Activating beige fat in humans could combat obesity

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This is an image of a weight scale. Credit: CDC/Debora Cartagena

The body's ability to harness heat production by converting white fat cells, which store calories, into beige fat cells, which burn energy, could help fight obesity, according to researchers at Georgia State University.

Their review paper suggests this natural mechanism in the body, which converts white fat cells into brownish fat cells—known as 'brite' or 'beige' fat cells—by using heat production and increasing the sympathetic nervous system's (SNS) supply of blood vessels to white fat tissue, could be a new and promising approach to fighting obesity. While this mechanism doesn't occur naturally on a large scale because of the connection of white fat tissue with other tissues, including the heart and blood vessels that could lead to coronary and hypertension diseases, understanding how it occurs could be beneficial. The paper was published in the *International Journal of Obesity Supplements*.

Almost 70 percent of Americans are overweight or obese, according to the National Heart, Lung and Blood Institute of the National Institutes of Health. Strategies for fighting obesity, such as pharmacological and behavioral approaches to decrease food intake, have been only marginally successful. Patients who have undergone various surgeries for the gastrointestinal system have found success, but these are extreme measures. Scientists are hopeful that increasing energy expenditure with brown or brite/beige fat cells could be an effective way to fight obesity.

The body has two types of fat tissue: white and brown. White adipose tissue, or white fat, stores energy or calories and produces hormones that are secreted into the bloodstream. Brown adipose tissue, or brown fat, is a dark-colored fat tissue with many blood vessels that burns energy and produces heat. It was originally thought that, in humans, only babies had brown fat, but researchers found small amounts of brown fat in adults in 2009.

In this review paper, the researchers investigate how the SNS, a part of the nervous system that helps prepare the body to react to situations of stress or emergency, 'browns' white fat tissue cells, transforming them into 'brite' or 'beige' fat cells and suggesting a potential mechanism for increasing heat production in the body. They reviewed published studies about the neural control of white, beige and brown fat tissue available in PubMed, a database of citations for biomedical literature.

"Perhaps the most important features of white adipose tissue for the conversion of white fat cells to brite/beige fat cells is the density of the SNS nerves being supplied to white adipose tissue, and the fat cell population surrounding this nerve supply having a genetic ability to brown," said Vitaly Ryu, co-author of the study and senior research scientist II in the Department of Biology and Center for Obesity Reversal at Georgia State. "SNS drive increases with cold exposure and food deprivation, so that's when a breakdown of fats and cell

'browning' occurs.

Very little is known about how the SNS supplies white adipose tissue with nerves to form beige fat cells. The researchers found the clearest neuroanatomical evidence of the SNS controlling the browning of white fat in mice after cold exposure for 10 days versus warm acclimated control mice. Cold exposure increased the number of fibers of tyrosine hydroxylase, the marker for SNS nerves, in contact with white fat cells, and this fiber contact was associated with triple the number of multilocular fat cells, or those with many vesicles, compared to accumulations of traditional white fat tissue. Studies infer that SNS innervation and stimulation of the white adipose tissue 3-adrenoreceptor is important in white adipose tissue browning.

The only specific brain site that appears to exclusively cause browning specifically in white fat tissue is the dorsomedial hypothalamic nucleus (DMH), according to a 2011 study by P.T. Chao and other researchers. When neuropeptide Y (NPY) gene expression with the DMH decreases, the SNS drive to specific subcutaneous white adipose fat depots, or fat just beneath the skin, increases and results in the browning effect.

The researchers conclude that because humans normally exist at thermoneutrality, or close to it, by altering the temperature of their living and working environment or adding and removing clothes, this most likely limits the number of naturally occurring brite/beige cells in humans and any significant role of these cells in the everyday production of heat.

More information: T J Bartness et al. Neural control of white, beige and brown adipocytes, *International Journal of Obesity Supplements* (2015). DOI: 10.1038/ijosup.2015.9