ORIGINAL ARTICLE

Rapid Eye Movement Sleep in Relation to Overweight in Children and Adolescents

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Context: Short sleep duration is associated with obesity, but few studies have examined the relationship between obesity and specific physiological stages of sleep.

Objective: To examine specific sleep stages, including rapid eye movement (REM) sleep and stages 1 through 4 of non-REM sleep, in relation to overweight in children and adolescents.

Design, Setting, and Participants: A total of 335 children and adolescents (55.2% male; aged 7-17 years) underwent 3 consecutive nights of standard polysomnography and weight and height assessments as part of a study on the development of internalizing disorders (depression and anxiety).

Main Outcome Measures: Body mass index (calculated as weight in kilograms divided by height in meters squared) *z* score and weight status (normal, at risk for overweight, overweight) according to the body mass index percentile for age and sex.

Results: The body mass index *z* score was significantly related to total sleep time ($\beta = -0.174$), sleep efficiency ($\beta = -0.027$), and REM density ($\beta = -0.256$). Compared with normal-weight children, overweight children slept about 22 minutes less and had lower sleep efficiency, shorter REM sleep, lower REM activity and density, and longer latency to the first REM period. After adjustment for demographics, pubertal status, and psychiatric diagnosis, 1 hour less of total sleep was associated with approximately 2-fold increased odds of overweight (odds ratio = 1.85), 1 hour less of REM sleep was associated with about 3-fold increased odds (odds ratio = 2.91), and REM density and activity below the median increased the odds of overweight by 2-fold (odds ratio = 2.18) and 3-fold (odds ratio = 3.32), respectively.

Conclusions: Our results confirm previous epidemiological observations that short sleep time is associated with overweight in children and adolescents. A core aspect of the association between short sleep duration and overweight may be attributed to reduced REM sleep. Further studies are needed to investigate possible mechanisms underpinning the association between diminished REM sleep and endocrine and metabolic changes that may contribute to obesity.

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CHILDHOOD OBESITY HAS become a major public health concern. During the past 3 decades, the childhood obesity rate has more than tripled for children aged 6 to 11 years[1,2]; currently, approximately 17% of US adolescents are overweight or obese as defined by having a body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared) greater than or equal to the 95th percentile for age and sex.[3] Obesity is associated with various short-term and long-term psychosocial, behavioral, and physical health problems.[4-6] Multiple psychosocial, lifestyle, nutritional, and familial or genetic factors are associated with childhood obesity.[7,8]

Obesity results from impaired balance between energy intake (food calories) and expenditure (physical activity), but little is known about what factors alter the balance.[9] Recent epidemiological and laboratory studies suggest that shortened sleep duration may be one of the risk factors that alters the energy balance in ways that are contributing to the obesity pandemic in modern society.[9-11]

A number of cross-sectional epidemiological studies have demonstrated a link between short self-reported sleep duration and obesity in adults and children.[9,10] It has been shown that adults who report sleeping on average less than 5 hours per night tend to have elevated BMIs.[12] A dose-response relationship between short sleeping hours and obesity has been observed in a large sample of Japanese children (n = 8274).[13] Several longitudinal studies have identified short sleep duration or inadequate sleep as a risk factor for weight gain or obesity in the fu-

ture.[6,12,14-16] Interestingly, a longitudinal study of UK children has shown that short sleep duration at an early age of 30 months predicts obesity at age 7 years.[6] Using objective sleep measures, several studies have confirmed the short sleep–obesity association. For example, Gupta et al[17] used 24-hour wrist actigraphy to assess sleep in 383 adolescents and found that 1 hour of sleep loss increased the odds of obesity by 80%. In one comparative study of 60 overweight adolescents and 20 control subjects, Beebe et al[18] reported that obese participants as compared with control subjects slept shorter (469 minutes vs 507 minutes, respectively) and had lower sleep efficiency (80% vs 87%, respectively) as assessed by 5-night actigraphy. However, total sleep duration and percentage of stages 1, 2, 3, 4, and rapid eye movement (REM) sleep as assessed by 1 overnight polysomnography (PSG) sleep in the laboratory did not significantly differ between the 2 groups.

Sleep loss has been hypothesized to contribute to overweight and obesity through endocrine changes, such as decreased levels of leptin (an adipocyte-derived hormone that suppresses appetite), increased levels of ghrelin (a stomach-derived peptide that stimulates appetite), and compromised insulin sensitivity.[14,19-21] Importantly, one experimental study[22] reported that sleep restriction in healthy young men is associated with decreased leptin levels, elevated ghrelin levels, and increased hunger and appetite. These findings have been confirmed by a large population-based study[21] (Wisconsin Sleep Cohort Study) that shows a significant association of sleep duration with leptin and ghrelin levels, independent of age, sex, sleep-disordered breathing, and self-reported exercise.

The combination of growing epidemiological and laboratory studies points to a conclusion that there is a potential causal relationship between short sleep duration and obesity mediated by endocrine and metabolic changes. However, many questions remain to be answered.[21] One of the questions is whether there is a significant interaction effect between sleep and obesity pertaining to specific sleep stage(s). During the course of a night, a person's sleep is divided into non-REM (NREM) sleep and REM sleep. The NREM sleep is further divided into 4 stages. However, it is unknown what sleep stage loss uniquely contributes to overweight and whether the association between short sleep time and overweight differs across sleep stages.

Human studies have shown that the sleeping metabolic rate is higher in REM sleep and electrophysiological alterations are sleep stage dependent.[23,24] Specifically, glucose utilization during REM sleep is higher than during NREM sleep.[25,26] In addition, brain glucose metabolic changes during sleep occur independent of slow-wave sleep stages but brain metabolism increases during REM sleep.[26] Research has also shown that children with short sleep duration (<6 hours) spend proportionally less time in REM sleep.[27] Thus, it is possible to speculate that the association between short sleep duration and obesity may also be sleep stage dependent. Specifically, REM-related sleep may be associated with obesity.

The goal of the current study was to examine whether the association between short sleep duration and BMI or overweight differs across sleep stages with a large clinical sample of children and adolescents who underwent 3 consecutive nights of standard polysomnography and weight and height assessments. Based on previous studies,[23,25-27] we hypothesized that REM sleep time and activity are negatively related to BMI and that overweight children are more likely to have reduced REM sleep than normal-weight peers.

METHODS

PARTICIPANTS

Participants were children and adolescents in an ongoing multidisciplinary study of neurobehavioral characteristics of pediatric affective disorders from January 1987.[28-30] A total of 339 children and adolescents had undergone PSG sleep assessment, and their sleep PSG had been scored by June 2006. Four children having no height and weight measurements were excluded, leaving 335 participants (98.8%) in the current report. Of the 335 participants, 166 had internalizing disorders (ie, major depressive disorder and anxiety disorders), 86 were at high risk for but had no history of mood disorder based on high family loading for major depressive disorder (≥ 1 first-degree and 1 second-degree relative with a history of major depressive disorder), and 83 were healthy, low-risk participants (absence of lifetime affective disorder in first-degree relatives and lifetime major depressive disorder in $<20\%$ of second-degree relatives) with no history of psychiatric disorder. In this article, high- and low-risk participants were called nonpsychiatric control subjects as appropriate. Participants in the internalizing group were recruited from the Child and Adolescent Depression Program at Western Psychiatric Institute and Clinic, Pittsburgh, Pennsylvania, and from radio and newspaper advertisements. Nonpsychiatric control subjects were recruited from advertisements.

Diagnoses were determined through administration of the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Present and Lifetime version.[31] Each participant and a parent (or guardian) were interviewed separately by a bachelor's-level research specialist trained according to local diagnostic reliability standards. Reliability for depressive and anxiety diagnoses was greater than 90% and was maintained through monthly department-wide diagnostic reviews. A child psychiatrist reviewed all of the data with the research specialist and provided the final best-estimate diagnoses. Participants in the internalizing groups were in a current episode. First- and second-degree relatives were interviewed using the Schedule for Affective Disorders and Schizophrenia (for adults) and the Schedule for Affective Disorders and Schizophrenia for School-Age Children–Epidemiologic version (for child siblings).[32]

Participants were medication free at the time of the study, with no use of medication affecting the central nervous system or hypothalamic-pituitary effects within the past 2 weeks; there was no use of fluoxetine hydrochloride within the past month. Other exclusionary criteria included the following: significant medical illness; extreme obesity (weight $>150\%$ of ideal body weight); obstructive sleep apnea; IQ lower than 70; eating disorder, developmental disorder, or schizophrenia; phobia of intravenous needles; learning disabilities; and use of nicotine, drugs, or alcohol.

Pubertal development was determined through physical examination by a trained physician or nurse practitioner using 5 stages of breast, genital, and pubic hair development as described by Marshall and Tanner.[33] Agreement for Tanner stage classification has been 90% or higher. Participants were categorized as prepubertal or early pubertal if they were below Tan-

ner stage 3 and as midpubertal or late pubertal if they were at Tanner stage 3 or higher.

PROCEDURE

The study protocol was approved by the University of Pittsburgh Institutional Review Board. Participants' parents or guardians were told about the procedures of the study and signed an informed consent form; participants aged 14 to 16 years provided consent; and participants younger than 14 years provided verbal assent. Participants were admitted to the Child and Adolescent Sleep and Neurobehavioral Laboratory at Western Psychiatric Institute and Clinic for a neurobiological assessment that included 3 consecutive nights of standard PSG.

During the week before the PSG sleep assessment, all of the participants maintained their usual sleep/wake schedules, were not permitted to nap during the day, and were instructed to abstain from caffeine, nicotine, and any medications; those participants who were enrolled in the program project after August 1991 were asked to keep detailed sleep logs in their home environment. While in the sleep laboratory, participants maintained their usual bedtime and wake time and were not allowed to nap.

Of the 335 participants who had both PSG sleep assessments and weight and height measurements, 181 had complete sleep logs. Habitual sleep duration was estimated by averaging sleep times (ie, the period from sleep onset to the final awakening minus the time spent awake during the sleep period) recorded in the sleep logs.

POLYSOMNOGRAPHY

Sleep data were analyzed from the second night of sleep (night 1 was considered an adaptation night, and the protocol for night 3 included sleep-disrupting procedures).[28] Sleep scoring was conducted in 30-second epochs using standard criteria.[34] Scorers were blinded to diagnosis and achieved adequate interrater reliability. The following variables were computed: total sleep time, sleep latency, wake after sleep onset, sleep efficiency, total REM time, REM latency, REM activity, REM density, time in sleep stages 1 through 4, and total delta sleep (sum of time in stages 3 and 4). Sleep onset was defined as the first of 10 consecutive minutes of stage 2 or deeper sleep. The total sleep time was computed within the total sleep period. Wake after sleep onset was computed as wakefulness after sleep onset and before the waking time in the morning. Sleep efficiency was the total sleep time divided by the time from lights out until arising in the morning. The sleep latency was computed as the difference between bedtime and sleep onset. The total REM time was computed as the time in REM sleep. The REM latency was computed as the time from sleep onset to the first epoch of the first REM period lasting at least 3 minutes. The REM activity was estimated as the total units of REM during sleep. The REM density was defined as the average semiquantitative estimate of eye movements per minute of REM sleep.

BODY MASS INDEX

Weight and height were recorded to the nearest 0.1 kg and 0.5 cm, respectively, by trained and reliable research associates. Participants were asked to remove socks, shoes, and heavy garments and to remove or push aside any barrettes, braids, or hairstyles that might interfere with the height measurement. Height was obtained with a standard stadiometer (Accustat Stadiometer; Genentech, Inc, South San Francisco, California). The child's feet were placed flat on the floor and either the knees or feet were together in the center of the measuring board. The horizontal headpiece was brought into contact with the most superior part of the child's head. Weight was measured with a Detecto balance scale (Detecto Scales Inc, Brooklyn, New York) that has a capacity of 140 kg and was calibrated once per month. The child was asked to stand on the center of the scale platform with arms at the side. Scale weights were pushed across the beam until the beam was balanced.

STATISTICAL ANALYSIS

Using the Centers for Disease Control and Prevention SAS version 9.1 statistical software program (SAS Institute Inc, Cary, North Carolina), the BMI z score and percentile by the Centers for Disease Control and Prevention growth charts for age and sex were computed for each child. The BMI z score reflects each child's BMI relative to children of the same age and sex, thus allowing for comparison of children of different ages and sexes. According to the Centers for Disease Control and Prevention criteria, participants were then divided into 3 groups: normal weight (BMI z score $<$ 85th percentile), at risk for overweight (BMI z score of 85th to $<$ 95th percentile), and overweight (BMI z score $\geq$ 95th percentile).[6]

Covariates in the current study were age, sex, ethnicity (white, black, or other), family socioeconomic status as assessed by the Hollingshead Four-Factor Index of Social Status, diagnosis (internalizing disorder, high-risk normal, or low-risk normal), and pubertal status (Tanner stage <3 or ≥ 3). These variables were considered as covariates because they are associated with sleep, obesity, or both in the literature.[7,8,35-38]

General linear models were used to examine the linear relationship between each sleep variable and BMI z score. Analysis of variance and analysis of covariance were then performed to examine whether there were group differences in sleep variables across weight status (ie, normal weight, at risk for overweight, and overweight) with and without adjustment for covariates. Post hoc tests were computed using 1-way analyses of variance with the least significant difference method.

Logistic regression analyses were performed to examine the association between each sleep variable and overweight. Multiple logistic regression analysis was then performed, with overweight vs not overweight as the dependent variable and PSG stage 1, stage 2, delta, and REM sleep as independent variables to determine which sleep stages were independently associated with overweight after adjustment for covariates. In logistic regression on the basis of medians, REM activity and density were dichotomized for explicit interpretation of the results.

All of the analyses were performed for the entire sample and separately for children with and without internalizing disorders to examine the interaction of sleep parameters by diagnosis. All of the statistical tests were 2-tailed. We used SPSS version 15.0 statistical software (SPSS Inc, Chicago, Illinois) for all of the statistical analyses.

RESULTS

DEMOGRAPHIC AND SLEEP CHARACTERISTICS

Of 335 participants who had both PSG sleep assessments and BMI measurements, the mean (SD) age was 10.84 (2.28) years (range, 7.0-17.0) years, 185 (55.2%) were boys, 49 (14.6%) were at risk for overweight, and 45 (13.4%) were overweight. As shown in **Table 1**, there were no significant differences in age, sex, family socioeconomic status, and pubertal status across weight sta-

Table 1. Sample Characteristics According to Weight Status

Characteristic	Weight Status[a]				Statistical Test	
	Total (N=335)	Normal (n=241)	At Risk for Overweight (n=49)	Overweight (n=45)	ANOVA *F* or χ^2	*P* Value
Age, mean (SD), y	**10.84 (2.28)**	10.72 (2.26)	11.36 (2.48)	10.92 (2.15)	1.64[b]	.20
Male, No. (%)	**185 (55.2)**	131 (54.4)	25 (51.0)	29 (64.4)	1.97[c]	.37
Ethnicity, No. (%)						
White	**285 (85.1)**	211 (87.6)	45 (91.8)	29 (64.4)	24.63[c]	<.001
Black	**40 (11.9)**	21 (8.7)	4 (8.2)	15 (33.3)		
Other	**10 (3.0)**	9 (3.7)	0	1 (2.2)		
Family SES, mean (SD)	**42.10 (13.30)**	42.91 (14.12)	40.10 (10.57)	39.86 (10.89)	1.58[b]	.21
Diagnosis, No. (%)						
Internalizing disorder	**166 (49.6)**	111 (46.1)	22 (44.9)	33 (73.3)	12.26[c]	.02
High-risk normal	**86 (25.7)**	66 (27.4)	15 (30.6)	5 (11.1)		
Low-risk normal	**83 (24.8)**	64 (26.6)	12 (24.5)	7 (15.6)		
BMI, mean (SD)	**19.24 (3.75)**	17.47 (2.14)	22.21 (2.26)	25.45 (3.17)	271.75[b]	<.001
BMI *z* score, mean (SD)	**0.45 (0.98)**	–0.01 (0.74)	1.35 (0.19)	1.92 (0.19)	232.49[b]	<.001
BMI percentile, mean (SD)	**62.93 (28.01)**	50.90 (23.85)	90.77 (3.06)	97.03 (1.16)	151.64[b]	<.001
Tanner stage of pubertal status, No. (%)						
<3	**233 (74.7)**	168 (76.0)	34 (70.8)	31 (72.1)	0.74[c]	.69
≥3	**79 (25.3)**	53 (24.0)	14 (29.2)	12 (27.9)		

Abbreviations: ANOVA, analysis of variance; BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); SES, socioeconomic status.

[a] Normal weight was below the 85th BMI percentile of the Centers for Disease Control and Prevention growth charts for age and sex; at risk for overweight was from the 85th percentile to less than the 95th percentile; and overweight was at or higher than the 95th percentile.

[b] Values were tested with ANOVA *F*.

[c] Values were tested with χ^2.

tus. However, overweight children were more likely than children at normal weight or at risk for overweight to be African American and had more internalizing disorders.

The mean (SD) total sleep duration was 524.40 (44.40) minutes as assessed by PSG in the sleep laboratory. According to sleep logs, habitual sleep duration (mean [SD], 555.00 [54.60] minutes) in the home environment was on average 31 minutes longer than PSG sleep duration. The correlation between habitual sleep duration and PSG total sleep time was 0.51 ($P<.001$).

There were 4 sleep parameters that differed significantly across psychiatric diagnoses. Subjects in the high-risk and low-risk control groups as compared with children with internalizing disorders slept longer (mean [SD], 542.66 [40.37] minutes, 521.68 [42.69] minutes, and 518.45 [44.36] minutes, respectively; $F=9.43$; $P<.001$), fell asleep slightly faster (mean [SD], 19.90 [18.58] minutes, 19.40 [15.06] minutes, and 25.43 [22.99] minutes, respectively; $F=3.48$; $P=.03$), and had longer wake after sleep onset (mean [SD], 26.52 [20.80] minutes, 29.70 [27.37] minutes, and 21.77 [20.51] minutes, respectively; $F=3.73$; $P=.02$). Delta sleep was longest in the high-risk group (mean [SD], 133.77 [44.78] minutes), followed by the low-risk group (mean [SD], 115.23 [39.05] minutes) and the internalizing disorder group (mean [SD], 111.11 [38.16] minutes) ($F=9.27$; $P<.001$).

HABITUAL SLEEP DURATION, PSG SLEEP PROFILE, AND BMI *z* SCORE

Table 2 presents results of linear regression analyses for each sleep variable in relation to the BMI *z* score. The BMI *z* score was significantly and negatively related to total PSG sleep time ($\beta=-0.174$; $P=.02$), sleep efficiency ($\beta=-0.027$; $P=.01$), and REM density ($\beta=-0.256$, $P=.02$). The relationship between REM activity and BMI *z* score was at the borderline of significance ($\beta=-0.001$, $P=.06$). Although habitual sleep duration was also negatively related to BMI *z* score ($\beta=-0.124$), the association was not statistically significant ($P=.13$). Similarly, all of the other sleep parameters were not significantly related to BMI *z* score.

According to the quartile on each significant sleep variable, children were divided into 4 groups to better illustrate the dose-response relationships between sleep parameters and BMI *z* score. As shown in the **Figure**, BMI *z* scores linearly declined with total PSG sleep time, sleep efficiency, and REM density, whereas BMI *z* scores markedly declined when the REM activity was above the median (ie, REM activity=202).

After adjustment for covariates, total sleep time ($\beta=-0.179$; SE=0.088; $t=2.03$; $P=.04$) and sleep efficiency ($\beta=-0.024$; SE=0.011; $t=2.28$; $P=.02$) remained significantly associated with BMI *z* score. Stratified analyses for children with and without internalizing disorders indicated that only sleep efficiency was significantly related to BMI *z* score ($\beta=-0.032$; SE=0.015; $t=2.21$; $P=.03$) in nonpsychiatric control subjects. The total sleep time–BMI *z* score relationships were very similar between children with internalizing disorders ($\beta=-0.142$; SE=0.104; $t=1.36$; $P=.18$) and nonpsychiatric control subjects ($\beta=-0.162$; SE=0.103; $t=1.56$; $P=.12$). Although the relationships between REM sleep parameters and BMI *z* score were slightly stronger in children with internalizing disorders than in nonpsychi-

Table 2. Linear Regression Analyses for Habitual Sleep Duration, Polysomnographic Sleep Profiles, and Body Mass Index *z* Score

	BMI *z* Score (N=335)			
Sleep Variable	**β**	**SE**	***t***	***P* Value**
Habitual sleep duration, h (n=181)	–0.124	0.081	1.53	.13
Polysomnographic sleep continuity				
Sleep latency, min[a]	0.114	0.081	1.41	.16
Wake time after sleep onset, min[a]	0.068	0.061	1.11	.27
Total sleep time, h	–0.174	0.073	2.40	.02
Sleep efficiency, %	–0.027	0.010	2.60	.01
NREM sleep stage, h				
Stage 1	–0.169	0.267	0.63	.53
Stage 2	–0.113	0.073	1.55	.12
Delta sleep	–0.016	0.078	0.20	.84
REM sleep				
Time, h	–0.127	0.140	0.91	.36
Latency, h	–0.067	0.065	1.03	.31
Activity, units of REM[b]	–0.001	0.001	1.88	.06
Density, units/min[b]	–0.256	0.107	2.39	.02

Abbreviations: BMI, body mass index (calculated as weight in kilograms divided by height in meters squared); NREM, non–rapid eye movement; REM, rapid eye movement.

[a] Log transformed for approximate normal distribution.

[b] The REM activity is the total units of REM during sleep, and the REM density is the average semiquantitative estimate of eye movements per minute of REM sleep.

atric control subjects (REM time: β=–0.116, SE=0.194 vs β=–0.089, SE=0.201, respectively; REM activity: β=–0.002, SE=0.001 vs β=–0.001, SE=0.001, respectively; and REM density: β=–0.310, SE=0.532 vs β=–0.167, SE=0.145, respectively), none was significant.

COMPARISON OF SLEEP PARAMETERS ACROSS WEIGHT STATUS

Table 3 shows the means and standard deviations of habitual sleep duration and PSG sleep parameters across weight status and statistical comparisons.

Analysis of variance showed that total PSG sleep time, sleep efficiency, and all of the REM sleep variables differed significantly across weight status. Compared with normal-weight children, overweight children slept approximately 22 minutes less and had lower sleep efficiency, less REM sleep time, longer REM latency, and less REM activity and density. Post hoc test results are presented in Table 3.

After adjustment for covariates, analysis of covariance showed that total PSG sleep time, REM time, and REM activity were still significantly different across weight status, and REM latency was at the borderline of significance (*P*=.06). Stratified analyses showed that most sleep parameters across weight status were very similar between children with and without internalizing disorders. However, REM activity had significant differences between the overweight group (mean [SD], 167.91 [71.30]) and the groups of normal weight (mean [SD], 205.10 [75.96]) and at risk for overweight (mean [SD], 207.55 [56.55]) (*F*=3.53; *P*=.03) in children with internalizing disorders. Among children without internalizing disorders, total PSG sleep time had significant differences across the overweight group (mean [SD], 509.40 [61.80] minutes), the group at risk for overweight (mean [SD], 520.80 [34.80] minutes), and the normal-weight group (mean [SD], 537.00 [41.40] minutes) (*F*=3.50; *P*=.03).

LOGISTIC REGRESSION ANALYSIS

Table 4 presents unadjusted and adjusted odds ratios (ORs) and 95% confidence intervals (CIs) of overweight for each sleep parameter. As shown in Table 4, unadjusted ORs were significant for reduced total PSG sleep time, sleep efficiency, and reduced REM time, activity, and density. After adjustment for covariates, reduced habitual sleep time became significant (OR=2.12; 95% CI, 1.05-4.28), whereas sleep efficiency was no longer significant. As another way to illustrate the magnitude of the effects, 1 hour less of total sleep time as assessed by both sleep logs and PSG was associated with about 2-fold increased odds of overweight. One hour less of REM sleep was associated with about 3-fold increased odds for overweight. The REM density and activity below the median were associated with 2- and 3-fold increased odds, respectively, for overweight.

Stratified analyses indicated that most sleep parameters had similar associations with overweight between children with and without internalizing disorders. Consistently, reduced REM time was significantly associated with overweight for both children with (OR=3.17; 95% CI, 1.16-8.68; Wald statistic=5.05; *P*=.02) and without (OR=5.13; 95% CI, 1.08-24.35; Wald statistic=4.23; *P*=.04) internalizing disorders. Reduced REM activity was significantly associated with overweight in children with internalizing disorders (OR=3.17; 95% CI, 1.33-7.54; Wald statistic=6.83; *P*=.009) but not in nonpsychiatric control children (OR=2.62; 95% CI, 0.76-9.06; Wald statistic=2.31; *P*=.13).

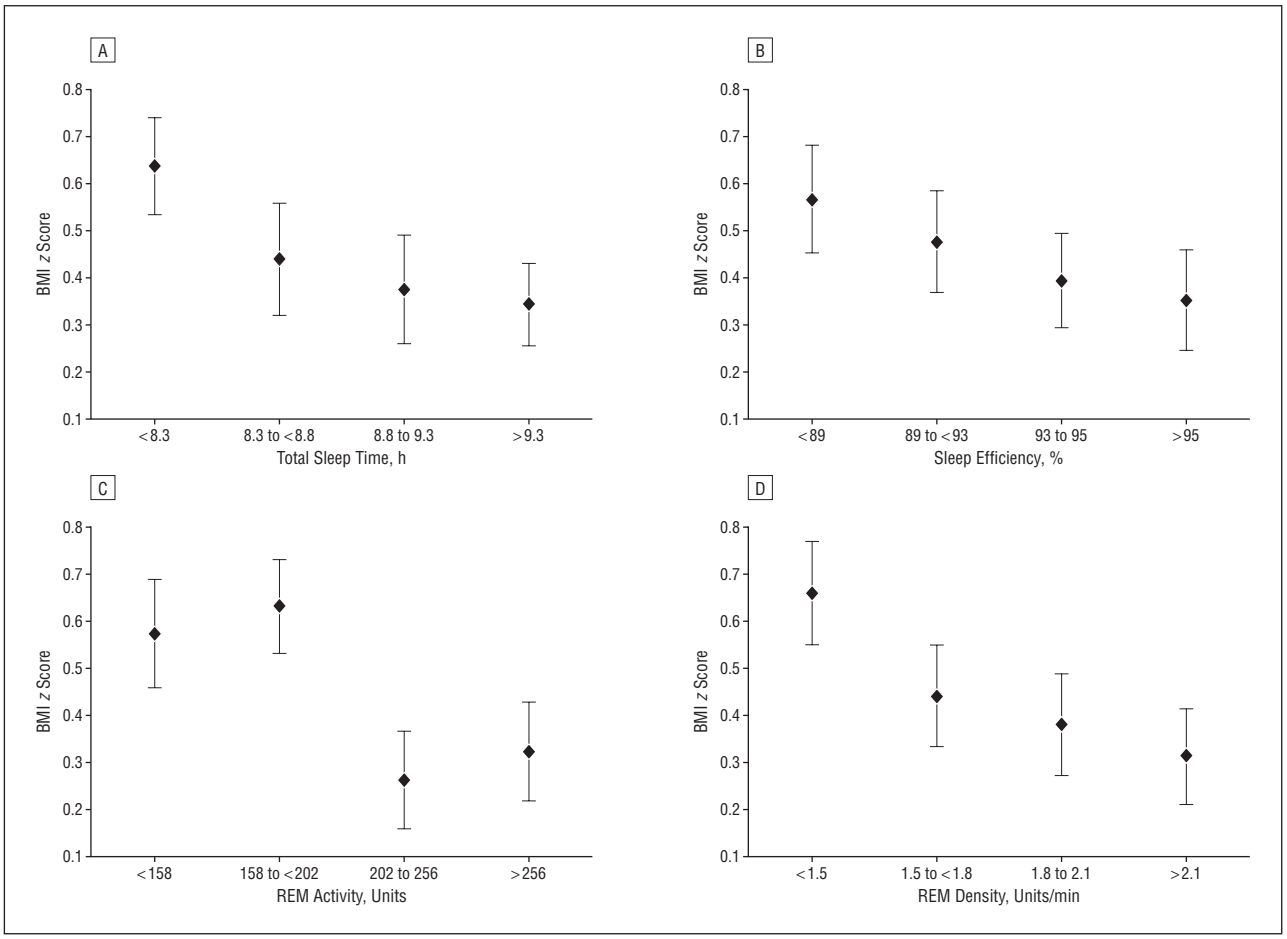

Figure. The associations between sleep parameters and body mass index (BMI) (calculated as weight in kilograms divided by height in meters squared) *z* score in 335 children and adolescents. Mean (SE) BMI *z* scores across 4 categories of total sleep time (A), sleep efficiency (B), rapid eye movement (REM) activity (C), and REM density (D) according to quartile. The BMI *z* scores are standardized BMI scores according to the Centers for Disease Control and Prevention growth charts for age and sex. The REM activity is the total units of REM during sleep, and the REM density is the average semiquantitative estimate of eye movements per minute of REM sleep.

Multiple logistic regression analysis was performed to determine which sleep stage (stage 1, stage 2, delta, or REM sleep) was independently associated with overweight after adjustment for other sleep stages and covariates. As indicated in **Table 5**, only reduced REM sleep was significantly and independently associated with overweight (OR=3.00; 95% CI, 1.14-7.90; *P*=.03). Separate analysis showed that reduced REM sleep was consistently but not significantly associated with overweight for both children with internalizing disorders (OR=2.18; 95% CI, 0.67-7.16) and nonpsychiatric control subjects (OR=4.86; 95% CI, 0.57-41.46).

COMMENT

This study investigated the associations between sleep profiles and high BMI and overweight in a large sample of children and adolescents who had participated in a project examining the neurobiology of pediatric affective disorders. This is the largest study to our knowledge that reports that short PSG sleep duration is significantly related to overweight in children and adolescents. This represents the first study to report specifically that REM sleep seems to be the stage most strongly associated with childhood overweight.

Consistent with previous epidemiological studies,[9,10] we found that elevated BMI and overweight in children and adolescents were associated with short sleep time as assessed by both sleep logs and PSG. Although the precise mechanisms are currently under investigation, the association between short sleep duration and overweight may be attributed to the interaction of behavioral and biological changes as a result of sleep deprivation.[9] First, sleep loss causes metabolic and endocrine changes, such as reduced leptin levels and increased ghrelin levels and insulin resistance.[20-22,39] Second, sleep loss may promote obesity through increased hunger and appetite and/or preference for calorie-rich foods.[22,40,41] Third, sleep loss causes extra time awake that provides increased opportunity for eating per 24 hours.[9,11] Fourth, sleep loss increases fatigue and/or excessive daytime sleepiness the following day and decreases daily physical activities, which in turn reduces energy expenditure. In addition, tiredness and irritability may interfere with inhibitory control and result in less effective avoidance of unhealthy eating.

Our analyses consistently indicated that reduced REM sleep time and activity, but not NREM sleep stages, were associated with elevated BMI or overweight. Because our

Table 3. Habitual Sleep Duration and Polysomnographic Sleep Profiles Across Weight Status and Statistical Comparisons

Sleep Variable	Weight Status, Mean (SD)[a]			Statistical Test[b]		
	Normal (n=241)	At Risk for Overweight (n=49)	Overweight (n=45)	ANOVA *F* (*P* Value)	ANCOVA *F* (*P* Value)	Post Hoc Test by LSD[c]
Habitual sleep time, h[d]	560.47 (52.91)	541.94 (51.57)	543.11 (63.46)	2.10 (.13)	1.49 (.22)	
Sleep continuity, min						
Sleep latency[e]	2.86 (0.63)	2.89 (0.70)	2.94 (0.77)	0.26 (.77)	0.10 (.91)	
WASO[e]	2.81 (0.89)	2.93 (0.81)	3.06 (0.84)	1.76 (.17)	1.36 (.26)	
Total sleep time	530.06 (41.87)	516.45 (33.66)	507.55 (58.65)	5.90 (.003)	4.43 (.01)	1 > 2, 3
Sleep efficiency, %	92.16 (4.41)	91.37 (4.77)	89.75 (8.25)	3.85 (.02)	1.87 (.16)	1 > 3
NREM sleep stage, min						
Stage 1	21.22 (11.84)	22.02 (9.62)	22.42 (15.37)	0.24 (.79)	0.14 (.87)	
Stage 2	276.84 (42.89)	268.89 (43.11)	267.74 (50.20)	1.27 (.28)	0.97 (.38)	
Delta sleep	119.78 (41.48)	111.36 (44.96)	117.04 (38.69)	0.78 (.46)	0.32 (.73)	
REM sleep						
Time, min	112.88 (22.49)	114.68 (20.33)	101.10 (26.33)	5.63 (.004)	3.12 (.04)	1, 2 > 3
Latency, min	117.88 (49.94)	98.66 (44.23)	122.68 (49.28)	3.65 (.03)	2.92 (.06)	1, 3 > 2
Activity, units of REM[f]	212.96 (75.08)	209.41 (66.88)	171.33 (84.44)	5.83 (.003)	3.08 (.047)	1, 2 > 3
Density, units/min[f]	1.87 (0.51)	1.82 (0.43)	1.62 (0.50)	4.72 (.009)	2.41 (.09)	1 > 3

Abbreviations: ANCOVA, analysis of covariance; ANOVA, analysis of variance; LSD, least significant difference; NREM, non–rapid eye movement; REM, rapid eye movement; WASO, wake after sleep onset.

[a] Normal weight was below the 85th percentile of body mass index (calculated as weight in kilograms divided by height in meters squared) of the Centers for Disease Control and Prevention growth charts for age and sex; at risk for overweight was from the 85th percentile to less than the 95th percentile; and overweight was at or higher than the 95th percentile.

[b] Without and with adjustment for age, sex, socioeconomic status, ethnicity (white, black, or other), pubertal status (prepubertal or postpubertal), and diagnosis (internalizing disorder, high-risk normal, or low-risk normal).

[c] For any significant variable with ANOVA. 1 indicates normal weight; 2, at risk for overweight; and 3, overweight.

[d] There were 127 normal-weight children, 30 children at risk for overweight, and 24 overweight children.

[e] Log transformed for approximate normal distribution.

[f] The REM activity is the total units of REM during sleep, and the REM density is the average semiquantitative estimate of eye movements per minute of REM sleep.

Table 4. Results of Logistic Regression Analyses[a]

Sleep Variable	Unadjusted			Adjusted		
	OR (95% CI)	Wald Statistic	*P* Value	OR (95% CI)	Wald Statistic	*P* Value
Reduced habitual sleep time, h[b]	1.32 (0.83-2.11)	1.34	.25	2.12 (1.05-4.28)	4.39	.04
Sleep continuity						
Sleep latency, min[c]	1.18 (0.73-1.89)	.05	.49	0.96 (0.55-1.68)	0.02	.88
Wake time after sleep onset, min[c]	1.37 (0.94-1.99)	2.75	.10	1.26 (0.83-1.92)	1.21	.27
Reduced sleep time, h	1.74 (1.16-2.61)	7.15	.007	1.85 (1.08-3.16)	5.00	.02
Sleep efficiency, %	0.94 (0.89-0.99)	6.11	.01	0.96 (0.90-1.02)	1.95	.16
NREM sleep stage, h						
Reduced stage 1	0.65 (0.14-2.98)	0.30	.58	0.73 (0.12-4.50)	0.12	.73
Reduced stage 2	1.26 (0.83-1.91)	1.21	.27	1.35 (0.82-2.23)	1.41	.24
Reduced delta sleep	1.03 (0.65-1.63)	0.01	.90	0.97 (0.50-1.86)	0.01	.92
REM sleep						
Reduced REM time, h	3.96 (1.71-9.15)	10.37	.001	2.91 (1.12-7.66)	4.70	.03
REM latency, h	1.21 (0.84-1.76)	1.03	.31	1.22 (0.80-1.87)	0.89	.35
Reduced REM activity below the median, units of REM[d]	3.20 (1.59-6.45)	10.62	.001	3.32 (1.47-7.50)	8.31	.004
Reduced REM density below the median, units/min[d]	2.27 (1.18-4.37)	6.02	.01	2.18 (1.03-4.62)	4.19	.04

Abbreviations: CI, confidence interval; NREM, non–rapid eye movement; OR, odds ratio; REM, rapid eye movement.

[a] Without and with adjustment for age, sex, socioeconomic status, ethnicity (white, black, or other), pubertal status (prepubertal or postpubertal), and diagnosis (internalizing disorder, high-risk normal, or low-risk normal). There were 45 overweight children and 290 children who were not overweight.

[b] There were 24 overweight children and 157 children who were not overweight.

[c] Log transformed for approximate normal distribution.

[d] The REM activity is the total units of REM during sleep, and the REM density is the average semiquantitative estimate of eye movements per minute of REM sleep.

sample comprised children and adolescents with and without internalizing disorders, whether these findings could be generalized to the general population of children and adolescents needs further research. However, while sleep PSG changes characterized by impaired sleep efficiency, reduced slow-wave sleep, and disinhibited REM sleep have been consistently demonstrated in adult depression,[42] findings of PSG studies in child depression are equivocal and

REM sleep abnormalities appear to occur less frequently in child depression than in adult depression.[43] In the current study, we did not find significant differences in REM sleep time and REM activity between children with and without internalizing disorders. A series of separate analyses indicated that the associations of high BMI with most sleep parameters were similar between children with and without internalizing disorders. Although the association between reduced REM sleep and BMI and overweight appeared to be slightly stronger in children with internalizing disorders than in nonpsychiatric control subjects, logistic regression analyses showed that reduced REM sleep was more strongly associated with overweight in nonpsychiatric control subjects than in children with internalizing disorders. Taken together, our findings suggest that the REM sleep–overweight association may exist independent of psychiatric diagnosis.

The significant association between reduced REM sleep and overweight suggests that the short sleep–obesity association may be attributed to reduced REM sleep. Compared with NREM sleep deprivation, REM sleep loss may be more likely to alter the balance of energy intake and expenditure—increasing food intake and decreasing energy expenditure. This speculation is supported by previous findings that sleeping metabolic rate and energy expenditure in humans differ across sleep stages, with sleeping metabolic rate being significantly higher in REM sleep,[23] and that diminished sleeping metabolic rate is associated with high BMI.[44] It is also speculated that endocrine changes may be more sensitive to reduced REM sleep, such as decreased leptin levels and increased ghrelin levels. These endocrine changes due to REM sleep loss may increase hunger and appetite, which in turn increase food consumption. These hypotheses and causal relationships between reduced REM sleep and endocrine and metabolic changes need to be tested in animal and human experimental studies. Specifically, further studies would be warranted to do the following: (1) investigate metabolic and endocrine changes across specific sleep stages; (2) examine whether REM sleep loss is more likely than NREM sleep loss to contribute to a decline in 24-hour energy expenditure and/or an increase in food consumption; and (3) examine whether the association between reduced REM sleep and obesity is mediated by peripheral changes in catecholaminergic tone as plasma catecholamine levels have been reported to be lowest in REM sleep.[45,46]

There are several limitations that should be kept in mind when interpreting our results. First, 1 overnight PSG sleep in the laboratory was used for our analysis, and this may not reflect real and stable sleep in the natural home environment. For instance, sleep duration measured by 1 night of PSG was 31 minutes less than that measured by 1 week of sleep logs, and the correlation between sleep times assessed by sleep logs and PSG was moderate (r=0.51). However, the associations of BMI with sleep duration as assessed by sleep logs and PSG were similar and in the same direction. Second, the associations between sleep parameters and overweight may be underestimated because our research design excluded extremely overweight children for the original project on the neurobiology of pediatric affective disorders. This may also explain why we did not find a *u*-shaped association between sleep time and BMI.[21] Third, a single measurement was taken for weight and height, whereas an average of 3 measurements is usually recommended. However, our measurements were taken on standard equipment by trained and reliable operators. Although there may be a certain margin of measurement error, this would not be expected to change the results of a study of this size. Fourth, fat mass was assessed with BMI, which is a surrogate measure of adiposity that correlates with fat-free mass as well as total body fat and does not account for differences in body fat distribution.[47] Additional anthropometric (eg, waist and neck circumferences) and endocrine (eg, fasting glucose, insulin, leptin, and ghrelin levels) measurements may be better to interpret the REM sleep loss and overweight association. Finally, although we statistically controlled for the effects of age, sex, ethnicity, socioeconomic status, pubertal status, and psychiatric diagnosis, we could not control for the effects of several other important variables, such as sleep-disordered breathing, food intake, daily activity, family history of obesity, and parental BMI, because we did not collect these data.

Table 5. Independent Associations Between Each Sleep Stage and Overweight[a]

Reduced Sleep Time, h	OR (95% CI)	Wald Statistic	*P* Value
Stage 1 sleep	0.91 (0.13-6.24)	0.01	.93
Stage 2 sleep	1.62 (0.86-3.06)	2.22	.14
Delta sleep	1.38 (0.59-3.19)	0.55	.46
REM sleep	3.00 (1.14-7.90)	4.92	.03

Abbreviations: CI, confidence interval; OR, odds ratio; REM, rapid eye movement.
[a] After adjustment for other sleep stages, age, sex, socioeconomic status, ethnicity, pubertal status, and diagnosis. There were 45 overweight children and 290 children who were not overweight.

In summary, our objective electrophysiological study of sleep with a large sample of children and adolescents confirms previous epidemiological observations that short sleep time is associated with elevated BMI and overweight. Given the fact that the prevalence of overweight among children and adolescents continues to increase and chronic sleep insufficiency becomes more prevalent in modern society, family- and school-based sleep interventions that aim to enhance sleep hygiene and increase sleep duration may have important public health implications for the prevention and intervention of obesity and type 2 diabetes in children. Furthermore, our results demonstrate an important relationship between REM sleep and high BMI and obesity, suggesting that the short sleep–obesity association may be attributed to reduced REM sleep time and decreased activity during REM sleep.

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