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Prenatal Cocaine Exposure and Small-for-Gestational-Age Status: Effects on Growth at 6 Years of age

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Abstract

OBJECTIVE—To evaluate the impact of prenatal cocaine exposure and small-for-gestational-age (SGA) status on childhood growth.

STUDY DESIGN—Cocaine exposure was defined by history or meconium metabolites. Hierarchical linear modeling was used to examine cocaine exposure and SGA status on growth, while controlling for exposure to other drugs and alcohol use.

RESULTS—At birth cocaine-exposed infants (n=364) had significantly lower growth parameters compared to non-exposed children (n=771). At 6 years, weight was similar between exposed and unexposed children. SGA infants continued to be growth impaired. There was a significant interaction between prenatal cocaine exposure and SGA status at 6 years. The negative effects of cocaine on weight and height were greater among non-SGA than SGA children (432 vs. 280 gm, and 0.7 and 0.5 cm, respectively) while negative effects of SGA status on weight and height were larger in non-cocaine exposed compared to the exposed children (2.3 kg vs. 1.6 kg and 2.2 and 1.0 cm).

CONCLUSIONS—Children exposed to prenatal cocaine were similar in weight to non-exposed children at 6 years of age. Cocaine had an unexplained greater detrimental effect on non-SGA than SGA children. SGA status at birth has an independent detrimental effect on childhood growth.

Keywords

Prenatal cocaine exposure; small for gestational age; childhood growth

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1.1 INTRODUCTION

Cocaine use during pregnancy has effects on fetal and childhood growth. In the largest prospective longitudinal study evaluating the impact of maternal lifestyle during pregnancy on acute birth outcomes, the Maternal Lifestyle Study (MLS), we noted that infants exposed to cocaine had lower birth weight, length and head circumference than infants not exposed to cocaine during pregnancy [2, 7]. We have continued to evaluate the growth of these offspring to childhood.

Investigators have noted that growth in childhood is poor following cocaine exposure. Covington and colleagues evaluated growth in childhood among 540 African American children (231 exposed to cocaine; 198 by maternal history, 20 by laboratory measures, 13 by biologic mothers' admission at 7 years) and meconium confirmation of metabolites for 20% of subjects. The investigators controlled for other drug exposures and other confounders including maternal age, pre-pregnancy weight and gestational age. They noted that at 7 years of age, cocaine exposed children were 1 inch shorter than and twice as likely to fall below the 10th percentile in height as the children in the control group [11]. Minnes and co-workers examined 154 prenatally exposed children and 131 non-exposed children belonging to similar race and social class, with exposure documented by maternal urine toxicology and infant meconium. At birth 19 children in the exposed group and 3 in the nonexposed group were small for gestational age (SGA). At 6 years of age, there was a relationship between cocaine exposure and growth parameters; higher prenatal exposure was associated with lower weight, and weight for height z score was predicted by level of prenatal cocaine exposure [18]. Richardson has reported on the impact of first trimester prenatal cocaine exposure using a model of repeated measures growth curves to 10 years of age. Women were enrolled prenatally into the study, and 99 cocaine exposed children were compared to 125 non-cocaine exposed children. At birth, cocaine exposure during the first trimester resulted in reduced gestational age, but no difference in growth parameters. SGA status at birth was noted in 11% of overall cohort of children studied. At 7 and 10 years of age, cocaine exposed children were smaller on all growth parameters compared to unexposed children [20].

Other investigators have not noted an impact of cocaine exposure on childhood growth. Chasnoff et al examined 95 children born to women with cocaine/polydrug exposure by history and urine toxicology compared to 75 matched children (by race and socio-economic status) born to women without exposure. The mean growth parameters were similar in both groups at 4, 5 and 6 years of age; rate of growth was also similar but head circumference was marginally smaller in the cocaine/polydrug exposed children at 6 years [8]. Lumeng and associates evaluated 123 cocaine exposed and 134 non-cocaine users with exposure confirmed by maternal report and meconium analysis. Women were characterized as heavier (n=38) or lighter (n=74) or non-users (n=89) based on quantification of cocaine metabolites. After controlling for polydrug use, child's gestational age, gender, ethnicity, and pre-pregnancy weight, the detrimental effects of cocaine noted at birth (heavier vs. unexposed differed by 0.33 standard deviation (SD) units, lighter vs. unexposed differed by 0.39 SD units) were no longer noted at 8 years [17].

Women who use cocaine prenatally often also use other illicit drugs and alcohol. Smoking during pregnancy has been found to have a negative impact on birth weight, head circumference, and length of the neonate [2]. During the course of childhood, however, this growth detriment appears to dissipate over time and studies have demonstrated that prenatal tobacco exposure is related to childhood obesity [10, 14, 16, 25]. Alcohol use during pregnancy is associated with a decrease of fetal growth parameters with continued

detrimental effect on growth during childhood [2,3,9,10,11,14,17]. Opiate exposure during pregnancy also has a detrimental effect on fetal growth parameters [2].

Infants exposed to prenatal cocaine may be small-for-gestational-age (SGA) at birth [3, 7], and in MLS, prenatal cocaine exposure increased the likelihood of SGA status (Odds Ratio 2.24). A gap in our knowledge about prenatal cocaine exposure and SGA status is whether these 2 conditions have independent effects on childhood growth; this has not been evaluated in previous studies. Prevention of substance use and prevention and treatment of SGA status at birth will have important clinical and public health implications; hence the need to examine the effects of cocaine exposure and SGA status at birth on the trajectory of growth. The hypothesis of this study was that prenatal cocaine exposure and SGA status would both have independent detrimental effects on childhood growth. The objective of this study was to evaluate the effects of prenatal cocaine exposure and SGA status at birth on growth to six years of age and to examine this effect while controlling for exposure to other drugs.

1.2 METHODS

This evaluation was undertaken as part of the longitudinal study examining the impact of maternal lifestyle during pregnancy on maternal, neonatal and childhood outcome conducted at Wayne State University, University of Tennessee at Memphis, University of Miami, and Brown University, participants in the *Eunice Kennedy Shiver* National Institute of Child Health and Human Development Neonatal Research Network. RTI International in Research Triangle Park, NC, was the Data Coordinating Center and the Neurodevelopmental Center was at Brown University. At one month of age, infants were enrolled in a cocaine exposed group or a comparison cohort. Exposure was defined by maternal self report of cocaine use during pregnancy or gas chromatography mass spectroscopy confirmation of metabolites of cocaine in the infants' meconium. In the comparison group, non-exposure was defined as a negative history of cocaine use and an absence of cocaine metabolites in meconium, and non-exposed infants were group matched at each site to exposed infants by gestational age, sex, and race. A history of alcohol, tobacco, opiate and marijuana use was also ascertained by the study research nurse among all mothers in the study and opiate use was also confirmed by the presence of metabolites in meconium. SGA status was defined as birth weight that was below the 10th percentile for gestational age on the Alexander curves [1]. Gestational age was based on the best obstetric estimate, derived from the last menstrual period and/or early sonography. The study nurses were trained to reliability on estimation of gestational age by the site study principal investigator. The physical growth trajectory was plotted on the Centers for Disease Control and Prevention and the National Center for Health Statistics Growth Charts [15].

At each clinic visit (1 month of age and each annual visit within one month of child's birthday) weight was measured by the research nurse using a physician's 2-beam scale with children wearing a hospital gown with no shoes, no outer clothing and no items that could add weight such as keys, belt, or watches. Weight was recorded to the nearest 0.1 kg. Height was measured with the child standing with feet together on the stadiometer recorded to the nearest 0.1 cm. Head circumference was measured to the closest 0.1 cm. Research nurses were trained to reliability by one of the site principal investigators (S.S). The protocol was approved by the Institutional Review Board of each of the study sites and informed consent obtained prior to enrollment. The study was conducted under a Certificate of Confidentiality from the National Institute on Drug Abuse. At each visit to the clinic the study subjects were given developmentally age appropriate books or toys.

1.2.1 Statistical Methods

T tests or ANOVA were used to compare means for continuous variables and chi-square tests to compare proportions for categorical variables. All of the variables for prenatal drug exposure are dichotomous (i.e. exposed vs. not exposed). To examine whether trajectories of growth up to 6 years of age were influenced by cocaine exposure or SGA status at birth, longitudinal analyses were performed using Hierarchical Linear Models (HLM). The HLM utilized the growth data (as continuous variables) at different time points to model the trajectory of each growth outcome (weight, height and head circumference) as a function of prenatal cocaine exposure, SGA status at birth and other covariates and confounders. Adjustments were carried out for the following covariates (selected *a priori*) regardless of statistical significance: clinical site, maternal race, maternal socio-economic status (SES) measured using the Hollingshead Index, maternal use of alcohol, tobacco, opiates and marijuana during pregnancy, and sex of the child. Current maternal alcohol or drug use was not considered as covariates. We selected variables in the model to ensure that our estimates for SGA and cocaine reflect the impact of SGA and cocaine on growth above and beyond these factors that have been shown to impact childhood growth. In addition, to account for change over time (temporal trends), all models included linear and quadratic terms for the age of visit (ages one through six years). Further adjustments were made for certain interaction terms only if the p value (overall or any category-wise) was ≤ 0.1 , or, if the inclusion of the variable substantially changed the relationship between cocaine, SGA and the outcomes (i.e. removal of the variable changes the directionality or size of the estimates by more than 20%). These included two-way interactions between cocaine and SGA, and cocaine and opiates, and three-way interactions between these two items and age of visit. The longitudinal modeling utilized any available outcome data; i.e. if data were available at the one-year visit but not during the two-year visit, the one-year data was still included in the model if all covariate data were also available.

1.3 RESULTS

1.3.1 Sample Description

There were 1388 infants enrolled at one month and of these, 1135 mother-infants dyads were followed to 6 years of age. Table 1 shows the baseline comparison of dyads with follow-up and those lost to follow-up. Compared to the dyads lost to follow up, those in the sample studied had a lower frequency of Medicaid insurance, illicit drug and alcohol use and higher frequency of prenatal care, tobacco use, and higher gestational age, birth weight, length and head circumference. Table 2 reflects the maternal and neonatal characteristics of the study cohort by prenatal cocaine exposure and SGA status at birth. The prenatal cocaine use cohort had higher Medicaid insurance, placental abruption, illicit drug, tobacco and alcohol use and SGA status and lower prenatal care, preeclampsia, maternal educational status, birth weight and birth length than the non-exposed group. The SGA cohort had higher frequency of Black mothers, chronic hypertension, and high tobacco and cocaine use in pregnancy than the appropriate for gestational age cohort.

1.3.2 Unadjusted Analyses

Table 3 shows decreases in growth parameters for cocaine exposed infants compared to those not exposed to cocaine. At birth, cocaine exposed infants were 150 g less in weight, 0.85 cm shorter and had 0.40 cm smaller head circumference compared to infants who were not cocaine exposed ($p < .05$). At one and two years of age, height was lower in the exposed infants compared to the non-exposed infants and there were non-significant differences from 3 to 6 years of age. At 6 years of age, exposed children were 300 g lighter, had shorter stature (0.3 cm) and lower head circumference (0.08 cm) as compared to the non-cocaine exposed children (all $p > 0.05$). Table 4 shows the growth trajectory for SGA and non-SGA

children. At birth, SGA infants were 800g lighter, 3.2 cm shorter and had a 1.8 cm smaller head circumference than the non-SGA infants ($p < .05$). SGA infants continued to be growth impaired in all three measurements at all ages, and at 6 years of age had weight that was 2.2 kg lower, height 2.0 cm lower and head circumference 0.90 cm smaller than the non-SGA children ($p < .05$).

1.3.3 Adjusted Analyses

Longitudinal modeling of growth data produced slightly different models for the three growth outcomes, depending on what interaction terms were statistically significant and thus retained in the final model. Table 5 reveals that for weight, a significant interaction is seen between prenatal cocaine and SGA status, as well as between SGA status and age of visit. The effect of SGA status at birth on a child's later growth depended both on the prenatal cocaine exposure, and age. The SGA effect thus was larger in children who were not exposed to cocaine (780g mean adjusted difference at birth, increasing to 2.3 kg by year 6) compared to those who were exposed to cocaine (63 g increasing to 1.6 kg by year 6). Conversely, the negative effect of exposure to cocaine was observed only in the non-SGA children compared to the SGA children (432 g adjusted mean deficiency in weight for exposed children, unchanged over time). The statistically significant covariates for weight included clinical site, race and sex of the child ($P < 0.05$) and trend for maternal SES ($P = 0.06$). There was no discernable effect of prenatal opiate exposure on weight.

Table 6 reveals significant interactions for child height between cocaine and SGA, as well as between cocaine and opiates. The SGA effect was larger in children who were not prenatally exposed to cocaine (2.2 cm) compared to those who were (1.0 cm). Overall, prenatal cocaine exposure had a significantly negative effect on height, with those exposed being, on average 0.9 cm shorter than those who were not exposed. The significant cocaine versus opiate interaction prompted a separate examination of the effect of cocaine/no opiate, opiate/no cocaine, and both cocaine and opiates, compared to those who were exposed to neither. The negative effect of prenatal cocaine exposure, but not opiate exposure (a deficiency of 0.7 cm) in height was only observable in the non-SGA children. There was no discernable effect of prenatal exposure to opiates on height. The negative effect of prenatal exposure of both cocaine and opiates (a deficiency of 1.5 cm) was only observable in the non-SGA children. Comparing this with the negative effect of prenatal exposure to cocaine, it was noted that for the non-SGA children there does appear to be an additive effect of simultaneous exposure of cocaine and opiates on height. There were no significant interactions with age of assessment. The statistically significant covariates for height included clinical site, sex of the child and maternal SES ($P < 0.05$).

Table 7 shows that SGA status at birth had a significant, independent and negative effect on head circumference that persisted up to 6 years of age. On average, children born SGA had a head circumference that was 0.8 cm smaller than non-SGA children. Prenatal exposure to cocaine had a significant independent and negative effect on head circumference that persisted up to 6 years of age. Children so exposed had head circumferences that were 0.3 cm smaller than non-exposed children. There was no discernable effect of prenatal exposure to opiate on head circumference. There were no significant interactions with age of assessment. The interactions (cocaine/SGA) were not significant for the head circumference model. The statistically significant covariates for head circumference included clinical site, sex of the child and maternal SES ($P < 0.05$).

Figure 1a shows the adjusted impact of SGA status at birth and cocaine exposure on weight up to 6 years. Detriment in weight is greater in the SGA children, whether exposed to cocaine or not. Figure 1b notes the impact of cocaine exposure and SGA status at birth on height at 6 years. The non-SGA, non-cocaine exposed children are taller than children in the

other groups, with SGA, cocaine exposed children with the greatest detriment in height. There was no cocaine by SGA interaction for head circumference, so the interaction term was dropped from the final model.

1.4 DISCUSSION

This is the largest study performed to date to examine the effect of prenatal exposure to cocaine on growth to age 6 years and the first to examine the independent effects of SGA and cocaine on growth to age 6 years. This study found detrimental effects of cocaine on growth to age 6 only in children who were AGA at birth, but not in those who were SGA at birth. In this multi-institutional, prospective longitudinal study we found that SGA status at birth had a greater negative impact on growth through 6 years of age than prenatal cocaine exposure. We have previously reported that consistent use of cocaine throughout each trimester was associated with detrimental effects on birth weight and head circumference when drug use was evaluated during each trimester of pregnancy [21] and that deceleration of growth following prenatal cocaine exposure occurred after 32 weeks gestation in a full term pregnancy [2]. We have also noted that prenatal cocaine exposure increased the likelihood of low birth weight with tobacco and cocaine having additive effects [3]. Bandstra and colleagues found a symmetrical negative impact on growth parameters following cocaine exposure that is partially mediated by gestational age in a full term pregnancy [4].

The effect of prenatal cocaine exposure on growth in childhood has been evaluated by many investigators. Chasnoff et al [8] and Lumeng and co-workers [17] found that catch up growth in the cocaine-exposed infants occurred early in childhood without any differences among exposure groups (heavy, light or no exposure). Neither of these 2 studies has noted the proportion of SGA children in their cohorts.

Richardson and co-authors recently reported slower growth at 10 years of age among cocaine exposed children (n=99) compared to those not exposed to cocaine (n=125) during the first trimester [20]. The study did include 11% of children who were SGA; however the impact of SGA status is not reported. Covington and colleagues have noted that children born to women exposed prenatally to cocaine were shorter and likely to fall below the 10th percentile in height as compared to control children; differential effects of cocaine and alcohol were noted with maternal age moderating the effects [11]. In their study, the investigators do not state if any of the children were SGA. Minnes and associates evaluated 154 six year old children prenatally exposed to cocaine and 131 high risk children of similar race and social class [18]. The authors noted greater prenatal cocaine exposure predicted lower weight for height z-scores. In their study 12.5% of the cohort was SGA, however, the impact of SGA status at birth on growth at 6 years is not reported.

In our study, we have examined, for the first time, the effects of SGA status at birth and prenatal cocaine exposure and suggest that SGA status at birth may account for some of the differences noted between our study and those of other investigators. SGA status at birth is associated with deficits in childhood growth in previous publications [22,23] and was confirmed in our study. Hediger evaluated growth of young children from the Third National Health and Nutrition Examination Survey with 423 SGA infants, 3,570 AGA and 438 who were large for gestational age [13]. At 47 months of age, children who were born SGA had a deficit of 0.75 standard deviation units for weight and 0.60 standard deviation units for height and head circumference compared to the children born AGA. In a nation-wide population-based study where a large cohort was followed longitudinally to adulthood, adults who were born SGA were shorter than their appropriate for gestational age peers at the age of 21 years [24]. As noted by Barker et al [6] and Bhargava and colleagues [7] the

growth of the fetus may be influenced by many factors including maternal weight and body mass index. An impaired growth rate in-utero is often accompanied by impaired growth during childhood; however, it has also been shown that growth restriction in-utero may be followed by rapid weight gain in childhood because of an increase in adiposity of the fetus [5,6,12].

We can only speculate on the potential mechanism of the moderating effect of cocaine on SGA status at birth or SGA on cocaine exposure. Fetal growth is influenced by placental size, perfusion of fetal nutrition, and genes linked to growth factors [12]. SGA status at birth may be due to *early* fetal growth deceleration secondary to fetal under nutrition often starting with the first trimester as a result of maternal health problems (under nutrition/hypertension/overweight status). The placenta is often compromised when the infant is SGA at birth. The impact of cocaine on fetal weight may be due to decreasing transport of amino acids through the placenta [19]. The impact of cocaine on fetal weight is noted late in gestation [2]. It is therefore possible that the detrimental effects of cocaine are less on the fetus and placenta that are already compromised throughout pregnancy as noted in SGA infants.

Our study has limitations; details of prenatal causes of SGA status such as poor maternal nutrition or placental insufficiency could not be elucidated. We did not have information on the pre-pregnancy weight of the mothers at the time of the 6 year visit to the clinic [26]. We did not include current maternal alcohol and drug use as covariates. It is possible that children who remained in this study differed from those who did not remain in the study on some factors that we did not measure.

In summary we have demonstrated in a large prospective longitudinal study that SGA status at birth has a greater negative impact on growth through 6 years of age than prenatal cocaine exposure. In future research it is very important to conduct these growth analyses either examining interactions with SGA status at birth, or stratifying analyses based on SGA status at birth. This study is important for clinical care and future research because understanding the causes of SGA status at birth and preventing these conditions as well as avoiding exposure to illicit drugs such as cocaine during pregnancy will optimize maternal and childhood outcomes. We plan to follow this high risk cohort and evaluate whether growth restriction continues to adulthood among those born SGA at birth and whether the other consequences of SGA status occur such as obesity, impaired glucose tolerance or risk for coronary heart disease [5, 6, 12, 22].

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Data collected at participating sites of the NICHD Neonatal Research Network (NRN) were transmitted to RTI International, the data coordinating center (DCC) for the network, which stored, managed, and analyzed the data for this study. On behalf of the NRN, Drs. Abhik Das (DCC Principal Investigator) and Sylvia Tan (DCC Statistician) had full access to all the data in the study and take responsibility for the integrity of the data and accuracy of the data analysis.

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Abbreviations

SGA	Small for gestational age
SES	socio-economic status

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Figure 1.

Figure 1a–b. Weight in Kg from birth to 6 years of age is noted in 1a, height in centimeters in 1b following adjustment for confounders (maternal race, socio-economic status and alcohol, tobacco, opiates, marijuana use and child gender) among the following groups: No SGA, no cocaine exposure, no SGA with cocaine exposure, SGA with no cocaine exposure and children who are SGA and cocaine exposed.

Table 1

Baseline comparison of dyads in the study compared with those with no follow-up. Results are expressed as a percentage or where indicated as mean $\pm$ SD.

Sample descriptors	No Follow-up N = 253	With follow-up (Analysis Sample) N = 1135	p value
Race: Black	72	78	0.09
White	17	16	
Hispanic/other	2	1	
Insurance: Medicaid	83	81	<0.01
Private/HMO	5	13	
Education (Highest Grade) ^I	11.17 $\pm$ 1.84	11.82 $\pm$ 1.91	0.03
Prenatal care	73	91	<0.01
Prenatal Alcohol	72	57	<0.01
Prenatal Tobacco	83	47	<0.01
Prenatal Cocaine	93	32	<0.01
Prenatal opiates	10	8	<0.01
Prenatal marijuana	37	20	<0.01
Chronic Hypertension	3	5	0.31
Preeclampsia	4	7	0.06
Abruptio Placentae	2	2	0.52
Prolonged rupture of membranes	11	8	0.06
SGA	22	24	0.6
Birth Weight (g) ^I	2536.46 $\pm$ 833.09	2648.95 $\pm$ 815.42	0.05
Gestational Age (weeks) ^I	35.71 $\pm$ 4.34	36.37 $\pm$ 3.94	0.03
Birth length (cm) ^I	45.99 $\pm$ 5.25	46.91 $\pm$ 4.97	0.01
Birth head circumference (cm) ^I	31.68 $\pm$ 3.18	32.21 $\pm$ 2.99	0.01

^I Mean $\pm$ SD

Baseline comparison of dyads by prenatal cocaine exposure and SGA status at birth. Results are expressed as percentage or where indicated as mean $\pm$ SD.

Table 2

Sample descriptors	Prenatal cocaine exposure			SGA status at birth		
	Yes N = 364	No N = 771	p value	Yes N = 272	No N = 863	p value
Race: Black	80	76	0.48	83	76	0.03
White	14	16		11	17	
Hispanic/other	1	1		2	1	
Insurance: Medicaid	89	77	<0.01	83	81	0.28
Private/HMO	5	18		11	15	
Education (Highest Grade) [/]	11.46 $\pm$ 1.53	11.98 $\pm$ 2.04	<0.01	11.78 $\pm$ 1.54	11.83 $\pm$ 2.01	0.64
Prenatal care	81	96	<0.01	90	92	0.35
Prenatal Alcohol	74	49	<0.01	61	55	0.08
Prenatal Tobacco	83	30	<0.01	61	43	<0.01
Prenatal Cocaine				44	28	<0.01
Prenatal opiates	11	6	0.01	10	7	0.1
Prenatal marijuana	43	10	<0.01	23	20	0.25
Chronic Hypertension	4	5	0.49	7	4	0.05
Preeclampsia	5	8	0.04	9	6	0.08
Abruptio Placentae	4	2	0.02	2	2	0.57
Prolonged rupture of membranes	7	8	0.77	6	8	0.1
SGA	33	20	<0.01			
Birth Weight (g) [/]	2542.14 $\pm$ 689.54	2699.37 $\pm$ 864.38	<0.01	2229.30 $\pm$ 454.38	2781.21 $\pm$ 858.33	<0.01
Gestational Age (weeks) [/]	36.30 $\pm$ 3.78	36.41 $\pm$ 4.02	0.68	37.17 $\pm$ 2.50	36.13 $\pm$ 4.27	<0.01
Birth length (cm) [/]	46.42 $\pm$ 4.41	47.14 $\pm$ 5.20	0.02	45.44 $\pm$ 3.62	47.37 $\pm$ 5.24	<0.01
Birth head circumference (cm) [/]	32.04 $\pm$ 2.70	32.29 $\pm$ 3.12	0.19	31.48 $\pm$ 2.24	32.44 $\pm$ 3.16	<0.01

[/] Mean $\pm$ SD

Table 3

Difference in Growth Parameters between non-cocaine exposed and exposed children from birth to 6 years of age

Year	<u>Difference between non-cocaine exposed and cocaine exposed)</u>		
	Weight (kg)	Height (cm)	Head Circumference (cm)
0 (Birth)	.15*	.85*	.4*
1	.04	.5*	.4
2	.1	.7*	.3
3	.2	.3	.2
4	.01	.4	.2
5	.3	.6	.07
6	.3	.3	.08

*
p <.05

Values reflect non-cocaine minus cocaine

Table 4

Difference in Growth Parameters between non-SGA and SGA children from birth to 6 years of age

Year	<u>Difference between non-SGA and SGA children</u>		
	Weight (kg)	Height (cm)	Head Circumference (cm)
0 (Birth)	.8*	3.2*	1.8*
1	.7*	2.0*	.8*
2	.9*	1.6*	.8*
3	1.1*	2.3*	.6*
4	1.4*	1.95*	.9*
5	1.8*	1.8*	.7*
6	2.2*	2.0*	.9*

* p <.05

Values reflect non-SGA minus SGA

TABLE 5

Interactions of Cocaine and SGA Status on Weight over time

Standard Effect	Estimate	Error	DF	t Value	Pr > t
Overall SGA Effect: Year 0	-0.4219	0.1962	4742	-2.15	0.0315
Overall SGA Effect: Year 2	-0.8206	0.1694	4742	-4.84	<.0001
Overall SGA Effect: Year 4	-1.3321	0.1722	4742	-7.73	<.0001
Overall SGA Effect: Year 6	-1.9566	0.2231	4742	-8.77	<.0001
SGA Effect for Coc: Year 0	-0.06304	0.2657	4742	-0.24	0.8125
SGA Effect for Coc: Year 2	-0.4617	0.2461	4742	-1.88	0.0608
SGA Effect for Coc: Year 4	-0.9733	0.2482	4742	-3.92	<.0001
SGA Effect for Coc: Year 6	-1.5977	0.2864	4742	-5.58	<.0001
SGA Effect for No Coc: Year 0	-0.7808	0.2258	4742	-3.46	0.0005
SGA Effect for No Coc: Year 2	-1.1794	0.2035	4742	-5.80	<.0001
SGA Effect for No Coc: Year 4	-1.6910	0.2057	4742	-8.22	<.0001
SGA Effect for No Coc: Year 6	-2.3155	0.2492	4742	-9.29	<.0001
Overall Coc Effect	-0.07316	0.1760	4742	-0.42	0.6776
Coc Effect: No SGA	-0.4320	0.1824	4742	-2.37	0.0179
Coc Effect: Yes SGA	0.2857	0.2707	4742	1.06	0.2913

Results obtained from longitudinal modeling of weight over time, adjusting for clinical site, maternal race, maternal socio-economic status (SES) at birth measured using the Hollingshead Index, maternal use of alcohol, tobacco, opiates and marijuana during pregnancy, and gender of the child (see Statistical Methods and Results for further details).

TABLE 6

Interactions of Cocaine, Opiates and SGA status on Height over time

Effect	Estimate	Error	DF	t Value	Pr > t
Overall SGA Effect	-1.5765	0.2704	4734	-5.83	<.0001
SGA Effect for Coc	-0.9787	0.4185	4734	-2.34	0.0194
SGA Effect for No Coc	-2.1743	0.3364	4734	-6.46	<.0001
Overall Coc Effect	-0.9165	0.4551	4734	-2.01	0.0441
Coc Only: No SGA	-0.7248	0.3336	4734	-2.17	0.0298
Coc Only: Yes SGA	0.4708	0.4921	4734	0.96	0.3387
Coc & Opt: No SGA	-1.5126	0.6598	4734	-2.29	0.0219
Coc & Opt: Yes SGA	-0.3170	0.7376	4734	-0.43	0.6674
Opi Only	0.7913	0.5496	4734	1.44	0.1500

Opi represents opiates

Results obtained from longitudinal modeling of height over time, adjusting for clinical site, maternal race, maternal socio- economic status (SES) at birth measured using the Hollingshead Index, maternal use of alcohol, tobacco, opiates and marijuana during pregnancy, and gender of the child (see Statistical Methods and Results for further details).

TABLE 7
Associations of Cocaine, Opiates and SGA status on Head Circumference over time

Label	Estimate	Error	DF	t Value	Pr > t
SGA Effect	−0.7777	0.1126	4688	−6.90	<.0001
Cocaine Effect	−0.2559	0.1238	4688	−2.07	0.0388
Opiate Effect	0.09283	0.1783	4688	0.52	0.6026

Results obtained from longitudinal modeling of weight over time, adjusting for clinical site, maternal race, maternal socio- economic status (SES) at birth measured using the Hollingshead Index, maternal use of alcohol, tobacco, opiates and marijuana during pregnancy, and gender of the child (see Statistical Methods and Results for further details).