

Sleep Problems in Children With Prenatal Substance Exposure

The Maternal Lifestyle Study

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Objective: To examine the associations between sleep problems and prenatal exposure to cocaine, opiates, marijuana, alcohol, and nicotine in children aged 1 month to 12 years.

Design: Sleep data were collected by maternal report in a prospective longitudinal follow-up of children participating in the Maternal Lifestyle multisite study.

Setting: Hospital-based research centers in Providence, Rhode Island; Miami, Florida; Detroit, Michigan; and Memphis, Tennessee.

Participants: There were 808 participants, 374 exposed to cocaine and/or opiates, and 434 comparison subjects.

Main Exposure: Prenatal cocaine, opiate, marijuana, alcohol, and/or nicotine exposure.

Outcome Measure: Sleep problems in early, middle,

and/or late childhood, assessed as composites of maternal report items.

Results: Of the 5 substances, prenatal nicotine exposure was the only unique predictor of sleep problems ($B=0.074$, R^2 change=0.008, $P=.01$), with adjustment for covariates, including socioeconomic status, marital status, physical abuse, prenatal medical care, and postnatal cigarette smoke exposure.

Conclusions: Prenatal exposure to nicotine was positively associated with children's sleep problems persisting throughout the first 12 years of life. Targeting of this group of children for educational and behavioral efforts to prevent and treat sleep problems is merited given that good sleep may serve as a protective factor for other developmental outcomes.

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SLEEP PROBLEMS IN CHILDREN are associated with daytime impairment, including altered psychomotor performance,¹ behavioral disturbance,² sleepiness,^{3,4} decreased physical activity and social interest,⁴ memory and learning deficits,⁵ and substance use.⁶ The role of sleep in the development of children with prenatal drug exposure, however, is not well understood. Sleep studies with prenatally exposed children have been limited almost entirely to infancy. Observable decrements in sleep duration and continuity and in sleep-state organization have been found in infants with prenatal cocaine exposure⁷⁻¹⁰ and, more recently, in infants with prenatal exposure to alcohol¹¹ and nicotine.^{11,12} In addition, differences in electroencephalographic sleep patterns between exposed and unexposed infants have been demonstrated in studies of prenatal exposure to opiates,¹³ alcohol,¹⁴ and nicotine.¹⁵

Until recently, there were no longitudinal sleep studies of prenatal exposure to cocaine, opiates, alcohol, or nicotine. One study in 3-year-old children found more disrupted sleep to be associated with prenatal exposure to marijuana.¹⁶ Furthermore, an association between sleep problems through 9 years of age and prenatal nicotine exposure

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has been documented in a small Maternal Lifestyle Study sample ($n=139$),¹⁷ meriting a larger study with better control of covariates and more power to investigate level of prenatal exposure. The aim of the current study, therefore, was to investigate the effects of prenatal exposure (including level of exposure) to cocaine, opiates, marijuana, nicotine, and alcohol on sleep problems over time (1 month to 12 years) in a large sample of children ($n=808$).

STUDY DESIGN

The Maternal Lifestyle Study is a multisite longitudinal investigation of the developmental effects of prenatal exposure to cocaine and other drugs.¹⁸⁻²⁰ The Maternal Lifestyle Study enrolled 1388 children at birth from 1993 to 1995 and was approved by an appropriate institutional review board at each of its 4 sites (Wayne State University, Detroit, Michigan; University of Tennessee at Memphis, Memphis, Tennessee; University of Miami, Miami, Florida; and Brown University, Providence, Rhode Island).²¹ Confidentiality regarding the participants' drug use was assured through each center's National Institute on Drug Abuse certificate of confidentiality.

Mothers were recruited in the hospital after delivery and informed consent was obtained at that time. All women delivering very-low-birth-weight newborns (ie, 501-1500 g) were approached to maximize likelihood of recruiting participants who either had prenatal cocaine exposure or were appropriate group-matched controls. During normal business hours, other mothers (ie, those delivering newborns >1500 g) were also approached. Mothers were eligible if they were aged 18 years or older and did not have psychiatric disorders, developmental delays, or language barriers. Neonates were eligible if they were inborn, likely to survive, a singleton, and were born before 43 weeks' gestation. Mother-infant dyads were excluded from the study, starting with the 1-month visit, if the infant had a chromosomal abnormality or toxoplasmosis, rubella, cytomegalovirus, herpes, or syphilis infection or if the mother planned to move out of the catchment area. Comparison participants were matched on ethnicity (black, white, Hispanic, and other), sex, and gestational age. Another match was generated when an infant in the comparison group did not attend the 1-month visit. It was not always possible, however, to replace exposed infants who withdrew, which yielded uneven groups: 658 in the cocaine or opiate-exposed group and 730 in the comparison group.

PARTICIPANTS

Mothers were assigned to the cocaine/opiate exposure group based on either maternal report and/or meconium toxicology with gas chromatography-mass spectroscopy assay confirmation. To be assigned to the comparison group, participants who denied cocaine or opiate use during pregnancy also had to have negative meconium toxicology results. The same procedure was followed for identification of marijuana exposure. Alcohol and tobacco use were assessed by maternal report alone. Level (ie, amount) of prenatal exposure to each of those 5 substances (cocaine, opiates, marijuana, alcohol, and nicotine) was determined at the 1-month visit using the Maternal Interview of Substance Use, which provides information about the frequency (eg, number of times used cocaine each week) and quantity (ie, number of cigarettes, joints, or ounces of alcohol used or consumed each day) of substance use during pregnancy. To be eligible for the current study, participants must have completed more than half of all the sleep measures administered from 1 month to 12 years. Eight hundred eight participants were eligible (374 exposed to cocaine and/or opiates and 434 comparison subjects), which is the final sample for this study.

DEMOGRAPHIC AND MATERNAL MEASURES

At the 1-month visit, self-report information about prenatal care, maternal age, marital status, education level, socioeconomic status (SES), and poverty status was gathered. The Caretaker In-

ventory of Substance Use was used at yearly visits to assess level of postnatal use of each of the 5 substances since pregnancy. Furthermore, questionnaires assessed the number of caretaker changes (number of times the child changed caregivers during the 12-year period); child abuse (yes or no each year, defined by medical examination findings suggestive of physical or sexual abuse or removal of the child from the home owing to suspicion or verification of physical or sexual abuse); and domestic violence, including physical and sexual abuse experienced by the caretaker (yes or no, years 5-12).

SLEEP MEASURES

The sleep problems index was created to measure global sleep difficulties, particularly difficulties falling or staying sleep, in our sample across the first 12 years of life using sleep items on the 4 pediatric questionnaires described below. All items within 3 periods (1 month to 4 years, 5-8 years, and 9-12 years) were summed for 3 age-relative indexes of sleep problems. We then computed a total sleep problems index summing all 45 items from 1 month to 12 years. Our sleep problems indexes were prorated for missing items. That is, we accounted for missing data by multiplying the mean of the items that were present by the total number of possible items. Other studies have created a composite score from questionnaires, such as the Child Behavior Checklist,^{22,23} with adequate internal consistency ($\alpha=0.64$).²² The Cronbach α for the sleep problems index at each period for our study was 0.64, 0.74, and 0.8, respectively. The Cronbach α for the overall sleep problems index was 0.88.

The Child Behavior Checklist²⁴ was administered at the 3-, 5-, 7-, 9-, and 11-year assessments. This standardized parent-reported questionnaire identifies behavioral and emotional problems of children during the past 6 months and includes the following sleep-related items: having problems sleeping at night, having trouble getting to sleep, talking in one's sleep, crying in one's sleep, sleepwalking, waking up often at night, and sleeping less than or more than most. The child was assigned 1 point for each item the parent endorsed. The Child Health and Illness Profile was administered at years 10 to 12. This validated questionnaire²⁵ assesses children's health and well-being and includes 1 item assessing "trouble falling asleep." If endorsed, the child was assigned 1 point. The child was also assigned 1 point if the parent endorsed "trouble sleeping" on the Pediatric Symptom Checklist, which was administered at years 8 to 12. The Pediatric Symptom Checklist is a 35-item psychosocial screener for cognitive, behavioral, and emotional problems.²⁶ A general health questionnaire administered yearly contained the following sleep items: problems with sleeping, falling asleep at an unreasonable time, waking at night and requiring attention, being medicated for insomnia, and sleep disorder diagnosis. The child was assigned 1 point for each item the parent endorsed.

STATISTICAL ANALYSIS

A χ^2 test or *t* test was used to compare sample characteristics of attrition (**Table 1**) and exposure (**Table 2**) groups. Analysis of variance was used to compare the cocaine or opiate exposure group to the comparison group on the overall sleep problems index.

A 2-step approach was used to determine which of the 5 substances (cocaine, opiates, marijuana, alcohol, and/or nicotine) were significant predictors of sleep problems. In step 1, all 5 substances were entered together in a regression model to determine which of the substances reached significance ($P < .05$), which would suggest an association with sleep problems un-

Table 1. Sample Characteristics by Attrition

Characteristic	No. (%)		P Value
	With 12-Year Data (n = 808) ^a	Without 12-Year Data (n = 580) ^b	
Maternal Characteristic			
Minority race	689 (86.4)	462 (80.5)	.003
Low SES, Hollingshead score of 5 at 1-month visit	193 (24.5)	116 (21.2)	.16
Below poverty line at 1-month visit	484 (64.5)	325 (62.6)	.49
Married	144 (17.8)	122 (21.1)	.13
Education <high school	311 (38.5)	234 (40.5)	.46
No prenatal care	89 (11.0)	79 (13.6)	.14
Age, mean (SD), y	28.6 (5.8)	28 (5.9)	.11
Prenatal drug use			
Cocaine	346 (42.8)	254 (43.8)	.72
Opiates	58 (7.2)	57 (9.8)	.08
Marijuana	173 (21.4)	151 (26)	.045
Alcohol	487 (60.3)	338 (58.3)	.46
Nicotine	422 (52.2)	326 (56.2)	.14
Postnatal drug use			
Cocaine ^c	102 (12.6)	46 (8.6)	.02
Opiates	32 (4.0)	26 (4.9)	.42
Marijuana	215 (26.6)	111 (20.8)	.02
Alcohol	667 (82.5)	389 (73)	<.001
Nicotine	519 (64.2)	339 (63.6)	.81
Domestic violence anytime during child age range of 5-12 y	108 (13.5)	45 (17.9)	.08
Child abuse anytime during child age range of 1 mo-12 y,	204 (25.2)	128 (22.4)	.22
No. of caretaker changes 4 mo-12 y, mean (SD)	1 (1.6)	0.8 (1.2)	.004
Newborn Medical Characteristic			
Premature	339 (42.1)	238 (41.1)	.72
Birth weight, mean (SD), g	2615.4 (833.8)	2649.9 (797.1)	.44
Length, mean (SD), cm	46.6 (5.1)	46.9 (4.9)	.35
Head circumference, mean (SD), cm	32.1 (3.0)	32.2 (3.0)	.44
Male sex	427 (52.8)	300 (51.7)	.68

Abbreviation: SES, socioeconomic status.

^aOf the total sample, 58.2% had 12-year data.

^bOf the total sample, 41.8% did not have 12-year data.

^cThe decrease in cocaine use postnatally may be attributable to the fact that mothers using cocaine during pregnancy in some cohorts of the Maternal Lifestyle Study (eg, Providence, Rhode Island) were required by state law to remain abstinent from cocaine to be reunified with their children. Either the mother remained abstinent from cocaine or the child was raised by a caregiver who reported abstinence from cocaine. Admitting postnatal cocaine use to our research team should not have been more threatening than admission of prenatal cocaine use. A National Institute on Drug Abuse certificate of confidentiality ensured confidentiality of the participant's drug use. The certificate superseded any mandatory reporting of illegal substance use and was explained in full to the mothers.

adjusted for covariates. Step 2 controlled for covariates using hierarchical linear regressions performed with the significant substances from step 1. From the candidate variables listed in Table 2, SES, marital status, abuse (physical or sexual [yes or no]), and prenatal medical care (yes or no) were selected as covariates, having met the following criteria: (1) differed significantly between exposure groups, (2) were associated with the overall sleep index at $P < .2$, and (3) were not highly cor-

related with other covariates ($r > .7$). Additionally, study site and postnatal cigarette smoke exposure were included as covariates, having been selected a priori. Pearson correlations were used to investigate the association between early and later sleep problems.

RESULTS

When comparing participants in the 12-year follow-up (those included in this study) with those not in the 12-year follow-up (Table 1), children in the 12-year follow-up were more likely to be a racial minority (African American, Hispanic, or other) and had more caretaker changes over time. Mothers or caregivers in this study were less likely to use marijuana prenatally and more likely to use cocaine, marijuana, and/or alcohol postnatally. There were no significant differences on newborn medical characteristics (prematurity, birth weight, length at birth, head circumference at birth, and sex). There were no significant differences in level (amount) of postnatal substance use (cocaine, opiates, marijuana, alcohol, or nicotine) among the 2 attrition groups.

There were also differences between the 2 exposure groups (Table 2). Compared with mothers who did not use cocaine during pregnancy, mothers in the exposed group were more likely to be of a low SES, more likely to be older, less likely to be married, less likely to have at least a high school education, and less likely to have had any prenatal care. Furthermore, mothers and caregivers in the exposed group were more likely to use substances (cocaine, opiates, marijuana, alcohol, or nicotine) both prenatally and postnatally. Children in the exposed group were more likely to have been physically or sexually abused and had more caretaker changes over time than children in the comparison group.

In the unadjusted analysis among the 5 substances, prenatal nicotine exposure was the only significant predictor of sleep problems ($\beta = .168$, $P < .001$). Importantly, multicollinearity was not a problem, as evidenced by tolerance remaining above 0.7 and the variance inflation factor remaining between 1 and 2. None of the prenatal exposure variables were highly correlated with each other (all $r < 0.4$). When adjusted for covariates (SES, marital status, physical or sexual abuse, prenatal care, clinic site, and postnatal cigarette smoke exposure), the effect of prenatal nicotine exposure predicting more sleep problems on the sleep problems index was still statistically significantly (unstandardized coefficient [B] = 0.074, $R^2 = 0.067$, R^2 change = 0.008, $P = .01$). Higher levels of prenatal exposure to nicotine predicted more sleep problems. Specifically, after controlling for covariates, each additional cigarette smoked per day during a pregnancy was associated with a 0.074 increase in the child's index score of sleep problems. Increases in this score indicate more difficulty falling and staying asleep from 1 month to 12 years.

In a separately tested model, postnatal cigarette smoke exposure was no longer significant when entered into a regression model after prenatal nicotine exposure and covariates; that is, it did not explain sleep problems above and beyond prenatal nicotine exposure and the other covariates.

The main finding from this study was that in a large sample of children with prenatal exposure to cocaine, opiates, marijuana, alcohol, and/or nicotine there is a unique effect on sleep problems between 1 month and 12 years for nicotine in both unadjusted and adjusted analyses. This was a dose-response effect for prenatal nicotine exposure with adjustment for covariates. Higher levels of prenatal nicotine exposure predicted more sleep problems, specifically difficulty falling and staying asleep from 1 month to 12 years. This effect was observed controlling for postnatal maternal/caregiver use of cigarettes.

The finding that prenatal nicotine exposure predicted sleep problems in children is consistent with studies of smokers showing sleep disruption attributable to nicotine^{27,28} and supports a recent study that found that prenatal maternal smoking resulted in less sleep and more fragmented sleep among newborns.¹² Preclinical studies of prenatal nicotine exposure have shown abnormal cardiorespiratory response during sleep,²⁹ altered sleep-state maturation,³⁰ and decreased rapid eye movement (REM) sleep.³¹ A recent study documented significantly less sleep in infants after drinking breast milk that contained nicotine than after drinking nicotine-free breast milk (53 vs 85 minutes).³²

There are several ways through which nicotine can affect sleep. Nicotine has been shown to excite pedunculo-pontine nucleus cells, which are involved in sleep-wake mechanisms³¹; to suppress pontogeniculooccipital spike activity, which influences the initiation and maintenance of REM sleep³³; and to inhibit sleep-promoting neurons in the ventrolateral preoptic area.³⁴

When investigating prenatal exposure to cocaine, opiates, marijuana, alcohol, and nicotine, we found dose-response effects of prenatal nicotine exposure only on sleep problems in a large sample of children aged up to 12 years. Caution should be taken when concluding that prenatal nicotine exposure is more damaging to sleep than other prenatal drug exposure, given the current study's specific limitations (namely the subjectivity of the sleep problems index) and the study's operationalization of "sleep problems" (ie, difficulty falling and staying asleep). Whether or not there are associations between prenatal drug exposure and other types of sleep problems (eg, sleep-disordered breathing) is unknown and was not investigated in this study. Our study is also limited by the use of maternal self-report for our measures both of sleep problems in the children and of caregiver postnatal substance use. Validated parent-reported sleep problems questionnaires would have been preferable to our index composed of items from the Child Behavior Checklist, the Child Health and Illness Profile, Pediatric Symptom Checklist, and general health questionnaire. To our knowledge, this type of validated instrument does not yet exist to measure sleep during the first 12 years of life or pediatric difficulties falling and staying asleep specifically, and therefore this limitation points to an important need in the field. Furthermore, it would be useful to conduct formal sleep studies on these children and validate environmental tobacco exposure and postnatal substance use with toxicological assays.

Table 2. Sample Characteristics by Original Maternal Lifestyle Study Exposure Groups

Characteristic	No. (%)		P Value
	Exposure ^a (n = 374)	Comparison ^a (n = 434)	
Maternal Characteristic			
Minority race	319 (86.9)	370 (86)	.72
Low SES, Hollingshead score of 5 at 1-month visit	100 (28.1)	93 (21.6)	.04
Below poverty line at 1-month visit	232 (68.2)	252 (61.5)	.05
Married	36 (9.7)	108 (24.9)	<.001
Education <high school	197 (52.8)	299 (68.9)	<.001
No prenatal care	79 (21.1)	10 (2.3)	<.001
Age, mean (SD), y	30.42 (4.98)	26.96 (5.93)	<.001
Prenatal drug use			
Cocaine	346 (92.5)	0	<.001
Opiates	58 (15.5)	0	<.001
Marijuana	138 (36.9)	35 (8.1)	<.001
Alcohol	270 (72.2)	217 (50.0)	<.001
Nicotine	300 (80.2)	122 (28.1)	<.001
Postnatal drug use			
Cocaine ^b	95 (25.4)	7 (1.6)	<.001
Opiates	29 (7.8)	3 (0.7)	<.001
Marijuana	130 (34.8)	85 (19.6)	<.001
Alcohol	326 (87.2)	341 (78.6)	<.001
Nicotine	314 (84.0)	205 (47.2)	<.001
Domestic violence anytime during child age range of 5-12 y	56 (15.2)	52 (12)	.19
Child abuse anytime during child age range of 1 mo-12 y	118 (31.6)	86 (19.8)	<.001
No. of caretaker changes during child age range of 4 mo-12 y, mean (SD)	1.64 (1.82)	0.39 (1.00)	<.001
Newborn Medical Characteristic			
Premature	159 (42.6)	180 (41.6)	.76
Birth weight, mean (SD), g	2568.24 (776.85)	2656.05 (878.74)	.13
Length, mean (SD), cm	46.43 (4.81)	46.82 (5.3)	.28
Head circumference, mean (SD), cm	31.97 (2.81)	32.14 (3.23)	.43
Male sex	173 (46.3)	208 (47.9)	.64
Sleep problems index score for child age range of 1 mo-12 y, mean (SD)	6.67 (5.65)	6.5 (5.78)	.67

Abbreviation: SES, socioeconomic status.

^aParticipants were recruited to be in 1 of 2 groups: the group with exposure to cocaine or opiates, or the comparison group, which was matched on ethnicity, sex, and gestational age.

^bThe decrease in cocaine use postnatally may be attributable to the fact that mothers using cocaine during pregnancy in some cohorts of the Maternal Lifestyle Study (eg, Providence, Rhode Island) were required by state law to remain abstinent from cocaine to be reunified with their children. Either the mother remained abstinent from cocaine or the child was raised by a caregiver who reported abstinence from cocaine. Admitting postnatal cocaine use to our research team should not have been more threatening than admission of prenatal cocaine use. A National Institute on Drug Abuse certificate of confidentiality ensured confidentiality of the participant's drug use. The certificate superseded any mandatory reporting of illegal substance use and was explained in full to the mothers.

This is the first longitudinal study of the effects of prenatal drug exposure on sleep problems over time with adjustment for multiple covariates (SES, marital status,

physical or sexual abuse, prenatal care, clinic site, and postnatal cigarette smoke exposure) and with adequate power to detect a dose-response association. Findings suggest a link between prenatal nicotine exposure and persisting sleep problems in children for the first 12 years of life. Understanding the persisting nature of sleep problems in children with prenatal adversity, including substance exposure, could be a critical component to improving developmental outcomes in this population. Sleep problems may mediate some of the other developmental effects of prenatal exposure to nicotine. Assessing the risk for sleep problems in children with prenatal exposure to nicotine and other drugs is the first step toward creating efficient, proactive services that will foster optimal sleep and corresponding daytime functioning.

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REFERENCES

- Anders TF, Keener MA, Kraemer H. Sleep-wake state organization, neonatal assessment and development in premature infants during the first year of life. *II. Sleep.* 1985;8(3):193-206.
- Thoman EB, Denenberg VH, Sievel J, Zeidner LP, Becker P. State organization in neonates: developmental inconsistency indicates risk for organizational dysfunction. *Neuropediatrics.* 1981;12(1):45-54.
- Carskadon MA. The second decade. In: Guilleminault C, ed. *Disorders of Sleeping and Waking: Indications and Techniques.* Menlo Park, CA: Addison Wesley; 1982:99-125.
- Carskadon MA, Harvey K, Duke P, Anders TF, Litt IF, Dement WC. Pubertal changes in daytime sleepiness. *Sleep.* 1980;2(4):453-460.
- Carskadon MA, Acebo C, Jenni OG. Regulation of adolescent sleep: implications for behavior. *Ann N Y Acad Sci.* 2004;1021:276-291.
- Carskadon MA. Patterns of sleep and sleepiness in adolescents. *Pediatrician.* 1990;17(1):5-12.
- DiPietro JA, Suess PE, Wheeler JS, Smouse PH, Newlin DB. Reactivity and regulation in cocaine-exposed neonates. *Infant Behav Dev.* 1995;18(4):407-414.
- Gingras JL, Feibel JB, Dalley LB, Muelenaer A, Knight CG. Maternal polydrug use including cocaine and postnatal infant sleep architecture: preliminary observations and implications for respiratory control and behavior. *Early Hum Dev.* 1995;43(3):197-204.
- Regalado MG, Schechtman VL, Del Angel AP, Bean XD. Sleep disorganization in cocaine-exposed neonates. *Infant Behav Dev.* 1995;18(3):319-327.
- Regalado MG, Schechtman VL, Del Angel AP, Bean XD. Cardiac and respiratory patterns during sleep in cocaine-exposed neonates. *Early Hum Dev.* 1996;44(3):187-200.
- Troese M, Fukumizu M, Sallinen BJ, et al. Sleep fragmentation and evidence for sleep debt in alcohol-exposed infants. *Early Hum Dev.* 2008;84(9):577-585.
- Stéphan-Blanchard E, Telliez F, Leke A, et al. The influence of in utero exposure to smoking on sleep patterns in preterm neonates. *Sleep.* 2008;31(12):1683-1689.
- Hutchings DE. Methadone and heroin during pregnancy: a review of behavioral effects in human and animal offspring. *Neurobehav Toxicol Teratol.* 1982;4(4):429-434.
- Chiriboga CA. Fetal effects. *Neurol Clin.* 1993;11(3):707-728.
- Pichini S, Garcia-Algar O. In utero exposure to smoking and newborn neurobehavior: how to assess neonatal withdrawal syndrome? *Ther Drug Monit.* 2006;28(3):288-290.
- Dahl RE, Scher MS, Williamson DE, Robles N, Day N. A longitudinal study of prenatal marijuana use: effects on sleep and arousal at age 3 years. *Arch Pediatr Adolesc Med.* 1995;149(2):145-150.
- Stone KC, High PC, Miller-Loncar CL, LaGasse LL, Lester BM. Longitudinal study of maternal report of sleep problems in children with prenatal exposure to cocaine and other drugs. *Behav Sleep Med.* 2009;7(4):196-207.
- Bada HS, Das A, Bauer CR, et al. Gestational cocaine exposure and intrauterine growth: maternal lifestyle study. *Obstet Gynecol.* 2002;100(5, pt 1):916-924.
- Bauer CR, Langer JC, Shankaran S, et al. Acute neonatal effects of cocaine exposure during pregnancy. *Arch Pediatr Adolesc Med.* 2005;159(9):824-834.
- Lester BM, El Sohly M, Wright LL, et al. The Maternal Lifestyle Study: drug use by meconium toxicology and maternal self-report. *Pediatrics.* 2001;107(2):309-317.
- Lester BM, Tronick EZ, LaGasse L, et al. The Maternal Lifestyle Study: effects of substance exposure during pregnancy on neurodevelopmental outcome in 1-month-old infants. *Pediatrics.* 2002;110(6):1182-1192.
- Alfano CA, Ginsburg G, Kingery J. Sleep-related problems among children and adolescents with anxiety disorders. *J Am Acad Child Adolesc Psychiatry.* 2007;46(2):224-232.
- Storch EA, Murphy TK, Lack CW, Geffken GR, Jacob ML, Goodman WK. Sleep-related problems in pediatric obsessive-compulsive disorder. *J Anxiety Disord.* 2008;22(5):877-885.
- Achenbach TM. *Manual for the Child Behavior Checklist/4-18.* Burlington: University of Vermont; 1991.
- Starfield B, Bergner M, Ensminger M, et al. Adolescent health status measurement: development of the Child Health and Illness Profile. *Pediatrics.* 1993;91(2):430-435.
- Jellinek MS, Murphy JM, Robinson J, Feins A, Lamb S, Fenton T. Pediatric Symptom Checklist: screening school-age children for psychosocial dysfunction. *J Pediatr.* 1988;112(2):201-209.
- Patten CA, Choi WS, Gillin JC, Pierce JP. Depressive symptoms and cigarette smoking predict development and persistence of sleep problems in US adolescents. *Pediatrics.* 2000;106(2):E23.
- Zhang L, Samet J, Caffo B, Punjabi NM. Cigarette smoking and nocturnal sleep architecture. *Am J Epidemiol.* 2006;164(6):529-537.
- Hafström O, Milerad J, Sundell HW. Prenatal nicotine exposure blunts the cardiorespiratory response to hypoxia in lambs. *Am J Respir Crit Care Med.* 2002;166(12, pt 1):1544-1549.
- Frank MG, Srere H, Ledezma C, O'Hara B, Heller HC. Prenatal nicotine alters vigilance states and AchR gene expression in the neonatal rat: implications for SIDS. *Am J Physiol Regul Integr Comp Physiol.* 2001;280(4):R1134-R1140.
- Garcia-Rill E, Buchanan R, McKeon K, Skinner RD, Wallace T. Smoking during pregnancy: postnatal effects on arousal and attentional brain systems. *Neurotoxicology.* 2007;28(5):915-923.
- Mennella JA, Yourshaw LM, Morgan LK. Breastfeeding and smoking: short-term effects on infant feeding and sleep. *Pediatrics.* 2007;120(3):497-502.
- Vazquez J, Guzman-Marín R, Salin-Pascual RJ, Drucker-Colin R. Transdermal nicotine on sleep and PGO spikes. *Brain Res.* 1996;737(1-2):317-320.
- Saint-Mleux B, Eggemann E, Bisetti A, et al. Nicotinic enhancement of the noradrenergic inhibition of sleep-promoting neurons in the ventrolateral preoptic area. *J Neurosci.* 2004;24(1):63-67.