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Reactivity and Regulation of Motor Responses in Cocaine-Exposed Infants

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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-second 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

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(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.

Keywords

cocaine; prenatal exposure; motor activity; reactivity; regulation

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 & 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 arms and leg flexion and 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 on 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 & 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; Mayes, et al., 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 & Hansen, 1992) while others suggest a decrease in movement (Alessandri, et al., 1993; Edmondson & 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 & Smith, 1994; Martin et al., 1996; Mayes et al., 1995, 1996; Struthers & 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 & 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 1,388 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 groupmatched 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 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 of tobacco, marijuana, and alcohol use, averaged over three trimesters, were not normally distributed. 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 = 1,127) 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 infants became inconsolable early in the procedure (within the first 5 of 17 items). The resulting sample of 825 infants was made up of 338 (41%) CE infants and 487 (59%) comparison infants. The percentage of CE infants in the study sample was not significantly different ($p > .05$) from those who did not attend the 4-month visit (47.6%) or the infants without data (42.5%).

The study sample and the infants not included in the study were different ($\alpha < .05$) with respect to socioeconomic status, marital status, heavy tobacco use, and some marijuana use. Specifically, the SES (modified Hollingshead, LaGasse et al., 1999) of the study sample ($M = 28.96$, $SD = 10.66$) was slightly higher, $t(1334) = 2.21$, $p = .027$, than the SES of those who did not attend ($M = 27.64$, $SD = 10.66$). The study sample also included a lower percentage of mothers who were single (79%) than those who did not attend (83.3%) or were without data (83.4%). Heavy tobacco use during pregnancy was less common in the study sample (19.6%) than for those who did not attend (29.8%) or those without data (30.3%). Similarly, some use of marijuana during pregnancy was reported less frequently by mothers in the study sample (21.5%) than by mothers who did not attend the visit (28.6%) and those without data (28%).

The medical and demographic characteristics of CE and comparison infants in the study sample are described in Table 1. The CE infants weighed slightly less than the comparison infants at birth (120 g), $t(825) = 2.08$, $p < .05$, but did not differ in terms of their gestational age, length, head circumference, or Apgar scores at 5-minutes of age. A greater percentage of the mothers of the CE infants had not completed high-school, were unmarried, without private insurance, and below the federal poverty line. In addition, they were much more likely to use tobacco, alcohol, and marijuana.

2.3 Measures

The data from this study were derived from the Behavioral Assessment of Infant Temperament (BAIT) (Garcia-Coll et al., 1988) which consists of the presentation of a series of 17 visual, auditory, and tactile stimuli for 30 seconds each. The stimuli were presented in a fixed order, designed so that the level of stimulation increased with each new stimulus (see Table 2 for a list of items in order of administration). The assessments were videotaped and behaviors were coded using the Action Analysis, Coding, and Training (AACT) system (Delgado, 1996).

2.4 Procedure

The BAIT was administered to the infants when they were 4 months old (3.5 to 4.5 months corrected for prematurity), by examiners that were masked to exposure status. The BAIT procedure was videotaped, and coded at a later time. The procedure began when the infants were placed in a slightly reclined infant car seat and secured with a lap belt. The child's caregiver often watched from the other side of a one-way mirror but did not interact with the infant. The examiner began the stimulus presentation as soon as the child was in a calm, awake state. The research assistant who operated the camera timed each item for the required 30 seconds, allowing only a few seconds for stimulus changes between items. If the infant became upset during the procedure, the examiner stopped the presentation to allow 15 seconds for the infant to quiet on his own. If the infant was unable to self-quiet, a fixed order of consoling procedures, each lasting 15 seconds, was used to determine the level of intervention required to calm the infant. If the child was not calmed by one of these levels, the infant was deemed inconsolable, and the procedure was interrupted so that examiner and/or the mother could soothe the infant. If the child calmed within 30 minutes and was able to maintain an alert state, the examiner repeated the stimulus during which the child had become upset and continued through the sequence. If the child was unable to calm or was not in an alert state, the exam was terminated.

2.5 Data reduction

Infant movement was coded from videotapes of the BAIT by research assistants masked to exposure status. The intensity of arm and leg movement as well as behaviors such as fussing and crying were coded at 1 second intervals. Coders rated the infants' arm and leg movements on the basis of the number of limbs moving as well as the speed in which they were moving. At the onset of each item the coders chose one of four mutually exclusive levels of movement that best described the level of movement exhibited by the child at that moment as described below. Every time the infant increased or decreased the movement of their arms and or legs, the coder would change the code to more accurately reflect the movement level of the infants' arms and/or legs. The result was a second by second account of the infant's movement level during each item.

There were four levels of movement. Low movement of arms and/or legs was coded when less than four limbs were moving at one time and the movements were slow. Moderate movement of arms and/or legs was coded when less than four limbs were moving at one time and the movements of the fastest limbs were moderate to fast or when movements were slow but involved all four limbs. High movement of arms and/or legs was coded when all four limbs were moving and the fastest limbs were moving at a moderate or fast speed. When an infant was not moving her arms and/or legs or if the movement was very slight or negligible, a code representing the absence of arm and/or leg movement was coded. Movement was not coded during transition periods between items or when the child was being consoled.

The seven research assistants who coded the BAIT trained using gold standard practice tapes, and ten gold standard reliability tapes originally coded by the first author. A mean kappa of .60 for the movement level variable was required before a research assistant was allowed to code movement levels without the assistance of a trainer. Additional inter-rater reliability tapes (1 of every 10) were coded to monitor coder drift, and thereby maintain a high level of reliability. Reliability tapes that resulted in a kappa statistic less than .60 were reviewed for consensus and any remaining disagreements were refereed by the first author.

Examination of the mean duration of the four levels of movement (no movement, low, moderate, and high movement) revealed that across all items, the infants in our sample were not moving 60% of the time. Because the focus of the study is movement, we omitted items from the data set that elicited less than average amounts of movement from the infants. Specifically, an item was excluded if the overall mean proportion of movement during that item was below 40% (the average mean for all items). Data from the 10 remaining items (see Table 2) sample the overall range of stimulus intensity in the procedure and were retained for further analyses.

The four levels of movement (none, low, moderate, and high) were used in the calculation of summary variables designed to measure the intensive and temporal characteristics of motor responses. The majority of the summary variables were significantly correlated with negative affect (the proportion of time infants were fussing and crying during items) as expected given that affect and activity are both modalities through which reactivity and regulation are expressed. Descriptions of each variable as well as the correlations between each variable and negative affect are provided in Table 3

3. Results

3.1 Statistical Analysis

Analysis of Covariance (ANCOVA) was used to test the effects of exposure status while controlling for covariates. The covariates were included for conceptual reasons or because they met the following statistical criteria: the variable was correlated with both cocaine exposure and one or more measures of reactivity and regulation ($p < .05$), and not highly correlated with other covariates (Pearson $r < .70$) (Jacobson & Jacobson, 1990; LaGasse et al. 1999; Leon, 1993; Richardson & Day, 1999). Birthweight, maternal tobacco use, and maternal marijuana use met the statistical criteria for inclusion. SES (modified Hollingshead, LaGasse et al., 1999) and maternal alcohol use were included for conceptual reasons. An additional factor, site was added as a nesting factor to the model, such that exposure status was nested within site. Previous analyses of data from this project have revealed strong site differences despite rigorous efforts to insure uniform protocol administration among the personnel at the four sites. Therefore, it was necessary to control for site variance statistically. Adjustments for multiple comparisons were made when appropriate by controlling false discovery rates (FDR; Benjamini & Hochberg, 2000). Means and standard errors are reported in Table 4.

To test the hypothesis that CE infants are more active in general, each infant’s activity level was calculated as the proportion of time movements were coded as moderate or high during each item. Proportions were calculated to adjust for minor variations in item duration. The activity level of CE infants averaged across all items did not differ from the activity level of infants in the comparison group, $F(4, 733) = 0.84$, $p > .05$.

CE infants were also hypothesized to exhibit increased movement in response to stimulation for a larger proportion of time than comparison infants. To test this hypothesis, three variables were calculated to measure the infants' general response to stimulation. Periods of time when the infant exhibited higher levels of movement than the level at presentation are referred to as an *increase from presentation level*. Periods of time when the infant exhibited lower levels of movement than the level at presentation are referred to as a *decrease from presentation level*. *Presentation level* describes the periods of time when the infant exhibited the same level of movement as the initial level. While the comparison infants exhibited presentation levels of movement for a larger proportion of time than the CE infants, $F(4, 733) = 3.87$, $p < .05$, CE infants showed an increase from presentation level for a larger proportion of time than the comparison infants, $F(4, 733) = 3.82$, $p < .05$). Together, these data suggest that CE infants increased movement in response to stimulation more than comparison infants. CE and comparison infants did not differ ($F(4, 733) = 0.624$, $p > .05$) in the proportion of time movement levels were decreased from presentation levels.

The hypothesis that the motor systems of CE infants are more reactive to stimulation was tested by comparing the CE and the comparison infants on a number of different measures of reactivity, each of which described an initial response of the infant's motor system to stimulation. The percent of first moves that were *increases* or *decreases* reflect an infant's initial tendency to alter motor activity when presented with stimulation. The timing of the responses was measured by the latencies to *first peak*, *highest peak*, *first valley*, and *lowest valley*. *First peak* measured the first increase in movement level while *highest peak* measured the highest level of movement exhibited. Similarly, *first valley* measured the first decrease in movement level while *lowest valley* measured the lowest level of movement exhibited. Differences between the CE and comparison infants were not found on any of the six reactivity variables.

Lability of motor activity reflects the infants' regulation capacity (i.e., ability to modulate reactivity). Two related but conceptually different measures of motor lability were used the test the hypothesis that CE infants are poorer regulators of the motor system. *Number of changes* measured the absolute number of movement level changes (increases and decreases) exhibited by the infants. *Number of peaks*, in contrast, measured the number of times the infants reached their highest level of movement. The data show some indication that CE infants had more peak movement levels than comparison infants, $F(4, 731) = 2.59$, $p < .025$. However, with alpha adjusted, the effect is not statistically significant. CE infants did not differ from the comparison infants in the number of changes in movement levels they exhibited, $F(4,731) = 1.94$, $p > .05$.

3.3 Tactile Item Analyses

A second set of exploratory analyses was conducted to examine the motoric reactivity and regulation of CE infants during items involving tactile stimulation. The BAIT items were administered in the order specified by Garcia-Coll et al., (1988) with each item providing more intense stimulation than the previous item. However, examiners and coders for this study noted that many infants responded negatively (fussed and cried) in response to *brush hair*, *wash face*, and *hat* items (referred to as the Irritability items by Garcia-Coll et al. 1988). Table 2 shows that two of the three tactile items (*wash face* and *hat*) may have been particularly aversive or irritating to the infants than the other items as evidenced by the average amount of negative affect exhibited by infants during those items. Therefore, the data from the three tactile items (bolded in Table 2) were analyzed separately to investigate whether motor systems of CE infants were more or less reactive than comparison infants in the context of tactile stimulation.

Table 5 shows that the CE and the comparison infants were not more active in general during the tactile items. The movement level of CE infants and comparison infants showed similar proportions of both increased movement and decreased movement in response to tactile stimulation. However, the movement level of the comparison infants were more often at the presentation level than the CE infants, $F(4, 734) = 2.62$, $p < .05$. Interestingly, while the movement level of CE infants were less often at the presentation level, they did not show more increased movement from presentation or decreased movement from presentation than comparison infants. These data suggest that CE infants show some response to tactile stimulation (as evidenced by a less time in the level of movement exhibited at presentation). However, the direction of the response (either a general increase in movement or a general decrease in movement) is not clear.

CE infants exhibited longer latencies to the highest peak than infants in the comparison group, $F(4, 732) = 2.48$, $p < .05$, possibly suggesting a slower reactivity. Differences between the groups were not found on the other five reactivity variables (see Table 5). Further, CE infants showed a larger number of changes in movement levels, $F(4, 734) = 3.18$, $p < .05$, as well as a larger number of peaks than the comparisons group infants $F(4, 732) = 3.50$, $p < .01$. Therefore, when stimulation is of a tactile nature CE infants' movements are more labile and intense, suggesting poorer capacity for regulation.

3.4 Covariate Effects

Birthweight was significantly correlated ($r(747) = .114$, $p = .002$) with the latency to highest peak in the analyses of the tactile items but not when all items were included in analyses. This is some indication that this specific measure of reactivity is related to birthweight such that, the lower the birthweight of an infant the shorter the latency to the *highest peak* of movement in the context of tactile stimulation.

When all items were included in the analyses, infants heavily exposed to tobacco, ($M = .76$, $SE = .016$) as opposed to infants with no exposure to tobacco ($M = .81$, $SE = .007$), showed fewer increases when the stimuli were first presented ($F(1, 733) = 9.47$, $p = .002$, $\eta_p^2 = .013$). The opposite was true for infants heavily exposed to marijuana $F(1, 733) = 5.36$, $p = .021$, $\eta_p^2 = .007$. Infants with heavy exposure to marijuana showed more increases in the level of movement as a first response to stimulation ($M = .86$, $SE = .027$) than infants with some or no exposure to marijuana ($M = .79$, SE .007). Infants heavily exposed to marijuana also showed fewer decreases in the level of movement as a first response to stimulation ($M = .10$, $SE = .022$) than infants with some or no exposure to marijuana ($M = .15$, $SE = .006$),

F(1, 733) = 4.39, p = .037, η_p^2 = .006. These data suggest that heavy tobacco and heavy marijuana exposure may have opposite effects on reactivity as measured by the tendency to decrease or increase movement respectively as an initial response to stimulation.

Opposite effects of marijuana and tobacco were also present when only the tactile items were analyzed. Infants exposed to some tobacco showed a longer latency to the *lowest valley* (M = 10.33, SE = .365) than comparison infants (M = 9.45, SE = .253), F(1, 729) = 5.71, p = .017, η_p^2 = .008, whereas infants exposed to some marijuana showed a shorter latency to the *lowest valley* (M = 9.28, SE = .361) than those with no exposure to marijuana (M = 10.06, SE = .23), F(1, 729) = 3.94, p = .047, η_p^2 = .005. Prenatal exposure to alcohol did not have a significant effect on any of the measures of reactivity or regulation.

4. Discussion

This study is the largest prospective study reported on the effects of prenatal cocaine exposure on infant motoric reactivity and self-regulation. By utilizing behavioral observation coding methods as opposed to maternal reports, we were able to analyze infants' general activity level and overall response to stimulation. In addition, we specifically examined reactivity and regulation, central components of Rothbart's theory of temperament (Rothbart & Derryberry, 1981), within the motor system.

The results of this study did not show support for the first hypothesis that CE infants exhibit higher levels of activity than infants in the comparison group in general. The CE infants did not exhibit active arm and leg movements for longer or shorter durations than the comparison infants. These findings are inconsistent with other behavioral observation studies that found CE infants to be more active (Mayes et al., 1995, 1996; Struthers & Hansen, 1992) or less active (Allesandri et al., 1993; Edmondson & Smith, 1994; Martin et al., 1996) than comparison infants.

We found some support for the hypothesis that CE infants would show increased movement in response to stimulation. CE infants showed increased movement in response to varied stimulation, but not under tactile stimulation conditions. One possible explanation for this finding is that when stimulation is of a tactile nature, some CE infants tend to increase movement while others tend to decrease movement; thus any effects are lost when the increases and decreases are combined. This possible divergence of behavior in CE infants has been noted previously by Lester, et al. (1995) where both an excited and depressed pattern of behavior emerged.

The hypothesis that CE infants are more reactive to stimulation than infants in the comparison group was not supported by our data under either level of stimulation. In fact, in contrast to a number of other studies (DePietro et al., 1995; Eiden et al, 2009; Mayes et al., 1995; Mayes et al., 1996; Stuthers & Hansen, 1992), our data indicate that infants in the CE group may be less reactive (as evidenced by longer latency to the highest peak) than the comparison group during the tactile items. Thus, the rise time of a motor response, as measured by the latency to the highest peak of movement, was longer for CE infants.

CE infants were found to be poorer regulators of the motoric response system than non-exposed comparison infants as predicted by the fourth hypothesis. Clearer evidence of poor regulation of the motor system was found during the tactile items where CE infants reached their peak movement level more frequently than comparison infants and showed a larger number of actual changes in movement levels, suggesting more lability of movement and poorer regulation in general. The finding discussed previously that CE infants show a general increase in movement as a response to stimulation appears to result from regulation difficulties as suggested by the higher number of peaks and movement lability rather than differences in reactivity. Interestingly, evidence of motor system dysregulation was more evident during items that elicited the most negative affect; specifically, the tactile stimulation items. Other studies have found evidence that CE infants have poor regulation of their affective or attentional states (DiPietro et al., 1995; Karmel & Gardner, 1996; Tronick et al., 1996), ours is the first to show poorer regulation within the motor system in particular.

The pattern of results observed between overall conditions and conditions involving tactile stimulation may be related to this construct. When measured across a range of stimulation, the overall response by cocaine exposed infants was an increase in movement level with no findings of higher or lower reactivity. But a different pattern of responding emerged in the context of tactile stimulation. First, CE infants were slower to respond to stimuli than comparison infants, suggesting a depressed reaction. Second, they no longer showed more increased movement than infants in the comparison group, but continued to show less time in their initial level of movement, suggesting that with tactile stimulation, some CE infants react with an increase in movement while others react by decreasing movement. This decrease in movement is consistent with animal studies that found a propensity for CE rat pups to “freeze” under conditions of stress. This excited/depressed finding in 4-month-old infants provides support for the Lester et al., (1995) suggestion that there are distinct neurobehavioral profiles of CE infants with some highly aroused (excitable) and others more lethargic (depressed). This study provides new evidence that these profiles are maintained at least four months after exposure to cocaine has ceased and that they may be related to higher, more aversive levels of stimulation such as the tactile items of the BAIT.

Several differences exist between the present study and the aforementioned behavioral observation studies that may account for discrepant findings. First, Martin et al. (1996) observed newborns before discharge from the hospital and the observations of activity were made during periods in the assessment protocol when little, if any stimulation occurred. In contrast, we measured the activity of older infants when responses were elicited by varying levels of stimuli. Second, examiners for the Edmondson and Smith (1994) study subjectively rated the infants’ activity level after administering a developmental test. It is possible that this global rating by an examiner may be influenced by many factors such as the child’s level of compliance during the task and the examiner’s memory. Allesandri et al. (1993), counted the number of arm pulls during a learning and extinction task to objectively measure the activity of 4-to-8-month old infants. However, one might argue that this contingency task promotes instrumental movement that is not likely to be present in our study. In addition, we measured the strength and duration of the movements of all four limbs.

Inconsistent findings might also be attributable to the system in which reactivity was measured. While we observed reactivity of the motor system, most of the other studies observed reactivity within an affective framework. Interestingly, our reactivity findings are more consistent with studies by Alessandri et al. (1993), Martin et al. (1996), and Edmondson and Smith (1994) who found less reactivity in CE infants.

Unique contributions of exposure to other drugs were also examined in this study. Although prenatal alcohol use was not associated with our measures of reactivity and regulation, tobacco and marijuana use accounted for significant amounts of variance in some of the measures. Interestingly, our findings suggest that prenatal marijuana exposure and prenatal tobacco exposure have the opposite effect on the reactivity of infants' motor systems. Under overall stimulation, infants with heavy exposure to marijuana were more likely to respond to stimulation by increasing their level of movement and reaching their lowest level of movement faster. Infants prenatally exposed to heavy amounts of tobacco were less reactive. When presented with higher levels of stimulation, infants with some exposure to tobacco had a longer latency to the lowest movement level. This may indicate that even infants with some nicotine exposure seem less reactive by exhibiting a slower response than comparison infants.

Many limitations of previous studies of the effects of prenatal cocaine exposure were eliminated by the design and scope of the Maternal Lifestyle Study. Its large sample size was sufficient for detecting subtle effects and allowed for the control of confounding factors through adjustment for covariates. The effect sizes reported here may reflect truly subtle effects or as is often the case when measures are newly-developed and untested, attenuation of larger effects result in smaller calculated effect sizes (Cohen, 1988). With continued refinement of the coding system and derived variables, the effects may become more pronounced.

Therefore, the main limitations of the study were within the coding system itself. First, coding did not occur during the time periods between the items. Therefore, a "baseline" measure of an infant's motor activity under non-stimulus conditions was not possible to obtain. Second, the movement levels were defined such that when arms and legs did not change position, the infant was coded as not moving. The problem with this definition is that at times some infants would become upset, extend their arms and legs and maintain a truly "activated" position, yet they would be coded as not moving. Fortunately, inclusion of this data was rare because when an infant was extremely upset, the item was terminated and repeated once the child was in a calmer state. Only the later, more complete administration of the item would be included in the data set. Third, we acknowledge that reactivity and regulation are difficult to separate and measure independently. Regulatory processes could be continuously active and modulating the infant's initial reaction to the stimulus, and variation in initial reaction could place different demands on the regulatory system. We also acknowledge that the behavioral repertoire of infants is comprised of motor activity, arousal, affect, and attention; all of which can be used as indices of reactivity and regulation when examining individual differences. Our selection of measures and focus on motor activity was based on other studies and Rothbart's conceptual framework.

The generalizability of the findings may be limited due to sample attrition. Infants in this particular study were slightly different from those MLS cohort infants who were not included in this study in terms of nicotine and marijuana use as well as marital and socioeconomic status. The direction of these differences indicates lower risk for those infants included in the study than for those not included in the study.

5. Conclusions

Young infants continuously respond to changing circumstances in their environments using affective and motoric modalities. Individual differences in reactivity and regulation reflect temperamental qualities that may be affected by prenatal exposure to cocaine and other drugs. This study finds that cocaine exposed infants are more dysregulated overall and show increases in movement in response to stimulation unless confronted by high levels of stimulation. In this case, CE infants may also show a decrease in movement. These variations in responding are characteristics of difficult temperament. Poorly regulated CE infants may be more difficult to understand and care for, especially by mothers with poor parenting skills (as is the case with many drug using mothers). Given a nonoptimal environment for which to learn self-regulation skills, these infants may be at risk for a myriad of disorders in regulation that emerge in infancy and continue through adolescence such as internalizing and externalizing behaviors. Continued follow-up of these infants is likely to determine whether dysregulation of the motoric response system in infancy is predictive of child and adolescent behavioral outcomes.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- CE infants showed more increased movement levels in response to stimulation.
- CE infants exhibited poorer self-regulation of the motor system than comparisons
- Excitable and depressed behavior patterns emerged with tactile stimulation.

Table 1

Infant Medical Characteristics, Maternal Characteristics, and Background Drug Use of Comparison and Cocaine-Exposed (CE) Groups

	Comparison (*n* = 487) Mean (*SE*), %	**Cocaine-Exposed (CE) (*n* = 338) Mean (*SE*), %**	***p***
Infant Medical Characteristics			
Gestational Age at Birth (weeks)	36.20 (.185)	36.01 (.225)	.527
Birth Weight (grams)	2667 (39)	2545 (42)	**.034**
Length at Birth (cm)	47.01 (.238)	46.42 (.265)	.100
Head Circumference (cm)	32.17 (.146)	31.80 (.163)	.095
Apgar (5 minute)	8.56 (.046)	8.55 (.057)	.991
% Male	52.8	55.3	.469
Maternal Characteristics			
Maternal Age	26.92 (.269)	30.31 (.249)	**< .001**
SES	29.76 (.49)	27.67 (.57)	**.007**
% Below Federal Poverty Line	58.2	74.0	**< .001**
% No Private Insurance	80.7	96.2	**< .001**
% Single	71.7	89.6	**< .001**
% < High School Degree/GED	30.9	49.4	**< .001**
Race			.885
% Black	76.4	76.3	
% White	15.2	13.9	
% Hispanic	6.8	8.0	
% Other	1.6	1.8	
Background Drug Use			
%Tobacco			**< .001**
High	8.9	38.3	
Some	21.5	48.5	
None	69.6	13.1	
% Alcohol			**< .001**
High	3.7	27.7	
Some	49.5	54.4	
None	46.8	17.9	
% Marijuana			**< .001**
High	1.2	8.4	
Some	10.8	40.5	
None	88.0	51.1	

Table 2

Mean Proportion of Movement and Negative Affect Elicited by Items Included in Analyses

BAIT Item	Movement	Negative Affect
Examiner's Face and Voice	.48	.06
Brush Hair	.52	**.14**
Wash Face	.68	**.22**
Hat	.60	**.26**
Ring Bell 1	.43	.13
Ring Bell 2	.41	.12
Mask 1 (scary, normal voice)	.44	.11
Mask 2 (human, normal voice)	.44	.10
Cry 1 (audio of an infant crying)	.41	.11
Cry 2 (audio of an infant crying)	.42	.14

[a]These 10 items included in the analyses elicited more than average amounts of movement.

[b]The bell and cry items consisted of 10 seconds of sound followed by 20 seconds of silence.

[c]Tactile items are bolded

Table 3

Correlations Between Negative Affect and Motoric Reactivity and Regulation Summary Scores

Summary Scores	Negative Affect	Description of Summary Scores
Activity Level	.277*	The proportion of time infant movement was coded as moderate or high during each item.
Presentation	−.301*	The periods of time when infants exhibited the same level of movement as the initial level.
Increase from Presentation	.314*	The proportion of time infants exhibited higher levels of movement than the level at presentation.
Decrease from Presentation	−.017	Periods of time when the infant exhibited lower levels of movement than the level at presentation.
Increases	.030	The proportion of items for which the second level of movement is higher than the level coded at the onset of the stimulus.
Decreases	.063	The proportion of items for which the second level of movement is lower than the level coded at the onset of the stimulus.
First Peak	−.214*	The number of seconds from the onset of the stimulus to the first peak of movement (defined as the onset of the highest level of movement reached before the first decline to a lower level) averaged across items.
Highest Peak	−.182*	The number of seconds from the onset of the stimulus to the highest level of movement (defined as the onset of the highest level of movement reached) averaged across items.
First Valley	−.202*	The number of seconds from the onset of a stimulus to the first lower level of movement (defined as the onset of the lowest level of movement reached before an increase to a higher level) averaged across items.
Lowest Valley	−.094	The number of seconds from the onset of a stimulus to the lowest level of movement (defined as the onset of the lowest level of movement reached) averaged across items.
Number of Changes	.125*	The number of changes in movement levels that occur during an item averaged across items.
Number of Peaks	.094	The number of peaks (defined as the onset of the highest level of movement reached before the first decline to a lower level) averaged across items.

*Indicates $p < .001$

Table 4

Group Differences in Reactivity and Regulation Measures Adjusted for Covariates.

	Comparison			Cocaine-Exposed (CE)				
	n	**Mean**	***SE***	***n***	**Mean**	***SE***	***p***	**(η_p^2)**
Activity								
Activity Level	482	.13	.008	268	.15	.011	.501	.005
Response to Stimulation								
Presentation	482	.54	.009	268	.50	.013	**.004**	**.021**
Increase from Presentation	482	.38	.009	268	.41	.013	**.004**	**.020**
Decrease from Presentation	482	.08	.005	268	.09	.007	.646	.003
Reactivity								
Increases	482	.79	.010	268	.78	.014	.871	.002
Decreases	482	.16	.009	268	.17	.012	.756	.003
First Peak	481	8.20	.168	267	7.74	.236	.060	.012
Highest Peak	481	11.20	.198	267	11.02	.279	.140	.009
First Valley	480	9.57	.175	267	9.36	.246	.231	.008
Lowest Valley	480	10.27	.188	267	10.54	.264	.193	.008
Regulation								
Number of Changes	482	7.67	.150	268	7.96	.210	.102	.010
Number of Peaks	481	3.64	.056	267	3.75	.079	.036	.014

[a]The *Number of Peaks* effect does not meet the significance criterion after adjusting for multiple comparisons

Table 5

Group Differences in Reactivity and Regulation Measures During Tactile Items Adjusted for Covariates.

	Comparison			Cocaine-Exposed (CE)				
	n	**Mean**	***SE***	***n***	**Mean**	***SE***	***p***	**(η_p^2)**
Activity								
Activity Level	482	.18	.010	267	.18	.015	.981	.001
Response to Stimulation								
Presentation	482	.46	.011	267	.43	.016	**.022**	**.015**
Increase from Presentation	482	.43	.012	267	.47	.018	.087	.011
Decrease from Presentation	482	.10	.008	267	.10	.012	.961	.001
Reactivity								
Increases	482	.79	.014	267	.79	.020	.789	.002
Decreases	482	.18	.014	267	.18	.019	.985	.001
First Peak	481	6.40	.192	266	6.38	.273	.115	010
Highest Peak	481	8.85	.276	266	9.90	.392	**.030**	**.015**
First Valley	480	8.45	.219	266	8.20	.311	.170	.009
Lowest Valley	480	9.81	.287	266	10.14	.407	.662	.003
Regulation								
Number of Changes	482	8.51	.173	266	8.70	.244	**.023**	**.015**
Number of Peaks	481	3.93	.070	266	3.97	.099	**.013**	**.017**