Prenatal Cocaine Exposure and Motor Performance at 4 Months

OBJECTIVE. The relation between prenatal cocaine exposure and quality of movement was studied at 4 mo using the Posture and Fine Motor Assessment of Infants (PFMAI–I).

METHOD. Posture and fine motor scores of 4-month-old infants exposed to cocaine in utero (n = 370) were compared with an unexposed group (n = 533) within the context of gestational age, medical and demographic characteristics, and level of prenatal substance exposure using the PFMAI–I.

RESULTS. Infants prenatally exposed to cocaine had significantly lower posture scores than infants in the unexposed group. There was no main effect of cocaine exposure on fine motor scores; however, there were independent effects of gestational age at birth on both posture and fine motor scores at 4-mo corrected age.

CONCLUSION. These findings demonstrate independent contributions of prenatal cocaine exposure and prematurity to risk of motor delay and support the validity of the PFMAI–I as a measure of motor competence in early infancy.

Substance abuse by women of child-bearing age has long been a public health concern. Prenatal cocaine exposure (PCE), in particular, is associated with increased risks to growth and development. PCE has the potential to alter blood flow to the fetal brain, subsequently restricting brain growth (Pollard, 2007) and continuing to restrict blood flow into adolescence (Avants et al., 2007; Rao et al., 2007). With such a possibility, it follows that neurodevelopmental outcomes in infancy and childhood may also be negatively affected. Several obstacles exist to obtaining reliable results with this study population, including the need to control for:

- Varying education and socioeconomic status (SES);
- Differing cultural, nutritional, and medical characteristics of cocaine-using mothers;
- Disparity in the availability of social and community supports for the family; and
- The strong probability that cocaine-using mothers also use other substances that potentially affect fetal development and childhood outcomes, such as tobacco, marijuana, alcohol, barbiturates, and heroin (Lester, LaGasse, & Seifer, 1998).

For more than a decade, studies of the relation between prenatal substance exposure and developmental outcomes have addressed these methodological...
issues with increasing success. Multisite studies with larger sample sizes and statistical modeling capable of dealing with multiple potentially interacting and confounding variables have revealed subtle but important effects of PCE on intellectual, language, and behavioral functioning (Ackerman, Riggings, & Black, 2010; Bada et al., 2007; Lester et al., 1998).

Although several studies that have addressed these methodological concerns have also included motor measures, the effect of PCE on motor development remains unclear (Singer et al., 2002). One explanation for the lack of clarity in examining this relationship is the competence and dynamic nature of newborn infants. Neurodevelopmental assessments during the newborn period typically focus on posture and reflex responses and are not sufficiently sensitive to predict later motor performance. An approach that combines these observations with assessment of qualitative aspects of movement, including the ability to perform flexibly organized movements, shows greater promise as a predictor of neuromotor outcome (Guzzeta et al., 2007). Disorganization in the motor presentation of the neonate with PCE may not be related to history of drug exposure; thus, combining such observations with longitudinal study is the optimal approach to investigating this relationship (Miller-Loncar et al., 2005). Studies that incorporate sensitive measures with a longitudinal perspective are needed to detect potentially subtle influences of PCE on neuromotor outcomes.

Conceptual Framework

Global measures of motor development, such as the Psychomotor Development Index of the Bayley Scales of Infant Development—II (Bayley, 1993) and the Peabody Developmental Motor Scales (Folio & Fewell, 2000), although commonly used in studies of PCE, are not sufficiently sensitive to detect subtle differences in motor development. These assessments were originally constructed using a hierarchical neuromaturation model, which assumes that the rate and sequence of normal motor development are fixed and directly tied to central nervous system (CNS) maturation. Studies of motor control have demonstrated that flexible organization is the critical aspect of motor performance that leads to proficiency (Lockman & Thelen, 1993). Current research indicates that basic units of motor control are organized as functional synergies or coordinated structures rather than as individual actions by specific muscles or muscle groups (Turvey & Fitzpatrick, 1993). Functional synergies cannot be attributed to particular nerve tracts. Instead, these coordinated motor structures are produced through activity in multiple regions of the brain in concert with certain unique characteristics of the individual, such as sensory processing ability, muscle tone, strength, body weight, cognition, motivation (Thelen & Spencer, 1998), and the affordances within the environment (Berger & Adolph, 2007; de Campos, Rocha, & Savelbergh, 2009). As such, functional movement synergies are exquisitely complex and endlessly adaptable.

In addition, a basic premise of the current conceptual framework for motor development is the role of discontinuity in the developmental process. Acquisition of motor milestones does not follow a linear trajectory (Trevarthan, 1982). Instead, typical motor development shows periods of positive linear change interrupted by dips in performance. These periods of regression, referred to as phase shifts (Smith & Thelen, 2003), introduce an element of disequilibrium, expanding the options for movement and providing opportunities to practice movement structures that may be more flexible in their organization. This process, by virtue of its dynamic nature, fuels adaptation, which ultimately fuels motor performance (Hedberg, Carlberg, Forsberg, & Hadders-Algra, 2005; Meyer-Lindenberg, Ziemann, Hajak, Cohen, & Berman, 2002).

The influence of dynamical theory in motor development has been seen in test construction. The Bayley Scales of Infant and Toddler Development—III (Bayley, 2005) includes a motor scale that encompasses some qualitative aspects of movement. To capture the dynamic nature of the developing motor system, however, an assessment tool must allow infants the opportunity to elaborate on movements and to demonstrate emerging skills. When motor assessment captures emerging skills (marked by instability in performance) as well as established skills (stable performance), clinicians can analyze both factors that are constraining development and those that promote new skills. Because the purpose of assessment is often to determine the need for and direction of intervention, understanding the variables that constrain or facilitate new skills is a worthy goal (Case-Smith & Bigsby, 2000, p. 10). Standardized tests do not lend themselves to this aspect of motor assessment as well as criterion-referenced or play-based assessments, in which variability can become the focus of observation instead of an indicator of abnormality (Kelly-Vance, Needelman, Troia, & Ryalls, 1999).

Although infants with PCE have been described as having postural tone and movements that may appear qualitatively different from those of unexposed infants during the newborn period and early infancy (Chiriboga, Kuhn, & Wasserman, 2007), over time their scores on
scales of motor development are reported to be largely within age expectations. Even when the extent of PCE is taken into consideration, no persistent effects of PCE appear in overall scores of motor development (Frank et al., 2002). In fact, the trajectory of motor development for infants with PCE has been shown to be one of improvement in motor development scores over the first 18 mo of life, even for infants with prenatal exposure to heavy cocaine use, and even when the potential effects of tobacco, low SES, and negative environmental factors are entered into the model (Miller-Loncar et al., 2005). Such findings could be interpreted as evidence for a model of recovery from the initial negative effects of PCE—even high levels of exposure—over time. However, the current expanded conceptual framework for motor development, which goes beyond acquisition of milestones and includes qualitative aspects of movement, has not yet been tested.

The purpose of this study was to examine potentially subtle differences in the quality of movement of term and preterm infants with PCE at 4 mo and 4-mo corrected age, respectively, and that of unexposed comparison groups, using the Posture and Fine Motor Assessment of Infants (PFMAI–I; Case-Smith & Bigsby, 2000) within the context of multiple potentially intervening factors, including gestational age at birth; maternal characteristics; SES; and level of exposure to cocaine, tobacco, alcohol, and marijuana. We hypothesized that qualitative evaluation of posture and fine motor performance can reveal the negative impact of PCE.

Description of the Posture and Fine Motor Assessment of Infants

The PFMAI–I was designed for infants ages 2–12 mo as a criterion-referenced tool. The goal of the PFMAI–I is to assess the acquisition not only of age-related motor milestones but also of motor skills characteristic of phase shifts—transitional periods when new skills emerge. Posture items include qualitative aspects of movement such as the infant’s weight-bearing position, postural alignment, and ability to adapt to challenges imposed by gravity. Fine motor items include components of reach, grasp, manipulation, and release using objects that offer differing affordances for action. For this study, a research version of the PFMAI–I including 45 items was administered to term infants at 4 mo and to preterm infants at 4-mo corrected age; each item was rated on a 5-point scale (0–4); higher scores indicated better quality of posture and fine motor performance.

Interobserver reliability for the PFMAI–I is .97 for the Posture scale and .99 for the Fine Motor scale (Case-Smith & Bigsby, 1997); test–retest reliability ranges from .49 for the Fine Motor scale to .90 for the Posture scale (Case-Smith, 1992); and Cronbach’s α, a measure of internal consistency, is high at .97 for the Posture scale and .99 for the Fine Motor scale (n = 59; Case-Smith & Bigsby, 1997). Strong correlations have been demonstrated between the PFMAI–I and the Psychomotor Scale of the Bayley Scales of Infant Development–II (n = 23; r = .75; Case-Smith, 1992) and infant age (n = 59; Posture r = .89; Fine Motor r = .92; Case-Smith & Bigsby, 1997). In addition, the performance results of 211 preterm infants and 162 term infants were combined (N = 373) and submitted to Rasch analysis to determine the spread of scores (item difficulty) within the context of ability level. The Rasch analysis resulted in elimination of three items from the Posture scale and three items from the Fine Motor scale to obtain a final “fair to good” spread of scores and re-structuring to a 4-point scale (Case-Smith & Bigsby, 1997).

Method

This study was part of the Maternal Lifestyle Study (MLS), a longitudinal investigation of the effects of prenatal cocaine exposure on child outcome. The MLS was conducted under the auspices of the National Institute of Child Health and Human Development Neonatal Research Network at four sites (Brown University, Providence, RI; University of Miami, Miami, FL; University of Tennessee, Memphis, TN; and Wayne State University, Detroit, MI). MLS participants were recruited postpartum at four hospital sites from 1993 to 1995. The institutional review board at each site approved the study. A National Institute on Drug Abuse Certificate of Confidentiality was obtained to ensure confidentiality of information regarding participants’ drug use, and the mother provided written informed consent. The MLS was conducted in two phases: (1) an acute phase (Bauer et al., 2005), which extended through hospital discharge, and (2) the longitudinal follow-up of a subset of mothers and infants. The PFMAI–I was included in the battery of tests administered at 4 mo (age corrected for prematurity; Lester et al., 2002).

Mothers and Infants in the MLS Study

The initial sample of 1,388 mothers enrolled their infants at 1 mo in the MLS longitudinal follow-up. The mothers were >18 yr old, and most were African American (78%), had at least a high school education (69%), received Medicaid benefits (79%), and had an income below the Federal Poverty Level (63.8%).
Exposed and comparison groups were matched on gestational age, race, and gender. The exposed group consisted of infants whose mothers used cocaine or opiates during pregnancy, based on maternal self-report at the time of delivery or the finding of cocaine or opiate metabolites in meconium by gas chromatography (ElSohly et al., 1999; Lester et al., 2001). The comparison group consisted of infants whose mothers denied cocaine and opiate use during pregnancy and with negative meconium analysis for the presence of cocaine and opiates. Meconium assays indicate the presence of drug metabolites in the stool of the newborn, and sensitivity can vary depending on the timing of drug use during pregnancy (e.g., early vs. late; Lester et al., 2001).

At the 1-mo visit, mothers reported the quantity and frequency of their use of legal and illegal drugs during pregnancy. Heavy cocaine use was defined as ≥3 days/wk in the first trimester, heavy alcohol use as ≥0.5 oz. of absolute alcohol/day, heavy tobacco use as ≥10 cigarettes/day, and heavy marijuana use as ≥0.5 joints/day. “Some use” was defined as any use not meeting the criterion for heavy use and “no use” was defined as denial of use during pregnancy. Other substances associated with cocaine use (alcohol, marijuana, tobacco) were present in both the exposed and the comparison groups. Maternal and child characteristics were collected postpartum in the MLS. Included in the demographics were race, maternal age, marital status, insurance, or maternal education. However, mothers excluded were less likely to have had prenatal care (p = .003) than mothers included in the study. Table 1 displays the medical and maternal characteristics of the two groups.

**Examiner Training and Administration of the PFMAI–I**

Psychometrists at each of the four MLS sites were trained in administration and scoring of the PFMAI–I; one of the authors (Bigsby) provided on-site instruction using videotaped and live administrations. Trained examiners practiced administration and scoring on pilot participants over a period of months and sent a minimum of six videotapes of completed assessments with scores to the trainer. The trainer viewed the videotaped exams for accuracy in administration according to the PFMAI–I manual and the MLS study protocol and corresponded with examiners regarding their administrations. Pilot data were not included in study analyses. Once examiners met certification requirements for administration of the PFMAI–I, they submitted videotaped administrations for comparison with independent scoring by the trainer.

Intraclass correlations (ICCs; Shrout & Fleiss, 1979) were used to calculate interobserver reliability. This method is more revealing of potential areas of disagreement than an overall percentage of agreement, and it allowed us to calculate scoring reliability on specific subsections of the exam (e.g., Head, Shoulder, Pelvis, Reach, Grasp, Manipulation). Examiner scoring for each subsection of the exam was compared with the trainer’s scoring of submitted videotapes using the analysis of variance (ANOVA) general linear model (GLM) procedure in SAS (version 9.1; SAS Institute, Cary, NC). The resulting mean squares were then entered into the calculation for the ICC as follows: (1) mean square for the model − mean square for error) / 2 df = X, then (2) X / (X + mean square for error) = ICC.

Examiners received feedback on their administration and scoring with pilot participants and continued to submit videotaped administrations and examiner scores to the trainer until the ICC coefficient for all subsections of the exam reached ≥80% agreement. The trainer’s scores were entered as study data until examiners achieved reliable scoring. All examiners, including the trainer, were blinded as to the exposure status of infants in the MLS.

Mothers brought their infants to the hospital clinics for the 4-mo visit. Administration of the PFMAI–I followed the instructions detailed in the manual (Case-Smith & Bigsby, 2000). The presence of parents or primary caregivers as observers was encouraged. When the entire exam was administered, the PFMAI–I was completed within 30 min and was scored immediately thereafter.

**Statistical Analyses**

ANOVA and χ² analyses were used to compare the cocaine-exposed and comparison groups on gestational age, birth weight, length, head circumference, and gender. One-min and 5-min Apgar scores were compared using Mann–Whitney median tests (Rosenthal & Rosnow, 1991). Chi-square analyses were also used to compare the
two groups on maternal drug use during pregnancy. Infants’ gestational age was recoded into two groups: high gestational age (≥33 wk) and low gestational age (<33 wk). GLM analyses were conducted to examine the main effects of cocaine and gestational age on posture and fine motor scores while adjusting for the effects of site; SES; and prenatal tobacco, alcohol, and marijuana exposure. The interaction between cocaine exposure and gestational age was also included in the model.

Results

Infant Medical and Maternal Characteristics

Table 2 presents the medical characteristics of the 903 infants with PFMAI–I data. No statistically significant differences (p > .05) were found between the cocaine-exposed and comparison groups on gestational age, birth weight, length, head circumference, 1-min and 5-min Apgar scores, or gender. Table 3 displays the demographic information for the mothers of infants in exposed and comparison groups. The two groups did not differ significantly in race distribution, p = .738. However, mothers in the exposed group were more likely to be older, to be never married or divorced, to be on Medicaid, to have lower SES, and to have completed less than a high school education. They were also less likely to have received prenatal care than mothers in the comparison group. In addition, mothers in the cocaine-exposed group were more likely to have used tobacco, alcohol, and marijuana during pregnancy than those in the comparison group.
Infant Posture and Fine Motor Scores

Some infants were unable to complete portions of the PFMAI–I. Table 4 shows the adjusted means and standard errors of measurement for the final sample of infants completing the posture portion (N = 893) and the fine motor portion (N = 823) by cocaine exposure status and gestational age group. A main effect of cocaine exposure on infant posture scores was found after adjusting for the effect of site; gestational age; SES; and prenatal exposure to alcohol, tobacco, and marijuana. Cocaine-exposed infants had poorer posture scores than the comparison infants (p = .043). Gestational age also had a significant effect on infant posture scores. Infants born at <33 wk gestational age had lower posture scores than infants born at >33 wk gestational age (p < .001). No interaction was found between the effect of cocaine and the effect of gestational age. Neither SES nor prenatal exposure to tobacco, alcohol, and marijuana had a significant effect on infant posture scores at 4 mo (p > .05).

No main effect of cocaine exposure on infant fine motor scores was found (p = .859). However, infants born at <33 wk gestational age had lower fine motor...
scores than infants born at >33 wk gestational age ($p = .000$). No significant interaction was found between the effects of cocaine and the effects of gestational age. As with posture scores, neither SES nor prenatal exposure to tobacco, alcohol, and marijuana had a significant effect on infant fine motor scores at 4 mo ($p > .05$).

We also tested the association between level of cocaine and other drug use during pregnancy and PFMAI–I scores. Of the 903 mothers, 760 reported their level of cocaine use: 77 reported heavy use, 160 reported some use, and 523 reported no use. In 85 of the remaining 143 cases, mothers had lost custody of their infants by the 1-mo visit; hence, level-of-use data were not collected. In 58 cases, mothers denied cocaine use despite a positive toxicology for cocaine metabolites in infant meconium; their data were excluded from level-of-use analyses.

We examined the effect of different levels of cocaine exposure on infant posture and fine motor scores while adjusting for the effects of gestational age, site, SES, and level of prenatal tobacco, alcohol, and marijuana exposure in GLM analysis. We also included the potential interaction between level of cocaine exposure and gestational age in the model. These analyses again revealed a main effect of gestational age on both infant posture ($p < .001$) and fine motor scores ($p = .016$). However, no effect of SES or of the level of cocaine use was detected on either posture or fine motor scores ($p > .05$). Moreover, no main effect was found for either level of prenatal exposure to tobacco or alcohol on infant posture or fine motor scores ($p > .05$) or level of prenatal exposure to marijuana on posture scores ($p = .199$). We did detect a significant effect of level of prenatal exposure to marijuana on fine motor scores, suggesting better fine motor scores among infants who were prenatally exposed to higher levels of marijuana ($p = .042$). However, differences in fine motor scores for the three levels of marijuana exposure were not maintained after post hoc analysis using Student–Newman–Keuls tests ($p = .362$; Keuls, 1952).

**Discussion**

This study represents an advance in assessment of the potential effects of PCE on infant motor outcomes. It contrasts with previous studies in two ways. First, instead of focusing on acquisition of motor milestones, which had not been found to be significantly affected by PCE (Mayes, Cicchetti, Acharyya, & Zhang, 2003), we incorporated into our study model the current conceptual framework for motor development emphasizing qualitative aspects of motor performance. Second, embedded within this conceptual framework is the concept that characteristics of the environment, including the affordances of stimulus objects, may have a direct impact on the quality of movement that is observed. The PFMAI–I affords infants the opportunity to demonstrate their full repertoire of movements in the least restrictive fashion by offering stimulus objects for fine motor exploration with three distinctly different sets of characteristics. Thus, use of the PFMAI–I allows the full range of potential responses to be elicited and subtle differences to be detected.

Our initial hypothesis, that the PFMAI–I would detect subtle differences between infants with PCE and an unexposed comparison group, was partially supported. A statistically significant main effect of PCE on posture scores, but not on fine motor scores, was demonstrated. The PFMAI–I may not have been sufficiently sensitive to detect a fine motor difference. However, because the tool was sensitive enough to detect subtle differences in both posture and fine motor performance among infants born at <33 wk gestation, a more likely interpretation is that PCE has a greater impact on areas of the brain that organize posture and gross motor functioning than on the areas that organize fine motor activity. For decades, researchers have known that the neuronal tracts directly involved in posture and gross motor activity are distinct from those involved in fine motor activity (Hadders-Algra, Bogren, & Forssberg, 1998; Kuypers, 1981). Thus, it is important to assess gross motor and fine motor performance separately, particularly when attempting to discern subtle effects on CNS function.

When fine motor performance is specifically examined and the potential effects of coinciding substances such as tobacco, alcohol, and marijuana are included in the model, evidence suggests that factors outside the infant, such as maternal vocabulary and features of the home environment, may have a stronger effect on fine motor scores than PCE (Arendt et al., 2004; de Campos et al.,

<table>
<thead>
<tr>
<th>Measure</th>
<th>Cocaine Exposed</th>
<th>Comparison</th>
<th>&lt;33 Wk Gestational Age</th>
<th>≥33 Wk Gestational Age</th>
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<tr>
<td></td>
<td>nM</td>
<td>SE</td>
<td>p</td>
<td>nM</td>
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<tr>
<td>Posture (N = 893)</td>
<td>367</td>
<td>58.22</td>
<td>0.74</td>
<td>526</td>
</tr>
<tr>
<td>Fine motor (N = 823)</td>
<td>322</td>
<td>56.00</td>
<td>1.10</td>
<td>491</td>
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Note. $M =$ mean; $SE =$ standard error.

Table 4. Adjusted Means and Standard Errors for 4-Month PFMAI–I Scores by Cocaine Exposure and by Gestational Age.
Our finding of a direct effect of PCE on posture but not on fine motor scores concurs with those observations and stands in contrast to results obtained using a presumably less sensitive global measure such as the Motor Scale of the Bayley Scales of Infant Development—II (Mayes et al., 2003).

Additional strengths of this study are the multisite sampling methodology, the size of the sample, and the statistical power these features afford. The main effect of cocaine exposure on infant posture was obtained after adjusting for the possibility of site differences and maternal characteristics in the statistical model. This approach was necessary because of significant differences between the exposure groups with regard to age, education, marital status, and SES, all of which are factors with the potential to influence the affordances for growth and development that a mother is able to provide within the home environment. These characteristics of the sample impose certain limitations on the interpretation of our findings, however. Substance-abusing women are clearly a diverse group with varying degrees of risk and protection. Discretion is advised when generalizing the results of any study of PCE, including our own, to other groups of women and their infants.

**Conclusion**

In this study, we incorporated the context for motor development into the study model and used the PFMAI–I, a tool that focuses on specific aspects of motor performance, to detect subtle differences in posture development between infants prenatally exposed to cocaine and an unexposed comparison group. The PFMAI–I was sufficiently sensitive to reveal a main effect of prenatal cocaine exposure on postural performance and differences in posture and fine motor development among infants born at or before 33 weeks gestation, even after correcting for prematurity. Independent contributions of prenatal cocaine exposure and prematurity to infant risk status are important for clinicians to consider when conducting assessments and intervening with infants at risk. These findings further demonstrate the validity of the PFMAI–I as a measure of motor competence in early infancy. ▲

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**References**


