, 1983; Wang & Schnoll, 1986). Animal studies have found that prenatal cocaine exposure is associated with increased catecholaminergic fiber densities in selected brain areas such as the posterior parietal cortex (Akbari & Azmitra, 1992; Posner & Peterson, 1988). Cocaine exposure may affect fetal brain development through its release and metabolism of monoamines, which are important in the definition of fetal brain structure and neuronal formation (Mayes & Bornstein, 1995). In addition, the reduction of blood flow prenatally to cocaine-exposed fetuses may affect later infant information processing or problem solving (Mayes & Bornstein, 1995).

The early behavioral development of cocaine-exposed infants has been studied using measures of sensory-motor processing such as the Brazelton Neonatal Behavioral Assessment Scale (NBAS), (Brazelton, 1984) neonatally, and later in life using standard developmental assessments, such as the Bayley Scales (Bayley, 1969, 1993). Findings have been inconsistent among studies. Some reports have found developmental deficits in cocaine-exposed infants compared to non-exposed infants (Arendt, Singer, Angelopoulos, Busdieker, & Mascia, 1998; Chasnoff, Griffith, Freier, & Murray, 1992; Coles, Platzman, Smith, James, & Falek, 1992; Eisen et al., 1991; Griffith, Azuma, & Chasnoff, 1994; Mayes, Bornstein, Chawarska, & Granger, 1995; Singer et al., 1997; Singer et al., 1994), while other reports have not found a difference based on exposure (Graham et al., 1992; Neuspiel, Hamel, Hochberg, Green, & Campbell, 1991; Richardson & Day, 1991; Woods, Eyler, Behnke, & Conlon, 1993; Hurt et al., 1995). In addition, cocaine's effects on arousal systems may differ from its effects on cognition (Mayes & Bornstein, 1995). Some studies have reported that early information processing is negatively affected by cocaine exposure (Eisen et al., 1991; Mayes, Granger, Frank, Schottenfeld, & Bornstein, 1993). Specifically, cocaine-exposed infants showed significant deficits in habituation, an early form of information processing requiring adaptation to novel stimuli. Sustained attention to a novel stimulus includes the active intake of information and alteration of arousal responses (Mayes & Bornstein, 1995), suggesting that deficits in the modulation or activation of arousal processes can influence attentional processes (Pribram & McGuiness, 1975; Ruff, 1988). The dopaminergic system, a key system affected by cocaine, is also implicated in arousal regulation (Coles & Robbins, 1989) and some reports of cocaine-exposed infants have identified their arousal mechanisms and attentional organization as inadequate (Karmel & Gardner, 1996; Singer et al., 1994).

A basic measure of visual perception and attention is operationalized through the tendency of the infant to fixate on some stimuli more than others (Fantz, 1956). Evidence of visual perception and discrimination is well documented in neonates (Fantz, 1961; Hershenson, 1964) and three-week-old infants (Brennan, Ames, & Moore, 1966). Werner and Siqueland (1978) found that infants from birth are able to discriminate among highly disparate targets on a recognition test. The emergence of infant visual preferences for a novel

over a previously exposed stimulus has been used to explore memory processes in infants as young as three months of age (Fagan, 1970). Recently, Slater, Mattock, Brown, Burnham, & Young (1991) found evidence, using infant-controlled habituation, that newborns process visual stimuli, confirming earlier studies of novelty preferences in newborns (Slater, Morison, & Rose, 1982, 1983, 1984). Moreover, prior studies have demonstrated significant differences in visual recognition memory between term healthy infants and risk groups, including infants with Down Syndrome (Cohen, 1981; Miranda & Fantz, 1974), institutionally reared children (Fantz & Nevis, 1967), central nervous system impaired infants (Fagan & Singer, 1983), preterm infants (Caron & Caron, 1981; Rose, 1981, 1983; Sigman & Parmelee, 1974), infants with prenatal polychlorinated biphenyl (PCB) exposure (Jacobson, Fein, Jacobson, Schwartz, & Dowler, 1985), intrauterine growth retarded infants (Gotlieb, Biasini, & Bray, 1988) and infants diagnosed with organic and non-organic failure-to-thrive (Singer & Fagan, 1984).

There are a limited number of studies which have investigated the association of fetal cocaine exposure to visual selectivity in early infancy. One study comparing non-cocaine and cocaine-exposed three-month-old infants using an infant-controlled habituation procedure found that cocaine-exposed infants were more likely to fail to attend visually to the habituation stimulus, but differences were not found between the cocaine-exposed infants and the non-exposed infants in their recovery to a novel stimulus (Mayes et al., 1995). Another study compared the visual recognition memory of non-drug exposed and poly drug exposed infants at 7-8 months (Struthers & Hansen, 1992). The drug-exposed infants showed poorer novelty preferences on the Fagan Test of Infant Intelligence (Fagan & Shephard, 1983). Cocaine exposure, however, was confounded with exposure to other illicit drugs and alcohol in addition to cocaine. In a large, well controlled study, Jacobson and colleagues (Jacobson, Jacobson, Sokol, Martier, & Chiodo, 1996) tested non-cocaine exposed and cocaine-exposed infants at 6.5 and 12 months corrected ages, and found that infants with history of heavy cocaine exposure, even after accounting for the effects of other drugs, had poorer recognition memory performance on the Fagan Test, while lightly exposed infants were comparable to non-exposed controls. These studies suggest that in utero cocaine exposure may affect infant visual selectivity and cognitive development. The purpose of the present study was to determine if cocaine-exposed infants would exhibit differences in visual selectivity, compared to non-cocaine exposed infants, on similar visual-perceptual tasks administered during the neonatal period.

METHOD

Participants

A total of 415 infants (218 cocaine-exposed, 197 non-exposed) were recruited at birth to participate in a longitudinal study of the sequelae of fetal drug exposure. All of the mothers and infants were recruited from a large, urban county teaching hospital. All of the women were identified from a high risk population that was screened for drug use at the hospital. Urine samples were obtained immediately before or after labor and delivery and were analyzed for the presence of cocaine metabolites (benzoylecgonine), cannabinoids, opiates, PCP, and amphetamines. Urine toxicology screens for drugs are performed by the hospital on all women who receive no prenatal care, appear to be intoxicated or taking drugs, who have a history of involvement with the Department of Human Services in previous pregnancies, or who self-admit or appear to be high risk for drug use after interview by a social worker or medical resident. The Syva Emit method (Syva Company, Palo Alto, CA) was used for urine analysis. The specificity for benzoylecgonine was 99% at a concentration

of 0.3 mg/mL. Follow-up thin layer chromatography or gas chromatography analyses were performed. The infants also had meconium drug analyses performed for cocaine and its metabolites (benzoylecgonine (BZE), metahydroxybenzoylecgonine (m-OH-BE), cocaethylene), cannabinoids (THC), opiates, PCP, and amphetamines, (Lewis, Moore, & Leikin, 1994; Ostrea, Brady, Parks, Asensio, & Naluz, 1989).

A nurse recruiter approached all women who had been screened shortly before or after infant birth. Six-hundred and forty-seven mothers and their infants were identified, of whom 54 subjects were excluded (20 cocaine positive, 34 cocaine negative). Reasons for exclusion included no meconium (15), Down syndrome (2), maternal psychiatric history (16), primary heroin user (2), HIV positive (5), maternal low IQ (1), fetal alcohol syndrome (1), maternal age < 19 years (2), maternal chronic illness (4), infant medical illness (3), and other (3). One-hundred and fifty-five mothers refused to participate (49 cocaine positive, 106 cocaine negative), and four infants died before the first visit. Of the mothers who agreed to participate, 23 (9 positive, 14 negative) did not show up for the first visit. Therefore, 415 women and their infants enrolled in the study. The visual attention assessment was given to 267 (131 cocaine-exposed and 136 non-exposed) of 382 infants who came for the initial visit within the time window of the assessment (between 38 and 44 weeks corrected ages) and who were not asleep or too fussy to be assessed during the visit.

Cocaine-exposed infants were identified by a positive response on any one of the following measures: infant meconium, urine, or maternal urine positive for cocaine, maternal report to hospital staff or maternal self-report during clinical interview. In order to be a control subject, all of the above indicators had to be negative. Women who used alcohol, marijuana, or tobacco during pregnancy were included in both groups. Infants who were cocaine positive were further sub-divided into heavy and light categories. The heavy cocaine use classification was determined by meconium screen or self report indication of use greater than the 70th percentile for the cocaine users. Of the infants assessed, there were 75 classified as heavily exposed, 56 lightly exposed, and 136 non-exposed. For 10 women who denied cocaine use, but whose infants' meconium screens were positive for cocaine, self-report data were estimated by assigning them the median score for the group (heavy/light) to which they were assigned based on meconium status.

Procedures

Infants and their biologic or foster mothers/caregivers were seen as soon as possible after birth, at which time, the biologic mother was interviewed regarding her drug use. The Maternal Post-Partum Questionnaire (Singer et al., 1997) was used to quantify maternal drug use the month prior to and during each trimester of pregnancy and to document drug taking behavior. For the month prior to pregnancy, and for each trimester of pregnancy, mothers were requested to recall frequency and amount of drug use. For tobacco, the number of cigarettes smoked per day was recorded. For marijuana, the number of joints per day, and for alcohol, the number of drinks of beer, wine, or hard liquor per day was computed, with each drink equivalent to .5 ounces of absolute alcohol. For cocaine, the number of rocks consumed and amount of money spent per day were noted. For each drug, the frequency of use was recorded on a Likert type scale ranging from 0 (not at all) to 7 (daily use), which was then converted to reflect the average number of days per week a drug was used. The frequency of use was multiplied by the amount used per day to compute a severity of use score for the month prior to pregnancy and for each trimester. This score was then averaged for a total score for the prenatal exposure for each drug.

Demographic and medical characteristics at the time of infant birth were taken from hospital birth record. These included maternal race,

age, gravida, parity, number of prenatal care visits, type of medical insurance, infant Apgar scores, and infant birth outcomes. At the initial visit, maternal socioeconomic status and maternal education were calculated, maternal vocabulary score was measured using the Peabody Picture Vocabulary Test - Revised (PPVT-R) (Dunn & Dunn, 1981) and two subtests of the Wechsler Adult Intelligence Scale - Revised (WAIS-R) (Wechsler, 1981) were administered, i.e., the Block Design (BD), and Picture Completion (PC) subtests to obtain an estimate of non-verbal intelligence. Mothers were also administered the Brief Symptom Inventory (Derogatis, 1992) to obtain an overall measure of self-reported severity of psychological distress, the General Severity Index (GSI) (see Singer et al., 1997 for details). The Hobel Neonatal Risk Index (Hobel, Gyvarinem, Okado, & Oh, 1973) was also computed by a research nurse practitioner from chart review to obtain a measure of neonatal medical complications.

The visual recognition testing apparatus consisted of a box like structure with a pivoting stage, a complete description of which can be found in Fagan and Shephard (1983). The infant and mother sat on one side while the observer sat on the other side. The stage was opened by the observer and the stimuli were attached outside of the infant's view. A peephole halfway between the two stimuli allowed the observer to record the infant's visual fixations. A digital timer was used to measure the length of each fixation. Mothers were instructed not to speak during the testing session.

The assessment consisted of four pairs of visual stimuli constructed on matte paper and mounted on grey cardboard (See Figure 1). The dimensions of the stimuli used in the first and second problems were 21.5 x 21.5 cm, of the third problem stimuli, 19 x 19 cm, and of the fourth problem stimuli, 19 x 17.5 cm. In the first problem, the familiarized stimulus had the amplitude spectrum of the schematic face and the face spectrum of a lattice (Kleiner, 1987). The novel stimulus was a schematic face (Fantz, 1961) with white features on a black background (D-A_1). In the second problem, the familiarized stimulus was an irregular lattice of white squares in a black circle with a 16 cm diameter. The novel stimulus was again the schematic face with white features on a black background (B-A_2). In the third problem, the familiarized stimulus consisted of 2 white 13 x 6.5 cm rectangles aligned side by side on a black background. The novel stimulus consisted of two white hourglass shapes of comparable size to the previous rectangles on a black background (K_2V-K_1V). The familiarized stimulus in the fourth problem consisted of six white, 14.5 x 1.5 cm vertical rectangles on a black background. The novel stimulus was a white bull's eye with a diameter of 16 cm on a black background (A_6-A_4).

Each infant was seated on the mother's lap approximately 35 cm from the stimuli. Each familiarized stimulus was presented on the left

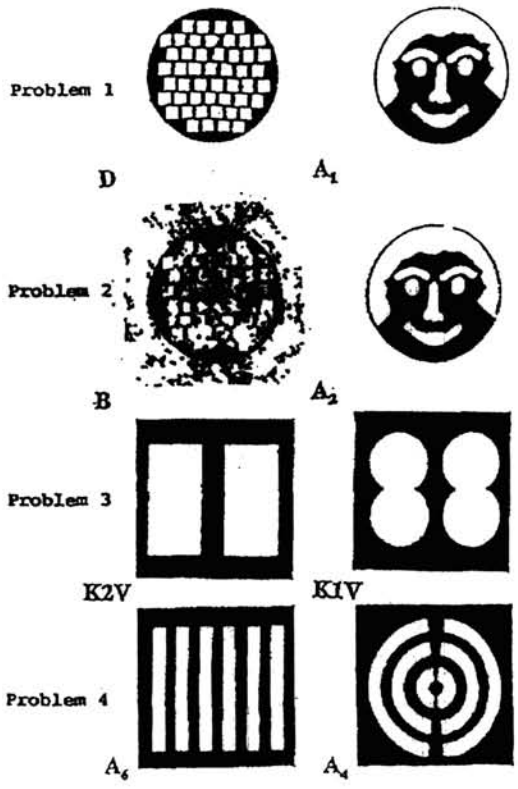

FIGURE 1
Stimuli Used in Visual Recognition Problems.

TABLE 1
Demographic Characteristics

Characteristic	Cocaine Mean ± SD	Non-Cocaine Mean ± SD	χ^2/t
Mother			
Age (years)	29.3 ± 5	25.6 ± 5	6.2***
Gravida	4.8 ± 2	3.7 ± 2	3.9****
Parity	3.3 ± 2	2.7 ± 2	2.6**
Prenatal care received	70.8%	88.2%	12.5***
Month began prenatal care	3.8 ± 2	3.2 ± 2	2.0*
Number of prenatal visits	5.6 ± 5	8.7 ± 5	5.5***
Use tobacco	90%	41%	66.1***
Use alcohol	80%	45%	32.7***
Use amphetamines	1%	2%	.3
Use barbituates	0%	1%	.9
Use heroin	2%	0%	2.1
Use PCP	2%	0%	2.1
Use marijuana	44%	12%	34.1**
PPVT-R Score	74.1 ± 13	77.9 ± 15	2.1*
WAIS PC Score	6.6 ± 2	6.9 ± 2	1.0
WAIS BD Score	7.0 ± 2	7.2 ± 2	.8
GSI Score	.80 ± .7	.53 ± .5	3.5***
Ethnicity			
Black	101 (77%)	108 (79%)	6.5
White	15 (12%)	17 (13%)	
Hispanic	3 (2%)	0	
Bi-racial	9 (7%)	11 (7%)	
Other	3 (2%)	0	
Maternal education			
Less than high school	52 (43%)	43 (32%)	
High school	46 (38%)	54 (41%)	4.8
Some college	20 (17%)	34 (26%)	
College Graduate	3 (3%)	2 (2%)	
Marital Status			
Married	12 (10%)	25 (18%)	
Single	90 (74%)	88 (66%)	14.2
Divorced	6 (5%)	11 (8%)	
Separated	11 (9%)	9 (8%)	
Widowed	2 (2%)	0 (0%)	
Work Status			
Full time	0 (0%)	2 (2%)	
Part time/at home	(14%)	(23%)	9.2*
Unemployed	33 (28%)	43 (33%)	
Never Employed	68 (58%)	55 (42%)	
Annual Income			
$0 - $10,000	116 (100%)	118 (93%)	8.5
$10,000 - $20,000	0	9 (7%)	
Infant			
Birthweight (gms)[1]	2765 ± 639	3108 ± 642	4.4***
Gestational Age (weeks)	37.9 ± 2	38.7 ± 2	2.6**
Birth length (cm)[1]	47.5 ± 4	49.2 ± 4	3.6*
Head circumference (cm)[1]	32.7 ± 3	33.7 ± 2	3.3*
Apgar - 1 minute	8.2 ± 1	8.0 ± 2	-.9
Apgar - 5 minutes	8.9 ± .4	8.8 ± 1	-.9
% Female	51.5%	47.7%	0.5
% AGA	87.4%	93.3%	7.6*
Hobel Score	5.3 ± 12	4.0 ± 13	.9

[1]p's adjusted for gestational age
+$p < .10$, *$p < .05$, **$p < .01$, ***$p < .001$, ****$p < .0001$

side until 15 seconds of looking were accumulated and then on the right side for 15 seconds. The familiar target was then paired with the novel target for 10 seconds of accumulated looking time, after which right and left positions were reversed and another pairing trial was performed. This procedure was performed for each of the four problems. The order of presentation was the same for all infants. The observer recorded looking time when the reflection of the stimulus was reflected in the center of the infant's cornea. All examiners were blinded to the cocaine status of the infant, and separate research personnel recruited and followed mothers into the study and conducted drug interviews. Examiners were balanced across exposure groups, and had been trained to reliability levels > .90 prior to the study.

This study was approved by the Institutional Review Board of the participating hospital, and maternal written informed consent was obtained for infant participation.

Statistical Analysis

Prior to analysis, cocaine, cigarette, alcohol, and marijuana self-report and meconium variables, which were positively skewed, were normalized by means of log x + 1 transformation. Means and standard deviations are reported in terms of the original distribution. Log transforms were used in correlation and regression analyses.

The cocaine negative and cocaine positive mothers and infants were compared on demographic variables, frequency and severity of drug use, and infant birth outcomes, using t tests for continuous data and χ^2 analyses for categorical variables. Additional analyses, comparing those infants who came to the follow-up visit versus those who did not and those who were able to be administered the assessment and those who were not, were also completed on the same demographic variables.

Percent novelty score, the ratio of time spent looking at the novel stimulus versus total looking time, was calculated for each problem. The mean novelty scores for each group for each of the 4 problems were compared utilizing a mixed models approach with restricted maximum likelihood estimation procedures. PROC from SAS version 6.12 was employed to assess group differences and the rate of change in the novelty scores over the problems between the heavily cocaine-exposed, lightly exposed, and the non-cocaine exposed infants and any interactions.

Pearson product moment or Spearman rank order correlations were used to assess the relationship of prenatal drug exposure and demographic and medical factors to infant novelty preferences. Hierarchical multiple regression analysis was used to evaluate the predictive power of cocaine exposure after control for confounding and mediating factors.

Sample Characteristics

Demographic and medical characteristics of the cocaine-exposed and the non-cocaine exposed infants seen at the neonatal follow-up visit are presented in Table 1. Cocaine using women were older, had more children and were less likely to have received prenatal care. The majority of both groups were Black, with a high school education or lower, of low income status and unemployed. Cocaine using women were less likely to be married. The majority of cocaine using women (84%) and non-using women (90%) received nutritional supplements (WIC) during pregnancy due to low income status, χ^2 (4, N = 389) = 1.8, $p < .18$. Cocaine-exposed infants were of lower gestational age, birthweight, and head circumference. There were significant differences between light and heavy cocaine users only on maternal GSI score, with heavy users having higher severity scores than light users (.92 ± 8 versus .60 ± .4, t (178) = -2.9, $p < .01$).

Table 2 shows the summary measures of frequency and severity of drug use for alcohol, marijuana, tobacco, and cocaine for cocaine positive (light and heavy) and cocaine negative users during the month prior to and during the trimesters of pregnancy. Because the data were skewed by two very heavy users, the means for

TABLE 2
Summary Measures of Drug Use by Group

	Cocaine Negative	Cocaine Positive	
		Light	Heavy
Number of Cigarettes/Day/Total	Mean ± SD 4.5 ± 9	Mean ± SD 9 ± 8	Mean ± SD 14 ± 13***a,b,c
Alcohol[1]			
Month Prior	2.2 ± 7	8.4 ± 11	19.2 ± 32***a,b
Trimester 1	1.2 ± 4	6.2 ± 10	18.3 ± 31***a,b,c
Trimester 2	.3 ± 1	4.9 ± 11	12.4 ± 27***a,b,c
Trimester 3	.6 ± 6	4.5 ± 11	8.1 ± 21***a,b,c
Average over pregnancy	1.1 ± 4	6 ± 8	14.5 ± 24***a,b,c
Marijuana[2]			
Month Prior	1.2 ± 7	1. ± 2	2.4 ± 5***b
Trimester 1	.8 ± 4	.9 ± 3	2.1 ± 5**b
Trimester 2	.3 ± 2	.5 ± 2	2.2 ± 6***b,c
Trimester 3	.1 ± 9	.5 ± 2	1.5 ± 5***b,c
Average over pregnancy	.6 ± 3	.8 ± 2	2 ± 5***b,c
Cocaine[3]			
Month Prior		7.5 ± 7	48.7 ± 67**
Trimester 1		8.1 ± 8	58.7 ± 85**
Trimester 2		4.2 ± 4	45.5 ± 81***
Trimester 3		3.3 ± 5	20.4 ± 37**
Average over pregnancy		6.2 ± 4	42.5 ± 52***

a negative/light *$p < .05$
b negative/heavy **$p < .01$
c heavy/light ***$p < .001$
[1]Number of drinks per occasion x number of days/week
[2]Number of joints per occasion x number of days/week
[3]Number of rocks per occasion x number of days/week

heavy users are somewhat misleading. The median unit of use averaged over the pregnancy for all cocaine users was 8.30 units; for heavy users, 24.75 units, and for light users, 5.25 units. Light and heavy cocaine users also differed in their severity of use of tobacco, alcohol, and marijuana (see Table 2). Heavy cocaine users, on average, ingested more than twice the amount of tobacco, alcohol, and marijuana over pregnancy than light users. The amount of cocaine used over pregnancy was increased more than five-fold for heavy users. The cut-off point indicating ≥ the 70th percentile for users was 17.5 rocks of cocaine per week.

Table 3 presents the amounts of nanograms/gram of cocaine metabolites extracted from the meconium for light and heavy users.

Infants were seen for assessment within a two month window after birth. The mean age (corrected for prematurity) for cocaine-exposed infants was 42.9 weeks ($SD = 2$) and for non-exposed infants was 43.0 weeks ($SD = 3$), $t\ (240) = -.03$, $p < .98$.

Within the non-cocaine exposed group, those infants who came to the visit had lower birthweights, $t\ (192) = 2.1$, $p < .05$ and lower gestational ages, $t\ (13) = 2.4$, $p < .05$ than those who did not. Within the cocaine-exposed group, infants who came to the visit differed from those who did not in five minute apgar scores, $t\ (38) = -2.6$, $p < .05$. Maternal characteristics were significantly different for number of prenatal visits, $t\ (211) = -2.5$, $p < .02$, and with a trend for parity, $t\ (212) = 1.8$, $p < .08$ and maternal education, $t\ (197) = -1.9$, $p < .06$, suggesting greater risk for cocaine-exposed infants who did not come to the visit. For those infants who were able to be assessed versus those infants who came to the first visit but were untestable, within the cocaine-exposed group, there were significant differences in the five minute, $t\ (74) = -2.4$, $p < .02$ apgar scores,

TABLE 3
Meconium Metabolites by Group

	Light (n = 36) Mean ± SD Range	*Heavy (n = 63) Mean ± SD Range*
Nanograms/gram Cocaine	1.9 ± 9 (0-51)	226.2 ± 453 (0-2271)
Nanograms/gram Benzoylecgonine	16.3 ± 38 (0-152)	853.9 ± 1377 (0-7088)
Nanograms/gram m-OH-benzoylecgonine	10 ± 21 (0-91)	564 ± 1782 (0-9998)

and in head circumference, t (190) = -2.4, $p < .02$, all indicating greater risk for the infants who did not complete the assessment. None of the maternal variables was significant. Within the non-exposed group, significant differences were found for infant gestational age, t (62) = -2.1, $p < .04$, and head circumference, t (57) = -2.3, $p < .03$, with those infants who did not complete the test at greater risk.

RESULTS

Prior to assessing group differences, relationships between the outcome variables (percent novelty for each of the 4 problems) and all demographic, medical and drug confounding or potentially mediating variables noted previously were tested through Pearson or Spearman correlational analyses. Those variables even weakly ($p < .10$) related to outcome were considered confounders or potential mediators. Percent novelty on any problem was unrelated to infant gender, Hobel score, gestational age, birthweight, length, head circumference, apgar score, severity of tobacco, alcohol, or marijuana exposure, maternal age, gravida, parity, education, number of prenatal care visits, socioeconomic status, vocabulary score, or WAIS subscale scores. GSI score was marginally related to percent novelty on problem 1 (r = -.11, $p < .1045$. Percent novelty was related to infant age at time of test, r = -.22, $p < .001$. Since groups did not differ in this variable, it could not be considered either a mediator or confounder (See Baron & Kenny, 1986; Jacobson, Jacobson, Sokol, Martier, & Ager, 1993).

TABLE 4
Mean Percent Novelty by Group

	Cocaine Negative	*Cocaine Positive*	
		Light	*Heavy*
Problem 1			
M	65.8%	62.8%	56.6%*
SD	27	25	27
Problem 2			
M	60.0%	65.5%	61.5%
SD	26	28	22
Problem 3			
M	51.6%	58.9%	51.8%
SD	28	24	29
Problem 4			
M	47.8%	51.8%	44.7%
SD	27	24	28
Mean Novelty Score			
M	57%	60.6%	54.6%
SD	15	14	16

*Post-hoc Comparisons:
t [df = 672] = .69, $p < .49$ for light vs. negative
t [df = 672] = 2.4, $p < .02$ for heavy vs. negative

Results of the multivariate analysis are illustrated in Table 4. The main effect of group (none, light or heavy exposure) had a trend toward significance, F (2,264) = 2.7, $p < .07$. Post-hoc group contrasts indicated that there was a significant difference of a low/medium effect size ($d = .37$) in percent novelty on problem 1 between the non-exposed and the heavily exposed infants with heavily exposed infants having lower novelty preferences. Heavily exposed infants had a mean novelty score of 57% while lightly exposed infants had a mean score of 63% which was not different from non-exposed infants. Severity of cocaine exposure continued to predict novelty preference on Problem 1 after control for maternal distress ($\beta = -.14$, t (2,230) = 2.0, $p < .04$). When novelty scores which were considered "at-risk" were compared, (i.e., ≤ 53% based on Fagan & Detterman, 1992, and Jacobson et al., 1993), heavily exposed infants were also more likely to be considered at risk, 54% versus 42%, χ^2, 1 (204) = 2.6, $p < .05$, one-tailed.

There was a significant effect for time, F (3,672) = 12.9, $p < .0001$. The novelty scores on Problem 1 were significantly higher than the scores observed on problem 4 for all groups, indicating a significant decrement in infant visual selectivity over time to chance levels. Differences between Problems 1 and 4 were 17.9% (SE = 3.4) for the non-exposed group, t (672) = 5.2, $p < .001$; 11.1% (SE = 5.6) for the lightly exposed group, t (672) = 2.0, $p < .05$; and 11.9% for the heavily exposed group, t (672) = 2.6, $p < .01$. The group (severity of cocaine exposure) x time interaction was not significant.

Mean novelty scores for problems 1 and 2 indicated that all groups of infants had reliable visual preferences for the schematic face when tested against chance performance (50%). By the fourth problem, no group of infants exhibited a novelty preference, likely demonstrating a fatigue effect. The average novelty scores across the problems were not different by group.

Cocaine's potentially interactive effects with other drugs were examined by comparing the percentages of infants who received percent novelty scores on problem 1 above (> 53%) or below (≤ 53%) the risk cut-off through contingency tables based on cocaine positive/negative and marijuana or alcohol positive/negative status. There were no interaction effects with alcohol or marijuana. Tobacco interactions could not be explored because virtually all cocaine users also smoked tobacco.

We also examined whether cocaine exposure was related to whether or not infants were unable to be tested or failed to complete the 4 problems. Out of 155 non-exposed infants, 44 (28%) were too fussy to be tested or did not complete the 4 problems, compared to 31 out of 70 lightly exposed (44%) and 21 of 82 (26%) heavily exposed infants. Infants with light cocaine exposure were less likely to be testable or to complete the test than the non-exposed, $z = 2.21$, $p < .03$, or the heavily exposed groups, $z = 2.16$, $p < .03$.

Relationship of Demographic, Medical, and Biologic and Self-Report Measures of Drug Exposure to Novelty Preference

A number of measures of cocaine use correlated with percent novelty on problem 1, i.e., the number of rocks of cocaine used per occasion for trimesters 2, $r = -.16$, $p < .01$, and 3, $r = -.16$, $p < .01$; the amount of money spent on cocaine the month prior, $r = -.11$, $p < .1$, and in trimesters 2, $r = -.18$, $p < .01$, and 3, $r = -.17$, $p < .05$; the number of days per week of cocaine use in trimesters 2, $r = -.17$, $p < .008$ and 3, $r = -.16$, $p < .001$, and the summary measure of cocaine use for trimesters 2, $r = -.16$, $p < .01$, and 3, $r = -.16$, $p < .01$.

Meconium assays of cocaine metabolites also were evaluated. Nanograms/gram of benzoylecgonine were significantly negatively related to novelty score on problem 1, $r = -.15$, $p < .05$, and there was a similar trend for m-O-H benzoylecgonine, $r = -.12$, $p < .07$. THC was unrelated, $r = .07$, $p < .31$. The average score across the 4 problems was also related to the amount of cocaine metabolite found in meco-

nium. Although there were no group differences in the average score across the 4 problems, i.e., nanograms/gram of cocaine, $r = -.13$, $p < .06$; benzoylecgonine, $r = -.13$, $p < .05$; and m-OH-benzoylecgonine, $r = -.14$, $p < .04$.

DISCUSSION

The present study examined early visual information processing in cocaine-exposed and non-exposed neonates. At a mean of three weeks corrected age, four separate visual recognition memory tasks were administered which exploited previously demonstrated normal infant visual preferences for face-like (Fantz, 1961; Kleiner, 1987) and curved forms (Fantz, Fagan, & Miranda, 1975) when other stimulus characteristics are equivalent. Cocaine-exposed infants demonstrated significantly lower novelty preference scores on the first problem, with heavily exposed infants performing more poorly than non-exposed infants. This dose-response relationship was found with both biologic measures of the quantity of cocaine metabolites in infant meconium and with maternal self-report measures, further strengthening this finding. On the second problem, while all groups continued to demonstrate reliable novelty preferences, there were no group differences. Novelty preferences decreased over the four problems for all groups, with only chance responding evident by the last trial.

The poorer novelty preferences of the heavily cocaine-exposed group in the present study are consistent with the lower visual recognition memory performance scores noted in heavily cocaine-exposed infants at 6 1/2 and 12 months of age in prior studies (Jacobson et al., 1996; Struthers & Hansen, 1992). In the perinatal period, other investigators have found cocaine-exposed neonates to demonstrate poorer habituation (which includes reaction to the repeated presentation of a visual stimulus) on the NBAS (Eisen et al., 1991; Mayes et al., 1993), poorer orientation (Mirochnick et al., 1997; Delaney-Black et al., 1996), and to demonstrate deficits in arousal-modulated attention similar to those noted in neonates with central nervous system compromise (Gardner, Karmel, & Magnano, 1992). Similarly, abnormalities in the left hemisphere visual attention system have been implicated in a study which found that cocaine-exposed infants are slower to orient to stimuli in the right visual field (Heffelfinger, Craft, & Skyken, 1997). A small study found signs of visual stress and poorer visual following in cocaine-exposed newborns (Napiorkowski et al., 1996), although obstetric drugs may have confounded these findings. The present study's findings are also consistent with reports of the relationship of cocaine exposure to attentional difficulties in preterm (Singer et al., 1994) and term (Arendt et al., 1998) infants at older ages, and to reports of relative impairment in visual-motor abilities in small samples of cocaine-exposed children at preschool age (Bender et al., 1995).

The present study also supports theories related to the neurobiological effects of cocaine exposure which suggest that early attention and information processing may be disrupted through cocaine's effects on developing monoaminergic transmitter systems (Mayes, 1994). Visual attention and memory tasks which tap into fundamental neurobehavioral processes in the neonatal period have the advantage of being mediated by neuropsychological processes which have not been as affected by environmental influences as tasks measured later in life.

Prenatal marijuana and alcohol exposure were unrelated to neonatal visual preferences in this study. Fried and Makin (1987) found altered visual responsiveness on the BNBAS, in a middle class, low risk sample, but others found no marijuana effects on BNBAS performance (Richardson, Day, & Taylor, 1989). The lack of alcohol effect is consistent with findings by Jacobson et al. (1993) on the Fagan Test of Infant Intelligence at older ages. Moreover, in the present study, the amount of cocaethylene, a metabolite formed through the

combined use of cocaine and alcohol, (Church, Holmes, Overbeck, Tilak, & Zajac, 1991) was unrelated to novelty preference, despite relationships of novelty preference with the quantity of two other cocaine metabolites.

The present study suggests that neonatal visual attention and discrimination tasks may be sensitive to teratologic effects. Such tasks have proved discriminating in assessments of a wide variety of risk conditions in the first year of life (Fantz & Nevis, 1967; Fagan & Singer, 1983; Singer & Fagan, 1984; Rose, 1983). Such tasks may prove useful in detecting teratologic effects since they encompass visual discrimination, attention, and memory processes important to later learning. In the present assessment, both cocaine-exposed and non-exposed infants were able to demonstrate novelty preferences on the first two problems, replicating Fantz's (1961) and Kleiner's (1987) studies with newborns, but heavily exposed infants had poorer scores. The significant decrement by all groups to chance levels by the fourth problem is likely a fatigue effect, but could also reflect that these comparisons were too difficult for the neonates. Since the four problems were given in univariate order, future studies should control for order effects, or attempt to incorporate rest periods between items.

The present study has several advantages which may have increased the likelihood of detecting significant drug effects. Maternal drug status was determined through both biologic (meconium and urine screen) and clinical means, enhancing reliability of classification. Moreover, severity of nicotine, alcohol, and marijuana use were quantified, reducing the likelihood that the effects of other drugs are undercontrolled and that the observed effects are actually due to other drugs. All infants were also tested when any drugs, including obstetric drugs, would have cleared the infant's system; thus the findings are not due to acute or withdrawal effects.

Some limitations to the present study should be considered. Although examiners were blinded to infant cocaine exposure status, it may have been possible to identify drug exposure through maternal or caregiver behaviors or characteristics since all infants were assessed with the caregiver present. Another issue concerns that the drug assessments were conducted retrospectively, making reliability of report problematic. The classification of cocaine users into heavy and light groups, however, was more reliable due to the additional meconium data.

Acknowledgments: The Department of Pediatrics, Case Western Reserve University School of Medicine, and the Department of Psychology, Case Western Reserve University, Cleveland, Ohio is supported by Grants RO1-07259 and R29 07358 from the National Institute on Drug Abuse and the General Clinical Research Center RR00080. Lynn T. Singer, Ph.D., The Triangle Building, 11400 Euclid Avenue, Suite 250-A, Cleveland, Ohio 44106. Thanks are extended to the participating families, to Drs. Marc Collin, Mary Lou Kumar, and Laurel Schauer and to the staff of The Center for the Advancement of Mothers and Children at MetroHealth Medical Center. Also, Terri Lotz-Ganley for manuscript preparation; Joanne Robinson, Kristen Weigand, Adela Kuc, Marilyn Davillier, Lois Klaus, Val Petran, and Dr. Carol Siegal for research and data analytic assistance.

REFERENCES

Akbari, H., & Azmitra, E. (1992). Increased tyrosine hydroxylase immunoreactivity in the rat cortex following prenatal cocaine exposure. *Developmental Brain Research, 66*, 277–281.

Arendt, R. E., Singer, L. T., Angelopoulos, J., Busdieker, O., & Mascia, J. (1998). Sensorimotor development in cocaine-exposed infants. *Infant Behavior and Development, 21*, 627–640.

Baron, R. M., & Kenny, D. A. (1986). The moderator-mediator variable distinction in social psychological research: conceptual, strategic, and statistical considerations. *Journal of Personality and Social Psychology, 51*, 1173–1182.

Bayley, N. (1969). *Bayley Scales of Infant Development*. New York: Psychological Corporation.

Bayley, N. (1993). *Bayley Scales of Infant Development* (2nd ed.). San Antonio, TX: The Psychological Corporation.

Bender, S. L., Word, C. O., DiClemente, R. J., Crittendon, M. R., Persand, N. A., & Ponton, L. E. (1995). The developmental implications of prenatal and/or postnatal crack cocaine exposure in preschool children. *Developmental and Behavioral Pediatrics, 16,* 418–424.

Brazelton, T. B. (1984). *Neonatal Behavioral Assessment Scale* (2nd ed.). London: Spastics International Medical Publications.

Brennan, W. M., Ames, E. W., & Moore, K. W. (1966). Age differences in infants' attention to patterns of different complexity. *Science, 151,* 335–356.

Caron, A. J., & Caron, R. F. (1981). Processing of relational information as an index of infant risk. In S. L. Friedman & M. Sigman (Eds.), *Preterm birth and psychological development* (pp. 219–240). New York: Academic Press.

Chasnoff, I. J., Griffith, D. R., Freier, C., & Murray, J. (1992). Cocaine/poly drug use in pregnancy: Two year follow–up. *Pediatrics, 89,* 284–289.

Church, M. W., Holmes, P., Overbeck, G., Tilak, J., & Zajac, C. (1991). Interaction effects of prenatal alcohol and cocaine exposure on postnatal mortality, development, and behavior in the Long-Evans rat. *Neurotoxicology and Teratology, 13,* 377–386.

Cohen, L. B. (1981). Examination of habituation as a measure of aberrant infant development. In S. L. Friedman & M. Sigman (Eds.), *Preterm birth and psychological development* (pp. 241–253). New York: Academic Press.

Coles, B. J., & Robbins, T. W. (1989). Effects of 6-hydroxydopamine lesions of the nucleus accumbens septi on performance of a 5-choice serial reaction time task in rats: Implications for theories of selective attention and arousal. *Behavioral Brain Research, 33,* 165–179.

Coles, C. D., Platzman, K. A., Smith, I. E., James, M. E., & Falek, A. (1992). Effects of cocaine and alcohol use in pregnancy on neonatal growth and neurobehavioral status. *Neurotoxicology Teratology, 14,* 23–33.

Delaney-Black, V., Covington, C., Ostrea, E., Romero, A., Baker, D., Tagle, M. T., Nordstrom-Klee, B., Silvestre, M. A., Angelilli, M. H., Hack, C., & Long, J. (1996). Prenatal cocaine and neonatal outcome: Evaluation of dose-response relationship. *Pediatrics, 98,* 735–740.

Derogatis, L. (1992). *The brief symptom inventory: Administration, scoring, and procedures manual* (2nd ed.). Baltimore, MD: Clinical Psychometric Research, Inc.

Dunn, L., & Dunn, L. (1981). *Peabody picture vocabulary test-revised.* Circle Pines, MN: American Guidance Service.

Eisen, L. N., Field, T. M., Bandstra, E. S., Roberts, J. P., Morrow, C., Larson, S. K., & Steele, B. M. (1991). Perinatal cocaine effects in neonatal stress behavior and performance on the Brazelton Scale. *Pediatrics, 88,* 477–480.

Fagan, J. F. (1970). Memory in the infant. *Journal of Experimental Child Psychology, 9,* 217–226.

Fagan, J. F., & Detterman, D. (1992). The Fagan test of infant intelligence: A technical summary. *Journal of Applied Developmental Psychology, 13,* 173–193.

Fagan, J. F., & Shephard, P. A. (1983). *Fagan test of infant intelligence: Training manual.* Cleveland, OH: Infantest Corporation.

Fagan J. F., & Singer, L. T. (1983). Infant recognition memory as a measure of intelligence. In L. Lipsitt & C. Rovee-Collier (Eds.), *Advances in Infancy Research* (Vol. 2, pp. 31–78). Norwood, NJ: Ablex.

Fantz, R. L. (1956). A method for studying early visual development. *Perceptual and Motor Skills, 6,* 13–15.

Fantz, R. L. (1961). The origin of form perception. *Scientific American, 204*(5), 66–72.

Fantz, R. L., Fagan, J. F., & Miranda, S. B. (1975). Early perceptual development as shown by visual discrimination selectivity and memory with varying stimulus and population parameters. In L. Cohen & P. Salapatek (Eds.), *Infant perception: From sensation to cognition: Basic visual processes* (pp. 258–270). New York: Academic Press.

Fantz, R. L., & Nevis, S. (1967). Pattern preferences and perceptual-cognitive development in early infancy. *Merrill-Palmer Quarterly, 13,* 77–108.

Fried, P. A., & Makin, J. E. (1987). Neonatal behavioral correlates of prenatal exposure to marijuana, cigarettes, and alcohol in a low risk population. *Neurotoxicology and Teratology, 9,* 1–7.

Gardner, J. M., Karmel, B. Z., & Magnano, C. L. (1992). Arousal/visual preference interactions in high risk neonates. *Developmental Psychology, 18,* 821–830.

Gotlieb, S. J., Biasini, F. J., & Bray, N. W. (1988). Visual recognition memory in IUGR and normal

birthweight infants. *Infant Behavior and Development, 11,* 223–228.

Graham, K., Feiginbaum, A., Pastuszak, A., Nulman, I., Weksberg, R., Emerson, T., Goldberg, S., Ashby, S., & Koren, G. (1992). Pregnancy outcomes and infant development following gestational cocaine use by social cocaine users in Toronto, Canada. *Clinical Investigations in Medicine, 15,* 384–394.

Griffith, D., Azuma, S., & Chasnoff, I. (1994). Three year outcome of children exposed prenatally to drugs. *Journal of the American Academy of Adolescent Psychiatry, 33*(1), 20–27.

Heffelfinger, A., Craft, S., & Skyken, J. (1997). Visual attention in children with prenatal cocaine exposure. *Journal of the International Neuropsychology Society, 3,* 237–245.

Hershenson, M. (1964). Visual discrimination in the human newborn. *Journal of Comparative and Physiological Psychology, 58,* 270–276.

Hobel, C., Gyvarinem, M., Okado, D., & Oh, W. (1973). Prenatal and intrapartum high-risk screening. *American Journal of Obstetrics and Gynecology, 114,* 1–9.

Hurt, H., Brodsky, N. L., Betancourt, L., Braitman, L. E., Malmud, E., & Giannetta, J. (1995). Cocaine-exposed children: Follow-up through 30 months. *Developmental and Behavioral Pediatrics, 16,* 29–35.

Jacobson, S. W., Fein, G. G., Jacobson, J. L., Schwartz, P. M., & Dowler, J. K. (1985). The effect of intrauterine PCB exposure on visual recognition memory. *Child Development, 56,* 853–860.

Jacobson, S. W., Jacobson, J. L., Sokol, R. J., Martier, S., & Ager, J. (1993). Prenatal alcohol exposure and infant information processing ability. *Child Development, 64,* 1706–1721.

Jacobson, S. W., Jacobson, J. L., Sokol, R. J., Martier, S. S., & Chiodo, L. M. (1996). New evidence of neurobehavioral effects of in utero cocaine exposure. *The Journal of Pediatrics, 129,* 581–588.

Karmel, B. Z., & Gardner, J. M. (1996). Prenatal cocaine exposure effects on arousal modulated attention during the neonatal period. *Developmental Psychology, 29,* 463–480.

Kleiner, K. A. (1987). Amplitude and phase spectra as indices of infants' pattern preferences. *Infant Behavior and Development, 10,* 45–55.

Lewis, D., Moore, C., & Leikin, J. (1994). Cocaethylene in meconium specimens. *Clinical Toxicology, 32,* 697–703.

Mayes, L. C. (1994). Neurobiology of prenatal cocaine exposure effect on developing monoamine systems. *Infant Mental Health Journal, 15,* 121–133.

Mayes, L. C., & Bornstein, M. H. (1995). Developmental dilemmas for cocaine-abusing parents and their children. In M. Lewis & M. Bendersky (Eds.), *Mothers, babies, and cocaine: The role of toxins in development* (pp. 251–272). Hillsdale, NJ: Lawrence Erlbaum Associates.

Mayes, L. C., Bornstein, M. H., Chawarska, K., & Granger, R. H. (1995). Information processing and developmental assessments in 3 month old infants exposed prenatally to cocaine. *Pediatrics, 95,* 539–545.

Mayes, L. C., Granger, R. H., Frank, M. A., Schottenfeld, R., & Bornstein, M. (1993). Neurobehavioral profiles of neonates exposed to cocaine prenatally. *Pediatrics, 91,* 778–783.

Miranda, S. B., & Fantz, R. L. (1974). Recognition memory in Down's syndrome and normal infants. *Child Development, 45,* 651–660.

Mirochnick, M., Meyer, J., Frank, D. A., Cabral, H., Tronick, E. Z., & Zuckerman, B. (1997). Elevated plasma norepinephrine after in utero exposure to cocaine and marijuana. *Pediatrics, 99,* 555–559.

Napiorkowski, B., Lester, B. M., Freier, M. C., Brunner, S., Dietz, L., Nadra, A., & Oh, W. (1996). Effects of in utero substance exposure on infant neurobehavior. *Pediatrics, 98,* 71–75.

Neuspiel, D. R., Hamel, S. C., Hochberg, E., Green, J., & Campbell, D. (1991). Maternal cocaine use and infant behavior. *Neurotoxicology Teratology, 13,* 229–233.

Ostrea, E. M., Brady, M. J., Parks, P. M., Asensio, D. C., & Naluz, Â. (1989). Drug screening of meconium in infants of drug dependent mothers. *Journal of Pediatrics, 115,* 474–477.

Posner, M. I., & Peterson, S. E. (1988). Structures and functions of selected attention. In T. Boll & B. Bryant (Eds.), *Master lectures of clinical neuropsychology* (pp. 173–202). Washington, DC: American Psychological Association.

Pribram, K. H., & McGuiness, D. (1975). Arousal, activation, and effort in the control of attention. *Psychological Review, 82,* 116–149.

Richardson, G. A., & Day, N. L. (1991). Maternal and neonatal effects of moderate cocaine use during pregnancy. *Neurotoxicology and Teratology, 13,* 455–460.

Richardson, G. A., Day, N. L., & Taylor, P. M. (1989). The effect of prenatal alcohol, mari-

juana, and tobacco exposure on neonatal behavior. *Infant Behavior and Development, 12,* 199–209.

Rose, S. A. (1981). Lags in cognitive competence of prematurely born infants. In S. L. Friedman & M. Sigman (Eds.), *Preterm birth and psychological development* (pp. 255–269). New York: Academic Press.

Rose, S. A. (1983). Differential rates of visual information processing in full term and preterm infants. *Child Development, 54,* 1189–1198.

Ruff, H. A. (1988). The measurement of attention in high risk infants. In P. M. Vietze & H. G. Vaughan (Eds.), *Early identification of infants with developmental disabilities* (pp. 282–296). New York: Grune and Stratton.

Sigman, M., & Parmelee, A. H. (1974). Visual preferences of four month old premature and full term infants. *Child Development, 45,* 959–965.

Singer, L. T., Arendt, R., Farkas, K., Minnes, S., Huang, J., & Yamashita T. (1997). Relationship of prenatal cocaine exposure and maternal psychological distress to child developmental outcome. *Development and Psychopathology, 9,* 473–489.

Singer, L. T., & Fagan, J. F. (1984). Cognitive development in the failure-to-thrive infant: A three year longitudinal study. *Journal of Pediatric Psychology, 9,* 363–383.

Singer, L. T., Yamashita, T., Hawkins, S., Cairns, D., Baley, J., & Kliegman, R. (1994). Increased incidence of intraventricular hemorrhage and developmental delay in cocaine-exposed very low birthweight infants. *Journal of Pediatrics, 124,* 765–771.

Slater, A., Mattock, A., Brown, E., Burnham, E., & Young, A. (1991). Visual processing of stimulus compounds in newborn infants. *Perception, 20,* 29–33.

Slater, A., Morison, V., & Rose, D. (1982). Visual memory at birth. *British Journal of Psychology, 73,* 519–525.

Slater, A., Morison, V., & Rose, D. (1983). Perception of shape by the newborn baby. *British Journal of Developmental Psychology, 1,* 135–142.

Slater, A., Morison, V., & Rose, D. (1984). Habituation in the newborn. *Infant Behavior and Development, 7,* 183–200.

Struthers, J. M., & Hansen, R. L. (1992). Visual recognition memory in drug-exposed infants. *Journal of Developmental and Behavioral Pediatrics, 13,* 108–111.

Tennyson, V., Gershon, P., Budinkas, M., & Rothman, T. (1983). Effects of extended periods of reserpine and alpha-methyl-p-tyrosine treatment on the development of putamen in fetal rabbits. *International Journal of Developmental Neuroscience, 1,* 305–318.

Volpe, J. (1992). Effects of cocaine on the fetus. *New England Journal of Medicine, 327,* 135–142.

Wang, C., & Schnoll, S. (1986). Prenatal cocaine use associated with down regulation of receptors in the human placenta. *Neurotoxicology Teratology, 6,* 263–269.

Wechsler, D. (1981). *Weschler Adult Intelligence Scale - Revised.* San Antonio, TX: The Psychological Corporation.

Werner, J. S., & Siqueland, E. R. (1978). Visual recognition memory in the preterm infant. *Infant Behavior and Development, 1,* 79–94.

Wise, R. A. (1984). Neural mechanisms of the reinforcing action of cocaine. *National Institute of Drug Abuse Research Monograph, 50,* 15–33.

Woods, N., Eyler, F., Behnke, M., & Conlon, R. (1993). Cocaine use during pregnancy: Maternal depressive symptoms and infant neurobehavior during the first month. *Infant Behavior and Development, 16,* 83–98.

Woods, N., Plessinger, M., & Clark, K. (1987). Effects of cocaine on uterine blood flow and fetal oxygenation. *Journal of the American Medical Association, 257,* 957–961.

11 February 1998; Revised 03 September 1998 ■