

# Assessment of ventilatory neuromuscular drive in patients with obstructive sleep apnea

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## Abstract

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The presence of abnormalities of the respiratory center in obstructive sleep apnea (OSA) patients and their correlation with polysomnographic data are still a matter of controversy. Moderately obese, sleep-deprived OSA patients presenting daytime hypersomnolence, with normocapnia and no clinical or spirometric evidence of pulmonary disease, were selected. We assessed the ventilatory control and correlated it with polysomnographic data. Ventilatory neuromuscular drive was evaluated in these patients by measuring the ventilatory response (VE), the inspiratory occlusion pressure ( $P_{i1}$ ) and the ventilatory pattern (VT/TI, TI/TTOT) at rest and during submaximal exercise, breathing room air. These analyses were also performed after inhalation of a hypercapnic mixture of CO<sub>2</sub> ( $\Delta P_{i1}/\Delta P_{ET}CO_2$ ,  $\Delta VE/\Delta P_{ET}CO_2$ ). Average rest and exercise ventilatory response (VE: 12.2 and 32.6 l/min, respectively), inspiratory occlusion pressure ( $P_{i1}$ : 1.5 and 4.7 cmH<sub>2</sub>O, respectively), and ventilatory pattern (VT/TI: 0.42 and 1.09 l/s; TI/TTOT: 0.47 and 0.46 l/s, respectively) were within the normal range. In response to hypercapnia, the values of ventilatory response ( $\Delta VE/\Delta P_{ET}CO_2$ : 1.51 l min<sup>-1</sup> mmHg<sup>-1</sup>) and inspiratory occlusion pressure ( $\Delta P_{i1}/\Delta P_{ET}CO_2$ : 0.22 cmH<sub>2</sub>O) were normal or slightly reduced in the normocapnic OSA patients. No association or correlation between ventilatory neuromuscular drive and ventilatory pattern, hypersomnolence score and polysomnographic data was found; however a significant positive correlation was observed between  $P_{i1}$  and weight. Our results indicate the existence of a group of normocapnic OSA patients who have a normal awake neuromuscular ventilatory drive at rest or during exercise that is partially influenced by obesity.

### Key words

- Ventilatory neuromuscular drive
- Sleep apnea
- Polysomnography
- Ventilatory control

## Introduction

Several studies have shown a reduction of ventilatory drive in patients with obesity-hypoventilation syndrome (1-4). However, it is not yet clear whether this abnormality is primary or secondary in its origin.

In contrast, alterations of the respiratory center in obstructive sleep apnea (OSA) are still controversial. Some investigators believe that obesity could stimulate the ventilatory drive. This hypothesis was raised by Sampson and Grassino (5) for obese patients without OSA with a normal ventilatory pattern, but with increased inspiratory occlusion pressure. The same has not been observed by others (6), who showed normal hypercapnic ventilatory response in these subjects. Studies of obese OSA patients have indicated a reduced hypercapnic ventilatory response compared to obese subjects without OSA (7) or when an inspiratory load was imposed (8).

The role of upper airway obstruction in decreasing the ventilatory drive of OSA patients has been suggested in studies in which tracheostomy (9) or continuous positive airway pressure (CPAP) (10) improved the hypercapnic response. Also, sleep deprivation as the cause of reduction in the hypercapnic ventilatory response has been shown to occur in normal subjects (11-13). The disparity of data reported in these studies is probably due to the use of different methods and a heterogeneous patient series.

In the present study we evaluated OSA patients presenting the following characteristics: a) moderate obesity (14); b) sleep deprivation and fragmentation reflected by reduced sleep efficiency and altered sleep architecture, with resulting daytime hypersomnolence assessed by a hypersomnolence score (15), and c) normocapnia with no spirometric alterations which might indicate obstructive or restrictive ventilatory disturbances.

The major objective of the present study

was to evaluate the possible abnormalities of the respiratory center by assessing ventilatory response, inspiratory occlusion pressure ( $P_{i1}$ ) and ventilatory pattern at rest (breathing either room air or a hypercapnic mixture) and during a metabolic increase induced by exercise. We also attempted to correlate possible alterations of these variables with polysomnographic findings.

## Patients and Methods

### Subjects

Twenty-two patients with a diagnosis of OSA who presented an apnea/hypopnea index (AHI: number of apneas and hypopneas/total sleep time) above 15 were included in the study. These patients were referred from the Sleep Disorders Section of the Respiratory Division, Universidade Federal de São Paulo, and were compared with normal subjects studied by Moura et al. (16) to determine normal values for the variables  $P_{i1}$  and ventilatory pattern at rest and during submaximal exercise, following the same protocol. The hypercapnic ventilatory response was compared to the normal range reported by Burki (17).

Exclusion criteria were 1) degree III of obesity: body mass index (BMI) above 40 kg/m<sup>2</sup> (14); 2) clinical diagnosis of chronic obstructive pulmonary disease, asthma, bronchiectasis, obstructive or restrictive ventilatory insufficiency (18) assessed by simple spirometry; 3) hypercapnia, i.e., partial arterial carbon dioxide blood pressure ( $P_{aCO_2}$ ) above 45 mmHg determined by arterial gasometry; 4) diseases that may lead to secondary OSA, such as hypothyroidism, acromegaly, Cushing syndrome, and other disturbances that may hinder the patient's ability to perform the exercise, such as peripheral vascular insufficiency, bone and/or joint and muscle alterations, cardiac insufficiency and acute coronary insufficiency.

## Protocol

*Clinical evaluation.* A modified questionnaire (15) containing questions about sleep, snoring, nocturnal apneas and daytime hypersomnolence was used. Answers were scored as 0 = never, 1 = rarely, 2 = occasionally, and 3 = frequently. The severity of hypersomnolence was classified as follows: 0.5 to 1 = mild, up to 2 = moderate, and greater than 2 to 3 = severe.

Otorhinolaryngologic evaluation consisted of nasofibroscope using an FLT-S Machida (Tokyo, Japan) apparatus connected to a monitor, a NISCO G10 CCD-25 control camera and a Machida RH 150 TL source (Japan). During examination, the patient was seated at a 45° angle in dorsal inclination during both spontaneous breathing and Müller maneuver. Following these procedures, abnormalities of nasal cavities, oropharynx, rhinopharynx and hypopharynx were recorded.

*Polysomnographic recording.* Polysomnography was carried out throughout the night. The apparatus consisted of a sleep analyzer computer (SAC, version 9.2, Oxford Instruments, Inc., Tampa FL, USA). Thirteen channels were distributed as follows: 2 for electroencephalography, 2 for the oculogram, 1 for chin electromyography, 2 for tibial electromyography, 1 for electrocardiography, 1 for airflow, 2 for thoracic-abdominal movements, 1 for pulse oxymetry and 1 for detection of body position. The system automatically analyzes sleep stages using the criteria of Rechtschaffen and Kales (19), detecting artifacts and arousals.

At the end of the recording period, a physician trained in polysomnographic reading reanalyzed the computer-generated staging following the criteria of Rechtschaffen and Kales (19) and making the necessary alterations. The normal values used for analysis of sleep variables were those proposed by Carskadon and Dement (20), and those for respiratory events were those of

Guilleminault (21).

The variables analyzed during polysomnography were sleep efficiency (ratio of total sleep time/total recording time), sleep stages 3, 4 and REM (percentage of sleeping time), AHI and percentage of total recording time with oxyhemoglobin saturation below 85%.

*Spirometry and flow-volume curve.* The Diagnostic System Med Graphic MGC-CPx (St. Paul, MN, USA) set on the flow mode was used. The difference in pressure in a linear pneumotachograph (Hans Rudolph, model 3800, Kansas City, MO, USA) was calculated to measure airflow. Patients were submitted to the test at rest, in a sitting position and breathing room air. Predicted values were based on the formulas reported by Knudson et al. (22) and Cherniack and Raber (23). A series of at least 3 measurements were obtained. Curves were accepted by the system when the criteria determined by the American Thoracic Society (24) were reached. We analyzed as percentage of predicted values the forced vital capacity (%FVC), the ratio of forced expired volume in the first second (FEV<sub>1</sub>) over FVC (FEV<sub>1</sub>/FVC in %) and the ratio of forced expired flow at 50% of FVC/forced inspired flow at 50% of FVC (FEF<sub>50%</sub>/FIF<sub>50%</sub>).

*Maximal voluntary ventilation.* After the determination of the flow-volume curves, patients were submitted to at least 3 maximal voluntary ventilation (MVV) maneuvers, which consisted of inhalations and exhalations using the highest possible tidal volume and respiratory frequency for a period of 15 s. Predictive values were those used by Cherniack and Raber (23).

*Measurements of maximal inspiratory (MIP) and expiratory pressures (MEP).* On the same day, following a 30-min period of rest, patients were instructed to perform maneuvers of maximum inspiratory and expiratory pressures measured with a manovacuometer ( $\pm 150$  cmH<sub>2</sub>O; IMEBRAS, São Paulo, SP, Brazil) and the best of 10 maneu-

vers was considered for analysis. The criteria of acceptance were those determined by Ringqvist (25), whereas normal range values of MIP and MEP were based on those reported by Wilson et al. (26).

*Arterial blood gases and pH measurements.* Arterial blood was anaerobically collected with the patient at rest and breathing room air. Blood gases ( $\text{PaO}_2$  and  $\text{PaCO}_2$ ) and pH were determined using an ABL 330 apparatus (Radiometer, Copenhagen, Denmark), and normal  $\text{PaO}_2$  values were calculated using regression of these variables, according to age, as established by Møllgaard (27).

*Ventilatory and metabolic evaluation at rest and during the submaximal exercise test.* The exercise test was performed on the same day employing an electromagnetic cycloergometer (Collins-Pedalmate, Braintree, MA, USA) and variables were monitored with a cardioscope and an electrocardiograph (FUNBEC, São Paulo, SP, Brazil). Pulse oximetry was determined with an oximeter (Sensor Medics, Oxysuttle TM, Anaheim, CA, USA). Ventilatory and metabolic variables (tidal volume (VT), respiratory rate, minute ventilation (VE), oxygen uptake and carbon dioxide output ( $\text{VCO}_2$ )) were analyzed by the Med Graphic MGC-CPx system set on the metabolic mode. Ventilation and  $\text{VCO}_2$  were obtained breath-by-breath by integration of flow and volume and the  $\text{CO}_2$  signal, as previously described (28,29). A period of 2 min at rest was followed by exercise which began with a 0 Watt load for 2 min followed by an increment of 25 Watts for 5 min, and a further increment of 25 Watts (total of 50 Watts) for another 5 min. Electrocardiography, oxyhemoglobin saturation and systemic arterial blood pressure were also measured simultaneously during each period.

*Determination of ventilatory pattern and inspiratory occlusion pressure.* Analysis of the ventilatory pattern was performed at rest and during the different exercise loads and

the values obtained were compared to those reported by Moura et al. (16). We analyzed VT, VE, respiratory rate, inspiratory time (TI)/total cycle time (TTOT) ratio and the VT/TI ratio.

During assessment of  $P_{i,1}$ , patients were acoustically and visually isolated from the environment (16). Ventilatory assessment was performed with the patient breathing through a mouthpiece connected to a two-way valve (Rudolph 2700) of low resistance and 90 ml of dead space. Inspiratory flow rate was measured with a Fleisch pneumotachograph coupled to a pressure transducer (Valyline MP,  $45.1 \pm 2.0$  cmH<sub>2</sub>O). The generated electric signal was recorded with a Beckman polygraph (model R-411) as inspiratory flow and sent to a Thompson integrator (Montreal, Canada), which generated another electric signal that corresponded to VT on the polygraph. After a 2-min period of adaptation, we began the recording of tidal volume and inspiratory flow with the polygraph set at a speed of 10 mm/s.  $P_{i,1}$  was recorded at a speed of 100 mm/s, using an inspiratory occlusion at the level of functional residual capacity produced by a pneumatic valve for a period of 300 ms (16,30). This procedure was repeated as many times as necessary to obtain 5-10 technically acceptable  $P_{i,1}$  curves (with no flow or volume alteration), with at least 4 curves of flow and tidal volume preceding each one. Bizarre curves were excluded from  $P_{i,1}$  calculation (16,30).

$P_{i,1}$  values were obtained, after discarding the first 50 ms, by measuring the pressure variations of the occluded airway during inspiration during the subsequent 100 ms. This assessment was performed at rest and during the 3rd (25 Watts) and 6th min (50 Watts). Normal ranges were those determined by Moura et al. (16) in our laboratory.

*Steady-state  $\text{CO}_2$  inhalation test.* The patient, sitting and wearing a nasal clip, breathed through a mouthpiece connected to a two-way Rudolph 2700 valve coupled to a 120-l

Douglas balloon containing an 8% CO<sub>2</sub> and 42% O<sub>2</sub> mixture. The system used for P<sub>1</sub> measurement was connected to the airways. The expiratory port was in contact with the environment. P<sub>1</sub> was assessed after 3 min of inhalation of the mixture. At the end of the 5th min, expiratory air was collected for 1 min through a connection with a 120-l Tissot gasometer (Warren E. Collins, Inc., Braintree, MA). The displacement generated by the volume of air obtained under BTPS conditions was recorded. Simultaneously, the end tidal CO<sub>2</sub> expired fraction was measured with an infrared CO<sub>2</sub> analyzer (Sensor Medics, model LBII) whose output signal was recorded with a polygraph (Beckman, model R 411). The end tidal CO<sub>2</sub> partial pressure (P<sub>ET</sub>CO<sub>2</sub>) was then calculated (16). The values of  $\Delta P_{1}/\Delta P_{ET}CO_2$  and  $\Delta VE/\Delta P_{ET}CO_2$  reported by Burki (17) were used as reference values.

This study was approved by the Ethics Committee of Hospital São Paulo and informed consent was obtained from the subjects.

### Statistical analysis

The ventilatory neuromuscular drive, respiratory impedance and ventilatory pattern of patients and normal volunteers from our laboratory (16) were compared by the Mann-Whitney U-test (31).

In a second phase of the analysis, patients were separated according to the median values of the score of hypersomnolence and polysomnographic variables, and the ventilatory drive and the respiratory pattern of these two subgroups were compared by the Mann-Whitney U-test.

The possible association between neuromuscular ventilatory drive (P<sub>1</sub>, P<sub>1</sub>/VCO<sub>2</sub>,  $\Delta P_{1}/\Delta P_{ET}CO_2$  and  $\Delta VE/\Delta P_{ET}CO_2$ ) and hypersomnolence score, and polysomnographic variables (sleep efficiency, arousals, AHI and oxyhemoglobin saturation) was determined by comparing their median values by

the chi-square test or the Fisher exact test (31).

The Spearman correlation test was used to evaluate the correlation between ventilatory drive variables and weight, hypersomnolence score, AHI and minimum oxyhemoglobin saturation (31).

### Results

The group of patients consisted of 17 men and 5 women ranging in age from 32 to 63 years, weighing 63 to 123 kg, and ranging in height from 151 to 178 cm, which resulted in a BMI of 25.5 to 39.3 kg/m<sup>2</sup>. Median values are shown in Table 1. The control group (16) consisted of 10 men ranging in age from 23 to 32 years, weighing 57 to 85 kg and ranging in height from 160 to 180 cm. The OSA patients were older and heavier than normal subjects.

The scores obtained from the clinical questionnaire showed that 4 patients presented mild hypersomnolence (score >0.5 and <1), 14 presented moderate hypersomnolence (score >1 and <2), and 4 severe hypersomnolence (score >2). None of the normal subjects complained of hypersomnolence.

Table 1 - Physical characteristics and polysomnographic data of OSA patients.

BMI: Body mass index; TST: total sleep time; TRT: total recording time; SPT: sleep period time, defined as the result of TST subtracted from the initial and final latencies; AHI: apnea/hypopnea index; SaO<sub>2</sub><85%: percentage of TRT with oxyhemoglobin saturation below 85%.

Variable	Median	Range
Age (years)	47	32-63
Weight (kg)	90.4	63-123.5
Height (cm)	167.7	151-178
BMI (kg/m <sup>2</sup> )	32.6	25.5-39.4
TST/TRT	71.5	46.1-93.2
Stages (%SPT) 3 and 4	3.5	0-29
REM	12.7	2-42.8
AHI	48	16.2-89.5
SaO <sub>2</sub> <85%	22	0-51

Otorhinolaryngological evaluation revealed that of the 22 patients 12 showed inferior turbinate hypertrophy and 11 presented septum deviation (10 of whom showed degrees II and III). Upon oropharynx examination, 12 patients presented uvula edema and 7 uvula stretching, 5 patients had hypertrophied tonsils and 1 had an increased tongue base. Nasofibroscopy during the Müller maneuver revealed obstruction at the level of the velopharyngeal sphincter in 18 patients. Of these, 2 presented obstruction at the tongue base level, 1 at the hypopharynx level, and 1 at all levels.

Polysomnographic findings revealed that patients presented reduced sleep efficiency and superficial sleep, with decreased stages 3, 4 and REM. AHI was above 30 in 13 patients, characterizing moderate to severe OSA (Table 1).

Spirometry, MVV, MIP and MEP revealed mostly normal results for the patients (Table 2). Analysis of the flow-volume curve revealed the presence of sawtooth values in 12 patients and an  $FEF_{50\%}/FIF_{50\%}$  ratio above 1 in eight patients. Analysis of arterial blood

gases showed that the patients were all normocapnic (Table 2). The normal group showed values of FVC between 76 and 104%, with  $FEV_1/FVC$  ranging from 79 to 89%.

Comparison of neuromuscular respiratory drive ( $P_{i1}$  and  $P_{i1}/VCO_2$ ), respiratory impedance ( $P_{i1}/VT/TI$ ), and ventilatory pattern ( $VT/TI$  and  $TI/TTOT$ ) showed no difference between our patients and the normal subjects (Table 3).

Figures 1 and 2 show that most patients presented a ventilatory drive within the normal range when it was evaluated by the ratio between the variation ( $\Delta$ ) of inspiratory occlusion pressure and the variation of  $P_{ET}CO_2$ , before and after the inhalation of a hypercapnic mixture ( $\Delta P_{i1}/\Delta P_{ET}CO_2$ ), and by the ratio between the variation of minute ventilation and the variation of  $P_{ET}CO_2$  ( $\Delta VE/\Delta P_{ET}CO_2$ ). Two of these patients, however, presented  $\Delta P_{i1}/\Delta P_{ET}CO_2$  values (0.11 and 0.10  $cmH_2O/mmHg$ ) slightly below the normal range (normal values are between 0.12 and 2.64  $cmH_2O/mmHg$ ) (17). These patients also presented reduced  $\Delta VE/\Delta P_{ET}CO_2$  values (0.94 and 1.09  $l\ min^{-1}\ mmHg^{-1}$ ), while the normal range is between 1.16 and 6.18  $l\ min^{-1}\ mmHg^{-1}$  (17). The former patient had the most reduced  $P_{i1}$  value at rest (0.8  $cmH_2O$ ), meaning a reduction of ventilatory drive but without evidence of alveolar hypoventilation. The other patient had the highest BMI value (39.3  $kg/m^2$ ) and reduced MIP (66  $cmH_2O$ ).

In order to establish whether clinical and polysomnographic abnormalities influence the ventilatory drive, our patients were reclassified based on a cut-off point that corresponded to the median value of hypersomnolence score, sleep efficiency, number of arousals, AHI, and the percentage of total recording time in which saturation remained below 85%. Comparison between subgroups did not reveal any difference in neuromuscular drive ( $P_{i1}$ ,  $P_{i1}/VCO_2$ ), respiratory impedance ( $P_{i1}/VT/TI$ ), ventilatory pattern ( $VT/TI$ ,  $TI/TTOT$ ) at rest and during exercise or the hypercapnic test ( $\Delta P_{i1}/\Delta P_{ET}CO_2$  and  $\Delta VE/$

Table 2 - Pulmonary function test and arterial blood gases in OSA patients.

#: Percent of predicted value, when % is placed before the variable; FVC: forced vital capacity;  $FEV_1$ : forced expired volume during the first second of FVC;  $FEF_{50\%}$ : forced expired flow at 50% of FVC;  $FIF_{50\%}$ : forced inspired flow at 50% of FVC; MVV: maximal voluntary ventilation; MIP: maximal inspiratory pressure; MEP: maximal expiratory pressure;  $PaO_2$ : partial  $O_2$  pressure in arterial blood;  $PaCO_2$ : partial  $CO_2$  pressure in arterial blood.

Variable	Median	Range
%FVC	105.5	76-133
$FEV_1/FVC(\%)$	81.5	68-88
$FEF_{50\%}/FIF_{50\%}$	0.84	0.32-2.86
%MVV	90.5	67-149
%MIP	112	73-162
%MEP	106.5	90-123
$PaO_2$	82	56-108
$PaCO_2$	38	30-43

$\Delta P_{ET}CO_2$ ).

Also, no correlation was found between the neuromuscular drive and the above variables, except for a weak but significant correlation between  $P_{i1}$  at rest and weight ( $r = 0.48$ ,  $P = 0.02$ ).

## Discussion

Our results point to a group of normocapnic obese OSA patients with ventilatory neuromuscular drive ( $P_{i1}$ ,  $P_{i1}/VCO_2$ ) and ventilatory pattern (VT/TI, TI/TTOT) in the normal range at rest and during exercise. Also, the positive correlation between  $P_{i1}$  at rest and weight may indicate a possible load effect stimulation of obesity on the ventilatory drive in our patients. This hypothesis is supported by the study of Sampson and Grassino (5) who described similar results, i.e., a positive correlation between obesity and  $P_{i1}$  values in obese non-OSA subjects. However, when the neuromuscular drive was evaluated by the hypercapnic ventilatory response (HVR), we found normal or slightly reduced values of  $\Delta P_{i1}/\Delta P_{ET}CO_2$  and  $\Delta VE/\Delta P_{ET}CO_2$ , which were not correlated with subject weight. Gold et al. (7) found a reduced HVR in obese OSA patients as compared to obese non-OSA subjects and, since the respiratory mechanics were similar for both groups, the authors postulated that a primary chemoresponsiveness defect may be responsible for the alterations found in OSA patients.

Other authors (8) have shown that normocapnic OSA patients have preserved HVR but a decreased response compared to normal subjects when an inspiratory load is imposed, suggesting that these patients have an altered ventilatory drive, since they did not increase ventilation in response to an inspiratory load. Furthermore, they hypothesized that daytime somnolence was the cause of such abnormality.

The hypothesis that sleep quality of OSA patients can interfere with chemoresponsive-

ness during waking is still controversial. Sleep deprivation can lead to altered body temperature, opiate secretion, and daytime hypersomnolence, all of which could explain the inhibition of the respiratory center (13). Studies that addressed this issue also report disputable results. Espinoza et al. (12) did not find changes in HVR in normal subjects following 2 nights of sleep fragmentation. In contrast, White et al. (13) found a 24% reduction of HVR and a 29% reduction of the ventilatory response to hypoxemia in 24-h sleep-deprived subjects. Similar results were reported by Cooper and Phillips (11), with a 20% decrease of HVR in subjects submitted to total sleep for 24 h. The deprivation reported in the above studies and that used here differ in two major aspects: normal

Table 3 - Ventilatory pattern, ventilatory drive and respiratory impedance in OSA patients and normal volunteers, both at rest (Rest) and during submaximal 50-Watt exercise (Ex).

Data are reported as median and range. VT: Tidal volume; TI: inspiratory time; TOT: total time;  $P_{i1}$ : inspiratory occlusion pressure;  $VCO_2$ :  $CO_2$  output; VE: minute ventilation.

	OSA patients (N = 22)	Normal volunteers (N = 10)
VT/TI (l/sec)		
Rest	0.42 (0.21-0.80)	0.5 (0.38-0.84)
Ex	1.09 (0.77-1.47)	1.06 (0.63-1.28)
TI/TOT		
Rest	0.47 (0.35-0.59)	0.39 (0.31-0.46)
Ex	0.46 (0.41-0.56)	0.46 (0.41-0.51)
Respiratory rate		
Rest	15.1 (10.4-27.6)	15.2 (10.8-17.5)
Ex	24.5 (10-49)	20.3 (14.1-29.9)
VT (l)		
Rest	0.73 (0.36-1.18)	0.83 (0.57-1.72)
Ex	1.45 (0.65-2.67)	1.38 (0.82-2.17)
VE (l/min)		
Rest	12.2 (5.4-18.2)	12.5 (8.9-23.12)
Ex	32.6 (23.4-42.3)	29 (16.34-35.71)
$P_{i1}$ (cmH <sub>2</sub> O)		
Rest	1.5 (0.8-6.2)	1.4 (0.51-2.42)
Ex	4.7 (2-14.3)	4.3 (2.39-5.60)
$P_{i1}/VCO_2$ (cmH <sub>2</sub> O/ml)		
Rest	6.1 (2.2-14)	4.5 (2.12-10.52)
Ex	5.1 (2.5-12)	4.7 (2.32-6)
$P_{i1}/VT/TI$ (cmH <sub>2</sub> O l <sup>-1</sup> s <sup>-1</sup> )		
Rest	3.5 (1.4-16.3)	2.9 (1.24-4.48)
Ex	4.4 (2.3-15)	4.5 (2.23-6.83)

subjects were used in all of them and these subjects were sleep deprived for 24-48 h, which is considered an acute deprivation. The HVR obtained for our patients (Figures

Figure 1 - Individual values of  $\Delta P_{.1}/\Delta P_{ET}CO_2$  in normocapnic patients with OSA. The horizontal line corresponds to the lower limit of normality at 0.12 cmH<sub>2</sub>O/mmHg (17).

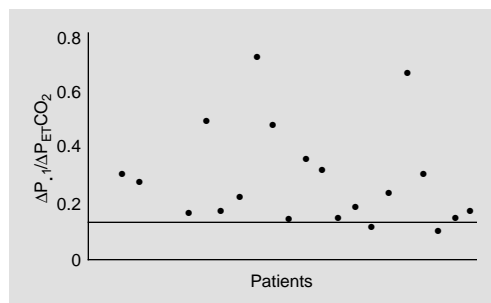
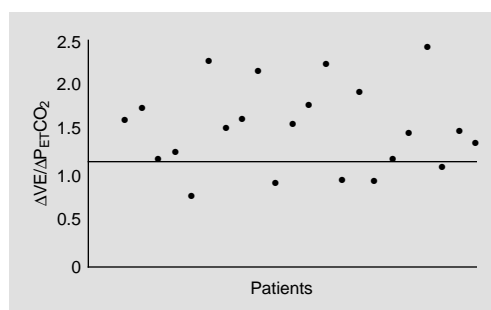


Figure 2 - Individual values of  $\Delta VE/\Delta P_{ET}CO_2$  in normocapnic patients with OSA. The horizontal line corresponds to the lower limit of normality at 1.16 l min<sup>-1</sup> mmHg<sup>-1</sup> (17).



1 and 2) who presented with chronic sleep deprivation and/or fragmentation might be considered blunted, since higher values would be expected, as reported by Gold et al. (7) for obese non-OSA subjects. However, no association or correlation was found between this response and AHI, sleep efficiency, arousals, or hypersomnolence score.

Some studies report an improvement of HVR following treatment of upper airway obstruction by tracheostomy (9) or with the use of nasal CPAP (10) in OSA patients. These results suggest a direct or secondary effect of obstructive sleep apnea reducing the hypercapnic ventilatory drive. Studies utilizing nasal CPAP in OSA patients are currently in progress in our service to test the above hypothesis.

Our results indicate the existence of a group of obese, normocapnic OSA patients who have a normal awake ventilatory drive at rest and during exercise which is partially influenced by obesity.

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