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New Study May Explain How Weight-loss Surgery Reverses Type 2 Diabetes

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(PhysOrg.com) -- A team of researchers, led by a UC Davis veterinary endocrinologist, has shown for the first time that a surgical procedure in rats that is similar to bariatric surgery in humans can delay the onset of type 2 diabetes. The researchers also have identified biochemical changes caused by the surgeries that may be responsible for that delay.

Findings from the study, published online in the journal Gastroenterology, should help researchers identify strategies for preventing and treating type 2 diabetes, a chronic condition in which the body is unable to properly metabolize sugar and fat, leading to serious complications including heart disease, blindness and kidney failure.

Type 2 diabetes affects more than 21 million people in the United States, where it results in more than $150 billion in direct and indirect annual costs, according to the National Institutes of Health.

“Bariatric surgery currently is considered to be the most effective long-term treatment for human obesity and often leads to marked improvements in diabetes,” said the study’s lead author Peter Havel, a professor with joint appointments in the School of Veterinary Medicine and Department of Nutrition.

“It has been thought that reduction of blood sugar, which indicates a reversal of type 2 diabetes, in patients following bariatric surgery was due to post-surgery weight loss,” Havel said. “This study, however, supports the observations from a number of earlier clinical studies

reporting that diabetes is often improved prior to substantial weight loss. It also suggests that endocrine changes in hormones produced by the gastrointestinal tract may contribute to the early effects of bariatric surgery, in addition to the later effects of weight loss."

"This study confirms our clinical observations that metabolic regulation -- specifically homeostasis of glucose -- occurs quickly after gastric bypass surgery," said Mohamed Ali, an associate professor of gastrointestinal surgery and a specialist in bariatric surgery at UC Davis Health System. "It's clear from the outcome that something physiologic is at work with controlling diabetes that is not related to weight loss.

"UC Davis has the perfect environment for collaboration between basic and clinical scientists to take this discovery to the next step, which is identifying the molecular signals that set these physiologic changes in motion," said Ali, who was not a participant in this study, but has collaborated with Havel on previous research.

About bariatric surgery in humans

In severe cases of obesity -- usually when the patient is 80 to 100 or more pounds overweight -- bariatric surgery is used to alter or reconstruct the stomach and/or the intestinal tract. In such cases, obesity is not just a weight issue but also a life-threatening health problem that often leads to type 2 diabetes, heart disease and sleep apnea.

There are several types of bariatric surgeries available in the United States. The most commonly performed surgical procedure, known as Roux-en-Y gastric bypass surgery, limits the amount of food the stomach can hold and reroutes the digestive tract, resulting in changes in intestinal function and hormones produced by the gastrointestinal tract.

In 2008, about 220,000 people with severe obesity in the U.S. had

bariatric surgery, according to the American Society for Metabolic and Bariatric Surgery.

The new study

Havel and colleagues set out to test a hypothesis that certain bariatric surgical procedures were successful in improving type 2 diabetes, at least in part, because the procedures increased the flux of unabsorbed nutrients to the far end of the small intestine and, in doing so, triggered increased secretion of two hormones. Those hormones -- glucagon-like peptide-1 (GLP-1) and peptide-YY (PYY) -- are known to have a role in controlling food intake and improving insulin secretion and insulin sensitivity, thereby helping to stabilize blood sugar levels.

To test the hypothesis, the researchers carried out a surgical procedure known as ileal interposition in a line of rats that were predisposed to obesity and type 2 diabetes. The rat model, developed in Havel's laboratory, was known as the UC Davis Type 2 Diabetes Mellitus (UCD-T2DM) Rat. The pathology of type 2 diabetes in these animals is more similar to type 2 diabetes in humans than other existing rodent models of the disease.

The ileal interposition procedure involves relocating a short portion of the small intestine known as the ileum further forward in the intestinal tract. Then the researchers compared how long it took for the animals to develop diabetes, compared with a control group of rats that had surgery but without rearrangement of the intestines.

They found that the rats receiving the ileal interposition surgery developed type 2 diabetes 120 days later than did the rats in the control group. Furthermore, by the time the rats were one year old, 78 percent of the control group rats were diabetic while only 38 percent of the rats that had received the ileal interposition procedure had developed

diabetes.

Havel said the delay in onset of diabetes in the rats would be similar to delaying the age of onset of diabetes by approximately 10 years in a person, which would be expected to significantly decrease the amount of time for diabetic complications to develop, and to reduce the health care costs associated with treating this costly and prevalent disease.

The researchers also found that, when compared with the control group, the rats receiving the ileal interposition surgery had:

• lower fluctuations in blood sugar levels;

• improved insulin production, making them better able to metabolize sugar; and

• decreased levels of lipids (cholesterol and triglyceride) in the bloodstream, which are known to be risk factors for cardiovascular disease in humans.

“In addition, results from the study also demonstrated that the ileal interposition surgery increases production of bile acids, which are involved in fat metabolism and can increase the production of GLP-1, the hormone that improves insulin secretion and insulin sensitivity,” Havel said. “This could contribute to the delay in the onset of type 2 diabetes that we observed in the rats in this study.”

He noted that further studies are needed to better understand how surgically induced improvements of metabolism can be achieved in order to discover new methods for preventing and treating type 2 diabetes. Havel, postdoctoral researcher Bethany Cummings and their colleagues have received funding from a National Institutes of Health Challenge Grant to continue to pursue research on the effects of

bariatric surgical procedures in the UCD-T2DM model of diabetes.

Collaborating with Havel on this study were Cummings, Kimber Stanhope, James Graham, Jennifer Lee and Helen Raybould, all at UC Davis; April Strader of Southern Illinois University School of Medicine; and Denis Baskin of the Department of Veterans Affairs Puget Sound Health Care System and the University of Washington, Seattle.

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Provided by UC Davis