# Cold temps may help to combat obesity and related metabolic diseases by reducing inflammation, researchers find

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More than 40 percent of American adults have obesity, a complex condition that can increase the risk of diabetes, cardiovascular disease

and certain cancers. One mechanism by which obesity can lead to other health problems is by causing low-grade chronic inflammation, the accumulation of immune cells in insulin-sensitive tissues. Scientists hypothesize that reversing—known as resolving—this chronic inflammation could prevent the onset of obesity-related diseases including diabetes and possibly facilitate weight loss.

In a new paper published in *Nature Metabolism*, researchers at Joslin Diabetes Center and Brigham and Women's Hospital found that exposure to cold temperatures resolved obesity-induced inflammation while improving insulin sensitivity and glucose tolerance in diet-induced obese mice. The team further revealed that the process depended on brown adipose (fat) tissue—sometimes considered "good fat"—producing a naturally occurring molecule called Maresin 2 when stimulated by cold. Recognized as an active endocrine organ because it secretes molecules that communicate with other tissues and regulate metabolism, brown adipose tissue helps dissipate stored energy and may potentially promote weight loss and metabolic health.

"Extensive evidence indicates that obesity and metabolic syndrome are linked with chronic inflammation that leads to systemic insulin resistance, so interrupting inflammation in obesity could offer promising therapies for obesity-related disease," said co-corresponding author Yu-Hua Tseng, Ph.D., a senior investigator in the Section on Integrative Physiology and Metabolism at Joslin Diabetes Center and professor of medicine at Harvard Medical School. "We discovered that cold exposure reduced inflammation and improved metabolism in obesity, mediated at least in part by the activation of brown adipose tissue. These findings suggest a previously unrecognized function of brown adipose tissue in promoting the resolution of inflammation in obesity."

In two previous studies, Tseng and colleagues discovered that cold exposure could activate brown fat to produce specific lipid mediators

that regulate nutrient metabolism. In the current study, the researchers identified a novel role for a lipid mediator produced from brown fat to resolve inflammation.

In the present study, the scientists created a mouse model that becomes obese when fed a typical high-fat, Western diet. When the animals were exposed to a cold environment (around 40 degrees Fahrenheit), the researchers observed that the animals' insulin sensitivity and glucose metabolism improved and their body weight decreased, compared to control animals maintained at a thermoneutral zone—the environmental temperature where the body does not need to produce heat for maintaining its core body temperature. What's more, the scientists also noticed a profound improvement in inflammation, as measured by reduced levels of a major inflammatory marker.

"We found that brown fat produces Maresin 2, which resolves inflammation systemically and in the liver," said co-corresponding author Matthew Spite, Ph.D., a lead investigator at Brigham and Women's Hospital and Associate Professor of Anesthesia at Harvard Medical School. "These findings suggest a previously unrecognized function of brown adipose tissue in promoting the resolution of inflammation in obesity via the production of this important lipid mediator."

Moreover, these findings also suggest that Maresin 2 could have clinical applications as a therapy for patients with obesity, metabolic disease, or other diseases linked to chronic inflammation; however, the molecule itself breaks down quickly in the body. Tseng and colleagues seek a more stable chemical analog for clinical use.

The team notes a shortcut to improved metabolic health may already exist. Multiple human studies conducted at Joslin and elsewhere show that exposure to mild cold temperatures (50 to 55 degrees Fahrenheit)

have been shown to be sufficient to activate brown adipose tissue and improve metabolism, though the mechanisms are not well understood.

**More information:** Satoru Sugimoto et al, Brown adipose tissue-derived MaR2 contributes to cold-induced resolution of inflammation, *Nature Metabolism* (2022). DOI: 10.1038/s42255-022-00590-0

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