Obstructive Sleep Apnea Syndrome, Sleepiness, and Quality of Life*

Marta A. Gonçalves, MD; Teresa Paiva, MD; Elizabeth Ramos, MS; and Christian Guilleminault, MD, BiolD

Objective: To evaluate the addition of short arousals of > 3 s on indexes of sleep-disordered breathing (SDB) and subjective sleepiness in patients with obstructive sleep apnea (OSA), and to evaluate the quality of life and reported difficulty driving with arousal index and indexes of SDB.

Method: Data was collected from a general clinical evaluation, and evaluations using the Epworth sleepiness scale (ESS), the sleep disorders questionnaire, the Beck depression inventory (BDI), the Medical Outcomes Study 36-item short form health survey (SF-36), a questionnaire on driving difficulties and accidents, and polysomnography.

Results: A total of 135 male subjects (mean [± SD] age, 52 ± 12.1 years; mean body mass index [BMI], 27.8 ± 5.6 kg/m²; mean apnea-hypopnea index [AHI], 48.7 ± 26.8 events per hour) were studied. Of these subjects, 70.4% acknowledged having driven while sleepy. ESS scores correlated significantly with the arousal index and AHI, and negatively with the lowest arterial oxygen saturation. The “physical functioning,” “general health,” and “role physical” subscales of the SF-36 correlated with the arousal index. No significant correlation was seen in multiple regression analyses after adjusting for age and BMI, using “reports of sleepiness while driving” as the dependent variable.

Conclusion: Several subjective complaints and subscales of the SF-36 correlated significantly with a frequency of SDB-related arousal of > 3 s. Patients perceived that an organic health problem had been impairing their quality of life more than an emotional problem, despite elevated scores on the BDI. However, if sleepiness while driving was common in OSA patients, it was not significant. Many clinical and polysomnographic variables may be considered as possible independent variables in the regression analysis. Other unrelated factors have a greater impact.

To relate sleepiness while driving only to the usually studied variables in OSA patients is an oversimplification.

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Key words: arousal index; obstructive sleep apnea; quality of life; short arousal; sleepiness driving

Abbreviations: AHI = apnea-hypopnea index; BDI = Beck depression inventory; BMI = body mass index; CPAP = continuous positive airway pressure; ESS = Epworth sleepiness scale; OSA = obstructive sleep apnea; REM = rapid eye movement; SaO₂ = arterial oxygen saturation; SDB = sleep-disordered breathing; SF-36 = Medical Outcomes Study 36-item short form health survey; SWS = slow-wave sleep

In the 1980s, the nocturnal sleep of obstructive sleep apnea (OSA) patients was scored using international criteria of Rechtschaffen and Kales. Often, no significant relationship was found between (1) the apnea-hypopnea index (AHI), the time spent awake during the night, and the daytime arterial oxygen saturation (SaO₂), and (2) complaints of tiredness, fatigue, and sleepiness.

In 1992, the American Sleep Disorders Association defined short arousal as an arousal with a duration of 3 to 15 s. Using a prospective, standardized protocol, we investigated whether the adjunction of short arousals to the scoring of sleep disturbance in OSA patients yielded a stronger relationship between (1) the AHI and subjective sleepiness mea-
sured by the Epworth sleepiness scale (ESS) and (2) the AHI and the number of arousals per hour of sleep (ie, the arousal index). We also evaluated the relationships among reported sleepiness, quality of life evaluated using the Medical Outcomes Study 36-item short form health survey (SF-36), the presence of depressive mood, and the reported difficulties of driving before treatment with nasal continuous positive airway pressure (CPAP).

**Protocol**

**Subjects**

During a 12-month period, male subjects between 20 and 65 years of age, who had been referred for snoring, fatigue, and/or daytime sleepiness, underwent a standardized prospective protocol that included a general clinical evaluation, and evaluations by a sleep specialist and psychiatrist.

Subjects who had experienced chronic psychiatric disorders, alcoholism, drug abuse, intake of psychotropic medications (including hypnotic and stimulant agents), unstable medical regimens, circadian rhythm disorders, and other sleep disorders leading to sleep disruption were excluded from the study. All other patients, including those with a stable medical regimen (eg, hypertension medication intake) for > 6 months, were included in the study. The protocol was restricted to men to avoid the influence of the menstrual cycle.

**Tools**

All of the subjects were interviewed by sleep disorder specialists and psychiatrists. They completed the ESS (which is an eight-item, 4-point scale evaluating sleepiness in daily situations), the sleep disorders questionnaire (which is a validated 180-question questionnaire using a 5-point Likert scale to evaluate sleep and its disorders), the Beck depression inventory (BDI), a quality-of-life questionnaire (the SF-36), and a questionnaire about the presence of sleepiness while driving and having an automobile accident due to sleepiness. The questions that addressed driving were as follows: Have you fallen asleep at the wheel any time during the last 2 years? Have you had any driving accident while sleepy during the last 2 years? Do you believe that this accident was related to being sleepy at the wheel?

**Polysomnography**

For the purpose of the study, each subject responding to the inclusion criteria underwent a nocturnal polysomnogram with a minimum of 8 h in bed. The following variables were systematically monitored using a computerized sleep system (EMBLA; Flaga; Reykjavik, Iceland): EEG (leads C3/A2, C4/A1, O1/A2, and O2/A1); electrooculogram; chin and leg electromyogram; ECG (modified V2 lead); and body position. Respiration was monitored using oral and nasal thermistors, uncalibrated thoracic and abdominal inductive respiratory plethysmography, pulse oximetry, and neck microphone.

**Data Analysis**

Apnea and hypopnea were subdivided into central, mixed, and obstructive types. They were scored following the American Academy of Sleep Medicine recommendations. Sleep was scored following the International and American Sleep Disorders Association criteria. An arousal index (ie, the number of arousals per hour of sleep) was calculated, and it included all arousals of ≥ 3 s in duration. Each scored arousal was examined, and a distinction was made between breathing-related arousals and non–breathing-related arousals.

**Statistical Analysis**

Descriptive statistics using mean ± SD were used. If normally distributed, continuous variables were analyzed by Student t test. Nonparametric analysis (ie, Kruskal-Wallis test) was performed on variables without normal distribution. χ² tests were performed on percentages with the Yates correction factor. If a comparison was performed with a number inferior to five subjects per cell, the Fisher exact test was applied. The Spearman correlation coefficient was calculated in the investigations of quality of life. Multiple regression analyses were performed after the identification of significant variables by simple linear regression and with appropriate adjustments.

**Results**

**Subjects**

The study included 135 male subjects. The mean (± SD) age was 52 ± 12.1 years, the mean body mass index (BMI) was 27.8 ± 5.6 kg/m², the mean AHI was 48.7 ± 26.8 events per h, the mean BDI was 8.0 ± 5.9, 60 subjects (44.4%) reported symptoms of esophageal reflux, 62 subjects (45.9%) reported more than one nightly episode of nocturia, and 25 patients (18.5%) received antihypertensive medication. All subjects had a drivers license and drove at least weekly. Twenty-five subjects (18.5%) reported automobile accidents due to sleepiness, and 95 subjects (70.4%) acknowledged having driven while sleepy. Nocturnal sleep variables and daytime scales of sleepiness are presented in Table 1. Other variables, including respiratory variables during sleep, are presented in Table 2.

**Apnea-Hypopnea Index, Sleep, and Sleepiness**

The AHI and the lowest SaO₂ were selected as polysomnographic variables indicative of sleep-
disordered breathing (SDB). These two variables are not independent of a correlation factor ($r = 0.665; \ p = 0.0001$), but they were each considered independently, as their impact on sleep EEG may not be the same. The arousal index presented here included all arousals $\geq 3$ s in duration. As calculated for the total group, a mean of $7 \pm 3\%$ of these arousals were not related to a breathing event.

The relationship between the AHI and the arousal index is presented in Figure 1. As can be seen, the correlation was highly significant, with a steep slope ($r = 0.783; \ p = 0.001$). It was also very significant when the lowest $\text{Sa}_{O_2}$ and arousal index were studied ($r = 0.502; \ p = 0.0001$).

When subjective measures of sleepiness were considered, the ESS scores correlated significantly with the arousal index, as shown in Figure 2 ($r = 0.303; \ p = 0.001$). ESS scores correlated with AHI ($r = 0.338; \ p = 0.0001$) and correlated negatively with the lowest $\text{Sa}_{O_2}$ ($r = 0.379; \ p = 0.0001$). The two other variables (ie, a report of experiencing sleepiness at the wheel and having had a driving accident while sleepy) were also significantly correlated with the AHI ($p = 0.0001$ for both variables).

An investigation of sleep stages showed that the degree of sleep disruption correlated with the selected indexes of SDB and the amounts of slow-wave sleep (SWS) and rapid eye movement (REM) sleep. The percentage of SWS correlated negatively with the arousal index ($r = -0.572; \ p = 0.0001$) and with the AHI ($r = -0.458; \ p = 0.0001$). Similarly, the percentage of REM sleep correlated negatively with the arousal index ($r = -0.317; \ p = 0.0001$) and with the AHI ($r = -0.354; \ p = 0.0001$).

The disruption of REM sleep was so important in some subjects that the timing of REM sleep also was disturbed. Four subjects had a REM sleep latency (ie, sleep-onset REM sleep period) of $< 15$ min without any signs or symptoms of narcolepsy syndrome. These four subjects had a mean age of

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Table 2—Subscale Scores of the SF-36 and Clinical Data From the Studied Subjects

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean</th>
<th>SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>SF-36 subscales</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Physical functioning</td>
<td>71.78</td>
<td>24.11</td>
</tr>
<tr>
<td>Role physical</td>
<td>72.50</td>
<td>37.28</td>
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<tr>
<td>Bodily pain</td>
<td>73.35</td>
<td>24.24</td>
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<td>General health</td>
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<td>16.60</td>
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<tr>
<td>Vitality</td>
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<tr>
<td>Social function</td>
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<td>25.56</td>
</tr>
<tr>
<td>Role emotional</td>
<td>68.78</td>
<td>39.31</td>
</tr>
<tr>
<td>Mental health</td>
<td>65.26</td>
<td>21.05</td>
</tr>
<tr>
<td>Age, yr</td>
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<tr>
<td>BDI</td>
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<td>5.60</td>
</tr>
<tr>
<td>ESS</td>
<td>15.11</td>
<td>4.60</td>
</tr>
<tr>
<td>BMI, kg/m$^2$</td>
<td>27.8</td>
<td>5.6</td>
</tr>
<tr>
<td>AHI, events/h</td>
<td>48.7</td>
<td>26.8</td>
</tr>
<tr>
<td>Lowest $\text{Sa}_{O_2}$, %</td>
<td>74.9</td>
<td>12.25</td>
</tr>
</tbody>
</table>

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Figure 1. Correlation between AHI and arousal index. The AHI is expressed as the number of events per hour of sleep, and the arousal index is expressed as the number of arousals of $> 3$ s per hour of sleep ($r = 0.783; \ p = 0.001$).

Figure 2. Correlation between ESS and arousal index. Arousal index is expressed as in Figure 1 ($r = 0.303; \ p = 0.001$). The regression line is significant but is not as steep as those for other variables. This difference may be related to the limitations of the ESS.11,12
41.5 ± 13.1 years, a mean BMI of 29.83 ± 3.5 kg/m², a mean AHI of 70.8 ± 19.55, a mean lowest SaO₂ of 61.8 ± 12.77%, and mean ESS of 16.8 ± 3.9. However, these results, including the measurement of BMI, were not significantly different from those for the total group (by Fisher exact test). They were situated in the lower quartile, however, for both AHI and lowest SaO₂. Overall, REM sleep latency was significantly correlated with the arousal index (r = 0.246; p = 0.004).

**Impact of Quality-of-Life Score**

The mean SF-36 subscale scores and mean BDI values are presented in Table 2. The overall SF-36 score had no positive correlation with AHI (r = -0.58; p = 0.533). Each subscale of the SF-36 was studied, and correlation coefficients were calculated. The following four different variables were considered: the AHI; the mean SaO₂; the lowest SaO₂; and the arousal index. They are presented in Table 3. The only significant correlations with the AHI were with the physical functioning and general health subscales of the SF-36. There was no correlation with the mean SaO₂, and only one correlation with the mean lowest SaO₂ (the bodily pain subscale). The significant correlations between the arousal index and the SF-36 subscales were the physical functioning sub scale with the AHI and the role physical sub scale. None of the coefficients, even if statistically significant, were very high, and all were indicative of the perception of an organic disorder.

**Relationship Between Subjective Sleepiness and Clinical Variables**

We consider high scores on the ESS and reports of sleepiness while driving as indicators of subjective daytime sleepiness. These variables were studied as dependent variables. We consider the following variables to be clinically relevant: arousal index; AHI; lowest SaO₂; total sleep time; age; professional activity; and BMI. A linear regression with appropriate adjustment was performed to identify the variables needed for a multiple regression analysis (ie, age, BMI, and AHI), with ESS as the dependent variable. After adjusting for age, AHI, and BMI, age (p = 0.001) and AHI (p = 0.005) were the significant variables. The model explained 41% of the variance (r = 0.41; F statistic = 11.7; variance with age: p = 0.02; β = 0.07; and variance with AHI: p = 0.01; β = 0.006).

When we consider the report of driving accidents as the dependent variable, none of the independent variables placed in the regression is significant. For example, the AHI has a p value of 0.20. With a report
of sleepiness while driving as the dependent variable, only AHI was initially significantly correlated \((p = 0.04)\), but the model explained only 3\% of the variance \((r = 0.03)\). When we adjust for BMI and age, this significant relation disappears. Thus, none of the studied variables are significant with respect to self-reported sleepiness while driving and/or having driving accidents.

Comments

Controversies exist about the relationship between OSA and daytime sleepiness.\(^2\)–\(^4\) There are also controversies about the relationship between polysomnographic indexes of OSA and disruptions in EEG during sleep. The latter controversy is of long standing, as studies\(^2\) in the 1980s showed no significant relationship between AHI and EEG changes during sleep, particularly those that indicate arousals. In theory, daytime consequences (ie, sleepiness and fatigue) are related to nocturnal sleep disruption. One possibility for the absence of correlation between OSA and EEG may relate to the scoring of sleep, particularly the absence of tabulating short arousals.

Our study indicates that the scoring of short (ie, \(> 3\) s) EEG arousals leads to a stronger correlation than those previously published. To assure scoring consistency in the scoring of short EEG arousals, one individual scored all of the obtained records. Also, the inclusion/exclusion criteria were designed to limit the risk of confounding conditions that could be responsible for short EEG arousals. Much effort was made to closely follow the protocol. The total number of arousals was taken into consideration, but most (mean, 93\%) were related to abnormal breathing during sleep in this group of clear OSA patients.

The results show that a correlation between the arousal index and OSA is shown when AHI and lowest \(\text{Sa}_\text{O}_2\) are selected as the indexes of SDB. Other sleep indexes, including the percentage of SWS, the percentage of REM, or REM sleep latency, also correlate well with AHI and lowest \(\text{Sa}_\text{O}_2\), as did the indicators of subjective sleepiness. These findings are not too surprising, and confirm that significant correlations can be obtained between subjective complaints and polygraphic findings. Often, a delay in the appearance of REM sleep is seen in OSAS patients, but, as already observed,\(^3\) sleep onset REM sleep periods can be seen in some patients. The four subjects in which these occurred were in the upper quartile for the number of arousals. At the end of the prospective study, treatment with nasal CPAP completely eliminated these periods of sleep onset REM sleep.

If there are significant correlations between nocturnal sleep disturbances and the frequency of SDB-related arousals, one may argue, however, that, even if strengthened with a tabulation of short arousals, the polysomnographic measures did not correlate strongly with the subjective measurements of sleepiness. The ESS, for example, explains only 9\% of the variance in subjective sleepiness. A strong debate exists on the relationship between data from one night of polysomnography and scales looking at a much longer time period.\(^11\)–\(^13\) One possibility is that other EEG markers of sleep disruption have to be integrated. Terzano et al\(^14\) have emphasized that cyclical alternating patterns should be systematically studied in patients with sleep disorders. Cyclical alternating patterns encompass not only the short EEG arousals described in 1992, but take into account the instability to sleep as related to abnormal breathing. Better analyses of EEG changes, including the recently proposed “detection of respiratory cycle-related EEG changes in SDB” by Chervin et al,\(^15\) also may provide further useful information.

Correlations between quality-of-life measurements and the polysomnographic variables were shown, and the arousal index was one of the variables. The role physical and physical functioning subscales of the SF-36 correlated with the arousal index, the general health and physical functioning subscales correlated with the AHI, and lowest \(\text{Sa}_\text{O}_2\) correlated with the bodily pain subscale. The abnormal scores obtained with the subscales general health, physical functioning, role physical, and bodily pain indicate that the patients perceived that an organic health problem had been impairing their quality of life more than an emotional problem, despite elevated scores on the BDI.

The controversy about the existence of OSA patients with AHI of 30 events per hour of sleep without subjective sleepiness could not be resolved with this study, since the entry criteria included complaints of daytime fatigue or sleepiness, as confirmed by ESS scores.\(^16\)

Despite the improvement in correlations between several polysomnographic variables and subjective reports, the complex issue of sleepiness while driving in patients with OSAS was incompletely resolved. A large number of subjects (91 subjects; 67\%) reported the presence of sleepiness while driving. The AHI was initially the only significant variable in the regression analysis that explored the role of several independent variables in the explanation of the driving problem, and when we adjusted the model for age and BMI, it became nonsignificant. Clearly, other factors not considered in the study, and not directly associated with the polysomnographic variables tabulated here, had a much greater impact on this report. As mentioned above, one possibility is
that other EEG markers of sleep disruption have to be integrated.\textsuperscript{14,15} Independently of the introduction of these new criteria and to better define the severity of the sleep impairment related to the breathing disorder, one should be critical in the risk attribution to only one variable (SDB here) when considering the complex behavior of driving.

Linking the obstructive sleep apneic events and their associated polygraphic changes to sleepiness while driving, which is a common tendency with these patients, may be an overgeneralization\textsuperscript{17} even if driving accidents may be reported more often in OSAS patients.\textsuperscript{18,19} Several studies of sleep deprivation and sleep restriction have shown that there are important individual differences in driving impairment due to sleep disturbance. Also, the presence of daytime fatigue or sleepiness may lead to behavioral adjustments to avoid it. Finally, the severity of sleepiness while driving may be unmasked only in specific conditions, such as long driving, driving at specific times of the day, or adjunct of another factor (eg, sleep restriction or the need for greater attention to driving). The OSAS may lead to sleep restriction related to difficulties on the job, the need to perform for longer periods of time due to secondary tiredness, slower performance during the day, and the secondary reduction of total sleep time. Our finding is of a cautionary nature. The treatment of OSA may eliminate one factor involved in sleepiness while driving but may not completely eliminate the problem. This should lead to a systematic reassessment of the driving difficulties after several months of treatment to avoid an unjustified sense of security with the prescription and appropriate use of nasal CPAP. Finally, another cautionary note. Our study was performed in men, and the age range (39 to 67 years) is well-suited to the majority of OSAS patients, but our study provides no information on women and does not consider elderly subjects.

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REFERENCES