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ABSTRACT. In the newborn period, infants prenatally exposed to cocaine and other drugs show low scores on the Neonatal Behavioral Assessment Scale. Beyond that period, research is limited on the effects of prenatal drug exposure on neurobehavioral functioning. In this study we compared infants exposed to cocaine and other drugs and control infants from low socioeconomic backgrounds on measures of neurobehavioral functioning during neuromotor assessment at 1, 4 and 7 months of life. None of the measures of neurobehavioral functioning showed any significant group differences. This study did not support the hypothesis of disrupted neurobehavioral functioning beyond the neonatal period in infants exposed to drugs prenatally. *[Article copies available for a fee from The Haworth Document Delivery Service: 1-800-342-9678. E-mail address: getinfo@haworthpressinc.com]*

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R I G H T S L I N K()

Since the 1980s, the availability of crack cocaine at low cost has contributed to an increase in the number of pregnant women who use it as well as other illegal drugs during pregnancy.[1] Reported incidences of prenatal cocaine use vary from 8% to 18%,[2-5] with a study conducted in Detroit revealing an incidence as high as 31% on meconium testing.[6] Due to its low molecular weight and its water and lipid solubility, cocaine readily crosses the placenta and the fetal blood-brain barrier.[7] Cocaine affects the monoaminergic neurotransmitter system (dopamine, norepinephrine and serotonin) in the central nervous system (CNS) through its action on the neurotransmitter release, reuptake, and recognition at the synaptic junction.[7-9] In humans, these neurotransmitters are present in neural pathways that project to brain areas involved in neurologic and behavioral functions including arousal, regulation of attention, response to sensory stimuli, and the modulation of mood states.[10,11]

Neurotransmitters play an important role in fetal brain development through their influence on neuronal migration and differentiation, synaptic proliferation and on the development of receptor sites.[12,13] Although full scientific support for the suspected cocaine-induced changes in the human fetal neurotransmitter system and their ensuing neurodevelopmental consequences is still lacking, preliminary research has shown results suggestive of such a relationship. In a recent study with newborn infants, Mirochnick and colleagues[14] showed that plasma norepinephrine concentrations were higher in infants who had been prenatally exposed to cocaine and marijuana than in unexposed infants. Among the exposed infants, plasma norepinephrine concentrations were associated with a decreased responsivity to social and non-social auditory and visual stimuli and higher levels of depressed behavior on the Neonatal Behavioral Assessment Scale (NBAS). Of note, these associations remained significant even when controlling for the effects of prenatal marijuana exposure. In a rare study with human infants, Needlman and his colleagues[15] examined the relation between prenatal cocaine exposure and the presence of monoamine precursors and metabolites in the central nervous system. Relative to unexposed infants, infants who had been prenatally exposed to cocaine had decreased levels of homovanillic acid, the principal metabolite of dopamine, in their cerebrospinal fluid. These findings suggest that prenatal cocaine exposure may result in changes in central dopaminergic systems in the human neonate.[15]

Many investigators have reported that prenatal cocaine and polydrug exposure is significantly related to compromised infant neurobehavioral performance on the NBAS, although specific findings vary across studies.[16-22] Compared to unexposed neonates, neonates with a history of prenatal cocaine and polydrug exposure exhibit poorer state regulation,[16,18,19] motor maturity,[16] orientation,[16] habituation[20,21] and greater excitability.[19] In some stud-

ies,[18,19] these findings remained significant even when the effects of confounding variables such as birthweight and prenatal exposure to other drugs were controlled analytically. Moreover, significant dose-related effects of prenatal cocaine exposure have been reported for infant NBAS performance.[18,19]

Clinically, full-term infants who have been exposed prenatally to cocaine and other drugs have been described as being easily overstimulated and requiring increased examiner intervention in order to maintain control of their hyperexcitable nervous systems.[16] This hypersensitivity and need for examiner intervention is still described at one month of age.[16] Some exposed infants are unable to tolerate even low levels of stimulation and quickly reach an agitated crying state.

Early detection of neurobehavioral abnormalities such as those revealed on the NBAS is important for infants prenatally exposed to drugs and other high risk infants. These behaviors may represent early manifestations of potential insult to the nervous system which may contribute to later compromised developmental outcome. Unfortunately, few developmental assessments designed to capture neurobehavioral organization beyond the newborn period are available.[23]

Most investigators have used the Bayley Scales of Infant Development (BSID) or other psychometric assessments to evaluate the effects of prenatal cocaine exposure on infant outcome beyond the neonatal period. In the majority of these studies, prenatal cocaine exposure was not significantly related to infants' performance on either the Mental Developmental Index (MDI) or the Psychomotor Developmental Index (PDI).[24-26] Billman and colleagues[27] reported that PDI scores varied according to infant exposure status, but only when infant ethnicity was considered. That is, black infants who had been exposed to cocaine and other drugs had higher PDI than black control infants; however, no significant difference was reported for white infants.[27] In other research Singer and associates[28] reported differences on the BSID MDI at 12 months favoring the control group.

Psychometric assessments such as the BSID may be too limited in sensitivity and specificity to detect subtle neurobehavioral deficits that may be associated with prenatal drug exposure.[26,29,30] Beeghly and Brazelton[23] have demonstrated that qualitative dimensions of two-year-old behavior assessed during the BSID can significantly discriminate biological at-risk small for gestational age (SGA) infants from non-SGA infants, even when the BSID scores did not. The instrument used in this study, the Qualifier Scoring System for Toddlers (QSS-T), was adapted from the NBAS supplementary items and measured the quality of a child's responsiveness during testing on the BSID. In their study, SGA toddlers exhibited more attentional dysregula-

tion and more negative affect during the BSID than non-SGA toddlers, and required more examiner persistence to complete testing.

Standard measurement systems for assessing qualitative dimensions of infant neurobehavior during the first year of life are lacking. This is unfortunate because empirical research suggests that prenatal drug exposure may exert significant compromising effects on dimensions of infant attention regulation and arousal modulation during this period. Struthers and Hansen[31] reported that infants exposed to cocaine and amphetamines performed significantly worse than unexposed infants on the Fagan Test of Infant Intelligence, a motor-free standardized test of visual attention and recognition. Alessandri and colleagues[32] found that infants who had been exposed to cocaine prenatally expressed less interest and joy during a learning task and less anger and sadness during extinction than unexposed infants. Mayes and her colleagues[33] reported that three-month-old infants with a history of prenatal cocaine and other drug exposure were more likely to cry and exhibit negative affect during a novel stimulus presentation task and show greater decrements in calming down to repeated presentations than same age unexposed infants.

In a related study, Mayes and colleagues[34] found that infants in the exposed group were more likely to fail to start an habituation procedure and were more irritable during the early part of the procedure than infants in the unexposed group. Among the subset of infants who successfully completed the habituation paradigm, however, no group differences in habituation performance were observed. Given the comparable performance between the two groups on the habituation task, Mayes et al.[34] suggest the early effects of drug exposure may be particularly evident in qualitative dimensions of infant behavior such as arousal modulation and attention regulation, rather than early cognitive abilities.

The aim of the present study was to evaluate the effect of prenatal cocaine and other drug exposure on infants' neurobehavioral functioning at 1, 4 and 7 months of age. Infants were observed longitudinally in multiple neuromotor testing contexts at 1, 4 and 7 months of age. We hypothesized that infants who had been exposed to cocaine would have poorer scores on measures of neurobehavioral functioning than unexposed infants at each assessment point.

METHOD

Subjects

Subjects included 49 infants: 23 control and 26 infants exposed to cocaine. Detailed maternal and infant demographic information is provided in Table 1. Of the 49 infants, 28 were females and 36 were African American. All were full-term at birth, with birth weights appropriate for gestational age. All

TABLE 1. Infant and Maternal Demographic Variables

	CONTROL (n = 23)	EXPOSED (n = 26)
Gender		
Male	8	13
Female	15	13
Race		
Black	14	22
Hispanic	5	1
White	4	3
Birthweight (g)**		
	3276.91(443.6)	2960.37(420.4)
Age at testing (days)		
1 month	33.87 (5.60)	33.64 (6.00)
4 month	127.83 (7.92)	124.43 (7.03)
7 month**	214.39 (4.46)	217.82 (5.11)
Age (years)*	22.9 (4.5)	28.3 (2.9)
Parity**	2.4 (1.1)	3.5 (2.0)
Education (years)	11.8	11.1
AFDC status***	100%	100%
ETOH*	2/20	19/21
MARIJUANA*	0/20	8/21
TOBACCO*	5/20	17/21

* p < 0.01
** p < 0.05
***AFDC: Aid to Families with Dependent Children

infants were from families living in urban, inner-city dwellings. Transportation to and from the study site was provided as well as a payment of $50 per visit for their participation in the study. Of the 59 mothers who originally agreed to participate in the study, 10 dropped out of the study: 1 from the control group and 9 from the drug group. One infant died of sudden infant death syndrome, 2 mothers were found to have used heroin during pregnancy and 7 failed to keep their appointments.

Both infant-mother dyads of infants exposed to drugs and control infants met the following criteria: (1) mother at least 18 years of age; (2) birth weight equal to or greater than 2000 grams; (3) no obvious major congenital malformations; (4) neonatal intensive care unit stay for no more than drug related reasons, minor routine observation or septic work-up but with no evidence of sepsis; (5) no requirements for mechanical ventilation; (6) no stigmata of fetal alcohol syndrome on neonatal examination; (7) no history of seroposi-

tivity for HIV noted in the mother's or infant's medical record; (8) mothers with no seizure disorder and no medication for any psychiatric illness; (9) infant discharged to mother's or foster mother's care from the nursery; and, (10) mother's willingness to give informed consent.

The mother-infant dyads of the drug exposed group were selected on the basis of documented history from the medical chart of substance use during pregnancy or on the basis of urine toxicology screens positive for cocaine metabolites in the infant following delivery, in the mother at delivery, or within one week before delivery as documented in the mother's or infant's medical record.

On the basis of medical record review, control dyads delivering within two months were matched to experimental dyads for mother's education and socioeconomic status as defined by method of payment for medical care. Control dyads also had no documentation in the mother's prenatal record of possible illicit substance use, no positive urine toxic screens for illicit substances at any time in the prenatal period, and no positive urine toxic screens noted in the infant's record. In addition, after receiving informed consent from the infant's mother, meconium samples were collected on all control infants and screened for the presence of cocaine, opiates, phencyclidine, amphetamine and marijuana by radioimmunoassay.

Procedure

This study was part of a larger study designed to examine neuromotor development in infants exposed to cocaine at 1, 4 and 7 months of age.[35] Items measuring neurobehavioral functioning were scored from videotapes of the neuromotor testing sessions. All subjects were tested under the same laboratory conditions and submitted to identical procedures during testing.

At 1 month of age, all infants were tested on kinematic analysis and the Alberta Infant Motor Scales (AIMS). At 4 and 7 months of age, all infants were tested on kinematic analysis, the AIMS and the Movement Assessment of Infants (MAI). All neuromotor testing sessions were videotaped. Of importance to this study was the "context" of testing rather than the actual motor test as the types of events and handling procedures occurring during testing became the stressful agent against which neurobehavioral functioning would be measured in the infants.

Kinematic analysis captures and analyzes movement in three dimensions through video tracking of the displacement of light reflecting markers placed on the infant. During kinematic testing at 1 and 4 months, the infants were placed in an infant seat and light reflecting markers were placed on their foreheads, wrists and ankles. The infants' movements were observed under three conditions lasting 2 minutes each: infant alone, with a rattle shaken in front of the infant, and with the examiner interacting with the infant. During

kinematic testing at 7 months, a reaching task was conducted. The infants were seated in a high chair and light reflecting markers were placed on their foreheads and wrists. The infants then reached up to 30 times for small objects presented by the examiner.

The AIMS is a motor screening assessment made of 58 motor items observed in four different positions: prone, supine, sitting and standing.[36] After kinematic testing, the infant was undressed, placed on a floor mattress and observed in each position. In order to pass an item, key motor descriptors must be observed: aspects of weight bearing, posture and antigravity movement. The AIMS involves minimal handling and is designed to score the observed motor behaviors elicited by the examiner, parent or age appropriate toys.

The MAI measures neurological and motor integrity through testing of 65 items divided into four sections on muscle tone, primitive reflexes, automatic reactions and volitional movement.[37] To score the MAI, a high-risk point is given when an item differs from the scores listed on the high-risk profile. The MAI involves extensive infant handling to produce the required reactions.

Ideally, an infant had to be in an alert state for testing. If the infant became fussy or cried, the examiner used different strategies in order to assist the infant in maintaining or reaching a state suitable for testing. These strategies could be mild (use of face, voice, touch, change of position, offer a toy, time-out), moderate (pacifier, arm and leg containment, hand to mouth facilitation, shortened duration of tested item, time-out) or maximal (pick up and hold, bottle, rock, walk, break with mother). If the baby still could not reach and maintain an alert state for testing, the session was considered incomplete and rescheduled. Even when rescheduled, some infants were still unable to complete the requirements for kinematic, AIMS or MAI testing; the kinematic session was either shortened or some items from the AIMS or MAI were left unscored. In these situations, the subject's testing session was coded as not completed.

Data Collection

The infants' kinematic and neuromotor testing sessions were conducted by examiners unaware of the exposure status of the infants. Measures of neurobehavioral functioning were coded from the videotaped neuromotor testing sessions by one of the examiners (Y.B.). At each age, neurobehavioral scores were determined based on the type of neuromotor testing (kinematics and AIMS at 1 month; kinematics, AIMS and MAI at 4 and 7 months). Infant and maternal demographic information was available from three sources: the infant's and mother's medical chart at recruitment, the Hobel, and a questionnaire completed by the mothers at the end of the study.

Measures

The neurobehavioral items are listed in Table 2. For those items using a scale from 1 to 9, a coding system was adapted from the NBAS supplementary items.[38] The scale from 1 to 9 reflected the testing situation used in the study and the typical responses seen in 1, 4 and 7 month old infants. An example of the scoring scale for general irritability is shown in Table 3.

In the first phase of the study, a pilot sample of ten subjects (the first ten subjects to be tested on kinematic, AIMS and MAI at 1, 4 and 7 months) was scored on each of the neurobehavioral items and the final definition of each score determined. Following this first phase, intra and inter-rater reliability was determined using intraclass correlation coefficients.[39] To determine intra-rater reliability, the experimenter (Y.B.) coded the neurobehavioral items from the testing sessions of the 10 pilot subjects and then recoded the items a second time. To determine inter-rater reliability, one of the project's research assistants was trained on the coding system and coded the neurobehavioral items from 4 subjects previously coded by the experimenter. Intra-class coefficients (ICC) were calculated and were as follows (intra-rater; inter-rater): number of state changes (0.97; 0.95); number of interruptions (1.0; 0.98); number of breaks (1.0; 1.0); predominant state (0.95; 1.0); general irritability (0.98; 1.0); quality of alert responsiveness (0.99; 0.94); regulatory capacity (0.99; 0.97); tolerance to testing (0.98; 0.95); and, examiner persistence (0.99; 0.96). All the ICC scores were indicative of high inter or intra-rater reliability.[39]

Data Analyses

The groups were first compared on all maternal and infant demographic variables using ANOVA or Chi-square analyses. For those continuous demographic variables on which significant group differences were found, correlations between that variable (confounder) and all outcome variables were determined. In order to examine the influence of a confounder on outcome, the study hypotheses were tested using hierarchical regression analyses for all those outcome variables significantly correlated with a confounder. All other outcome variables were compared using ANOVA or Chi-square tests.

RESULTS

Group Comparisons on Infant and Maternal Demographic Variables (Table 1)

The exposed infants were significantly lower in birth weight than the control infants (p = 0.03) but birth weight was not significantly correlated

TABLE 2. Definitions of Measures of Neurobehavioral Functioning

- # of state changes/minute: the total number of state changes divided by the total number of minutes needed to complete testing.
- # breaks/minute: the total number of breaks divided by the total number of minutes needed during testing. A break was a rest period that occurred when the infant could not reach and maintain an alert state for testing.
- # interruptions/minute: the total number of interruptions divided by the total number of minutes needed for testing. An interruption occurred when the infant had to be handled for adjustment or repositioning.
- # visits: number of visits needed to complete testing.
- Time duration: the length of time in minutes and seconds required for testing.
- Session completed: to indicate if testing was completed (yes) or partially/not completed (no). Results are presented as the percentage of infants who completed the testing session.
- Predominant state: the most common state of consciousness observed during testing: deep sleep, light sleep, drowsy, alert, fussy, crying. Results are presented as the percentage of infants with the alert state as the predominant state during testing.
- *Quality of alert responsiveness: quality of the alert infant's capacity to invest himself in a response to an animate or inanimate stimuli (scale 1-9).
- *Regulatory capacity: ability of the infant to maintain an alert state by himself during testing and the strategies demonstrated to maintain and/or return to an alert state before requiring examiner assistance (scale 1-9).
- *General irritability: infant's response to handling and stimulus situations encountered during testing. It measures the number of times the infant was irritable, the level of irritability and the kind of stimuli causing the irritability (scale 1-9).
- *Tolerance to testing: amount of stress induced by the demands of attention required during testing on the physiologic, motor and state systems (scale 1-9).
- *Examiner persistence: summary score of the amount of examiner assistance necessary to facilitate the infant's optimal performance during testing (scale 1-9).

*scored only during AIMS and MAI testing.

with any of the outcome variables. The age at testing at 7 months was statistically higher for the exposed group when compared with the control group (p = 0.02) and was significantly correlated with ratings of examiner persistence at 7 months (r = −0.444, p = 0.04 Bonferroni corrected). The exposed mothers were significantly older (p < .01), had more children (p = 0.04), and were more likely to use alcohol (p < .01), marijuana (p < .01) and tobacco (p < .01) during pregnancy than control mothers (Table 1). Of these variables only maternal parity was significantly correlated with the number of interruptions per minute during kinematic testing at 1 month (r = 0.458, p = 0.002) and 7 months (r = 0.366, p = 0.02).

Group Comparisons on Measures of Neurobehavioral Functioning

In the first phase of this analysis, group comparisons using ANOVA or Chi-square tests were conducted for all outcome variables that were not

TABLE 3. General Irritability Scoring Scale

The general irritability score reflected the infant's response to handling and stimulus situations encountered during the examination. Measures the number of times the infant was irritable, the level of irritability and the kind of stimuli which made him/her irritable.

1–Irritable throughout the testing session. State 6 (crying) during most of the session. Irritability at beginning of examination that increased with time. Examiner unsuccessful at calming infant, testing session terminated early.

2–Irritability began early during the testing procedure. Reached state 6 (crying) or 5 (fussing); needed break early in testing. Remained irritable, calmed for brief periods but not long enough for testing to be continued. Testing procedure not completed.

3–Irritability began during or after AIMS was completed. Remained easily irritable, reaching state 6 (crying) 1 or 2 times but mostly in state 5 (fussing) during testing. Might not complete exam.

4–Easily irritable. However, state 6 (crying) reached only for very brief periods or baby heard crying briefly during testing. Increased fussiness and irritability over time. Needed break, recovered, but examiner might decide not to complete exam.

5–Some irritability with 2-3 episodes of state 5 (fussing). Fussiness was heard but able to complete session with examiner intervention and time-out periods.

6–Reached state 5 (fussing) 1 or 2 times briefly. Returned to quiet alert state spontaneously or with mild examiner intervention. Exam completed.

7–2 or more brief episodes of fussiness during testing but self-control regained rapidly, i.e., within 5 seconds. Might briefly reach state 5 (fussing) once. Exam completed.

8–1-2 brief episodes of fussiness, did not reach state 5 (fussing) but fussing heard.

9–No irritability; infant responded to all stimulus and handling conditions with well-maintained self-control.

correlated with a confounder. None of these analyses resulted in significant group differences (Tables 4 and 5).

The second phase of analysis was conducted for those outcome variables reported above that were significantly correlated with infant or maternal demographic variables (confounders). Hierarchical regressions, as an approach to analyses of covariance, [40] were used for this purpose. This approach allows interpretation of the data in terms of variance accounted for by the covariate and then any additional variance accounted for by group membership, in this case drug exposure (increment in R^2). For each analysis, the confounder was entered first and then group membership. The increment in R^2 was then tested for significance and partial R^2s computed for the group variable. Prior to these analyses all interactions between the confounder and group member-ship were tested to rule out violation of the homogeneity of regression as-sumption. The inclusion of the interaction term in the regression analysis tests for slope differences between drug exposed and control groups.

As can be seen in Table 6 the infants' age at testing significantly predicted examiner persistence at 7 months accounting for 9.7 percent of the variance ($R^2 = .097$). Drug exposure did not account for any additional variance indicated by a zero increment in R^2. A significant interaction between mater-nal parity and group for number of interruptions during kinematics testing at 1 month was found thus violating the homogeneity of variance assumption

TABLE 4. Means, Standard Deviations and Percentages of Scores During Kinematic Testing at 1, 4 and 7 Months

Dependent Variables	1 Month		4 Months		7 Months	
	Exposed	Control	Exposed	Control	Exposed	Control
# visits	1.17(.38)	1.13(.34)	1.19(.40)	1.17(.39)	1.22(.42)	1.14(.35)
% session completed	63%	78%	81%	74%	77%	77%
# breaks/minute	0.05(.07)	0.05(.09)	0.01(.03)	0.02(.05)	0.02(.04)	0.01(.03)
# interruptions/minute	0.46(.31)	0.27(.22)	0.24(.21)	0.27(.19)	0.83(.67)	0.89(.75)
Time duration	8.35(1.8)	8.16(2.1)	7.43(1.1)	7.54(1.5)	10.81(2.1)	10.16(3.6)
% predominant state 4	75%	83%	86%	91%	100%	91%
# state changes/minute	0.19(.18)	0.15(.20)	0.08(.19)	0.10(.17)	0.07(.16)	0.07(.17)

TABLE 5. Means, Standard Deviations and Percentages of Scores During AIMS Testing at 1 Month and AIMS/MAI Testing at 4 and 7 months

Dependent Variables	1 Month		4 Months		7 Months	
	Exposed	Control	Exposed	Control	Exposed	Control
% session completed	96%	95%	95%	83%	86%	67%
# breaks/minute	0.00(.00)	0.03(.13)	0.03(.06)	0.04(.07)	0.03(.07)	0.03(.06)
# interruptions/minute	0.07(.17)	0.03(.09)	0.01(.03)	0.02(.05)	0.02(.05)	0.002(.01)
Time duration	3.20(1.2)	3.73(1.1)	17.14(3.4)	18.03(2.3)	16.02(2.9)	17.49(3.2)
% predominant state 4	88%	73%	100%	96%	100%	86%
# state changes/minute	0.18(.30)	0.25(.31)	0.08(.16)	0.10(.17)	0.09(.15)	0.07(.13)
General irritability			7.33(1.6)	6.65(2.4)	6.96(2.1)	6.71(2.4)
Tolerance to testing			7.29(1.4)	6.61(2.3)	6.91(2.2)	6.52(2.4)
Examiner persistence			6.86(1.9)	6.39(2.4)	7.09(2.1)	6.48(2.6)
Quality alert responsiveness			7.24(1.5)	6.87(2.1)	7.05(1.8)	7.05(1.9)
Regulatory capacity			7.57(1.6)	6.87(2.3)	7.18(2.2)	6.95(2.5)

indicating a significant slope difference and therefore making a regression analysis invalid. Within group regressions of parity on this outcome variable, however, indicated that parity predicted interruptions for the control infants but was unrelated within the group of infants exposed to drugs. An outlier within the group of infants exposed to cocaine (one mother with 10 children) was then removed and the analysis rerun. Analysis of the interaction between parity and group on interruptions at one month was still significant after removal of this outlier. Within group regressions indicated that parity was now significantly related to number of interruptions at one month for both groups (see Table 6). Figure 1, however, illustrates that the slope of the regression within the group of infants exposed to cocaine is much greater indicating that increases in the need to interrupt testing occurred for infants with fewer siblings in this group than for the control infants. The interaction between parity and group was not significant for interruptions at 7 months

TABLE 6. Hierarchical Regression Analyses of Covariance Results

| Covariate Age at testing	r	Cum R^2	F	p	I_R^2	p	partial R^2
Examiner Persistence at 7 mos/							
Age at test × Group	.137		<1	ns			
Age at testing	.311	.097	4.4	.04			
Group/drug exposure	.312	.097	<1	ns	0	ns	0
Maternal Parity	r	Cum R^2	F	p	I_R^2	p	partial R^2
With outlier							
# of interruptions Kinematics 1 mo							
Parity × Group	.323		4.7	.037			
Within Group Regressions							
Cocaine exposed	.352		2.7	ns			
Controls	.543		7.9	.011			
Without outlier							
# of interruptions Kinematics 1 mo							
Parity × Group	.315		4.3	.045			
Within Group Regressions							
Cocaine exposed	.523		6.7	.018			
Controls	.543		7.9	.011			
# of interruptions Kinematics 7 mo							
Parity × Group	.245		2.8	.102			
Parity	.366	.134	6.2	.017			
Group/drug exposure	.368	.135	<1	ns	.001	ns	.001

and hierarchical regression analyses indicated that drug exposure did not account for a significant amount of variance over and above that accounted for by parity on this variable.

DISCUSSION

This study was designed to examine the possibility of persisting difficulties in neurobehavioral functioning beyond the neonatal period for infants prenatally exposed to cocaine and other drugs. The available research, though limited, suggests that the neurodevelopmental sequelae of prenatal drug exposure appear to be expressed primarily in the general domain of arousal regulation experienced in novel or stimulating situations.[32,33] Impaired arousal regulation, in turn, influences infants' attentional capacities and their reactivity to stimulation, including their responsivity to both inanimate and animate stimuli.[38] In this indirect way, prenatal drug exposure may exert long-term compromising effects on children's learning. The lack of sensitive instruments able to capture, at times subtle, neurobehavioral markers has potentially contributed to the limited amount of research in this area beyond the newborn period. This study represents a first attempt to examine neurobehavioral functioning beyond the newborn period in infants exposed prenatally to cocaine and other drugs.

FIGURE 1. Relation Between Maternal Parity and Interruptions/Minute During Kinematic Testing at One Month
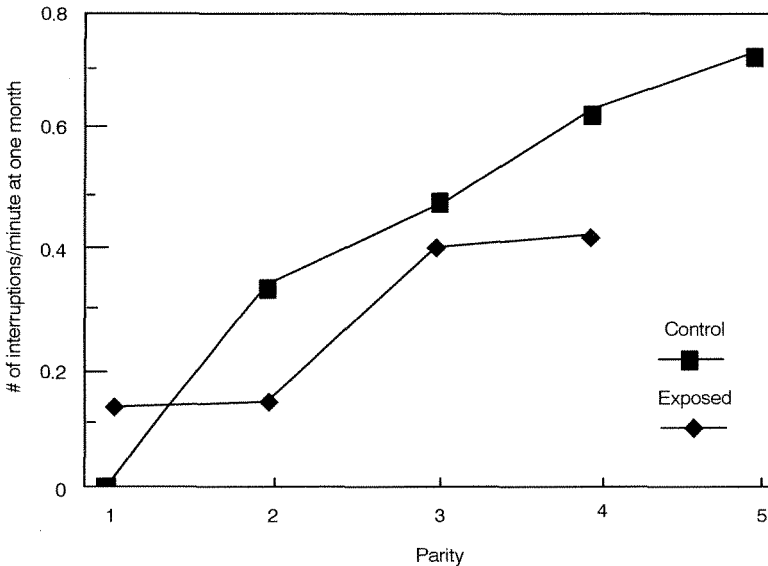
The results of this longitudinal study, however, did not offer significant support to prior empirical or clinical reports of increased irritability and disrupted neurobehavioral functioning among older infants exposed to drugs. None of the measures of neurobehavioral functioning showed any significant group differences. Interestingly, some maternal and infant demographic variables showed more effects on neurobehavioral functioning than group exposure status. Age at testing at 7 months significantly predicted examiner persistence at 7 months but drug exposure did not (Table 6). The results shown in Table 6 show a positive correlation between examiner persistence and age at testing at 7 months (0.311) indicating that older infants had higher scores on examiner persistence, ie, they required less examiner persistence. Older infants were thus easier to test. This relationship was as would be expected even though measures of examiner persistence have not been normed for infants beyond the newborn period.

A significant interaction was found between parity and group for the number of interruptions during kinematic testing at 1 month of age. After removal of an outlier in the drug exposed group (one mother had 10 children), parity was shown to be significantly related to number of interruptions during kinematic testing at 1 month for both control (r = 0.543) and exposed

groups ($r = 0.523$). As can be seen on the slopes shown in Figure 1, however, this relationship was different between exposure groups. Fewer children were required in the cocaine group to change the slope of the relationship between the two variables. At one month of age, in the exposed group, an increase in one child in the family caused the number of interruptions to increase whereas in the control group, an increase in two children in the family was needed to cause an increase in the number of interruptions during kinematic testing. The number of interruptions per minute was an indicator of the number of additional or unplanned handling procedures introduced during testing. For example, interruptions occured to reposition infants or when velcro bands holding the reflecting markers moved or detached; if an infant was very active, the bands would move and the markers could no longer be seen by the two recording cameras. Additionally, during kinematic testing at one month, interruptions occured when the infant's posture had to be corrected. Some infants showed an influence of the asymmetrical tonic neck reflex on their posture; testing had to be interrupted to place the infant's head in midline in order to minimize the influence of this reflex. Our results suggest that infants with more siblings were more demanding in attention during kinematic testing at one month and that among the infants exposed to cocaine and other drugs, the effects of parity occur with fewer siblings in the family. The reason why parity influenced the number of interruptions at one month during kinematic testing is difficult to interpret. Possibly mothers who use drugs differ in their handling of their infants when multiple children are in the home and perhaps are less able to divide their attention and respond to their infant's needs for consoling. Mothers who use drugs may also be more stressed by an additional child which could lead to difficulties in the development of organized behavior.

In this study, we could not determine if the infants' neurobehavioral scores were within or below established norms. No such norms exist and very little is known about neurobehavioral functioning beyond the newborn period. As in most studies of prenatal drug exposure, the families from both groups in this study were from low socioeconomic backgrounds and were benefiting from AFDC assistance, more commonly known as welfare services. This bias in the studied populations was also found in a study examining the prevalence of substance use during pregnancy.[41] The results of that study showed that, even though no racial or social class differences among the identified substance using pregnant women were noted, black and poor women were more likely to be reported for substance abuse while pregnant than their white and middle class counterparts. Frank and colleagues[42] have proposed that long-term negative effects of prenatal cocaine exposure might be more representative of outcome in a population of poor children living in difficult and chaotic home environments. In a long-term follow-up study of children

prenatally exposed to drugs, Chasnoff and colleagues suggested that low-income children, regardless of their prenatal drug exposure status, are at risk for developmental delays early in life. In their study, children from both groups scored below national norms on the Bayley Scales of Infant Development.[16] The infants of this study also showed scores on the neuromotor assessments, i.e., AIMS and MAI, that were below average for both groups.[35] To examine the effects of prenatal drug exposure without the co-morbid influences of poverty, future studies would need to include groups of exposed and control subjects from higher socioeconomic levels. In fact, socioeconomic status and mother's level of education have long been recognized as significant predictors of developmental outcome in infants born prematurely.[43,44]

For this study, detailed information on the family home environment was not collected. Although understudied, postnatal environmental factors such as consistent, sensitive caregiving or early intervention services can significantly moderate the toxic effects of prenatal cocaine exposure and help promote healthy adaptation in children exposed to drugs prenatally.[45,46] In one longitudinal study, increased maternal sensitivity and maternal psychological adaptation during the first year of life predicted higher Bayley scores in infants prenatally exposed to cocaine and other drugs.[47] In other research,[48] mothers using drugs who received support services were more likely than other mothers to provide a developmentally supportive environment for their infants and to have infants whose developmental skills were age-appropriate at age one. Similarly, Frank and colleagues[49] showed that, among infants heavily exposed to cocaine in utero, BSID scores during the first two years of life were significantly higher if the infants or their caregivers had received early intervention services. Although these factors were not measured in the present study, their influence may have masked actual effects of prenatal drug exposure on infant neurobehavioral functioning. In future studies with drug exposed samples, the moderating effects of these environmental variables should be assessed.

While neurobehavioral dysfunction has been reported for newborn infants exposed to cocaine and other drugs, these findings have not been consistently replicated and have not been found to indicate severe neurobehavioral dysfunction. As these signs of dysfunction have not been readily demonstrated beyond the newborn period, they might reflect only transient effects of prenatal exposure that are not present later in development. The possibility exists that the outcome variables in this study were not sensitive enough to capture subtle difficulties in neurobehavioral functioning in 1-, 4- and 7-month-old infants. This is unlikely as the measures used in this study were adapted from the NBAS neurobehavioral qualifiers, which are designed to assess these dimensions. Besides the Qualifier Scoring System for Toddlers (QSS-T),[23] no other comparable neurobehavioral assessments for older infants are avail-

able. The QSS-T, an adaptation of the NBAS supplementary items designed for use with two-year-old children during structured testing contexts, was able to discriminate between biologically high risk infants and lower risk infants. The results of this study suggest that qualitative dimensions of functioning are sensitive measures of risk. More efforts in the design of such instruments need to be made in the future.

Similar to the NBAS which uses the neurological examination as the vehicle to induce stress in the newborn infant, the testing conditions imposed in this study during kinematic assessment, AIMS, and MAI testing placed challenging demands on the infants. In fact, the general measures of neurobehavioral functioning at 4 and 7 months during AIMS and MAI testing showed a range of scores from 2 to 9. Although most of the infants showed scores between 7 and 9, the presence of low scores indicated that the testing conditions were able to elicit a wide range of behaviors, from organized to disorganized, in the tested infants.

Some of the early research on prenatal cocaine exposure presented methodological weaknesses such as lack of control for polydrug use including opiates, small sample size, inclusion of preterm infants, and lack of blind examiners.[42] In this study, we attempted to control for confounding variables and biases although still using a relatively small sample of polydrug users. The subjects were all fullterm infants with birth weight above 2500 grams and from the same (low) socioeconomic class, all control infants were free of drug exposure, and the examiner was unaware of the exposure status of the infants. All infants were tested in the same rooms at the three ages under an identical protocol of testing. Despite these precautions, group differences were not detected. Our findings do not support the presence of a marked or persisting dysfunction in neurobehavioral organization among infants exposed to cocaine and other drugs. In future studies, infants and children from all sub-groups of drug users, including middle class mothers, should be examined in order to separate the effects of prenatal cocaine exposure from the potential effects of suboptimal rearing environments.

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