Obesity Without Sleep Apnea Is Associated With Daytime Sleepiness

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Background: Daytime sleepiness and fatigue is a frequent complaint of obese patients even among those who do not demonstrate sleep apnea.

Objective: To assess in the sleep laboratory whether obese patients without sleep apnea are sleepier during the day compared with healthy controls with normal weight.

Methods: Our sample consisted of 73 obese patients without sleep apnea, upper airway resistance syndrome, or hypoventilation syndrome who were consecutively referred for treatment of their obesity and 45 controls matched for age. All patients and healthy controls were monitored in the sleep laboratory for 8 hours at night and at 2 daytime naps, each for 1 hour the following day.

Results: Obese patients compared with controls were sleepier during the day and their nighttime sleep was disturbed. During both naps, sleep latency, wake time after onset of sleep, and total wake time were significantly lower, whereas the percentage of sleep time was significantly higher in obese patients compared with controls. In contrast, during the nighttime testing, obese patients compared with controls demonstrated significantly higher wake time after onset of sleep, total wake time, and lower percentage of sleep time. An analysis of the relation between nighttime and daytime sleep suggested that daytime sleepiness in obese patients is a result of a circadian abnormality rather than just being secondary to nighttime sleep disturbance.

Conclusions: Daytime sleepiness is a morbid characteristic of obese patients with a potentially significant impact on their lives and public safety. Daytime sleepiness in individuals with obesity appears to be related to a metabolic and/or circadian abnormality of the disorder.

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IN 1988 TO 1991, 33.4% of US adults aged 20 years or older were estimated to be overweight (at least an increase of 24% for men and 20% for women above ideal body weight).1 Obesity is associated with significant mortality and morbidity, including diabetes, cerebral and cardiovascular disorders, and obstructive sleep apnea.2,3 In a large group of severely or morbidly obese patients, 40% of men and 3% of women demonstrated obstructive sleep apnea severe enough to warrant therapeutic intervention.4

Daytime sleepiness and fatigue is a frequent complaint of obese people even among those who do not demonstrate sleep apnea or any degree of sleep disordered breathing.4 However, to our knowledge, no study has assessed objectively the degree of daytime sleepiness in obese patients without sleep apnea. The aim of our study was to assess in the sleep laboratory whether obese patients without sleep apnea are sleepier during the day compared with healthy controls with normal weight.

RESULTS

NIGHTTIME SLEEP

Compared with controls, obese patients demonstrated a significantly higher WTASO (82.4 ± 6.9 vs 46.1 ± 6.1 minutes; P<.01) and TWT (117.3 ± 8.8 vs 72.3 ± 7.2 minutes; P<.01) and a significantly lower percentage of sleep time (75.5% ± 1.8% vs 84.9% ± 1.5%; P<.01) (Table 1). Also, the percentage of WTASO during the sleep period was higher in obese patients compared with controls (18.9% ± 1.7% vs 10.7% ± 1.4%; P<.01). In addition, compared with controls, obese patients demonstrated a significantly higher percentage of stage 1 sleep (10.3% ± 0.8% vs 7.3% ± 0.7%; P<.01) and a significantly lower
PATIENTS, SUBJECTS, AND METHODS

PATIENTS AND SUBJECTS

Seventy-three patients, 7 men (9.6%) and 66 women (90.4%) (6 of them postmenopausal [9.1%]), with a diagnosis of obesity (body mass index [BMI], a measure of weight in kilograms divided by the square of the height in meters) ≥27.8, mean ± SE, 45.4 ± 1.3; range, 27.8-85.8) and 45 healthy control subjects (mean ± SE BMI, 23.5 ± 0.42; range, 18.6-30.6) participated in this study. Sixty-eight of the obese patients were either severely (BMI ≥32) or morbidly (BMI ≥39) obese. Overall 91 patients were referred consecutively to the University Weight Management Center of the Milton S. Hershey Medical Center, Hershey, Pa, for treatment of their obesity. Eighteen of them were excluded from the study because they were found to have some type of sleep disordered breathing or other disorder of excessive daytime sleepiness. The mean ± SE age of these obese patients was 37.4 ± 1.0 years (range, 16-55 years). A complete medical history was recorded and a complete physical examination was performed, including neurologic assessment and a battery of clinical tests (including complete blood cell count, urinalysis, thyroid indexes, and electrocardiography). No abnormalities were detected in the clinical or laboratory assessment, including blood cell counts and thyroid indexes, which could have accounted for the daytime sleepiness.

The obese patients who demonstrated obstructive sleep apnea of sufficient severity to warrant therapeutic recommendations or had an apnea plus hypopnea index of 5 or more events per hour of sleep were excluded from the study. Also the patients who demonstrated symptoms and/or signs consistent with hypoventilation syndrome or a resting hemoglobin oxygen saturation of less than 92% were excluded from the study. In addition, obese patients who had a complaint of daytime sleepiness or fatigue and their polysomnographic study demonstrated loud snoring, waking up at night because of snoring or gasping, and frequent brief electrophysiologic semiarousals that appeared to be related to snoring were excluded from the study.

Finally, obese patients who were diagnosed as having a primary disorder of excessive daytime sleepiness, ie, narcolepsy or idiopathic hypersomnia, were excluded from the study.

The controls consisted of 28 women (62.2%) (3[10.7%] of them postmenopausal) and 17 men (37.8%) (mean ± SE age, 41.2 ± 1.7 years; range, 17-58 years). The controls were selected from a large pool of subjects by controlling for age with the obese patients (the mean age of the controls was not significantly different from the mean age of the obese patients); the controls were selected solely based on age without knowledge of sleep laboratory findings. Control subjects were recruited from the medical and technical staff and student population of the medical center as well as from friends and acquaintances of the medical center personnel. A careful screening process was used to ensure that the control subjects had no sleep complaints, no major psychiatric disorders, were in good general health, and were not using any medication. The project was approved by our institutional review board and a written informed consent was obtained from the subjects.

SLEEP LABORATORY PROCEDURES

All the patients and control subjects were monitored using 16-channel polygraphs (Model 78c, Grass Instrument Co, Quincy, Mass) in the sleep laboratory for one 8-hour nocturnal polysomnogram and for 2 daytime naps the next day in sound-attenuated, light- and temperature-controlled rooms. The 2 nap sessions lasted 60 minutes each and began at approximately 9:00 AM and 12:30 PM. This test provides a quantitative assessment of pathologic diurnal sleepiness and has been suggested as an alternative to

percentage of REM sleep (16.7% ± 0.9% vs 19.7% ± 0.9%; P<.01). The amount of REM sleep was significantly decreased in the first and second third of the night in obese patients compared with controls. Furthermore, REM latency and REM interval were significantly increased in obese patients compared with controls.

DAYTIME SLEEP

In the morning nap, 72 (100%) of 72 obese patients and 41 (81.8%) of 146 controls had some sleep. In the afternoon nap, 62 (100%) of 62 obese patients and 37 (80.4%) of 46 controls had some sleep. The percentage of obese patients compared with healthy controls who slept during the 2 naps was significantly higher (for both, P<.01).

PROPENSITY TO FALL ASLEEP (SLEEP LATENCY)

During both naps obese patients fell asleep significantly faster than healthy controls. Specifically, obese patients compared with controls demonstrated a significantly shorter sleep latency during the first nap (13.7 ± 1.9 vs 22.7 ± 2.8 minutes; P<.01) (Table 2). A similar difference was noted between these 2 groups during the second nap (18.7 ± 1.6 vs 27.6 ± 2.8 minutes; P<.01) (Table 3).

AMOUNT AND STRUCTURE OF DAYTIME SLEEP

During both naps, obese patients compared with controls slept more. Specifically, during the first nap obese patients had significantly lower WTASO (4.7 ± 0.6 vs 8.6 ± 1.4 minutes; P<.01) and TWT (18.5 ± 1.4 vs 30.4 ± 2.6 minutes; P<.01) and a significantly higher percentage of sleep time (69.3% ± 2.8% vs 49.4 ± 4.4%; P<.01) (Table 2). Also, the percentage of WTASO during the sleep period was lower in obese patients compared with healthy controls (10.3% ± 1.4% vs 21.0% ± 3.4%; P<.01). During the second nap, obese patients had a significantly lower TWT (26.9 ± 1.8 vs 35.0 ± 2.7 minutes; P<.01) and a significantly higher percentage of sleep time (55.1% ± 3.0% vs 41.5 ± 4.4%; P<.01) (Table 3). Also, the percentage of WTASO during the sleep period was lower in obese patients compared with controls (18.8% ± 3.0% vs 23.1% ± 3.9%; P = .32). There were no differences between the 2 groups in terms of sleep stages in either of the 2 naps with the exception of a significantly higher amount of
the Multiple Sleep Latency Test for determining sleepiness in disorders of excessive daytime sleepiness.\textsuperscript{7}

Electroencephalographic, electro-oculographic, and electromyographic recordings were obtained in accordance with standard methods.\textsuperscript{8} The sleep records were subsequently scored, independent of any knowledge of the experimental conditions according to standardized criteria.\textsuperscript{9} Of the 73 obese patients 1 did not complete the first nap whereas 11 did not complete the second nap. All controls completed both naps. Daytime sleepiness was assessed subjectively using a sleep questionnaire on a 3-point scale (mild, moderate, or severe).

The following sleep parameters were calculated for each subject: sleep induction (sleep latency); sleep maintenance (wake time after onset of sleep [WTASO] and percentage of WTASO during the sleep period); total wake time (TWT, the combined measure of sleep induction and sleep maintenance); percentage of total sleep time; percentage of sleep stages (rapid eye movement [REM], 1-4); number of REM periods; and REM latency.

Onset of sleep and REM latency were determined for each recording in the following manner: the onset of sleep was established by the presence of any sleep stage for a duration of 1 minute or longer. However, if the initial stage of sleep was stage 1, it had to be followed, without any intervening wakefulness, by at least 60 seconds of stages 2, 3, 4, or REM. Sleep latency was defined as the time elapsed from lights out to onset of sleep; a sleep latency value of 60 minutes was assigned to those who failed to sleep during the naps. The REM latency was then defined as the total amount of time from onset of sleep to the first appearance of REM sleep. During the naps, REM latency and percentage of REM was calculated only for those who demonstrated REM sleep.

The distribution of wakefulness and REM sleep through the night was examined by thirds of the night. A third of the night was established by subtracting sleep latency from REM sleep during the first nap in the obese patients compared with controls.

**SUBJECTIVE ESTIMATES OF DAYTIME SLEEPINESS**

Approximately 42 (57%) of the 73 obese patients reported daytime sleepiness that was on average moderately severe. Approximately 1 (2%) of 45 controls reported daytime sleepiness (mild).

**RESPIRATORY DATA**

The mean ± SE number of apneic and hypopneic events in an 8-hour sleep recording was 5.2 ± 1.0 in the obese group and 5.5 ± 1.1 in the control group (\(P = .88\)). Mean ± SE presleep hemoglobin oxygen saturation values were similar in the obese and control groups (95.6% ± 0.2% vs 96.1% ± 0.2%; \(P = .13\)). The mean ± SE minimum hemoglobin oxygen saturation associated with sleep apneic events was 86.7% ± 0.6% in the obese group and 89.6% ± 0.9% in the control group (\(P<.01\)).

**EFFECTS OF NIGHTTIME SLEEP, BMI, AND SNORING ON DAYTIME SLEEP**

In obese patients, nighttime sleep latency was positively correlated to daytime sleep latency (average of the sleep latencies of the 2 naps) \((r_{xy} = 0.24; P<.05)\) and amount of daytime wakefulness (average TWT of both naps) \((r_{xy} = 0.32; P<.01)\) and negatively correlated to amount of daytime sleep (average percentage of sleep time of both naps) \((r_{xy} = -0.32; P<.01)\). Furthermore, nighttime percentage of sleep time, TWT, and WTASO were positively correlated to daytime average percentage of sleep time \((r_{xy} = 0.27; P<.05)\), to average TWT \((r_{xy} = 0.27; P<.05)\), and to average WTASO \((r_{xy} = 0.33; P<.01)\), respectively. In controls, nighttime sleep latency was positively correlated to average daytime TWT \((r_{xy} = 0.33; P<.05)\) and negatively to average percentage of daytime sleep time \((r_{xy} = -0.32; P<.05)\). However, in contrast to obese patients, in controls nighttime percentage of sleep time, TWT, and WTASO were not correlated to average daytime percentage of sleep, TWT, and WTASO, respectively. There was a positive correlation between percentage of nighttime REM sleep and percentage of REM in...
The primary finding of our study is that severe obesity even in the absence of sleep apnea or other breathing disorders in sleep is associated with increased daytime sleepiness.

Obesity affects about one third of adult Americans and its prevalence appears to be on the rise particularly among minorities and women.1 Daytime sleepiness is a significant problem for 5% of the adult population9 and has been underestimated. Our study provides strong objective evidence that obesity alone can be a significant factor leading to daytime sleepiness and fatigue.

In our study none of the obese patients were referred with a chief complaint of daytime sleepiness or fatigue. Our data indicate that obese patients tend to underestimate the degree of their sleepiness. This is consistent with previous findings that self-reported sleepiness is an underestimate of the physiological state of sleepiness.14

**Table 1. Nocturnal Sleep of Obese Patients and Healthy Controls**

<table>
<thead>
<tr>
<th>Sleep efficiency</th>
<th>Obese Patients (n = 73)</th>
<th>Healthy Controls (n = 45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep latency (SL, min)</td>
<td>34.9 ± 3.8</td>
<td>26.2 ± 3.4</td>
</tr>
<tr>
<td>Wake time after onset of sleep (WTASO, min)</td>
<td>82.4 ± 6.9†</td>
<td>46.1 ± 6.1</td>
</tr>
<tr>
<td>Total wake time (TWT, min)</td>
<td>117.3 ± 8.8†</td>
<td>72.3 ± 7.2</td>
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<tr>
<td>Sleep time (ST, %)</td>
<td>75.5 ± 1.8†</td>
<td>84.9 ± 1.5</td>
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</table>

**Table 2. Daytime Sleep of Obese Patients and Healthy Controls**

<table>
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<th>Sleep efficiency</th>
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<th>Healthy Controls (n = 45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep latency (SL, min)</td>
<td>13.7 ± 1.9†</td>
<td>22.7 ± 2.8</td>
</tr>
<tr>
<td>Wake time after onset of sleep (WTASO, min)</td>
<td>4.7 ± 0.6†</td>
<td>8.7 ± 1.4</td>
</tr>
<tr>
<td>Total wake time (TWT, min)</td>
<td>18.5 ± 1.4†</td>
<td>30.4 ± 2.6</td>
</tr>
<tr>
<td>Sleep time (ST, %)</td>
<td>69.3 ± 2.8†</td>
<td>49.4 ± 4.4</td>
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**Table 3. Daytime Sleep of Obese Patients and Healthy Controls**

<table>
<thead>
<tr>
<th>Sleep efficiency</th>
<th>Obese Patients (n = 62)</th>
<th>Healthy Controls (n = 45)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sleep latency (SL, min)</td>
<td>18.7 ± 1.6†</td>
<td>27.6 ± 2.8</td>
</tr>
<tr>
<td>Wake time after onset of sleep (WTASO, min)</td>
<td>8.2 ± 1.3</td>
<td>9.3 ± 1.5</td>
</tr>
<tr>
<td>Total wake time (TWT, min)</td>
<td>26.9 ± 1.8†</td>
<td>35.0 ± 2.7</td>
</tr>
<tr>
<td>Sleep time (ST, %)</td>
<td>55.1 ± 3.0†</td>
<td>41.5 ± 4.4</td>
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The first nap in the obese group ($r_s = 0.44; P<.01$) but not in the control group. Correlations between BMI and objective indexes of daytime sleepiness (average sleep latency and percentage of sleep time based on both naps) in the group of obese patients were not significant. Correlations between the presence of snoring and the nighttime and daytime sleep variables in the group of obese patients were not significant.

**COMMENT**

The most frequently cited probable cause of mass transportation crashes is fatigue.11 The National Transportation Safety Board has found that fatigue and fatigue-drug interactions are greater factors in fatalities involving heavy trucks than alcohol or other drugs of abuse alone.12 While there has been an appropriate emphasis on probable common underlying causes of daytime sleepiness, such as sleep deprivation and sleep apnea,13 the potential role of obesity per se, which is a common disorder, has been underestimated. Our study provides strong objective evidence that obesity alone can be a significant factor leading to daytime sleepiness and fatigue.
The underlying mechanisms of daytime sleepiness associated with obesity are not clear. At first glance it appears that nocturnal sleep disturbance in our obese patients, which is consistent with our previous findings, is the cause of their daytime sleepiness. However, our analysis of the relation between daytime and nighttime sleep does not appear to support such a conclusion. Our data show that obese patients who sleep more at night also sleep more during the day and vice versa. One would have expected that those obese patients who slept worse at night would have slept better during the day to compensate for the amount of previous night sleep loss. A possible explanation for this inconsistency is that obese patients who are not sleeping well at night, because of presumably mechanical effects of obesity on their sleep, are also not sleeping well during the daytime for the same reasons. However, such a hypothesis is not supported by our findings. In fact, we found that the daytime sleep of obese patients is less fragmented compared with the daytime sleep of controls as indicated by the significant decrease in WTAOS (both in terms of absolute time and percentage during the daytime naps).

An alternative explanation is that daytime sleepiness and nighttime disturbance are manifestations of a circadian and/or metabolic abnormality that is associated with hyperarousal during the night and hypoarousal during the day. Such a hypothesis is suggested by at least 3 of our findings. First, obese patients have a higher sleep propensity (sleep latency) during the day but it is more difficult for them to fall asleep at night compared with controls. One would have expected that obese patients, who are chronically deprived of sleep, would fall asleep more easily compared with controls regardless of the time of the 24-hour cycle. Second, obese patients, compared with controls, maintain their sleep better during the day but not so during the night. One would have expected that the mechanical effects of excess weight on sleep would operate uniformly both during the day and night. Finally, the presence of lower amounts of REM sleep during the early part of the night in contrast to the higher amounts of REM sleep during the early morning hours in obese patients compared with controls (an increase that cannot be interpreted as a result of REM deficit) suggests a possible circadian shift of REM sleep also. All these factors combined lead us to hypothesize that daytime sleepiness in obese patients appears to be primarily a manifestation of a circadian and/or metabolic abnormality of obesity per se and secondarily a result of mechanical effects of excessive weight on the sleep of these patients. Our hypothesis that obesity is associated with hyperarousal during the night and hypoarousal during the day is consistent with the reported high prevalence of the night eating syndrome in obese patients.

The pathophysiological mechanism of daytime sleepiness in obesity is unknown. In a recent study we demonstrated that the plasma levels of inflammatory cytokines (tumor necrosis factor α [TNF-α] and interleukin 6 [IL-6]) are elevated in disorders of excessive daytime sleepiness. Also in this study we demonstrated that TNF-α and IL-6 levels were highest in the obese patients with sleep apnea and there was a strong correlation between BMI and IL-6 levels. Plasma TNF-α concentrations are significantly elevated in obese animals with the levels best correlating with massive obesity and insulin resistance. We hypothesize that cytokines play a role in mediating sleepiness in obesity and the use of TNF-α or IL-6 humanized neutralizing antibodies or specific antagonists may be indicated when these factors become available for use.

In conclusion, severe obesity per se is a frequent causative factor of daytime sleepiness and fatigue significant both in terms of occupational and social function as well as public safety. Obesity-related daytime sleepiness appears to be a manifestation of a metabolic and/or circadian abnormality. Finally, cytokines, particularly TNF-α and IL-6, may play a role in mediating sleepiness in patients with obesity.

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