METABOLISM

Imaging studies suggest a role for brown adipose tissue in adult humans

Long thought to have little or no physiological function in adult humans, brown adipose tissue has now been implicated in cold-activated thermogenesis by the authors of two independent studies published in the *New England Journal of Medicine*.

Brown adipose tissue is characterized by the presence of large numbers of mitochondria. Unlike white adipose tissue, which essentially stores energy, brown adipose tissue regulates energy expenditure: mitochondrial electron transport is uncoupled from production of ATP and energy is dissipated as heat. Brown adipose tissue is abundant in newborn infants, where it provides a vital heat source. By contrast, brown adipose tissue was not considered to have any functional relevance in adult humans.

Wouter van Marken Lichtenbelt (Maastricht University, The Netherlands) has worked on adaptive thermogenesis—the phenomenon of increased production of heat in response to cold or diet—for several years. His research group previously reported mitochondrial uncoupling in skeletal muscle after exposure to cold. A chance conversation with Jaap Teule, a nuclear physician at the same institution, led van Marken Lichtenbelt's team to extend their studies to brown adipose tissue, which shares the same developmental lineage as skeletal muscle.

The researchers used ^{18}F-fluorodeoxyglucose (FDG) PET-CT imaging to investigate the presence, distribution and activity of brown adipose tissue under thermoneutral conditions (22 °C) and during mild cold exposure (16 °C) in a group of healthy men. "FDG behaves to some extent like glucose," explains van Marken Lichtenbelt. "All glucose-consuming tissues will accumulate this radioactive tracer, which can be visualized by PET. Under mild cold conditions brown adipose tissue is activated and starts to use glucose. The PET scan is combined with CT in order to anatomically determine the tissues that show PET scan activity."

Brown adipose tissue was active in 23 of the 24 participants when assessed at 16 °C, but not at 22 °C. Cold-induced FDG uptake was highest in brown adipose tissue located within the supraclavicular region, and its activity was related to energy expenditure (heat production). Activity and mass of brown adipose tissue were both considerably reduced in men with a BMI ≥25 kg/m^2. In general, lean men had a greater amount of brown adipose tissue than did those who were overweight or obese.

The second study, which was performed by a research group in Boston, reported similar results. Aaron Cypess and colleagues retrospectively analyzed 3,640 consecutive FDG PET-CT scans that had been performed for various diagnostic purposes. The researchers found that 106 of 1,972 adult patients (5.4%) had detectable brown adipose tissue, particularly within the supraclavicular region. Of note, the prevalence of brown adipose tissue was far greater in women than in men (7.5% versus 3.1%, respectively), and women had a higher capacity to increase the mass and activity of their brown adipose tissue than did men.

In agreement with van Marken Lichtenbelt's findings, exposure to cold correlated with activation of brown adipose tissue. Cypess and coworkers noted the dates on which brown adipose tissue activity was maximal and compared them with the mean outdoor temperature in Boston during the same period. Activity of the brown adipose tissue was highest in the winter and lowest in the summer.

These two studies are extremely important, as they are the first to show that brown adipose tissue might play a part in cold-activated thermogenesis in adult humans. The fact that brown adipose tissue promotes energy expenditure rather than energy storage is of particular interest. Methods that aim to increase either the amount or responsiveness of brown adipose tissue in individuals who are overweight or obese have obvious therapeutic applications.

"We will now start to study the activity of brown adipose tissue in other groups of people, like the elderly," says van Marken Lichtenbelt. "We will also study whether different climate conditions or regular cold exposure will improve availability of brown adipose tissue."

Vicky Heath

Original articles van Marken Lichtenbelt, W. D. *et al.* Cold-activated brown adipose tissue in healthy men. *N. Engl. J. Med.* **360**, 1500–1508 (2009).
Cypess, A. M. *et al.* Identification and importance of brown adipose tissue in adult humans. *N. Engl. J. Med.* **360**, 1509–1517 (2009).