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Increased Behavioral Morbidity in School-Aged Children With Sleep-Disordered Breathing

Carol L. Rosen, MD; Amy Storfer-Isser, MS; H. Gerry Taylor, PhD; H. Lester Kirchner, PhD; Judith L. Emancipator, MA; and Susan Redline, MD, MPH

ABSTRACT. *Objective.* **To assess whether sleep-disordered breathing (SDB), ranging from primary snoring to obstructive sleep apnea (OSA), is associated with increased behavioral morbidity.**

Methods. **A cross-sectional study was conducted of school-aged children in an urban, community-based cohort, stratified for term or preterm (<37 weeks' gestation) birth status. A total of 829 children, 8 to 11 years old (50% female, 46% black, 46% former preterm birth) were recruited from a cohort study. All children had unattended in-home overnight cardiorespiratory recordings of airflow, respiratory effort, oximetry, and heart rate for measurement of the apnea hypopnea index (number of obstructive apneas and hypopneas per hour). SDB was defined by either parent-reported habitual snoring or objectively measured OSA. Functional outcomes were assessed with 2 well-validated parent ratings of behavior problems: the Child Behavioral Checklist and the Conners Parent Rating Scale–Revised:Long.**

Results. **Forty (5%) children were classified as having OSA (median apnea hypopnea index: 7.1 per hour; interquartile range: 3.1–10.5), 122 (15%) had primary snoring without OSA, and the remaining 667 (80%) had neither snoring nor OSA. Children with SDB had significantly higher odds of elevated problem scores in the following domains: externalizing, hyperactive, emotional lability, oppositional, aggressive, internalizing, somatic complaints, and social problems.**

Conclusions. **Children with relatively mild SDB, ranging from primary snoring to OSA, have a higher prevalence of problem behaviors, with the strongest, most consistent associations for externalizing, hyperactive-type behaviors.** *Pediatrics* **2004;114:1640–1648;** ***sleep-disordered breathing, primary snoring, child behavior disorders, epidemiology.***

ABBREVIATIONS. SDB, sleep-disordered breathing; OSA, obstructive sleep apnea; CBCL, Child Behavior Checklist; CPRS-R:L, Conners Parent Rating Scale-Revised:Long; BMI, body mass index; OR, odds ratio; CI, confidence interval.

From the Department of Pediatrics, Rainbow Babies and Children's Hospital, University Hospitals of Cleveland, Case Western Reserve University School of Medicine, Cleveland, Ohio.

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Reprint requests to (C.L.R.) Department of Pediatrics, Rainbow Babies and Children's Hospital, 11100 Euclid Ave, RB&C 790 Mail Stop 6003, Cleveland, OH 44106-6003. E-mail: carol.rosen@case.edu

There is increasing evidence that childhood sleep-disordered breathing (SDB) is associated with behavioral problems, including hyperactivity, inattention, and aggression.[1–15] Improvements in behavior and learning after treatment for SDB suggest that these deficits may be partially reversible.[2,4,6,9,16–18] Unfortunately, many of the previous studies supporting this relationship are subject to methodologic criticisms, including (1) failure to account for the children's background characteristics; (2) recruitment from clinical populations that may oversample children with behavioral problems[1,2,4,8–10,13,16,18,19]; (3) lack of objective measures of obstructive sleep apnea (OSA) in all patients[3,5–7,10–12,14,16,20]; and (4) use of nonvalidated measures of behavior outcomes.[2,4,6,16,20] In view of these limitations, past associations of SDB and behavior problems are of uncertain significance.

In this analysis, a unique community-based cohort of school-aged children was studied to assess the behavioral outcomes of SDB using both objective measures of OSA and parent reports of snoring. Our primary interest was to assess the association of SDB and increased behavioral morbidities, controlling for confounding. We hypothesized that SDB in children would be associated with increased behavioral morbidities, specifically in the domains of inattention, hyperactivity, and other externalizing ("acting out") type behaviors. Some of the behavioral data in this study have been previously published in abstract form.[18]

METHODS

Study Sample

The Cleveland Children's Sleep and Health Study is a nonclinical, unreferred, urban, community-based cohort of 907 children who were studied at 8 to 11 years of age. This cohort was originally assembled as a stratified random sample of term and preterm (<37 weeks' gestational age) children who were born between 1988 and 1993. This unique cohort was specifically assembled to overrepresent black and former preterm children to have internally valid and stable estimates of the relationship of these factors to SDB and other health outcomes. Methods for cohort assembly and recruitment have been previously reported.[21] A total of 73 children were excluded from analysis because of incomplete data: 48 with technical failures of their home overnight cardiorespiratory study (behavioral scales and snoring data complete), 9 with missing parent-reported behavior scales and snoring data (all non-OSA children based on respiratory data), 8 with missing parent-reported behavioral scales (complete respiratory and snoring data), 3 with missing snoring data (non-OSA based on respiratory data, behavioral data were complete), and 5 with missing data for all 3 assessments (behavior scales, snoring, and respiratory). An additional 5 children were excluded, 1 because of

severe illness, 2 because of congenital conditions, and 2 children who did not meet criteria for term or preterm birth. There were no significant differences in the demographic and subject characteristics of the 829 children in the final analytic sample compared with the 78 excluded children except for an age difference of ~2 months considered to be clinically insignificant. Institutional Review Boards at participating hospitals approved the protocol. The child's legal guardian provided informed consent, and the child gave assent.

Measures

Demographic and medical data were assessed with the Child Sleep Questionnaire, a pediatric modification of a validated questionnaire.[22] For analytic purposes, race/ethnicity was dichotomized as black or nonblack on the basis of previous studies showing that black race/ethnicity was a risk factor for SDB.[21,23,24] Asthma was defined as a parent report of doctor-diagnosed asthma plus either wheezing symptoms or asthma medication use. Parents completed 2 well-validated behavioral rating instruments: the Child Behavior Checklist (CBCL)[25] and the Conners Parent Rating Scale-Revised:Long version (CPRS-R:L).[26] Height and weight were measured directly.

SDB

Details on the methods for the overnight, limited-channel home cardiorespiratory studies, validation compared with in-laboratory polysomnography, and scoring of respiratory events have been previously reported.[21,27] In brief, limited-channel cardiorespiratory recordings included thoracic and abdominal excursions and estimated tidal volume (by inductance plethysmography), pulse oximetry with wave form display, heart rate, and body position (PT-2 system; SensorMedics, Yorba Linda, CA). OSA was defined as an obstructive apnea hypopnea index of ≥5 events per hour and/or an obstructive apnea index ≥1 events per hour.[21,28] Children without OSA were categorized as having primary snoring when the caregiver answered "yes" to the statement "loud snoring in the past month" at least 1 to 2 times per week. Children with either OSA or primary snoring were categorized as having SDB, whereas children who neither snored nor had OSA were categorized as no-SDB.

Behavioral Assessments

The CPRS-R:L is a well-validated, 80-item measure of childhood behavior problems.[26] This instrument yields 7 behavioral subscales—oppositional, cognitive/inattention, hyperactivity, anxious-shy, perfectionism, social, and psychosomatic—as well as 4 composite indices. The CBCL is a widely used 118-item instrument that assesses multiple dimensions of psychopathology, including individual problem scales (attention, delinquent, aggressive, somatic, social, anxious/depressed, withdrawn, and thought), 2 composite scales for externalizing (delinquent and aggressive) and internalizing (withdrawn, somatic complaints, and anxiety/depression) behaviors, a total problem score summing nearly all problem items; and child competencies (activities, social relationships, and school performance).[25,29,30] For each instrument, raw behavior scores were converted to age- and gender-adjusted t scores (mean: 50; SD: 10) on the basis of published norms constructed from population-based samples. Scale scores were dichotomized such that t scores in the borderline clinical or clinically abnormal range were defined as behavior problems.[25,26]

Statistical Analysis

Analyses were done using SAS v8.2 (SAS Institute, Inc, Cary, NC). Group differences were compared with 2-sample t tests and Pearson χ^2 tests for continuous and categorical data, respectively. Logistic regression was used to assess the relationship between SDB and each outcome while controlling for key covariates: age, gender, race/ethnicity, preterm status, and caregiver education. Models were constructed with and without the covariates body mass index (BMI) and asthma as exploratory assessments for potential confounding. Interactions between SDB and race and SDB and preterm status were evaluated. Associations between SDB and the outcomes are expressed as odds ratios (ORs) with corresponding 95% confidence intervals (CIs). All reported P values are 2-tailed with statistical significance set at $<.05$. Sensitivity analyses were conducted to explore differences between the adjusted ORs for the behavioral outcomes for children with OSA compared with children with primary snoring and potentially to justify combining these 2 groups into a single SDB exposure variable. When SDB was significantly associated with a specific behavioral outcome, sensitivity analyses were also conducted via stratified analyses to explore the stability of the relationship within key subgroups (black/nonblack; term/preterm; male/female) while controlling for any other confounders identified in the primary analyses.

RESULTS

Participant characteristics according to SDB status are summarized in Table 1. The sample was 50% female and 36% black and had a mean age of 9.5 years (SD: 0.8). Children who were born prematurely composed 46% of the sample and had a mean gestational age of 31 weeks (SD: 3). The sample included 40 (5%) children with OSA (median apnea hypopnea

TABLE 1. Participant Characteristics Stratified by SDB Status

Characteristics*	SDB Categories			
	None (N = 667)	Primary Snoring (N = 122)	OSA (N = 40)	Analytic Sample (N = 829)
Age, y, mean ± SD	9.5 ± 0.8	9.5 ± 0.8	9.3 ± 0.9	9.5 ± 0.8
Female, n (%)	332 (49.8)	60 (49.2)	23 (57.5)	415 (50.1)
Black race/ethnicity,* n (%)	213 (31.9)	57 (46.7)	27 (67.5)	297 (35.8)
Preterm birth, n (%)	285 (42.7)	67 (54.9)	29 (72.5)	381 (46.0)
Caregiver education less than high school, n (%)	39 (5.9)	9 (7.5)	6 (15.4)	54 (6.6)
Height percentile for age, mean ± SD	54.4 ± 29.2	55.1 ± 30.3	58.9 ± 29.5	54.8 ± 29.4
BMI percentile for age, gender, mean ± SD	57.0 ± 30.9	64.3 ± 32.5	60.7 ± 35.6	58.3 ± 31.5
BMI, kg/m^2, mean ± SD	17.9 ± 3.5	19.5 ± 5.0	19.0 ± 4.7	18.2 ± 3.9
BMI >95th percentile, n (%)	88 (13.2)	35 (28.9)	9 (22.5)	132 (16.0)
Apnea hypopnea index, events per hour, mean ± SD	1.1 ± 1.1	1.4 ± 1.2	9.7 ± 9.6	1.5 ± 3.0
Oxygen saturation nadir, %	91.6 ± 2.4	91.3 ± 2.9	86.7 ± 6.9	91.4 ± 3.0
Usual hours of sleep/night, parent-reported, mean ± SD				
Weekdays	9.3 ± 0.9	9.1 ± 1.1	9.0 ± 1.2	9.2 ± 1.1
Weekends	9.2 ± 1.2	9.2 ± 1.6	9.0 ± 1.5	9.1 ± 1.3
Asthma, n (%)	85 (12.7%)	25 (20.5%)	8 (20%)	118 (14.2%)

Primary snoring is defined as snoring loudly at least 1 to 2 times per week during the past month. OSA is defined as an apnea hypopnea index of ≥5 events per hour or an obstructive apnea index ≥to 1 event per hour and contains children with and without parent-reported snoring symptoms.

* The parent-identified race/ethnicity for the analytic sample was as follows: white, 495 (59.7%); black, 97 (35.8%); multiracial, 18 (2.2%); Hispanic, 13 (1.6%); Asian, 3 (0.4%); and Native American, 3 (0.4%).

index: 7.1 events per hour; interquartile range: 3.1–10.5), 55% of whom had parent-reported snoring; 122 (15%) children with only primary snoring and no OSA; and 667 (80%) children with neither snoring nor OSA. On the basis of parent report, the mean total hours of sleep per night were 9.2 (SD: 1.1) hours on week nights and 9.2 (SD: 1.3) hours on weekend nights, with no differences among the groups. Fourteen percent of the sample had doctor-diagnosed asthma.

Because snoring and OSA represent a spectrum of childhood SDB, preliminary analyses first compared children who had OSA with children who had primary snoring. Because these 2 groups had generally comparable distributions of behavioral outcomes, they were combined into a single SDB exposure group and compared with children without SDB for subsequent analyses.

Relationship of Covariates to Behavioral Outcomes

Many behavioral outcomes were significantly associated with race/ethnicity, preterm status, and caregiver education. Among the behavioral scales in which SDB was a significant predictor of adverse behavioral outcomes, caregiver education was a significant predictor for every outcome except the CBCL somatic complaints. Black race/ethnicity was a significant predictor only for the CBCL Total Problem scale, whereas preterm birth was significantly related to CBCL Total Problem, CBCL Social Problems, and CPRS-R:L Hyperactivity scales. In these models, the former covariates, when significant, identified children with higher odds of behavior problems when respectively compared with unexposed children. All logistic models were adjusted for the same covariates (black race/ethnicity, preterm status, and caregiver education) to improve the comparability of the models presented below.

Relationship of SDB to Behavioral Outcomes

Children with SDB had twice the odds of having CBCL total problem scores in the borderline or clinical range compared with children without SDB, and these differences persisted after covariate adjustment (adjusted OR: 2.2; 95% CI: 1.4–3.4; $P = .001$). Because the CBCL and CPRS-R:L identify many similar behavioral constructs, the remaining behavioral outcomes were grouped into 2 broad problem categories: externalizing, internalizing, and social problems and competencies. The unadjusted and adjusted relationships between SDB and these behavioral outcome groups are summarized in Tables 2, 3, and 4, respectively. Compared with children without SDB, children with SDB had 2.6 times the odds of having a borderline or clinically abnormal score for the CBCL externalizing scale (95% CI: 1.6–4.3; $P < .001$). Analyses of individual scales indicated that compared with children without SDB, children with SDB had significantly higher odds of the following acting-out behavior problems: hyperactivity (1.8; 95% CI: 1.2–2.8; $P = .010$), emotional lability (2.9; 95% CI: 1.7–4.8; $P < .001$), oppositional (2.3; 95% CI: 1.4–3.9; $P = .010$), aggressive (4.9; 95% CI: 2.4–9.9; $P < .001$), and another index of hyperactivity, the CPRS-R:L Global Total Index (1.9; 95% CI: 1.1–3.1; $P = .015$). Although unadjusted analyses for attentional scales (CBCL attention, CPRS-R:L cognitive/inattention, and CPRS-R:L attention-deficit/hyperactivity disorder) showed a significant association with SDB, these relationships were not statistically significant after controlling for confounders. SDB was not significantly associated with thought problems in either unadjusted or adjusted analyses.

Children with SDB had approximately twice the odds of a borderline or clinically abnormal CBCL internalizing scale (1.7; 95% CI: 1.0–2.7; $P = .034$) and more than twice the odds of having CBCL somatic complaints in the borderline or clinical range com-

TABLE 2. Externalizing/Attention Problem Behaviors Rated in the Borderline or Clinical Score Range Variation by SDB Status ($N = 829$)

Behavior Problem	No SDB ($n = 667$; 80%)	SDB ($n = 162$; 20%)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Adjusted OR *P* Value
Attention					
CBCL, Thought	33 (5.1%)	12 (7.6%)	1.54 (0.78–3.06)	1.11 (0.53–2.29)	.789
CBCL, Attention	48 (7.4%)	22 (13.9%)	2.04 (1.19–3.49)	1.55 (0.87–2.76)	.137
CPRS-R:L, Cognitive/Inattention	95 (14.3%)	33 (20.8%)	1.57 (1.01–2.44)	1.31 (0.82–2.09)	.255
CPRS-R:L, ADHD	88 (13.3%)	33 (21.2%)	1.75 (1.12–2.73)	1.36 (0.85–2.19)	.200
CPRS-R:L, Hyperactivity	93 (14.0%)	40 (25.0%)	2.05 (1.35–3.11)	1.80 (1.15–2.80)	.010
CPRS-R:L, Restlessness, Impulsive	85 (12.9%)	34 (21.8%)	1.89 (1.21–2.94)	1.54 (0.96–2.47)	.073
CPRS-R:L, Emotional Lability	48 (7.3%)	30 (19.2%)	3.04 (1.85–4.99)	2.87 (1.69–4.85)	<.001
CPRS-R:L, Global Total Index†	65 (9.8%)	29 (18.6%)	2.09 (1.30–3.38)	1.88 (1.13–3.14)	.015
Other externalizing, acting out					
CPRS-R:L, Oppositional	52 (7.8)	27 (16.9%)	2.39 (1.45–3.95)	2.28 (1.35–3.87)	.002
CBCL, Delinquent	51 (7.8%)	19 (12.0%)	1.61 (0.92–2.82)	1.28 (0.71–2.32)	.411
CBCL, Aggressive	19 (2.9%)	20 (12.7%)	4.84 (2.51–9.30)	4.92 (2.43–9.94)	<.001
CBCL, Externalizing‡	59 (9.0%)	36 (22.8%)	2.97 (1.88–4.70)	2.63 (1.61–4.30)	<.001

ADHD indicates attention-deficit/hyperactivity disorder. For complete definition of SDB, see Table 1. Reference category: no SDB.
* ORs were adjusted for preterm birth status (preterm vs term), race/ethnicity (black vs nonblack), and caregiver education (less than high school education vs at least high school education).
† Consists of a combination of items from the Restless/Impulsive, Emotional Lability problem scales. Previously known as the Hyperactivity Index, the Global Total Index is usually elevated when attention problems exist and will also be elevated when there are other kinds of psychopathology and behavioral problems.
‡ Consists of a combination of Delinquent and Aggressive behavior problem scales.

TABLE 3. Internalizing Problem Behaviors Rated in the Borderline or Clinical Score Range Variation by SDB Status (N = 829)

Problem	No SDB (n = 667; 80%), n (%)	SDB (n = 162; 20%), n (%)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Adjusted OR P Value
Internalizing					
CBCL, Withdrawn	18 (2.8)	10 (6.3)	2.38 (1.08–5.27)	1.87 (0.81–4.34)	.143
CBCL, Somatic	38 (5.8)	19 (12.0)	2.21 (1.24–3.95)	2.22 (1.22–4.06)	.010
CBCL, Anxious/Depressed	21 (3.2)	8 (5.1)	1.61 (0.70–3.69)	1.53 (0.65–3.61)	.336
CPRS-R:L, Anxious/Shy	72 (10.8)	23 (14.4)	1.38 (0.83–2.29)	1.22 (0.72–2.07)	.451
CPRS-R:L, Perfectionism	54 (8.1)	15 (9.4)	1.17 (0.64–2.23)	1.08 (0.58–2.01)	.805
CPRS-R:L, Psychosomatic	77 (11.6)	31 (19.4)	1.84 (1.16–2.90)	1.61 (1.00–2.60)	.051
CBCL, Internalizing†	79 (12.1)	32 (20.3)	1.85 (1.17–2.90)	1.68 (1.04–2.71)	.034

Reference category: no SDB.
* ORs were adjusted for preterm birth status, black race/ethnicity, and caregiver education (less than high school education).
† Consists of a combination of Withdrawn, Somatic, and Anxious/Depressed problem scales.

TABLE 4. Social Problems and Competencies Rated in the Borderline or Clinical Score Range Variation by SDB Status (N = 829)

Problem	No SDB (n = 667; 80%), n (%)	SDB (n = 162; 20%), n (%)	Unadjusted OR (95% CI)	Adjusted OR* (95% CI)	Adjusted OR P Value
Social problems					
CBCL, Social	28 (4.3)	16 (10.1)	2.52 (1.33–4.77)	2.13 (1.08–4.20)	.029
CPRS-R:L, Social	58 (8.7)	24 (15.0)	1.85 (1.11–3.08)	1.42 (0.83–2.45)	.202
Competencies					
CBCL, Activities	17 (2.6)	12 (7.5)	3.04 (1.42–6.50)	1.61 (0.71–3.65)	.257
CBCL, Social	56 (8.6)	18 (11.7)	1.41 (0.80–2.48)	1.23 (0.68–2.23)	.485
CBCL, School	78 (12.1)	33 (20.9)	1.92 (1.22–3.02)	1.43 (0.88–2.31)	.148
CBCL, Total	138 (21.6)	50 (32.9)	1.78 (1.21–2.63)	1.28 (0.84–1.95)	.259

Reference category: no SDB.
* ORs were adjusted for preterm birth status, black race/ethnicity, and caregiver education (less than high school education).

pared with children without SDB (2.2; 95% CI: 1.2–4.1; P = .010). A similar trend was seen for CPRS-R:L psychosomatic complaints (1.6; 95% CI: 1.0–2.7; P = .051). SDB was not significantly associated with the remaining individual internalizing scales (withdrawn, anxious/depressed, anxious/shy, and perfectionism). Children with SDB were significantly more likely to have social problems in the borderline or clinical range as measured on the CBCL compared with children without SDB (2.1; 95% CI: 1.1–4.2; P = .029), but this association was not statistically significant for social problems as measured by the CPRS-R:L (1.4; 95% CI: 0.8–2.5; P = .20). SDB was not significantly associated with any of the CBCL competency scales.

Adjusting for BMI, Obesity, or Asthma

After adjusting for other covariates, the addition of the BMI percentile, obesity (defined as BMI ≥95th percentile), or asthma to the final model did not appreciably change the relationship between SDB and the key significant behavioral outcomes.

Interactions Between SDB and Covariates

Two-way interactions for race and prematurity with SDB were evaluated to identify potential differences within subgroups. There was a significant interaction between SDB and race/ethnicity for the CPRS-R:L Global Total Index score (P = .048) such that black children with SDB had 3.3 times the odds of having a Global Total Index score in the borderline/clinical range compared with black children without SDB (95% CI: 1.6–7.0; P = .012). Comparisons among the other SDB race groups were not statistically significant. No statistically significant interactions between SDB and prematurity were identified.

Sensitivity Analyses

The extent to which the associations between SDB and the behavioral outcomes could be attributable to primary snoring was explored in a series of sensitivity analyses that compared children who had OSA with children who had only primary snoring. These analyses showed that the odds for borderline or clinically abnormal behavioral scores for hypothesized outcomes of interest were generally comparable in children with OSA or primary snoring (Fig 1). Even when the children with OSA were excluded and SDB was based on primary snoring alone, the odds of

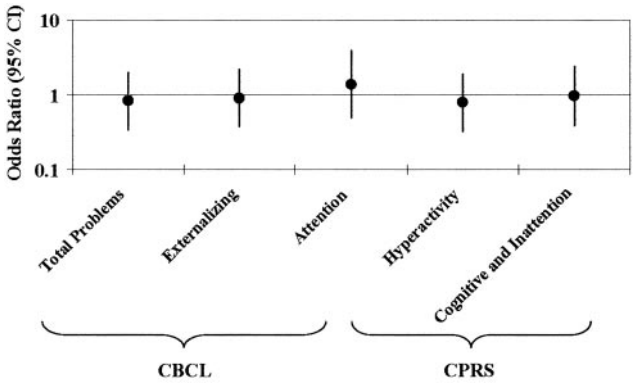

Fig 1. Sensitivity analysis for adjusted ORs for the relationship between the SDB group (OSA [n = 40] compared with children with primary snoring [n = 122]) and hypothesized behavioral outcomes of interest from 2 rating scales for children. Adjusted for preterm birth status, black race/ethnicity, and caregiver education. Primary snoring is the referent group.

borderline or clinically abnormal behavioral scores were comparable to those presented for the combined OSA and snoring groups (data not shown). Furthermore, a dose-response relationship between degrees of snoring was suggested by an exploratory analysis for the outcome aggressiveness. Even after adjusting for apnea-hypopnea index, increasing frequency of snoring (number of nights per week) was associated with a trend of increasing odds for aggressive behavior. Compared with a reference group of 519 children who never snored, the adjusted OR for increased aggressive behavior was 2.5 (95% CI: 0.9–7.1; $P = .654$) in 119 children who snored less than once a week, 3.7 (95% CI: 1.2–11.2; $P = .001$) in 71 children who snored 1 to 2 times per week, and 10.7 (95% CI: 4.2–27.5; $P = .077$) in 73 children who snored 3 to 7 times per week.

Finally, sensitivity analyses stratified by key subgroups (term/preterm, black/nonblack, and male/female) were performed to explore whether significant behavioral outcomes associated with SDB might be "driven" by certain subgroups (Fig 2). Compared with the findings from the analytic sample, the magnitude and the direction of the adjusted ORs were comparable among the various subgroups for all statistically significant behavioral outcomes except for CBCL somatic complaints and CPRS-R:L Global Index Total. For somatic complaints, the OR for SDB was >1 in the preterm group but <1 in the term group. For the Global Total Index, the OR for SDB was >3 for black children but was close to 1 for nonblack children.

DISCUSSION

This study assessed the relationship between childhood SDB and behavioral outcomes in a large urban community sample of US children with substantial black representation. A rigorous method included assessment of all participants with objective overnight measurements of SDB and 2 well-validated behavioral measures that provided convergent tests for the validity of the observed associations. This work confirms previous studies showing an association between SDB and behavioral problems reported in clinical samples[1,2,4,8–10,13,16,18,19] and extends these findings by specifying the behavioral constructs most consistently associated with SDB. Children with SDB, defined as primary snoring and/or an elevated number of apneas and hypopneas, had higher odds of behavior problems including externalizing and internalizing behaviors, somatic and psychosomatic complaints, and social ("unpopular") problems. Externalizing acting-out behaviors (including hyperactive, emotional labile, oppositional, and aggressive) seemed to be the most robust correlates of SDB. The results also revealed similar increased behavioral morbidity for children with primary snoring compared with children who have OSA.

Suggested mechanisms linking nocturnal upper airway obstruction and SDB to daytime cognitive and behavioral deficits include sleep disruption and blood gas abnormalities that prevent sleep-related restorative processes. Sleep disruption associated with SDB may cause fatigue and a general "irritability" that may impair regulation of impulsivity and control of emotions, all of which could facilitate hyperactivity and other externalizing acting-out behaviors.[31] In addition, intermittent airflow obstruction causing sleep disruption and intermittent hypoxemia, especially when occurring at key developmental periods, may produce central nervous system cellular injury that leads to cortical dysfunction in prefrontal regions[32] and manifests as behavioral dysregulation that may have a broad negative impact on learning and academic performance. Cognitive and executive deficits may also be present but were not examined in this study.

On the basis of previous studies,[5,7,10,14,19,20] we had hypothesized that inattention also would be strongly associated with SDB. Although unadjusted analyses showed greater odds of attentional problems in children with SDB compared with children without SDB, these differences were not significant after controlling for confounders. The significant association reported in previous studies could relate to use of different constructs of "inattention," which may have combined inattentive and hyperactive behaviors.[7,14,33] Biases introduced by oversampling referral children with both inattention and SDB[10,18,19] or by failing to account for confounding factors such as prematurity may also be partially responsible for the significant association with inattention observed in past studies. Overall, the CBCL identified more behavior problems in the SDB group than in the CPRS-R:L. The increased detection of problems by the CBCL may be related, in part, to the greater number of items in the CBCL.

One of the remarkable findings in this study was the comparable increased behavioral morbidity in children with primary snoring and children with OSA, suggesting that snoring alone may be associated with adverse behavioral outcomes. It is possible that we may have observed a larger impact of OSA on behavioral outcomes if the sample had included a larger number of more severely affected children. Nonetheless, our data support an association between primary snoring and behavior problems that does not seem to be attributable to unrecognized moderate to severe levels of OSA because the objective respiratory measurements likely precluded misclassification of OSA at this level. These findings are consistent with mounting evidence from other studies that suggest an increased risk of school and learning problems in children with primary snoring or relatively low levels of obstructive breathing events.[17,20,34–36]

The mechanism by which primary snoring alone without significant OSA might have an impact on daytime behavior is less clear but may be mediated by more subtle physiologic disturbances whereby chronicity and individual vulnerability may be important determinants of impact. Middle school–aged children who currently have primary snoring may have had more severe SDB, possibly OSA, when younger. If so, then exposure to more severe airflow obstruction and intermittent hypoxemia during critical periods during early brain development may

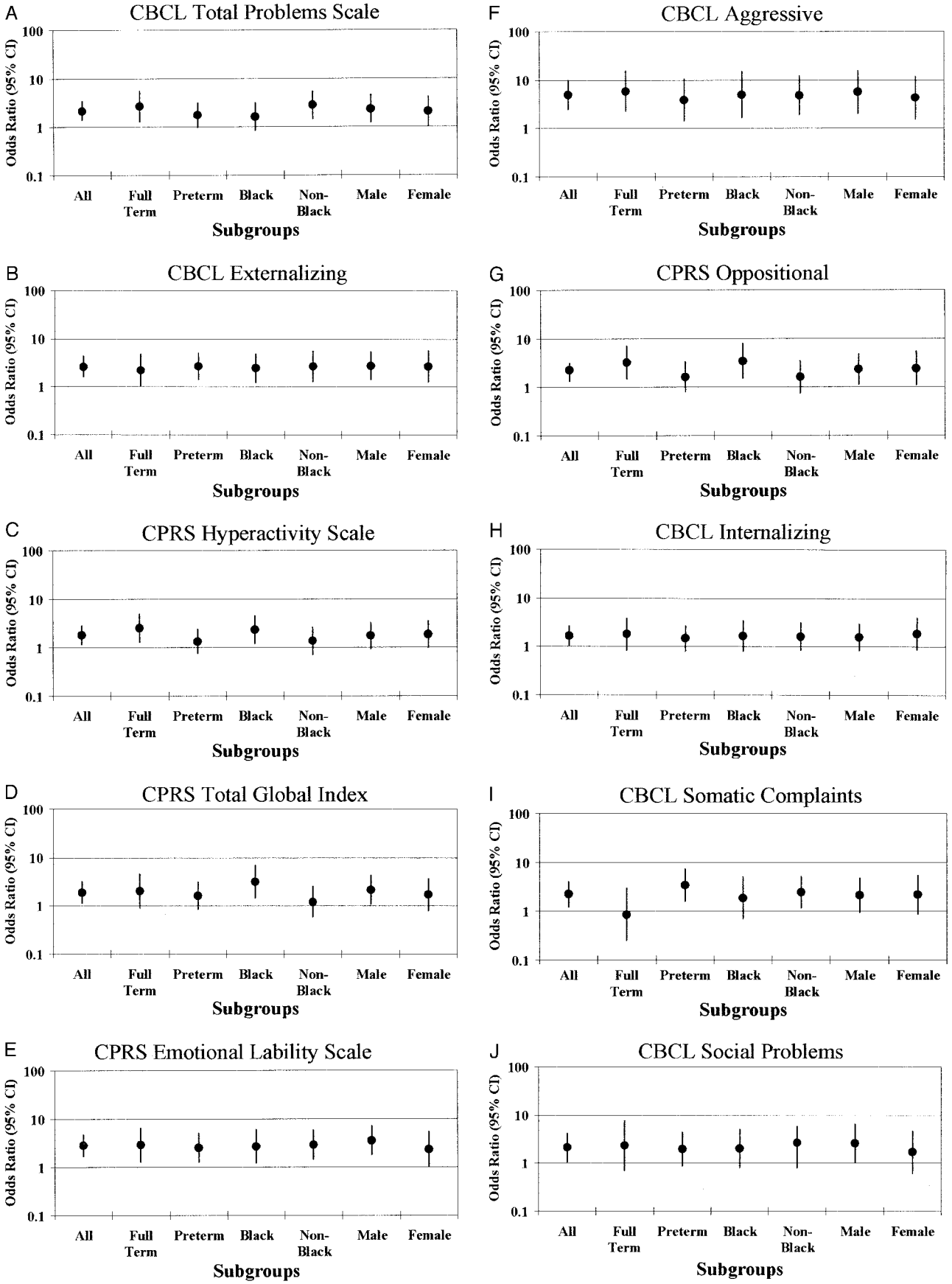

Fig 2. Sensitivity analyses for the adjusted ORs for SDB and the significant behavioral outcomes from 2 rating scales for children, stratified by potential key subgroups (term/preterm, black/nonblack, and male/female). Each analysis was adjusted for the remaining covariates (preterm birth status, black race/ethnicity, and caregiver education). Non-SDB is the referent group.

have led to persistent behavioral changes later in childhood. This hypothesis is supported by a retrospective study that showed that children with lower academic performance in middle school were significantly more likely to have snored during early childhood and to have undergone adenotonsillectomy for snoring compared with better performing schoolmates.[34] This mechanism is also consistent with the experimental rodent models showing that early exposure to chronic episodic hypoxia results in both cellular changes within neural regions associated with cognitive functions and impaired performance during acquisition of a cognitive spatial task.[37] Nonetheless, our finding suggests that children who snore may manifest excessive behavioral problems and possibly that primary snoring may not be as "benign" a marker as previously thought.[38–40]

Several limitations of this study must be considered. First, it is possible that the associations between SDB and poorer behavioral outcomes may be driven by population subgroups. For example, poorer behavioral outcomes among children with SDB may be driven by preterm birth status because the original cohort was constructed by overrecruiting former preterm infants, a group also known to be at increased risk for behavioral problems.[41,42] Although the logistic regression analyses were adjusted for former preterm birth status, it is possible that this adjustment did not completely eliminate other unmeasured explanatory variables. To address this issue, we conducted separate sensitivity analyses excluding the premature children and found qualitatively similar ORs for the term and preterm subgroups for all outcomes in which SDB was a significant predictor except for the CBCL somatic complaints. Specifically for this scale, data on physical symptoms (eg, headache, dizzy, nausea, stomach pain) included in the somatic complaints subscale are known to be more ambiguous or unstable when children who are more vulnerable to compromised health status (such as former preterm infants) are included in the sample.[43] ORs for the relationship between SDB behavioral scale scores in the borderline or clinical range were similar for both genders. Finally, we were concerned that BMI, obesity, or asthma may have confounded the relationship between SDB and behavioral outcomes, but secondary analyses showed that this was not the case.

Because race is associated with SDB and may be associated with behavioral morbidity, we explored extensively the extent of confounding and effect modification caused by race. As only 1 interaction between race and SDB was statistically significant (CPRS-R:L Global Index Total subscale, an index of hyperactivity), the results suggest that the effect of SDB was comparable among black and nonblack subgroups. For the CPRS-R:L Global Index Total, among black children, the odds of a borderline or clinically abnormal score was ~3-fold higher in children with SDB compared with children without SDB. However, this difference was not seen in the specific Hyperactivity scale from the same instrument. The differential effect of SDB by race for the CPRS-R:L Global Index Total may be spurious or is possibly attributable to greater vulnerability among the SDB black subgroup to sleep disruption.

Second, there may be methodologic limitations related to the behavioral assessments used in this study.[43] Although these measures provide reliable and valid assessments of behavioral problems, this validity is based largely on their ability to discriminate problem behaviors in clinically affected children versus nonreferred children on a range of symptoms. The instruments may have limited sensitivity to identify less serious behavioral problems that are below the threshold for clinical disturbance. Specifically, the CBCL was not designed to discriminate physical symptoms related to organic disorders from somatic symptoms created by emotional problems or stresses related to those same organic disorders. Moreover, the CBCL provides only limited assessment of social competence.[43] Despite these potential limitations, similar externalizing acting-out behaviors were identified by both the CBCL and the CPRS-R:L and persisted after adjustment for key covariates. Furthermore, the CBCL and CPRS-R:L both are validated measures of behavior disorders, and classifying children with borderline ratings as abnormal is likely to have increased their sensitivity to clinically meaningful problems.[25,26]

A third limitation is a potential bias by reliance on parent reports. Our definition of SDB included either parent report of habitual snoring or objectively measured OSA. Snoring may be differentially reported by parents according to any number of factors, including their attentiveness to their children's sleep habits and underlying concerns about sleep and its possible impact on health and behavior. Given the increasing public awareness of the relationship between OSA and daytime problems, parents of children with behavioral problems may be more likely to report snoring. However, analyses were adjusted for maternal education and race/ethnicity, and any referral bias should be less in a community cohort than in a clinic-based sample.

Fourth, our assessment of apnea hypopnea index was based on a single overnight, in-home, unattended, limited-channel cardiorespiratory recording. Unattended studies have been shown to be reliable for measuring apnea hypopnea indices in children.[44] Our preliminary validation studies showed excellent agreement in classifying SDB by apnea hypopnea indices from full laboratory-based polysomnography to technology selected for our limited-channel home studies.[21] Although nasal pressure technology may have provided a more sensitive index of airflow obstruction and hypopneas,[45] this sensor was not part of available ambulatory equipment at the time of this study's data collection. Furthermore, a recent study of ambulatory unattended data collection in children found that the poorest signal quality came from the nasal cannula.[44] Had more sensitive measures of airflow been available, it is possible that some of the children with primary snoring may have been classified as having modest levels of OSA. However, our recordings were especially unlikely to misclassify children with moderate to severe levels of OSA, underscoring the validity of our conclusions regarding

associations between modest levels of SDB and behavioral outcomes. Because sleep and arousals were not measured, we could not separate the effects of respiratory abnormalities and sleep fragmentation on behavior. In summary, the limited-channel approach extends the data available from questionnaire studies, identifying significant associations between behavioral morbidity in children who are primary snorers, which did not seem to be explained by unrecognized moderate to severe levels of OSA.

Fifth, we examined the relationship between SDB and each of the 26 behavioral outcomes without any adjustment for multiple testing. However, this analysis was exploratory and our primary interest was to estimate the association between SDB and behavioral problems after adjusting for confounders. Finally, the cross-sectional design of the study limits implications of the findings with regard to a causal relationship between SDB and behavioral problems.

CONCLUSIONS

Children with primary snoring and children with relatively mild degrees of OSA have an increased odds of behavioral problems compared with children without SDB, especially externalizing acting-out behaviors that may have a negative impact on daytime functioning, learning, and school performance. Future large, well-controlled, prospective studies are needed to understand better the extent to which this association is causal, to examine the potential reversibility of associated behavioral problems, and to investigate cognitive consequences of SDB. Given the relatively high prevalence of SDB in school-aged children (2%),[21] any causal association would likely have a large public health impact, necessitating more aggressive screening, diagnosis, and treatment strategies aimed at identifying and treating a potentially treatable cause of behavioral problems. Even if not causal, these associations suggest a means for identifying children who are at increased risk for behavioral morbidity and might benefit from interventions. Given the association of behavior problems with difficulties in social adjustment and academic competence,[46,47] effective treatments may also yield improvement in other areas of functioning.

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Marcus AD. *Wall Street Journal*. September 29, 2004

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Increased Behavioral Morbidity in School-Aged Children With Sleep-Disordered Breathing

Carol L. Rosen, Amy Storfer-Isser, H. Gerry Taylor, H. Lester Kirchner, Judith L. Emancipator and Susan Redline

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