COMMENTS AND RESPONSES

Abdominal Fat and Sleep Apnea: the Chicken or the Egg?

Response to Pillar and Shehadeh

I read with great interest the article by Pillar and Shehadeh (1) on the coherences between obstructive sleep apnea (OSA) syndrome and associated metabolic alterations apparently linked by obesity. The authors give a good overview of the current literature about sleep disturbances in OSA and various aspects related to the metabolic syndrome, particularly obesity, such as glucose intolerance and insulin resistance. Notwithstanding, as the authors correctly mention, the clinical picture of OSA is characterized by both sleep fragmentation and recurrent hypoxic periods, which were somewhat neglected in their article.

As the authors mentioned, the underlying mechanism of insulin resistance in OSA is not fully understood. The potential options presented in the article were effective sleep deprivation associated with OSA and an additional involvement of elevated sympathetic activity. Concerning the role of hypoxia in this context, merely one study in an animal model was indicated: Polotsky et al. (2) examined the effect of intermittent hypoxia on glucose metabolism in mice, which resulted in improvements in glucose tolerance. By contrast, our group (3) clearly demonstrated in healthy humans that brief periods of moderate hypoxia, i.e., 30 min of oxygen desaturation to a level of 75%, are sufficient to cause glucose intolerance, which persists for an additional 2 h after normalization of oxygenation levels despite the fact that sympathetic activation upon this intervention is rather weak (unchanged blood pressure and moderate rise in epinephrine) and parameters of the hypothalamus-pituitary-adrenal axis were not affected at all.

Moreover, our study can help to clarify the question raised by Pillar and Shehadeh of whether OSA worsens obesity. We found that experimentally induced hypoxia leads to a persistent suppression of resting energy expenditure in healthy subjects (4), an aspect centrally involved in the development and worsening of obesity, which is most likely also of relevance for weight gain in OSA.

On the other hand, leptin secretion was not altered upon short-term hypoxia. This adipokine is tightly involved in the endocrine control of energy expenditure and body weight regulation by sending a feedback signal to the brain concerning the size of peripheral fat stores. Although leptin is predominantly released by subcutaneous and not by abdominal fat tissue (5), its role in the development of obesity is certainly unquestioned. However, the divergent impact that hypoxia apparently exerts on glucose and energy metabolism, stress axis activation, and leptin secretion suggests that OSA-associated alterations in these parameters are determined by multifactorial mechanisms, i.e., sleep fragmentation, hypoxia, and obesity development. Thus, as Pillar and Shehadeh rightly state, the future challenge in elucidating the pathogenesis of OSA and related metabolic changes will be to clarify: Which came first: the chicken or the egg?

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