Autonomic Arousals in Sleep Related Breathing Disorders: A Link Between Daytime Somnolence and Hypertension?

Carolina Lombardi, MD, PhD[1]; Paolo Castiglioni, PhD[2]; Elio Lugaresi, MD[3]; Pietro Cortelli, MD[3]; Pasquale Montagna, MD[3]; Gianfranco Parati, MD, FESC[1]

[1]Department of Clinical Medicine and Prevention, University of Milano-Bicocca, Department of Cardiology, S.Luca Hospital, IRCCS, Istituto Auxologico Italiano, Milan, Italy; [2]Biomedical Technology Dept., S. Maria Nascente Research Hospital, Don Gnocchi Foundation, Milan, Italy; [3]Center for Sleep Disorders, Dept. of Neurological Sciences, University of Bologna, Bologna, Italy

WE HAVE READ WITH EXTREME INTEREST THE RECENT ARTICLE PUBLISHED ON YOUR JOURNAL BY KAPUR ET AL.[1] THE FINDINGS OF THIS STUDY EMPHASIZE the important role of daytime sleepiness in determining the risk of hypertension in patients with sleep-related breathing disorders. In particular, in Figure 1 the authors clearly show that only in patients with daytime somnolence there is an increase in the risk of hypertension, in parallel with the increase in apnea-hypopnea index. The important and clinically relevant contribution carried by this excellent study, is the identification of daytime sleepy patients as a group at greater risk of cardiovascular events. However, this study was not designed to investigate the mechanisms responsible for the association between sleepiness and hypertension, an important issue which thus remains unresolved.

We have hypothesized that excessive daytime sleepiness (EDS) in patients with sleep related breathing disorders may be associated with subcortical arousals. Apnea-related autonomic arousals may not produce detectable EEG changes. However, since they involve brainstem neurons controlling both sleep/vigilance and cardiovascular regulation, they may simultaneously trigger daytime somnolence and appreciable changes in cardiac autonomic regulation. Therefore alterations in cardiac autonomic control might be considered as markers of the occurrence of autonomic arousals in patients with sleep related breathing disorders. These alterations can be easily assessed by estimating changes in spontaneous baroreflex sensitivity[2] or in specific indexes of heart rate variability[3] from polysomnographic recordings.

Shortly before Kapur et al reported their findings, we demonstrated the association between EDS and impaired autonomic cardiac modulation in a study[4] published online in May 2008. To test our hypothesis we applied a multiple latency sleep test to quantify EDS in normotensive patients with sleep related breathing disorders ranging from snoring to obstructive apnea; these patients then underwent a complete overnight polysomnography associated with non-invasive beat-by-beat blood pressure monitoring. We found that patients with and without EDS had similar values of apnea-hypopnea index, similar sleep characteristics, and also similar overnight values of blood pressure (hypertension was among the exclusion criteria in our study). However, patients with EDS showed a significantly lower baroreflex sensitivity (known to be potentially linked to development of hypertension), and a higher ratio of the low-frequency to high-frequency powers of heart rate variability (an acknowledged indirect indication of changes in cardiac sympatho/vagal balance towards a predominant sympathetic modulation). In a successive analysis we confirmed these results also after excluding obese patients (BMI $\geq$30 kg/m^2) in the EDS group, in order to completely exclude the obese hypoventilation syndrome as a possible cause of somnolence.[5] Our findings demonstrate an association between daytime sleepiness and impaired autonomic cardiac modulation even in subjects who have not yet developed overt hypertension (preclinical stage), but who are at high risk for its future development.

Our results may thus help understanding the mechanisms responsible for the association between daytime sleepiness and hypertension demonstrated by Kapur et al.[1] Our hypothesis is that autonomic arousals, which may occur in some of the patients suffering from sleep related breathing disorders, are associated with both daytime sleepiness and alterations of cardiac autonomic modulation. These changes in autonomic cardiovascular regulation, on top of the well known alterations in chemoreflex activity, in mechanics of ventilation and in sleep structure characterizing obstructive sleep apnea, could explain why daytime sleepiness is associated with a higher risk of developing arterial hypertension.

The work by Kapur et al[1] provides data which are clearly supporting our hypothesis, and which unequivocally indicate the importance of taking the level of daytime somnolence into account to prevent cardiovascular events in patients with sleep related breathing disorders.

DISCLOSURE STATEMENT

The authors have indicated no financial conflicts of interest.

REFERENCES

1. Kapur V, Resnik H, Gottlieb D. Sleep disordered breathing and hypertension: does self-reported sleepiness modify the association? Sleep 2008;31:1127-32.
2. Bonsignore MR, Parati G, Insalaco G, et al. Baroreflex control of heart rate during sleep in severe obstructive sleep apnoea: effects of acute CPAP. Eur Respir J 2006;27:128-35.
3. Task Force of the European Society of Cardiology and the North American Society of Pacing and Electrophysiology. Heart rate

Submitted for publication February, 2009
Accepted for publication February, 2009
Address correspondence to: Gianfranco Parati MD, FESC, Department of Cardiology, Ospedale San Luca, Istituto Auxologico Italiano, via Spagnoletto 3, 20149 - Milan, Italy; Tel +39-02-619112980; Fax +39-02-619112956; E-mail: gianfranco.parati@unimib.it

variability. Standards of measurement, physiological interpretation, and clinical use. Eur Heart J 1996;17:354-81.
4. Lombardi C, Parati G, Cortelli P, et al. Daytime sleepiness and neural cardiac modulation in sleep-related breathing disorders. J Sleep Res 2008;17:263-70.
5. Castiglioni P, Lombardi C, Di Rienzo M, et al. What are the causes of excessive daytime sleepiness in patients with sleep-disordered breathing? Eur Respir J 2008;32:526-7.