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SCIENTIFIC INVESTIGATIONS

Obstructive Sleep Apnea and Sleep Architecture in Adolescents With Severe Obesity: Effects of a 9-Month Lifestyle Modification Program Based on Regular Exercise and a Balanced Diet

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Study Objectives: Physical exercise and lifestyle modification are recognized as adjunct therapy for obstructive sleep apnea (OSA) in overweight adults. The objectives of this study were to investigate the effects of long-term physical exercise combined with a balanced diet on sleep architecture, sleep duration, and OSA in adolescents with severe obesity.

Methods: This interventional study was conducted in a nursing institution. Participants were aged 14.6 ± 1.2 years with obesity (body mass index (BMI) = 40.2 ± 6.5 kg/m^2). At admission and at 9 months, participants underwent ambulatory polysomnography and incremental maximal exercise testing to determine cardiorespiratory fitness.

Results: Twenty-four subjects completed the study. Analyses were performed on the whole population and on a subgroup of subjects with OSA (OSA-subgroup). OSA, defined as obstructive apnea-hypopnea index (OAHI) ≥ 2 events/h, was diagnosed in 58.3% of the population. OAHI was only associated with fat mass in males (r = .75, P < .05). At 9 months postintervention, weight loss (−11.1 kg, P < .0001) and improved cardiorespiratory fitness (VO_2peak: +4.9 mL/min/kg, P < .001) were found in the whole population. Sleep duration was increased (+34 minutes, P < .05) and sleep architecture was changed with an increase of rapid eye movement sleep (+2.5%, P < .05) and a decrease of stage N3 sleep (−3.1%, P < .001). Similar results were found in the OSA subgroup. However, OAHI remained unchanged (P = .18).

Conclusions: A combination of supervised aerobic exercise and a balanced diet led to weight loss, improved aerobic capacity, and modified sleep architecture without changes in OSA.

Commentary: A commentary on this article appears in this issue on page 907.

Clinical Trial Registration: Registry: ClinicalTrials.gov, Title: Exercise and Venous Compression on Upper Airway Resistance in Obese Teenagers With OSA (OBESOMAC), URL: https://clinicaltrials.gov/ct2/show/NCT02588469, Identifier: NCT02588469

Keywords: cardiorespiratory fitness, obesity, OSA, chronic exercise, polysomnography, sleep architecture, sleep-disordered breathing, teenager, weight loss

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BRIEF SUMMARY

Current Knowledge/Study Rationale: The progression of pediatric obesity is associated with the development of obstructive sleep apnea (OSA). Multidisciplinary programs with physical exercise and weight loss are the first line of obesity management. Because it is recognized that weight loss and physical exercise decrease OSA, we hypothesized that this program would contribute to reducing OSA in a severely obese adolescent population.

Study Impact: This study is the first to objectively assess both cardiorespiratory fitness and polysomnographic parameters in obese adolescents, in a context of obesity management. Our results suggest that this type of management may be insufficient to treat OSA, and point to a need for further investigations to better manage OSA, and to study the association between weight loss and changes in sleep architecture.

INTRODUCTION

Over the past few decades, the prevalence of pediatric overweight and obesity has increased dramatically worldwide.[1] There is currently a large body of evidence suggesting that obesity during youth is a risk factor for the development of several conditions, including low-grade inflammation, metabolic syndrome, type 2 diabetes,[2] and obstructive sleep apnea (OSA).[3,4]

Pediatric obesity is a multifactorial disease that results from an impaired balance between energy intake and expenditure. Moreover, lifestyle modifications, such as spending time watching television[5,6] or using a mobile phone late into the evening,[7,8] lead to sleep disturbances and short sleep duration. Numerous studies[9–13] have suggested a strong relationship between short sleep duration and the development of obesity in both adulthood and childhood. However, obesity is known to alter sleep quality, because of OSA. In the general pediatric population, the prevalence of OSA is about 1% to 3%,[4,14,15] whereas it ranges from 33% to 61% in the obese pediatric population.[16–18] Over the past decade, studies have shown the beneficial effects of weight loss induced by lifestyle intervention on the severity of OSA in adults.[19,20] Furthermore,

exercise training is also recognized as an adjunct therapy for OSA treatment[21–23] and sleep improvement.[24] Accordingly, it is well accepted that lifestyle modification based on a healthy diet and increased physical activity is useful as a therapeutic treatment to manage obesity. Nevertheless, only a few studies have focused on the effects of long term pediatric obesity management on OSA.[25–28] Studies have been conducted on the effects of weight loss therapy on sleep in obese adolescents and young adults aged between 15 and 19 years (Corgosinho et al.[25]), and aged between 14 and 23 years (Siegfried et al.[26]). They used adult definition for OSA (apnea-hypopnea index [AHI] ≥ 5 events/h) and found a decrease of OSA prevalence about 60% and 67%, respectively, at the end of the program. Verhulst et al.[27] studied younger adolescents (mean age 14.8 years) and used AHI ≥ 2 events/h to define OSA. At the end of the 5-month program, an average weight loss of 24 kg was observed and OSA (measured by respiratory polygraphy) was treated in 62% of the subjects. Finally, in the context of a pediatric obesity management program, a 12-week exercise program increased sleep duration, assessed by polysomnography (PSG) without change in AHI or weight (Mendelson et al.[28]). In view of the discrepancies between the use of devices for sleep assessment, definitions of OSA, modalities, and evaluations of exercises, it remains unknown whether weight reduction and enhanced cardiorespiratory fitness, achieved through both long-term modified dietary habits and exercise training, can improve sleep architecture and decrease OSA in obese youths.

Therefore, the purpose of this study was first to investigate the effects of physical exercise combined with a balanced diet on sleep architecture in severe obese adolescents with or without OSA, and second, to focus on the effects of this intervention on a subgroup of adolescents presenting OSA. Our hypotheses were that this lifestyle modification would (1) improve the duration and quality of sleep and (2) decrease OSA via the induced weight loss and increased cardiorespiratory fitness.

METHODS

Subjects

Thirty-two adolescents (16 females and 16 males) with severe obesity were recruited from a nursing institution specialized in the management of adolescent obesity. Obesity was defined as age-specific body mass index (BMI) greater than the French 97th percentile and severe obesity as BMI z-score greater than 3.[29] All subjects were free of cardiac disorders.

Protocol Overview

Obese adolescents spent an academic year in a specialized residential nursing institution with the aim of weight reduction. Experts in nutrition and physical activity and pediatricians oversaw the lifestyle intervention for a period of 9 months without the involvement of the subjects' parents. The weight reduction program, which aimed to promote a healthier lifestyle, was based on the introduction of physical exercise, modification of eating habits, and individual psychological care.

The study was performed in accordance with the Declaration of Helsinki and approved by the medical ethics committee of the University Hospital Center of Franche-Comté (n°2015-A00763-46). All participants and their parents or legal guardians were fully informed of the experimental procedures and gave written informed consent before enrollment in the study.

Experimental Procedures and Lifestyle Intervention

At enrollment, clinical evaluation, maximal exercise testing, and nocturnal recordings were performed for all subjects. These measurements were repeated at the end of a 9-month lifestyle modification program, during which diet and nutritional education were proposed.

Clinical Evaluation

Weight was measured to the nearest 0.1 kg using a calibrated scale and height was determined to the nearest 0.01 meter using a standing stadiometer. Body mass and height were measured barefoot while wearing underwear. BMI was computed as body mass divided by height (kg/m^2). Waist circumference (WC) and hip circumference (HC) were measured to the nearest 0.5 cm in a standing position with a standard nonelastic tape that was applied horizontally midway between the last rib and the superior iliac crest and from both sides of the greater trochanter respectively. Waist-hip ratio was calculated as WC/HC (in cm). BMI *z*-score was calculated for age and sex reference values adapted to the French pediatric population.[30]

Fat mass (FM) and fat-free mass (FFM) were measured by bioelectrical impedance (BIA, Impedimed Limited, Pinkenba, QLD 4008 Australia) in the supine position, with an impedance analyzer using four body-surface electrodes.

Maximal Exercise Test

Maximal exercise test was performed at least 2 days before nocturnal PSG, because of possible modifications in sleep architecture the night following intense exercise. Each subject underwent an ambulatory incremental exercise test on a fixed-cycle ergometer with gas exchange measurement (MetaMax, Matsport, Saint Ismier, France).

During warm-up, subjects were required to pedal continuously for 3 minutes at 30 W and then the workload was increased by 10 W every minute until exhaustion to determine individual maximal aerobic power, ventilation minute (V_E), and peak oxygen uptake (VO_2peak). The subjects pedaled at a frequency between 60 and 70 rpm, which is the recommended standard to achieve highest oxygen uptake. During each test, the assessor spurred the subject on, stimulating them to reach maximal effort, as materialized by a peak in oxygen uptake. All subjects were instructed to stop the test only when they felt maximal fatigue. During recovery, the subjects were asked to pedal at 50 W per minute for at least 5 minutes.

Nocturnal Recordings

All subjects underwent, under the same conditions, a standard ambulatory PSG on a weekday and during the school period at entrance and at the end of the intervention. Recordings were performed in the specialized residential nursing institution with an ambulatory PSG (Morpheus, Micromed, Italy). Sleep was assessed with standard PSG techniques using the 10–20 system[31] and the following variables were also continuously

measured and recorded for at least 6 hours: Fz, Cz, F4-M1, C4-M1, O2-M1, F3-M2, C3-M2, and O1-M2, left and right electrooculogram, chin electromyogram, left and right anterior tibialis electromyogram, and electrocardiogram.

Respiratory efforts were studied by thoracic and abdominal inductance plethysmography (SleepSense, S.L.P Inc., Elgin, Illinois, United States). Airflow was measured with a thermistor and nasal pressure cannula (ThermoCan, SleepSense, S.L.P Inc., Elgin, Illinois, United States) and snoring was determined by filtration of the nasal pressure signal.

Peripheral oxygen saturation (SpO_2) and heart rate were both recorded by pulse oximetry (Nonin Medical, Inc. Plymouth, Minnesota, United States). PSG data were recorded directly to a data acquisition, storage, and analysis system (SleepRT software; Brain RT, OSG, Rumst, Belgium).

The electroencephalogram recordings were visually scored in 30-second periods by an experienced board-certified sleep physician using the American Academy of Sleep Medicine's standard rules to obtain the overnight pattern of sleep stages.[32]

The following sleep parameters were recorded: sleep latency (time from lights out to sleep onset, defined as the first epoch of any sleep stage, minutes), total sleep time (TST, minutes), sleep efficiency (TST / time in bed × 100, %), arousal index (number of arousals / TST, %), wake after sleep onset (WASO, minutes), percentage of stage N1 sleep (%TST), percentage of stage N2 sleep (%TST), percentage of stage N3 sleep (%TST), percentage of stage R sleep (%TST), and stage R sleep latency (time from sleep onset to the first stage R sleep epoch).

Respiratory events were scored in 3-minute periods for airflow by an experienced board-certified sleep physician according to the criteria of the American Academy of Sleep Medicine.[33] Apnea was defined as ≥ 90% reduction in airflow for at least the duration of 2 breaths, associated with the presence of respiratory effort for obstructive apnea, or associated with absent respiratory effort during one portion of the event and the presence of inspiratory effort in another portion for mixed apnea. Central apnea was defined as ≥ 90% reduction in airflow, for at least 20 seconds with absent inspiratory effort throughout the entire event, or for at least the duration of 2 breaths associated with ≥ 3% fall in oxygen saturation and/or arousal. Hypopnea was defined as ≥ 30% reduction in airflow for at least 2 breaths associated with ≥ 3% fall in oxygen saturation and/or arousal. Respiratory effort-related arousal (RERA) was defined as increasing respiratory effort for at least 2 breaths, characterized by a flattening of the inspiratory portion of the nasal pressure, and leading to arousal from sleep.[33] Apnea, obstructive apnea, central apnea, mixed apnea, and hypopnea index (AI, OAI, CAI, MAI, and HI respectively; events/h) and RERA index were determined by dividing the number of apnea, obstructive apnea, central apnea, mixed apnea, hypopnea and RERA events, respectively, by hours of sleep. Obstructive apnea-hypopnea index (OAHI; events/h) was determined by dividing the number of obstructive apnea plus mixed apnea and hypopnea by hours of sleep. Apnea-hypopnea index (AHI; events/h) was determined by dividing the number of apneas plus hypopneas by hours of sleep. Respiratory disturbance index (RDI) was defined by the sum of AHI and RERA index. RDI in stage R sleep was determined by dividing the number of apnea, hypopnea and RERA events during stage R sleep by total hours spent in stage R sleep. Oxygen desaturation index (ODI) was determined by dividing the number of oxygen desaturation ≥ 3% by hours of sleep.

The diagnosis of OSA was defined by the presence of an OAHI ≥ 2 events/h of total sleep time (TST).

9-Month Lifestyle Intervention Program

Over the duration of the study, subjects performed physical exercise at least 5 times/wk for 45 to 60 minutes, including an interval training program consisting of nine sessions of 5 minutes each, twice a week. Each training session alternated 4 minutes of moderate work (50% of VO_2peak) and 1 minute of intense work (85% of VO_2peak) based on initial testing. Workloads were readjusted (+10 W) to maintain target heart rate over time. In addition, moderate and high activities, such as walking, swimming, cycling, climbing, and group games (handball, football, basketball, badminton), and muscle strengthening were performed 3 times/wk during the program. Adolescents also had physical education lessons on how to incorporate exercise into their daily life (leisure physical activities with their family) and how to reduce sedentary behaviors (such as watching television and computer or video game playing).

Diet and Nutritional Education

Changes in dietary habits included the consumption of a balanced diet and nutritional education sessions. Total daily calorie intake was controlled at about 2300–2500 kcal, according to age and recommended French allowances,[34] and contained 30% fat, 14% proteins, and 57% carbohydrates. Moreover, individual and group nutritional education sessions, consisting of promoting healthy cooking methods, portion size control, and food labeling, were held twice a week. Finally, special attention was paid to the subjective feelings of hunger and satiety, and the pleasure of eating.

Statistical Analysis

Statistical analysis was performed using GraphPad software (version 8.00, Tulsa, Oklahoma, United States). Data are presented as mean ± standard deviation (SD), with a level of significance set at $P < .05$. The Kolmogorov-Smirnov test was used to test the assumption of distribution normality for quantitative parameters.

Sleep latency, sleep efficiency, WASO, percentage of stage R sleep, OAHI, AHI, AI, OAI, MAI, CAI, ODI, and relative VO_2peak were not normally distributed. Wilcoxon matched-pairs tests were used to compare these nonparametric data in the whole population and in the OSA-subgroup before and after the 9-month lifestyle intervention.

Paired *t* tests were used to compare every other parametric data in the whole population, in female and in male subjects, and in the OSA-subgroup before and after the 9-month lifestyle intervention program.

Unpaired *t* tests were used to compare anthropometric characteristics and body composition between females and males at entrance.

Table 1—Spearman correlations between anthropometric variables and OAHI at admission.

	Whole Population		Females		Males	
	r	*P*	*r*	*P*	*r*	*P*
Body mass index (kg/m^2)	.31	.17	−.06	.86	.52	.13
Body mass index z-score	.28	.20	−.20	.50	.63	.06
Waist circumference (cm)	.22	.33	.01	.97	.57	.10
Hip circumference (cm)	.14	.53	.07	.84	.22	.55
Waist-hip ratio	.17	.44	−.03	.94	.52.	.13
Fat mass (%)	−.20	.39	−.57	.07	.75	.03
Fat-free mass (%)	.20	.39	.57	.07	−.75	.03

OAHI = obstructive apnea-hypopnea index.

Table 2—Clinical characteristics in obese adolescents at admission and at 9 months postintervention (n = 24).

	Whole Population (n = 24)		Females (n = 13)		Males (n = 11)	
	Admission	9 Months	Admission	9 Months	Admission	9 Months
Age (years)	14.66 ± 1.30	15.30 ± 1.34 ***	14.78 ± 1.30	15.47 ± 1.29 ***	14.51 ± 1.36 ns	15.09 ± 1.41 ***
Weight (kg)	111.7 ± 19.95	100.60 ± 16.84 ***	102.50 ± 16.32	94.29 ± 15.3 ***	122.70 ± 18.77 ††	108.80 ± 15.76 ***
Height (cm)	166.6 ± 6.74	168.4 ± 7.04 ***	164.90 ± 6.48	165.9 ± 6.32 ***	168.50 ± 6.78 ns	171.60 ± 6.90 **
BMI (kg/m^2)	40.27 ± 6.82	35.33 ± 5.68 ***	37.59 ± 4.78	34.23 ± 5.08 ***	43.43 ± 7.69 ††	36.75 ± 6.35 ***
BMI z-score	4.71 ± 0.95	3.97 ± 1.06 ***	4.20 ± 0.69	3.58 ± 0.89 ***	5.32 ± 0.87 ††	4.48 ± 1.10 ***
WC (cm)	121.60 ± 15.88	98.41 ± 12.85 ***	112.80 ± 11.85	97.69 ± 13.83 ***	132.10 ± 13.76 ††	99.44 ± 12.01 ***
HC (cm)	126.80 ± 10.75	114.80 ± 10.04 ***	121.50 ± 9.61	114.00 ± 9.98 ***	133 ± 8.68 ††	116.00 ± 10.63 ***
Waist-hip ratio	0.96 ± 0.71	0.86 ± 0.08 ***	0.93 ± 0.05	0.85 ± 0.08 ***	0.99 ± 0.08 †	0.86 ± 0.08 ***
FFM (%)	60.72 ± 5.22	65.85 ± 5.21 **	62.88 ± 4.23	65.85 ± 6.50 ns	60.34 ± 8.69 ns	66.22 ± 5.99 *
FM (%)	39.28 ± 5.22	34.15 ± 5.21 **	37.12 ± 4.23	34.15 ± 6.50 ns	39.66 ± 8.69 ns	31.78 ± 5.99 *

Values are presented as mean ± standard deviation. Unpaired *t* test for comparison at admission between male and female: ns = not significant, † = $P < .05$, †† = $P < .01$. Paired *t* test for comparison in the whole population and per sex between admission and postintervention: ns = not significant, * = $P < .05$, ** = $P < .01$, *** = $P < .001$. BMI = body mass index, FFM = fat-free mass, FM = fat mass, HC = hip circumference, WC = waist circumference.

Spearman correlation coefficient was used to assess the association between OAHI and anthropometric and body composition characteristics in the whole population, in females and in males at admission.

RESULTS

Characteristics of the Population

Eight subjects (5 males, 3 females) were excluded from the study; 2 males were treated by continuous positive airway pressure (CPAP), 1 PSG recording failed and 5 subjects failed to complete the 9-month lifestyle intervention program. In total, 24 subjects (11 males, 13 females) were considered for analysis with a mean age (± SD) of 14.7 ± 1.3 years.

At entrance in the study, OAHI was not associated with BMI, BMI z-score, WC, HC, waist-hip ratio, FFM, and FM in the whole population. Similar results were found in females. In males, OAHI was positively associated with percentage of FM ($r = .75$, $P = .03$) and negatively associated with percentage of FFM ($r = -.75$, $P = .03$) (**Table 1**).

On the basis of the OAHI results, OSA was diagnosed in 58.3% (14 subjects; 7 males, 7 females) of the studied population, who represents the OSA subgroup.

Comparison of Clinical Characteristics Between Sex

At entrance, females and males presented at the same age and height ($P < .05$). Males exhibited higher BMI and waist-hip ratio than females ($P < .05$). Weight, BMI z-score, WC, and HC were also higher in males ($P < .01$) (**Table 2**).

Effects of a 9-Month Lifestyle Intervention Program in the Whole Population

Anthropometric Characteristics and Body Composition by Sex

Females and males both presented a significant decrease in weight, BMI, BMI z-score, WC, and HC ($P < .01$). Waist-hip ratio also decreased in females ($P < .05$) and males ($P < .001$). Change in percentage in FFM and FM was found in males ($P < .05$) whereas no modification was found in females ($P > .05$) (**Table 2**).

Anthropometric Characteristics and Body Composition in the Whole Population

Paired *t* tests showed a significant decrease in weight, BMI, BMI z-score, WC, HC, and waist-hip ratio ($P < .0001$). A decrease in FM ($P < .01$), and an increase in FFM ($P < .01$) and height ($P < .001$) were also found at the end of the program (**Table 2**).

Table 3—Polysomnography characteristics in obese adolescents at admission and at 9 months postintervention (n = 24).

	Admission	9 Months	*P*
Sleep latency (minutes)	17.65 ± 13.83	13.55 ± 7.55	.06
TST (minutes)	451.20 ± 30.39	485.50 ± 48.49	.03
Sleep efficiency (%)	88.90 ± 5.83	91.30 ± 3.74	.18
Arousal index (events/h)	7.76 ± 2.50	10.94 ± 5.30	.03
WASO (minutes)	31.29 ± 36.40	29.45 ± 19.18	.24
NREM and REM sleep			
Stage N1 sleep (%TST)	4.97 ± 2.77	7.17 ± 2.46	< .01
Stage N2 sleep (%TST)	54.00 ± 4.58	52.39 ± 6.60	.34
Stage N3 sleep (%TST)	21.12 ± 4.77	18.03 ± 4.36	< .001
Stage R sleep latency (minutes)	111.50 ± 39.34	110.20 ± 44.09	.97
Stage R sleep (%TST)	19.89 ± 3.20	22.40 ± 3.93	.03
Respiratory events			
OAHI (events/h)	2.35 ± 2.49	2.07 ± 2.54	.24
AHI (events/h)	2.73 ± 3.40	2.28 ± 2.54	.32
Apnea index (events/h)	0.84 ± 2.10	0.77 ± 1.10	.99
Obstructive apnea index (events/h)	0.33 ± 0.62	0.55 ± 1.05	.88
Mixed apnea index (events/h)	0.13 ± 0.54	0.01 ± 0.03	.25
Central apnea index (events/h)	0.38 ± 1.00	0.21 ± 0.35	.50
Hypopnea index (events/h)	1.89 ± 1.54	1.51 ± 1.70	.23
RERA index (events/h)	5.72 ± 3.18	8.09 ± 4.8	.04
RDI (events/h)	8.45 ± 4.62	10.37 ± 6.43	.23
RDI in REM sleep (events/h)	21.73 ± 12.62	26.25 ± 14.38	.28
RDI in NREM sleep (events/h)	5.18 ± 4.05	6.24 ± 5.41	.36
Snoring index (events/h)	199.10 ± 182.70	237.80 ± 295.00	.33
ODI (events/h)	3.92 ± 4.05	3.97 ± 3.45	.97
Mean SpO_2 (%)	95.04 ± 1.62	95.33 ± 2.28	.35

Values are presented as mean ± standard deviation. Paired *t* test for parametric data, Wilcoxon matched-pairs test for nonparametric data. AHI = apnea-hypopnea index, NREM = non-rapid eye movement, OAHI = obstructive apnea-hypopnea index, ODI = oxygen desaturation index, RDI = respiratory disturbance index, REM = rapid eye movement, RERA = respiratory event-related arousal, SpO_2 = peripheral oxygen saturation, TST = total sleep time, WASO = wake after sleep onset.

Polysomnography Analysis and Respiratory Events in the Whole Population

A tendency toward a decrease in sleep latency at the end of the program was observed with Wilcoxon matched- pairs test, although the modification did not reach statistical significance ($P = .06$). TST and arousal index were significantly increased ($P < .05$) without a significant modification in sleep efficiency and WASO. Analyses showed an increase of the amount of stage N1 sleep ($P < .01$) and a decrease of the amount of stage N3 sleep ($P < .001$) at the end of the program. No significant change in the amount of stage N2 sleep was found. Stage R sleep was significantly increased ($P < .05$) without modification of stage R sleep latency.

At the end of the program, OAHI, OAI, MAI, HI, AHI, CAI, RDI in TST in rapid eye movement (REM) sleep and non-rapid eye movement (NREM) sleep, snoring index, ODI, and mean SpO_2 were not significantly changed ($P > .05$). RERA was increased ($P < .05$) (**Table 3**).

Maximal Cardiorespiratory Values in the Whole Population

Maximal cardiorespiratory values are presented in **Table 4**. We observed a significant increase in maximal aerobic power ($P < .0001$), absolute ($P < .01$) and relative ($P < .001$) VO_2peak. V_E was also increased at the end of the program ($P < .01$).

Effects of a 9-Month Lifestyle Intervention Program in the OSA-Subgroup (Table 5)

Anthropometric Characteristics and Body Composition

At the end of the program, weight, BMI, BMI-z score, WC, waist-hip ratio ($P < .001$), and FM ($P < .05$) were significantly decreased.

Polysomnography Analysis and Respiratory Events

TST was significantly increased ($P < .01$) whereas no modification was found for sleep latency, arousal index, or WASO ($P > .05$). Stage N1 and N2 sleep were not modified ($P > .05$). Stage R sleep was significantly increased whereas stage N3 sleep was significantly decreased ($P < .05$).

At the end of the program, subjects with OSA still exhibited the same OAHI, OAI, MAI, and HI as at enrollment ($P > .05$). Similarly, AHI, CAI, RERA index, RDI in TST, in REM sleep and in NREM, snoring index, ODI, and mean SpO_2 also remained unchanged.

Table 4—Maximal cardiorespiratory values in obese adolescents at admission and at 9 months postintervention (n = 24).

	Admission	9 Months	*P*
Maximal aerobic power (W)	138.60 ± 29.00	178.70 ± 37.45	< .0001
VO_2peak (L/min)	2.51 ± 0.50	2.74 ± 0.59	< .01
VO_2peak (mL/min/kg)	22.77 ± 3.18	27.71 ± 5.26	< .001
Maximal heart rate (bpm)	185.50 ± 8.94	182.00 ± 14.29	.06
V_E (L/min)	90.15 ± 21.74	101.60 ± 26.95	< .01

Values are presented as mean ± standard deviation. Paired *t* test for parametric data, Wilcoxon matched pairs test for nonparametric data. V_E = ventilation minute, VO_2peak = peak oxygen uptake.

Maximal Cardiorespiratory Values

Maximal aerobic power ($P < .001$), absolute ($P < .05$) and relative VO_2peak ($P < .01$) significantly increased at the end of the program and V_E ($P = .08$) and maximal heart rate ($P = .11$) remained unchanged.

DISCUSSION

The main findings of this study are: first, that the decrease in body mass and improvement in cardiorespiratory fitness induced by the 9-month lifestyle modification program increase TST and change sleep architecture in obese youths; and second, that this program has no effect on OSA.

Before the 9-month lifestyle modification program, the subjects slept on average 7.5 h/night, which is less than recommended for adolescents aged 14 to 17 years. Indeed, according to National Sleep Foundation's guidelines, Hirshkowitz et al.[35] recommended a range of sleep duration from 8 to 10 h/d. This short sleep duration in our adolescents may have potentially led to obesity and poor health. A large body of evidence suggests a strong relationship between short sleep duration and development of obesity.[9–13] In the current study, sleep deprivation was accompanied by an alteration of sleep architecture, with reduced REM sleep. Some authors have previously reported a relationship between reduced REM sleep and obesity,[36–38] but the underlying mechanisms remain unclear. Some studies have shown that the sleeping metabolic rate is higher in REM sleep, with elevated brain glucose utilization.[39] In case of a decrease in REM sleep, such as observed in the current study, it may be hypothesized, as already suggested by Liu et al.,[38] that energy expenditure is reduced.

Horne[37] speculated that REM sleep is involved in feeding behavior and more specifically, the final REM period of sleep, which may be an appetite suppressant. Thus, the low amount of REM sleep, as measured in our subjects, might explain their high BMI, or contribute to weight gain by enhancing their appetite. Nevertheless, further investigations are needed to clarify the loss of REM sleep in obese adolescents.

Sleep loss leads to obesity, and obesity itself is recognized to be a main risk factor for sleep-disordered breathing, and more precisely for OSA. In pediatric populations, the risk of OSA increases by a factor of 4.59 in case of obesity.[3] In our population, OSA was observed in 58.3% of participants. These data are consistent with those of Verhulst et al.[27] in whose study OSA was diagnosed with the same threshold in about 60.7% of severe obese adolescents, with a BMI z-score equal to 2.7, slightly lower than that observed in our study. Similarly, Li et al.[40] observed OSA in 64% of obese children, although they used a criterion of AHI > 1 event/h. This prevalence confirms the consequences of obesity on nocturnal respiration, despite the lack of positive associations between anthropometric parameters of the whole population and the OAHI.

Because a multidisciplinary program with physical exercise and weight loss is the first line of obesity management, we hypothesized that this program would contribute to reducing OSA in our population. It is indeed well recognized that both weight loss[25–27] and physical exercise[21] decrease OSA. As expected, our population experienced a significant decrease in anthropometric parameters and an improvement in body composition, with a decrease in FM and an increase in FFM at the end of the program. Similar results were found by our team in a previous study.[41,42] At entrance, males had higher weight and BMI z-score than females but both experienced significant weight loss at the end of the program. Males exhibited a mean weight loss of 13.9 kg, compared with 8.2 kg in females. Despite this encouraging outcome, we failed to show any decrease of OAHI in patients with OSA (still ≥ 2 events/h of TST), although other authors[25–27] have previously reported a significant reduction of OSA in obese adolescents after a similar program. Verhulst et al.[27] studied 61 obese children and adolescents (mean age 14.8 years) who were recruited in a revalidation center for 5.2 months. The prevalence of OSA, defined as AHI ≥ 2 events/h, was 61% at the start of the study, and at the end of the program, 8 of 21 subjects (38%) continued to have residual OSA. At baseline, mean BMI z-score was 2.7 ± 0.4, and the subjects experienced a median weight loss of 24 kg, corresponding to a relative decrease in BMI z-score of 34.8% (16.2% to 76.3%), or 0.9. In our study, BMI z-score decreased by 0.8 in the OSA subgroup. Nevertheless, our subjects with OSA were morbidly obese with a mean BMI z-score of 4.98 before therapy.

Two studies[25,26] assessed the effects of long-term weight loss therapy on sleep, respectively in severe[25] and morbidly[26] obese adolescents and young adults. Because of the age of the subjects, both groups of authors used adult definition for OSA (AHI ≥ 5 events/h).

Corgosinho et al.[25] recruited 55 obese subjects (age range: 15–19 years, mean BMI: 37.6 kg/m^2) for a 1-year interdisciplinary program. At entrance, OSA was diagnosed in 21.9% of the population. In addition to nutritional and psychological

Table 5—Anthropometric characteristics, sleep characteristics, and cardiorespiratory values in obese adolescents with OSA at admission and at 9 months postintervention (n = 14).

	Admission	9 Months	*P*
Age (years)	14.53 ± 1.48	15.15 ± 1.56	< .0001
Weight (kg)	115.20 ± 22.53	102.00 ± 19.78	< .001
BMI (kg/m^2)	42.37 ± 7.72	36.43 ± 6.74	< .0001
BMI z-score	4.98 ± 1.10	4.17 ± 1.29	< .0001
WC (cm)	124.30 ± 17.37	98.75 ± 12.96	< .0001
Waist-hip ratio	0.97 ± 0.08	0.86 ± 0.07	< .001
FM (%)	39.90 ± 6.14	34.06 ± 5.05	< .05
Sleep characteristics			
Sleep latency (minutes)	17.31 ± 14.21	11.18 ± 6.17	.18
TST (minutes)	441.90 ± 21.87	494.90 ± 47.57	< .01
Arousal index (events/h)	8.37 ± 2.08	11.38 ± 5.69	.13
WASO (minutes)	27.23 ± 20.64	31.46 ± 23.18	.98
NREM and REM sleep			
Stage N1 sleep (%TST)	5.69 ± 3.15	6.32 ± 2.69	.31
Stage N2 sleep (%TST)	53.37 ± 4.60	51.61 ± 7.00	.50
Stage N3 sleep (%TST)	21.40 ± 5.36	19.20 ± 3.11	< .05
Stage R sleep (%TST)	19.51 ± 3.29	22.88 ± 4.78	< .05
Respiratory events			
OAHI (events/h)	3.67 ± 2.62	2.98 ± 3.04	.32
AHI (events/h)	4.23 ± 3.90	3.09 ± 3.08	.18
Apnea index (events/h)	1.37 ± 2.71	1.03 ± 1.33	.31
Obstructive apnea index (events/h)	0.59 ± 0.73	0.92 ± 1.28	.69
Mixed apnea index (events/h)	0.22 ± 0.72	0.00 ± 0.03	.50
Central apnea index (events/h)	0.56 ± 1.30	0.11 ± 0.19	.06
Hypopnea index (events/h)	2.86 ± 1.32	2.06 ± 2.06	.13
RERA index (events/h)	7.24 ± 2.86	9.23 ± 5.58	.22
RDI (events/h)	11.47 ± 3.17	12.32 ± 7.64	.72
RDI in REM sleep (events/h)	29.75 ± 9.61	31.47 ± 15.79	.86
RDI in NREM sleep (events/h)	6.93 ± 4.32	7.41 ± 6.58	.80
Snoring index (events/h)	207.30 ± 237.30	214.00 ± 249.20	.37
ODI (events/h)	5.48 ± 4.77	4.56 ± 4.41	.12
Mean SpO_2 (%)	95.10 ± 2.02	95.70 ± 2.34	.15
Maximal cardiorespiratory values			
Maximal aerobic power (W)	129.20 ± 28.13	170.60 ± 38.03	< .001
VO_2peak (L/min)	2.53 ± 0.52	2.71 ± 0.63	< .05
VO_2peak (mL/min/kg)	22.31 ± 2.39	27.09 ± 4.48	< .01
Maximal heart rate (bpm)	184.50 ± 11.38	181.50 ± 11.71	.14
V_E (L/min)	86.95 ± 19.92	98.37 ± 24.84	.08

Values are presented as mean ± standard deviation. Paired *t* test for parametric data, Wilcoxon matched pairs test for nonparametric data. AHI = apnea-hypopnea index, BMI = body mass index, FM = fat mass, HC = hip circumference, NREM = non-rapid eye movement, OAHI = obstructive apnea-hypopnea index, ODI = oxygen desaturation index, OSA = obstructive sleep apnea, RDI = respiratory disturbance index, REM = rapid eye movement, RERA = respiratory effort-related arousal, SpO_2 = peripheral oxygen saturation, TST = total sleep time, V_E = ventilation minute, VO_2peak = peak oxygen uptake, WASO = wake after sleep onset, WC = waist circumference.

therapy, the subjects underwent 3 hours of combined aerobic and resistance exercise per week. At the end of the program, mean weight loss was about 9.4 kg and prevalence of OSA was decreased by 60% (7/12 subjects). Siegfried et al.[26] studied 38 morbidly obese adolescents and young adults (mean age 17.98 years). The prevalence of OSA was 24%. At the end of a 3- to 9-month program, mean BMI decreased from 45.3 to 35.8 kg/m^2 and OSA was treated in 67% of the subjects. Our results are partially divergent from those obtained in these two studies, because of the different definition of OSA, and because of different severity of obesity at entrance[25] and lesser weight loss than Siegfried et al.[26] at the end of the period of care.

Finally, the lack of any decrease in OAHI in our study may be explained by the fact that our subjects with OSA exhibited

morbid obesity (grade 3 obesity, BMI > 40 kg/m^2) before the 9-month lifestyle program, and despite a significant weight loss, remained severely obese (grade 2 obesity, BMI > 35 kg/m^2) at the end of the program. Greater weight loss was probably required to observe an improvement in nocturnal respiration in this particular population.

When considering physical training we found a significant enhancement of cardiorespiratory fitness and maximum workload during maximal exercise at the end of the 9-month lifestyle modification program in our studied subjects. Unfortunately, we cannot compare our results with other pediatric studies since Verhulst et al.[27] and Siegfried et al.[26] did not assess these parameters, despite the presence of physical activity rehabilitation in their program. Nevertheless, physical exercise has been recognized in adult populations as an interesting tool and an inexpensive alternative for OSA management. Even if the underlying mechanisms remain unclear, some authors have hypothesized that first, exercise increases respiratory muscle recruitment and might result in increased upper airway (UA) muscle activation to increase UA diameter, reduce UA resistance, and oppose pharyngeal collapse during sleep.[43] Second, exercise reduces rostral fluid shift. Because a sedentary lifestyle is associated with fluid retention in the legs, the recumbent position during sleep contributes to fluid displacement accumulation in the neck, thus increasing OSA severity.[44] Conversely, exercise contributes to improving leg fluid dynamics, and decreases OSA severity.[45] Finally, exercise leads to reduced weight. Previous reports have shown that a 10% reduction in BMI is associated with a 30% reduction in AHI.[19,46,47]

In a moderate to severe OSA overweight adult population, Sengul et al.[23] reported an increase in relative VO_2peak after a 12-week training program based on moderate-intensity aerobic exercise (45 to 60 minutes, 3 times/wk), with a decrease in OSA and no modification of anthropometric parameters. Other studies[21,22,48] also found a decrease in OSA after a training program in adults. These results are not in accordance with those observed in our adolescent population. Nevertheless, our subjects with OSA presented less AHI at entrance compared to other studies, which may explain this discrepancy.

After a 12-week program of exercise training, Kline et al.[22] reported a 25% decrease in OSA (evaluated by AHI) and a modification in the amount of stage N3 sleep compared to a control group in an overweight/obese adult population. The program included twice-weekly aerobic sessions and resistance exercise, and led to a significant increase in the percentage of TST spent in stage N3 sleep. Another study reported comparable changes in stage N3 sleep after acute exercise.[24] Stage N3 sleep (or slow wave sleep) is known for being involved in hormonal and metabolic homeostasis,[49] neurophysiologic recuperation,[50] and its increase in response to exercise can thus lead to more restorative sleep. Surprisingly, at the end of our program, in addition to an increase in TST, a significant decrease in stage N3 sleep was found in every subject, in favor of stage R sleep. Mendelson et al.[28] reported an increase in stage R sleep in obese adolescents (age 14.5 ± 1.7 years) after a 12-week supervised program consisting of 4 hours of moderate to high aerobic exercise and resistance training per week without weight loss. A significant decrease in NREM sleep was also found, explained by a decrease in stage N1 sleep.[28] In agreement with Mendelson et al.,[28] our physical activity program is able to change sleep architecture, and increase sleep duration. Corgosinho et al.[25] also reported an increase in stage R sleep in obese adolescents after 1 year of interdisciplinary therapy, without modification of TST, and with a significant weight loss and a 60% reduction of OSA. Nevertheless, the authors did not discuss this result.

This study has some limitations that must be recognized: the sample size was relatively small and it would have been useful to have one adaptation night prior to the ambulatory PSG recording used for study purposes. The logistic conditions of this study, plus the drawbacks of PSG, such as high cost and time-consuming process, were limitations on the feasibility of allowing a single night of adaptation. Furthermore, the measurement of carbon dioxide concentrations by capnometry during the night could have been interesting for the assessment of the obesity hypoventilation syndrome, as often found in obese subjects. However, because of the planning of the protocol, this measurement could not be achieved.

In addition, because of the duration of the program (9 months), it was difficult to control some parameters, such as food consumption and the physical activity intervention. In further studies, it would be useful to objectively consider these parameters during comparable but shorter programs. We used waist circumference and waist-hip ratio for the estimation of abdominal obesity, but it would have been interesting to perform a direct measure of visceral fat (eg, dual-energy x-ray absorptiometry, magnetic resonance imaging).

In conclusion, our results show that a 9-month lifestyle modification program, with induced weight loss and enhanced cardiorespiratory fitness by exercise training, improves sleep duration and changes sleep architecture. However, despite these changes, the OAHI did not decrease.

The absence of any change in OSA might be explained by the low, albeit significant, weight loss. At the end of the program, subjects remained nonetheless severely obese, which may explain the persistence of nocturnal respiratory events. In view of the alarming prevalence of OSA in this population, and the long-term implications for health of these two diseases, further studies are needed to better explore the combined effects of weight loss and exercise training on OSA and sleep architecture in severe obese adolescents.

ABBREVIATIONS

AHI, apnea-hypopnea index
AI, apnea index
BMI, body mass index
CAI, central apnea index
FM, fat mass
FFM, fat-free mass
HC, hip circumference
HI, hypopnea index
MAI, mixed apnea index
NREM, non-rapid eye movement
OAHI, obstructive apnea-hypopnea index

OAI, obstructive apnea index
ODI, oxygen desaturation index
PSG, polysomnography
RDI, respiratory disturbance index
REM, rapid eye movement
RERA, respiratory effort-related arousal
SDB, sleep-disordered breathing
SpO_2, peripheral oxygen saturation
TST, total sleep time
V_E, ventilation minute
VO_2peak, peak oxygen uptake
WASO, wake after sleep onset
WC, waist circumference

REFERENCES

1. Han JC, Lawlor DA, Kimm SY. Childhood obesity. *Lancet*. 2010;375(9727):1737–1748.
2. Weiss R, Caprio S. The metabolic consequences of childhood obesity. *Best Pract Res Clin Endocrinol Metab*. 2005;19(3):405–419.
3. Redline S, Tishler PV, Schluchter M, Aylor J, Clark K, Graham G. Risk factors for sleep-disordered breathing in children. Associations with obesity, race, and respiratory problems. *Am J Respir Crit Care Med*. 1999;159(5 Pt 1):1527–1532.
4. Rosen CL, Larkin EK, Kirchner HL, et al. Prevalence and risk factors for sleep-disordered breathing in 8- to 11-year-old children: association with race and prematurity. *J Pediatr*. 2003;142(4):383–389.
5. Wells JC, Hallal PC, Reichert FF, Menezes AM, Araújo CL, Victora CG. Sleep patterns and television viewing in relation to obesity and blood pressure: evidence from an adolescent Brazilian birth cohort. *Int J Obes*. 2008;32(7):1042–1049.
6. Erik Landhuis C, Poulton R, Welch D, Hancox RJ. Programming obesity and poor fitness: the long-term impact of childhood television. *Obesity*. 2008;16(6):1457–1459.
7. Munezawa T, Kaneita Y, Osaki Y, et al. The association between use of mobile phones after lights out and sleep disturbances among Japanese adolescents: a nationwide cross-sectional survey. *Sleep*. 2011;34(8):1013–1020.
8. Van den Bulck J. Adolescent use of mobile phones for calling and for sending text messages after lights out: results from a prospective cohort study with a one-year follow-up. *Sleep*. 2007;30(9):1220–1223.
9. Touchette É, Petit D, Tremblay RE, et al. Associations between sleep duration patterns and overweight/obesity at age 6. *Sleep*. 2008;31(11):1507–1514.
10. Chaput JP, Lambert M, Gray-Donald K, et al. Short sleep duration is independently associated with overweight and obesity in Quebec children. *Can J Public Health*. 2011;102(5):369–374.
11. Eisenmann JC, Ekkekakis P, Holmes M. Sleep duration and overweight among Australian children and adolescents. *Acta Paediatr*. 2006;95(8):956–963.
12. Fatima Y, Doi SA, Mamun AA. Longitudinal impact of sleep on overweight and obesity in children and adolescents: a systematic review and bias-adjusted meta-analysis. *Obes Rev*. 2015;16(2):137–149.
13. Cappuccio FP, Taggart FM, Kandala NB, et al. Meta-analysis of short sleep duration and obesity in children and adults. *Sleep*. 2008;31(5):619–626.
14. Brunetti L, Rana S, Lospalluti ML, et al. Prevalence of obstructive sleep apnea syndrome in a cohort of 1,207 children of southern Italy. *Chest*. 2001;120(6):1930–1935.
15. Gislason T, Benediktsdóttir B. Snoring, apneic episodes, and nocturnal hypoxemia among children 6 months to 6 years old. An epidemiologic study of lower limit of prevalence. *Chest*. 1995;107(4):963–966.
16. Kalra M, Inge T, Garcia V, et al. Obstructive sleep apnea in extremely overweight adolescents undergoing bariatric surgery. *Obes Res*. 2005;13(7):1175–1179.
17. Verhulst SL, Schrauwen N, Haentjens D, et al. Sleep-disordered breathing in overweight and obese children and adolescents: prevalence, characteristics and the role of fat distribution. *Arch Dis Child*. 2007;92(3):205–208.
18. Wing Y, Hui S, Pak W, et al. A controlled study of sleep related disordered breathing in obese children. *Arch Dis Child*. 2003;88(12):1043–1047.
19. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. *JAMA*. 2000;284(23):3015–3021.
20. Tuomilehto H, Seppä J, Uusitupa M. Obesity and obstructive sleep apnea – Clinical significance of weight loss. *Sleep Med Rev*. 2013;17(5):321–329.
21. Iftikhar IH, Kline CE, Youngstedt SD. Effects of exercise training on sleep apnea: a meta-analysis. *Lung*. 2014;192(1):175–184.
22. Kline CE, Crowley EP, Ewing GB, et al. The effect of exercise training on obstructive sleep apnea and sleep quality: a randomized controlled trial. *Sleep*. 2011;34(12):1631–1640.
23. Sengul YS, Ozalevli S, Oztura I, Itil O, Baklan B. The effect of exercise on obstructive sleep apnea: a randomized and controlled trial. *Sleep Breath Schlaf Atm*. 2011;15(1):49–56.
24. Kredlow MA, Capozzoli MC, Hearon BA, Calkins AW, Otto MW. The effects of physical activity on sleep: a meta-analytic review. *J Behav Med*. 2015;38(3):427–449.
25. Corgosinho FC, Dâmaso AR, Tufik S, et al. One year of interdisciplinary therapy decreases predictors and prevalence of sleep-breathing disorder in obese adolescents. *J Health Biol Sci*. 2015;3(1):10–17.
26. Siegfried W, Siegfried A, Rabenbauer M, Hebebrand J. Snoring and sleep apnea in obese adolescents: effect of long-term weight loss-rehabilitation. *Sleep Breath*. 1999;3(3):83–88.
27. Verhulst SL, Franckx H, Van Gaal L, De Backer W, Desager K. The effect of weight loss on sleep-disordered breathing in obese teenagers. *Obesity*. 2009;17(6):1178–1183.
28. Mendelson M, Borowik A, Michallet AS, et al. Sleep quality, sleep duration and physical activity in obese adolescents: effects of exercise training. *Pediatr Obes*. 2016;11(1):26–32.
29. Rolland-Cachera MF, Cole TJ, Sempé M, Tichet J, Rossignol C, Charraud A. Body mass index variations: centiles from birth to 87 years. *Eur J Clin Nutr*. 1991;45(1):13–21.
30. Mellerio H, Alberti C, Druet C, et al. Novel modeling of reference values of cardiovascular risk factors in children aged 7 to 20 years. *Pediatrics*. 2012;129(4):e1020–e1029.
31. Jasper HH. The ten twenty electrode system of the international federation. *Electroencephalogr Clin Neurophysiol*. 1958;10:371–375.
32. Berry RB, Gamaldo CE, Harding SM, et al. AASM Scoring Manual version 2.2 updates: new chapters for scoring infant sleep staging and home sleep apnea testing. *J Clin Sleep Med*. 2015;11(11):1253–1254.
33. Berry RB, Budhiraja R, Gottlieb DJ, et al. Rules for scoring respiratory events in sleep: update of the 2007 AASM Manual for the Scoring of Sleep and Associated Events. Deliberations of the Sleep Apnea Definitions Task Force of the American Academy of Sleep Medicine. *J Clin Sleep Med*. 2012;8(5):597–619.
34. Martin A. The "apports nutritionnels conseillés (ANC)" for the French population. *Reprod Nutr Dev*. 2001;41(2):119–128.
35. Hirshkowitz M, Whiton K, Albert SM, et al. National Sleep Foundation's sleep time duration recommendations: methodology and results summary. *Sleep Health*. 2015;1(1):40–43.
36. Horne J. Obesity and short sleep: unlikely bedfellows? *Obes Rev*. 2011;12(5):e84–e94.
37. Horne JA. Human REM sleep: influence on feeding behaviour, with clinical implications. *Sleep Med*. 2015;16(8):910–916.
38. Liu X, Forbes EE, Ryan ND, Rofey D, Hannon TS, Dahl RE. Rapid eye movement sleep in relation to overweight in children and adolescents. *Arch Gen Psychiatry*. 2008;65(8):924–932.
39. Kayaba M, Park I, Iwayama K, et al. Energy metabolism differs between sleep stages and begins to increase prior to awakening. *Metabolism*. 2017;69:14–23.
40. Li AM, Chan MH, Chan DF, et al. Insulin and obstructive sleep apnea in obese Chinese children. *Pediatr Pulmonol*. 2006;41(12):1175–1181.
41. Gueugnon C, Mougin F, Simon-Rigaud ML, Regnard J, Nègre V, Dumoulin G. Effects of an in-patient treatment program based on regular exercise and a balanced diet on high molecular weight adiponectin, resistin levels, and insulin resistance in adolescents with severe obesity. *Appl Physiol Nutr Metab*. 2012;37(4):672–679.

42. Gueugnon C, Mougin F, Nguyen NU, Bouhaddi M, Nicolet-Guénat M, Dumoulin G. Ghrelin and PYY levels in adolescents with severe obesity: effects of weight loss induced by long-term exercise training and modified food habits. *Eur J Appl Physiol*. 2012;112(5):1797–1805.
43. Vincent HK, Shanely RA, Stewart DJ, et al. Adaptation of upper airway muscles to chronic endurance exercise. *Am J Respir Crit Care Med*. 2002;166(3):287–293.
44. Redolfi S, Yumino D, Ruttanaumpawan P, et al. Relationship between overnight rostral fluid shift and obstructive sleep apnea in nonobese men. *Am J Respir Crit Care Med*. 2009;179(3):241–246.
45. Mendelson M, Lyons OD, Yadollahi A, Inami T, Oh P, Bradley TD. Effects of exercise training on sleep apnoea in patients with coronary artery disease: a randomised trial. *Eur Respir J*. 2016;48(1):142–150.
46. Dobrosielski DA, Patil S, Schwartz AR, Bandeen-Roche K, Stewart KJ. Effects of exercise and weight loss in older adults with obstructive sleep apnea. *Med Sci Sports Exerc*. 2015;47(1):20–26.
47. Newman AB, Foster G, Givelber R, Nieto FJ, Redline S, Young T. Progression and regression of sleep-disordered breathing with changes in weight: the Sleep Heart Health Study. *Arch Intern Med*. 2005;165(20):2408–2413.
48. Norman JF, Von Essen SG, Fuchs RH, McElligott M. Exercise training effect on obstructive sleep apnea syndrome. *Sleep Res Online*. 2000;3(3):121–129.
49. Hanlon EC, Van Cauter E. Quantification of sleep behavior and of its impact on the cross-talk between the brain and peripheral metabolism. *Proc Natl Acad Sci U S A*. 2011;108(Suppl 3):15609–15616.
50. Benington JH, Heller HC. Restoration of brain energy metabolism as the function of sleep. *Prog Neurobiol*. 1995;45(4):347–360.

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DISCLOSURE STATEMENT

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