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Editorial

The driver of sympathetic overactivity in obstructive sleep apnea: hypoxia or arousal?

It is now accepted that untreated obstructive sleep apnea (OSA) is associated with numerous cardiac and vascular complications including hypertension, atrial fibrillation, myocardial infarction, and stroke. While several pathophysiological mechanisms are likely involved, increasing evidence suggests that overaction of the sympathetic nervous system plays a major role. Previous studies have demonstrated positive correlations between sympathetic overactivity and hypoxemia [1], increased negative intrathoracic pressure [2], and frequent cortical arousals [3], all of which are common in patients with OSA. Yet, how (and how much) each of these risk factors increases sympathetic output—and by extension their role in the development of vascular complications in OSA—remains uncertain. Prior work has suggested that frequent arousals from sleep, even in the absence of increased ventilatory effort or hypoxia, can produce a rise in blood pressure similar to what is observed at apnea termination in OSA [4]. This begs the question: What role does cortical arousal play in sympathetic overactivity in OSA?

Kim and colleagues [5] attempted to better answer this in their current article “Effect of arousal on sympathetic overactivity in patients with obstructive sleep apnea,” in which the authors evaluated the independent effect of apnea and arousal on sympathetic activity in a large cohort of patients with OSA. The authors used frequency analysis of heart rate variability (HRV) during overnight polysomnography to calculate high frequency (HF) power, low frequency (LF) power, and the LF/HF ratio. High-frequency RR signal (greater than 0.15 Hz) is thought to be influenced by the vagus nerve-mediated respiratory sinus arrhythmia of deep breathing and is associated with parasympathetic tone, while the low-frequency RR signal (0.04–0.15 Hz) is thought to be influenced by the baroreflex-mediated heart rate response to blood pressure and is associated with sympathetic tone. A greater LF/HF ratio suggests greater sympathetic drive, and a lower LF/HF ratio suggests greater parasympathetic drive. Patients in this retrospective study were grouped into mild, moderate, and severe OSA using standard apnea-hypopnea index (AHI) cutoffs. The arousal index (AI) was calculated by combining apnea-hypopnea arousals, limb movement arousals, and spontaneous arousals. Controls consisted of patients without OSA who were referred to the sleep clinic for other sleep-related complaints. Patients with other comorbid sleep disorders such as insomnia and restless legs syndrome were excluded.

The authors found, not surprisingly, that the more severe patients' AHI, the greater the severity of sympathetic overactivity, as measured by the LF band and the LF/HF ratio. Furthermore, the authors also found that the greater the AI, the greater the magnitude of sympathetic overactivity. Notably, when the authors compared the effects of AHI to the effects of arousals, they found that the AI had a more robust correlation with sympathetic overactivity. This correlation was more striking in those with more severe OSA and tended to be less robust in patients with mild OSA. These findings support the theory that frequent arousals alone may be an independent risk factor for sympathetic overactivity and, by extension, cardiovascular risk. The authors also noted that age and male sex were associated with an increase in LF power and the LF/HF ratio, and a corresponding decrease in HF power. The Epworth sleepiness scale (ESS) score did not correlate with LF, HF, or the LF/HF ratio.

The limitations of this study include the first night effect, whereby the artificial nature of the sleep laboratory may lead to sleep fragmentation and thus increase sympathetic activity. In addition, control subjects consisted of patients referred to the sleep clinic for various sleep-related complaints and were not “sleep healthy” controls; therefore, this control group may have presented with inherent autonomic imbalance. Nonetheless, the study by Kim et al.'s a valuable addition to the growing literature on the importance of the autonomic nervous system in regulating sleep and homeostatic well-being, and provides further evidence that frequent arousals, and not just hypoxia, may serve as a potent trigger of sympathetic activity as well as cardiovascular risk.

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