Rearing temperature and the sympathetic nervous system regulation of white and brown adipose tissue

REGIS R. VOLLMER AND OLE SKØTT
Department of Pharmaceutical Sciences, School of Pharmacy, University of Pittsburgh, Pittsburgh, Pennsylvania 15261; and Physiology and Pharmacology, University of Southern Denmark, DK-5000 Odense, Denmark

THE PHYSIOLOGICAL CHANGES that result in response to cold exposure clearly demonstrate the close interrelationship between thermal and caloric homeostasis. This point is exemplified by the adjustments made in the two major types of fat tissue, the heat-generating brown adipose tissue (BAT) that provides warmth and the energy-storing white adipose tissue (WAT) that provides metabolic substrate. It is becoming clear through neuroanatomic and functional studies that BAT is connected to central loci that are important to setting sympathetic tone and thus the level of thermogenic activity (1, 4, 6). On exposure to cold, central nervous system activation of sympathetic neurons to BAT stimulates lipolysis, leading to intracellular oxidative metabolism of released fatty acids. The energy produced is uncoupled from ATP formation, resulting in heat release that is transferred to blood perfusing BAT, thereby providing an effective mechanism for the maintenance of body core temperature when an animal is exposed to a cold environment.

Like BAT, sympathetic neurons to WAT stimulate lipolysis; however, the sympathetic innervation is one of many factors that influence WAT. After stimulation of lipolysis, released fatty acids diffuse out of the adipocytes and into the circulation. During cold exposure, the released fats can serve as fuel for accelerated heat production.

BAT is rapidly activated via its noradrenergic innervation at the initiation of cold exposure, but continued cold exposure leads to hypertrophy and increased expression of several proteins crucial to augmenting the heat-generating function of BAT (2). WAT tissue also increases in mass as cold exposure is extended, resulting in expansion of the depot for the substrate needed for heat production (7). However, the role that the sympathetic nervous system plays with regard to WAT adaptive changes is not clear.

The changes that occur in BAT and WAT when adult animals are exposed to cold appear to be reversible when the animals are returned to normal temperatures. However, early life exposure to cold appears to reduce the reversibility. Postnatal rearing at cool or cold temperatures was shown to increase the mass of WAT and BAT, but the increases were not reversed when animals were returned to normal temperatures (7). In fact, the animals remain obese. In addition, a unique change that occurs in the young animals reared in the cold is that the density of sympathetic innervation of BAT and the content of norepinephrine present in the tissue were found to be increased (5). The changes in the noradrenergic neurons were sustained when the animals were restored to normal laboratory temperatures, although it was unclear whether the sustained density of sympathetic innervation was related to a sustained increment in tonic sympathetic outflow.

In this issue of the American Journal of Physiology-Regulatory, Integrative and Comparative Physiology, Dr. Young and collaborators (8) provide evidence that there is a sustained increase in sympathetic activity to BAT in cold-reared animals returned to normothermic temperatures compared with animals reared at 30°C. This point is supported by an increase in the turnover of the neurotransmitter norepinephrine and evidence for increased expression of several proteins that are markers of increased metabolic activity in BAT. These proteins include uncoupling protein and the glucose uptake transporter GLUT-4. These observations seem to imply that central regulation of sympathetic outflow to BAT had been augmented in a sustained fashion.

Although the sustained alterations in BAT and WAT mass that occur in animals reared at 18°C may serve to beneficially adapt the animals for future cold exposure, it will be of interest to determine if the obesity and chronic stimulation of BAT are maladaptive for animals kept at lower temperatures. In addition, the extrapolation of these findings in the rodent to humans is as yet unclear (3). Infant humans have considerable BAT, which diminishes with aging. Perhaps the loss of...
this tissue in human during maturation is related to the fact that human babies are typically reared in a warm environment. Additionally, it will be of interest to determine if rearing in a cold environment is in any way related to the development of chronic obesity.

REFERENCES


