What are the causes of excessive daytime sleepiness in patients with sleep-disordered breathing?

To the Editors:

Recently, the *European Respiratory Journal* published a study by MEDIANO *et al.* [1] on the determinants of excessive daytime sleepiness (EDS) in obstructive sleep apnoea (OSA) patients. The study did not find differences in body mass index (BMI), age or apnoea/hypopnoea index (AHI) between OSA patients with and without EDS, but found significantly more pronounced nocturnal hypoxaemia in patients with EDS, and concluded that nocturnal oxygen desaturation is involved in the pathogenesis of EDS. In his letter commenting on this work, BAHAMMAM [2] pointed out that the possible role of obesity hypoventilation syndrome (OHS), a known cause of EDS, was not ruled out by MEDIANO *et al.* [1]. OHS patients have the same AHI of pure OSA patients matched by age and BMI, but are characterised by apnoeas of longer duration and more severe nocturnal hypoxaemia [3], like the EDS patients studied by MEDIANO *et al.* [1]. In other words, BAHAMMAM [2] suggests that the lower nocturnal oxygen saturation and the associated daytime somnolence observed by MEDIANO *et al.* [1] in the EDS group might be due to OHS. Thus, BAHAMMAM [2] also concludes that low nocturnal blood oxygen saturation has a fundamental role in EDS, whether or not it is related to OHS.

However, data we have collected from patients with sleep-disordered breathing support the hypothesis that EDS is not always associated with low nocturnal blood oxygen saturation in sleep-related breathing disorders, and that other factors are involved. We have recently demonstrated an association between EDS and impaired autonomic cardiac modulation, suggesting that autonomic arousals may be an additional cause of EDS [4]. Autonomic arousals involve brainstem neurons controlling both sleep/vigilance and cardiovascular regulation. They might not produce detectable electroencephalogram (EEG) changes but are responsible for changes in cardiac autonomic regulation, as reflected by baroreflex sensitivity [5] and heart rate variability indices [6]. To test our hypothesis, we studied sleep-disordered breathing patients with a wide spectrum of disease severity, from simple snoring to OSA [4]. We found that EDS is actually associated with reduced baroreflex sensitivity occurring at night and with an increased ratio of the low- to high-frequency (LF/HF) heart rate power, the latter of which is an indirect index of sympatho/vagal balance [6]. Baroreflex sensitivity and the LF/HF power ratio were inversely correlated, and only the LF/HF power ratio was found to be a statistically independent predictor of daytime somnolence at multivariate analysis. Compared to the population studied by MEDIANO *et al.* [1], overall, our patients were characterised by lower BMI (29 *versus* 32 $kg \cdot m^{-2}$) and AHI (35 *versus* 61 $n \cdot h^{-1}$). Like MEDIANO *et al.* [1], we did not find differences in age, BMI and AHI between patients with and without EDS. Nor, however, did we find the significant differences between non-EDS and EDS patients in apnoea durations and in the minimum value of arterial oxygen saturation at night that MEDIANO *et al.* [1] reported in their study.

TABLE 1 Comparison of patients without excessive daytime sleepiness (EDS) and non-obese patients with EDS

	EDS		p-value
	With	Without	
Subjects n	23	13	
AHI $n \cdot h^{-1}$	29.2±25.8	30.5±27.3	0.89
Apnoea duration s	25.0±7.6	25.5±7.3	0.86
Sa,O_2 min %	90.0±5.4	90.2±3.8	0.92
LF/HF power ratio	6.1±4.2	3.3±2.3	<0.03

Data presented as mean±SD. All p-values were calculated using an unpaired t-test, after log transformation of the low- to high-frequency (LF/HF) power ratio data. AHI: apnoea/hypopnoea index; Sa,O_2: arterial oxygen saturation. Data presented are based on a subset of data analysed in [4].

The discrepancy between our study and that of MEDIANO *et al.* [1] could be related to a lower prevalence of OHS in our EDS group. Although we too cannot completely exclude the presence of OHS in our study group, this is unlikely because the mean BMI was $<30\ kg \cdot m^{-2}$ and because analysis of daytime blood gases did not reveal hypercapnia. To better assess this issue, and to completely rule out the presence of OHS in our EDS patients, we have reanalysed our data after excluding all the obese patients, *i.e.* all subjects with a BMI $\geqslant 30\ kg \cdot m^{-2}$, in the EDS group. The mean±SD BMI of this selected subgroup of our EDS patients decreased to $26.6 \pm 2.2\ kg \cdot m^{-2}$. However, in spite of such careful exclusion of OHS, a significantly higher LF/HF power ratio was still found as compared to that in non-EDS patients, while AHI, apnoea duration and the minimum nocturnal oxygen saturation were practically the same as in patients without EDS (table 1).

In conclusion, the study of MONTANO *et al.* [1] and our study [4] together suggest that at least two independent factors are associated with the pathogenesis of excessive daytime sleepiness in sleep-disordered breathing patients. One is a low nocturnal oxygen saturation, probably caused by obesity hypoventilation syndrome, as BAHAMMAM [2] pointed out; another is an enhanced sympathetic cardiac modulation at night, probably caused by repeated nocturnal autonomic arousals, as we have hypothesised [4].

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STATEMENT OF INTEREST

None declared.

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Lung volume measurements

To the Editor:

I read with interest the impressive paper by CAZZOLA *et al.* [1] in a recent issue of the *European Respiratory Journal*.

However, I felt somewhat uneasy reading the recommendations on lung volume measurements, *i.e.* closing circuit dilution methods and body plethysmography.

CAZZOLA *et al.* [1] state ''either method can be used... However they are not interchangeable, since moderate-to-severe airflow obstruction dilution methods tend to underestimate and body plethysmography tends to overestimate TLC''.

Therefore, according to CAZZOLA *et al.* [1], in moderate-to-severe airflow obstruction no method is accurate. What, therefore, is the choice? To accept underestimation of lung volume since the dilution methods are ''less expensive and less demanding''? Or, in spite of the overestimation of total lung capacity, to use a body plethysmograph, since it is ''time saving''?

In fact, dilution methods do underestimate lung volume in moderate-to-severe airflow obstruction [2–4]. The more severe the airflow obstruction, the larger the underestimation [4].

Body plethysmography might indeed overestimate total lung capacity in airflow obstruction if incorrectly measured [5, 6]. However, the plethysmographic method is accurate even in moderate and severe airflow obstruction by breathing or panting at <1 Hz [7, 8].

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STATEMENT OF INTEREST

None declared.

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