

How leptin, the 'satiety hormone,' reverses diabetes

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(Medical Xpress)—Treatment with leptin, the hormone associated with fullness or satiety, reverses hyperglycemia in animals models of poorly controlled type 1 (T1D) and type 2 (T2D) diabetes by suppressing the neuroendocrine pathways that cause blood glucose levels to soar, a Yale-led team of researchers has found. The study appears in the Advance Online Publication of *Nature Medicine*.

The leptin hormone regulates metabolism, appetite, and body weight. The researchers discovered that, in a fasting state, rats with poorly

controlled T1D and T2D diabetes had lower plasma insulin and leptin concentrations and large increases in concentrations of plasma corticosterone—a stress hormone made in the adrenal glands that raises levels of [blood glucose](#).

The researchers then found that normalizing plasma leptin concentrations in the T1D rats with a leptin infusion resulted in marked reductions in plasma [glucose concentrations](#), which could mostly be attributed to reduction in rates of liver conversion of lactate and amino acids into glucose.

The question was why this happened. The team's data revealed that leptin normalized plasma corticosterone and [plasma](#) glucose concentrations by inhibiting the hypothalamic-pituitary-adrenal axis, a critical neuroendocrine pathway consisting of three major glands that regulate many body processes, including reactions to stress, energy storage, and energy utilization.

Researchers believe their finding about leptin may lead to development of new types of therapies to reduce and reverse uncontrolled hyperglycemia in patients with type 1 and type 2 diabetes.

"Previous studies by our group found that leptin replacement therapy reversed [diabetes](#) and insulin resistance in patients with severe lipodystrophy—a loss of fatty tissue that leads to those disorders—by reducing fat deposits in the liver and skeletal muscle," said senior author Dr. Gerald Shulman, the George Cowgill Professor of Medicine (Endocrinology) and Cellular & Molecular Physiology, and a Howard Hughes Medical Institute investigator. "These new data provide an additional mechanism by which leptin therapy reverses hepatic insulin resistance and hyperglycemia in animal models of poorly controlled type 1 and [type 2 diabetes](#)."

More information: "Leptin reverses diabetes by suppression of the hypothalamic-pituitary-adrenal axis." Rachel J Perry, Xian-Man Zhang, Dongyan Zhang, Naoki Kumashiro, Joao-Paulo G Camporez, Gary W Cline, Douglas L Rothman & Gerald I Shulman. *Nature Medicine* (2014) [DOI: 10.1038/nm.3579](https://doi.org/10.1038/nm.3579)

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