

Supplemental Figure Legends

Supplementary Figure 1. Postprandial plasma concentrations of exendin9-39 (Ex9-39)

Time courses (-30-240 minutes) and AUCs of postprandial plasma concentrations of Ex9-39 after metformin and placebo with saline and Ex9-39, respectively in 12 patients with type 2 diabetes. Data are means $\pm$ SEM. Comparisons performed by paired Student's t-test

Supplementary Figure 2. Postprandial insulin:glucose ratios

Time courses (0-240 minutes) and iAUCs of postprandial plasma insulin:glucose ratios, after receiving a single dose of metformin (1,500 mg) or placebo with subsequent i.v. infusion of saline or exendin9-39 (Ex9-39), respectively, in 12 patients with type 2 diabetes. Data are means $\pm$ SEM. *P < 0.05, **P < 0.01, ***P < 0.001. Comparisons performed by paired Student's t-test. Comparisons performed by one-way repeated measures ANOVA with Tukey's multiple comparison post hoc test.

Supplementary Figure 3. Postprandial serum concentrations of acetaminophen

Time courses (0-240 minutes) and iAUCs of postprandial serum concentrations of acetaminophen, after receiving a single dose of metformin (1,500 mg) or placebo with subsequent iv-infusion of saline or exendin9-39 (Ex9-39), respectively in 12 patients with type 2 diabetes. Data are means $\pm$ SEM. *P < 0.05, **P < 0.01, ***P < 0.001. Comparisons performed by paired Student's t-test. Comparisons performed by one-way repeated measures ANOVA with Tukey's multiple comparison post hoc test.

Supplementary Figure 4. Visual analog scales

Time courses (0-240 minutes) of postprandial scores on visual analog scales of hunger, fullness, prospective food consumption, general well-being, nausea and thirst after metformin and placebo with saline and exendin9-39 (Ex9-39), respectively, in 12 patients with type 2

diabetes. Data are means $\pm$ SEM. Comparisons performed by one-way repeated measures ANOVA with Tukey's multiple comparison post hoc test.

Supplementary Figure 5. Ad libitum meal test

Scatter plot of ad libitum food intake after metformin (MET) and placebo (PLA) with saline and exendin9-39 (Ex9-39), respectively in 12 patients with type 2 diabetes. Data are raw data with means $\pm$ SEM. Comparisons performed by one-way repeated measures ANOVA with Tukey's multiple comparison post hoc test.

Supplementary Figure 6. Postprandial serum concentrations of plasma cholecystokinin (CCK)

Time courses (0-240 minutes) and iAUCs of postprandial plasma concentrations of cholecystokinin, after receiving a single dose of metformin (1,500 mg) or placebo with subsequent iv infusion of saline or exendin9-39 (Ex9-39), respectively in 12 patients with type 2 diabetes. Data are means $\pm$ SEM. *P < 0.05, **P < 0.01, ***P < 0.001. Comparisons performed by paired Student's t-test. Comparisons performed by one-way repeated measures ANOVA with Tukey's multiple comparison post hoc test.

Supplementary Figure 7. Postprandial gallbladder volumes

Time courses (0-240 minutes) and iAUCs of postprandial gallbladder volumes, after receiving a single dose of metformin (1,500 mg) or placebo with subsequent iv-infusion of saline or exendin9-39 (Ex9-39), respectively in 12 patients with type 2 diabetes. Data are means $\pm$ SEM. *P < 0.05, **P < 0.01, ***P < 0.001. Comparisons performed by paired Student's t-test. Comparisons performed by one-way repeated measures ANOVA with Tukey's multiple comparison post hoc test.

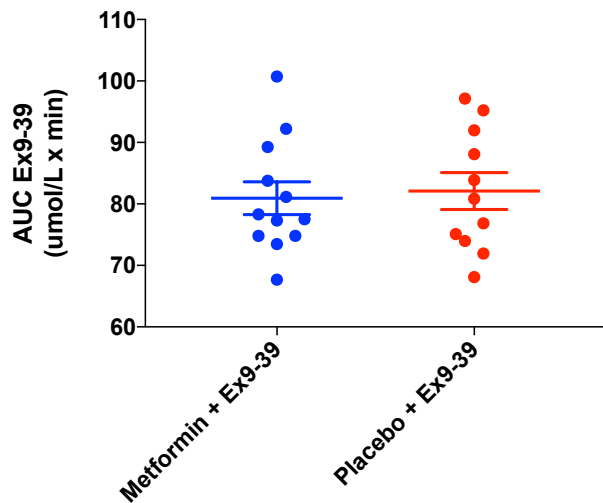
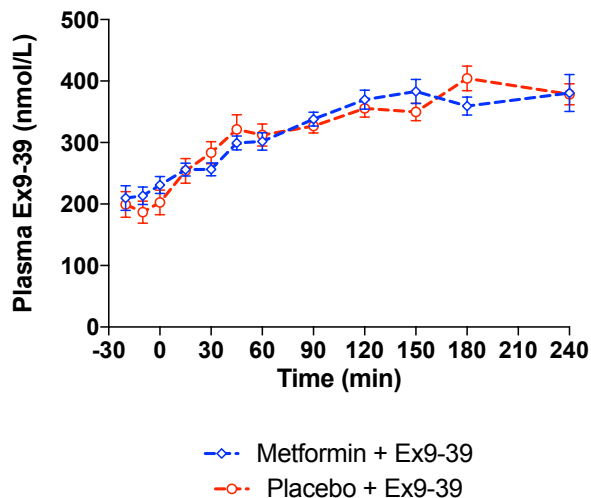
Supplementary Figure 8. Postprandial serum concentrations of total bile acids

Time courses (0-240 minutes) and iAUCs of postprandial serum concentrations of total bile acids, after receiving a single dose of metformin (1,500 mg) or placebo with subsequent iv-infusion of saline or exendin9-39 (Ex9-39), respectively in 12 patients with type 2 diabetes. Data are means $\pm$ SEM. * $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$. Comparisons performed by paired Student's t-test. Comparisons performed by one-way repeated measures ANOVA with Tukey's multiple comparison post hoc test.

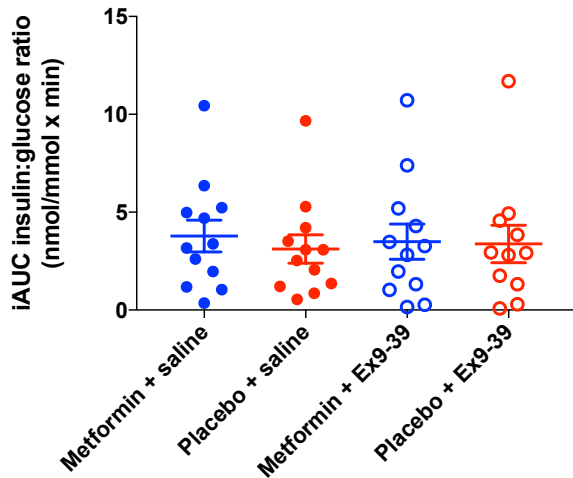
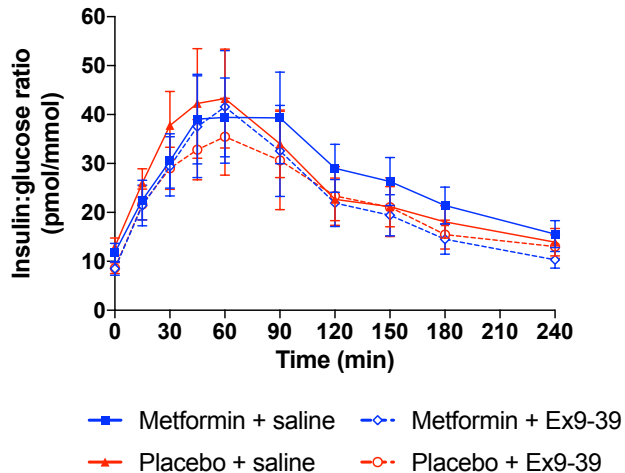
Supplementary Figure 9. Metformin-induced colonic L cell secretion

Metformin-induced colonic L cell secretion does not change in obesity or diabetes. (A) No correlation exists between BMI and (A) basal and (B) stimulated glucagon-like peptide-1 (GLP-1) release ($N = 46$). (C) Basal and (D) stimulated GLP-1 release were similar in samples from non-diabetic individuals (ND, $N = 35$) and patients with type 2 diabetes (T2D, $N = 11$). Bar graph data are means $\pm$ SEM, ns indicates no significant correlation.

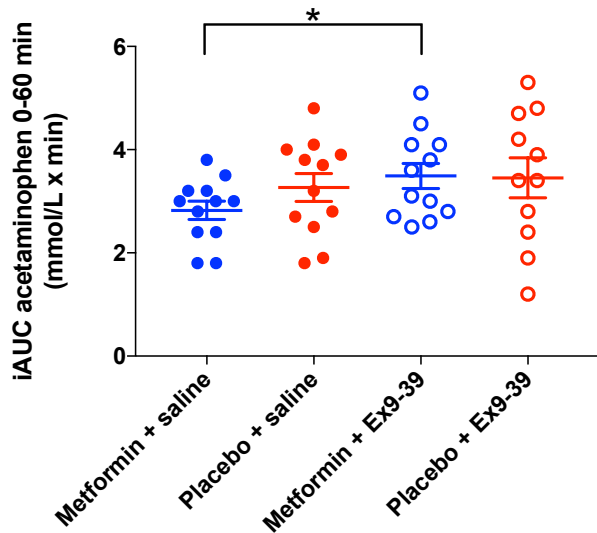
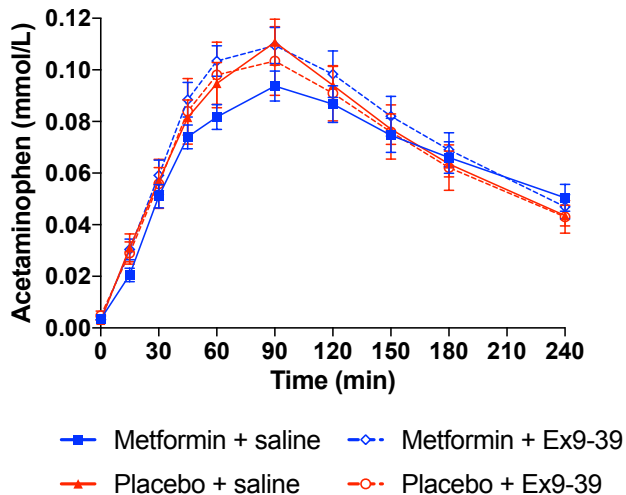
Supplementary Figure 1 – Postprandial plasma concentrations of exendin9-39



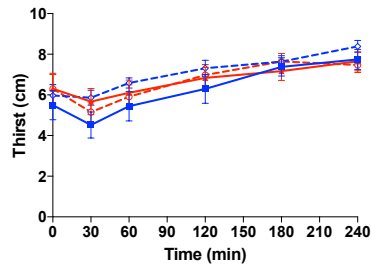
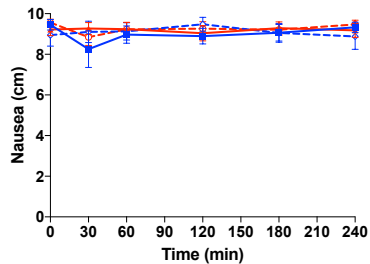
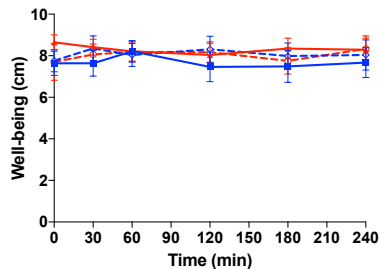
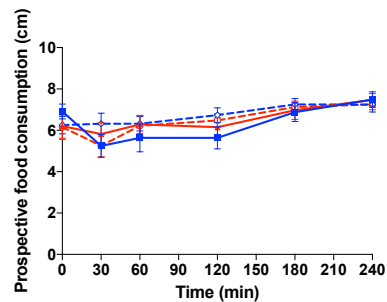
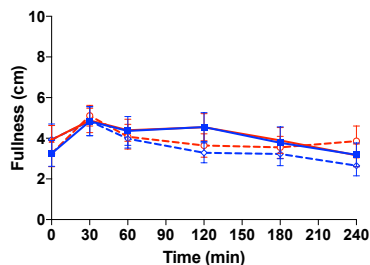
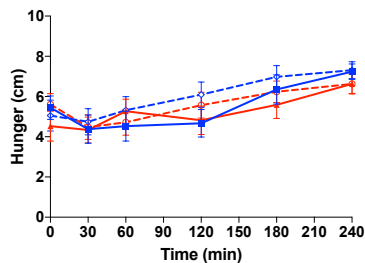
Supplementary Figure 2 – Postprandial insulin:glucose ratios



Supplementary Figure 3 – Postprandial serum concentrations of acetaminophen

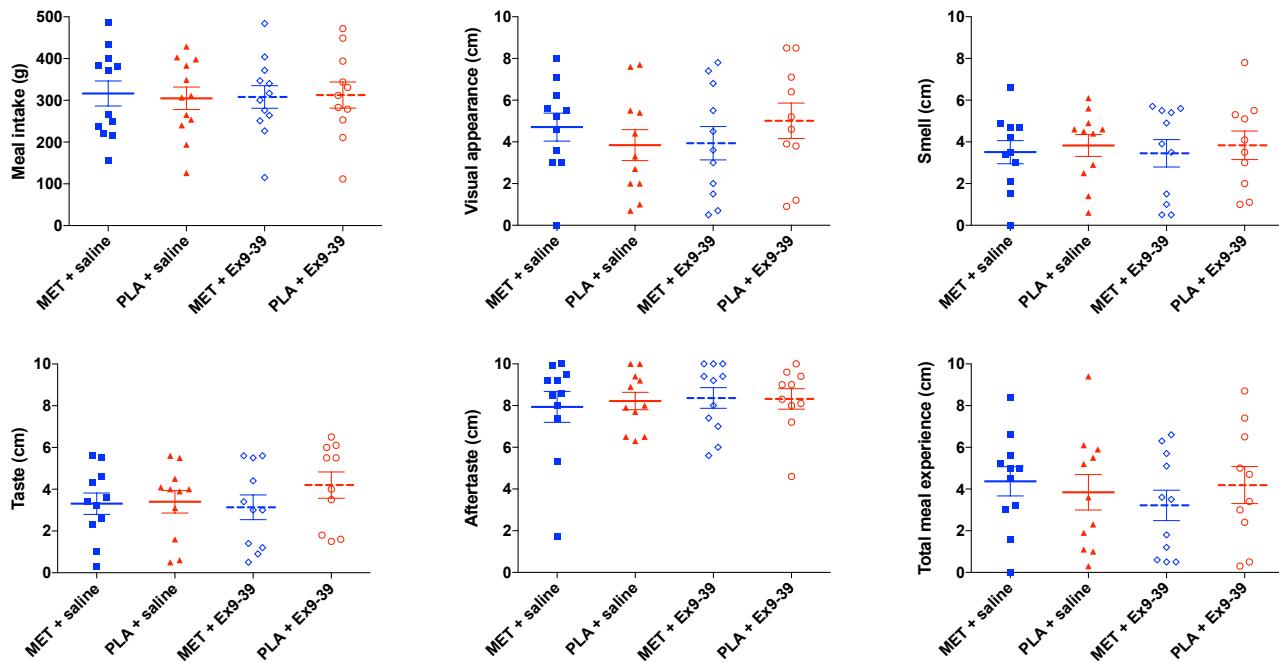


Supplementary Figure 4 – Visual analog scale

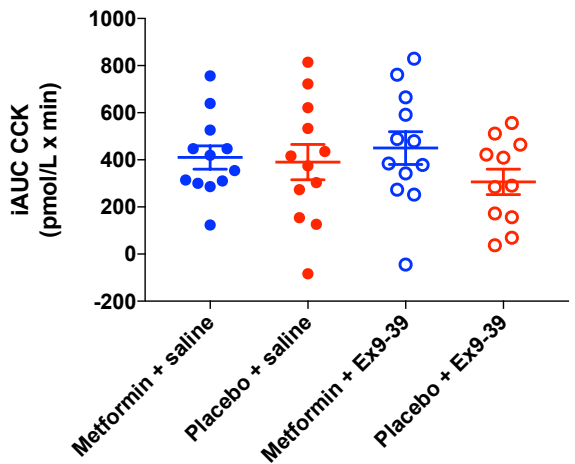
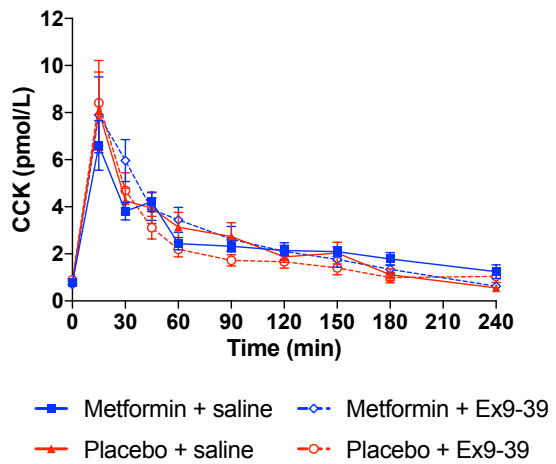


Metformin + saline Metformin + Ex9-39
Placebo + saline Placebo + Ex9-39

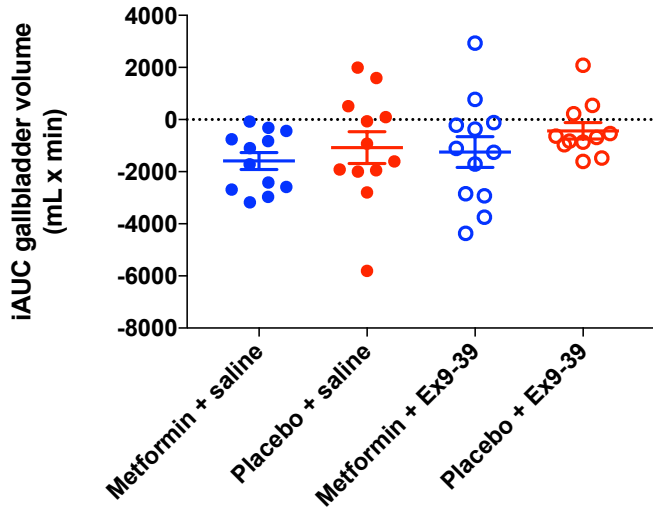
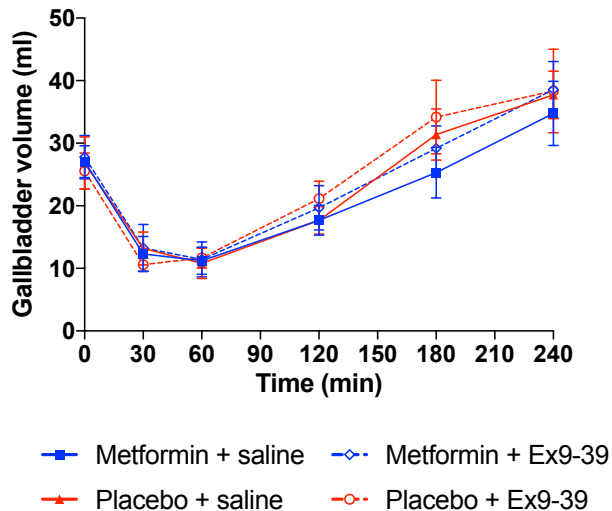
Supplementary Figure 5 – Ad libitum meal test



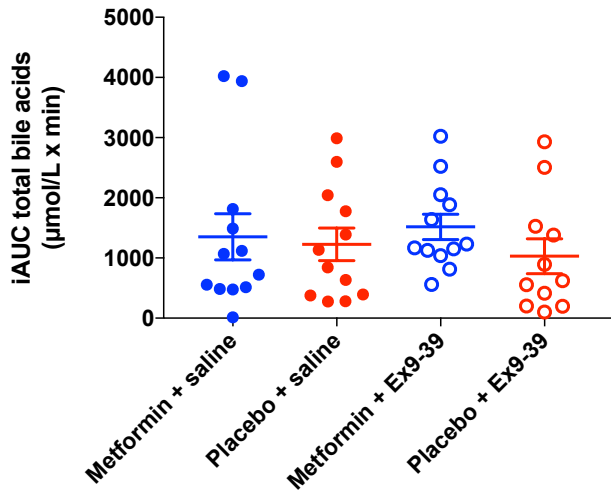
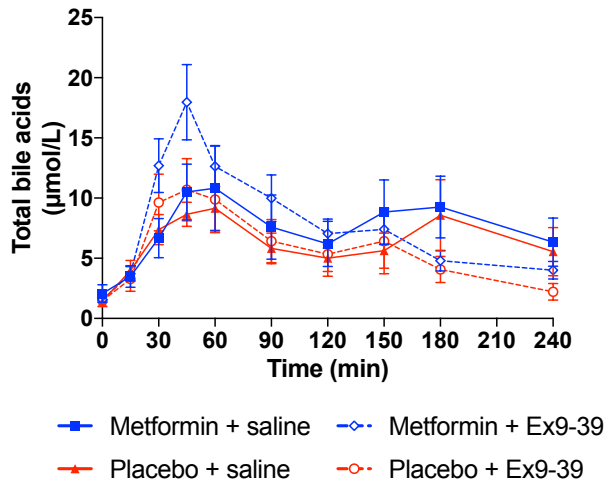
Supplementary Figure 6 – Postprandial serum concentrations of plasma cholecystokinin



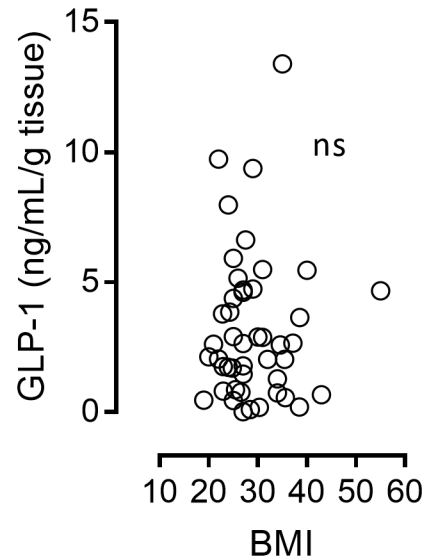
Supplementary Figure 7 – Postprandial gallbladder volumes



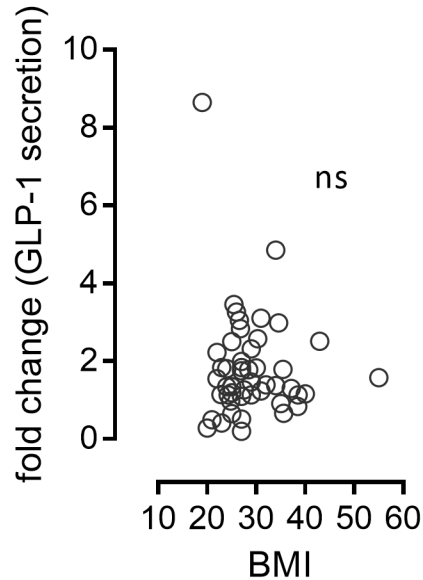
Supplementary Figure 8 – Postprandial serum concentrations of total bile acids



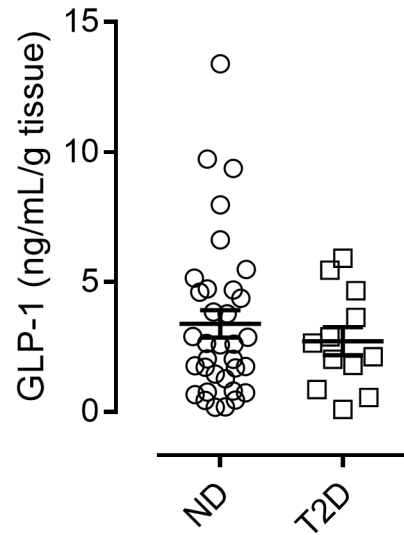
A



B



C



D

