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Human hormone blocker found to help prevent obesity and diabetes: study

BETHESDA, MD - A new study finds that a chemical found in the body is capable of promoting weight loss, improving insulin resistance and reversing diabetes in an animal model. The hormone is gastric inhibitory polypeptide (GIP) receptor blockade.

Background

GIP is a peptide hormone that is secreted in response to food. It inhibits the secretion of acids stimulates the releases insulin as part of the digestive process in response to food. It is found in a variety of tissues, including the intestine, heart, stomach, brain and in adipose (fat).

While the significance of its action is largely unknown, its potent and prolonged stimulation after a high-fat diet has led researchers to speculate it may play a key role in metabolizing fat. Research has shown that high fat feeding results in elevated circulating GIP concentrations, traits often found in patients who are obese with diabetes. GIP also effects the growth of fat cells. Other studies have shown that mice injected with the GIP receptor antagonist - (Pro3)GIP - can reverse or prevent many of the metabolic abnormalities associated with obesity.

The Study

A new study examined whether prolonged GIP receptor antagonism using daily injections of (Pro3) GIP was able to reverse well established diet-induced obesity and related metabolic abnormalities.

The new study is entitled, "GIP Receptor Antagonism Reverses Obesity, Insulin Resistance, and Associated Metabolic Disturbances Induced in Mice by Prolonged Consumption of High-Fat Diet." It was conducted by Paula L. McClean, Nigel Irwin, Roslyn S. Cassidy, Victor A. Gault and Peter R. Flatt, all of the School of Biomedical Sciences, University of Ulster, Coleraine, Northern Ireland, UK; and Jens J. Holst, Department of Medical Physiology, The Panum Institute,

University of Copenhagen, Copenhagen, Denmark. It is entitled The findings appear in the American Journal of Physiology - Endocrinology and Metabolism (doi:10.1152/ajpendo.00460.2007), a publication of the American Physiological Society (APS; http://www.the-aps.org/).

Methodology

The researchers used a model for diet-induced obesity that has been used extensively alongside genetic models and has close parallels with obesity, increasingly found in humans who consume a high-fat, energy-rich diet. In this model, young (8-week old) male, age matched mice were age-divided into groups and housed individually in an air-conditioned room at 22°± 2ΓXC with a 12 hour light: 12 hour dark cycle. Experimental animals had free access to drinking water and a high fat diet (45 percent fat, 20 percent protein and 35 percent carbohydrate; percent of total energy of 26.15kj/g). Age-matched control mice from the same colony had free access to a standard rodent maintenance diet (10 percent fat; 30 percent protein; 60 percent carbohydrate; percent of total energy of 12.99kj/g.). The two were used for comparison purposes.

Prior to the study, mice were maintained on a high fat diet for 160 days. In addition, a separate set of mice were maintained on a high fat diet for 112 days prior to measuring circulating GIP and GLP-1 levels. On both occasions, obesity and diabetes were clearly evident.

The mice which had previously been fed a high fat diet for 160 days received only daily injections of either saline or (Pro3)GIP over a 50-day period. Food intake and body weight were recorded daily while plasma glucose and insulin concentrations were monitored at 5-7 day intervals.

Blood was taken on day 50 to measure cholesterol, triglycerides, glucagon (the hormone involved in metabolizing carbohydrate), corticosterone (involved with carbohydrates in the liver) and circulating adipokines (which play a key role in obesity-related diseases). Glucose tolerance and insulin sensitivity tests were performed at the end of the study period. The metabolic response of both groups of mice was also analyzed.

Key Findings

Highlights of the research findings include the following:

- Compared with the standard rodent diet (control), the mice that were fed the high-fat diet for the previous 160 days exhibited increased body weight, energy intake, and circulating glucose concentrations. The levels remained elevated throughout the study. The cholesterol and triglycerides levels increased at day 50.

- consumption of the high fat diet resulted in progressive weight gain and elevations of plasma glucose and gyrated hemoglobin, leading to impaired insulin sensitivity and glucose intolerance by 10 days. Fat (adipose) tissue deposits were increased as were circulating cholesterol and triglyceride concentration levels.

- (Pro3)GIP was able to counter many of the detrimental effects of high fat diet on body weight and indices of glucose and lipid metabolism.

Conclusion

This study showed that blocking GIP activity using (Pro3)GIP in mice with established, high fat diet-induced obesity and diabetes results in significant weight loss, improvement of insulin resistance and amelioration of diabetes. These findings represent an interesting new approach to the treatment of obesity and metabolic disturbances.

According to the research team๐s Nigel Irwin, Ph.D., "Interestingly, possible parallels exist with the benefits of Roux-en-Y surgery (gastric bypass surgery) in treating gross obesity and associated diabetes in people. In this procedure, nutrients surgically bypass the area of the small intestine, resulting in a deficiency of circulating GIP. We are looking to better understand how and why."

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NOTE TO EDITORS: To schedule an interview with a member of the research team, please contact Donna Krupa at 301.634.7209 (direct dial) or DKrupa@the-APS.org.

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