Association Between Sleep Architecture and Measures of Body Composition

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Study Objectives: To determine whether slow wave sleep (SWS) is inversely associated with body mass index (BMI) and other measures of body composition.

Design: Cross-sectional, observational study.

Setting: Community-based.

Participants: 2745 older men from the MrOS Sleep Study who completed polysomnography.

Interventions: N/A

Measurements and Results: SWS as a percentage of total sleep duration was obtained from in-home, overnight polysomnography. Measures of body composition including BMI, weight, waist circumference and total body fat mass were determined by standard techniques. Other covariates in the analysis were age, race/ethnicity, clinic site, physical activity, respiratory disturbance index (RDI), total sleep time, and sleep efficiency. In the multivariate analysis, there was a significant inverse association between quartiles of SWS and BMI (P-trend = 0.0095). Older men in the lowest quartile of SWS had an average BMI of 27.4 kg/m^2, compared to 26.8 for those in the highest quartile of SWS. This association was attenuated in men with RDI ≥ 15. Furthermore, participants in the lowest quartile of SWS had a 1.4-fold increased odds for obesity (P = 0.03, 95% CI 1.0, 1.8) compared to those in the highest quartile. A similar inverse association between SWS and waist circumference as well as weight was observed. REM sleep was not associated with measures of body composition.

Conclusions: Independent of sleep duration, percentage time in SWS is inversely associated with BMI and other measures of body composition in this population of older men. Participants in the lowest quartile of SWS (compared to those in the highest quartile) are at increased risk for obesity.

Keywords: slow wave sleep, obesity, weight, body composition, sleep architecture

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THE PREVALENCE OF OBESITY IN THE US HAS DOUBLED OVER THE PAST 3 DECADES.[1] DURING THIS SAME TIME PERIOD, SELF-REPORTED SLEEP DURATION has decreased,[2,3] and it is estimated that only one-quarter of adults sleep ≥ 8 hours per day.[3] A number of recent epidemiologic studies have suggested an association between total sleep time and the risk of obesity.[4-7] Specifically, body mass index (BMI) has been shown to increase as total sleep duration decreases. However, few studies have assessed the relationship between sleep architecture and BMI.

Sleep is regulated by 2 distinct processes: (1) a homeostatic process that depends on the amount of prior sleep and wakefulness; and (2) a circadian process that is driven by an endogenous pacemaker. Of the various stages of sleep, slow wave sleep (SWS) is the deepest stage and has the highest arousal threshold.[8] In subjects with previous sleep loss, SWS appears to be preferentially recovered compared with REM sleep which may reflect increased homeostatic drive (i.e., sleep pressure).[9] Studies have shown that on recovery nights following a period of sleep loss, there is first rebound and recuperation of SWS, after which recovery of other sleep stages occurs.[10-13]

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Despite this preservation of SWS, its functional significance is unclear. It has been hypothesized that SWS is important for the consolidation of memory.[14,15] The role of SWS in metabolism and energy conservation in human beings is unknown. Small clinical studies performed 20-30 years ago evaluated the relationship between REM sleep (but not SWS) and body weight, with inconsistent results.[16-19] A recent small experimental study in healthy subjects showing insulin resistance occurring the morning after selective SWS sleep deprivation has provided intriguing data implicating SWS as a mediator of glucose homeostasis.[20]

We recently reported from the Outcomes of Sleep Disorders in Older Men study (MrOS Sleep Study) that decreased total sleep time (TST) assessed by actigraphy was related to increased odds of obesity.[21] This study examines whether, in the same large cohort of community-dwelling older men, SWS specifically, rather than just TST, is associated with BMI and other measures of body composition, independent of confounding factors (including age, race, physical activity, sleep disordered breathing, and sleep efficiency). A secondary aim of this study was to determine whether REM sleep (as a percentage of TST) is associated with measures of body composition, independent of other confounding factors.

METHODS

Participants and Study Design

The Osteoporotic Fractures in Men Study (MrOS) is a cohort of 5995 community-dwelling men, aged ≥ 65 years, who

were enrolled between 2000-2002 at 6 clinical centers (Birmingham, Alabama; Minneapolis, Minnesota; Palo Alto, California; Monongahela Valley, Pennsylvania; Portland, Oregon; and San Diego, California). To be eligible, men had to be able to walk without assistance and have no history of bilateral hip replacement. Further details of this cohort are published elsewhere.[22,23]

The Outcomes of Sleep Disorders in Older Men Study (MrOS Sleep Study), an ancillary study of the parent MrOS Study, enrolled 3,135 participants from 2003-2005. Of the 2,860 participants from the main cohort who did not participate in the sleep study, 1997 were unwilling, 332 were not screened because recruitment goals were met, 344 died before the sleep study visit, 150 were ineligible due to exclusion criteria, and 37 stopped the study before the sleep visit. Men were screened for use of mechanical devices during sleep, including pressure mask for sleep apnea (CPAP or BiPAP), mouthpiece for snoring or sleep apnea, or oxygen therapy. In general, those who reported nightly use of any of these devices were excluded from the MrOS Sleep Study; however the study sample includes 49 men who reported use of one of these devices. Seventeen men were able to forego use of their sleep devices during the night of the in-home PSG study. The other 32 men did not complete the PSG measure and thus, were not included in this analysis. Of the 3135 enrolled participants, 2911 had usable PSG data. Of these, sleep staging could not be performed on 39 studies (due to poor quality), and in 132 records, there was difficulty differentiating stage 2 and SWS; 5 studies fell into both categories. Thus, of the 2911 subjects with usable PSG data, the 2745 (94.3%) with evaluable SWS data comprise our study sample. Of these, 2 participants did not have a weight measurement, 6 did not have waist circumference measurement, and 45 did not have evaluable DEXA scans. All protocols were approved by the institutional review boards at the respective enrollment sites, and participants signed informed consent to participate in the MrOS Sleep Study.

Data Collection

Measures of Body Mass and Body Composition

Weight was measured using a standard balance beam or digital scale, and height using a wall-mounted Harpenden stadiometer (Holtain, UK). These measurements were used to calculate BMI [weight (kilograms) divided by height (meters) squared]. Obesity was defined as a BMI $\geq$30 kg/m^2. Waist and hip circumferences were measured using standard techniques.[24] Percentage total body fat was obtained by DEXA (Hologic QDR-4500 W, Bedford, MA). A central quality control lab (San Francisco Coordinating Center), certification of DEXA operators, and standardized procedures for scanning were used to ensure reproducibility of measurements.

PSG

In-home, single night sleep studies using unattended polysomnography (Safiro, Compumedics, Inc., Melbourne, Australia) were performed. The recording montage consisted of C3/A2 and C4/A1 electroencephalograms, bilateral electrooculograms, a bipolar submental electromyogram, thoracic and abdominal respiratory inductance plethysmography, airflow (using nasal-oral thermocouple and nasal pressure cannula), finger pulse oximetry, electrocardiogram, body position (mercury switch sensor), and bilateral leg movements (piezoelectric sensors). Trained certified staff members performed home visits for setup of the sleep study units. After sensors were placed and calibrated, signal quality and impedance were checked, and sensors were repositioned as needed to improve signal quality, replacing electrodes if impedances were > 5000 ohms, using approaches similar to those in the Sleep Health Heart Study.[25]

After studies were downloaded, they were transferred to the Case Western Reserve University Reading Center (Cleveland, OH) for centralized scoring by a trained technician using standard criteria.[26,27] Polysomnography data quality was excellent, with > 70% of studies graded as being of excellent or outstanding quality and a failure rate < 4%. Quality codes for signals and studies were graded using previously described approaches, including coding of the duration of artifact-free data per channel and overall study quality (reflecting the combination of grades for each channel).[25] Sleep stages (REM, stages 1-4 NREM) were scored by the centralized Case Reading Center, using standard criteria.[26] Data from EEG leads C3 and C4 were used to score sleep stages 3 and 4, using the criteria of Rechtschaffen and Kales.[26] The inter-scorer reliability of percent time in SWS was high (intraclass correlation coefficient [ICC] = 0.958, 95% CI = 0.921-0.982). The intra-scorer reliability was also high, with the ICC ranging from 0.964-0.998.

SWS (stage 3 and 4 sleep) defined as a percentage of TST, determined by PSG, was the primary predictor, and REM sleep was the secondary predictor. Respiratory disturbance index (RDI), an indication of the severity of sleep disordered breathing (SDB), was defined as the number of apneas and hypopneas (based on the Sleep Heart Health Study criteria) per hour of sleep, associated with a desaturation of 4% or greater. Moderate to severe SDB was defined by RDI $\geq$ 15 and mild to no SDB was defined by RDI < 15.[28] Of note, apneas and hypopneas per hour of sleep (regardless of desaturation) were also analyzed as a measure of sleep disordered breathing. Because the results were similar, we have presented the results using RDI associated with a desaturation $\geq$ 4%. Central apnea index (CAI) is the number of apneas and hypopneas per hour of sleep associated with no displacement of either chest or abdominal inductance channels. Central apnea was defined as CAI $\geq$ 5. TST at night and sleep efficiency, defined as the percentage of the sleep period (time in bed) spent asleep, were also obtained from PSG. TST was examined both as a continuous variable and categorical ($\leq$ 5 h, > 5 to < 8 h, $\geq$ 8 h) variable.

Other Covariates

Race/ethnicity was determined by questionnaire with a choice of 5 categories (Caucasian/White, African American/Black, Asian, Hispanic, and Other). Physical activity was assessed through the Physical Activity Scale for the Elderly (PASE), a validated questionnaire that was used to obtain a summary score regarding activity levels in this population.[29] Comorbidities were determined by self-reported history of current or prior diabetes mellitus, cardiovascular disease, hyper-

tension, or chronic lung disease. Smoking status and pack years smoked were also obtained by self-report.

Statistical Analysis

Baseline characteristics were summarized across quartiles of SWS and REM using mean and standard deviation (SD) for continuous covariates, and counts and percentages for categorical data. These characteristics were compared across quartiles of SWS and REM, using ANOVA for continuous variables with normal distributions, Kruskal-Wallis tests for continuous variables with skewed distributions, and chi-square tests for categorical data.

Linear regression was used to assess the relationship of quartiles of SWS and REM with the continuous outcomes of BMI, weight, percent fat mass, waist circumference and waist-to-hip ratio. We categorized SWS and REM sleep into quartiles, to account for any non-linear associations with the outcomes. Adjusted means and 95% confidence intervals across quartiles were calculated using the least-squares means procedure. Logistic regression was used to assess the association of SWS and REM with the binary outcome, obesity (BMI $\geq$ 30 kg/m^2), and results were presented as odds ratios with 95% confidence intervals. All models were first adjusted for age and clinic site, and then further adjusted for multiple confounding variables. Potential confounding variables were identified a priori, and their association with the predictor was assessed. The confounding variables examined included age, race/ethnicity, physical activity, SDB, TST, sleep efficiency, comorbid conditions, smoking status, and central apnea index (CAI). If the covariate was associated with SWS or REM, with $P < 0.10$ in univariate analyses, it was included within the multivariate model. These covariates were entered into sequential models, thereby assessing their incremental effects. In the first multivariate model, the covariates were age, race/ethnicity, clinic site, and physical activity score. In the second model, TST and sleep efficiency were added. The final model included all of these covariates, plus SDB.

Several secondary analyses were conducted to assess confounding or mediation. Average TST derived by wrist actigraphy (collected over a mean of 5 consecutive 24-hour periods) rather than PSG-derived TST, was also assessed in the multivariate model; however, as the results of our analyses were unchanged, only data with PSG-derived TST are presented. TST was assessed in all models as both a continuous and categorical variable, and because the results did not significantly differ, only data with TST as a continuous variable are presented. Lastly, we tested for interaction of PSG-derived TST and sleep staging exposures.

Because SDB was considered a potential confounder of the association between SWS and outcomes, we accounted for it by adjusting the multivariate models for RDI (< 15 and ≥ 15). Of note, RDI was examined as both a dichotomous variable as well as a continuous one, with the results yielding similar conclusions. For simplicity, we present only the results using the dichotomous RDI variable. We also repeated the analyses, restricting to individuals without appreciable levels of SDB (RDI < 5). Finally, models were repeated restricting to individuals without central sleep apnea (CAI < 5). All analyses were performed using SAS statistical software (version 9.1, SAS Institute, Inc., Cary, NC).

Table 1—Characteristics of Sleep Architecture

Sleep variables (n = 2745)	mean ± SD
Total Sleep Time, min	356 ± 69
REM Sleep	
Duration, min	70 ± 28
% time	19 ± 7
Stage 1 sleep	
Duration, min	24 ± 13
%	7 ± 4
Stage 2 sleep	
Duration, min	223 ± 54
%	63 ± 10
Slow wave sleep (stages 3 & 4)	
Duration, min	40 ± 33
%	11 ± 9
Sleep efficiency %	74 ± 12

REM = rapid eye movement, SD = standard deviation

RESULTS

Baseline Characteristics and Univariate Analysis

The study population was predominantly (over 90%) Caucasian, with a mean age of 76 years (SD, 5.5; range 67-96). Nearly 73% had one or more comorbidities, including cardiovascular disease (42%), hypertension (50%), diabetes mellitus (13%), and chronic lung disease (14%), while only 2% were current smokers. The mean TST derived by PSG was 356 minutes (Table 1). On average, the total duration of SWS was 40 minutes and accounted for 11% of TST, while REM duration was 70 minutes and accounted for 19% of TST.

Increased amount of SWS was associated with younger age, more physical activity, lower RDI, longer TST, and greater sleep efficiency (Table 2). The percentage of Caucasians increases as the quartiles of SWS increase. Comorbidities, smoking status, and central apnea index were not associated with SWS. The covariates significantly associated with REM sleep were age, physical activity, RDI, TST, sleep efficiency, and comorbid conditions (data not shown). Age, RDI, and comorbid conditions were inversely associated with REM sleep, whereas physical activity, TST and sleep efficiency were positively associated.

Sleep Architecture and Body Composition

SWS was significantly associated with BMI after adjusting for age and clinic site (Table 3). Specifically, increasing quartiles of SWS were associated with decreasing BMI. On average, participants in the lowest SWS quartile had an adjusted BMI of 27.5, those in quartiles 2 and 3 had a BMI of approximately 27.1, and those in the highest quartile had the lowest BMI of 26.7 ($P = 0.0002$ for trend). The model was then sequentially adjusted with covariates. As shown in Table 4, the average BMI increased with decreasing SWS in each of the 3 multivariate models. This association remained significant after adjustment for all identified potential confounders (e.g., race, physical activity, TST, sleep efficiency, SDB), with men in the

Table 2—Univariate Association Between Slow Wave Sleep Quartile and Confounders

	Quartile of slow wave sleep (SWS as a % of total sleep time)				
	Quartile 1 0% to ≤ 3.8% (n = 688)	Quartile 2 > 3.8% to ≤ 9.9% (n = 685)	Quartile 3 > 9.9% to ≤ 16.7% (n = 686)	Quartile 4 > 16.7% (n = 686)	P-value (for trend)
Age (years), mean ± SD	77.2 ± 5.7	76 ± 5.4	75.9 ± 5.4	76.4 ± 5.5	<0.0001
Race/ethnicity-non-Caucasian, n (%)	80 (11.6)	64 (9.3)	62 (9.0)	46 (6.7)	0.018
Physical activity (PASE Score), mean ± SD	143 ± 73	147 ± 73	153 ± 71	143 ± 69	0.018
History of diabetes mellitus, n (%)	100 (14.5)	87 (12.7)	86 (12.5)	85 (12.4)	0.608
History of cardiovascular disease, n (%)	312 (45.4)	283 (41.4)	274 (40.0)	281 (41.0)	0.188
History of hypertension, n (%)	350 (50.9)	337 (49.2)	344 (50.2)	339 (49.4)	0.924
History of chronic lung disease, n (%)	92 (13.4)	88 (12.9)	92 (13.4)	100 (14.6)	0.817
Smoking (current or prior), n (%)	404 (58.72)	413 (60.29)	406 (59.18)	426 (62.1)	0.585
Pack-years smoked, mean ± SD	16 ± 23	17 ± 25	16 ± 23	16 ± 22	0.876
RDI (events/hr), mean ± SD	15.2 ± 16.0	11.7 ± 12.5	10.1 ± 11.0	9.9 ± 11.0	<0.0001
RDI ≥ 15, n (%)	244 (35%)	174 (25%)	154 (22%)	151 (22%)	<0.0001
RDI ≥ 5, n (%)	471 (68%)	420 (61%)	391 (57%)	386 (56%)	<0.0001
CAI, mean ± SD	1.84 ± 5.02	1.48 ± 4.06	1.32 ± 3.42	1.31 ± 3.84	0.511
CAI ≥ 5, n (%)	59 (9%)	50 (8%)	44 (7%)	45 (7%)	0.375
Total sleep time (min), mean ± SD	344.1 ± 72.5	360.6 ± 67.7	360.8 ± 65.8	358.3 ± 67.9	<0.0001
Sleep efficiency (%), mean ± SD	71.1 ± 12.8	73.9 ± 12.2	75.3 ± 11.2	75.7 ± 11.9	<0.0001

SD = standard deviation, RDI = respiratory disturbance index, CAI = central apnea index
P-value is from comparison across quartiles of SWS using ANOVA (continuous variables with normal distribution), Kruskal-Wallis test (continuous variable with skewed distribution) or chi-square test (categorical variables)

Table 3—Age and Clinic Adjusted Association of Body Composition Outcomes and SWS

		Quartile of slow wave sleep (SWS as a % of total sleep time)				
Outcomes	N	Quartile 1 0 to < 3.8%	Quartile 2 > 3.8 to < 9.9%	Quartile 3 > 9.9 to < 16.7%	Quartile 4 > 16.7%	*P-value for trend
BMI (kg/m²)	2743	27.5	27.1	27.17	26.7	0.0002
Weight (kg)	2743	83.3	82.2	82.3	80.6	0.0001
Waist circumference (cm)	2739	100.3	99.3	99.4	98.8	0.012
Waist-to-hip ratio	2737	1.04	1.04	1.04	1.04	0.575
% Fat mass	2700	26.1	26.2	26.2	.26.4	0.255

*P-value for linear regression (assessing linear trend across quartiles of SWS)
BMI = body mass index, SWS = slow wave sleep

lowest quartile of SWS having an average BMI of 27.4 while those in the highest quartile had a BMI of 26.8 (P = 0.0095 for trend) (Table 4, model 3).

Similarly, in the minimally adjusted model (Table 3), waist circumference and weight showed statistically significant negative associations with SWS quartiles. On average, men in the lowest SWS quartile weighed 2.7 kg more and had a waist circumference 1.5 cm greater than those in the highest SWS quartile. Weight remained inversely associated with SWS in the fully adjusted model (Table 4, model 3). Men in the lowest SWS quartile weighed 83 kg, whereas those in the highest quartile weighed 80.6 kg (P = 0.001 for trend). Waist circumference also remained significantly inversely associated with SWS quartile (models 1 and 2). However, the association between waist circumference and SWS quartiles was attenuated (P = 0.089) after adjustment for SDB (model 3), although the adjusted mean values were similar to those of the minimally adjusted model, suggesting that lower power may have been partially responsible for this. Because percentage total body fat mass and waist-to-hip ratio were not significantly associated with SWS in models minimally adjusted for age and clinic, further multivariate analyses were not performed for these outcomes. There were no significant trends observed between quartiles of REM sleep and any of the designated primary or secondary outcomes after adjusting for age and clinic site (data not shown).

Potential effect modification associated with SDB was examined further (Table 5). In analyses stratified by SDB (RDI < 15 or ≥ 15), a significant relationship between SWS and BMI, weight and waist circumference was observed in those with a RDI < 15. However, in the RDI ≥ 15 strata (26% of participants), there was no relationship between SWS and any of the outcomes studied. A formal assessment of interaction (between quartile 4 of SWS and SDB) indicated that interaction between these terms was present with respect to BMI (P = 0.03 for the interaction term), weight (P = 0.077), and waist circumference (P = 0.07). There was no significant interaction between SWS and TST (P > 0.10).

Table 4—Sequential Multivariate Analysis of Body Composition by Quartiles of SWS

Outcomes	N	Quartile of slow wave sleep (SWS as a % of total sleep time) Quartile 1 0 to ≤ 3.8%	Quartile 2 > 3.8 to ≤ 9.9%	Quartile 3 > 9.9 to ≤ 16.7%	Quartile 4 > 16.7%	*P-value for trend
Model 1						
BMI (kg/m²)	2743	27.5	27.1	27.2	26.7	0.0001
Weight (kg)	2743	83.5	82.1	82.3	80.4	< 0.0001
Waist circumference (cm)	2739	100.5	99.3	99.5	98.6	0.003
Model 2						
BMI (kg/m²)	2743	27.5	27.1	27.2	26.7	0.0009
Weight (kg)	2743	83.3	82.1	82.4	80.5	0.0001
Waist circumference (cm)	2739	100.3	99.3	99.6	98.8	0.02
Model 3						
BMI (kg/m²)	2743	27.4	27.1	27.3	26.8	0.0095
Weight (kg)	2743	83.0	82.2	82.5	80.6	0.001
Waist circumference (cm)	2739	100.0	99.3	99.7	98.9	0.089

Model 1: adjusted for age, race/ethnicity, PASE, clinic
Model 2: adjusted for age, race/ethnicity, PASE, clinic, TST and sleep efficiency
Model 3: adjusted for age, race/ethnicity, PASE, clinic, TST, sleep efficiency and SDB
Results unchanged when TST used as categorical (rather than continuous) variable (data not shown)
*P-value for linear regression (assessing linear trend across quartiles of SWS)

Sleep Architecture and Obesity

We assessed the association between SWS and obesity (i.e., BMI ≥ 30) in a multivariate logistic model adjusted for age, race/ethnicity, clinic, TST, sleep efficiency, and RDI. We found 1.4-fold increased odds (95% CI 1.03, 1.8) for obesity in participants in the lowest SWS quartile, compared to those in the highest SWS quartile. When stratified by SDB, participants with RDI < 15 in the lowest quartile of SWS had 1.5-fold increased odds for obesity (95% CI 1.1, 2.2, P = 0.03) compared with the highest SWS quartile. In participants with RDI ≥ 15, the odds for obesity did not differ significantly for those in the lowest versus highest SWS quartiles (odds ratio = 1.08, 95% CI 0.7, 1.7). REM sleep was not associated with obesity in the unadjusted logistic model and therefore, multivariate analysis was not performed.

Additional Analyses

To address potential confounding due to mild to moderate levels of SDB, we analyzed the association between SWS and measures of body composition in the subset of participants with RDI < 5 (n = 1077, 39% of participants), and found no difference in the results compared to participants with RDI < 15 (data not shown). A statistically significant, negative relationship between SWS and BMI, weight, and waist circumference was still present. Furthermore, to exclude participants with any central sleep apnea, we also assessed the multivariate model subset to those with CAI < 5. The results were similar to the subjects with RDI < 15 (data not shown). Lastly, we assessed the relationship between percentage of time in stage 1 sleep and measures of body composition (i.e., BMI, weight, waist circumference, waist-to-hip ratio, and percentage fat mass). We found no significant association between these measures of body composition and either stage 1 sleep or stage 2 sleep. We also found no significant relationship between arousal index (as a measure of sleep fragmentation) and measures of body composition.

DISCUSSION

With the increasing incidence of obesity over the past decade, the role of sleep duration in energy metabolism and obesity has been assessed in multiple epidemiologic studies.[5-7] However, this is the first large scale study to examine the relationship of sleep architecture and, specifically, slow wave sleep, with measures of body composition such as BMI, waist circumference and percentage body fat. In this cohort study of community-dwelling, older men, we found a significant negative relationship between SWS and BMI, after controlling for various confounding factors including RDI and TST. Furthermore, this relationship was independent of total sleep duration. Specifically, men in the lowest quartile of SWS had an average 0.6 kg/m² greater BMI than those in the highest quartile. The magnitude of this effect on BMI is consistent with the results of other studies which assessed the effect of total sleep duration on BMI,[5-7] in which the differences in BMI ranged from 0.8-1.2. A rigorous series of analyses showed that these associations were not due to confounding from SDB, nor were they explained by reductions in total sleep duration. However, we found that this association was most significant and substantial in men with mild or no SDB. This association was no longer present in participants with modest to severe SDB. Finally, similar findings were observed between SWS and waist circumference, a measure considered more specific for central body fat distribution and diabetes risk than BMI.

However, we did not find a consistent relationship between SWS and percentage fat mass, possibly because of limitations in the measurement of body fat with DEXA, or because total body fat is not as strongly associated with sleep as a measure of central body fat would be. In this study population, BMI and percentage body fat were correlated at an r-value of 0.69, which

Table 5—Stratified Multivariate* Adjusted Association of Body Composition and SWS

Outcomes	N	RDI	Quartile of slow wave sleep (SWS as a % of total sleep time) Quartile 1 0 to ≤ 3.8%	Quartile 2 > 3.8 to ≤ 9.9%	Quartile 3 > 9.9 to ≤ 16.7%	Quartile 4 > 16.7%	**P-value for trend
BMI (kg/m²)	2022	< 15	26.9	26.8	26.8	26.2	0.003
	721	≥ 15	28.6	28	28.4	28.5	0.947
Weight (kg)	2022	< 15	81.8	81.6	81.6	79.2	< 0.001
	721	≥ 15	86	83.7	85.2	84.8	0.459
Waist circumference (cm)	2022	< 15	99	98.4	98.6	97.4	0.017
	721	≥ 15	102.9	101.8	103	103.3	0.666

*Adjusted for: age, clinic, race, physical activity, TST, and sleep efficiency.
**P-value for linear regression (assessing linear trend across quartiles of SWS)

is similar to that found in other studies.[30-32] A discrepancy between BMI and percent fat mass in predicting outcomes has been noted in other studies.[33-36] The relationship between BMI and percent body fat is known to be dependent on age, gender, and ethnicity.[37,38] Furthermore, discrepancies between BMI and percentage body fat occur with increasing age and body fat mass.[30,39] The MrOS Sleep cohort consists of older men, of which 9% are non-Caucasian. Another possible explanation for the discrepancy between BMI and percent fat mass is that these subjects have an accumulation of visceral adipose tissue, which would not be assessed by the whole body DEXA. In support of this hypothesis is the observed association between SWS and waist circumference. A sensitive measure of visceral adiposity (such as abdominal CT scan) is not currently available for this cohort. In the MrOS Sleep Study population, we also did not find a significant association between percentage of REM sleep and measures of body composition, suggesting that SWS may be more specifically important than TST or other sleep stages.

We postulated that SWS would play an important role in energy homeostasis for a number of reasons. First, a recent study in humans has shown that selective deprivation of SWS for 3 nights induces insulin resistance,[20] indicating a potentially crucial role of SWS in metabolism. Second, studies have suggested a relationship between hormone secretion by the hypothalamus/pituitary gland and SWS. Specifically, SWS appears to be associated with decreased secretion of cortisol and ACTH, and increased secretion of growth hormone.[40-42]

Studies published 20-30 years ago assessed the relationship between obesity and REM sleep, but not SWS. Although some studies found a significant positive relationship between REM sleep (as a percentage of total sleep) and BMI,[16,17] other studies did not find this relationship.[18,19] Furthermore, these studies were performed on a very small number of individuals (approximately 50).

In this current study, we did not find a significant relationship between REM sleep and body composition. Our cohort consisted of a large number of participants (over 2000) and our population of older men fundamentally differed from the previous studies that included young and middle-aged men. A more recent study that analyzed sleep architecture in a large cohort of men and women found that SWS (as a percentage of total sleep) was significantly higher in participants in the lowest quartile of BMI (< 24.8); however, no significant relationships were seen across the highest 3 quartiles of BMI.[43] Notably, SWS percentage varied significantly between men and women, which may have contributed to the difficulty in assessing the relationship between BMI and SWS. In this current study, the uniformity of gender and restriction to older age (≥ 65 years) allowed us examine the effects of sleep architecture on obesity and other measures of body composition more closely.

Limitations of this study include the lack of generalizability to women or younger men. Furthermore, given the cross-sectional nature of these analyses, we are unable to assess the causative relationship between SWS and BMI. It is possible that increased BMI (through factors such as SDB) may alter sleep architecture and decrease SWS. We have tried to account for SDB by including it within our multivariate models and by performing stratified analyses. However, it is possible that residual confounding remains. The major strengths of this study are its large size, population (community dwelling men), objective characterization of sleep duration and architecture, and comprehensive measures of body composition. In conclusion, we found that higher levels of SWS were associated with decreased BMI and other measures of obesity. These associations were most notable in participants with no evidence of SDB. Furthermore, the odds of obesity were 40% higher for participants in the lowest quartile of SWS than those in the highest quartile. These findings suggest a link between sleep architecture, in particular SWS, and obesity risk among older men. Additional studies in other cohorts will need to be performed to confirm these results and to further expand the generalizability of these observations.

ABBREVIATIONS

BMI = body mass index
CAI = central apnea index
CI = confidence interval
DEXA = dual energy x-ray absorptiometry
ICC = intraclass correlation coefficient
MrOS = Osteoporotic Fractures in Men Study
NREM = non-rapid eye movement
PASE = Physical Activity Scale for the Elderly
PSG = polysomnography
RDI = respiratory disturbance index
REM = rapid eye movement

SDB = sleep disordered breathing
SWS = slow wave sleep
TST = total sleep time

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