Cardiopulmonary Integration – the Dark Side

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Normally neural and chemical mechanisms coordinate the actions of the circulatory system and the respiratory system to deliver the oxygen required by the tissues, regardless of their activity and to remove the metabolically produced carbon dioxide. But there is a dark side. The two systems are so dependent on each other that dysfunction in one pump may cause the other to fail as well. For example inadequacies in the circulation such as deficiencies in the blood supply to the brain can interfere with its operation, causing breathing to be too little or too much. Heart failure allows fluid to accumulate in the alveoli and pleural spaces so that breathing is inadequate because of poor oxygenation. More often it is the other way round, i.e. problems with breathing give rise to damaged blood vessels or pathology in the heart itself.

The persistent hypoxia produced by chronic lung diseases has long been recognized as a significant cause of circulatory abnormalities and heart failure. The chronic hypoxia constricts the pulmonary vessels, raising vascular pressure, increasing the load on the right ventricle and ultimately causing heart failure (cor pulmonale).

However, it seems that an even more common cause of circulatory problems is the intermittent hypoxia that occurs in both central and obstructive sleep apnea syndromes [1]. There is substantial and possibly overwhelming evidence that sleep apneas are risk factors not only for pulmonary but also for systemic hypertension and left ventricular failure [1, 2]. More recently biochemical evidence of vascular injury in sleep apnea patients has been

reported, e.g. increases in cell adhesion, coagulation and proinflammatory molecules [3, 4]. Increases in C-reactive protein have also been demonstrated [5]. In this issue of *Respiration* Tanriverdi et al. [6] confirm studies that demonstrated anatomical and functional changes in the blood vessels of patients with obstructive sleep apnea. They used newly developed noninvasive ultrasonographic methods to show increased aortic stiffness, increased carotid intima thickness and decreased flow-mediated vasodilatation, all signs of arteriosclerosis which occurred more frequently in the patients with obstructive sleep apnea than in the controls.

There are two potential mechanisms for these pathological changes in sleep apnea. The first is repeated intermittent hypoxia and reoxygenation leading to oxygen radical formation and damage to the blood vessel endothelium [1, 7]. The second is the repeated bursts of increased sympathetic activity that occur with the frequent arousals in sleep apnea [8]. These arousals, besides causing tachycardias, make blood vessels stiffer, thus accelerating pulse wave transmission. These episodic waves of sympathetic activity arising from conventional arousals may predispose to systemic hypertension. In addition to conventional arousals that produce alpha wave desynchronization and behavioral changes, so-called ‘autonomic arousals’, commonly occurring even during normal sleep, are associated with delta wave activity and are important triggers of increased sympathetic discharge [8]. It is not yet clear if these arousals affect the quality of

sleep, but it is possible that too many autonomic arousals may also predispose to vascular changes. Appropriate studies need to be carried out. The noninvasive methods described by Tanriverdi et al. [6] could be valuably employed in such studies.

It is important to recognize that failure in either the respiratory or the circulatory system can produce a vicious cycle that might shorten life expectancy. Heart failure and long circulation times as well as problems in the perfusion of the brain increase the likelihood of central

and probably obstructive apneas causing the intermittent episodes of hypoxia that result in further damage to the heart and the brain [9].

The take home message is that patients with circulatory disease need careful evaluation of their respiratory system, including their breathing during sleep. Similarly patients with breathing or sleep disorders need thoughtful evaluation of their cardiovascular function. The new techniques described by Tanriverdi et al. [6] may be extremely useful adjuncts in such an evaluation.

References

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