

## EFFECT OF THE DEFINITION OF HYPOPNEA ON APNEA/HYPOPNEA INDEX

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**Abstract** The objective of this study was to determine whether different decreases in oxygen saturation ( $\text{SaO}_2$ ) or the presence of electroencephalographic arousals (EEGA) in the definition of hypopnea modify hypopnea index and apnea/hypopnea index and the prevalence of obstructive sleep apnea/hypopnea syndrome (OSAHS). A total of 20 polysomnographies performed in patients with OSAHS were analyzed. There are four different definitions of hypopnea:  $\geq 30\%$  reduction in airflow or 50% decrease in abdominal movement associated with  $\geq 3\%$   $\text{SaO}_2$  (type 1);  $\geq 3\%$   $\text{SaO}_2$  or EEGA (type 2);  $\geq 4\%$   $\text{SaO}_2$  (type 3);  $\geq 4\%$   $\text{SaO}_2$  or EEGA (type 4). The prevalence of OSAHS was calculated for an apnea/hypopnea index (AHI)  $\geq 10$  and  $\geq 15$ . Hypopnea index (HI) and AHI types 2 and 4 were higher than type 3 (HI: type 2:  $20 \pm 10.6$ , type 4:  $18.6 \pm 10$ , type 3:  $11.4 \pm 10$ ,  $p < 0.001$ ; AHI: type 2:  $23.3 \pm 11.6$ , type 4:  $21.4 \pm 11.2$ , type 3:  $14.7 \pm 11.6$ ,  $p < 0.001$ ). No differences were observed between HI and AHI types 1 and 2 (HI: type 1:  $17.4 \pm 10$ , type 2:  $20 \pm 10.6$ ; AHI: type 1:  $20.6 \pm 11.8$ , type 2:  $23 \pm 11.6$ ,  $p > 0.05$ ). The prevalence of OSAHS was 30-55% in type 3, 70-85% in type 4 ( $p < 0.05$ ), and 70-85% in types 1 and 2 ( $p > 0.05$ ). In our patient's population, the presence of EEGA in the definition of hypopnea significantly increased the HI, the AHI and the prevalence of OSAHS when associated with a  $\geq 4\%$  decrease in  $\text{SaO}_2$ .

**Key words:** diagnosis, hypopnea, sleep apnea syndrome

**Resumen** *Influencia de la definición de hipopnea sobre el índice apnea/hipopnea.* El objetivo del estudio fue evaluar si diferentes niveles de descenso de la saturación de  $\text{O}_2$  ( $\text{SaO}_2$ ) o la presencia de microdespertares electroencefalográficos (MDEEG) en la definición de hipopnea, modifican el índice de apnea/hipopnea y la prevalencia del síndrome apnea/hipopnea del sueño (SAHS). Se analizaron 20 polisomnografías de pacientes con SAHS. Hipopnea (H) se definió de cuatro formas: descenso del flujo aéreo  $\geq 30\%$  o caída del 50% del movimiento abdominal asociado a:  $\geq 3\%$   $\text{SaO}_2$  (tipo 1);  $\geq 3\%$   $\text{SaO}_2$  o MDEEG (tipo 2);  $\geq 4\%$   $\text{SaO}_2$  (tipo 3);  $\geq 4\%$   $\text{SaO}_2$  o MDEEG (tipo 4). La prevalencia del SAHS se calculó para un índice apnea/hipopnea (IAH)  $\geq 10$  y  $\geq 15$ . El índice hipopnea (IH), el IAH tipo 2 y 4 fue mayor respecto al tipo 3 (IH: tipo 2:  $20 \pm 10.6$ , tipo 4:  $18.6 \pm 10$ , tipo 3:  $11.4 \pm 10$ ,  $p < 0.001$ ; IAH: tipo 2:  $23.3 \pm 11.6$ , tipo 4:  $21.4 \pm 11.2$ , tipo 3:  $14.7 \pm 11.6$ ,  $p < 0.001$ ). No hubo diferencias entre el IH y el IAH tipo 1 y 2 (IH: tipo 1:  $17.4 \pm 10$ , tipo 2:  $20 \pm 10.6$ ; IAH: tipo 1:  $20.6 \pm 11.8$ , tipo 2:  $23 \pm 11.6$ ,  $p > 0.05$ ). La prevalencia de SAHS fue del 30-55% con el tipo 3, 70-85% con el tipo 4 ( $p < 0.05$ ) y del 70-85% con los tipos 1 y 2 ( $p > 0.05$ ). En nuestra población de pacientes, la presencia de MDEEG en la definición de hipopnea aumentó significativamente el IH, el IAH y la prevalencia de SAHS cuando se asoció a un descenso de la  $\text{SaO}_2 \geq 4\%$ .

**Palabras clave:** diagnóstico, hipopnea, síndrome apnea del sueño

Obstructive sleep apnea/hypopnea syndrome (OSAHS) is diagnosed due to the presence of frequent episodes of apnea/hypopnea during sleep, and is associated with symptoms such as excessive daytime sleepiness or cognitive disorder<sup>8, 13</sup>.

Although apnea has been defined in the literature as the absence of oronasal airflow  $\geq 10$  sec, controversy exists about the definition of hypopnea. The criteria used for the identification of hypopneas, such as magnitude of the decrease in airflow, level of oxygen desaturation and presence of electroencephalographic arousals dif-

fer considerably in the literature<sup>2,10,11</sup>. Gould<sup>2</sup> demonstrated that a 50% fall in thoracoabdominal movements examined with calibrated inductance plethysmography better correlated with arousals and oxygen desaturation than 25% or 75% reductions in the dimension of respiratory movements. In a study carried out by 44 accredited sleep disorder centers in the United States<sup>1</sup>, in addition to the reduction in ventilation, a decrease in oxygen saturation ( $\text{SaO}_2$ ) was included as a criterion of hypopnea by 82% of the centers. The decrease in  $\text{SaO}_2$  was higher than 4% in 30% of the centers, higher than 2% and lower than or equal to 4% in 22%, and any degree of oxygen desaturation was used in the remaining 42%. The presence of an electroencephalographic arousal associated with the end of hypopnea was included by 75% of the laboratories. These differences could play a significant

role in the diagnosis of OSAHS and in the comparison of the results obtained from epidemiological studies.

Little data exist regarding the impact of different definitions of hypopnea on the apnea/hypopnea index (AHI). Using different levels of SaO<sub>2</sub> fall (0% to > 5%), Redline<sup>9</sup> found an 11-fold difference in the median of AHI and a 16-fold difference in the prevalence of OSAHS. Tsai<sup>7</sup> demonstrated that the addition of electroencephalographic arousals (EEGA) to the decrease in SaO<sub>2</sub> in the definition of hypopnea brought about no significant changes in AHI, but it did in the prevalence of OSAHS.

The objective of this study was to determine whether the use of EEGA as an alternative criterion of the decrease in SaO<sub>2</sub> in the definition of hypopnea modifies the HI, the AHI and the prevalence of OSAHS.

## Material and Methods

### Study subjects and design

Polysomnographies performed in patients with suspicion of OSAHS, who had been filed in a database from 12/01/98 to 07/31/00, were revised by a physician from the Sleep Laboratory in the Hospital Alemán. Patients selected for this study should meet the following inclusion criteria: 1) more than 50% of hypopneas upon respiratory compression analysis (oronasal airflow, abdominal movement and SaO<sub>2</sub>), and 2) a proper signal for all the recorded variables. The criteria for exclusion from the study included: patients < 18 years of age and clinical diseases that might result in oxygen desaturation and sleep respiratory alterations during the sleep, such as neuromuscular disease, severe chronic obstructive pulmonary disease (FEV1 < 50% of the baseline value), severe coronary disease (unstable angina, myocardial infarction or aortocoronary bypass in the previous 6 months), chronic sleeplessness, restless legs syndrome, psychiatric disorders and use of tranquilizers. A group of 20 patients were recruited. The present study was approved by the Hospital Alemán bioethics committee.

### Methods

Polysomnographies were performed with an AKONIC version 8.0 computing polysomnographer. The following variables were registered: four channels of electroencephalogram (EEG: C3, C4, O1, O2), bilateral electrooculogram (EOG), chin electromyogram (chin-EMG), right and left anterior tibialis surface electromyogram (LAT AND EMG), electrocardiogram (EKG), oronasal airflow measured with thermistors, abdominal movements measured with a pressure transducer, and SaO<sub>2</sub> measured with a finger sensor. SaO<sub>2</sub> was measured with a NOVAMETRIX 505 oximeter, and an average frequency of 4 sec was used. Sleep stages were identified based on international guidelines<sup>4</sup>. We used the criteria of the American Sleep Disorders Association (ASDA) for EEGA<sup>5</sup>. Apnea was defined as the absence of oronasal airflow for <sup>≥</sup> 10 sec. Hypopneas (H) were defined according to four different types: a discernible decrease in oronasal airflow or a 50% reduction in abdominal movements associated with one of the following criteria: a) a 3% reduction in SaO<sub>2</sub> (type 1), b) a 3% decrease in SaO<sub>2</sub> or EEGA (type 2), c) a <sup>≥</sup> 4% reduction in SaO<sub>2</sub> (type 3), d) a <sup>≥</sup> 4% decrease in SaO<sub>2</sub> or EEGA (type 4). A discernible decrease in airflow was represented by a <sup>≥</sup> 30% fall in

thermistor signal amplitude. AHI was defined as the total number of apneas plus hypopneas divided by the total sleep time. Hypopnea index (HI) was defined as the total number of hypopneas divided by the total sleep time.

Polysomnographies were analysed by a skilled physician other than the observer who selected the tracings. The following algorithm was used for the classification of hypopneas: 1) identification of the decrease in ventilation; 2) identification of the highest decrease in SaO<sub>2</sub> (either 3% or <sup>≥</sup> 4%). The latter was achieved given that the program constantly shows SaO<sub>2</sub> values on the screen, thus allowing the operator to identify 1%, 2%, 3% or >4% falls in SaO<sub>2</sub>; 3) the presence or absence of an EEGA associated with the end of hypopnea was determined. These data were used to design a table that allowed determining the number of hypopneas according to each definition.

### Statistical analysis

A descriptive analysis was performed. AHI and HI were calculated according to each definition of hypopnea. Analysis of variance was used for repeated measurements and the Scheffe test for the differences in HI and AHI according to the different definitions of hypopnea. Two cut-off values were used as diagnostic criteria of OSAHS: a <sup>≥</sup> 10 AHI and a <sup>≥</sup> 15 AHI. Mc Nemar test was used in order to determine the differences in the prevalence of OSAHS between hypopnea type 1 vs. 2 and type 3 vs. 4. A p < 0.05 significance level was used. The strength of association between polysomnographic indexes based on different criteria of hypopnea was determined by the intraclass correlation coefficient (ICC). Considering a relatively high correlation does not necessarily imply good agreement, Bland-Altman plots were constructed in order to assess the extent of agreement<sup>14</sup>.

## Results

Table 1 summarizes patients' anthropometric characteristics and the results of polysomnographies. According to the definition used, hypopneas accounted for 78% to 85% of the whole respiratory events (apneas plus hypopneas) (Table 2). The addition of EEGA to the definition contributed to the identification of 13% and 53% of hypopneas (type 1: 1572 vs. type 2: 1779; type 3: 1053 vs. type 4: 1608).

The ICCs were calculated for paired comparisons between the different HIs and AHIs derived from four methods for scoring hypopneas. The ICC of HI between method 1 and method 2 was 0.91 (95% CI 0.78 to 0.96). The ICC of HI between method 3 and method 4 was 0.79 (95% CI 0.53 to 0.91). The ICC of AHI between method 1 and method 2 was 0.93 (95% CI 0.82 to 0.97). The ICC of AHI between method 3 and method 4 was 0.83 (95% CI 0.62 to 0.93). Figure 1 and 2 are Bland-Altman plots of the agreement between HI type 1 / HI type 2 and AHI type 3 / AHI type 4. The mean difference between HI type 1 / HI type 2 and AHI type 1 / AHI type 2 were -2.6±9/h (mean±2SD). Notwithstanding, substantial differences between HI type 3 / HI type 4 and AHI type 3 / AHI type 4 were observed (-6.75±13.3/h, mean±2SD).

TABLE 1.– Anthropometrics and polysomnographics data of the patients

Patients data	Mean $\pm$ SD <sup>+</sup>	Range
n: 20		
AGE (YEARS)	52 $\pm$ 7	31 - 65
WEIGHT (KG)	94 $\pm$ 23	73 - 156
HEIGHT (CM)	173 $\pm$ 7	156 - 182
BMI (KG/M2)*	31 $\pm$ 7	25 - 49
TST (MIN)**	268 $\pm$ 61	152 - 346
NREM (MIN)***	231 $\pm$ 48	146 - 303
REM (MIN)****	37 $\pm$ 20	0 - 74

Abbreviations: \*BMI: body mass index, \*\*TST: total sleep time, \*\*\*NREM: NREM total time (stages 1, 2, 3, 4), \*\*\*\*REM: REM total time, <sup>+</sup> Arithmetic mean and standard deviation

TABLE 2.– Number and type of hypopneas according to the definition of hypopnea

Number of hypopneas	Number of apnea and hypopneas	Rate of hypopneas (%)
TYPE 1: 1572	1884	83
TYPE 2: 1779	2091	85
TYPE 3: 1053	1355	78
TYPE 4: 1608	1920	84

Type 1: hypopneas with  $\bar{SaO}_2$   $\geq$  3%; Type 2: hypopneas with  $\bar{SaO}_2$   $\geq$  3% or EEGA; Type 3: hypopneas with  $\bar{SaO}_2$   $\geq$  4%; Type 4: hypopneas with  $\bar{SaO}_2$   $\geq$  4% or electroencephalographic arousals (EEGA).

TABLE 3.– Apnea/hypopnea index (AHI) and hypopnea index (HI) according to the definition of hypopnea

	Type 1	Type 2	Type 3	Type 4	P
AHI+	21 $\pm$ 12	23 $\pm$ 12	15 $\pm$ 12	21 $\pm$ 11	* < 0.001
Range	2 - 48	0 - 43	0 - 43	6 - 44	
HI+	17 $\pm$ 10	20 $\pm$ 11	11 $\pm$ 10	19 $\pm$ 10	** < 0.001
Range	2 - 40	3 - 35	0 - 33	2 - 37	

Abbreviations: AHI: Apnea/hypopnea index; HI: Hypopnea index; Type 1: hypopneas with  $\bar{SaO}_2$   $\geq$  3%; Type 2: hypopneas with  $\bar{SaO}_2$   $\geq$  3% or EEGA; Type 3: hypopneas with  $\bar{SaO}_2$   $\geq$  4%; Type 4: hypopneas with  $\bar{SaO}_2$   $\geq$  4% or EEGA.

<sup>+</sup> Arithmetic mean and standard deviation.

\* Difference between AHI type 2, 4 and 3. \*\* Difference between HI type 2, 4 and 3.

Table 3 shows the different values of AHI and HI, according to the different definitions of hypopnea. HI and AHI types 2 and 4 were higher than type 3 (HI type 2 = 20  $\pm$  11.6, HI type 4 = 18.6  $\pm$  10 vs. HI type 3 = 11.4  $\pm$  10,  $p$  < 0.001; AHI type 2 = 23.3  $\pm$  11.6, AHI type 4 = 21.4  $\pm$  11.2 vs. AHI type 3 = 14.7  $\pm$  11.6,  $p$  < 0.001). HI and AHI types 1 and 2 were similar (HI type 1 = 17.4  $\pm$

10, AHI type 1 = 20.6  $\pm$  11.8 vs. HI type 2 = 20  $\pm$  10.6, AHI type 2 = 23  $\pm$  11.6,  $p$  > 0.05).

Table 4 shows the prevalence of OSAHS according to both AHI cut-off value and the definition of hypopnea. The diagnostic frequency of OSAHS in the population herein studied was 30% to 55% when a  $\geq$  4% decrease in  $SaO_2$  was used as criterion of hypopnea, and 70% to

TABLE 4.– Prevalence of OSA according to the definition of hypopnea and the apnea/hypopnea index (AHI)

Type of Hypopnea	Prevalence of OSA (%)	
	AHI $\geq$ 10	AHI $\geq$ 15
TYPE 1	85	70
TYPE 2	85	70
TYPE 3	55	30
TYPE 4	85	70

Type 1: hypopneas with  $\geq$  SaO<sub>2</sub>  $\geq$  3%; Type 2: hypopneas with  $\geq$  SaO<sub>2</sub>  $\geq$  3% or EEGA; Type 3: hypopneas with  $\geq$  SaO<sub>2</sub>  $\geq$  4%; Type 4: hypopneas with  $\geq$  SaO<sub>2</sub>  $\geq$  4% or EEGA.

85% when a  $\geq$  4% fall in SaO<sub>2</sub> and/or EEGA was used ( $p < 0.05$ ). Definitions 1 and 2 showed no differences in the frequency of OSAHS (type 1: 70% to 85%, type 2: 70% to 85%,  $p > 0.05$ ).

## Discussion

In the present study we compared apnea/hypopnea indices according to four different definitions of hypopnea: 1) type 1:  $\geq$  SaO<sub>2</sub>  $\geq$  3%; 2) type 2:  $\geq$  SaO<sub>2</sub>  $\geq$  3% or EEGA; 3) type 3:  $\geq$  SaO<sub>2</sub>  $\geq$  4%; 4) type 4:  $\geq$  SaO<sub>2</sub>  $\geq$  4% or EEGA. Results show that when the definitions including EEGA (H type 2 and 4) are used, the average number of hypopneas, as well as HI and AHI are significantly higher than the same variables in type 3. HI and AHI type 2 were 76% and 59% higher than HI and AHI type 3. Moreover, HI and AHI type 4 were 64% and 46% higher than HI and AHI type 3.

Our results reveal that HI or AHI type 1 and HI or AHI type 2 show a high level of correlation and agreement (ICC 0.9 to 0.93, mean difference between HI /AHI type 1 and HI /AHI type 2 =  $-2.6 \pm 9/h$ , Fig. 1). Therefore, the addition of an arousal requirement to the oxygen desaturation criterion for hypopnea causes only a small change in HI and AHI. On the other hand, the correlation and agreement between HI or AHI type 3 and HI or AHI type 4 was poor, showing that a definition of hypopnea requiring an arousal associated to oxygen desaturation yields substantially different results than one based solely on oxygen desaturation (ICC 0.78 to 0.83, mean difference between HI or AHI type 3 and HI or AHI type 4 =  $-6.75 \pm 13.3/h$ , Fig. 2). Indeed, a statistically significant difference was found between the mean values of HI or AHI type 3 and 4 ( $p < 0.001$ ).

The above mentioned definitions of hypopnea were chosen for several reasons. The "discernible" decrease in airflow was selected due to observations indicating that small decreases in thermistor signal amplitude could be associated with up to 50% reductions in the current

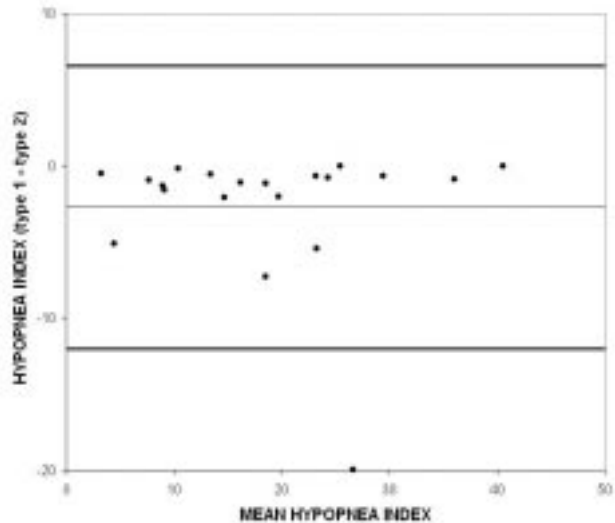


Fig. 1.– Bland Altman plot illustrating the agreement in HI scored with type 1 and type 2 criteria. The mean of the difference (bias) in HI with the two scoring methods was  $-2.61$  (thin solid line). The difference between the two test results will fall within 9/h of this mean difference 95% of the time (thick lines, limits of agreement).

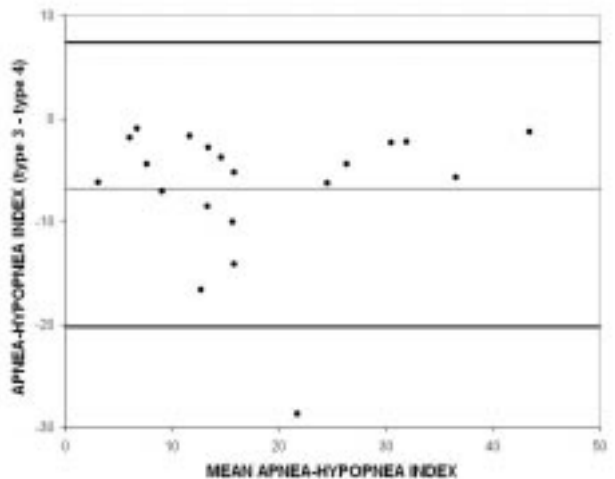


Fig. 2.– Bland Altman plot illustrating the agreement in AHI scored with type 3 and type 4 criteria. The mean of the difference (bias) in AHI with the two scoring methods was  $-6.75$  (thin line). The difference between the two test results will fall within 13.3/h of this mean difference 95% of the time (thick lines, limits of agreement).

volume measured with a pneumotachograph<sup>6</sup>. A  $\geq$  50% fall in abdominal movements was herein included as an alternative criterion of ventilation reduction. The cut-off value chosen for this study has been largely reported in the literature<sup>7</sup> and allows a higher correlation with oxygen desaturation and arousals<sup>2</sup>. We chose either the 3% or  $\geq$  4% SaO<sub>2</sub> decreases, since they are the most frequently used in the different sleep laboratories with a variability higher than the 2% shown by pulse oximetry.

TABLE 5.– Comparison studies of apnea-hypopneas indices derived from different definitions of hypopnea

Nº Patients	Author	Rate of Hypopnea(%)	Criteria Hypopnea	Results
94	Tsai	55 - 75	- 30% T or A movements (respirtrace) plus: 1)Type A: - SaO <sub>2</sub> 3 4% 2)Type B:- SaO <sub>2</sub> 3 4% or EEGA	HI type B 9 / HI type A 14, p < 0.001 AHI type B 19 / AHI type A 16, p > 0.05
48	Manser	3 80	Type B: - TA movements (respirtrace) Plus - SaO <sub>2</sub> 3 3% or EEGA Type C: - airflow (thermistors/respirtrace) plus - SaO <sub>2</sub> 3 3%	HI type C 24 / HI type B 35, p < 0.0005 AHI type C 30 / AHI type B 42, p < 0.0005
20	Nigro	3 78	- 30% AF (thermistors) or - 3 50% AM (strain gauge) plus: Type 1: - SaO <sub>2</sub> 3 3% Type 2: - SaO <sub>2</sub> 3 3% or EEGA Type 3: - SaO <sub>2</sub> 3 4% Type 4: - SaO <sub>2</sub> 3 4% or EEGA	HI type 1, 17 / HI type 2, 20, p > 0.05 AHI type 1, 21 / AHI type 23, p > 0.05 HI type 3, 11 / HI type 4, 19, p < 0.001 AHI type 3, 15 / AHI type 4, 21, p < 0.001

T = thoracic; A = abdominal; TA = thoracoabdominal; AF = airflow; AM = abdominal movements; HI = hypopnea index; AHI = apnea/hypopnea index. EEGA = electroencephalographic arousal.

The findings herein reported are similar from the study by Tsai et al<sup>7</sup>, who found a HI type B higher than HI type A (HI type B = 14, HI type A = 9, p < 0.004) in a group of 98 patients with OSAHS. These authors defined hypopnea as 3 30% decrease in the dimension of thoracic or abdominal movements 3 10 seg. associated with one of the following parameters: 1) type A: - SaO<sub>2</sub> 3 4%; 2) type B: - SaO<sub>2</sub> 3 4% or EEGA. However, the AHI type B and type A were similar in both definitions (AHI type A = 16, AHI type A = 19, p > 0.05). These differences could be explained because the population of patients studied by Tsai, presented a lower rate of hypopneas (57% - 75%) than our population (78% - 85%). Thus, although HI in definition "type B" was higher than in "type A", AHI was similar in both definitions, due to a "dilution effect" derived from the higher rate of apneas in their population. Similarly to us, Redline et al<sup>9</sup> revealed a 40% increase in AHI in hypopneas identified by oxygen desaturation or electroencephalographic arousals compared with definitions that only required SaO<sub>2</sub> fall. On the other hand, Manser et al<sup>12</sup> observed in a population of 48 patients with predominately hypopneas, an increase in HI and AHI of 24 to 35 and 30 to 42 (p < 0.0005) when he used as criteria of hypopnea a decrease in the oxygen saturation 3 3% vs oxygen desaturation or arousal. By contrast, we did not observe significant differences between HI type 1 (- SpO<sub>2</sub> 3 3%) and type 2 (- SpO<sub>2</sub> 3 3% or EEGA). These differences could be explained by several reasons: 1) Although we observed a trend towards a higher HI type 2 than HI type 1 (HI type 2 = 20, HI type 1 = 17), it did not reach statistical significance.

This possibly was because of the few number of patients we studied (type II error) 2) The methodology we used to detect descent of airflow (thermistors) may underestimate the number of hypopneas when it is compared with the respirtrace<sup>15</sup> 3) Finally, we used an airflow reduction to define hypopnea higher (- 3 50% AM) than Manser (- 3 30% respirtrace) therefore we may have failed to detect some hypopneas. In table 5 we compare our results with those of Tsai and Manser.

The prevalence of OSAHS depends on both the cut-off value used in AHI<sup>8</sup> and the definition of hypopnea<sup>9</sup>. Although the prevalence of OSAHS with the definition type 2 was higher than type 1 (85% and 70%), it did not reach statistical significance. This was probably due to the smaller number of patients in our study compared to Manser's paper. Nevertheless, we found that the prevalence of OSAHS using a cut-off value of AHI 3 10 increased from 55% (type 3 - - SaO<sub>2</sub> 3 4%) to 85% (type 4 - - SaO<sub>2</sub> 3 4% or EEGA), and using AHI 3 15, from 30% to 70% (type 3 and 4, respectively, p < 0.05).

We conclude that, in our patients' population with high frequency of hypopneas, the use of EEGA as an alternative criterion of a 3 4% decrease in SaO<sub>2</sub> in the definition of hypopnea, significantly increased the number of identified hypopneas, HI, AHI and the prevalence of OSAHS.

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*Dans les champs de l'observation le hazard ne favorise que les esprits préparés.*

En los campos de la observación el azar no favorece sino a las mentes preparadas.

Louis Pasteur (1822-1895)