INFANT BEHAVIOR AND DEVELOPMENT **18,** 407–414 (1995)

Reactivity and Regulation in Cocaine-Exposed Neonates

JANET A. DIPIETRO
Johns Hopkins University
PATRICIA E. SUESS
National Institute on Drug Abuse
JEAN S. WHEELER AND PATRICIA H. SMOUSE
Johns Hopkins Medical Institution
DAVID B. NEWLIN
National Institute on Drug Abuse

This study examined behavioral and physiologic regulation in 14 full-term neonates who were exposed to cocaine antenatally. A group of 14 non-cocaine-exposed infants served as controls. Data on behavioral state, cardiac patterning (heart period and vagal tone), and habituation to a standardized stimulus were collected. There were no differences between cocaine-exposed and nonexposed infants in heart period or vagal tone during an undisturbed period. There were significant differences in behavioral state regulation: Cocaine-exposed infants displayed significantly greater state lability and shorter sleep bouts, fussed or cried more often, and spent less time asleep and more time in transitional states. Both groups responded to an auditory stimulus with shorter heart period, but cocaine-exposed neonates demonstrated a larger response. In addition, cocaine-exposed neonates displayed less behavioral response decrement to repeated presentations of the stimulus. Although there are limitations to attribution of these results to cocaine alone, the results are discussed in relation to prevailing clinical impressions of cocaine-exposed neonates.

neonate cocaine teratogen vagal tone behavioral state

The potential effects of intrauterine substance exposure on neonatal and infant developmental function have captured the interest of the clinical and research communities. In particular, the accelerated use of cocaine by women of childbearing age in the 1980s focused national attention on this issue. From this, a portrait of the typical "crack baby" emerged, representing the perception that cocaine-exposed neonates manifest multiple symptoms of neurologic damage, including poor state regulation, excessive irritability, and hypersensitivity to stimulation (Hawley & Disney, 1992). Although 486 research publications on cocaine use during pregnancy were generated during the 27 months commencing January 1988 (National Institutes of Health, 1990), the high level of interest has generated much heat and little light concerning the actual sequelae of intrauterine cocaine exposure. Early predictions suggested grave developmental sequelae resulting from cocaine exposure, but such effects have not been well documented (Hutchings, 1993).

Knowledge concerning neonatal functioning can help direct subsequent inquiry on developmental effects of intrauterine substance exposure and can confirm or defuse the general clinical impressions concerning cocaine-exposed infants. Although it is possible to have longer term sequelae without obvious neonatal impact, the identification of early patterns of effects provides impetus for investigation of subsequent neurological development. Research on neonatal neurobehavioral functioning of cocaine-exposed infants using a standardized assessment (the Neonatal Behavioral Assessment Scale [NBAS]; Brazelton, 1984) has generated conflicting results. Both Eisen et al. (1991) and Mayes, Granger, Frank, Schottenfeld, and Bornstein (1993) have found significant differences between cocaine-exposed and matched control groups *only* on the habituation cluster, with cocaine infants demonstrating poorer habituation performance. Conversely, Chasnoff, Griffith, MacGregor, Dirkes, and

Portions of this research were presented at the International Conference on Infant Studies, Paris, June 2–5, 1994. This research was supported in part by intramural research funds of the National Institute on Drug Abuse and by award MCJ-000106 from the MCH Bureau, Department of Health and Human Services.

The authors wish to thank Ellen Hutchins and Kathy Klusman for their assistance in data collection.

Correspondence and requests for reprints should be sent to Janet A. DiPietro, Department of Maternal and Child Health, Johns Hopkins University, 624 N. Broadway, Baltimore, MD 21205.

Burns (1989) documented an effect of cocaine exposure on all NBAS clusters *except* habituation. Two other research groups (Neuspiel, Hamel, Hochberg, Greene, & Campbell, 1991; Woods, Eyler, Behnke, & Conlon, 1993) failed to find any significant cocaine effect on any neonatal NBAS cluster in the 1st week of life.

There have been a few other studies targeting specific aspects of antenatal and neonatal neurobehavioral functioning. Both fetal and neonatal state regulation have been described as disorganized as a result of cocaine exposure (Hume, O'Donnell, Stanger, Killam, & Gingras, 1989), although state criteria parameters were poorly specified in that study. Some investigators have reported increased atypical behaviors such as excessive yawning or tremoring (Eisen et al., 1991; Hume et al., 1989). But when compared to groups exposed to narcotics, there is either no difference in these behaviors when systematically rated through the use of the Neonatal Abstinence Syndrome scale (Ryan, Ehrlich, & Finnegan, 1987) or narcotic-exposed newborns appear more affected (Oro & Dixon, 1987), suggesting that these effects may not be specific to cocaine.

The existing literature does not produce a cohesive portrait of neonatal behavioral functioning associated with intrauterine cocaine exposure. If effects of cocaine are manifest in neonatal behavior, they are either limited to a circumscribed aspect of functioning or are quite subtle. Given the limited behavioral repertoire of the neonate, it is possible that observations of neonatal behavior may be relatively insensitive in the detection of nervous system compromise, particularly autonomic functioning. Variability in fetal heart rate, typically considered to be an index of neurologic integrity and fetal well-being, has been reported to be reduced in cocaine-exposed fetuses (Chazotte, Forman, & Gandhi, 1991; Tabor, Soffici, Smith-Wallace, & Yonekura, 1991). Although regulation of heart rate is also thought to reflect autonomic function and neural status in neonates, data exist from only two studies of cocaine-exposed newborns. Decreased heart rate has been reported in cocaine-exposed neonates when compared to control subjects (Silvestri, Long, Weese-Mayer, & Barkov, 1991). Mehta et al. (1993) found no differences in baseline heart rate or heart rate variability between cocaine-exposed and nonexposed neonates. However, spectral analysis of these data indicated that cocaine-exposed infants had significantly greater high-frequency power, which suggests higher vagal tone. Both of these findings are unexpected because *faster* heart rate and *reduced* variability or vagal tone have been documented for other groups of infants with suspected neural damage (Cabal, Siassi, Zanini, Hodgman, & Hon, 1980; DiPietro, Caughy, Cusson, & Fox, 1994; Porges, 1992).

These inconclusive and often contradictory research findings can neither confirm nor deny the most persistent clinical impressions of cocaine-exposed infants which focus on irregularities in autonomic integrity, state regulation, and reactivity to stimulation. The goal of this study was to investigate autonomic and behavioral regulation and responsivity in cocaine-exposed and nonexposed neonates. Tonic autonomic and state organization as well as reactivity to a stimulus presented under standardized conditions were measured in cocaine-exposed and nonexposed neonates. The protocol was designed to test the following:

1. Cocaine-exposed neonates will display different baseline levels of autonomic control, as measured by vagal tone, as a result of chronic or temporal effects of cocaine exposure.
2. Cocaine-exposed neonates will display poorer state organization.
3. Cocaine-exposed neonates will be more behaviorally and autonomically reactive to the stimulus, a rattle, and will take longer to demonstrate response decrement to repeated presentations of that stimulus.

METHOD

Subjects

Subjects were recruited from the full-term nursery at an urban hospital. Standard procedure at this facility is to provide urine toxicology screen for cocaine, opiate, marijuana, and barbiturate metabolites for all women admitted for delivery. Medical charts for each new delivery were examined several times per week to identify potential participants. Infants were eligible as subjects if they fulfilled the following criteria: gestational age $\geq$ 37 weeks; birthweight $\geq$ 2500 gms; and no congenital anomalies. Study inclusion was also restricted to mothers who were $\geq$ 18 years old and had an unremarkable pregnancy history.

Potential control (non-cocaine-exposed) participants were identified if there was evidence of a negative maternal toxicology screen and no other report of drug use in their medical history. Potential non-cocaine-exposed participants