

Combining exercise with hormone could prevent weight gain

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Once heralded as a promising obesity treatment, the hormone leptin lost its fat-fighting luster when scientists discovered overweight patients were resistant to its effects. But pairing leptin with just a minor amount of exercise seems to revive the hormone's ability to fight fat again, University of Florida researchers recently discovered.

The combination of leptin and a modest dose of wheel running prevented obese rats on a belt-busting, high-fat diet from gaining weight, even though neither tactic worked alone, say UF researchers, writing in the journal *Diabetes*.

"They don't run enough to use sufficient energy to prevent weight gain," said Philip Scarpace, Ph.D., a professor of pharmacology and therapeutics in the UF College of Medicine and the senior author of the study. "What the act of running appears to do is allow the leptin to work again. It's a demonstration that this simple act can reverse leptin resistance."

More than 34 percent of American adults — about 72 million people — are obese or overweight, according to the Centers for Disease Control and Prevention. Scientists had hoped to wield leptin, a hormone that sends the body chemical signals to stop eating and use stored energy, as a weightloss weapon. Studies in lean animals were promising, but overweight animals and people don't respond the same way, likely because their bodies already overproduce leptin, causing them to develop resistance to the hormone, Scarpace said.

"Obese animals and humans don't respond to leptin at all," he said. "Our lab is interested in elucidating why this is the case. We know that often single-entity treatments are not successful. The concept was maybe a dual-entity treatment would work."

To test this, the researchers decided to pair leptin with exercise, comparing the effects on both

normal-weight and obese rats kept on high-fat diets, which simulate the type of fast-food-filled fare many Americans eat.

The rats were further separated into three groups to test three approaches. One group received leptin, another group got an exercise wheel and the third group got both leptin and a wheel. In the normal-weight rats, leptin and exercise both worked to prevent weight gain. The normal-weight rats ran significantly more than their bulkier peers, logging in about two and a half miles a day on their wheels, and kept off weight proportionally to how much they ran. The rats were allowed to run as much as they chose.

In the obese rats, which ran six to eight times less, neither running nor leptin alone kept the weight from accruing. Giving the rats leptin actually caused them to gain more weight than eating a high-fat diet alone, the study shows.

"This is a startling finding. Leptin is expected to reduce body weight, not promote weight and fat gain," Scarpace said.

But the obese rats that ran and took leptin kept the extra weight off, Scarpace said. More research is needed to understand exactly why this combination works, but the scientists speculate that the low level of running triggered a metabolic change in the rats that cleared the way for the leptin signal to get through.

"They should have been gaining weight," Scarpace said. "They don't run enough to make any difference."

Christopher Morrison, Ph.D., an assistant professor at the Pennington Biomedical Research Center at Louisiana State University who wrote a commentary about the UF study in Diabetes, said he thinks the discovery has potential to help combat obesity in humans.



"That's the hope and the reason for doing this type of work," he said. "The study raises many questions. If we can improve leptin sensitivity and enhance the ability of the signal to get through, maybe it will lead to weight loss."

UF researchers are now aiming to team with doctors and test the leptin and exercise combination in humans. They also are working on additional studies to better understand leptin's effects and its signaling pathway. Scientists still can't pinpoint exactly why overweight people develop resistance to leptin and what role the hormone really plays in obesity.

"Leptin may be the cause of obesity rather than a cure," Scarpace said. "Unless you run."

Source: University of Florida

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