Sleep apnea may increase insulin resistance

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Sleep apnea may cause metabolic changes that increase insulin resistance, according to researchers from the University of Pittsburgh Medical Center. The intermittent hypoxia associated with sleep apnea causes a distinct drop in insulin sensitivity in mice, even though chronic hypoxia, such as that associated with high altitude, did not.

The research will be reported at the ATS 2010 International Conference in New Orleans.

To determine whether intermittent hypoxia (IH) and chronic hypoxia (CH) would have different metabolic effects, Dr. Lee and colleagues fitted adult male mice with arterial and venous catheters for continuous rapid blood monitoring of glucose and insulin sensitivity. They then exposed the mice to either seven hours of IH, in which treatment, oxygen levels oscillated, reaching a low of about 5 percent once a minute, or CH, in which they were exposed to oxygen at a constant rate of 10 percent, and compared each treatment group to protocol-matched controls.

When compared to the control group, the IH mice demonstrated impaired glucose tolerance and reduced insulin sensitivity; the CH group, however, showed only a reduction in glucose tolerance but not insulin sensitivity compared to controls. "Both intermittent hypoxia and continuous hypoxia exposed mice exhibited impaired glucose tolerance, but only the intermittent hypoxia exposed animals demonstrated a reduction in insulin sensitivity," said Euhan John Lee, M.D., a fellow at the Medical Center.

"The intermittent hypoxia of sleep apnea and the continuous hypoxia of altitude are conditions of hypoxic stress that are known to modulate glucose and insulin homeostasis. Although both forms of hypoxia worsen glucose tolerance, this research demonstrated that the increase in insulin resistance that accompanies intermittent hypoxia, or sleep apnea, is greater than that seen with continuous hypoxia, or altitude," explained Dr. Lee.

The specific finding that intermittent, but not continuous, hypoxia induced insulin resistance was not expected.

Increased generation of reactive oxygen species, initiation of pro-inflammatory pathways, elevated sympathetic activity, or upregulation of insulin counter-regulatory hormones in IH may contribute to the greater development of insulin resistance in those mice versus those exposed to continuous hypoxia.

"As sleep apnea continues to rise with the rate of obesity, it will be increasingly important to understand both the independent and interactive effects of both morbidities on the development of metabolic disorders. This research demonstrated that intermittent hypoxic exposure can cause changes in insulin sensitivity and insulin secretion, which may have important consequences in metabolically vulnerable diabetic patients who present with co-morbid sleep apnea," said Dr. Lee. "Future research will explore potential inflammatory and lipotoxic pathways by which intermittent hypoxia disrupts glucose and insulin homeostasis."

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