

Changes in Pancreatic Islet Function and Morphology Following Gastric Bypass Surgery In Rats.

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Bariatric surgery improves glycemic control in patients with type II diabetes, but the mechanism of this phenomenon is not well established. Clinical studies in humans following Roux-en-Y gastric bypass (RYGB) have shown a postprandial (after a meal) increase in GLP-1 and glucagon, and many believe these changes in hormone levels are linked to the observed improvement in glycemic control following RYGB. The physiology leading to altered hormone expression is largely unknown.

Pancreatic alpha cells release glucagon in response to lowered plasma glucose and protein containing meals. Glucagon primarily stimulates glycogenolysis and gluconeogenesis in the liver, and also lipolysis in fat. Its actions prevent or correct hypoglycemia.

L cells in the distal ileum release glucagon-like peptide 1 (GLP-1) in response to nutrients in the gut lumen. GLP-1 potentiates insulin secretion from pancreatic beta cells, slows gastric emptying, increases satiety, and stimulates glycogenesis and lipogenesis. Its actions decrease blood glucose and stimulate insulin secretion.

We hypothesized that hyperglucagonemia and hyperGLP-1emia following RYGB result from a common mechanism. In our model, RYGP will alter the physiology of the proximal alimentary limb (gut) to increase the expression of proglucagon and cleave it to both GLP-1 and glucagon. To test this hypothesis we studied rats fed a high fat diet who had a RYGB or a sham operation (jejunal transection and reanastomosis). The RYGB animals weighed significantly less and had lower body adiposity than the sham group.

There was a small elevation in gut proglucagon mRNA expression by quantitative PCR in the RYGB group vs the sham-surgerized control group. This finding is consistent with our hypothesized upregulation of proglucagon in the proximal RYGB gut. However, preliminary measurement by ELISA of GLP-1 and glucagon in protein extracts from RYBG and sham-surgerized rats did not demonstrate significant differences in the relative synthesis of proglucagon derived peptides.

Based on these findings neither the mRNA proglucagon expression nor processing of proglucagon is altered substantially after RYGB in regions of the GI tract examined in our study. This suggests that expression of any differences in circulating concentrations of proglucagon-derived hormones could be due to differences in the rat model or secondary to differences in stimulation and secretion of GLP-1 and glucagon.