Pancreatic Amylase and Lipase Plasma Concentrations Are Unaffected by Increments in Endogenous GLP-1 Levels Following Liquid Meal Tests

David P. Sonne,[1] Tina Vilsbøll,[1] and Filip K. Knop[1,2]

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Recent findings have suggested that incretin-based therapies promote pancreatic inflammation and possibly cell proliferation within the endocrine and exocrine pancreas (1). However, these studies have been met with substantive criticism based on technical and methodical issues (2). Nevertheless, incretin-based therapies seem to result in small increases (within normal range) in plasma concentrations of amylase and lipase in patients receiving these treatments. For example, in the SCALE Maintenance study (3), which examined the efficacy of high-dose liraglutide (3.0 mg once daily) for maintenance of weight loss achieved with low-calorie diet in obese/overweight individuals without diabetes, median lipase concentration was increased throughout the treatment period. The nature of the increase in amylase and lipase concentrations in patients receiving incretin-based therapies is at present not known. It has been speculated that elevated GLP-1 receptor agonist concentrations may be the direct cause. Interestingly, it has never been shown whether plasma concentrations of pancreas-specific amylase or lipase exhibit postprandial changes, which could arise from endogenous GLP-1 reaching the pancreatic acini. To explore this hypothesis, we measured pancreas-specific amylase and lipase in plasma following the ingestion of oral glucose and three isocaloric and isovolemic liquid meals—all of which exerted normal endogenous GLP-1 secretion (4)—in patients with type 2 diabetes and matched control subjects.

Detailed description of the experimental procedures and subjects was provided previously (4). In short, pancreas-specific amylase and lipase concentrations were measured in plasma from 15 patients with type 2 diabetes (mean duration of diabetes: 7.5 years [range 6–20]; age: 59.4 ± 9.6 years [mean ± SD]; BMI: 28.0 ± 2.2 kg/m^2; HbA_{1c}: 7.5 ± 1.4% [58.0 ± 15.4 mmol/mol]) and 15 healthy age-, sex-, and BMI-matched control subjects (age: 59.7 ± 10.0 years; BMI: 27.9 ± 2.0 kg/m^2; HbA_{1c}: 5.2 ± 0.2% [33.0 ± 2.2 mmol/mol]) undergoing four separate "meal" tests: a 75-g oral glucose tolerance test (OGTT) and three isocaloric (500 kcal) and isovolemic (350 mL) liquid meals (Fig. 1). Pancreas-specific amylase and lipase concentrations were measured with enzyme colorimetric assays (Modular Analytics; Roche Diagnostics GmbH).

In both groups, amylase and lipase concentrations were within normal range (13–53 units/L and 13–60 units/L, respectively). Amylase concentrations were slightly higher in control subjects versus patients with type 2 diabetes ($P < 0.05$), whereas lipase concentrations were similar. Neither of the enzymes increased following nutrient ingestion, suggesting that postprandial elevations of endogenous GLP-1 (two- to threefold) cannot trigger enzyme release from the human pancreas, at least not acutely.

These results suggest that the observation of elevated plasma amylase and lipase concentrations in patients treated with GLP-1 receptor agonists is unlikely to reflect potentiation or prolongation of an endogenous GLP-1 effect but rather indicates that pharmacologic effects of GLP-1 receptor agonists on pancreatic acini could be the cause. However, as the current study reflects acute experimental administration of 500 kcal liquid meals, it remains unknown if larger and/or solid meals may induce different effects, especially if accompanied with alcohol intake.

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[1]*Center for Diabetes Research, Gentofte Hospital, University of Copenhagen, Hellerup, Denmark*
[2]*The NNF Center for Basic Metabolic Research, Department of Biomedical Sciences, Faculty of Health and Medical Sciences, University of Copenhagen, Copenhagen, Denmark*

Corresponding author: David P. Sonne, dpsonne@gmail.com.

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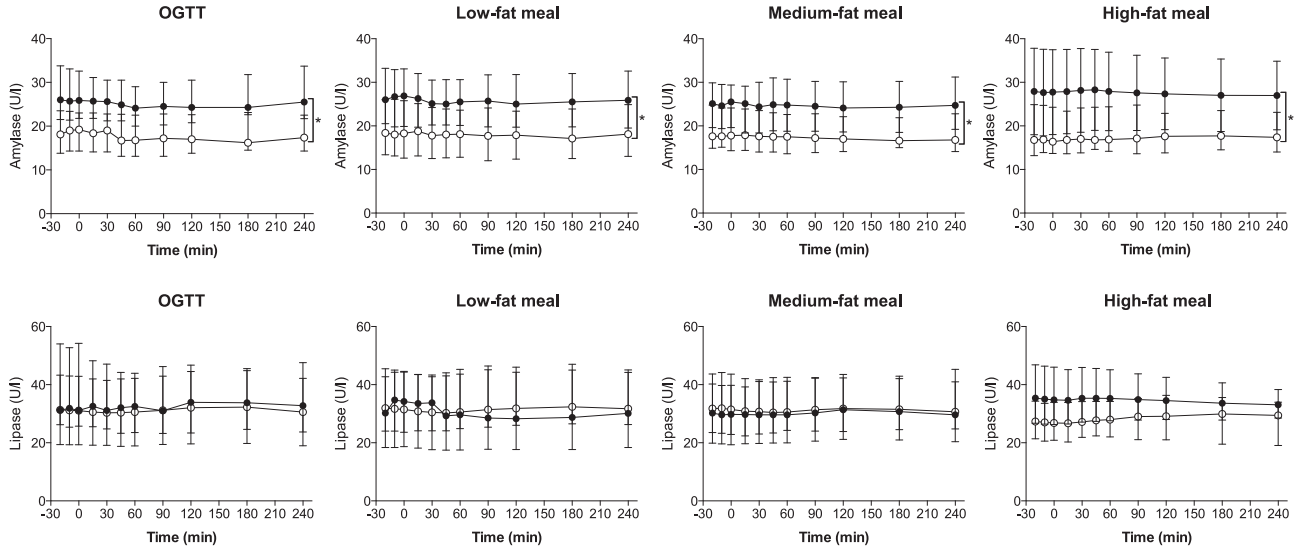

Figure 1—Plasma pancreatic amylase and lipase activity during a 75-g OGTT and three isocaloric (500 kcal) and isovolemic (350 mL) liquid meals (low fat: 2.5 g fat, 107 g carbohydrate, and 13 g protein; medium fat: 10 g fat, 93 g carbohydrate, 11 g protein; high fat: 40 g fat, 32 g carbohydrate, and 3 g protein) in healthy control subjects ($N = 15$, closed symbols) and patients with type 2 diabetes ($N = 15$, open symbols). Median and interquartile range values are shown. *Significant differences ($P < 0.05$) between groups were compared using two-way repeated-measures ANOVA.

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