

Cysteine Restriction Plays Key Role in Weight Loss

A diet that's low in the amino acid cysteine reprograms fat to burn more calories, triggering weight loss and reduced inflammation.

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The standard advice for losing weight is to take in fewer calories than you burn through a combination of healthy eating and exercise. Studies have suggested that calorie-restricted diets may also slow aging and delay chronic health conditions to help you live longer.

To examine the effects of a calorie-restricted diet in people, a research team led by Dr. Vishwa Deep Dixit at Yale School of Medicine used an approach called metabolomics. They looked for changes to thousands of metabolites (compounds formed as our bodies break down food and store energy) within fat tissue samples taken from people after a year of calorie restriction and weight loss.

The tissue samples came from participants in a clinical trial called CALERIE, in which healthy young and middle-aged men and women reduced their calorie intake by an average of about 14% over two years. This reduction led to weight loss along with other metabolic benefits, including improved muscle health. Results from the new analysis appeared in [Nature Metabolism](#) on June 3, 2025.

The researchers found substantial changes in study participants' fat metabolomes. A careful look at those changes revealed that calorie restriction came with an unexpected consequence: reduced levels of cysteine. The researchers also saw changes in a metabolic pathway to make cysteine.

To find out if lowering cysteine could lead to weight loss, the researchers created mice that lack the ability to make cysteine and gave them a diet restricted in cysteine but with plenty of calories. The animals lacking cysteine rapidly lost body weight. When cysteine was added back into their diets, the mice put the weight back on.

Further study revealed how low cysteine led to weight loss. The cysteine-deficient diet prompted white fat, which stores energy, to convert into brown fat, which burns energy to produce heat. When obese mice were deprived of cysteine, they showed a rapid browning of their fat as they lost weight. They also had lower levels of inflammation. The researchers found that these changes depended on signals from the sympathetic nervous system, which activates in stressful or

dangerous situations.

In a related paper in [Nature](#) on May 21, 2025, another team looked at weight changes when mice were fed diets lacking individual amino acids. Similar to the study from Dixit's team, they also found that a low-cysteine diet led to the most weight loss, with animals losing about a third of their body weight in just a week. The team also showed how cysteine restriction leads to widespread changes in metabolism.

"There's a pathway in the body that can make cysteine," Dixit explains. "During abundance it's normally dormant, but if you're getting less cysteine from your diet, your body activates this pathway in an effort to make more. And it appears that awakening this dormant pathway produces metabolic and health benefits."

The findings point to an unexpected role for dietary cysteine and cysteine metabolism in body weight and overall health. They also suggest new strategies for addressing obesity-related health problems that might not involve cutting calories.

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