Nutrient infusion bypassing duodenum-jejunum improves insulin sensitivity in glucose-tolerant and diabetic obese subjects

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1Department of Computer and System Science, University of Rome “La Sapienza”, Rome, Italy; 2Merck A/S, Copenhagen, Denmark; 3Department of Internal Medicine, Catholic University, Rome, Italy; 4Institute of Systems Analysis and Computer Science, CNR, Rome, Italy; 5Merck A/S, Rome, Italy; and 6Department of Surgery, Endoscopy Service, Catholic University, Rome, Italy

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Nutrient infusion bypassing duodenum-jejunum improves insulin sensitivity in glucose-tolerant and diabetic obese subjects. Am J Physiol Endocrinol Metab 305: E59–E66, 2013. First published May 7, 2013; doi:10.1152/ajpendo.00559.2012.—The mechanisms of type 2 diabetes remission after bariatric surgery is still not fully elucidated. In the present study, we tried to simulate the Roux-en-Y gastric bypass with a canonical or longer biliary limb by infusing a liquid formula diet into different intestinal sections. Nutrients (NutriSon Energy) were infused into mid- or proximal jejunum and duodenum during three successive days in 10 diabetic and 10 normal glucose-tolerant subjects. Plasma glucose, insulin, C-peptide, glucagon, incretins, and nonesterified fatty acids (NEFA) were measured before and up to 360 min following. Glucose rate of appearance (Ra) and insulin tolerance during three successive days in 10 diabetic and 10 normal glucose-tolerant subjects. Plasma glucose, insulin, C-peptide, glucagon, incretins, and nonesterified fatty acids (NEFA) were measured before and up to 360 min following. Glucose rate of appearance (Ra) and insulin tolerance during three successive days in 10 diabetic and 10 normal glucose-tolerant subjects. Plasma glucose, insulin, C-peptide, glucagon, incretins, and nonesterified fatty acids (NEFA) were measured before and up to 360 min following. Glucose rate of appearance (Ra) and insulin tolerance during three successive days in 10 diabetic and 10 normal glucose-tolerant subjects. Plasma glucose, insulin, C-peptide, glucagon, incretins, and nonesterified fatty acids (NEFA) were measured before and up to 360 min following.

The aim of the present study was to investigate insulin secretion and β-cell response, as well as insulin sensitivity and incretin secretion, during a graded mixed infusion of a liquid formula diet (carbohydrates, proteins, and fat) in the duodenum or the proximal or mid-jejunum. The infusion of nutrients into the proximal jejunum was aimed at simulating gastric bypass where gastroenteroanastomosis is performed immediately after the Treitz ligament, while the mid-jejunum infusion might mimic a modified gastric bypass with a longer than canonical biliary limb.

ANATOMIC CHANGES of the gastrointestinal tract induced by bariatric surgery and which include the bypass of different portions of the small intestine are followed by a net improvement in insulin sensitivity (15, 24, 25). The mechanisms underlying these changes in the peripheral tissues and/or liver have not yet been fully elucidated. The association of type 2 diabetes mellitus with obesity and the observation that diabetes undergoes remission after bariatric surgery (20) make further investigation most relevant. In this respect, it is not coincidental that surgical treatment of obesity is one of the most rapidly growing areas of surgical practice today (5).

It is generally agreed (2) that the severity of diabetes is markedly improved following bariatric surgery, with 85.4% of patients experiencing complete resolution or substantial improvement. However, the degree of improvement differs depending on the surgical technique used, ranging from 98.9% for biliopancreatic diversion (BPD) or duodenal switch, to 83.7% for Roux-en-Y gastric bypass (RYGB), to 71.6% for gastric bypass, and to 47.9% for gastric banding. These types of bariatric surgery not only differ in their effects on food intake, being subclassified into two major categories, restrictive and malabsorptive surgical procedures (with a variety of intermediate forms, where food restriction or malabsorption are alternatively prominent), but also, most importantly, these different types of surgery differ in relation to the particular portion of intestine that is bypassed by food, which, in our opinion, is particularly intriguing.

We (15) have recently demonstrated that both BPD and gastric bypass determine a prompt reversibility of type 2 diabetes by improving peripheral insulin sensitivity and enhancing β-cell sensitivity to glucose (24–26); these changes occur within a few days after these procedures, largely before changes in body weight occur (15, 25).

The response of pancreatic β-cells to glucose is reduced in type 2 diabetic subjects (9). In addition to this specific β-cell dysfunction, the inability to sense the fall or rise of plasma glucose concentration to provide adequate insulin secretion is another peculiar defect of β-cells (8).

Different methods for glucose administration, including hyperglycemic clamp, intravenous glucose tolerance test, oscillatory glucose infusion, and graded glucose infusion, are used to assess β-cell responsiveness to glucose. A characteristic feature and advantage of the graded glucose infusion protocol over the other glucose infusion techniques is its ability to describe the transient response of insulin secretion to a changing glucose stimulus and, therefore, the dose-response relationship between glucose and secretion rate during a physiological challenge. Although graded infusion of glucose is used largely in human studies (12, 32), its application during intestinal infusion of glucose or glucose plus other nutrients is lacking.

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RESEARCH DESIGN AND METHODS

Subjects. Studies were carried out in 20 obese subjects of both sexes, 10 with type 2 diabetes and 10 with normal glucose tolerance (Table 1), recruited from the outpatient clinics of the Catholic University.

Inclusion criteria were men and women 30–60 yr old, BMI between 30 and 40 kg/m², HbA1c between 6.5 and 8.5% (for diabetic patients). Normal-glucose-tolerant subjects (hereafter defined as control subjects) were recruited on the basis of absence of diabetes or impaired glucose tolerance after a standard oral glucose tolerance test. All diabetic subjects were drug naïve. Women of reproductive age engaged themselves in avoiding pregnancy during the study protocol. Before the start of each experimental session, a pregnancy test was performed, and pregnant women were excluded from the investigation. All women were studied in the follicular phase of their menstrual cycle.

Exclusion criteria were past or active medical history of major endocrinological, renal, cardiac, respiratory, liver, or gastrointestinal diseases.

The protocol was approved by the Catholic University in Rome (Italy) School of Medicine Ethics Committee. All of the subjects signed written informed consent.

Intestinal infusion of liquid formula diet. Subjects underwent three studies, single-blind, during which intraintestinal infusions of a liquid formula diet were administered. The intestine was cannulated by means of a 10 French tube 240 cm long (Cook Medical, Bloomington, IN). The tube was connected to a balloon which was used to occlude the intestinal lumen proximal to the site of infusion.

The three studies were performed on three successive days after a 12-h fast at 8:00 AM. On the first day, the tube was positioned during endoscopy in the mid-jejunum (120 cm from the nose). The second day, the tube was retracted by 30 cm (proximal jejunum, 90 cm distant from the nose), and on the third day it was retracted to the duodenum (60 cm distant from the nose). The position of the tube’s terminus was confirmed by fluoroscopy. In no case did the fluoroscopy show that the tube was in the stomach. The subjects kept the nasogastric tube for the whole 3 days, and they were able to eat and drink normally between the study sessions. Therefore, no changes in nutritional and hydration status occurred.

The lipid-glucose-protein test meal was a mixture of Nutrisun Energy (Nutricia) diluted with 1/6 water to avoid abdominal discomfort. One hundred milliliters of Nutrisun Energy (total caloric value 524 kcal) contains 18.5 g (49% of energy) carbohydrates, 6.0 g (16% of energy) fat, and 5.8 g (35% of energy) protein. A graded perfusion was performed using a continuous pump with the following infusion rates: 100 ml/h for 30 min, 110 ml/h for 60 min, 123 ml/h for 60 min, and 133 ml/h for 30 min. This graded infusion protocol was chosen to simulate the step-up phase of a test meal, and the infusion rates were adjusted on the basis of preliminary experiments. On the basis of the study by Capaldo et al. (3), demonstrating that the absorption of a mixed meal is still incomplete at 5 h after ingestion, we drew blood samples for 6 h, taking into account that our liquid formula diet was infused directly into the intestine.

Blood samples for glucose, nonesterified fatty acids (NEFA), insulin, C-peptide, glucagon, glucagon-like peptide-1 (GLP-1), and gastric inhibitory polypeptide (GIP) were drawn at 30 min and at 0, 15, 30, 40, 60, 80, 100, 120, 150, 180, 240, 300, and 360 min during each of the test periods.

Assay analytic methods. Plasma insulin, C-peptide, and glucagon were measured in duplicate with commercially available double-antibody RIAs purchased from Linco Research (St. Charles, MO). Intra-assay variation for insulin, C-peptide, and glucagon were 4.9, 2.4, and 6.8%, respectively. The interassay variation was 5.9, 7.1, and 8.4% for insulin, C-peptide, and glucagon, respectively. Plasma glucose was monitored immediately after blood withdrawal with an Analox GM9 Glucose Analyzer (Beckman Instruments, Fullerton, CA). Plasma triglycerides and free fatty acids were measured by enzymatic colorimetric methods.

Immunoreactive GIP levels were determined using 0.1 ml plasma in a human GIP RIA kit (Peninsula Laboratories, Belmont, CA). Intra-assay variation was less than 6%, and interassay variation was ~8 and 12% for 20 and 80 pmol/l standards, respectively.

GLP-1 (7–36)amide/(7–37) was measured by a GLP-1 (active) enzyme-linked immunoassay kit (Linco). This assay is based on a monoclonal antibody fixed in a coated microwell plate that binds the NH₂-terminal region of active GLP-1. The concentration of active GLP-1 is proportional to the fluorescence generated by umbelliferone, which is produced by the reaction between alkaline phosphatase (conjugated with anti-GLP-1 monoclonal antibodies) and methyl umbelliferyl phosphate. The lowest reported detection limit is 2 pmol/l, the reported within-assay coefficient of variation (CV) is 8% at low and high concentrations (range 4–76 pmol/l), and the between-assay CV is 12% at 4–8 pmol/l and 7% at 28–76 pmol/l. Assay cross-reactivity is 100% for GLP-1 (7–36)amide and GLP-1 (7–37), but it is not detectable for GLP-1 (9–36)amide, GLP-2, and glucagon.

Mathematical models. The data of glucose, insulin, and GLP-1 plasma concentrations were analyzed by a mathematical model similar to what we have previously used for analysis of the oral glucose tolerance test (OGTT) (27). The model represents the transport of glucose along the intestinal tract and its absorption from gut lumen into portal blood, assuming the presence of two glucose absorption components related to proximal and distal transporters, respectively, and estimates the time course of the rate of appearance Ra of enteral glucose in plasma, and of the rate of release of incretin hormones as related to glucose transit into gut lumen. The absorption model, coupled with the minimal model of glucose kinetics (4), was validated by fitting glucose and GLP-1 data in healthy controls and type 2 diabetic patients during the OGTT, and the model-derived estimates of insulin sensitivity were well correlated to those obtained from the euglycemic hyperinsulinemic clamp (27).

In the present study, the model utilizes the known rates of enteral nutrient infusion to provide the time courses of glucose and GLP-1 concentrations. The model-predicted time courses were fitted to the measured concentrations to estimate the values of model parameters. The following parameters were estimated for each subject: the rate coefficient γ of intestinal absorption, the velocity u of the luminal glucose bolus, glucose effectiveness Sgi, insulin sensitivity Sγ, the rate constant p of insulin action, the basal value of plasma GLP-1 concentration GLP₀, and the coefficient of GLP-1 release bGLP. The glucose distribution volume was computed for each subject by a formula that accounts for sex, age, total body fat, and basal glucose concentration (6). We note that glucose effectiveness is defined as the

Table 1. Anthropometric and clinical parameters of the subjects

<table>
<thead>
<tr>
<th>Subjects</th>
<th>Sex</th>
<th>Age, yr</th>
<th>Weight, kg</th>
<th>Height, cm</th>
<th>Fat-Free Mass, kg</th>
<th>Fat Mass, kg</th>
<th>BMI, kg/m²</th>
<th>Hb A₁c, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Glucose-tolerant subjects</td>
<td>7M 3F</td>
<td>45.9 ± 9.1</td>
<td>113.2 ± 11.9</td>
<td>169.7 ± 8.5</td>
<td>56.2 ± 8.0</td>
<td>56.8 ± 6.6</td>
<td>39.1 ± 0.7</td>
<td></td>
</tr>
<tr>
<td>Diabetic subjects</td>
<td>6M 4F</td>
<td>47.4 ± 7.7</td>
<td>111.2 ± 17.3</td>
<td>168.3 ± 12.3</td>
<td>56.1 ± 8.6</td>
<td>55.1 ± 9.7</td>
<td>39.0 ± 0.9</td>
<td>7.6 ± 0.7</td>
</tr>
<tr>
<td>P</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
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</tr>
</tbody>
</table>

Values are means ± SE.

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rate constant of glucose uptake independent of insulin. The central nervous system is the major utilizer of glucose without insulin regulation; therefore, \( S_G \) has a relevant clinical importance.

The means and standard deviations of model parameters were estimated by the NONMEM method (29). Minimization was performed using a constrained Levenberg-Marquardt minimization routine of the MATLAB library. The coefficients of variation of the estimates were found to be smaller than 20%.

Determination of C-peptide plasma concentrations allowed us to measure the rate of insulin secretion, ISR, by means of a deconvolution procedure, using the two-compartment model of C-peptide kinetics (7) with the standard values of C-peptide kinetic parameters computed for each subject (35). A rough estimate of the insulin clearance of each individual subject was obtained as the ratio between the area under the curve (AUC) of the ISR, as assessed by deconvolution, and the AUC of the insulin concentration measurements. The AUC values were computed by the trapezoidal rule.

From NEFA concentration data, the initial decrease of NEFA concentration that accompanies glucose infusion was computed, for each subject, as \( \Delta \text{NEFA} = \text{NEFA}_b - \text{NEFA}_{\text{min}} \), where subscript “b” denotes basal value and “min” the minimal NEFA concentration attained. Similarly, from insulin concentration data, the initial increase

Fig. 1. Plasma concentrations (means ± SE) of glucose (A), insulin (B), NEFA (C), C-peptide (D), GIP (E), and GLP-1 (F) in control subjects during the meal test. Each panel reports the data recorded during the infusion in duodenum, proximal jejunum, and mid-jejunum. To avoid superposition of the error bars, we anticipated by 5 min the data of duodenal time course and delayed by 5 min those of mid-jejunum. Significance: *P < 0.05 duodenum vs. mid-jejunum.
of insulin concentration (I) was computed as $\Delta I = I_{\text{max}} - I_b$, with $I_{\text{max}}$ the maximal insulin concentration. The ratio $\Delta \text{NEFA}/\Delta I$ gave an index of the sensitivity to insulin of the NEFA production.

**Statistics.** All of the data were expressed as means ± SD unless otherwise specified. In the figures, in particular, means ± SE are reported. Two-factor ANOVA followed by Tukey’s test was used for intergroup comparisons and one-factor ANOVA followed by Tukey’s test for intragroup comparisons. $P < 0.05$ was considered significant.

**RESULTS**

The control and diabetic subjects were well matched by sex (7 W and 3 M in control vs. 6 W and 4 M in diabetic subjects), age ($45.9 ± 9.1$ yr in control vs. $47.4 ± 7.7$ yr in diabetic subjects), and BMI ($39.1 ± 0.7$ kg/m$^2$ in control vs. $39.0 ± 0.9$ kg/m$^2$ in diabetic subjects) (Table 1). The average Hb A$_1c$ was $7.62\%$, meaning that the subjects were in a moderate decompen-sated diabetic state.

![Fig. 2. Plasma concentrations (means ± SE) of glucose (A), insulin (B), NEFA (C), C-peptide (D), GIP (E), and GLP-1 (F) in diabetic subjects during the meal test. Each panel reports the data recorded during the infusion in duodenum, proximal jejunum, and mid-jejunum. To avoid superposition of the error bars, we anticipated by 5 min the data of duodenal time course and delayed by 5 min those of mid-jejunum.](http://ajpendo.physiology.org/)(Fig. 2. Plasma concentrations (means ± SE) of glucose (A), insulin (B), NEFA (C), C-peptide (D), GIP (E), and GLP-1 (F) in diabetic subjects during the meal test. Each panel reports the data recorded during the infusion in duodenum, proximal jejunum, and mid-jejunum. To avoid superposition of the error bars, we anticipated by 5 min the data of duodenal time course and delayed by 5 min those of mid-jejunum.)
The time courses of the concentrations of glucose, insulin, NEFA, C-peptide, GIP, and GLP-1 after the test meal are reported in Figs. 1 and 2 for control and diabetic subjects, respectively. Glucagon concentration time courses are reported in Fig. 3. For control subjects, glucagon concentrations during infusion were larger in mid- and proximal jejunum vs. duodenum ($P < 0.0001$), whereas they were larger in mid-jejunum vs. duodenum ($P < 0.0001$) in diabetic subjects. As expected, plasma glucose concentration both while fasting and during the nutrient infusion was significantly higher in diabetic subjects than in control subjects (compare Fig. 1A vs. Fig. 2A, $P < 0.005$ in all comparisons).

In control subjects, GLP-1 seemed to be higher when nutrients were infused into the mid-jejunum (Fig. 1F) but without reaching statistical significance, as shown by the repeated-measures ANOVA. A tendency toward a larger GLP-1 response to the nutrient infusion was also observed in control compared with diabetic subjects without reaching statistical significance due to the large interindividual variability.

The correlation coefficients of NEFA with insulin average time courses in duodenal and proximal and mid-jejunal infusion were as follows: $-0.92 \ (P < 0.002)$, $-0.82 \ (P < 0.02)$, $-0.77 \ (P < 0.03)$ in control subjects and $-0.93 \ (P < 0.0005)$, $-0.83 \ (P < 0.004)$, $-0.96 \ (P < 0.0002)$ in diabetic subjects.

The sensitivity of NEFA production to insulin ($\Delta$NEFA/$\Delta$I) was doubled in mid-jejunal compared with duodenum in control subjects ($2.80 \pm 1.36 \times 10^6$ in mid-jejunal vs. $1.56 \pm 0.65 \times 10^6$ in proximal jejunum vs. $1.13 \pm 0.78 \times 10^6$ in duodenum, $P < 0.005$ mid-jejunal vs. duodenum and $P < 0.05$ mid-jejunal vs. proximal jejunum). The sensitivity values were not significantly different in diabetic subjects ($2.35 \pm 2.60 \times 10^6$ in mid-jejunal vs. $1.72 \pm 0.92 \times 10^6$ in proximal jejunum vs. $1.87 \pm 1.72 \times 10^6$ in duodenum).

The most prominent feature in the data was a progressive reduction of plasma insulin concentration from duodenal to proximal and mid-jejunal infusion in control subjects as seen in Fig. 1B. Accordingly, the insulin concentration incremental AUC was significantly different ($P < 0.05$) between duodenum and mid-jejenum $6.36 \pm 1.72 \text{ vs. } 4.20 \pm 1.03 \times 10^4$ pM·min. A similar trend, although less pronounced, was found for the C-peptide time course. In diabetic subjects, by contrast, no significant difference was found among duodenal and proximal and mid-jejunal infusion.

The values of total ISR, estimated by the C-peptide deconvolution, tended to be lower, without reaching significance, in diabetic subjects than in controls with no significant difference among infusion sites ($57.52 \pm 35.1$ vs. $61.98 \pm 18.9 \text{ pmol in duodenum; } 58.38 \pm 31.3 \text{ vs. } 65.18 \pm 13.7 \text{ pmol in proximal jejunum; } 52.32 \pm 36.1 \text{ vs. } 70.30 \pm 11.3 \text{ pmol in mid-jejunum}$). The insulin clearance, computed as the ratio between the AUC of the insulin secretion rate and the AUC of insulin concentration, was significantly increased in control subjects only when mid-jejenum was compared with duodenum ($2.05 \pm 1.05 \text{ vs. } 1.09 \pm 0.38 \text{ l/min, } P < 0.03$). No significant changes were observed, however, in diabetic subjects.

Figure 4 illustrates the model fitting of glucose and GLP-1 data (duodenal vs. proximal vs. mid-jejunal infusion from top to bottom) in control subjects and, respectively, diabetic patients. The AUC of the R$_g$ in plasma of infused glucose was not statistically different among the infusion sites in both groups (between 85 and 90% of the amount administered).

The estimates of model parameters are reported in Table 2 for control and diabetic subjects. The coefficient of the rate of glucose intestinal absorption ($\gamma$) increased significantly from duodenum to mid-jejenum ($P < 0.0001$ for all comparisons in controls, and $P < 0.001$ mid-jejenum vs. duodenum and proximal jejunum in diabetic subjects). As expected, diabetic subjects were more insulin resistant than control subjects independently of the intestinal tract where the nutrients were delivered. In both groups of subjects, insulin sensitivity progressively increased from duodenum to proximal jejunum to mid-jejenum. In the control subjects, the insulin sensitivity was significantly higher ($P < 0.015$) when nutrients were infused in mid-jejenum vs. duodenum, reaching values observed in lean subjects (27). Also in diabetic subjects insulin sensitivity was improved ($P < 0.05$) without reaching normal values. The NEFA sensitivity to insulin was linearly correlated with the glucose insulin sensitivity independently of the intestinal tract.
of nutrient infusion in control subjects (duodenum $r = 0.69$, $P < 0.05$, proximal jejunum $r = 0.66$, $P < 0.05$, mid-jejunum $r = 0.70$, $P < 0.025$, with overall values of $r = 0.58$, $P < 0.001$). The parameter $b_{\text{GLP}}$ of GLP-1 release doubled from duodenum to mid-jejunum in controls ($P < 0.05$) while remaining statistically nonsignificant in diabetic subjects.

**DISCUSSION**

The major findings of the present study are the following. 1) Insulin sensitivity was significantly increased in both control and diabetic subjects when nutrients were infused in the mid-jejunum compared with duodenum. 2) The improvement in insulin sensitivity translated into a larger inhibitory effect of insulin on lipolysis, as shown by the significantly larger sensitivity of NEFA production to insulin in control subjects. 3) The glucose absorption rate coefficient, derived from the simultaneous fitting of glucose and GLP-1 concentration, progressively increased from duodenum to proximal and mid-jejunum in both control and diabetic subjects. 4) The insulin clearance was significantly increased in control subjects from
The NEFA insulin sensitivity and glucose insulin sensitivity were well correlated, suggesting that a significant improvement in insulin sensitivity during nutrient administration translated into a larger antilipolytic effect of insulin, as shown by the larger decrease of plasma NEFA concentration per unit increase of insulin concentration in control subjects. In this regard, it has been ascertained that impaired insulin suppression of NEFA reflects NEFA flux from the adipose tissue rather than impaired NEFA uptake (13, 14). Therefore, the improvement of NEFA insulin sensitivity observed in our study should reflect the improvement of insulin action.

As shown by the increase in the glucose absorption rate coefficient, glucose absorption was enhanced in mid-jejunum compared with both duodenum and proximal jejunum, possibly as a compensatory effect. In fact, the model parameter $b_{GLP}$, which represents the efficiency of GLP-1 secretion in response to glucose absorption, increased significantly from duodenum to mid-jejunum in normal-glucose-tolerant subjects (Table 2). After a 50% proximal enterectomy in dogs, the net absorptive fluxes of water, electrolytes, or simple nutrients were in fact unmodified even early after the operation, suggesting that ileum vicariates the absorptive function of duodenum and jejunum (34). On the other hand, we have shown that in BPD glucose is efficiently absorbed and metabolized (31). Although it is well ascertained that insulin secretion is the major determinant of the hyperinsulinemia observed in obesity, a reduction in the metabolic clearance rate of insulin contributes to maintaining elevated circulating levels of this hormone (1, 22). In the present study, insulin clearance was increased when nutrients were infused into the mid-jejunum. However, our measurement of the insulin clearance did not allow us to determine whether this change occurs at hepatic or nonhepatic sites, although it is clearly ascertained that ~80% of endogenously secreted insulin is cleared by the liver (10). Impaired insulin clearance is a typical feature of insulin resistance (17).

The rapid rise of incretins, with an early peak about 30 min after the beginning of nutrient intestinal infusion observed in our series, might reflect the effect of proteins, whereas the late peak at a time between 180 and 240 min might depend on fat stimulation, as shown by Lindgren et al. (18).

In conclusion, bypass of duodenum and proximal jejunum by nutrients enhances insulin sensitivity, inhibits lipolysis, and increases insulin clearance. These results might help our comprehension of the effect of bariatric surgery on insulin resistance and diabetes.

**GRANTS**

Clinical Trials NIH no. NCT00994435.

**DISCLOSURES**

No conflicts of interest, financial or otherwise, are declared by the author(s).

**Table 2. Estimates of mathematical model parameters**

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<th>Parameters</th>
<th>Duodenum</th>
<th>Proximal Jejunum</th>
<th>Mid-Jejunum</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\gamma$ (min$^{-1}$)</td>
<td>14.08 ± 3.07</td>
<td>18.01 ± 2.20</td>
<td>25.13 ± 3.26*</td>
</tr>
<tr>
<td>$\alpha$ (cm·min$^{-1}$)</td>
<td>2.47 ± 0.42</td>
<td>2.34 ± 0.39</td>
<td>2.58 ± 0.24</td>
</tr>
<tr>
<td>$S_G \times 10^5$ (min$^{-1}$)</td>
<td>3.12 ± 1.48</td>
<td>3.68 ± 1.00</td>
<td>3.22 ± 1.02</td>
</tr>
<tr>
<td>$S_I \times 10^4$ (min$^{-1}$)</td>
<td>0.62 ± 0.22</td>
<td>0.73 ± 0.33</td>
<td>1.11 ± 0.44†</td>
</tr>
<tr>
<td>$p \times 10^2$ (min$^{-1}$)</td>
<td>1.18 ± 0.77</td>
<td>0.97 ± 0.46</td>
<td>0.84 ± 0.28</td>
</tr>
<tr>
<td>$GLP_0$ (pm)</td>
<td>1.96 ± 0.93</td>
<td>2.10 ± 0.94</td>
<td>1.99 ± 1.06</td>
</tr>
<tr>
<td>$b_{GLP} \times 10^3$ (l·min$^{-1}$)</td>
<td>0.21 ± 0.14</td>
<td>0.36 ± 0.20</td>
<td>0.45 ± 0.09§</td>
</tr>
</tbody>
</table>

**Diabetic subjects**

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Duodenum</th>
<th>Proximal Jejunum</th>
<th>Mid-Jejunum</th>
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<tbody>
<tr>
<td>$\gamma$ (min$^{-1}$)</td>
<td>14.30 ± 3.97</td>
<td>17.01 ± 0.84</td>
<td>25.12 ± 4.09‡</td>
</tr>
<tr>
<td>$\alpha$ (cm·min$^{-1}$)</td>
<td>2.51 ± 0.42</td>
<td>2.33 ± 0.06</td>
<td>2.49 ± 0.67</td>
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<tr>
<td>$S_G \times 10^5$ (min$^{-1}$)</td>
<td>2.51 ± 1.68</td>
<td>3.42 ± 1.46</td>
<td>2.17 ± 2.49</td>
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<td>$S_I \times 10^4$ (min$^{-1}$)</td>
<td>0.40 ± 0.20</td>
<td>0.60 ± 0.35</td>
<td>0.79 ± 0.34†</td>
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<td>$p \times 10^2$ (min$^{-1}$)</td>
<td>1.05 ± 0.73</td>
<td>0.86 ± 0.32</td>
<td>0.55 ± 0.13</td>
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<tr>
<td>$GLP_0$ (pm)</td>
<td>1.47 ± 0.41</td>
<td>1.90 ± 0.73</td>
<td>1.31 ± 0.79</td>
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<tr>
<td>$b_{GLP} \times 10^3$ (l·min$^{-1}$)</td>
<td>0.28 ± 0.33</td>
<td>0.30 ± 0.35</td>
<td>0.32 ± 0.19</td>
</tr>
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</table>

Values are means ± SD. See text for definitions. Significance: *P < 0.0001 mid- vs. proximal jejunum and duodenum, †P < 0.015 mid-jejunum vs. duodenum, §P < 0.05 mid-jejunum vs. duodenum, ‡P < 0.001 mid-jejunum vs. duodenum.
REFERENCES


