Neurotoxicology and Teratology 43 (2014) 25–32

Contents lists available at ScienceDirect

Neurotoxicology and Teratology

journal homepage: www.elsevier.com/locate/neutera

Reactivity and regulation of motor responses in cocaine-exposed infants

Melissa Duncan Fallone [a,b,*], Linda L. LaGasse [b,c,d], Barry M. Lester [b,c,d], Seetha Shankaran [e], Henrietta S. Bada [f], Charles R. Bauer [g]

[a] Missouri State University, Department of Psychology, 901 S. National Avenue, Springfield, MO 65897, USA
[b] Brown Center for the Study of Children at Risk, Department of Pediatrics, Women & Infants Hospital, 101 Dudley Street, Providence, RI 02905, USA
[c] Department of Pediatrics, Warren Alpert Medical School of Brown University, Providence, RI, USA
[d] Department of Psychiatry & Human Behavior, Warren Alpert Medical School of Brown University, Providence, RI, USA
[e] Department of Pediatrics, Wayne State University School of Medicine, 3901 Beaubien Blvd., Detroit, MI 48201, USA
[f] Department of Pediatrics, University of Kentucky Hospital, 800 Rose St., Rm MS-473, Lexington, KY 40536, USA
[g] Department of Pediatrics, University of Miami, Miller School of Medicine, P.O. Box 016960 (R-131), Miami, FL 33136, USA

ARTICLE INFO

Article history:
Received 29 May 2013
Received in revised form 17 February 2014
Accepted 17 February 2014
Available online 28 February 2014

Keywords:
Cocaine
Prenatal exposure
Motor activity
Reactivity
Regulation

ABSTRACT

Effects of prenatal exposure to cocaine on the reactivity and regulation of the motor system of 825 four-month-old infants enrolled in the Maternal Lifestyle Study were examined. Videotaped assessments of 338 cocaine-exposed (CE) infants and 487 non-exposed comparison infants were coded by examiners masked to exposure status. Exposure status was determined by meconium assay and maternal self-report of prenatal cocaine use. Infants were presented with a series of 17 visual, auditory and tactile stimuli for 30-s each. Intensity and latency of limb movement responses on a subset of items were analyzed to test the following hypotheses: CE infants are more active in general; CE infants exhibit increased movement levels for a larger proportion of time in response to stimulation; the motor systems of CE infants are more reactive to stimulation (e.g., shorter latencies to respond); and CE infants are poorer regulators of the motor system.

Results: CE infants were not more active in general and data do not indicate a more highly reactive motor system. However, CE infants exhibited increased movement levels for a larger proportion of time in response to stimulation. Additional analysis of movement exhibited during three tactile items found increased movement lability in CE infants and different patterns of responding, suggesting that the effects of prenatal cocaine exposure on the motor system may vary by context. Covariate effects for tobacco, alcohol, and marijuana are also reported.

1. Introduction

Prenatal exposure to cocaine is believed to affect the regions of the fetal brain where arousal regulation and motor activity are modulated by the monoaminergic system, specifically the limbic, hypothalamic, and extrapyramidal systems (Volpe, 1992). The relevant monoamines (i.e., dopamine, norepinephrine, and serotonin 5-HT) affect brain development by influencing cell proliferation, neural outgrowth, and synaptogenesis (Lauder, 1988). Deviations in normal levels during the gestational period may adversely affect the development of the neurotransmitter systems and the formation of brain structures in infants (Mayes, 1994). The specific effects of prenatal cocaine exposure are subtle (Lester et al., 1998), and are more consistent with behavioral regulation deficits than deficits in global cognitive or motor functioning. Thus, sensitive behavioral measures are more likely to detect exposure effects than standardized developmental tests of intelligence or motor milestones (Lester et al., 2002). The present study examines the reactivity and regulation of the infant motor system during a laboratory assessment of infant temperament. Because cocaine directly affects brain systems believed to be responsible for the regulation of arousal and motor movement, measures of motor reactivity and regulation are likely to show effects of cocaine exposure.

Reactivity and self-regulation are central concepts in Rothbart's theory of temperament (Rothbart and Derryberry, 1981; Rothbart et al., 1994). Rothbart's psychobiological approach to the study of temperament focuses on the intensive and temporal characteristics of responses to stimulation. The intensity or strength of a response and the latency to respond represent reactivity whereas regulation refers to the ability to return to homeostasis following a response (Marshall et al., 2000). Individual differences in temperament are the result of variations in reactivity and regulation that are expressed through attentional and affective behaviors as well as motor behavior. These variations in motor behavior are associated with the amygdala, a limbic system structure that has projections to areas known to mediate arm and leg flexion and

* Corresponding author at: Missouri State University, Department of Psychology, 901 S. National Avenue, Springfield, MO 65897, USA. Tel.: +1 417 836 6528; fax: +1 417 836 8330.
E-mail addresses: mfallone@missouristate.edu (M.D. Fallone), linda_lagasse@brown.edu (L.L. LaGasse), barry_lester@brown.edu (B.M. Lester), sshankar@med.wayne.edu (S. Shankaran), hbada2@uky.edu (H.S. Bada), cbauer@peds.med.miami.edu (C.R. Bauer).

http://dx.doi.org/10.1016/j.ntt.2014.02.005
0892-0362/

extension in response to stimulation (Kagan et al., 1992). As prenatal cocaine exposure affects these same systems, it is reasonable to expect prenatal cocaine exposure to impact the reactivity and regulation of the motor system. Several lines of research support the assertion that cocaine affects reactivity and regulation in infancy. Studies assessing newborn behavior have found that exposed infants scored higher in excitability dimensions (exhibit higher levels of activity, lability of state, rapidity of buildup, and levels of irritability) and exhibit poorer state regulation (DiPietro et al., 1995; Lester et al., 2002; Schuler and Nair, 1999; Tronick et al., 1996). These findings provide some evidence that cocaine-exposed (CE) infants are more reactive to stimulation and dysregulated in the newborn period.

Heightened reactivity to stimulation and dysregulation has also been found in CE infants beyond the newborn period. Mayes and her colleagues (Mayes et al., 1995, 1996) noted that 4-month-old CE infants cried more often and for longer periods of time and displayed frequent and longer negative facial expressions in response to novel stimuli. Similarly, Struthers and Hansen (1992) found that 6-month-old CE infants were more distractible and active in response to stimulation during a visual recognition memory test.

A direct behavioral assessment of reactivity and regulation in CE infants was recently conducted by Eiden and her colleagues (Eiden et al., 2009). Reactivity and regulatory behaviors of 7-month-old CE infants were assessed during a procedure designed to elicit frustration. After allowing the child to interact with a toy, the examiner restrained the infants' arms for two consecutive 30-second trials. Four measures of reactivity (intensity of anger and sadness and latency to anger and sadness) and the number of regulatory behaviors exhibited by the infant were used for analyses. Results indicated that CE infants were quicker to respond with anger on the second trial than the first trial, and unlike the comparison infants, the exposed infants did not increase their use of regulatory strategies during the second trial. The authors concluded that under conditions of stress (a repeated arm restraint trial), CE infants were more reactive and dysregulated. This finding is consistent with the results of animal research showing that behavioral differences in CE rat pups emerge under conditions of stress (Spear et al., 1998).

The results reported by Eiden et al. (2009) suggest that prenatal cocaine exposure affects the emotional reactivity and affective regulation of infants. However, little is known about how prenatal cocaine exposure affects the expression of reactivity and regulation via the motor system. Some studies have reported the effects of prenatal cocaine exposure on infants' activity level. However, the findings are largely inconsistent, with some suggesting increases in movement (Mayes et al., 1995, 1996; Struthers and Hansen, 1992) while others suggest a decrease in movement (Alessandri et al., 1993; Edmondson and Smith, 1994; Martin et al., 1996).

Overall, prenatal cocaine exposure has been found to be associated with higher levels of excitability, poorer state regulation, and increased reactivity to stimulation. However, less reactivity has also been reported. With the exception of Struthers and Hansen (1992), no studies of CE infants have explicitly examined reactivity and regulation specifically within the motor response system. A number of studies have looked at the activity level (i.e., amount of activity in general) CE infants exhibit (Alessandri et al., 1993; Edmondson and Smith, 1994; Martin et al., 1996; Mayes et al., 1995, 1996; Struthers and Hansen, 1992). However, reactivity of the motor system in response to specific stimuli has not been investigated to date in CE infants.

The present study examines the effects of prenatal cocaine exposure on motoric reactivity and self-regulation of infants. Motoric reactivity refers to the recruitment of the motor system in the expression of arousal, and can be assessed by observing the limb movement of infants immediately following exposure to visual, auditory, or tactile stimulation. Although the motor system is one of the primary modalities through which young infants exhibit signs of arousal (affect being another), no studies have directly examined the effects of cocaine exposure on infant motor reactivity.

Although some studies have found an association between CE infants and depressed levels of activity (Alessandri et al., 1993, 1995; Edmondson and Smith, 1994; Martin et al., 1996), the preponderance of evidence suggests that the affective responses of CE infants are more highly reactive and more excitable in response to stimulation. Thus, data from this investigation were analyzed to test the following hypotheses: When compared with comparison infants, CE infants (a) are more active in general; (b) exhibit increased movement levels in response to stimulation (c) have motor systems that are more reactive to stimulation (e.g., shorter latencies to respond); and (d) are poorer regulators of the motor system.

2. Method

2.1. Study design

Data for this study were collected through the Maternal Lifestyle Study (MLS), a study of children at risk due to prenatal exposure to cocaine and other substances. The research was approved by the institutional review board at each of the four NICHD Neonatal Research Network sites: University of Miami, the University of Tennessee at Memphis, Wayne State University, and Brown University. Mothers and their infants were enrolled between May 1993 and May 1995 prior to discharge. Specific enrollment procedures and exclusion criteria are described elsewhere (Bauer et al., 2002; Lester et al., 2001).

The early follow-up phase of MLS consisted of a 3-year longitudinal study of 1388 eligible children whose mothers agreed to participate and did not plan to move out of the catchment area. Children were categorized as “exposed” or “comparison” based on maternal self-report and drug assay of meconium samples. All meconium samples were screened for illicit drug metabolites using and enzyme multiplied immunoassay technique (EMIT). Positive samples were confirmed by gas chromatography–mass spectroscopy (GC/MS). The study definition of “exposed” was maternal admission of cocaine or opiate use during this pregnancy or positive GC/MS confirmation of cocaine or opiate metabolites. Opiates were included in the exposed group because of hospital reports indicating that many cocaine users were also using opiates. “Comparison” was defined as denial of cocaine or opiate use during this pregnancy and a negative EMIT screen for cocaine and opiate metabolites. Comparison infants were group-matched to exposed infants within each site on race, sex and gestational age resulting in 658 mother/infant dyads in the exposed group and 730 in the comparison group. Groups are uneven because it was not possible to replace exposed participants who withdrew their consent, while comparison subjects were replaced if they withdrew their consent prior to the 1-month follow-up visit.

The data on use of alcohol, marijuana, and nicotine by participants in both groups were obtained from the biological mother at the 1-month visit using the Maternal Interview of Substance Use (MISU). The distributions of reported tobacco, marijuana, and alcohol use, averaged over three trimesters, were not normal. Therefore, 3 categories of use (heavy, some, and no use) were created using established cutoffs for the patterns of use (Lester et al., 2002). Heavy use of nicotine and marijuana was defined as 10 or more cigarettes per day and 0.50 joints or more per day respectively. Heavy use of alcohol was defined as 0.50 oz of alcohol or more per day which translates to one standard drink. Some use of a substance was defined as any other use of the substance.

2.2. Participants

Infants were included in this study if they attended the 4-month visit ($N = 1127$) and had high quality videotapes from which to code limb movement and were not prenatally exposed to opiates ($N = 901$). An additional 10 cases were excluded due to administration errors, while an additional 66 cases were removed from the data set because the