Incretin levels and effect are markedly enhanced one month after Roux-en-Y gastric bypass surgery in obese patients with type 2 diabetes.

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Objective: Limited data on patients undergoing Roux-en-Y gastric by pass surgery (RY-GBP) suggest that an improvement in insulin secretion after surgery occurs rapidly thus may not be wholly accounted for by weight loss. We hypothesized that in obese patients with type 2 diabetes mellitus (T2DM) the impaired levels and effect of incretins changed as a consequence of RY-GBP.

Research Design and Methods: Incretin (GIP and GLP-1) levels and their effect on insulin secretion were measured before and 1 month after RY-GBP in eight obese women with T2DM and in seven obese non-diabetic controls. The incretin effect was measured as the difference in insulin secretion (area under the curve, AUC) in response to oral glucose tolerance test (OGTT) and to an isoglycemic IV glucose test (isoG IVGT).

Results: Fasting and stimulated levels of GLP-1 and GIP were not different between Controls and Patients with T2DM before the surgery. One month after RY-GBP, body weight decreased by 9.2±7.0 kg, oral glucose-stimulated GLP-1 (AUC) and GIP peak levels increased significantly by 4368±1418 pM.L⁻¹.min⁻¹ (p<0.0001) and 131±85 pg/ml (p=0.007) respectively. The blunted incretin effect markedly increased from 7.6±28.7 to 42.5±11.3% (p=0.005) after RY-GBP, time at which it was not different from the Controls (53.6±23.5%, p=0.284).

Conclusions: These data suggest that early after RY-GBP, the greater GLP-1 and GIP release could be potential mediators of improved insulin secretion.
Introduction
The prevalence of obesity and T2DM (1) is increasing in the US. More and more patients seek bariatric surgery (surgical weight loss) for treatment of their obesity. Up to 30% of patients presenting for bariatric surgery have T2DM (2,3). Although weight loss surgeries generally result in a loss of 50-70% excess body weight and ‘cure’ the diabetes in 77% of cases (4), the rapidity in the onset and the magnitude of the benefits of RY-GBP on diabetes has thus far baffled clinical scientists.

It has been proposed that the incretins could be one of the key mediators of the anti-diabetic effects of certain types of bariatric surgery. The incretins are gut peptides secreted in response to meals, which enhance insulin secretion. The two main incretins are gastric inhibitory peptide (GIP), secreted by the K cells in the proximal small intestine (5) and glucagon like peptide-1 (GLP-1), secreted by the L cells of the distal small intestine (6). Both incretins affect meal-related insulin secretion (7, 8). GLP-1 also delays gastric emptying (9), decreases appetite (9-11), inhibits glucagon (12), and may improve insulin sensitivity (13), all effects that are anti-diabetogenic. The incretin effect is impaired in patients with T2DM (14). GLP-1 levels are blunted (15), but the effect of administered GLP-1 on insulin secretion persists (16). Contrary to GLP-1, GIP levels are normal in patients with T2DM, but the effect of administered GIP on insulin secretion is blunted (17,18). GIP and GLP-1 have additive insulinotropic effects during hyperglycemia. Both GLP-1 and GIP analogues are being developed as anti-diabetic agents (19).

Previous data have shown that the significant weight loss observed after various bariatric procedures was accompanied by improvement of diabetes control and increased GLP-1 levels. However, most studies were cross sectional (20,21), reported fasting (22) rather than post-prandial GLP-1 levels, and compared various types of surgery such as jejuno-ileal bypass (JIB) (23,24) or bilio-pancreatic diversion (BPD) (24), often leading to inconclusive results. Data on fasting GIP levels after bariatric surgery are inconsistent, reporting either a decrease (22, 25, 26) or an increase (20, 24).

GLP-1 levels increase after a meal in patients after RY-GBP (27) or with oral glucose after BPD (28). Meal-stimulated GIP levels have been reported to increase after JIB (20), or to decrease after GBP or JIB surgery (23, 26, 29). None of these studies however measured GLP-1 and GIP simultaneously, reported the incretin levels and effect on insulin secretion, or was done in diabetic patients.

Our goal was to investigate the role of incretins as the mechanism for rapid improvement in insulin secretion in obese patients with T2DM after RY-GBP. Specifically, we wished to measure the changes in GLP-1 and GIP levels in response to oral glucose, as well as the changes in the incretin effect on insulin secretion in obese patients with T2DM before and 1 month after RY-GBP.

Methods
Subjects
Obese patients with BMI >35 kg/m², scheduled for RY-GBP surgery, with T2DM diagnosed for less than five years, not on insulin, with an HbA1C less than 8%, less than 60 years of age, of both genders and all ethnic groups were recruited. They were studied prior to and within one month after the surgery, in order to minimize the amount of
weight loss at the time of the second study. A group of obese non-diabetic controls were studied for incretin levels and effect. Fat mass was measured by anthropometrics (30).

**Roux-en-Y Gastric Bypass (RY-GBP) Protocol**
All patients underwent a laparoscopic RY-GBP with a 30 ml gastric pouch, 40 cm afferent limb, 150 cm Roux-limb, and 12 mm gastro-jejunostomy. The post-RY-GBP diet recommendations included a daily intake of 600-800 kcal, 70 g of protein and 64 oz of fluid. This was achieved, on an individual basis, with multiple small meals and snacks with various commercial protein supplements. The diet after RY-GBP was monitored by food records but not directly supervised. The diet in the few days preceding the testing in Patients prior to surgery or in Controls was not controlled.

**Methods to measure incretin effect: insulin secretion after oral and isoglycemic IV glucose load (IsoG IVGT)**
Subjects were studied for the OGTT and the IsoG IVGT in the morning after a 12-h overnight fast, on two different days, separated by less than 5 days.

**3-h oral glucose tolerance test (OGTT)** All patients underwent first a 3-h OGTT with 50 g of glucose (in a total volume of 300ml). After IV insertion, at 8:00 A.M., subjects received orally 50 g of glucose. Blood samples, collected on chilled EDTA tubes with added aprotinin (500 KIU (kallikrein inhibitory units)/ml of blood) and DPPIV inhibitor (Linco St. Charles, MO) (10µl/ml of blood), were centrifuged at 4ºC prior to storage at -70ºC.

**Isoglycemic IV glucose test (IsoG IVGT)** The goal of the IsoG IVGT was to expose the pancreas to blood glucose levels matched to the ones obtained during the OGTT in the same subject. Glucose (sterile 20% dextrose solution in water) was infused intravenously over 3 hours using a Gemini pump (Gemini, Inc.). A sample of blood was collected every 5 minutes, using a contra lateral antecubital IV catheter, then transferred in a picofuge tube without any additive and centrifuged for bed side immediate measure of glucose levels. The glucose infusion rate was adjusted in order to match the glucose concentrations obtained for the same patient during the OGTT at each time point for 3 hours. During the OGTT and the isoG IVGT, the arm used for blood sampling was kept warm with a heating pad.

**Incretin Effect (INC)** The difference in β-cell responses (insulin total area under the curve or INS AUC 0-180”) to the oral and the isoglycemic IV glucose stimuli represents the action of the incretin factor expressed as the percentage of the physiological response to oral glucose, which is taken as the denominator (100%) (14). The formula is:

\[
\text{INC} = \frac{\text{INS AUC}_\text{oral} - \text{INS AUC}_\text{isoglycemic IV}}{\text{INS AUC}_\text{oral}} \times 100\%
\]
Assays. Total GLP-1, indicator of secretion, was measured by radio-immuno assay (RIA) (Phoenix Pharmaceutical, Belmont, CA.) after plasma ethanol extraction. The intra assay and interassay CV were 3-6.5% and 4.7-8.8% respectively. This assay has 100% specificity for GLP-1 (7-36) and GLP-1 (9-36), 60% specificity for GLP-1 (7-37) and does not cross react with glucagon (0.2%), GLP-2 (<0.001%) or exendin (<0.01%). Active GLP-1, indicator of potential action, was measured by ELISA (Linco St. Charles, MO). The intra assay and interassay CV were 3-7% and 7-8% respectively. The assay is 100% specific for GLP-1 (7-36) and GLP-1 (7-37) and does not react with GLP-1 (9-36), glucagon or GLP-2. Total GIP was measured by ELISA (Linco St. Charles, MO). The assay is 100% specific for GIP 1-42 and GIP 3-42, and does not cross react with GLP-1, GLP-2, oxyntomodulin or glucagon. The intra-assay and interassay CV were 3.0 -8.8% and 1.8-6.1% respectively. Plasma insulin and C-peptide concentrations were measured by RIA (Linco St. Charles, MO) with intra assay CV respectively of 5-8% and 3-6%, and interassay CV of 7.2% and 5.2 to 7.7%. Glucose concentration was measured at the bedside by the glucose oxidase method (Beckman glucose analyzer, Fullerton, CA). All hormonal and metabolites assays were performed at the Hormone and Metabolite Core Laboratory of the New York Obesity Research Center.

Statistical analysis
Outcome variables were serum glucose and plasma insulin, C-peptide, GLP-1 and GIP concentrations. Total areas under the curve 0-180’ (AUC) for outcome variables were calculated using the trapezoidal method. ANOVA with repeated measures was used to detect hormonal changes over time during the OGTT within each condition and for comparison before and after RY-GBP, or between Controls and Patients with T2DM. Paired t-tests were used to compare data between before and after RY-GBP. Data are expressed as the mean ± SD except in the figures where SEM are used. Statistical significance was set at p<0.05. Statistical analyses were performed with SPSS 13.0 (SPSS Inc., Chicago, IL) (31).

Results
Subject characteristics are shown in Table 1. Eight obese women with T2DM of 20.1 ± 12.9 months duration, HbA1C 6.9 ± 0.7 %, liver enzymes, thyroid function tests and blood pressure within normal limit, were studied before and 1 month (31 ± 14 days) after RY-GBP. One patient was diagnosed with T2DM at the time of screening for surgery. Patients’ diabetes medications, sulfonylureas and/or metformin were discontinued 3 days prior to being studied before the surgery. None of the patients were taking insulin, thiazolidinedione or beta-blocker before RY-GBP or any diabetes medication after RY-GBP. Seven obese non-diabetic women were studied as controls, while on their regular diet, at stable weight, on no medications. Controls did not differ from patients in terms of age, body weight, BMI (Table 1).

Side effect
Although 50 g of glucose drink was used rather than 75g to minimize the risk of dumping syndrome after RY-GBP, three patients experienced stomach cramping and discomfort,
nausea, sweating, flushing and palpitations 5 to 20 minutes into the OGTT. No severe adverse effects were observed.

**Glucose and insulin levels during the OGTT.**
Changes in outcome variables after RY-GBP are shown in Table 1. After RY-GBP, body weights and BMIs decreased significantly. Fasting and 120 minutes glucose levels decreased to non-diabetic range while peak insulin increased significantly.

**GLP-1 and GIP levels during the OGTT**
Fasting and stimulated GLP-1 and GIP levels were not different between Controls and Patients prior to RY-GBP (Table 1, Figure 1a, 1b, 1c).
GLP-1 AUC and peak GIP increased significantly after surgery by a factor of 4.2 and 1.6 respectively (Table 1, Figure 1a, 1b). There was no change of GLP-1 or GIP levels during the IsoG IVGT (data not shown). The blunted active GLP-1 levels increased significantly at 15’ during the OGTT after GBP (Figure 1c). In order to assess indirectly the activity of the enzyme dipeptidyl-peptidase IV (DPP IV), the ratio of GLP-1 active to GLP-1 total (using OGTT peak values) was calculated. The ratio, which was not statistically different between Controls and Patients before surgery (p=0.132) decreased significantly from 0.70 ± 0.12 to 0.18 ±0.06 (p<0.0001) after RY-GBP.

**Incretin Effect**
In Controls, the glucose concentrations were well matched between the IsoG IVGT and the OGTT (mean levels 5.87 ± 0.76 mmol/L vs. 5.92 ± 0.82 p=0.639). As expected, the insulin levels were greater during the OGTT (AUC insulin 252±147 pmol.L⁻¹.min⁻¹) than during the IsoG IVGT (132±101 pmol.L⁻¹.min⁻¹, p=0.045) with a calculated incretin effect on insulin of 53.6±23.5%. In Patients before RY-GBP, the glucose levels were well matched between the IsoG IVGT and the OGTT (11.06 ±1.93 mmol/L vs. 10.76±1.97 mmol/L, p=0.058) (Figure 2a). Contrary to the Controls, as expected, the insulin response was not greater after oral (AUC insulin 356±199 pmol.L⁻¹.min⁻¹) than IV glucose (AUC insulin 305±161 pmol.L⁻¹.min⁻¹, p=.195) (Figure 2b), with a resulting blunted incretin effect of 7.6±28.7% (Figure 1c). After RY-GBP, glucose levels were higher during the IsoG IVGT (mean levels 9.39±1.00 mmol/L) compared to the OGTT (8.42±1.04 mmol/L, p=0.046) (Figure 2d). However the insulin response was greater during the oral test (323±137 pmol.L⁻¹.min⁻¹) than during the IV test (184±80 pmol.L⁻¹.min⁻¹ p=0.001) (Figure 2e), and the incretin effect was markedly increased by a factor of 5, to 42.5±11.3 % (mean increase 34.8±24.2%, p=0.007) (Figure 1c), level at which it was not significantly different from the Controls (53.6±23.5%, p=0.284) (Figure 1d). The incretin effect on C-peptide increased significantly after RY-GBP, to a level not statistically different (p=0.157) than the Controls (Table 1). There was a correlation between GIP AUC and insulin incretin effect in Patients before the surgery (r=0.737, p=0.037), but neither in Patients after RY-GBP nor in Controls. GLP-1 AUC was positively correlated to the C-peptide incretin effect in Controls and Patients after RY-GBP (r=0.915, p=0.046).
Discussion

We investigated the changes in incretin levels and effect after RY-GBP in patients with morbid obesity and T2DM. Our main findings are that the release of incretin after oral glucose is of greater magnitude and the incretin effect on insulin secretion is markedly improved one month after RY-GBP.

It has long been hypothesized that the incretins could play a role in the marked immediate improvements of diabetes control observed after bariatric surgery (32). Limited data (23,24,25,27,33) suggest that the improvement in insulin secretion after bariatric surgery occurs rapidly, thus may not be wholly accounted for by weight loss, but could be a consequence of changes of the enteroinsular axis, particularly in the incretins. However, most of the studies to date have been cross-sectional (20,23,24) or measured only fasting levels of incretins (22,25).

In our study, fasting and glucose-stimulated levels of GLP-1 and GIP were not different between Patients before the surgery and Controls. This is contrary to findings by others showing lower fasting levels and impaired stimulated release of incretins in patients with T2DM (7,14,17). This discrepancy could be due to different patients’ populations. Our patients were relatively young (45 years old) and with recently diagnosed T2DM (less than 2 years).

One month after RY-GBP, our data demonstrate a clear and significant increase of GLP-1 (total and active) and GIP release in response to oral glucose in Patients with T2DM. An increase in levels of circulating incretins was previously reported in non-diabetic patients after RY-GBP (27) or BPD (28). Some cross-sectional and longitudinal studies have shown an increase in the stimulated levels of incretins, after a meal- or oral glucose, after JIB (24,34) or after RY-GBP (27,35). Our data show that the changes in stimulated incretins levels occur as early as 1 month after RY-GBP, similarly to changes in enteroglucagon obtained after JIB (34). Future studies will address the long term changes of incretin and help clarify the controversy about β-cell hypertrophy after RY-GBP (36,37).

The mechanisms by which incretin levels increase after surgery are not fully understood. After RY-GBP, as a consequence of the bypass of the upper gut, the lower gut is exposed sooner to the ingested nutrients, thus changing the timing of the physiological release of gut incretins. The time of the peak release of GLP-1 and GIP after oral glucose was at 15 minutes, although GIP is released by the K cells of the proximal small intestine and GLP-1 by the more distal L cells of the small intestine (5,6). More frequent blood sampling could possibly identify different release time for each incretin, according to the anatomical distribution of the secretory cells. Our stimulus was a solution of glucose. Future studies should investigate whether other stimuli, such as amino acids, lipids or change in pH stimulate the secretion of the incretins with the same magnitude as a solution of oral glucose. Elegant studies in a rat model of diabetes suggest that the exclusion of the upper gut, rather than weight loss, benefits glucose tolerance (38). Rats after gastrojejunal bypass have better glucose tolerance than sham operated pair fed control animals with equivalent body weight (38). Similarly, ileal transposition results in an early improvement of glucose tolerance with increase of GLP-1 levels in a non-obese type 2 diabetes rat model, compared with sham-operated animals (39). The improvement in glucose tolerance was shown to be independent of weight and food intake (40). These rodent studies underline potential mechanisms by which diabetes
improves after bariatric surgery and support a role for the gut incretins in glucose tolerance after RY-GBP.

Additionally, the change in circulating incretin levels could result from changes in the level and/or activity of the enzyme dipeptidyl peptidase IV (DPPIV). Both GLP-1 and GIP are highly susceptible to enzymatic degradation in vivo. The cleavage by DPPIV is an important determinant of incretin action, as it occurs rapidly and generates non-insulinotropic metabolites. The modulation of incretin levels by the use of DPPIV inhibitors is used for the treatment of T2DM (41). We found that the release of GLP-1 active is also increased after RY-GBP, although short lived. The ratio of circulating active GLP-1 levels to total GLP-1 levels decreased after RY-GBP. It is difficult to speculate to the significance of these findings which could represent a change in levels and/or activity of the enzyme DPPIV. To our knowledge, there are no available data on in vivo DPPIV activity and/or levels in T2DM, or on the effect of diabetes control and/or weight loss on the activity or levels of the enzyme.

As shown by others (14, 42), we found that our patients with T2DM had impaired incretin effect. After RY-GBP, in addition to increases in the levels of stimulated circulating GLP-1 and GIP levels, the severely impaired incretin effect on insulin and/or C-peptide improved significantly reaching a magnitude similar to that of the non-diabetic Controls. To our knowledge, this is the first report of simultaneous increase in stimulated incretin levels and incretin effect (by comparing the insulin response to oral and matched IV glucose load) in patients with T2DM after RY-GBP. Although the incretin effect of the Patients normalized to the levels of Controls after RY-GBP, the magnitude of the increase of stimulated GIP and GLP-1 levels was far greater than Controls, with a five fold increase for GLP-1. Interestingly, a similar discrepancy between incretin levels and effect occurred in Patients before RY-GBP. Stimulated GLP-1 and GIP levels of Patients were not different than Controls, yet the incretin effect, normal for the Controls, was severely impaired for the Patients with T2DM. Other have shown discrepancies between circulating levels of incretins in response to the ingestion of glucose and the incretin effect (43), underlining the importance of looking at both incretin effect and plasma levels.

The changes in incretin levels and effect, albeit very significant, are likely not the only factor responsible in the improvement of insulin secretion early after RY-GBP. We did find significant correlation between incretin output during the OGTT and the incretin effect. However, the small sample size does not allow pertinent comments on these findings. Other determinants of impaired insulin secretion in T2DM, such as glucose toxicity (44,45), lipotoxicity (46,47) likely improve after weight loss. At 1 month after RY-GBP, the daily calorie intake was minimal (range of 500 kcal to 700 kcal by 24-h diet recall, data not shown) and the participants had lost about 10kg. It is known that both caloric restriction and weight loss improve diabetes control (48-51). Diet-induced weight loss also improves the release of incretins in obese non-diabetic individuals (52, 53). However, as all of these events occur simultaneously, it is hard to isolate one factor from the others. Future studies will have to separate the weight loss effect from the effect of the surgical bypass.
Insulin secretion in DM is extremely variable (54,55), depending on, among other factors, the age of the patient (56), the duration of the disease (impossible to measure accurately), the degree of diabetes control (45,46) and the degree of insulin resistance (57). The effects of weight loss will depend upon the pre-diet β-cell capacity (58). In this study, the mean age of our patients was 45 years, the duration of diagnosed diabetes was less than 2 years and the HbA1C at baseline was less than 7%. After RY-GBP, the patients discontinued their anti-diabetic medications and fasting and post-prandial glucose levels decreased significantly to non-diabetic levels. The changes in insulin and C-peptide (data not shown) levels after the RY-GBP were very variable and changes were not statistically significant. However the relative amount of insulin secreted in response to glucose (insulin to glucose ratio) was greater after the surgery, a marker of improved insulin secretion.

Our study has some weaknesses. Our sample was of small size and ethnically diverse (data not shown) with only women, therefore did not allow us to assess gender or ethnic differences. We did not control for the diet prior to the OGTT testing. Indeed, after the RY-GBP, patients were calorie restricted and their amount of carbohydrate (CHO) intake likely much lower than prior to RY-GBP. It has been shown that caloric and CHO restriction could affect the result of the OGTT (59). It is possible that this caloric and CHO restriction could have affected the incretin release during the OGTT. Future diet-controlled studies will address this issue. Finally, the matching of the glucose levels was not perfect between OGTT and IsoG IVGT in Patients after RY-GBP, and the levels of glucose were higher during the IsoG IVGT. However this does not affect the interpretation of the results. If anything, it strengthens our findings. Although the glycemia is greater during the IsoG IVGT, Patients still released significantly more insulin during the OGTT than the IsoG IVGT.

These data clarify the incretin effect on insulin in the early period after RY-GBP. Our main finding is that incretin levels and effect are markedly increased one month after RY-GBP, in parallel with a significant improvement of the diabetes control. The magnitude of the incretin release may be specific to the anatomical changes of the gut secondary to RY-GBP surgery. Future experiments will have to separate the effect of the weight loss from the effect of RY-GBP. These results may lead investigators to study other therapeutic maneuvers to alter the incretins and develop new treatments for the growing diabetic and pre-diabetic population. As more obese patients with diabetes undergo RY-GBP, a clear understanding of the mechanism underlying short and long term improvement in T2DM is increasingly important.

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Table 1: Subject Characteristics

Subject Characteristics for Controls (obese without T2DM, n=7), and Patients (obese with T2DM, n=8) before and after RY-GBP. Data are mean ± SD. Fasting (average of 2 baseline values). Peak, 120’ value, and AUC (total area under the curve, 180’) values are obtained during the OGTT. ∆ is difference between pre- and post-RY-GBP.

<table>
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<th>Controls</th>
<th>Patients pre-RY-GBP</th>
<th>p (vs. Controls)</th>
<th>Patients post-RY-GBP</th>
<th>∆</th>
<th>p (Δ)</th>
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<td>Age (years)</td>
<td>38.8±7.8</td>
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<td>Weight (kg)</td>
<td>100.4±29.9</td>
<td>113.9±16.4</td>
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<td>BMI (kg/m²)</td>
<td>37.1±11.6</td>
<td>43.6±6.8</td>
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<td>40.1±7.0</td>
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<td>Fat mass (%)</td>
<td>41.1±8.3</td>
<td>47.1±1.3</td>
<td>0.06</td>
<td>45.3±3.1</td>
<td>1.8±1.8</td>
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<td>Fasting glucose (mmol/L)</td>
<td>5.4±0.4</td>
<td>8.05±1.82</td>
<td>0.001</td>
<td>6.45±0.84</td>
<td>1.60±1.45</td>
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<td>Fasting insulin (pmol/L)</td>
<td>123±93</td>
<td>171±74</td>
<td>0.303</td>
<td>128±54</td>
<td>43±53</td>
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<td>20'glucose (mmol/L)</td>
<td>6.04±1.48</td>
<td>11.2±1.72</td>
<td>&lt;0.0001</td>
<td>7.10±1.72</td>
<td>4.10±1.62</td>
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<td>Peak glucose (mmol/L)</td>
<td>749±532</td>
<td>507±304</td>
<td>0.301</td>
<td>723±327</td>
<td>216±245</td>
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<td>↓ glucose (mmol.L. min⁻¹)</td>
<td>1113±191</td>
<td>2018±343</td>
<td>&lt;0.0001</td>
<td>1500±212</td>
<td>517±187</td>
<td>&lt;0.0001</td>
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<td>↓ insulin (pmol.L.min⁻¹)</td>
<td>252±147</td>
<td>356±199</td>
<td>0.294</td>
<td>323±137</td>
<td>32±134</td>
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<td>↓ TGLP-1 (pmol.L⁻¹.min⁻¹)</td>
<td>948±551</td>
<td>1358±503</td>
<td>0.155</td>
<td>5727±1458</td>
<td>4368±1418</td>
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<td>JC GIP (pmol.L⁻¹.min⁻¹)</td>
<td>6682±3775</td>
<td>9174±1732</td>
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<td>9480±3409</td>
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<td>Peak GIP (pmol/L)</td>
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<td>213±52</td>
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<td>Etin effect on Insulin (%)</td>
<td>53.6±23.5</td>
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<td>42.5±11.3</td>
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<td>26.6±18.1</td>
<td>44.4±43.6</td>
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**Figure 1**
Total GLP-1 (Figure 1a), GIP (Figure 1b) and active GLP-1 (Figure 1c) levels during the OGTT in Patients before (diamond) and after (square) RY-GBP (Figure 1a) and in Controls (triangle). Incretin Effect on insulin secretion (Figure 1d) in Controls (clear), Patients before RY-GBP (stripes) and Patients after RY-GBP (black). The incretin effect was calculated by comparing the insulin response to oral and matched IV glucose load. Data are mean ± SEM. * p<0.05 compared to Patients pre-RY-GBP. # p<0.05 compared to Controls.
Figure 2
Glucose (Figure 2a and 2d), insulin (Figure 2b and 2e) and C-Peptide (Figure 2c and 2f) concentrations during OGTT (diamond) and isoglycemic IV Glucose test (IsoG IVGT) (square) before (Figures 2a-c) and after (Figures 2d-f) RY-GBP. Data are mean ± SEM. * p<0.05 significant difference between OGTT and IsoG IVGT values within each condition (before or after RY-GBP).