Resting Energy Expenditure in Adults With Sleep Disordered Breathing

Eric J. Kezirian, MD, MPH; Ceyda E. Kirisoglu, MD; Robert W. Riley, MD, DDS; Edward Chang, DDS, MD; Christian Guilleminault, MD, BiolD; Nelson B. Powell, MD, DDS

Objective: To examine the association between sleep disordered breathing severity and resting energy expenditure (REE).

Design: Cross-sectional.

Setting: University-based academic medical center.

Participants: Two hundred twelve adults with signs or symptoms of sleep disordered breathing underwent medical history, physical examination, level I attended polysomnography, and determination of REE using an indirect calorimeter.

Main Outcome Measure: Mean REE.

Results: Seventy-one percent (151 of 212) of the study population were male, and the mean (SD) age was 42.3 (12.6) years. The mean (SD) body mass index, calculated as weight in kilograms divided by height in meters squared, was 28.3 (7.3). The mean (SD) apnea-hypopnea index was 25.4 (27.2), and the lowest oxygen saturation during the sleep study was 86.9% (9.5%). The mean (SD) REE was 1763 (417) kcal/d. Analysis of variance and univariate regression analysis showed an association between REE and several measures of sleep disordered breathing severity that persisted after adjustment for age, sex, and self-reported health status in multiple regression analysis. Only REE and the apnea-hypopnea index demonstrated an independent association after additional adjustment for body mass index (or body weight and height separately). This association did not differ between individuals with normal vs elevated body mass index.

Conclusions: Sleep disordered breathing severity is associated with REE. Although this association is largely confounded by body weight, there is an independent association with the apnea-hypopnea index.


Obesity is a major risk factor for the development of sleep disordered breathing (SDB), and changes in body weight are associated with changes in SDB severity. Using data from 690 adults in the Wisconsin Sleep Cohort Study, Peppard et al found that a 10% weight gain during 4 years was associated with a 32% increase in apnea-hypopnea index (AHI) and that a 10% weight loss was associated with a 26% decrease in AHI. This same 10% weight gain was associated with a 6-fold increase in the odds of developing moderate to severe SDB. Because of this and other similar findings, there has been considerable interest in treating SDB using a range of obesity interventions such as dietary changes, behavioral modification, and, for selected patients, bariatric surgery. Unfortunately, the success of these interventions has been inconsistent. It is unclear whether weight gain is simply a cause of SDB or whether SDB may be associated with alterations in energy metabolism that, in turn, lead to weight gain and complicate the treatment of these 2 disorders that often coexist. Studies have identified hormonal changes related to weight homeostasis that occur in SDB, but data are limited concerning the association between SDB and metabolic rates.

Ultimately, body weight is based on the balance between energy intake and expenditure. Total energy expenditure (TEE) includes resting energy expenditure (REE [60%-75% of TEE]), dietary thermogenesis, thermic effect of exercise, and facultative thermogenesis (energy expenditure that occurs in response to environmental stressors). All of these may be affected by SDB. For example, REE may be affected by adrenergic changes that occur in SDB using a range of obesity interventions such as dietary changes, behavioral modification, and, for selected patients, bariatric surgery. Unfortunately, the success of these interventions has been inconsistent.
of exercise and related energy expenditure. In addition, facultative thermogenesis is, in part, regulated by the hypothalamic-pituitary axis and other hormonal factors that have demonstrated reversible abnormalities in patients with SDB.

The objective of this study was to examine the association between SDB severity and REE. This was evaluated in a large population of adults.

This study was approved by the institutional review board at Stanford University, Stanford, California. Women and men aged 18 to 65 years were eligible if seeking treatment for or if recently diagnosed as having SDB. Subjects were healthy and were without significant pulmonary or cardiac disease, unstable psychiatric disorder, or history of alcohol or other drug abuse. Pregnant women were excluded from the study. A convenience sample of patients was recruited after undergoing routine medical history and physical examination. Height and weight were recorded on physical examination, and patients provided a self-report of their health status (good, moderate, fair, or poor). Daytime sleepiness was evaluated by completion of the Epworth Sleepiness Scale.13

Resting metabolic rate was evaluated using indirect calorimetry according to the validated method by Weir.14 All subjects were fasting for a minimum of 6 hours. For 24 hours before testing, they were instructed not to engage in exercise or strenuous physical activity and to avoid caffeine intake. A handheld indirect calorimeter (MedGem; HealtheTech, Inc, Golden, Colorado) was used to measure oxygen consumption and carbon dioxide production, and these were used to determine REE (in kilocalories per day). Each subject completed a baseline evaluation before polysomnography (if previous polysomnography was not performed) or before any treatment, whether the association between SDB severity and REE varied according to BMI, an interaction term (the product of SDB severity measures as continuous variables and a dichotomous BMI variable, with the following categories: normal (BMI, ≤25 mm Hg), moderate increase in respiratory effort (BMI, >25 to ≤30), and obesity (BMI, ≥30)) was included in the regression equations that incorporated BMI. Re-gression coefficient estimates are given with their 95% confidence intervals. For all analyses, P < .05 was considered statistically significant.

Data were analyzed using commercially available statistical software (STATA 8.0; StataCorp LP, College Station, Texas). Resting energy expenditure, descriptive statistics, and polysomnography results are given as means (SDs). One-way analysis of variance was used to test for differences in REE between SDB severity groups defined by commonly used cutpoints (based on AHI and Pes). Univariate linear regression analysis was used to test the association between REE and polysomnography measures. Multiple linear regression analysis was used to test these associations with adjustment for age, sex, and self-reported health status. Additional adjustment was performed with inclusion of body mass index (BMI; calculated as weight in kilograms divided by height in meters squared) or, separately, body weight and height in the multiple regression equation. To evaluate whether the association between SDB severity and REE varied according to BMI, an interaction term (the product of SDB severity measures as continuous variables and a dichotomous BMI variable corresponding to whether BMI was >25 or ≥28.3, with the latter representing the mean BMI of the sample) was included in the regression equations that incorporated BMI.

A convenience sample of 212 patients was enrolled. Seventy-one percent (151 of 212) of the study group members were male, and the mean (SD) age was 42.3 (12.6) years. The mean (SD) BMI was 28.3 (7.3); body weight was 85.9 (24.5) kg, and height was 174 (10) cm. The distribution among BMI categories was as follows: overweight (BMI, ≤20) in 5.7% (12 of 212), normal (BMI, >20 to ≤25) in 50% (65 of 212), overweight (BMI, >25 to ≤30) in 34.4% (73 of 212), and obesity (BMI, >30) in 29.2% (62 of 212). Self-reported health status was good (64.2% [124 of 193]), medium (25.4% [49 of 193]), fair (7.3% [14/193]), or poor (3.1% [6 of 193]). The mean (SD) Epworth Sleepiness Scale score was 9.3 (±7.0).

Polysonmography results are given in Table 1. Ninety-four percent (200 of 212) of patients had polysomnography performed at Stanford University Sleep Disorders and Research Center. Overall, the population demonstrated a roughly even distribution of AHI across the fol-
Increased REE is associated with greater SDB severity. This association is largely confounded by BMI or body weight. However, there is an independent association with AHI (and a trend toward association with the obstructive apnea index and hypopnea index separately) but not with other measures of SDB severity such as LSAT and Pes. This association between AHI and REE does not differ between individuals with normal and elevated BMI.

The independent association between REE and AHI, among the various measures of SDB severity, is interest-
sleep fragmentation in healthy adults. Sulit et al. demonstrated an increase in REE related to the frequency of events such as oxygen desaturations per hour (analogous to REE during sleep). Stenlöf et al. found higher TEE and SEE in 5 adults with OSA vs 6 controls with snoring and found that continuous positive airway pressure therapy reduced TEE and SEE. No difference was noted in the ratio of TEE to SEE between the 2 groups.

For 8 adults with OSA compared with a control group of 86 adults without apnea, Hins et al. found no association between OSA and TEE or sleep metabolic rates (analogous to REE during sleep). Stenlöf et al. found higher TEE and SEE in 5 adults with OSA vs 6 controls with snoring and found that continuous positive airway pressure therapy reduced TEE and SEE. No difference was noted in the ratio of TEE to SEE between the 2 groups.

The bulk of earlier work related to metabolic rates and SDB focused on TEE or sleep energy expenditure (SEE). Stenlöf et al. found higher TEE and SEE in 5 adults with OSA vs 6 controls with snoring and found that continuous positive airway pressure therapy reduced TEE and SEE. No difference was noted in the ratio of TEE to SEE between the 2 groups. For 8 adults with OSA compared with a control group of 86 adults without apnea, Hins et al. found no association between OSA and TEE or sleep metabolic rates.

### Table 4. Multiple Linear Regression Results for Resting Energy Expenditure and Apnea-Hypopnea Index

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient Estimate (95% CI)</th>
<th>P Value</th>
<th>Coefficient Estimate (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apnea-hypopnea index</td>
<td>5.37 (3.27 to 7.46)</td>
<td>&lt;.001</td>
<td>2.69 (0.63 to 4.74)</td>
<td>.01</td>
</tr>
<tr>
<td>Age</td>
<td>-5.59 (-9.57 to -1.42)</td>
<td>.008</td>
<td>-5.86 (-9.52 to -2.19)</td>
<td>.002</td>
</tr>
<tr>
<td>Male</td>
<td>304 (189 to 419)</td>
<td>&lt;.001</td>
<td>268 (164 to 372)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Health</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Good</td>
<td>-4 (-196 to 188)</td>
<td>.97</td>
<td>43 (-129 to 217)</td>
<td>.62</td>
</tr>
<tr>
<td>Medium</td>
<td>-26 (-230 to 177)</td>
<td>.80</td>
<td>-8 (-191 to 175)</td>
<td>.93</td>
</tr>
<tr>
<td>Poor</td>
<td>683 (360 to 1005)</td>
<td>&lt;.001</td>
<td>595 (305 to 885)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Body mass index</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### Table 5. Multiple Linear Regression Results for Resting Energy Expenditure and Other Polysomnographic Measures

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficient Estimate (95% CI)</th>
<th>P Value</th>
<th>Coefficient Estimate (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Obstructive apnea index</td>
<td>5.24 (2.64 to 7.83)</td>
<td>&lt;.001</td>
<td>2.03 (-0.43 to 4.49)</td>
<td>.10</td>
</tr>
<tr>
<td>Hypopneas per hour of sleep</td>
<td>5.62 (1.83 to 9.42)</td>
<td>&lt;.004</td>
<td>2.75 (-0.62 to 6.12)</td>
<td>.11</td>
</tr>
<tr>
<td>Arousal index</td>
<td>5.79 (3.77 to 7.81)</td>
<td>&lt;.001</td>
<td>3.12 (1.13 to 5.12)</td>
<td>.002</td>
</tr>
<tr>
<td>Lowest oxygen saturation during sleep</td>
<td>-9.93 (-15.70 to -4.16)</td>
<td>.001</td>
<td>-2.16 (-7.68 to 3.37)</td>
<td>.44</td>
</tr>
<tr>
<td>Slow wave sleep</td>
<td>1.80 (-3.92 to 7.53)</td>
<td>.53</td>
<td>1.76 (-3.12 to 6.64)</td>
<td>.48</td>
</tr>
<tr>
<td>Rapid eye movement sleep</td>
<td>-4.19 (-10.80 to 2.45)</td>
<td>.21</td>
<td>-0.91 (-6.67 to 4.84)</td>
<td>.75</td>
</tr>
<tr>
<td>Periodic limb movement index</td>
<td>-0.07 (-3.83 to 3.68)</td>
<td>.97</td>
<td>-0.80 (-4.02 to 2.42)</td>
<td>.62</td>
</tr>
<tr>
<td>Maximum negative esophageal pressure</td>
<td>-3.60 (-7.19 to -0.01)</td>
<td>.05</td>
<td>-1.07 (-4.49 to 2.34)</td>
<td>.54</td>
</tr>
</tbody>
</table>

### Notes

**Abbreviations:** CI, confidence interval; ellipsis, not applicable.

- **Model 1a results** are coefficient estimates for a regression equation that includes apnea-hypopnea index and adjustment for age, sex, and self-reported health status.
- **Model 2b results** are coefficient estimates from a similar model, adding adjustment for body mass index.
(no difference between measured and predicted values); however, there was an association between severity of nocturnal desaturation (percentage of sleep time with an oxygen saturation of <90% on polysomnography) and both TEE and sleep metabolic rate (greater desaturation associated with lower than predicted values). Finally, Lin et al. found higher SEE (but not morning basal metabolic rate) in a group of 25 adults with moderate to severe OSA compared with 15 controls. After undergoing laser-assisted uvulopalatoplasty, 6 patients with OSA who responded to this surgical treatment (AHI decreased by ≥50% to an absolute level <20) demonstrated a reduction in SEE but no change in basal metabolic rate; there were no changes among 19 nonresponders.22

The evidence concerning SDB and metabolic rates in children is also mixed. In 11 children with OSA compared with controls, Bland et al. showed no differences in overall TEE. Li et al. also demonstrated no relationship between SEE and OSA severity (measured using AHI) in a group of 24 children with OSA. In 14 children experiencing resolution of OSA after undergoing adenotonsillectomy, Marcus et al. showed reduction in SEE.

The major limitation of this study is the lack of data regarding body composition or lean body mass. Body composition has a well-described association with REE because, for example, muscle has greater metabolic activity than adipose tissue. Data on body composition would enhance this examination; however, the complexity of such an assessment is the basis for the fact that the studies described herein that assessed body composition or lean body mass have small sample sizes. We believe our findings are valid because, although we are unable to adjust for body composition, the study findings are robust to 2 different methods of adjustment for body weight. Our larger sample size enables a broader distribution of SDB severity, increasing statistical power and enhancing generalizability. Finally, this sample included 30.7% with normal BMI, and the association between SDB severity and REE did not differ for subjects with normal BMI vs elevated BMI. It would have been more challenging to assess body composition in a study population of this size, but future research can incorporate such evaluations.

This study advances our knowledge concerning SDB and metabolic rates, but it does not define the connection between SDB and body weight. Body weight is determined by the balance between energy intake and expenditure. Although the findings of this study suggest that SDB increases energy expenditure, it ignored 2 important aspects of this balance. First, SDB often results in fatigue and other decrements in daytime functioning that can limit physical activity. Second, this work does not specifically incorporate the emerging evidence that suggests that SDB may alter energy intake, whether through hormonal or other mechanisms. Future research considering the effect of SDB on body weight can include the effects on energy intake and expenditure.

Increasing SDB severity is associated with increasing SEE. Although this association is largely confounded by body weight, there is an independent association with AHI.

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Correspondence: Nelson B. Powell, MD, DDS, Department of Psychiatry and Behavioral Science and Stanford University Sleep Disorders and Research Center, Stanford University School of Medicine, 750 Welch Rd, Ste 317, Palo Alto, CA 94304 (npowell@stanford.edu).

Author Contributions: Dr Kezirian had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. Study concept and design: Kirisoglou, Guilleminault, and Powell. Acquisition of data: Kirisoglou, Riley, Chang, Guilleminault, and Powell. Analysis and interpretation of data: Kezirian and Powell. Drafting of the manuscript: Kezirian, Kirisoglou, Chang, Guilleminault, and Powell. Critical revision of the manuscript for important intellectual content: Riley, Guilleminault, and Powell. Statistical analysis: Kezirian. Obtained funding: Riley and Powell. Administrative, technical, and material support: Kirisoglou, Riley, Guilleminault, and Powell. Study supervision: Riley, Guilleminault, and Powell.

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