

# Study reveals weight loss drug's effect on the brain

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Various pills. Credit: Wikipedia

A weight-loss drug dampened the response to food cues in regions of the brain associated with attention and emotion, leading to decreases in caloric intake, weight and body mass index (BMI), a team led by scientists at Beth Israel Deaconess Medical Center (BIDMC) reported. In the first study of the drug lorcaserin in the human brain, the research revealed the mechanism underlying the drug's efficacy and provides insight into which individuals may benefit most from the medication. The paper was published today in the journal *Diabetes*, the journal of the American Diabetes Association.

"Human feeding behaviors involve areas of the brain responsible for cognitive control and decision-making," said Christos S. Mantzoros,

MD, Director of the Human Nutrition Unit in the Division of Endocrinology, Diabetes and Metabolism at BIDMC and Professor of Medicine at Harvard Medical School. "We wanted to find out if lorcaserin was acting on these brain regions and, if so, where and how. One-third of the U.S. population is obese, and another one-third is overweight. This is a huge burden on individuals and the health care system. In addition, it increases the risk of diabetes, cardiovascular disease and many types of cancer. We need to continue to develop safe and effective therapies to combat this epidemic."

Approved by the FDA in 2012, the generic drug lorcaserin is a medication prescribed for obese or overweight adults who also have weight-related health complications such as diabetes. Several studies have shown the drug helps about half of the people who take it lose more than 5 percent of their [body mass](#) within a year, but there's a great deal of variability in individual results, and the mechanism underlying its effect was previously unknown.

To determine how the drug works in the [human brain](#), Mantzoros and colleagues observed 48 obese men and women - half taking the drug, half taking a placebo - over the course of a four-week experiment. Participants came into the clinic on four occasions for blood work, physical exams, measurements and weight-loss counseling with a registered dietician. They were also expected to keep records of the food they ate during the study.

On three visits - before receiving any medication (Week 0), after a week of medication (Week 1), and after four weeks of medication (Week 4) - exams were followed by two brain scans: one after the patients had fasted for at least 12 hours, the other after they had eaten a meal. The scans were taken using functional magnetic resonance imaging (fMRI) to measure changes in blood flow in an active brain, which suggests which regions play a role during a given task. During each scan, participants

were shown 150 images of foods generally considered highly desirable, such as cake and onion rings; foods generally considered less desirable like vegetables; and nonfood items like rocks and trees.

At Week 1, the fMRI scans in the fasting state revealed that people taking the drug showed decreased brain activity in response to images of highly desirable foods in the attention-related parietal and visual cortices. At Week 4, the lorcaserin group in the fed state showed less activity in the parietal cortex - which is responsible for integrating sensory information - when looking at any of the food images.

The data also revealed that subjects who had the strongest brain responses to food prior to taking lorcaserin saw the most success with the weight-loss medication.

"Decreases in [caloric intake](#), weight, and BMI were linked to strong responses to food cues in the areas of the [brain](#) related to emotion, pleasure and attention prior to taking the weight-loss drug, which suggests that lorcaserin could prove to be of particular benefit to 'emotional eaters,' " Mantzoros said.

Lorcaserin targets only a very specific serotonin receptor (known as 5-HT<sub>2c</sub>), shown in animal studies to play a role in abnormal food consumption. A previous generation of weight loss drugs was linked to this receptor, but because their scope was broader, those products also had dire cardiac side effects including pulmonary hypertension and valve problems. Lorcaserin could produce weight loss without these cardiac risks, the authors noted.

"In addition, the different mechanism of action in comparison to other drugs for obesity creates an opportunity for combination drugs for the treatment of obesity," Mantzoros said. "This might create more powerful solutions and is something that remains to be explored."

Provided by Beth Israel Deaconess Medical Center

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