Brief Report: HIV-Exposed Newborns Show Inferior Orienting and Abnormal Reflexes on the Brazelton Scale

Frank Scafidi and Tiffany Field
University of Miami Medical School

Assessed 48 infants of HIV-positive and HIV-negative mothers on the Brazelton Neonatal Behavioral Assessment Scale. Infants exposed to HIV-positive mothers were disadvantaged from birth due to their mothers having obstetric complications and to the infants having orienting problems and abnormal reflexes on the Brazelton Newborn Scale. These problems may be early precursors of the later visual-spatial delays and hypertonicity noted in these infants.

KEY WORDS: HIV infants' Brazelton assessment.

Acquired immune deficiency syndrome (AIDS) is rapidly becoming the leading infectious cause of mental retardation in pediatric populations (Armstrong, Seidel, & Swales, 1993). Perinatal transmission of the human immunodeficiency virus (HIV-1) is the primary source of infection in children (Centers for Disease Control, 1989; Olson, Huszti, Mason, & Seibert, 1989). Although the perinatal factors that control the transmission of the infection remain unclear, growing empirical evidence suggests that perinatal transmission occurs during the prenatal period (Goedert, Mendez, Willoughby, & Landesmann, 1989; Jovaisas,

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2All correspondence should be sent to Tiffany Field, Touch Research Institute, University of Miami School of Medicine, PO Box 016820, Miami, Florida 33101.
Koch, Schafer, Stauber, & Lowenthal, 1985; Lapointe, Michaud, Pekocic, Chausseau, & Dupuy, 1985). This hypothesis is supported by the detection of HIV in fetal tissues and by reports of low birth weight and younger gestational ages in infants born to HIV-positive women. Infants born to HIV-seropositive women have maternally derived antibodies to HIV. Despite those antibodies, however, studies report that approximately 22 to 39% of these infants will be HIV-positive (Blanche et al., 1989; Johnson et al., 1989; Peckhan, Ades, & Newell, 1989; Wolinsky et al., 1992).

Prenatal transmission of HIV raises significant concern since infection during the fetal period has been associated with poor outcome. Several complications have been identified in HIV-positive offspring. Among pediatric patients, common neuropathological and neuroradiological findings include (a) atrophy of the cerebral cortex; (b) early calcification of the basal ganglia; and (c) attenuation and deterioration of white matter (Barnes, 1986; Belman, 1990; Curless, 1989; Kozlowski, 1992; Wiley et al., 1990). Significant cognitive differences have also been reported. For example, in a longitudinal follow-up of pediatric AIDS children a mean IQ of 57 was reported (Ultmann, 1985). Similar findings were also noted in other studies (Belman et al., 1988, 1986). Developmental delays are also a common finding in HIV-infected children. Both delays in the acquisition of new skills and the loss of previously acquired skills are seen. These delays include (a) motor impairments such as failure to acquire motor milestones, hypertonicity, and hyperflexia (Belman et al., 1988; Diamond et al., 1987; Epstein et al., 1986); (b) receptive and expressive language delays (Epstein et al., 1986; Johnson et al., 1989); and (c) visual-spatial delays (Diamond et al., 1987).

HIV encephalopathy is noted to have the most serious effects because of its progressive, deteriorating pattern and associated CNS abnormalities (Armstrong et al., 1993), although static encephalopathy can be characterized by severely delayed cognitive functioning and neuromotor deficits without deterioration (Brouwers, Belman, & Epstein, 1991). The major problem interpreting research findings, however, is that neurodevelopmental functioning in infants with HIV is further complicated by other factors such as prenatal drug exposure and fetal malnutrition. This problem is highlighted by a well-controlled study of children hospitalized with HIV that revealed a high rate of severe neurological involvement (100%) and cognitive delays (90%) (Diamond et al., 1987). However, high rates of these problems were also noted in the control group in this study, suggesting that mere exposure to HIV or other perinatal factors may have contributed to these findings.

To date, studies have focused on the development of older infants and children with AIDS. Very little is known about the neonatal outcome of infants who are simply exposed to HIV and do not necessarily become HIV-positive.
The present study was designed to determine the effects of being exposed to HIV on newborn behavior.

**METHOD**

**Participants**

The sample comprised 48 full-term infants and their HIV-positive and HIV-negative mothers who gave informed consent to participate. Twenty-four infants were born to women who were seropositive for HIV-1, and 24 infants were born to women who were seronegative. The women were low SES (based on the Hollingshead Index), single (86%) women who were distributed 11% Caucasian, 11% Hispanic, and 78% African American. The groups did not differ on these demographic characteristics. Infants were excluded from the study based on the following criteria: (a) major congenital malformations and chromosomal aberrations; (b) maternal substance abuse based on maternal and infant urine screens; (c) positive echoencephalograms; (d) documented congenital infections other than HIV, and (e) CNS infections such as meningitis and herpes encephalitis. To ensure that birth weight or intrauterine growth deprivation factors did not contribute to differences across the two groups, an attempt was made to ensure equal numbers of infants with high, medium, and low values on these factors in both groups.

**Measures**

The Ponderal Index \(\text{wt/ht}^3 \times 100\) was used to assess intrauterine growth deprivation.

**Urine Toxicology and Screens.** Routine urine toxicology screens were conducted on all mothers and infants eligible for this study. Enzyme immunoassays (EMIT) were used to measure cocaine metabolites (benzylecgonine) and cannabinoids in maternal urine. Maternal specimens were also assayed for five additional substances (opiates, amphetamines, barbiturates, benzodiazepines, and phencyclidine). Due to the difficulty in obtaining adequate volumes of urine, infant samples were limited to three assays: cocaine metabolites, cannabinoids, and opiates. If maternal urine was not obtained, the five assays listed for maternal urine were performed on the infant sample. Mothers or infants with positive urine toxicologies were eliminated from this study.

**Seroological Testing for Human Immune Deficiency Virus (HIV-1) Antibody.** All women were tested for human immunodeficiency virus. Maternal testing for HIV-1 antibody was performed using the ELISA method. A positive
result was confirmed by the Western blot technique using nitrocellulose strips from Epitope. If the mother’s blood was positive, the infant’s blood was also tested. Informed consent was obtained from the women to do HIV testing. The counselor obtaining consent explained the potential uses of the HIV test, its limitations, the meaning of test results, and an explanation of the procedures, including the voluntary nature of the testing, the right to withdraw consent at any time prior to HIV testing, and the confidential treatment of information identifying the subject.

**Obstetric Complications.** Obstetric complications were quantified using the Obstetric Complications Scale (OCS) consisting of 41 items obtained from the medical record and rated as optimal or nonoptimal for the summary score (Littman & Parmelee, 1978).

**Postnatal Complications.** Perinatal complications were quantified using the Perinatal Risk Index (Scheiner & Sexton, 1991). This 14-item scale weights complications on a 4-point scale according to severity and duration. Items include Apgar scores, EEG, presence of seizures, intracranial hemorrhage, presence of hydrocephalus, head ultrasound, weight for gestational age (2 items), dysmorphic features, ventilation, hematocrit, meningitis, and head growth (2 items).

**Neonatal Behavior Assessment Scale with Kansas Supplements.** The NBAS-K (Brazelton, 1973) consists of 28 behaviors scored on a 9-point scale and 18 elicited reflexes scored on a 3-point scale. The infant’s performance was summarized according to seven factors: habituation, orientation, motor behavior, range of state, regulation of state, autonomic stability and abnormal reflexes (Lester, Als, & Brazelton, 1982). Examiners were blind to group membership.

**Procedure**

The NBAS-K was administered to each infant within 48 hours after birth and midway between feedings to control for hunger and satiation effects. The examinations were performed by a trained psychology graduate student who was blind to the infant’s HIV status. The infant’s performance was summarized according to seven factors: habituation, orientation, motor behavior, range of state, regulation of state, autonomic stability, and abnormal reflexes (Lester et al., 1982).

**RESULTS**

Group comparisons were made by a MANOVA followed by univariate analyses of variance using SPSS. As can be seen in Table 1, the mothers of the HIV-exposed infants were older, had been pregnant more often, and had more
Table I. Means for Demographics and Birth Measures

<table>
<thead>
<tr>
<th>Variable</th>
<th>HIV (n = 24)</th>
<th></th>
<th>Non-HIV (n = 24)</th>
<th></th>
<th>F(1, 46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mother’s age</td>
<td>25.9</td>
<td>4.9</td>
<td>18.6</td>
<td>3.7</td>
<td>13.08*</td>
</tr>
<tr>
<td>Mother’s gravida</td>
<td>3.2</td>
<td>0.5</td>
<td>1.6</td>
<td>0.2</td>
<td>12.93*</td>
</tr>
<tr>
<td>Obstetric Complications Scale</td>
<td>90.2</td>
<td>19.2</td>
<td>105.7</td>
<td>20.1</td>
<td>6.19*</td>
</tr>
<tr>
<td>Gestational age</td>
<td>38.7</td>
<td>4.3</td>
<td>38.1</td>
<td>4.1</td>
<td>0.69</td>
</tr>
<tr>
<td>Birth weight</td>
<td>3,039.7</td>
<td>1,861</td>
<td>3,112.4</td>
<td>1,828</td>
<td>1.72</td>
</tr>
<tr>
<td>Length</td>
<td>49.5</td>
<td>8.7</td>
<td>49.6</td>
<td>7.3</td>
<td>0.78</td>
</tr>
<tr>
<td>Head circumference</td>
<td>33.2</td>
<td>4.7</td>
<td>33.4</td>
<td>4.5</td>
<td>0.65</td>
</tr>
</tbody>
</table>

*p = .01.

obstetric complications (lower OCS scores indicate more complications). Even though the groups differed on obstetric complication scores which were entered into the data analyses as a covariate, the HIV and non-HIV groups did not differ on birth measures including gestational age, length, and head circumference, and the attempt to match the groups on birth weight and Ponderal Index was successful. However, despite the similarity between groups on the standard birth measures, the HIV-exposed infant group showed inferior performance on the orienting items and had more deviant reflexes (Table II).

Table II. Means for Brazelton Scale Scores

<table>
<thead>
<tr>
<th>Brazelton scores</th>
<th>HIV (n = 24)</th>
<th></th>
<th>Non-HIV (n = 24)</th>
<th></th>
<th>F(1, 46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M</td>
<td>SD</td>
<td>M</td>
<td>SD</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Habituation</td>
<td>6.2</td>
<td>0.6</td>
<td>5.9</td>
<td>0.5</td>
<td>1.47</td>
</tr>
<tr>
<td>Orientation</td>
<td>4.6</td>
<td>0.8</td>
<td>5.5</td>
<td>0.9</td>
<td>5.17*</td>
</tr>
<tr>
<td>Motor</td>
<td>4.4</td>
<td>0.7</td>
<td>4.7</td>
<td>0.7</td>
<td>0.63</td>
</tr>
<tr>
<td>Range of state</td>
<td>3.4</td>
<td>0.5</td>
<td>3.7</td>
<td>0.5</td>
<td>0.71</td>
</tr>
<tr>
<td>Regulation of state</td>
<td>5.2</td>
<td>0.8</td>
<td>5.0</td>
<td>0.8</td>
<td>0.59</td>
</tr>
<tr>
<td>Autonomic stability</td>
<td>5.8</td>
<td>0.7</td>
<td>5.8</td>
<td>0.7</td>
<td>0.00</td>
</tr>
<tr>
<td>Reflexes</td>
<td>3.0</td>
<td>0.4</td>
<td>1.4</td>
<td>0.2</td>
<td>9.24*</td>
</tr>
</tbody>
</table>

*p = .05.

*p = .005.
DISCUSSION

Despite the fact that only 22 to 39% of infants born to HIV-positive mothers are HIV positive themselves, the HIV exposure itself appears to disadvantage the infants from birth. Their mothers experienced more obstetric complications, and the infants had inferior orienting scores and a greater number of abnormal reflexes on the Brazelton scale. It is of course possible that these effects could be explained by other maternal factors such as potential drug use not detected by our urine screens or poor maternal nutrition resulting in intrauterine growth deprivation not detected by the Ponderal Index. The HIV may indirectly affect the infants by compromising the mother’s capacity to support intrauterine development. It is not just the direct effects of HIV on the infant that place the fetus at risk. As far as we could determine, demographic and health characteristics besides HIV status (e.g., prenatal medical care and drug abuse) were similar. The three non-HIV factors that were different across the two groups could have contributed to differential fetal development, namely, the older mothers of greater gravida and less optimal obstetric complications scores. Statistically covarying the effects of obstetric complications may not have been adequate.

It should be noted that even though orienting and reflex factor scores were inferior for HIV-exposed newborns, most of the NBAS measures were not different between the groups. This may be surprising since all of these factors depend upon similar functional systems. However, there is a potential way the nonoptimal performance on the orientation and abnormal reflexes may be related to the adequate performance on the other factors. The nonoptimal orientation ratings derived from these infants having higher thresholds to stimulation, thus requiring more stimulation to orient to the stimuli. This same characteristic would contribute to high thresholds for irritability and disorganized behavior which could explain their adequate performance on the range of state, regulation of state, and autonomic stability factors. Their high reflex scores related to hypertonicity, which paradoxically because of good muscle tone and lack of flaccid motor behavior, may have contributed to their adequate motor scores.

Inferior performance on these Brazelton factors may be precursors of the later problems noted in this population. For example, the greater number of abnormal reflexes (mainly hypertonicity) may be a precursor of the later hypertonicity and hyperflexia documented by several investigators (Belman et al., 1988; Diamond et al., 1987; Epstein et al., 1986). Similarly, the newborn problem of orienting to visual and auditory stimuli may be a precursor of the visual-spatial delays noted in later development (Diamond et al., 1987). All of these deficits may relate to the neuropathological and neuroradiological problems reported for HIV offspring including atrophy of the cerebral cortex, early calcification of the basal ganglia and attenuation/deterioration of white matter (Barnes, 1986; Belman, 1990; Curless, 1989; Wiley et al., 1990).
These data suggest that future studies are needed to assess more subtle perceptual and cognitive functions in HIV-exposed newborns such as habituation and conditioning studies. Further, longitudinal studies are needed to track the developmental trajectory of these functions from the newborn period to later infancy to determine whether deficits persist even in HIV-exposed infants who do not become HIV positive. At least two recent studies converge to suggest that in HIV-exposed infants who are not infected themselves development proceeds normally (Nozyce et al., 1994), particularly in the absence of confounding drug exposure effects (Mellins, Levenson, Zawadzki, Kairam, & Weston, 1994). Finally, early interventions seem to be needed to reduce these early differences.

REFERENCES


