Prenatal Origins of Poor Sleep in Children

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Study Objectives: We examined whether small body size at birth and prenatal tobacco or alcohol exposure predict poor sleep and more sleep disturbances in children.

Design: An epidemiologic cohort study of 289 eight-year-old children born at term.

Measurements and results: Sleep duration and efficiency were measured by actigraphy for 7 consecutive nights (mean = 7.1, SD = 1.2). We used both continuous measures of poor sleep and binary variables of short sleep and low sleep efficiency (≤ 10th percentiles). Parents completed the Sleep Disturbance Scale for Children. Lower birth weight and shorter length at birth were associated with lower sleep efficiency. For every 1-SD decrease in weight and length at birth, the odds for low sleep efficiency increased by 1.7 fold (95% confidence interval [CI]: 1.1 to 2.7) and 2.2 fold (95% CI: 1.3 to 3.7), respectively. For every 1-SD decrease in ponderal index at birth, the risk of parent-reported sleep disorders increased by 1.4 fold (95% CI: 1.0 to 2.0). Moreover, children exposed prenatally to alcohol had a 2.9-fold (95% CI: 1.1 to 7.6) and 3.6-fold (95% CI: 1.3 to 10.0) increased risk for having short sleep and low sleep efficiency, respectively. The associations were not confounded by sex, gestational length, prenatal and perinatal complications, body mass index at 8 years, asthma, allergies, or parental socioeconomic status.

Conclusions: Poor sleep in children may have prenatal origins. Possible mechanisms include alcohol consumption during pregnancy and other conditions associated with small body size at birth.

Keywords: Body size at birth, epidemiological, actigraphy, alcohol, tobacco

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POOR SLEEP AND SLEEP DISTURBANCES ARE COMMON IN CHILDREN. WE OPERATIONALIZE POOR SLEEP AS SHORT SLEEP DURATION AND LOW SLEEP efficiency measured by actigraphy, and sleep disturbances as parent-reported sleep disorders, eg, parasomnias, bedtime resistance, motor activity during sleep, sleep disordered breathing, daytime somnolence, and sleep hyperhydrosis. According to some estimates, 20% to 33% of children are affected by these sleep-related problems. For those with sleep problems, about half have persistent problems.[1-5]

In experimental and epidemiologic studies in adults, poor sleep and sleep disturbances have a wide spectrum of detrimental sequelae, from neuroendocrine and cardiovascular alterations to poor psychological well-being and psychiatric disorders.[6-8] These associations are apparent in not only adults. Studies in children also suggest that poor sleep and sleep disturbances are associated with obesity and related traits[9-11]; internalizing, externalizing,[12-14] and depressive symptoms[15]; attention deficit hyperactivity disorder[14]; and poor neurobehavioral functioning.[16] However, in contrast to the abundant evidence available on the consequences of poor sleep and sleep disturbances, information about the origins of poor sleep and sleep disturbances remain scanty. In addition to genetic factors, environmental influences, such as inconsistent parental care, may induce poor sleep. Environmental influences are not restricted to periods of postnatal development but may have origins in prenatal life.

A suboptimal prenatal environment is known to exert lifelong effects on organ structure and organization of physiologic systems,[17] including circadian rhythms.[18] One marker of a suboptimal prenatal environment is low birth weight. Indeed, evidence from animal models indicates that prenatal stress[19-21] and prenatal malnutrition[22] predict altered circadian rhythms and poor sleep quality in offspring. These findings are supported by emerging epidemiologic evidence in humans. For example, maternal prenatal mood disturbance may predict poor sleep quality in toddlerhood.[23] Intrauterine growth retardation among children born full-term or late preterm is associated with an increased likelihood of poor sleep quality in 4- to 7-year-old children.[24] Our previous studies in young adults showed that very low birth weight (< 1500 gm) increases the risk for children to develop sleep disordered breathing,[25] and shorter gestational length within both prematurely and term-born subjects is associated with delayed sleep onset.[26]

Other environmental factors are also important to consider. Maternal smoking and alcohol consumption during pregnancy are associated with smaller infant body size at birth, [27-30] and infants exposed in utero to alcohol have more sleep problems as neonates[31] and at the ages of 2[32] and 12 months.[31] Prenatal tobacco exposure predicts sleep-related problems in both full-term[31] and prematurely born neonates,[33] as well as in 3-year-olds.[34] Whether these associations are independent of body size at birth and whether they extend to childhood is unknown.

In this study, we examined whether smaller body size at birth predicts poor sleep and a higher risk of having sleep disturbances in 8-year-old children born between 37 and 42 weeks of ges-

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tation. A secondary aim was to investigate the roles of prenatal tobacco and alcohol exposure as predictors of children's sleep characteristics and sleep disturbances, independent of body size at birth.

METHODS

Participants

The children came from an urban cohort comprising 1049 infants born between March and November 1998.[35] Altogether, 912 parents of participants (86.9% of the initial cohort) gave their permission to be included in the follow-up, and, of these, 890 (84.8% of initial cohort) were traced. Since 1 of the initial study objectives was to assess how maternal licorice consumption during pregnancy affects gestational length, body size at birth, and child development, the invited sample was weighted upon maternal licorice consumption during pregnancy. We invited the parents of all 88 children belonging to the group prenatally exposed to high levels of glycyrrhizin in licorice; 64 participated. The other invited parents of children had to live within a 35-mile radius from Helsinki, the capital of Finland, to manage costs related to participant and researcher travel and accommodation. Of the 271 children whose mothers consumed no or low levels of glycyrrhizin in licorice who were invited, 211 participated. Parents of 54 children exposed to moderate levels of glycyrrhizin in licorice were invited, and 46 participated. Nonparticipation was not related to child's sex; weight, length, or head circumference at birth; birth order; mode of delivery; or mother's occupational status, age, body mass index (BMI), alcohol consumption, licorice consumption, or stress during pregnancy (P values > 0.10). Nonparticipation was, however, related to more frequent maternal smoking during pregnancy (P = 0.02). The Ethics Committees of the City of Helsinki Health Department and Helsinki University Hospital of Children and Adolescents approved the study protocol. Each child and her/his parents gave written informed consent.

Of the 321 families participating in the follow-up, 305 took part in the sleep portion of the study. Of these children, 297 (97.3%) provided information on sleep for at least 3 nights. Children with a parent-reported diagnosis of developmental delay (n = 3) or Asperger syndrome (n = 1) were excluded, and an additional 4 children were excluded because they were born before term gestation (< 37 weeks). The analyzed sample, thus, comprised 289 participants.

Sleep Characteristics

Sleep was objectively measured using actigraphs (Actiwatch AW4, Cambridge Neurotechnology Ltd., UK). The devices were worn on the nondominant wrist for an average of 7.1 days (SD = 1.2; range 2 - 14), including nights on weekdays (mean = 5.1, SD = 1.0; range 1-10) and weekends (mean = 2.0, SD = 0.4; range 1-4). We instructed the parents to keep a sleep log on bedtimes and waking times, temporary pauses in actigraph registration (eg, while taking a shower), and significant events that might affect sleep quantity or quality (illness, pain, injury, travel, or other events likely to disturb sleep). The child was instructed to press a button (event marker) in the actigraph at bedtime and waking times. A completed sleep log was obtained from all participants, including both parent-reported sleep log and event markers on bedtimes and waking times reported by the child. The activity data were visually inspected to detect significant discrepancies among the sleep log, event markers, and the activity pattern. If there were several event markers for 1 night, the most recent was used and compared with the sleep log. If the sleep log was not synchronous with the event marker, the event marker was used to define the bedtime. We found high compliance in the sleep-log registrations in relation to the event markers; for 71% of the participants, no discrepancies were found; for 21%, a discrepancy was found for 1 or 2 nights; and, for 8%, a discrepancy was found for 3 or more nights. Nights were excluded from further sleep analysis if (a) the actigraph was not in use, (b) information on bedtimes was missing, (c) the child was asleep according to the data of reported bedtime, (d) information on waking time was missing and the activity pattern was not unequivocally interpretable, or (e) the parent reported a change in normal life due to, for example, illness or travel. There were 257 participants (89%) without excluded nights, and 97.6% had data for more than 5 valid sleep-registration nights available. Data were scored with Actiwatch Activity & Sleep Analysis version 5.42 software with medium sensitivity and a 1-minute epoch duration. The scored sleep data were averaged for each study subject over the valid registration nights and separately for weekday and weekend nights (4 children did not have data on weekends). Sleep duration refers to the actual sleeping time. We used the validated Actiwatch algorithm, [36] which defines "sleep start" as 10 minutes of consecutively recorded immobile data. Sleep efficiency was defined as the actual sleep time divided by the time in bed. Sleep duration and efficiency were analyzed as both continuous and dichotomous variables. We dichotomized sleep duration and efficiency at the 10th percentile of the distribution (short sleep: ≤ 7.7 hours/mean of all nights; ≤ 7.6 hours/mean of weekdays; ≤ 7.5 hours/mean of weekends; low sleep efficiency: ≤ 77.2%/mean of all nights; ≤ 76.4%/mean of weekdays; ≤ 77.2%/mean of weekends).

Sleep Disturbances

The parents filled out a 26-item sleep questionnaire (Sleep Disturbance Scale for Children, SDSC).[37] A total score of sleep disturbance and its 6 subscales (disorders of initiating and maintaining sleep, sleep breathing disorders, disorders of arousal/nightmares, sleep-wake transition disorders, disorders of excessive somnolence, sleep hyperhydrosis) was also calculated. Following Bruni et al,[37] we dichotomized the total score for analyses at the 75th percentile (1 = sleep disturbance ≥ 75th percentile, 0 = others) because the distribution was highly skewed.

Prenatal and Birth Variables

We obtained mode of delivery, weight (gm), length (cm), head circumference at birth (cm), date of birth, and gestational age (days) confirmed by ultrasound before 20 weeks of gestation from birth records. Ponderal index at birth was calculated

(kg/m^3). Birth weight, birth length, and head circumference were transformed into z scores (SD scores) for gestational age and sex based on Finnish standards.[38] The birth variables were normally distributed, and 2 of the participants were born small for gestational age (birth weight < -2 SD) .

While still at the maternity ward after delivery, the mothers reported their use during pregnancy of alcohol (number of 12-gm pure alcohol beverages/week) and tobacco (0 = no, 1 = 1 to 10 cigarettes per day, 2 = 11 to 20 cigarettes per day, > 20 cigarettes per day). Because only 12 mothers smoked more than 10 cigarettes per day, and only 14 reported consuming more than 1 standard dose of alcohol per week, both variables were analyzed as binary (0 = no; 1 = yes, daily smoking or more than 12 gm of alcohol per week).

Background Variables

Pregnancy complications (gestational diabetes and hypertension, preeclampsia) were derived from hospital records. The mothers reported their prenatal licorice consumption from lists prepared by the National Food Administration in 1993 and updated by the manufacturers (mg/wk) while still at the maternity ward after delivery. The child's BMI (weight in kilograms divided by length in meters squared) was measured in conjunction with the clinical visit. The parents also completed a questionnaire that included questions on the medical history of the child, parent education, and mothers' current alcohol use (AUDIT-C)[39] and smoking habits (nonsmoker, occasionally smoke, daily). Socioeconomic status of the family was classified according to the highest self-reported level of education of either parent in 2006.

Statistical Analyses

We used regression models to examine both linear and nonlinear associations among body size at birth, prenatal tobacco and alcohol exposure, and sleep duration and efficiency (all nights, weekdays, weekends) as continuous outcomes. Next, we applied binary logistic regression models to examine the associations between body size at birth and prenatal alcohol and tobacco exposure and (1) dichotomized actigraphy-based sleep parameters (short sleep, low sleep efficiency), and (2) clinically significant sleep disturbances based on the total sleep disturbance score and subscales above the 75th percentile cut-off. In addition to sex and family socioeconomic status, all associations were adjusted for common prenatal and perinatal conditions that may be associated with small birth size and shorter length of gestation, namely mode of delivery, gestational diabetes, gestational hypertension, and preeclampsia. In addition, all associations were adjusted for maternal licorice consumption, which, in this cohort, has been associated with shorter length of gestation.[35] We also adjusted for child factors known to be associated with poor sleep, i.e., child's current BMI,[11] atopic eczema or other allergies,[40] and asthma.[41] Finally, we examined whether body size at birth and prenatal alcohol and tobacco exposure exerted independent effects on sleep characteristics and sleep disturbances and, for prenatal alcohol and tobacco exposure, whether effects were also independent of current maternal alcohol use and smoking.

RESULTS

Initial Analyses

The correlation coefficient between average sleep duration and sleep efficiency was 0.81 ($P < 0.001$). The correlation coefficient between mean sleep duration on weekdays and weekends was 0.65, with the corresponding coefficient for sleep efficiency being 0.86 (P for both < 0.001). Of the 27 children who belonged to the category of short sleepers on weekdays, only 10 (38.5%) were short sleepers on weekends ($\chi^2 = 23.5$, $P < 0.001$). The corresponding proportion for sleep efficiency was 61.5% ($P < 0.001$). Of the 26 children with low sleep efficiency, 12 (46.2%) belonged to the group of short sleepers.

Characteristics of the participants according to the sleep-efficiency category ($\leq 10^{th}$ percentile vs $> 10^{th}$ percentile based on all nights) are presented in Table 1. Participants with low sleep efficiency were exposed to higher amounts of alcohol during gestation, were born smaller and shorter, and had shorter sleep duration in relation to children with better sleep efficiency. We also tested whether any of these variables were differentially distributed across categories of sleep duration ($\leq 10^{th}$ percentile vs $> 10^{th}$ percentile based on all nights) and found that children with short sleep duration were more likely to have been born via Caesarean section than were children sleeping longer (23.1% vs 8.4%, respectively, $P = 0.03$ in χ^2 test).

Prenatal alcohol exposure was associated with lower ponderal index at birth (mean difference [MD] = -0.4 SD, 95% confidence interval [CI] -0.7 to -0.1, P = 0.03), and prenatal tobacco exposure was associated with shorter length at birth (MD = -0.4 SD, 95% CI -0.8 to -0.0, P = 0.03).

Relations Between Body Size at Birth, Prenatal Alcohol and Tobacco Exposure, and Continuous Sleep Parameters

For every 1-SD decrease in birth weight, sleep efficiency decreased by -0.1 SD (95% CIs -0.3 to -0.0, P = 0.04, R^2's = 0.01) across all nights and on weekend nights. For every 1-SD decrease in length at birth, sleep efficiency decreased by 0.1 SD across all nights and on weekdays (95% CIs -0.3 to -0.0, P = 0.04; R^2's = 0.01). Prenatal alcohol exposure was associated with a 0.3-SD decrease in sleep efficiency over all nights (95% CI -0.5 to -0.0, P = 0.01, $R^2 = 0.02$) and on weekdays (95% CI -0.5 to -0.1, P = 0.01, $R^2 = 0.02$). Head circumference at birth (Bs ranging from 0.0 to 0.1; 95% CIs from -0.2 to 0.2, P values > 0.14), ponderal index at birth (Bs ranging from 0.0 to 0.1; 95% CIs from -0.1 to 0.2, P values > 0.13), and prenatal tobacco exposure (Bs ranging from -0.3 to 0.3; 95% CIs from -0.6 to 0.8, P values > 0.24) were not significantly associated with the continuous sleep variables. Neither were there significant nonlinear associations between the body size at birth and sleep characteristics.

Relations Between Body Size at Birth, Prenatal Alcohol and Tobacco Exposure, and Dichotomized Sleep Parameters

Table 2 shows that, for every 1-SD decrease in weight, the odds for low sleep efficiency increased by 1.7-fold (P values for all nights and weekday nights = 0.03). For every 1-SD decrease

Table 1—Characteristics of the Participants and Sleep Variables According to Groups Based on Sleep Efficiency

	Sleep efficiency on all nights		P value
	> 10th percentile	≤ 10th percentile	
Maternal alcohol consumption during pregnancy, 20-gm doses/wk			
0	222 (84.4)	16 (61.5)	0.03
> 0 and ≤ 1	31 (11.8)	8 (30.8)	
> 1 and ≤ 2	7 (2.7)	1 (3.8)	
> 2	3 (1.1)	1 (3.8)	
Mean	0.2 ± 0.5	0.5 ± 0.8	0.01
Maternal smoking during pregnancy, cigarettes/day			
0	235 (89.4)	25 (96.2)	0.47
1-10	16 (6.1)	1 (7.2)	
11-20	12 (4.6)	0	
> 20	0	0	
Gestational diabetes	5 (1.9)	1 (3.8)	0.44
Gestational hypertension	8 (3.1)	1 (3.8)	0.58
Preeclampsia	1 (0.4)	0	0.91
Neonatal characteristics			
Weight, gm[a]	3596.1 ± 448.8	3391.0 ± 460.4	0.03
Length at birth, cm[a]	50.5 ± 1.8	49.4 ± 1.9	0.006
Head circumference, cm[a]	35.7 ± 1.4	35.4 ± 1.1	0.23
Ponderal index, kg/m^3	27.9 ± 2.2	27.9 ± 1.8	0.92
Delivered via Cesarean section	23 (8.7)	5 (19.2)	0.09
Characteristics in child			
Age, y	8.1 ± 0.3	8.1 ± 0.3	0.32
Weight, kg	28.8 ± 5.3	26.8 ± 4.5	0.07
Height, cm	131.2 ± 5.5	129.4 ± 5.7	0.11
BMI, kg/m^2	16.6 ± 2.2	15.9 ± 1.9	0.12
Parent-report of child's medical diagnosis by a physician			
Asthma	14 (5.3)	3 (11.5)	0.19
Allergic rhinitis	23 (8.7)	1 (3.8)	0.34
Atopic eczema	29 (11.0)	6 (23.1)	0.08
Other allergic disorder	42 (16.0)	5 (19.2)	0.42
Parent characteristic			
Maternal age, y	38.7 (4.5)	39.8 (3.2)	0.23
Highest education in the family			
High-school diploma	39 (14.8)	1 (3.8)	0.32
Vocational education	71 (27.0)	6 (23.1)	
Bachelor's degree	42 (16.0)	4 (15.4)	
Master's degree	111 (42.2)	15 (57.7)	
Maternal current alcohol consumption, 12-gm doses/wk	0.8 ± 0.8	0.7 ± 0.6	0.43
Maternal current smoking			
No	199 (75.7)	23 (88.5)	0.12
Occasionally	26 (9.9)	3 (11.5)	
Daily	38 (14.4)	0	
Child's sleep measured by actigraphy			
Sleep duration, h			
Weekdays	8.5 ± 0.6	7.6 ± 0.5	< 0.001
Weekends	8.5 ± 0.6	7.6 ± 0.5	< 0.001
All nights	8.5 ± 0.7	7.7 ± 0.5	< 0.001
Sleep efficiency, %			
Weekdays	85.1 ± 5.1	74.0 ± 4.5	< 0.001
Weekends	85.4 ± 5.3	74.1 ± 4.5	< 0.001
All nights	85.2 ± 5.0	74.1 ± 3.4	< 0.001

Data are presented as mean ± SD or number (%). BMI refers to body mass index.
[a]Ranges for birth weight, height, and head circumference are 2505-4995 gm, 45-56 cm, and 32-40 cm, respectively.

in length at birth, the odds for being in the low-sleep-efficiency category increased by 2.2 fold for all nights and to 2.0 fold for weekdays (P values < 0.004). Children prenatally exposed to alcohol had a 2.9-fold (P = 0.03) risk for having short sleep duration on weekdays and a 3.6-fold (P = 0.01) risk for having low sleep efficiency on all nights.

Body size at birth and parent-reported sleep disturbance (dichotomous total sleep disturbance score) were not associated,

Table 2—Logistic Regressions between Prenatal Alcohol and Tobacco Exposures, Body Size at Birth, and Sleep Characteristics

	Short sleep, 10th percentile			Low sleep efficiency, 10th percentile		
	Allnights	weekdays	weekends	All nights	weekdays	weekends
Birth weight SD[a]	1.2 (0.7 to 1.9)	1.4 (0.9 to 2.2)	1.0 (0.7 to 1.6)	1.7 (1.1 to 2.7)	1.7 (1.1 to 2.6)	1.1 (0.7 to 1.8)
Length at birth SD[a]	1.1 (0.7 to 1.8)	1.4 (0.9 to 2.2)	1.1 (0.7 to 1.6)	2.2 (1.3 to 3.7)	2.0 (1.3 to 3.2)	1.4 (0.9 to 2.2)
Head circumference at birth SD[a]	1.0 (0.7 to 1.3)	1.2 (0.8 to 1.8)	1.4 (0.9 to 2.1)	1.4 (0.9 to 2.1)	1.3 (0.8 to 2.0)	1.0 (0.7 to 1.5)
Ponderal index at birth SD[a]	1.1 (0.7 to 1.7)	1.0 (0.6 to 1.6)	1.0 (0.6 to 1.4)	0.9 (0.6 to 1.4)	0.9 (0.6 to 1.4)	0.8 (0.5 to 1.5)
Prenatal alcohol exposure[b]	2.5 (1.0 to 6.4)	2.9 (1.1 to 7.6)	1.9 (0.7 to 5.3)	3.6 (1.3 to 10.0)	2.1 (0.7 to 5.7)	2.5 (0.9 to 6.7)
Prenatal tobacco exposure[3c]	1.5 (0.9 to 10.5)	1.1 (0.2 to 5.7)	2.4 (0.5 to 11.5)	1.2 (0.1 to 13.0)	2.0 (0.3 to 13.8)	1.7 (0.3 to 11.7)

Data are shown as odds ratios (95% confidence intervals).
[a]Associations adjusted for sex, gestational length, maternal licorice consumption during pregnancy, gestational diabetes and hypertension, preeclampsia, prenatal tobacco and alcohol exposure, mode of delivery, current body mass index (BMI), parent education attainment, and chronic somatic illnesses (atopic eczema, asthma, allergy).
[b]Associations adjusted for sex, gestational length, maternal licorice consumption during pregnancy, gestational diabetes and hypertension, preeclampsia, prenatal tobacco exposure, mode of delivery, current BMI, parent education attainment, chronic somatic illnesses (atopic eczema, asthma, allergy), birth weight SD, length at birth SD, and current maternal alcohol consumption. B refers to change in sleep parameters as a function of a prenatal alcohol exposure (yes/no).
[c]Associations adjusted for sex, gestational length, maternal licorice during pregnancy, gestational diabetes and hypertension, preeclampsia, prenatal alcohol exposure, mode of delivery, current BMI, parental educational attainment, chronic somatic illnesses (atopic eczema, asthma, allergy), birth weight SD, length at birth SD, and current maternal smoking. B refers to change in sleep parameters as a function of a prenatal tobacco exposure (yes/no).

except that, for every 1-SD decrease in ponderal index at birth, the odds for being in the category of clinically significant sleep disturbance increased by 1.4 fold (95% CI 1.0 to 2.0, P = 0.02). We then analyzed the subscales of the SDSC and found that, for every 1-SD decrease in ponderal index at birth, the odds of having disorders of initiating and maintaining sleep increased by 1.4 fold (95% CI, 1.1 to 1.8, P = 0.02) and disorders of arousal/nightmares increased by 1.3 fold (95% CI, 1.0 to 1.6, P = 0.07).

DISCUSSION

Smaller body size at birth was associated with poor sleep and with a higher risk for clinically significant sleep disturbances among children born at term. More specifically, lower weight and shorter length at birth were associated with lower sleep efficiency, and a lower ponderal index was associated with the presence of sleep disturbances. In addition, prenatal alcohol exposure significantly increased the odds for having a shorter sleep duration and lower sleep efficiency, independent of body size at birth and current maternal alcohol use. Contrary to our hypotheses, prenatal tobacco exposure did not have any effects on children's sleep characteristics or sleep disturbances.

Our observations are in agreement with evidence from animal models showing that prenatal adversity is associated with poor sleep quality in offspring[19-21] and with evidence from human cohorts revealing associations of prematurity,[25, 26] intrauterine growth retardation,[24] and prenatal alcohol exposure[32] with poor sleep quality in children and young adults. Our results add to the literature by demonstrating that, among children born healthy and at full-term, a linear relationship exists between smaller body size at birth and poor sleep quality 8 years from birth. Although the linear relationships were only moderate—the shared variance ranging from 1% to 2%—the effect sizes in the logistic regressions were considerable, 1-SD decrease in size at birth or prenatal alcohol exposure associating with 1.7- to 3.6-fold risks for poor sleep.

Small body size at birth is thought to function as a crude marker of disturbances in the fetal environment, possible reasons of which include malnutrition and programming by glucocorticoids.[42, 43] The developmental-origins hypothesis has gained extensive support from findings showing associations of low birth weight, shorter length at birth, and thinness at birth with alterations in the hypothalamic-pituitary-adrenocortical axis and sympathetic nervous system activity later in life, as well as with risk for cardiovascular disease, type 2 diabetes, and psychiatric disorders and their subclinical symptoms.[44-47] We suggest that altered function of the hypothalamic-pituitary-adrenocortical axis, which is associated with both smaller body size at birth[48] and prenatal alcohol exposure[49, 50] and participates in regulation of the sleep infrastructure,[51] may function as 1 potential mechanism underlying these associations. Thus, the question arises of whether impaired sleep quality and morbidity share common fetal origins.

This study has some limitations. First, sleep is regulated and affected by a multitude of environmental factors that could not be measured. We are therefore only able to speculate about possible mechanisms underlying our findings. Second, we do not have a ready explanation of why the different birth measures failed to yield an entirely consistent picture with regard to objectively measured and parent-rated sleep variables. Some of the results were specific to measurements for either weekday or weekend nights, although the associations that did not reach statistical significance were in the expected direction. A prior validation study concluded that reliable measurement of sleep efficiency requires at least 5 nights, and 7 nights may be needed for reliable sleep-duration measurement.[55] We obtained more than 7 successful registration nights for the entire measurement period, more than 5 nights for weekdays, and an average of 2 nights for weekends. The reliability of results for weekend nights may be thus lower than other results based either on weekday nights or on the entire measurement period. Another important sleep-registration issue concerns the sensitivity of

activity chosen for the sleep analysis. A recent study contrasted different sensitivity settings of the sleep analysis program used in this study against polysomnography and found the highest agreement for low- and auto-sensitivity settings.[56] Medium sensitivity was shown to underestimate sleep duration relative to low- or auto-sensitivity settings in children. However, medium- and high-sensitivity were the most accurate in detecting wakefulness, and all sensitivity settings were highly valid compared with polysomnography, with agreement rates varying from 85% to 89% for sleep time.[56] In addition, although polysomnography is likely to be more accurate in measuring total sleep time in young children,[57] actigraphy has the benefit of being an ecologically valid sleep-assessment option for studying sleep patterns over many consecutive nights. [58, 59]

The third limitation is related to the assessment of prenatal alcohol exposure retrospectively in the maternity ward, causing potential underreporting. However, mean consumption in our study was similar to a recent epidemiologic study among pregnant women.[60] It may also be more likely that mothers underestimate rather than overestimate their alcohol consumption during pregnancy.[60] The effects of body size at birth and prenatal alcohol and tobacco exposures were adjusted for the effects of each other, thus being examined as independent phenomena. However, the mechanisms suggested are likely to also concern prenatal tobacco exposure,[61] which was not associated with any of the sleep measures, because very few mothers smoked during pregnancy, and none reported smoking more than a pack a day. Thus, mechanisms are speculative. Finally, because there was no objective measurement of neurodevelopmental problems, children with mild neurodevelopmental problems may have remained in the cohort.

In summary, we found significant associations between smaller body size at birth and poor sleep and increased risk for sleep disturbances. In addition, prenatal alcohol exposure increased the risk for poor sleep. Ours is among the few studies in children that have used objective measures of sleep, decreasing the likelihood of response bias. Even low levels of prenatal exposure to alcohol and normal variation in body size at birth of full-term infants are important to sleep during childhood.

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DISCLOSURE STATEMENT

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