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Neurocognitive and Behavioral Functioning in Adolescents with Sleep Disordered Breathing: A Population-based, Dual-energy X-ray Absorptiometry Study

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Abstract

Background/Objectives—Sleep disordered breathing (SDB) has been associated with neurocognitive and behavioral problems in young children; however, this association is less studied in adolescents. Evidence suggests that obesity plays a key role in the development of SDB, although its relative association with neurobehavioral functioning remains unclear. We examined whether SDB and obesity are associated with neurocognitive and behavior problems in adolescents.

Subjects/Methods—421 adolescents (17.0±2.2y, 53.9% male) from the Penn State Child Cohort, a general population sample, underwent a 9-hour polysomnography, clinical history, physical examination, neurocognitive evaluation, and Dual-energy X-ray Absorptiometry (DXA) scan, and completed the Child or Adult Behavior Checklist. Obstructive sleep apnea (OSA) was defined as an apnea-hypopnea index (AHI) ≥ 2, primary snoring (PS) as AHI<2+snoring, and no-SDB as AHI<2 without snoring. Body weight measures included body mass index (BMI) percentile, waist circumference (WC), and DXA-measured total adipose tissue (TAT).

Results—WC and TAT were significantly associated with impaired vigilance, processing speed, working memory, and control interference and greater internalizing and externalizing behaviors, while BMI percentile was marginally associated. SDB per se (PS, AHI, or OSA) was not significantly associated with impaired neurocognitive outcomes or greater behavioral problems. However, TAT was significantly associated with impaired vigilance and greater internalizing and externalizing behaviors and, to a lesser extent, slower processing speed and greater control interference, only in adolescents with OSA.

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Conclusions—Central obesity, an etiopathogenic mechanism of OSA, is more strongly associated with neurocognitive and behavioral problems in adolescents than SDB alone. Deficits in low-order (vigilance) and high-order (executive) functions and behavioral problems observed in adolescents with OSA are primarily associated with increased central adiposity, a finding not entirely captured with less precise measures of obesity. These data support that OSA and its associated neurocognitive and behavioral morbidity are related to underlying metabolic dysfunction as early as adolescence.

INTRODUCTION

Sleep disordered breathing (SDB) is a spectrum of sleep-related breathing abnormalities ranging from primary snoring (PS) to obstructive sleep apnea (OSA). SDB has been associated with parent-reported behavioral problems and objectively measured neurocognitive deficits in young children, typically 5–12 years old.[1–23] However, inconsistencies exist across studies with regard to which neurocognitive functions and behaviors are affected by SDB, as well as the degree of independent relationship between the SDB severity and these outcomes.[6,8,15–16,17–20,22] These discrepancies in the literature may be partially explained by the lack of control for potential confounders such as body weight in the vast majority of previous studies. Furthermore, recent well-designed SDB clinical trials have suggested limited improvement in behavioral or neurocognitive functioning following adeno/tonsillectomy in young children.[24]

In a recent study, we reported that the prevalence of moderate OSA increases 10-fold (from 1.4% to 10.5%) from childhood to adolescence.[25] Despite this sharp increase, limited data has been published exclusively in adolescents on the association of SDB with neurocognition and behavioral problems during this important developmental period. To our knowledge, only six published studies have reported on the association between objectively-measured SDB and neurocognitive and/or behavioral functioning during middle to late childhood comparing those with SDB to controls, and only one of which was a general population study. [26–31] Consistent with the idea that behavior and neurocognitive problems exist in increased frequency in children with SDB and in children who are obese, four studies in clinical samples of adolescents reported on the association between SDB in overweight or obese adolescents and neurocognitive and/or behavioral functioning. Overall, study results indicated increased parent-reported internalizing[27,28] and externalizing problems,[28,29] and teacher-reported learning problems,[29] lower academic grades,[29] lower math computation scores[30] and poorer executive functioning[27] in those with SDB and obesity/overweight status when compared to obese children without SDB[27–30] and/or lean control groups.[27] In contrast, no neurocognitive differences in IQ,[28–30] memory,[28–30] attention,[29] fine motor,[29] problem-solving,[29] or academic achievement[28,30] were found after controlling for various confounders. A pilot study reported lower scores on measures of memory, learning and verbal intelligence in morbidly obese children and adolescents with OSA as compared to those without OSA.[31] In a longitudinal study of 263 children and adolescents from the Tucson Children's Assessment of Sleep Apnea (TuCASA) cohort followed up 5 years later, increased externalizing problems (hyperactivity, inattention, aggression) and poorer communication and social competency in youth with persistent or incident SDB were reported after controlling for body mass index (BMI).[26] Thus, given the

inconsistencies and limited studies reporting on the impact of SDB and body weight on neurocognition and behavior in adolescents, as well as the likelihood that neurocognitive and behavioral problems associated with SDB in adolescents differ from those reported in young children, our study aims to examine, for the first time, the association between objectively-measured SDB with a wide range of neurocognitive and behavioral problems from a large general population sample of adolescents.

We sought to fill in a key gap in the literature by determining the associations of SDB with neurocognitive and behavioral functioning in adolescents, hypothesizing that the more severe the SDB, the poorer the neurocognitive and behavioral functioning. Second, we examined the relative association, as compared to SDB, of measures of body weight such as BMI, waist circumference, and DXA-measured adiposity with neurocognitive and behavioral functioning. Finally, we propose that the greater severity of lower-order and higher order neurocognitive deficits and greater internalizing and externalizing behavioral problems present in adolescents with OSA is associated with increased adipose tissue, above and beyond global less precise measures of body weight (i.e., BMI).

METHODS

Population

The Penn State Child Cohort (PSCC) has been described in detail in previous studies.[25,32] In brief, the PSCC is a representative population sample of 700 children (aged 5–12 years old), of whom 421 were followed-up approximately 8 years later in 2010–2013 as adolescents and consisted of 48.8% females, 16.9 ± 2.3 years old with an age range of 12–23 years old, and 22.4% identified as belonging to a racial/ethnic minority, including 13.0% Black not Hispanic and 6.5% Hispanic. There were no differences in demographic or clinical characteristics between the 421 children and the 279 lost to follow-up.[25] All participants underwent a full clinical history, physical examination, an overnight in-lab sleep study, whole-body dual-energy x-ray absorptiometry (DXA) scan and neurocognitive evaluation including behavioral measures. The study protocol was approved by Penn State University College of Medicine Institutional Review Board. Written informed consent was obtained from all participants, and their parents or legal guardians if younger than 18 years.

Key Measurements

Sleep disordered breathing—The participant's sleep was continuously monitored for 9 hours with a seven-channel electroencephalography (EEG), electrooculography (EOG), and electromyography (EMG) polysomnography (PSG; Gamma Research Data Acquisition and Analysis System; Grass-Telefactor, West Warwich, RI). Respiration was monitored with nasal pressure (Pro-Tech PTAF Lite, Mukilteo, WA), thermocouple (Salter Laboratories, Lake Forest, IL), and thoracic and abdominal strain gauges (Model 1312, Sleepmate Technologies, Midlothian, VA). Snoring sounds were monitored by a microphone attached to the throat and were defined as the presence or absence of any snoring sounds. Hemoglobin oxygen saturation (SpO_2) was obtained from the finger. The sleep records were scored according to standardized criteria by a registered PSG technologist who was blinded to participant characteristics.[33] Apneas and hypopneas were defined following standardized

criteria,[34] while taking into account the age of the subjects as previously described [25,32]. The apnea-hypopnea index (AHI) was calculated as the number of apneas and hypopneas summed per hour of sleep. Objectively monitored snoring was used in this study. Based on the AHI and objectively measured snoring we created mutually exclusive SDB groups. We defined the absence of SDB as an AHI < 2 without any evidence of snoring. Primary snoring was defined as an AHI < 2 with evidence of snoring. The presence of OSA was defined as an AHI ≥ 2; for detailed analyses, we also identified mild (2 ≤ AHI < 5) and moderate (AHI ≥ 5) OSA. These cutoffs were based on prior pediatric research,[24] including studies indicating that this level of AHI is already associated with significant adverse outcomes in adolescents.[25,52]

Anthropometric measures and body fat composition—All participants underwent a physical examination that included measurements of Tanner stage, height, weight, hip, waist, and neck circumference. Tanner staging was measured by self-report using a standardized scale.[35] Height was measured in centimeters using a stadiometer (SECA Corp., Hanover, MD, USA) and weight was assessed in kilograms (Cardinal Scale Manufacturing, Webb City, MO, USA). The age- and sex-adjusted body mass index (BMI) percentile for each participant was calculated based on growth charts for height and weight.[36] Three groups based on BMI percentile were also defined as normal weight (i.e., < 85%), overweight (i.e., ≥ 85% and < 95%), and obese (i.e., ≥ 95%). The waist circumference was measured in centimeters at the top of the iliac crest and the neck at the cricothyroid membrane. Whole-body DXA scan was used to measure the adipose tissue distribution. The DXA scan was performed by using Hologic Discovery W scanner (Hologic Inc., Waltham, MA). Participants were required to remove all metal, plastic, and rubber materials to avoid any impact on x-ray beams. Android region (waist), gynoid region (hips), visceral adipose tissue (VAT), subcutaneous adipose tissue (SAT), and total adipose tissue (TAT) were selected as regions of interest (ROI) to assess abdominal obesity. Detailed ROI defining methods have been described elsewhere.[37–38] All ROI were identified by Hologic APEX 4.0 software (Hologic Inc., Bedford, MA) and visually verified by an experienced technician. Among all potential indices, TAT area (cm^2) was our primary DXA-measured predictor in this study.

Neurocognitive functioning—All participants underwent a 2.5-hour neurocognitive evaluation prior to their overnight stay in the sleep laboratory at approximately the same time each afternoon. The standardized tests were administered individually to each participant by a trained psychometrist over one session. Tests in the neurocognitive battery were selected to assess intelligence and a range of key neurocognitive functions. Our primary neurocognitive outcomes in this study were vigilance and processing speed as well as working memory and control interference as they capture low-order and high-order, respectively, neurocognitive processes. The *Gordon Diagnostic System* (GDS), which is a continuous performance test and well-established measure of attention, was administered to measure vigilance (subtest).[39] Processing speed and working memory were assessed using two subtests from either the *Wechsler Intelligence Scale for Children, Fourth Edition* (WISC-IV) or *Wechsler Adult Intelligence Scale, Third Edition* (WAIS-III) depending on the participant's age (i.e., younger or older than 16 years old).[40–41] The Digit Span (Ds)

subtest is a measure of attention span and working memory (backward) and the Coding (Cd) subtest is a measure of speed of information processing. The *Stroop Color and Word Test, Child and Adult Version,* was used as a measure of executive functioning that involves response inhibition and cognitive flexibility.[42] The Stroop test comprises 3 trials of word (W), color (C), and color-word (CW); the difference score (I_D) between the C and CW scores is calculated (e.g., $I_D = C - CW$) and lower scores indicate less interference from incongruent W when naming the C in the CW condition and, thus, is a purer measure of response inhibition / control interference.[43]

Other secondary outcomes reported in supplemental analyses included verbal learning, academic achievement and intelligence. *The Wechsler Abbreviated Scales of Intelligence* (WASI) is a measure of verbal, performance, and full scale intelligence derived from four subtests: Block Design, Matrix Reasoning, Vocabulary, and Similarities.[44] Academic achievement was assessed using the Math Computation and Word Reading subtests from the *Wide Range Achievement Test, Third Edition* (WRAT-3).[45] The *California Verbal Learning Test-Child or Adult Version* (CVLT) was administered as a measure of verbal learning and memory.[46–47]

Behavioral functioning—Parent and self-reported questionnaires were administered to measure behavior, including internalizing and externalizing symptoms. All participants older than 18 years old completed the self-reported Adult Behavior Checklist (ABCL, 2003), while the parents of participants younger than 18 years old completed the Child Behavior Checklist (CBCL, 2001), which are widely used and equivalent tools for the assessment of behavioral problems. For each scale and subscale, T-scores with a mean of 50 and a standard deviation of 10 were obtained following standard procedures.[48–49] Our primary behavioral outcomes in this study were the Internalizing and Externalizing global scales comprising anxious/depressed, withdrawn/depressed and somatic complaints scores and rule-breaking and aggressive behavior scores, respectively. Other secondary behavioral outcomes reported in supplemental analyses included each of these subscale scores.

Data Analyses

Categorical and continuous variables were analyzed with Chi-square test and analysis of variance (ANOVA), respectively. Neurobehavioral outcomes were continuous variables and normally distributed. Multivariable-adjusted linear regression models were performed to examine the relationship between measures of SDB (i.e., AHI, SDB groups, and OSA groups), and measures of body weight (i.e., BMI percentile, BMI groups, waist circumference, and DXA-measured TAT) with neurocognitive and behavioral functioning. Second, the cohort was divided into those with (AHI ≥ 2) and without OSA (AHI < 2) and the relationship between DXA-measured TAT and neurocognitive and behavioral functioning was examined using Pearson correlations. The critical statistical confidence level for all analyses was $p < 0.05$, two-tailed. All analyses were performed using SPSS Statistics version 23 (IBM, Armonk, NY, USA).

RESULTS

Characteristics of the sample

The average AHI was 2.5 ± 0.2 events / hour of sleep with a maximum value of 91.9 events / hour of sleep and an interquartile range of 0.6, 1.4, and 2.7 events / hour of sleep. The prevalence of primary snoring, 2 ≤ AHI < 5, and AHI ≥ 5 was 25.4%, 27.3%, and 10.5%, respectively. When examining the cohort of adolescents as function of SDB status (Table 1), we observed a significantly increased frequency of males ($p < 0.01$) and ethnic minority ($p = 0.022$) with increasing SDB severity. Adolescents with SDB were significantly older ($p < 0.01$) and had greater BMI percentile, neck circumference, and waist circumference (all $p < 0.01$). DXA-measured TAT was significantly elevated as SDB severity increased ($p = 0.016$), an association primarily reflective of increased VAT ($p < 0.01$) rather than SAT ($p = 0.121$).

The average BMI percentile was 62.9 ± 1.4 and the prevalence of obesity (15.2%) was similar to that reported in the general population for this age group. When the sample was stratified by BMI percentile status (Table 1), overweight and obesity were associated with a significantly greater frequency of ethnic minority ($p < 0.01$), later stages of pubertal development ($p = 0.014$), a lower minimum SpO_2 ($p = 0.049$), and, as expected, greater neck circumference, waist circumference, and DXA-measured TAT (all $p < 0.01$).

Relative association of SDB and body weight with neurocognitive and behavioral functioning

First, we examined the associations of various measures of SDB and body weight with neurocognitive (vigilance, processing speed, working memory, and control interference) and behavioral (internalizing and externalizing behaviors) functioning (Table 2). No measures of sleep apnea – neither AHI, SDB groups (none, snore, 2≤AHI<5, AHI≥5), OSA groups (AHI<2 vs. AHI≥2), nor minimum SpO_2 – were significantly associated with any measures of neurocognitive or behavioral functioning (all p values > 0.10). In contrast, body weight was significantly associated with all domains of neurocognitive and behavioral functioning. Importantly, the more precise the body weight measures (i.e., DXA-measured TAT > waist circumference > BMI percentile), the stronger the associations between body weight and neurocognitive and behavioral outcomes (Table 2). For example, although elevated BMI percentile was significantly associated with poorer working memory ($\beta = -0.115$, $p < 0.05$) and only marginally associated with decreased vigilance, greater control interference, and greater externalizing behaviors (all $p < 0.10$), DXA-measured TAT was more strongly associated with decreased vigilance ($\beta = -0.114$, $p < 0.05$), poorer working memory ($\beta = -0.119$, $p < 0.05$), slower processing speed ($\beta = -0.139$) and greater internalizing ($\beta = 0.176$) and externalizing ($\beta = 0.139$) behaviors (all $p < 0.01$) in the overall sample. Importantly, there were no significant associations between body weight measures and other measures of cognition such as IQ, achievement or verbal learning (Supplemental Table 1), suggesting that the associations found between body weight and specific lower-order and higher-order cognitive functions (i.e., vigilance, processing speed, working memory and control interference) were not related to or explained by an underlying association with decreased general ability (e.g., IQ).

Association of adiposity with neurocognitive and behavioral functioning in adolescent OSA

Second, given that body weight measures were significantly associated with OSA (Table 1) and more strongly related to neurocognitive and behavioral outcomes than SDB measures alone (e.g., AHI, SpO2), we examined whether this association was primarily found in adolescents with OSA. We divided the cohort into those with (n = 159) and without (n = 262) OSA as defined by an AHI ≥ 2 and examined the association between adiposity, neurocognitive, and behavioral outcomes (Table 3).

As shown in Table 3, while DXA-measured TAT was not associated with any cognitive domains in adolescents without OSA (all $p > 0.10$), it was significantly associated with decreased vigilance ($\beta = -0.233$, $p \leq 0.05$) and marginally associated with slower processing speed ($\beta = -0.136$, $p \leq 0.10$) and greater control interference ($\beta = 0.154$, $p \leq 0.10$) in those with OSA. Furthermore, DXA-measured TAT was significantly associated with internalizing ($\beta = 0.237$, $p \leq 0.01$) and externalizing behaviors ($\beta = 0.217$, $p \leq 0.01$) in those with OSA, while only marginally associated among those without OSA ($\beta = 0.115$ and $\beta = 0.105$, respectively, $p \leq 0.10$).

These stratified analyses also showed differential associations between neurocognition and behavior as a function of OSA status. In those with OSA, greater control interference was significantly associated with greater internalizing ($\beta = 0.185$, $p \leq 0.05$) and externalizing ($\beta = 0.371$, $p \leq 0.01$) behaviors, while slower processing speed ($\beta = -0.248$, $p \leq 0.01$) and poorer working memory ($\beta = -0.200$, $p \leq 0.05$) were significantly associated with greater externalizing behaviors (Table 3). Among those without OSA, slower processing speed was significantly associated with greater internalizing ($\beta = -0.182$, $p \leq 0.01$) and externalizing ($\beta = -0.287$, $p \leq 0.01$) behaviors, while greater control interference ($\beta = 0.216$, $p \leq 0.01$) was significantly associated only with greater externalizing behaviors (Table 3).

DISCUSSION

In this general population study of 421 adolescents, we found that increased body weight, particularly measures of central adiposity, is more strongly associated with neurocognitive and behavioral functioning than the severity of SDB per se. Overall, no measure of SDB was significantly associated with any measure of neurocognitive or behavioral functioning. In contrast, we demonstrated that increased body weight was significantly associated with poorer vigilance, processing speed, and working memory as well as internalizing and externalizing behaviors, and that increased precision of body weight measures (i.e., DXA-measured adipose tissue > waist circumference > BMI percentile) yielded the strongest associations between increased body weight and neurocognitive and behavioral outcomes in adolescents. Importantly, we also found that DXA-measured adiposity was significantly associated with decreased vigilance, greater internalizing and externalizing behaviors and, marginally with slower processing speed and greater control interference, only in those adolescents with OSA. Thus, we demonstrated that the greater deficits associated with adolescent OSA in lower-order (vigilance) and higher-order (executive) control of attention are primarily associated with increased DXA-measured adiposity, a finding that cannot be entirely captured with global measures of body weight such as BMI percentile. These

findings have direct implications for the way we currently screen, diagnose and treat SDB and its associated neurobehavioral sequelae in adolescents, which may require the integration of weight loss as part of the routine clinical care of adolescents with OSA beyond surgical and/or positive airway pressure interventions.

In our study, SDB alone was not associated with any objectively-measured neurocognitive deficits. Rather, body weight measures were associated in a dose-response manner with specific neurocognitive functions of working memory, processing speed, and vigilance. This finding suggests that central obesity, an etiopathogenic mechanism of OSA, is more strongly associated with neurocognitive problems in adolescents than the presence or severity of SDB alone. Interestingly, DXA-measured adiposity was most strongly associated with decreased vigilance, and not with increased distractibility, in adolescents with OSA. One of the proposed mechanisms for such an association of central adiposity with decreased vigilance in those with OSA is the role of chronic, low-grade inflammation, as indexed by increased pro-inflammatory cytokines.[50–53]

Similarly, we reported that SDB alone was not associated with internalizing or externalizing behaviors, but rather with body weight. This is interesting in light of the fact that one of the most commonly reported findings in the literature is the comorbidity of OSA and behavioral problems, including disorders such as attention deficit hyperactivity disorder (ADHD).[54] While children and adolescents with ADHD are typically below average in terms of body weight, those with OSA are typically overweight or obese and still found to commonly receive a comorbid diagnosis of ADHD.[55] In the present study, central adiposity as measured by DXA scan was associated with the neurocognitive functions typically impaired in adolescents diagnosed with ADHD, i.e., vigilance, processing speed, and control interference, but not with the self- or parent-reported severity of attention problems (see Supplemental Table 2). Furthermore, ADHD in adolescence is typically characterized by attention deficits rather than hyperactivity.[28, 29] Our data suggests that the link between OSA and attention deficits observed in previous adolescent studies and clinical samples may be primarily related to adolescents with decreased vigilance and increased central adiposity, [6, 8, 11] a finding that may not be entirely captured by global measures of body weight such as BMI percentile, which is the norm in most previous SDB studies.[5, 26] This finding has significant implications for interpreting previous findings in the literature and should guide future studies in adolescents with SDB by including body fat distribution measures when studying samples of adolescents with SDB as compared to healthy controls.

Another interesting finding of our study was that DXA-measured adiposity was associated with internalizing and externalizing problems in adolescents, and more strongly in those with OSA. Our study supports the findings of others[56–57] that childhood and adolescent obesity is associated with increased anxiety and depression, lower self-esteem, and psychosomatic complaints as well as aggressive behaviors (see Supplemental Table 2), especially during this developmental period of adolescence in which psychosocial factors such as peer-pressure, bullying and discrimination peak. It is also plausible that underlying systemic mechanisms such as activation of the stress system or increased inflammation also observed in dysfunctional mood states may be at play in adolescent with OSA. Moreover, executive components of attention (i.e., control interference) were significant neurocognitive

correlates of internalizing behaviors such as anxiety and depression in adolescents with OSA, while lower-order components of attention (i.e., slower processing speed) were in those without OSA. Indeed, multiple studies have shown slowed processing speed in children or adolescents with anxiety or depressive disorders. Our novel findings indicate that executive deficits in control interference and working memory may also contribute to anxiety and depression and aggressive behaviors, respectively, in adolescents with OSA. Taken together, our findings suggest that the presence of OSA helps identify those adolescents in whom the association between central adiposity and neurocognitive and behavioral deficits is stronger.

From a clinical stand point, the results of this study demonstrate the benefit of using more precise measures of body weight in order to disentangle the underlying mechanisms driving the association of SDB with neurocognitive and behavioral outcomes, and in turn influence treatment. These findings have direct implications for the way we currently screen, diagnose and treat SDB and its associated neurobehavioral sequelae in adolescents, which may require the integration of weight loss as part of the standard treatment of SDB in adolescents, which may include anatomical and surgical interventions of the upper-airway or positive airway pressure. Previous studies aimed at treating SDB have not been successful in demonstrating improvements in neurocognitive outcomes, potentially because the intervention did not address the underlying metabolic factors of the condition (e.g., central adiposity) that may be present even in non-obese children or adolescents.[24] Furthermore, the results align with prior studies that generally did not detect significant neurocognitive differences between adolescents with and without OSA.[26–30] One prior study reported deficits in executive functioning in adolescents with obesity and OSA, as compared to obese adolescents and lean controls.[27] These results fit within the context of the present study in that the association of central obesity with neurocognitive deficits was more strongly associated in those with OSA. The present findings may also help explain discrepancies in the literature, as many studies failed to control for body weight[30–31] or utilized less precise measures (i.e., BMI percentile).[5, 26]

Several limitations apply to this study. The study is cross-sectional and does not allow causal conclusions. Capnography was not included in the PSG recording, which limited the ascertainment of hypoventilation syndrome; however, this type of SDB is more common in clinical versus general population samples. Despite these limitations, this study extends the limited previous knowledge on behavioral and objectively-measured neurocognitive functioning in adolescents with SDB using a random general population sample and objective measures of sleep and body weight. Future studies should examine the role of pro-inflammatory cytokines to further delineate the relationship between SDB and adiposity with neurocognitive deficits and behavioral problems.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

Acknowledgments

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Table 1

Characteristics of the sample stratified by sleep disordered breathing and body mass index groups

	None(n = 155)	Snoring(n = 107)	2≤AHI<5(n = 115)	AHI≥5(n = 44)	P	BMI%<85(n = 278)	85≤BMI%<95(n = 79)	BMI%≥95(n = 64)	P
Male (%)	41.9	50.5	67.0	70.5	**<0.01**	54.0	53.2	54.7	0.983
Ethnic-Minority (%)	16.8	17.8	31.3	25.0	**0.022**	18.7	20.3	37.5	**<0.01**
White	83.2	82.2	68.7	75.0	**0.024**	81.3	79.7	62.5	**0.016**
Black	9.7	10.3	20.0	9.1		10.4	11.4	23.4	
Hispanic	4.5	5.6	8.7	9.1		5.0	7.6	10.9	
Other	2.6	1.9	2.6	6.8		3.2	1.3	3.1	
Age (years)	16.4±2.1	16.7±2.2	17.3±2.2	18.4±2.1	**<0.01**	16.9±2.2	17.3±2.5	16.8±2.1	0.326
Adeno/tonsillectomy (%)	7.1	11.2	13.9	18.2	0.189	10.8	7.6	18.8	0.097
Tanner (%)					0.064				**0.014**
Pre-pubertal	0.7	0.9	1.8	0.0		1.1	0.0	1.6	
Early pubertal	3.4	0.0	0.0	0.0		1.5	1.3	0.0	
Mid puberty	14.2	17.9	10.8	7.3		14.9	11.8	9.7	
Late puberty	45.9	44.3	52.3	41.5		50.0	40.8	40.3	
Adulthood	35.8	36.8	35.1	51.2		32.5	46.1	48.4	
AHI	0.8±0.6	1.0±0.5	3.1±0.9	12.1±13.9	**<0.01**	2.3±5.9	3.1±4.6	3.9±5.1	0.076
SpO_2	92.0±5.6	91.7±4.1	91.1±5.0	90.1±6.6	0.130	91.7±4.9	91.8±3.7	90.0±7.6	**0.049**
BMI%	60.1±28.4	62.2±28.9	70.1±26.6	79.0±25.6	**<0.01**	50.7±24.1	90.5±3.0	97.8±1.4	**<0.01**
Neck circumference (cm)	34.1±2.9	34.9±3.2	37.0±7.2	38.6±4.7	**<0.01**	34.4±4.9	36.3±3.1	39.7±4.3	**<0.01**
Waist circumference (cm)	76.3±10.5	79.1±12.4	83.1±12.9	90.8±18.3	**<0.01**	73.8±7.3	85.5±7.5	102.4±13.2	**<0.01**
Total adipose tissue (cm^2)	247.4±149.8	270.3±202.9	292.4±203.4	349.0±228.8	**0.016**	182.6±95.3	353.2±145.3	576.4±183.8	**<0.01**
Subcutaneous (cm^2)	197.9±126.9	214.8±171.6	225.1±167.4	261.8±180.4	0.121	142.5±88.3	278.1±127.5	452.1±149.6	**<0.01**
Visceral (cm^2)	49.6±29.5	55.6±35.9	67.4±41.3	87.3±53.9	**<0.01**	40.1±15.9	75.2±27.5	124.2±42.8	**<0.01**

AHI = apnea hypopnea index. BMI% = body mass index percentile for sex and age. SpO_2 = nocturnal oxygen desaturation.

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Table 2

Multivariable-adjusted standardized linear regression coefficients of the relationship between measures of sleep disordered breathing and body weight with neurocognitive and behavioral functioning

	Vigilance	Processing Speed	Working Memory	Control Interference	Internalizing Behaviors	Externalizing Behaviors
AHI	.004	−.007	−.070	−.022	.012	.012
SDB	−.006	.018	−.079	−.038	−.043	−.013
OSA	−.024	.016	−.081	.016	−.006	−.025
SpO_2	.007	−.023	−.015	.014	−.008	.012
BMI%	**−.087**^{T}	−.038	**−.115***	**.084**^{T}	.025	**.082**^{T}
BMI% groups	−.054	**−.079**^{T}	−.073	.021	.072	.072
Waist circumference	−.068	**−.113***	**−.112***	.057	**.126***	**.120***
Total adipose tissue	**−.105***	**−.139****	**−.119***	**.089**^{T}	**.176****	**.139****
Subcutaneous	**−.103**^{T}	**−.144****	**−.121***	**.094**^{T}	**.192****	**.145****
Visceral	**−.114***	**−.124****	**−.109***	.065	**.121****	**.119***

Data are standardized linear regression coefficients (β) adjusted for gender, age and race. AHI = apnea hypopnea index. SDB = dummy variable of none (0), primary snoring (snoring + AHI < 2 = 1), mild OSA (2 ≤ AHI < 5 = 2), and moderate OSA (AHI ≥ 5 = 3). OSA = dummy variable of no (AHI < 2 = 0) and yes (AHI ≥ 2 = 1). SpO_2 = dummy variable of normal (SpO_2 > 0.5 = 0) and low (SpO_2 < 0.4 = 1). BMI% = body mass index percentile. BMI% groups = dummy variable of normal weight (BMI% < 85 = 0), overweight (85 ≤ BMI% < 95 = 1), and obese (BMI% ≥ 95 = 2). P values ≤ 0.05 (*), including ≤ 0.01 (**), were considered statically significant, while P values 0.05–0.10 (^{T}) were considered marginally significant (trend).

Table 3

Relationship between DXA-measured total adipose tissue and neurocognitive and behavioral functioning in adolescents with and without obstructive sleep apnea

	Total Adipose Tissue	Vigilance	Processing Speed	Working Memory	Control Interference	Internalizing Behaviors	Externalizing Behaviors
Total Adipose Tissue	---	−.041	.035	−.035	.088	**.115**^{T}	**.105**^{T}
Vigilance	**−.223***	---	**.203****	.047	−.089	−.005	**−.121**^{T}
Processing Speed	**−.136**^{T}	.137	---	**.255****	**−.140***	**−.182****	**−.287****
Working Memory	−.088	.035	**.185***	---	−.002	−.022	−.096
Control Interference	**.154**^{T}	−.042	**−.172***	−.133	---	.049	**.216****
Internalizing Behaviors	**.237****	.008	−.132	−.070	**.185***	---	**.518****
Externalizing Behaviors	**.217****	−.097	**−.248****	**−.200***	**.371****	**.587****	---

Data are Pearson correlation coefficients in adolescents with OSA (below the diagonal) and without OSA (above the diagonal). OSA = obstructive sleep apnea, defined as an apnea/hypopnea index greater or equal to 2 events per hour of sleep. P values ≤ 0.05 (*), including ≤ 0.01 (**), were considered statically significant, while P values 0.05–0.10 (^{T}) were considered marginally significant (trend).

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