SUPPLEMENTARY DATA

Additional Description of Calculations.

Clamp glucose infusion rates (GIRs) were divided per individual total body weight, averaged for 20-min periods and are given in $mg \cdot kg^{-1} \cdot min^{-1}$, as done in the original paper by DeFronzo et al. (1) (see also **additional results** and **Fig.S1A**).

M-values (*M*) were calculated by adding clamp GIRs and hepatic glucose production (HGP) with regard to space correction during 20-min intervals of the clamp-test and are given in $mg \cdot kg^{-1} \cdot min^{-1}$, again as initially described (1) (see also **additional results** and **Fig.S1B**).

M/I is the ratio between *M* and prevailing insulin concentrations, multiplied by 100, and given in $(mg \cdot kg^{-1} \cdot min^{-1}) / (\mu U/mL)$.

Insulin Sensitivity - Homeostatic Model Assessment (ISI-HOMA) (2) was calculated as:

$$ISI\text{-}HOMA = \frac{22.5}{\text{Fasting plasma glucose (mmol/L)} \times \text{fasting plasma insulin } (\mu U/mL)}$$

The Clamp-like Index (CLIX) (3). The formula to compute the insulin sensitivity index CLIX is:

$$CLIX = SC \times f/(mAUC \text{ glucose} \times mAUC \text{ C-peptide}) \times F,$$

where SC is baseline serum creatinine concentration (in mg/dl), mAUC glucose is the area under the curve (AUC) of plasma glucose during OGTT from 0 min to the end of the time span (in $mg \cdot dl^{-1} \cdot min$) divided by the total amount of time (min), and mAUC C-peptide is the same for plasma C-peptide (in ng/mL·min, then divided by time amount). The term "mAUC" means "mean AUC" and is obtained by dividing AUC by the entire study time (for AUC see below). The constant f is 0.85 for males and 1.00 for females. The value of F depends upon the OGTT sampling schedule: when glucose and C-peptide are frequently measured until 120min or **180min** (i.e. in this study), F equals 6600 or **5900**, respectively.

Gut glucose absorption (4;5). In brief, the increase of postprandial circulating glucose ($dgluc_{circ}$) over time (dt) is the result of gain from gut glucose absorption (ABS) and HGP, and loss because of insulin-mediated glucose uptake (Rd), predominantly by skeletal muscle. Thus, the *dynamic* changes in glucose concentration over time can be expressed as:

$$dgluc_{circ}/dt = 1/VG \times [BW \times (HGP - Rd) + ABS]$$

with initial condition: gluc(0) = fasting glucose concentration; ABS(0) = 0; and HGP(0) = Rd(0). BW is the body weight, and VG is the oral glucose distribution volume assumed as ~15% of BW.
Dynamic HGP and Rd during the OGTT were estimated as follows: previous works from others (6) and ourselves (4) report that both glucose utilization and HGP suppression follow a dose-responsive curve with insulin concentrations in logarithmic manner. Because plasma insulin concentrations were frequently determined during the OGTT, measurements of insulin-mediated glucose uptake (M) and HGP from the clamp-test could be individually used for dynamic estimation of Rd and HGP applying the formula shown above. Thus, only one unknown variable remained, namely ABS so that the equation became solvable.

SUPPLEMENTARY DATA

Furthermore, this equation was implemented using Simulink® for Matlab® (MathWorks Inc., Boston, MA), and ABS was estimated by solving nonlinear least-squares problem fitting the plasma glucose values during the OGTT (MatLab® function used LSQNONLIN with 10·000 iterations at maximum). Every time sample of ABS was treated as an independent parameter to be estimated. Common criteria of model performance (best fit, residuals, variance-covariance Fisher's matrix) were evaluated for accepting the final model's prediction. ABS is calculated as the average value for each time interval between consecutive blood samples.

Beta cell function during the clamp-test was assessed from plasma C-peptide concentrations by the deconvolution method, as described in detail elsewhere (7;8). The gradients of insulin secretion during the clamp-test were calculated as the slope of the linear fit of its values over time.

Beta cell function during the first hour of the OGTT was either assessed from the **Insulinogenic Index (IGI)** for the first 30 min, as previously described in detail elsewhere (5;9), or from the **slope of C-peptide** released during the first 60 min (see also **additional results** and **Fig.S1C**). In brief, the **IGI** represents the quotient of the dynamic area under the curve of plasma C-peptide concentrations and the dynamic area under the curve of plasma glucose concentrations during the first OGTT hour (for 'dynamic area under the curve' see below). Whereas the IGI reflects insulin secretion in relation to acute hyperglycaemia, the slope of C-peptide released during the first 60 min reflects the absolute insulin secretion regardless of plasma glucose concentrations.

Beta cell function during the entire OGTT was estimated by calculating the dynamic area under the curve of plasma C-peptide concentrations (for 'dynamic area under the curve' see below).

Area under the curve (AUC) during the 3h OGTT. AUCs were calculated by the trapezoidal rule. Dynamic AUCs (dyn AUCs or ΔAUCs) were calculated as total AUC-(180 × basal concentration).

Others. For each participant, the total glucose absorbed was calculated by integrating glucose absorption rates (ABS) over the 180-min OGTT (4;5). The relative glucose retention is the amount of absorbed glucose at each OGTT time point in relation to total glucose absorbed (4;5). Gastrointestinal glucose half-life (t½) and hepatic insulin sensitivity during clamp-test (i.e. duration of halving clamp HGP by insulin, reflecting insulin-mediated HGP-suppressibility) were individually determined by relative glucose retention in the gastrointestinal tract during the OGTT, and linear curve interpolation of clamp HGP, respectively, by using the closest time points to cross the 50% threshold (4;5).

Additional Results
As visible from **Fig.S1A**, clamp GIRs were highest (each p<0.05 vs. the other groups) in CON_{lean}; post–OP had higher clamp GIRs by 0.8-1.7mg·kg^{-1}·min^{-1} -except at 80min- than before surgery (each p<0.05). GIRs did not differ between post–OP and CON_{ob}. M-values (*M*) are depicted in **Fig.S1B**. At the final common 20-min interval (100-120min), CON_{lean} had the highest *M*, while *M* in pre-OP was the lowest (each p<0.05 vs. the other groups). *M* did not differ between post–OP and CON_{ob}.
Data in **Fig.S1C** and **Fig.S2A-D** are described in the "Results" section of the paper.
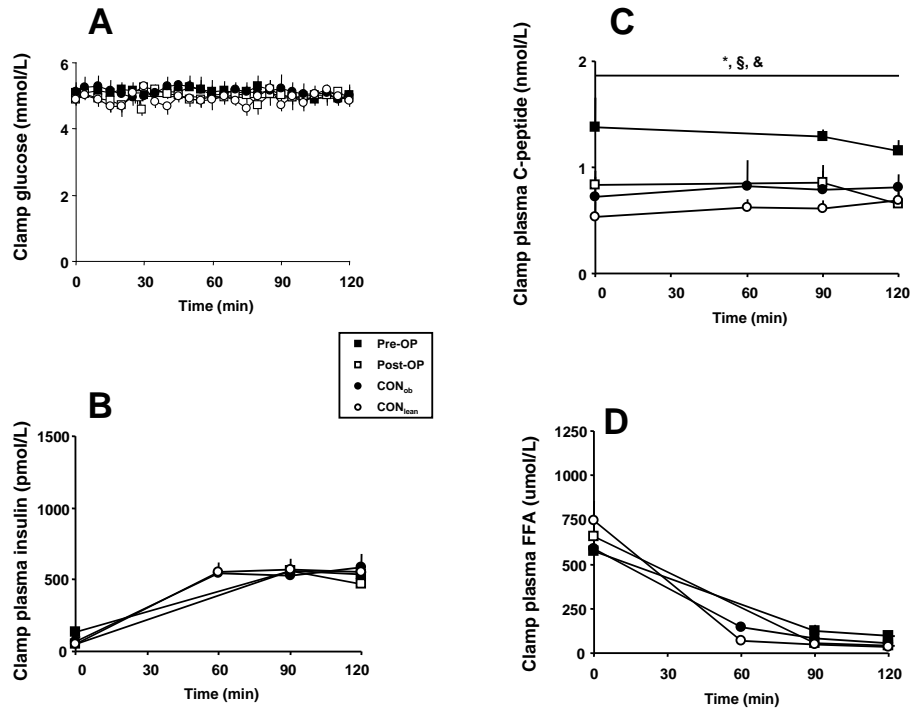
SUPPLEMENTARY DATA

Supplementary Figure 1. Clamp-test glucose infusion rates (**A**), M-values (**B**), and (**C**) the slope of C-peptide released during the first 60 min in obese patients before (pre-OP, n=6, ■ or black columns) and after bariatric surgery (post-OP, n=6, □, or dark-grey columns), as well as matching obese (CON$_{ob}$, n=6, ● or light-gray columns) and lean controls (CON$_{lean}$, n=6, ○ or uncolored columns).
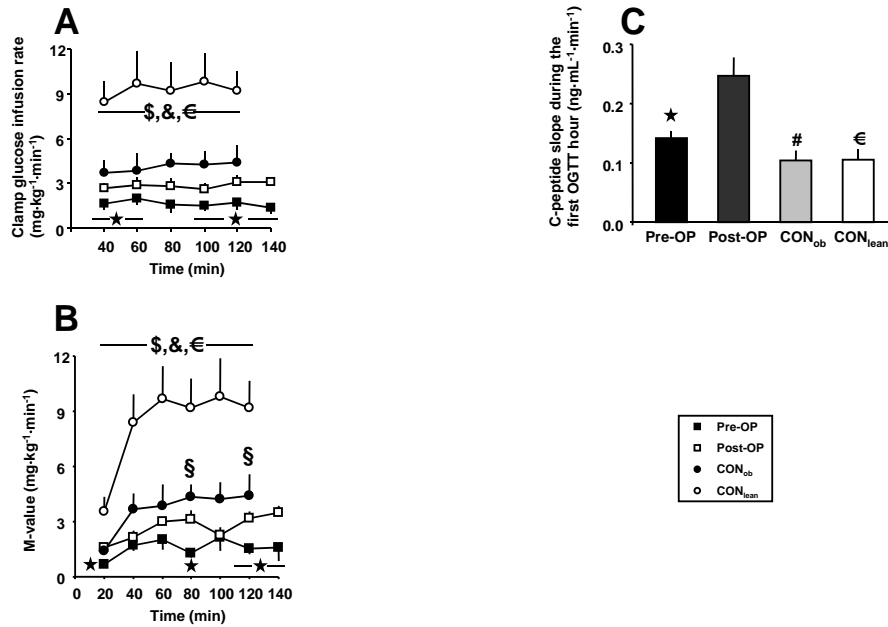
*, $p < 0.05$, pre-OP vs. post-OP; §, $p < 0.05$, pre-OP vs. CON$_{ob}$; &, $p < 0.05$, pre-OP vs. CON$_{lean}$; #, $p < 0.05$, post-OP vs. CON$_{ob}$; €, post-OP vs. CON$_{lean}$; $, $p < 0.05$, CON$_{ob}$ vs. CON$_{lean}$ (*Kruskal Wallis* test).

SUPPLEMENTARY DATA

Supplementary Figure 2. Plasma concentrations of (**A**) glucose, (**B**) insulin, (**C**) C-peptide, and (**D**) free fatty acids during the hyperinsulinaemic-isoglycaemic clamp-test in obese patients before (pre-OP, n=6, ■) and after bariatric surgery (post-OP, n=6, □), as well as matching obese (CON$_{ob}$, n=6, ●) and lean controls (CON$_{lean}$, n=6, ○).

*, $p < 0.05$, pre-OP vs. post-OP; §, $p < 0.05$, pre-OP vs. CON$_{ob}$; &, $p < 0.05$, pre-OP vs. CON$_{lean}$ (*Kruskal Wallis* test).

SUPPLEMENTARY DATA

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