

# **Evidence for the hindgut hypothesis after ileal interposition associated with sleeve gastrectomy: increased number of GLP-1-producing cells in interposed ileum and pancreatic islets in rats**

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**Background/Aim:** Based on the hindgut hypothesis, ileal interposition with sleeve gastrectomy (II-SG) has been proposed as a procedure in metabolic surgery. The aim of the present study was to study the underlying mechanism of II-SG in rats.

**Methods:** Male Sprague-Dawley rats were subjected to laparotomy, ileal interposition (II), sleeve gastrectomy (SG), or II-SG. Metabolic parameters were monitored by an open-circuit indirect calorimeter composed in comprehensive laboratory animal monitoring system. The number of GLP-1-producing cells was examined by quantitative immunohistochemistry

**Results:** After II alone, satiety ratio i.e., intermeal interval/meal size, was reduced while calorie intake was increased at two weeks postoperatively. Respiratory exchange ratio, i.e.,  $VCO_2/VO_2$ , was increased to above 1.0 (i.e., carbohydrate metabolism) during both daytime and nighttime two and six weeks postoperatively. After SG alone, satiety ratio and respiratory exchange ratio were unchanged, and the number of GLP-1-producing cells was not increased in the ileum (in terms of volume density), but increased in the pancreatic islets (number of cells per islet). After II-SG, rate of eating was reduced, while meal duration (minutes/gram) was increased during both daytime and nighttime at two and six weeks postoperatively. The number of GLP-1-producing cells increased by about 2.5-fold in the interposed ileum, and also increased to the same extent in the pancreatic islets as seen after SG alone. The increased GLP-1-producing cells in the pancreas were distributed around the insulin-producing  $\beta$  cells.

**Conclusion:** The present study provides evidence that II-SG stimulates GLP-1 production not only in the interposed ileum (to act by endocrine mechanism) but also in the pancreatic islets (to act on the  $\beta$  cells by paracrine mechanism), leading to the metabolic beneficial effects and the altered eating behavior as manifested by eating slowly.

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