

## Determinants of respiratory disturbance and oxygen saturation drop indices in obstructive sleep apnoea syndrome

M.A. Quera-Salva, C. Guilleminault, M. Partinen, A. Jamieson

*Determinants of respiratory disturbance and oxygen saturation drop indices in obstructive sleep apnoea syndrome. M.A. Quera-Salva, C. Guilleminault, M. Partinen, A. Jamieson.*

**ABSTRACT:** Although chronic sleep fragmentation and oxygen saturation ( $\text{SaO}_2$ ) drops alone do not induce obstructive sleep apnoea (OSA), both are part of the feedback loop leading to obstructive sleep apnoea syndrome (OSAS). To determine factors in respiratory disturbance and  $\text{SaO}_2$  drops, we used polysomnographic and cephalometric data from 120 OSAS patients to construct a model which we then applied prospectively to 25 new OSAS patients, calculating the correlation between observed and predicted values. We found body mass index and the amount of stage 1 non-rapid eye movement sleep to be significant variables when considering both the respiratory disturbance index (RDI) and  $\text{SaO}_2$  drops. Posterior airway space was also a significant variable for RDI. Forced expiratory volume in one second, expressed as the percentage of forced vital capacity ( $\text{FEV}_1/\text{FVC}$ ), was significant when considering  $\text{SaO}_2$  drops. Upper airway abnormalities were also significant variables in the models and must be considered when treating OSAS patients. *Eur Respir J.*, 1988, 1, 626-631.

Sleep Disorders Centre, Stanford University School of Medicine, Stanford, CA 94305.

Correspondence: C. Guilleminault, Sleep Disorders Centre, Stanford University School of Medicine, 701 Welch Road, Suite 2226, Palo Alto, CA 94304, USA.

Keywords: COLD; nocturnal  $\text{O}_2$  saturation; obesity; obstructive sleep apnoea syndrome; sleep; sleep fragmentation; upper airway anatomical abnormalities.

Received: August 21, 1987; accepted after revision March 22, 1988.

This work was supported by grant AG 06066 from the National Institute of Aging. Dr. Partinen was supported by U.S. Public Health Service International Research Fellowship 1 FO 5TWO3648-01 and Dr. Quera-Salva by a fellowship from Barcelona University School of Medicine (Spain).

Unfortunately little is known about the progressive development of obstructive sleep apnoea syndrome (OSAS). In a study of 120 consecutive OSAS patients, interviews with family members and patients revealed that 68% of the patients were regular snorers by twenty years of age, but less than 5% were reported to be overweight at that age [1]. In many patients there often appears to be a more or less rapid progression from snoring to OSAS. When partial or complete upper airway obstruction occurs during sleep, the resulting disturbances will undoubtedly induce sleep states and stage switches, and when severe, OSAS will be associated with a significant sleep disruption. The sleep disruptions induced by the abnormal breathing pattern can be expected to feed back and to play a role in the progressive worsening of the syndrome.

Experimental repetitive sleep disturbance (sleep fragmentation) decreases hypoxic and hypercapnic responses during sleep in dogs [2]. Sleep deprivation prolongs the duration of obstructive sleep apnoea (OSA) in mild to moderately severe OSAS and leads to more pronounced oxygen saturation ( $\text{SaO}_2$ ) drops [3]. It also causes small but significant drops in forced expiratory volume in one second ( $\text{FEV}_1$ ), forced vital capacity (FVC), minute ventilation and maximal inspiratory pressure in severe chronic obstructive lung disease (COLD) patients [4, 5]. However, 'sleep disturbance' is rarely, if ever, considered in OSAS

when the components responsible for partial or complete upper airway obstruction during sleep, or the importance of  $\text{SaO}_2$  drops associated with abnormal breathing, are analysed. Should 'sleep disturbance' continue to be systematically eliminated from all models dealing with determinants of OSAS, or should we now integrate the repetitive disturbance of states of alertness? As a first step, we have tried to assess the relative importance to OSAS patients of different factors, including sleep disturbance, that may affect a) the number of apnoeas and hypopnoeas experienced (apnoea = absence of air exchange at nose and mouth for a minimum of ten seconds; hypopnoea = 50% reduction in maximal thermistor output compared with baseline and association with a decrease in  $\text{SaO}_2$  to <92% from a baseline of at least 94%, or a drop in  $\text{SaO}_2$  of at least 3% if baseline was <90%), and b) the number of  $\text{SaO}_2$  drops. The variables, other than sleep disturbance, selected for the study came from a review of the literature: age, body mass index (BMI) [6-8], presence or absence of lung disease [6, 9] and size of the upper airway, particularly in the hypo- and nasopharynx [10-12]. Being also based upon clinical experience, the rationale for the selection of these factors appears sound: gas exchange may be impaired by lung diseases [9, 13] and, in a supine subject, by morbid obesity [7, 9, 14]; retrognathia is known to be

associated with OSA and  $\text{Sao}_2$  drops even in slender subjects with intact lungs [10].

A statistical model was derived from our study using a) stepwise multiple regression analysis and b) multiple regression analysis of data obtained on 120 OSA patients. This statistical model was then prospectively applied to a smaller group of 25 OSAS patients.

## Methods

### Definition of variables and indices

Recent pulmonary function tests and blood gases obtained on patients awake and seated were collected. Three variables are usually selected to define chronic obstructive lung disease (COLD): ratio of residual volume to total lung capacity, maximal mid-expiratory flow, and forced expiratory volume in one second expressed as the percentage of forced vital capacity ( $\text{FEV}_1/\text{FVC}$ ) [15, 16]. Considering the obesity of the patients, the literature [15, 16], and the definition of COLD, we decided to select  $\text{FEV}_1/\text{FVC}$  for the purpose of the study and as the variable to enter the statistical model, since it is the only variable of the three not affected by marked obesity [15, 16]. Similarly, awake/seated arterial  $\text{O}_2$  and  $\text{CO}_2$  tension expressed in torr were also selected. Since a prior study involving 155 OSAS patients had shown that posterior airway space (PAS) (the space behind the base of the tongue) and the distance from mandibular plane to hyoid bone (MP-H) were the only two variables obtained from cephalometric roentgenograms [1, 17] that explained meaningful variations in the respiratory disturbance index (RDI), they were selected as indicative of marked airway anatomical abnormality. To measure the number of abnormal breathing events per hour of sleep, RDI was defined as  $[\text{apnoea} + \text{hypopnoea}] \times 60/\text{total sleep time (TST)}$  in minutes. Finally, BMI was calculated, using the method of KHOSLA and LOWE [8] ( $\text{weight} \times \text{height}^2$ , expressed in  $\text{kg} \cdot \text{m}^2$ ).

### Oxygen saturation indices during sleep

Several  $\text{Sao}_2$  indices were calculated: the percentage of TST spent with an  $\text{Sao}_2 < 90\%$ , the mean nocturnal sleep  $\text{Sao}_2$  (mean  $\text{Sao}_2$ ), and an arbitrarily defined  $\text{Sao}_2$  index called oxygen-80-index ( $\text{O}_2\text{-80-I}$ ). The mean nocturnal sleep  $\text{Sao}_2$  was calculated using the formula of BRADLEY and co-workers [6]. The highest and lowest  $\text{Sao}_2$  of each polygraphically recorded 'epoch' were measured. Because the pattern of desaturation and resaturation in OSA approximates a sine wave, the mean  $\text{Sao}_2$  of each polygraphic epoch, *i.e.*, 30 s, was estimated by averaging the high and low values. Mean nocturnal  $\text{Sao}_2$  for TST was then calculated, using the mean values of all epochs. To further focus on events leading to significant  $\text{Sao}_2$  drops, even if short-lived, we calculated the number of  $\text{Sao}_2$  drops related to apnoea and hypopnoea  $\leq 80\%$  and, as with the RDI, calculated the number of  $\text{Sao}_2$  drops per hour of sleep ( $\text{O}_2\text{-80-I}$ ).

### Sleep disturbance index

Several measures of sleep disturbance have been advocated. Using the criteria of RECHTSCHAFFEN and KALES [18], sleep is scored in 30 s epochs. Wake is scored when at least half of an epoch can be scored as such. Cumulative time spent awake, as defined, is called 'wake after sleep onset' (WASO) and has been used as an index of sleep disturbance. However, this index may ignore sleep disturbances of shorter duration. Short EEG alpha arousals lasting 1–14 s have also been considered. To decide which criteria should be selected to define 'sleep disturbance' we first analysed forty randomly selected sleep apnoeas or hypopnoeas in forty different nocturnal polygraphic recordings. In 8% of the cases, two independent observers disagreed on the scoring of an EEG alpha arousal at the end of an apnoea or a hypopnoea, as they considered some of the termination of the partial or complete obstructions to be unassociated with an EEG alpha arousal. Conversely, there was  $< 1\%$  discrepancy in the independent scoring when stage 1 non-rapid eye movement (NREM) sleep (S1) was scored on a 10 s epoch started at the end of the apnoea or hypopnoea. As there was also a high correlation (Pearson correlation coefficient = 0.80) between WASO and percentage of S1, it was decided to consider the percentage of S1 sleep, as classically defined [18], as the index of sleep disturbance in our study.

### Tests

Nocturnal polygraphy was systematically performed. We monitored respiration by inductive respiratory plethysmography and airflow using thermistors.  $\text{Sao}_2$  was monitored with an ear oximeter (Biox™). The following variables were monitored: EEG ( $\text{C}_3/\text{A}_2$ ), electro-oculogram, chin electromyogram, and electrocardiogram (ECG) (modified  $\text{V}_2$  lead). Sleep and sleep states and stages were scored following the criteria of RECHTSCHAFFEN and KALES [18].

During the day-time, lateral cephalometric roentgenograms were obtained, using the Werner cephalostat. Films were analysed following the criteria outlined by RILEY *et al.* [17].

Spirometry and arterial blood gases were also obtained (awake, standing or seated) within three weeks of the time of polygraphic recording.

### Patient population and methodology

Criteria for entering the study were presence of clinical symptoms of OSAS, with heavy snoring at night and an  $\text{RDI} \geq 10$  during nocturnal polygraphic recording.

*A. Initial patient population (Population A).* Over a 6-month period, 120 patients (109 men and 11 women) seen consecutively met the above criteria. Their mean age was  $49.0 \pm 11.2$  yrs; mean BMI was  $31.1 \pm 5.9$   $\text{kg} \cdot \text{m}^2$ ; awake mean  $\text{PaO}_2$  was  $78 \pm 6.9$  torr and mean  $\text{Paco}_2$  was  $38 \pm 1.8$  torr (see table 1).

Table 1. – Variables for initial and prospective populations and statistical comparison

Variable	OSAS n=120 Mean±SD	Prospective group n=25 Mean±SD	Statistical significance
Age yrs	49.2±11.3	51.2±12.1	++NS
BMI	31.1± 5.9	35.8± 7.0	+p<0.0001
% S1	42.4±20.7	52.1±20.1	++p<0.02
RDI	53.0±29.0	68.0±23.0	+p<0.01
O <sub>2</sub> -80-I	8.6±17.0	20.0±22.0	+p<0.003
% TST<90% SaO <sub>2</sub>	8.5± 9.7	11.4±10.2	++NS
Mean O <sub>2</sub> %	92.9± 2.7	91.7± 3.0	+p<0.05
PAS mm	5.2± 3.1	5.0± 3.6	+NS
MP-H mm	27.0± 6.7	26.4± 6.3	++NS
FEV <sub>1</sub> /FVC	78.0± 5.0	76.1±16.4	+NS
PaO <sub>2</sub> torr	78.0± 6.9	74.6±13.0	+p<0.05
PaCO <sub>2</sub> torr	38.0± 1.8	37.9± 3.2	+NS

+: t-test; ++: Mann-Whitney U test. The prospective group was more obese, with more perturbation of the oxygen desaturation indices during sleep and lower arterial PO<sub>2</sub> during the day.

#### B. Prospective patient population (Population B).

Twenty-five patients were prospectively examined. They included 21 men and 4 women; mean age was 51.2±12.2 yrs. Their BMI was 35.6±7 kg·m<sup>2</sup>; mean awake PaO<sub>2</sub> was 73.2±13.2 torr, and mean PaCO<sub>2</sub> was 37.9±3.1 torr (see table 1).

#### Statistical analysis

Using a statistical programme (SYSTAT, Evanston, IL) [19], we submitted our data to stepwise multiple regression analysis, with RDI and O<sub>2</sub> desaturation indices as dependent variables. This analysis allowed us to select independent variables to use as a second step in a multiple linear regression analysis where RDI and O<sub>2</sub> desaturation variables were again the dependent variables. If the kurtosis of the distribution of a variable was >2, logarithmic transformation was carried out and the logarithm was added to the model for both analyses. The number of collected patient observations (n=120) allowed us at least 24 variables in our model even if we took the conservative number of five observations per variable. We have, in fact, considered only eight independent variables in our modelling: BMI, age, PAS, MP-H, S1, FEV<sub>1</sub>/FVC, PaO<sub>2</sub> and PaCO<sub>2</sub>, which is well within the permissible limits for our analysis. Pearson correlation coefficient analysis was also performed on the collected variables [19].

### Results

**Population A.** As in any group of OSAS patients, some presented with abnormal FEV<sub>1</sub>/FVC, but none was hypercapnic (table 1).

The stepwise multiple regression analysis showed a

statistically significant link between the percentage of S1, BMI, age and PAS as independent variables when RDI was the dependent variable. Using the multiple linear regression analysis, the variables with a significant coefficient were BMI (p<0.0001), S1 (p<0.0001), age (p<0.003), and logarithmic transformation of PAS (p<0.02). These independent variables accounted for 66% of the variance (R<sup>2</sup>=0.665). The model obtained was RDI=11.14+1.22(BMI)+0.87(S1)-[0.45 (age)+7.5 (log PAS)]. S1 represented 51% of the variance, while BMI accounted for 9%, age for 4% and PAS for 2%, for a total of 66%.

We next considered different SaO<sub>2</sub> variables. When O<sub>2</sub>-80-I was the dependent variable, the stepwise multiple regression indicated BMI, S1, and FEV<sub>1</sub>/FVC as the independent variables. The multiple linear regression analysis indicated the significance of these variables: BMI (p<0.0001); S1 (p<0.0001); and logarithmic transformation of FEV<sub>1</sub>/FVC (p<0.002). This model, however, accounted for only 53% of the variance (R<sup>2</sup>=0.529). The model was [log O<sub>2</sub>-80-I]=21.9+0.14 (BMI)+0.06 (S1)-6.6 [(log FEV<sub>1</sub>/FVC)]. S1 accounted for 40% of the variance, while BMI accounted for 9% and FEV<sub>1</sub>/FVC for 4%, for a total of 53%. The two other SaO<sub>2</sub> indices considered were a) mean SaO<sub>2</sub> and b) percentage of TST spent below 90% SaO<sub>2</sub> (%TST <90% SaO<sub>2</sub>). Using the same approach, with each of these indices as dependent variables and with stepwise multiple regression and multiple linear regression analyses, the results indicated a) S1, BMI, FEV<sub>1</sub>/FVC, PaO<sub>2</sub>, PAS, and MP-H as independent variables with the following significance: S1 (p<0.0001); BMI (p<0.005); FEV<sub>1</sub>/FVC (p<0.01); PaO<sub>2</sub> (p<0.025). This model accounted for 41% of the variance, (R<sup>2</sup>=0.412). The model was  $\bar{X}$  SaO<sub>2</sub>=84.5+8.2 (FEV<sub>1</sub>/FVC)-[0.05(S1)+0.1 (BMI)+0.02 (PaO<sub>2</sub>)]. S1 accounted for 30% of the variance, while BMI accounted for 3%, FEV<sub>1</sub>/FVC for 3%, PaO<sub>2</sub> for 2% (PAS and MP-H each accounted for 1%); b) for the % TST <90% SaO<sub>2</sub> model, R<sup>2</sup>=0.53 (i.e. accounted for 53% of the variance). The statistically significant variables were: S1 (p<0.0001); BMI (p<0.003) and FEV<sub>1</sub>/FVC (p<0.001). The model was 329+1.4 (BMI)+0.90 (S1) - [130.58 FEV<sub>1</sub>/FVC]. The partial R<sup>2</sup>'s were: S1=0.41, BMI=0.17, and FEV<sub>1</sub>/FVC=0.05.

It is obvious that in each model, S1 accounted for a large percentage of the partial variance.

**Population B.** Of the prospective OSAS group, 6 of the 25 patients also presented with abnormal FEV<sub>1</sub>/FVC. But once again, none was considered to have day-time hypercapnia based on awake, seated blood gas analysis (table 1).

#### Prospective validation of the statistical models

The same data (similar clinical evaluation, nocturnal polygraphic recordings, cephalometric roentgeno-

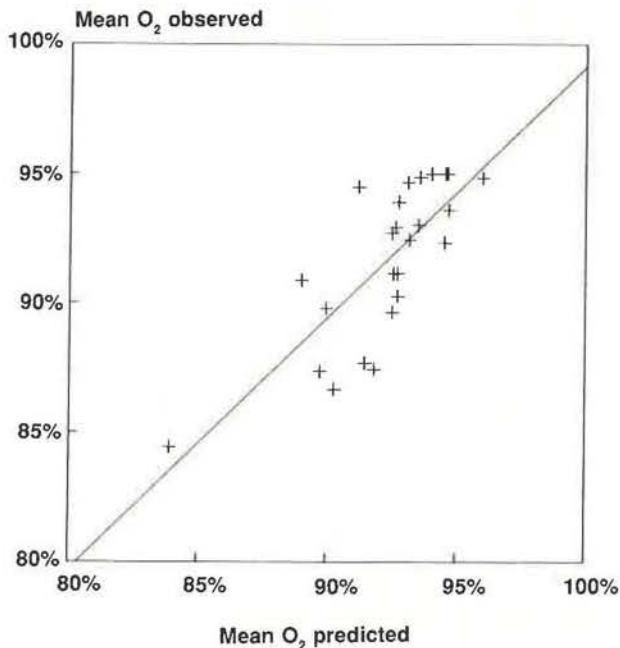


Fig. 1. Relationship between mean arterial oxygen saturation ( $\text{SaO}_2$ ) calculated according to model presented in text and  $\text{SaO}_2$  measured on prospective patient population (B) during overnight sleep study. Solid line: regression line.

grams, and standard pulmonary function tests with arterial blood gas readings obtained with patients awake and seated) were collected and are presented in table 1.

RDI and  $\text{SaO}_2$  indices for this smaller prospective group were tested against the pre-established models. The degree of correlation (Pearson coefficient) between observed and predicted values were as follows: RDI=0.70, O-80-I=0.81, %TST < 90%  $\text{SaO}_2$ =0.88, mean  $\text{SaO}_2$ =0.67. The statistical model on the average underestimated the mean RDI by  $16 \pm 11$  (apnoea + hypopnoea per hour); the mean O<sub>2</sub>-80-I by  $1.2 \pm 1.1$  (drops per hour); and overestimated the mean % TST < 90%  $\text{SaO}_2$  by  $4.4 \pm 3.5\%$ ; and the mean  $\text{SaO}_2$  by  $1.5 \pm 1.2\%$  (fig. 1 and table 1).

### Discussion

Several findings can be emphasized in our study:

A) Our OSAS population was a group of patients seen in a sleep disorders clinic and, *a priori*, the symptoms leading to consultation were related to sleep: *i.e.* presence of daytime tiredness, fatigue or sleepiness in the index case, or serious disturbance of the spouse's sleep due to the patient's heavy snoring; and despite a subgroup with a combination of OSAS and moderate COLD, day-time hypercapnia was not noted. Another important factor to note is that our initial patients were not extremely obese: the mean BMI was  $31 \text{ kg} \cdot \text{m}^{-2}$  [8]. Standard data in the USA for men aged 40–65 yrs show that 26.7% have a BMI  $> 27.8 \text{ kg} \cdot \text{m}^{-2}$  [20]. This patient population is representative of the overall OSAS patients seen in sleep

clinics, and includes patients with a large variation in the severity of symptoms and abnormalities on the nocturnal recording.

B) We have obtained information on the determinants of  $\text{SaO}_2$  drops in our OSAS population. One may question why we decided to consider three different indices of  $\text{SaO}_2$  which were, not surprisingly, correlated (Pearson correlation coefficient = O<sub>2</sub>-80-I and %TST < 90%  $\text{SaO}_2$  = 0.70,  $\bar{X}$   $\text{SaO}_2$  and O<sub>2</sub>-80-I = 0.80,  $\bar{X}$   $\text{SaO}_2$  and % TST < 90%  $\text{SaO}_2$  = 0.83). The three indices approach  $\text{SaO}_2$  drops associated with apnoeas differently. For example, the percentage of time spent below a certain  $\text{SaO}_2$  ignores the fact that there are abrupt  $\text{SaO}_2$  drops and returns to baseline or near baseline levels with each apnoea or hypopnoea. This is better indicated by our O<sub>2</sub>-80-I. Similarly, with mean  $\text{SaO}_2$ , there is a blunting of the saturation changes with each apnoea or hypopnoea. We thus decided to calculate the three indices and study three models. We also resolved to select FEV<sub>1</sub>/FVC for our model, as it would not be affected by marked obesity. Finally, blood gas values from patients who were awake and supine rather than seated would have been desirable; however, these data points were not available for all subjects.

Data in the literature have already given important information on interaction between ventilatory variables and  $\text{SaO}_2$  values during sleep. BRADLEY and co-workers [6] found that mean  $\text{SaO}_2$  during sleep correlated with supine  $\text{PaO}_2$ , expiratory reserve volume and percentage of time spent in apnoea. CATTERALL *et al.* [13] have emphasized the relationship between daytime  $\text{SaO}_2$  (patients awake and supine) and nocturnal  $\text{SaO}_2$  in patients with chronic obstructive pulmonary disease (COPD) with or without apnoea. In an experimental study of normal subjects, FINDLEY *et al.* [21] showed that initial lung volume is an important determinant of hypoxia during apnoea. Undoubtedly, the previous studies have convincingly emphasized the roles of lung volume and wake supine  $\text{SaO}_2$  in the sleep-related  $\text{SaO}_2$  drops associated with OSA. BRADLEY and co-workers [7] also emphasized the role of obesity (and its impact on lung volume) in the development of hypercapnia in morbidly obese OSA patients. Our data largely support these reports, but we have tried to add new dimensions and have analysed other than purely respiratory variables. This study confirmed our expectation that  $\text{SaO}_2$  indices are dependent on FEV<sub>1</sub>/FVC and, more notably, on BMI; and that RDI is dependent not only on obesity, but also on the size of the PAS. In each of the different models, however, the percentage of S1 is a major component when one includes 'sleep disturbance' in a model.

The percentage of S1 sleep, an index of sleep disruption and fragmentation, which also strongly correlates in our patients with WASO (*i.e.* awakening lasting longer than 30 s), is a controversial variable to consider in OSAS: the sleep fragmentation is considered as a consequence of disturbed breathing. However, as indicated in our introduction, sleep

fragmentation *per se* has an impact on ventilatory variables during wakefulness and sleep. Most proposed statistical models, on the one hand, and clinicians dealing with clinical complaints, on the other, have considered patients with OSAS: *i.e.* a problem that has evolved over time. Patients seen at this stage have a sleep fragmentation that cannot be ignored and that has an impact on brain controls. Could marked, long-term sleep fragmentation also lead to abnormal breathing patterns during sleep?

We have recently monitored two subjects with a very severe periodic leg movement syndrome (PLMS), a condition leading to significant sleep fragmentation and repetitive periodic breathing. The treatment of the PLMS and secondary sleep fragmentation by a benzodiazepine was associated with a disappearance of the repetitive short central apnoeas (Guilleminault, personal observation). To include sleep variables in our models thus appears very appropriate. However, the fact that a statistical link exists between S1 and RDI, for example, should be carefully analysed. We could have focused our study on S1 alone. We could have considered our index of sleep distribution, S1, as a dependent variable and delineated the statistically significant independent variables, with the obvious expectation of finding RDI in the model. We have performed this analysis on our initial patient group and have obtained the expected model  $S1 = 0.45(\text{age}) + 0.54(\text{RDI}) - 8.4$ , where age ( $p < 0.0001$ ) represents 2% of the variance and RDI ( $p < 0.0001$ ), 52%. However, after analysis of all initially outlined variables in our 120 OSAS patients, the  $R^2$  was again equal to 0.57 (*i.e.* this model accounted for 57% of S1 variance). As indicated above, however, when the clinical syndrome linked to presence of OSA is noted, there is continuous feedback between sleep fragmentation and repetitive  $\text{Sao}_2$  drops.

One can hypothesize that OSAS patients with marked sleep fragmentation will be sleepier than others, will show slower arousal responses during sleep and more pronounced blunting of hypoxic and hypercapnic responses. This will lead to longer apnoea duration and more pronounced  $\text{Sao}_2$  drops. Another issue is the increased daytime sleepiness normally associated with reduction of wake movement time and physical exercise, a factor often associated with weight increase. Obesity will have a secondary impact on hypoxic and hypercapnic responses, etc. Different components will increasingly interact as the syndrome worsens clinically.

Whilst it is obvious that continuous interruption of regular breathing is one determinant of the disruption of sleep as an organized state, the cost of disrupted nocturnal sleep and its impact on central controls of breathing are too often forgotten in considering OSAS. Central controls of ventilation and upper airway muscles have different set-points during sleep than those during wake. Repetitive sleep disturbances inhibit the orderly functioning of the sleeping brain, as indicated by the disappearance of the normal

progression of sleep stages and states. There is, for example, a known inverse relationship between the presence of apnoea and stage 3-4 NREM sleep (S3-4), demonstrated in our patient population by the negative correlation between S1 and S3-4 (Pearson correlation coefficient = -0.60).

Disordered breathing results in  $\text{Sao}_2$  drops and sleep disruption. The factors that initiate the abnormal breathing patterns are not clearly defined, but the presence of snoring at an early age, well before the appearance of lung disease and obesity in 68% of OSAS patients, suggests that local anatomical factors play a role early on. However, the consequences of abnormal breathing, *i.e.*  $\text{Sao}_2$  drops and sleep disturbance, may feed back to the sleeping brain and the controls of local reflexes, neuronal network, etc.

### Conclusion

Our study indicates that the continuous disruption of sleep considered as an organized state is one of the RDI determinants in OSAS. Sleep disruption alone obviously does not 'create' the initial obstructive apnoeas and hypopnoeas, even if severe sleep fragmentation may lead to periodic breathing.

Similarly,  $\text{Sao}_2$  drops during sleep appear to be absent in the 'pure' young heavy snorers [22] and hypoxaemia does not induce obstructive apnoea in many COPD patients, even those also presenting OSA. Nevertheless, once the process begins and clinical symptoms of OSAS are noted, the determinants of  $\text{Sao}_2$  drops include not only obesity and lung function [6, 7] but also the width of the upper airway and the severity of sleep disturbance.

These two components are also important in RDI determinants of the clinical syndrome. It must be acknowledged that width of the upper airway may be related to anatomical abnormalities and eventual dysfunction of local upper airway reflexes, and that 'sleep disturbance' is only the final, gross expression of the disintegration of normal sleep and basic brain function during sleep. The normal sleep EEG pattern is profoundly disturbed and, even if we cannot make any assumptions concerning specific neuronal dysfunctions, we can at least monitor the severity of the disturbance of stages and states.

*Acknowledgements:* We would like to thank B. Hayes and D. Cobasko for providing technical assistance and A. Grant for editing the manuscript.

### References

1. Guilleminault C, Quera-Salva MA. - Obstructive sleep apnea syndrome: clinical aspects and review of a large population. *In: Chronic Rhonchopathy*. C.H. Chouard ed., John Libbey and Co., London, 1988.
2. Phillipson EA, Bowes G, Sullivan CE, Woolf GM. - The influence of sleep fragmentation on arousal and ventilatory responses to respiratory stimuli. *Sleep*, 1980, 3, 281-289.
3. Guilleminault C, Rosekind M. - The arousal threshold: sleep deprivation, sleep fragmentation and obstructive sleep apnea. *Bull Eur Physiopathol Respir*, 1981, 17, 341-349.

4. Cooper KR, Phillips BA. – Effect of short-term sleep loss on breathing. *J Appl Physiol: Respirat Environ Exercise Physiol*, 1982, 53, 855–858.
5. Phillips BA, Cooper KR, Burke TV. – The effect of sleep loss on breathing in chronic obstructive pulmonary disease. *Chest*, 1987, 91, 29–32.
6. Bradley TD, Martinez D, Rutherford R, Lue F, Grossman RF, Moldofsky H, Zamel N, Phillipson EA. – Physiological determinants of nocturnal arterial oxygenation in patients with obstructive sleep apnea. *J Appl Physiol*, 1985, 59, 1364–1368.
7. Bradley TD, Rutherford R, Lue F, Moldofsky H, Grossman RF, Zamel N, Phillipson EA. – Role of diffuse airway obstruction in the hypercapnia of obstructive sleep apnea. *Am Rev Respir Dis*, 1986, 134, 920–924.
8. Khosla T, Lowe FR. – Indices of obesity derived from body weight and height. *Brit J Prev Soc M*, 1967, 21, 121–128.
9. Shepard JW Jr. – Gas exchange and hemodynamics during sleep. *Med Clin North Am*, 1985, 69, 1243–1269.
10. Jamieson A, Guilleminault C, Partinen M, Quera-Salva MA. – Obstructive sleep apneic patients have cranio-mandibular abnormalities. *Sleep*, 1986, 9, 469–477.
11. Lowe AA, Gionhaku N, Takeuchi K, Fleetham JA. – Three-dimensional CT reconstruction of tongue and airway in adult subjects with obstructive sleep apnea. *Am J Ortho Dentofacial Orthop*, 1986, 90, 364–374.
12. Rivlin J, Hofstein V, Kalbfleisch J, McNicholas W, Zamel N, Bryan AC. – Upper airway morphology in patients with idiopathic obstructive sleep apnea. *Am Rev Respir Dis*, 1984, 129, 355–360.
13. Catterall JR, Douglas NJ, Calverly PMA *et al.* – Transient hypoxemia during sleep in chronic obstructive pulmonary disease is not a sleep apnea syndrome. *Am Rev Respir Dis*, 1983, 128, 24–29.
14. Wittels EH. – Obesity and hormonal factors in sleep and sleep apnea. *Med Clin North Am*, 1985, 69, 1265–1280.
15. Boren HG, Kory RC, Syner JC. – The Veterans Administration-Army cooperative study of pulmonary function. II. The lung volume and its subdivision in normal men. *Am J Med*, 1966, 41, 96–114.
16. Kory RC, Callahan R, Boren HG, Syner JC. – The Veterans Administration-Army cooperative study of pulmonary function. I. Clinical spirometry in normal men. *Am J Med*, 1961, 30, 243–258.
17. Riley RW, Guilleminault C, Herraw J, Powell NB. – Cephalometric analysis and flow volume loops in obstructive sleep apneic patients. *Sleep*, 1986, 6, 303–311.
18. Rechtschaffen A, Kales A eds. – A manual of standardized terminology, techniques and scoring system for sleep stages of human subjects. Brain Information Service, Brain Research Institute, Los Angeles, 1968.
19. Wilkinson L. – SYSTAT: The System for Statistics. Systat, Inc., Evanston, IL, 1986.
20. Health United States 1985. – U.S. Department of Health and Human Services, National Center for Health Statistics, Hyattsville, MD, 1985.
21. Findley LJ, Ries AL, Tisi GM, Wagner PD. – Hypoxemia during apnea in normal subjects: mechanisms and impact of lung volume. *J Appl Physiol: Respirat Environ Exercise Physiol*, 1983, 55, 1777–1783.
22. Guilleminault C, Winkle R, Korobkin R, Simmons B. – Children and nocturnal snoring: evaluation of the effects of sleep-related respiratory resistive load and daytime functioning. *Eur J Pediat*, 1982, 139, 165–172.

**RÉSUMÉ:** Le syndrome d'apnée occlusive du sommeil est caractérisé par des troubles respiratoires et par des chutes de la saturation oxyhémoglobinée au cours du sommeil. Pour déterminer les facteurs qui pourraient conduire à ces anomalies, nous avons étudié, sur le plan statistique, des données provenant de 120 sujets atteints de syndrome d'apnée occlusive du sommeil, qui avaient subi un monitoring polysomnographique et des radiographies céphalométriques. Nous avons ajouté des indices de trouble du sommeil et des anomalies anatomiques des voies aériennes supérieures aux facteurs classiques (comme l'obésité et les maladies pulmonaires) qui sont habituellement pris en compte dans une analyse d'un modèle statistique. Après la construction de modèles utilisant les indices des troubles respiratoires et des chutes de saturation oxyhémoglobinée, nous les avons appliqués de manière prospective à 25 nouveaux cas de syndrome d'apnée occlusive du sommeil, et nous avons calculé le degré de corrélation entre les valeurs observées et les valeurs prédites. L'index de masse corporelle et la largeur de la voie aérienne postérieure ont une influence statistique sur l'index des troubles respiratoires. Toutefois, la quantité de sommeil de stade I non-REM, qui est un index de désagrégation du sommeil nocturne, est également une variable indépendante significative dans le modèle statistique lorsque l'index des troubles respiratoires est la valeur dépendante. De même, lorsque l'on considère les indices de chute de la saturation oxyhémoglobinée pendant le sommeil, plusieurs autres variables sont significatives dans le modèle statistique, comme l'index de masse corporelle, le rapport VEMS/CVF, et le sommeil de stade I non-REM. Les modèles ne parviennent pas à expliquer l'apparition de l'apnée occlusive partielle ou totale, puisque ni la fragmentation chronique du sommeil ni les chutes de saturation oxygénée seules n'induisent le syndrome d'apnée occlusive. Toutefois, les deux font partie de la courbe de feedback qui conduit au syndrome d'apnée occlusive, dont les déterminants peuvent être appréciés par l'utilisation des indices de perturbation respiratoire et de chute de saturation oxyhémoglobinée. Nos résultats indiquent également que les anomalies anatomiques de la voie aérienne supérieure sont une variable importante dans les modèles statistiques et doivent être considérées lorsque l'on traite les patients atteints de syndrome d'obstruction des voies aériennes.