COMMENTS AND RESPONSES

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

Response to Oltmanns

We thank Dr. Oltmanns for the important, eye-opening comments raised in her online letter to the editor (1). Indeed, in our article we discuss the complex relationships between obesity/abdominal fat and sleep disordered breathing (SDB) (2). While the effects of obesity on upper airway collapsibility are well established, the potential SDB-induced weight gain is less understood.

The major processes in obstructive sleep apnea (OSA) are sleep fragmentation (and consequently daytime somnolence and sympathetic nerve activation) and intermittent hypoxia/reoxygenation (and consequently oxidative stress, reactive oxygen species formation, and inflammatory response). Sleep fragmentation can lead to effective sleep deprivation, daytime somnolence, reduced physical activity, and eventually weight gain. The effects of intermittent hypoxia are less obvious. Acute hypoxia has been recently shown to result in reduced resting energy expenditure (3), which, as stated by Oltmanns, may partially relate to weight gain in patients with OSA. However, these patients have been shown to demonstrate an increased metabolic rate, which is probably due to the increased work of breathing associated with recurrent upper airway collapse and elevated respiratory effort against obstructed airway (4).

As mentioned in Oltmanns' letter, insulin resistance is one important mechanism that may lead to weight gain in patients with OSA. Although the underlying mechanism resulting in insulin resistance in patients with OSA is not fully understood, several options, such as effective sleep deprivation and elevated sympathetic activity, may play a role. Concerning the role of hypoxia, we described the study by Polotsky et al. (5) who suggest that the increase in insulin resistance in response to prolonged intermittent hypoxia was dependent on the disruption of leptin pathways. The study mentioned in Oltmanns' letter (6) examined the effects of acute hypoxia (of 30 min duration) on glucose tolerance in 14 healthy men under the conditions of a euglycemic clamp. Their finding that acute hypoxia results in glucose intolerance is of great interest and importance and may relate to the insulin resistance observed in patients with OSA, albeit in the latter case the hypoxia is of shorter duration and with a characteristic intermittent pattern. In addition, their finding of elevated epinephrine release with hypoxia suggests that sympathetic activation may play a role in the glucose intolerance they reported.

Thus, it seems that indeed the relationships between OSA and obesity are complex. We thank Dr. Oltmanns for her important comments that further emphasize the complexity of this issue, which indisputably requires further investigation.

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References

1. Oltmanns KM: Abdominal fat and sleep apnea: the chicken or the egg (Letter)? *Diabetes Care* 31:e61, 2008. DOI: 10.2337/dc08-0677
2. Pillar G, Shehadeh N: Abdominal fat and sleep apnea: the chicken or the egg? *Diabetes Care* 31 (Suppl. 2):S303–309, 2008
3. Oltmanns KM, Gehring H, Rudolf S, Schultes B, Schweiger U, Born J, Fehm HL, Peters A: Persistent suppression of resting energy expenditure after acute hypoxia. *Metabolism* 55:669–675, 2006
4. Stenlof K, Grunstein R, Hedner J, Sjostrom L: Energy expenditure in obstructive sleep apnea: effects of treatment with continuous positive airway pressure. *Am J Physiol* 271:E1036–E1043, 1996
5. Polotsky VY, Li J, Punjabi NM, Rubin AE, Smith PL, Schwartz AR, O'Donnell CP: Intermittent hypoxia increases insulin resistance in genetically obese mice. *J Physiol* 552:253–264, 2003
6. Oltmanns KM, Gehring H, Rudolf S, Schultes B, Rook S, Schweiger U, Born J, Fehm HL, Peters A: Hypoxia causes glucose intolerance in humans. *Am J Respir Crit Care Med* 169:1231–1237, 2004