Sympathetic nervous system activity may link hyperphagia and fat deposition in human obesity

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TO THE EDITOR: The increasing prevalence of human obesity is posing a major threat to global health. This concern has prompted great interest in the mechanisms responsible for the development of obesity. In their review paper, Nedergaard et al. (6) discuss the evidence indicating that the brown adipose tissue plays a significant and contributory role in the pathogenesis of human obesity through the stimulation of the sympathetic nervous system. As outlined by Nedergaard et al., the link between the brain and the adipose tissue occurring via the sympathetic nervous system might be critical in the pathogenesis of obesity. Indeed, recent data complement and corroborate the review of Nedergaard et al.

In their recent paper, Kuo et al. (2) provide important new clues to the better understanding of the role of the autonomic nervous system in the development of obesity, by showing that the sympathetic neural transmitter neuropeptide Y (NPY) is critical in adipose tissue remodeling. In particular, NPY appears to be involved in stress-induced augmentation of diet-induced obesity and metabolic syndrome (2). These data underline the role of the sympathetic nervous system in the pathogenesis of obesity and point to stress as a triggering agent. In fact, stressor agents, like cold exposure or aggression, lead to the release of NPY from sympathetic nerves, which in turn upregulates the NPY receptors (NPY2R) in the abdominal fat through new adipocyte proliferation and differentiation, fat angiogenesis, and macrophage infiltration. All these factors result in abdominal obesity and metabolic syndrome-like condition in mice.

These experimental data are consistent with clinical observations recently reported, which strengthen the relevance to human obesity and metabolic syndrome of stress-induced activation of the sympathetic nervous system. Both in animal models and in humans, sleep curtailment (4, 5, 7) and particularly total sleep deprivation are considered stress conditions that lead to marked hyperphagia (1). Although the exact molecular mechanisms linking the stressing condition of sleep curtailment to the control of appetite and food intake are not completely understood, Spiegel et al. (8) recently showed that sleep duration affects the circulating levels of neuroendocrine factors that regulate hunger and appetite in young healthy men. In particular, sleep restriction was associated with average reductions in the anorexigenic hormone leptin, elevations in the orexigenic factor ghrelin, and increased hunger and appetite, especially for calorie-dense foods with high carbohydrate content. Interestingly, it has been demonstrated that sleep deprivation increases sympathetic activity in normal humans (9), this evidence possibly linking clinical (2, 8) with experimental data (2). Also, a recent clinical study suggests that the sympathetic nervous system may influence body mass index in humans (3).

By combining experimental and clinical data, it appears conceivable that stressing conditions may promote hyperphagia by increasing orexigenic/inhibiting anorexigenic stimuli acting in the hypothalamus. At the same time, the activation of the sympathetic nervous system appears to direct the utilization of excessive calories by enhancing fat deposition via the release of NPY, thereby favoring the onset of obesity and metabolic syndrome. The better molecular characterization of the neural and biochemical pathways involved in these complex interactions will provide new therapeutic avenues for the prevention and treatment of obesity.

REFERENCES