Comparative effects of intraduodenal infusions of lauric and oleic acids on antropyloroduodenal motility, plasma cholecystokinin and peptide YY, appetite, and energy intake in healthy men1–3

Kate L Feltrin, Tanya J Little, James H Meyer, Michael Horowitz, Thomas Rades, Judith Wishart, and Christine Feinle-Bisset

ABSTRACT

Background: The regulation of gastrointestinal function and energy intake by fatty acids depends on their chain length. Animal studies suggest that lauric acid (C12) may have more potent suppressive effects on energy intake than does oleic acid (C18).

Objective: We compared the effects of equicaloric loads of C12 and C18 on antropyloroduodenal (APD) motility, plasma concentrations of cholecystokinin (CCK) and peptide YY (PYY), appetite, and energy intake.

Design: Thirteen healthy men (aged 20–46 y) were studied on 3 occasions in double-blind, randomized fashion. APD pressure waves, plasma hormones, and appetite perceptions were measured during 60-min intraduodenal infusions of 1) C12, 2) C18, or 3) 0.9% saline as control (rate: 4 mL/min; energy load for C12 and C18: 0.4 kcal/min); between 60 and 90 min, the subjects consumed a meal. Energy intake at a buffet meal was quantified.

Results: C12 and C18 both reduced antral (P < 0.001) and duodenal (P < 0.01) pressure waves and stimulated isolated pyloric pressure waves (P < 0.01) and plasma CCK (P < 0.001), with no differences between them. Although C12 and C18 both increased basal pyloric pressure (P < 0.05), C12 had a greater effect than did C18 (P < 0.01). In contrast, although both C12 and C18 increased plasma PYY (P < 0.001), C12 had a greater effect than C12. C12, but not C18, suppressed energy intake (P < 0.05).

Conclusions: At the load administered, C12, but not C18, suppressed energy intake, and C12 was a more potent stimulant of basal pyloric pressure. These discrepant effects are not apparently accounted for by changes in CCK or PYY secretion. Am J Clin Nutr 2008;87:1181–7.

INTRODUCTION

Although dietary fat is ingested in the form of triacylglycerols, its effects on gastrointestinal function and energy intake are mediated by the digestive products, free fatty acids. Accordingly, the effects of lipid to slow gastric emptying (9), modulate antropyloroduodenal motility (10, 11) and gastrointestinal hormone secretion (10–12), and suppress energy intake (10, 13) more than fatty acids with ≥10 carbon atoms.

Indirect comparison of results from different studies suggests that the effects on gastrointestinal function and energy intake may vary among fatty acids with ≥12 carbon atoms (3, 10). For example, we have reported that intraduodenal infusion of the fatty acid, lauric acid, a saturated fatty acid with 12 carbon atoms (C12), at a load of 0.4 kcal/min, resulted in a peak plasma CCK concentration of ≈12 pmol/L (10), whereas a long-chain triacylglycerol emulsion consisting mainly of oleic acid, a monounsaturated fatty acid with 18 carbon atoms (C18), only resulted in a peak plasma CCK concentration of ≈6 pmol/L, despite being infused into the duodenum at a much higher load (2.8 kcal/min) (3).

In rodents, Meyer et al (14) reported that small intestinal infusions of C12 or C18, in equimolar concentrations (0.96 mmol/h), have comparable effects on energy intake; however, at this concentration C18 delivered twice the amount of energy compared with C12. Given that fatty acids are emptied from the stomach at loads of ≈0.2–0.4 kcal/min (9, 15) and that we have reported recently that the effects of intraduodenal C12 on energy intake depend on the energy load, but not the concentration (16), it is probable that if the 2 fatty acids were administered in equicaloric amounts, C12 would be more effective in reducing energy intake than would C18. To our knowledge the comparative effects of C12 and C18 on gastrointestinal function and energy intake in humans have not been determined.

1 From the University of Adelaide Discipline of Medicine, Royal Adelaide Hospital, Adelaide, South Australia, Australia (KLF, TJJ, JHM, MH, JW, and CF-B), and the School of Pharmacy, University of Otago, Dunedin, New Zealand (TR).

2 Supported by a Dawes Postgraduate Research Scholarship provided by the Royal Adelaide Hospital (KLF), by a Postgraduate Research Scholarship from the University of Adelaide (TJJ), by a Career Development Award from the National Health & Medical Research Council in Australia (CF-B), and by a project grant provided by the Royal Adelaide Hospital Research Committee in 2005.

3 Reprints not available. Address correspondence to C Feinle-Bisset, Discipline of Medicine, Royal Adelaide Hospital, Adelaide SA 5000, Australia. E-mail: christine.feinle@adelaide.edu.au. Revisions received November 22, 2007. Accepted for publication January 16, 2008.
The aims of this study were to evaluate the hypotheses that 1) at equicaloric loads intraduodenal C12 would suppress appetite and energy intake more than C18 and that 2) these effects would be associated with specific changes in gastrointestinal function, such that C12 would inhibit antral and duodenal pressures, stimulate pyloric pressures, and increase plasma concentrations of CCK and PYY more than C18.

SUBJECTS AND METHODS

Thirteen healthy men were included in the study. The number of subjects was derived from power calculations based on our previous work (17). We calculated that with 12 subjects we would observe a 15% decrease in energy intake at \( \alpha = 0.05 \), with a power of 80%. The subjects had a mean (±SD) age of 26 ± 2 y (range: 20–46 y) and were of normal body weight for their height [body mass index (BMI; in kg/m\(^2\)): 22.9 ± 0.6; range: 19.2–25.5]. All subjects were unrestrained eaters [scoring < 12 on the eating restraint part (factor 1) of the 3-factor eating questionnaire (18)], had no gastrointestinal disease or symptoms, and were not taking medication known to affect gastrointestinal motility or appetite. No subject smoked or habitually consumed >20 g alcohol/d. The Royal Adelaide Hospital Research Ethics Committee approved the study protocol, and each subject provided written, informed consent before his inclusion.

Study design

Each subject was studied on 3 occasions, separated by 3–10 d, to evaluate, in a double-blind, randomized fashion, the effects of intraduodenal infusion of the fatty acids, 1) lauric acid (C12), 2) oleic acid (C18), or 3) control (0.9% saline) for 60 min on antro-pyloroduodenal motility, plasma concentrations of CCK and PYY, appetite, and energy intake.

Preparation of C12 and C18 solutions

Commercially available, food-grade lauric acid, a saturated fatty acid (Sigma-Aldrich, Milwaukee, WI), and sodium oleate, a monounsaturated fatty acid (Pfaltz & Bauer Inc, Waterbury, CT) were administered. The C12 solution was prepared by dissolving 4.52 g of C12 with 0.6 g of sodium hydroxide (Sigma-Aldrich, St Louis, MO) in 0.9% saline, to a total volume of 400 mL, with a resulting pH of 8.2. The C18 solution was prepared by dissolving 4.88 g of C18 in distilled water to a volume of 400 mL. The pH of the C18 and control (0.9% saline) solutions was adjusted to 8.2 by the addition of hydrochloric acid (Merck Pty Ltd, Victoria, Australia) and sodium hydroxide, respectively. All solutions were prepared on the morning of the study and infused at 37°C to maintain the C12 and C18 in solution. Both fatty acid solutions delivered the same energy content, ie, 0.4 kcal/min (total: 24 kcal); the concentration of the C12 solution was 56 mmol/L and that of the C18 solution was 43 mmol/L. All solutions were infused at a rate of 4 mL/min; thus, the total volume infused was 240 mL.

Both the solutions and their rate of delivery were selected on the basis of previous studies in humans that have quantified the rate at which fatty acids empty from the stomach into the small intestine at ≈0.2–0.4 kcal/min (9, 15) and established that the concentrations of fatty acids in the small intestine after triacylglycerol digestion are ≈30–70 mmol/L (19). We have shown that the intraduodenal C12 load of 0.4 kcal/min (at concentrations of 40–72 mmol/L) is well tolerated by healthy human subjects for ≤90 min and does not induce nausea (16, 17).

Protocol

Each subject attended the laboratory at 0830 after fasting from 2200 the previous night from both solids and liquids. They were intubated with a 16-channel manometric catheter (Dentsleeve International Ltd, Ontario, Canada), which was inserted through an anesthetized nostril and allowed to pass through the stomach and into the duodenum by peristalsis (20). The catheter incorporated 16 side holes, spaced at 1.5-cm intervals, to measure pressures in the antrum, pylorus, and duodenum. Six side holes (channels 1–6) were positioned in the antrum, a 4.5-cm-sleeve sensor (channel 7), with 2 channels (channels 8 and 9) present on the back of the sleeve, to measure pressure waves occurring over the entire pyloric region, was positioned across the pylorus, and 7 side holes (channels 10–16) were positioned in the duodenum. An additional lumen, used for the intraduodenal infusion, terminated 11.75 cm distal to the end of the sleeve sensor. The correct positioning of the catheter, so that the sleeve sensor straddled the pylorus, was maintained by continuous measurement of the transmucosal potential difference (TMPD) between the most distal antral (channel 6; ≃−40 mV) and the most proximal duodenal (channel 10; ≃0 mV) channels (20). For this purpose, an intravenous cannula filled with sterile saline was placed subcutaneously in the left forearm and used as a reference electrode (20). All manometric channels were perfused with degassed, distilled water, except for the 2 TMPD channels, which were perfused with degassed 0.9% saline, at 0.15 mL/min (20). An intravenous cannula was placed into a right forearm vein to obtain blood samples for subsequent measurement of plasma concentrations of CCK and PYY.

Once the catheter was positioned correctly, fasting motility was monitored until the occurrence of phase III of the interdigestive migrating motor complex (MMC) (21). Immediately after the cessation of phase III activity (t = 0–10 min), a baseline venous blood sample was taken, and a visual analogue scale (VAS) questionnaire (see Measurements) (22), assessing appetite-related sensations, as well as nausea and bloating, was administered. At t = 0 min (ie, during phase I of the MMC), duodenal infusions were commenced. Antropyloroduodenal pressures were monitored throughout the infusion period, blood samples were taken, and the VAS questionnaire was administered, every 10 min from t = 0 to 60 min. At t = 60 min the infusion was terminated, and the subject was extubated and immediately provided with a cold, buffet-style meal. The amount of food offered was in excess of what the subject was expected to consume. The types of food, macronutrient composition, and energy content of the meal were described in detail previously (10). The subject was given 30 min (ie, t = 60–90 min) to consume the meal and instructed to eat until comfortably full. After ingestion of the meal, the subject completed another VAS questionnaire, the intravenous cannula was then removed, and the subject was allowed to leave the laboratory.

Measurements

Appetite perceptions and energy intake

Perceptions of hunger and fullness were assessed with the use of the validated VAS questionnaire (22). Nausea and bloating
were also quantified. Each VAS questionnaire evaluated a sensation on a 100-mm horizontal line, in which 0 represented “sensation is not felt at all” and 100 represented “sensation is felt the greatest.” Subjects were asked to place a vertical stroke on the 100-mm line in relation to what they were feeling at that particular time. Energy intake from the buffet meal (energy consumption (in kcal), amount of food consumed (in g), and macronutrient distribution (% of energy]) were analyzed with the use of commercially available software (FOOD WORKS 3.0; Xyris Software, Highgate Hill, Queensland, Australia) (23).

**Antropyloroduodenal pressures**

Manometric pressures were digitized and recorded on a computer-based system running commercially available software (OAKDALE FLEXISOFT; Assoc Prof GS Hebbard, Melbourne, Australia), written in LABVIEW 3.1.1 (National Instruments, Austin, TX) and stored for subsequent analysis. Antropyloroduodenal pressures were analyzed for the number and amplitude of isolated pyloric pressure waves and pressure waves in the antrum and duodenum with the use of custom-written software (Gastrointestinal Motility Unit, University Hospital Utrecht, The Netherlands (24)), modified to our requirements. Basal pyloric pressures (tone) were also calculated for each minute by subtracting the mean basal pressure (excluding phasic pressures) recorded at the most distal antral side hole from the mean basal pressure recorded at the sleeve (25), with the use of custom-written software (MAD; Prof Charles-Henri Malbert, French National Institute for Agricultural Research, Rennes, France). Phasic pressure waves in the antrum and isolated pyloric pressure waves were defined by an amplitude ≥ 10 mmHg, with a minimum interval of 15 s between peaks. Phasic duodenal pressure waves were defined by an amplitude ≥ 10 mmHg, with a minimum interval of 3 s between peaks (24).

**Plasma concentrations of CCK and PYY**

Venous blood samples (10 mL) were collected in ice-chilled EDTA-treated tubes containing 400 kIU aprotinin (Trasylol; Bayer Australia Ltd, Pymble, Australia)/mL blood. Plasma was separated by centrifugation (1488 × g, 15 min, 4 °C) within 30 min of collection and stored at −70 °C until assayed.

Plasma CCK concentrations (in pmol/L) were determined after ethanol extraction with the use of a previously described radioimmunoassay (26). A commercially available antibody (C258, Lot 105H4852; Sigma Chemical, St Louis, MO) raised in rabbits against the synthetic sulfated CCK-8 was used. This antibody binds to all CCK peptides containing the sulfated tyrosine residue in position 7, shows a 26% cross-reactivity with unsulfated CCK-8, <2% cross-reactivity with human gastrin, and does not bind to structurally unrelated peptides. The intraassay CV was 9%, and the interassay CV was 27%, with a detection limit of 1 pmol/L.

Plasma PYY concentrations (in pmol/L) were measured by radioimmunoassay with the use of an antiserum (kindly donated by Dr B Otto, Medizinische Klinik, Klinikum Innenstadt, University of Munich, Munich, Germany) raised in rabbits against human PYY-1–36 (Sigma-Aldrich, St Louis, MO); ie, the assay does not distinguish between PYY-1–36 and PYY-3–36. This antiserum showed <0.001% cross-reactivity with human pancreatic polypeptide or sulfated CCK-8 and 0.0025% cross-reactivity with human neuropeptide Y. Tracer (NEX3410) was purchased from Perkin-Elmer (Boston, MA). Standards (1.6–50 fmol/tube) or samples (200 μL plasma) were incubated in assay buffer (0.05 mol/L phosphate containing 0.5% bovine serum albumin and 0.02% azide, pH 7.4) with 100 μL antiserum at a final dilution of 1:10 000 for 24 h at 4 °C, then 100 μL iodinated PYY (10 000 cpm) was added, and the incubation was continued for another 24 h. Separation of the antibody-bound tracer from free tracer was achieved by adding 200 μL of dextran-coated charcoal containing gelatin (0.015 g gelatin, 0.09 g dextran, 0.15 g charcoal/30 mL assay buffer), incubating at 4 °C for 20 min, then centrifuging at 2000 × g at 4 °C for 25 min. Radioactivity of the bound fraction was determined by counting the supernatant fluids in a gamma counter. The intraassay CV was 12.3%, and the interassay CV was 16.6%, with a detection limit of 1.5 pmol/L.

**Data and statistical analysis**

Baseline (0) values were calculated as the means of values obtained at t = −10 and 0 min for VAS scores and hormones, and between t = −10 and 0 min for basal pyloric pressures and total numbers and mean amplitudes of isolated pyloric pressure waves and for antral and duodenal pressure waves. During the infusion period basal pyloric pressures were expressed as means during 10-min periods, whereas numbers and amplitudes of isolated pyloric pressure waves and antral and duodenal pressure waves were expressed as total numbers and mean values, respectively. All data are expressed as changes from baseline, except plasma concentrations of CCK and PYY, which are shown as raw data.

Repeated-measures analysis of variance (ANOVA), with time and treatment as within-subject factors, was used to analyze the data with multiple measurements within one treatment, ie, VAS scores, basal pyloric pressures, and plasma hormone concentrations. One-factor ANOVA was used to assess the effect of treatment on those variables with only 1 data point per treatment, ie, total numbers and mean amplitudes of isolated pyloric pressure waves, antral and duodenal pressure waves, energy intake, and macronutrient distribution. Post hoc comparisons, with the use of Student’s t test, adjusted for multiple comparisons by Bonferroni’s correction, were performed if ANOVAs showed significances. VAS scores obtained after the test meal were not evaluated statistically, because we assumed a priori that the amount eaten would differ substantially between treatments. Statistical significance was accepted at P < 0.05, and data are presented as means ± SEMs. The statistical analysis was performed with the use of STAT VIEW (version 5.0; Abacus Concepts, Berkeley, CA).

**RESULTS**

All subjects completed the 3 study days and tolerated the experimental conditions well.

**Antropyloroduodenal motility**

**Antral pressure waves**

A significant effect of treatment was observed on both the number and amplitude of antral pressure waves (P < 0.001) (Table 1). C12 and C18 both reduced the number and amplitude of antral pressure waves substantially compared with control (P < 0.01), with no difference between them.
Pyloric pressures

Basal pyloric pressure. A significant treatment \times time interaction was observed for basal pyloric pressure ($P < 0.05$) (Figure 1). C12 and C18 both increased basal pyloric pressure compared with control, C12 between $t = 0$ and 60 min ($P < 0.01$) and C18 between $t = 10$ and 40 min ($P < 0.05$). The effect of C12 was greater than that of C18 between $t = 20$ and 60 min ($P < 0.01$).

Isolated pyloric pressure waves. A significant effect of treatment was observed on the number and amplitude of isolated pyloric pressure waves ($P < 0.01$) (Table 1). C12 and C18 caused an approximately 3-fold increase in the number compared with control ($P < 0.01$), with no difference between them. C12 and C18 both also increased the amplitude of isolated pyloric pressure waves compared with control ($P < 0.05$), with no difference between them.

Duodenal pressure waves

A significant effect of treatment was observed on the amplitude, but not the number, of duodenal pressure waves ($P < 0.01$). C12 and C18 both reduced the amplitude of duodenal pressure waves modestly compared with control ($P < 0.05$), with no difference between them.

TABLE 1

<table>
<thead>
<tr>
<th>Total numbers and mean amplitudes of antral, pyloric, and duodenal pressure waves during 60-min intraduodenal infusion of lauric acid (C12), oleic acid (C18), or control (0.9% saline)</th>
<th>Control</th>
<th>C12</th>
<th>C18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antral pressure waves</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>50 ± 13</td>
<td>0 ± 2</td>
<td>5 ± 2</td>
</tr>
<tr>
<td>Amplitude (mm Hg)</td>
<td>62 ± 13</td>
<td>19 ± 6</td>
<td>22 ± 6</td>
</tr>
<tr>
<td>Isolated pyloric pressure waves</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>38 ± 7</td>
<td>121 ± 17</td>
<td>120 ± 18</td>
</tr>
<tr>
<td>Amplitude (mm Hg)</td>
<td>23 ± 3</td>
<td>30 ± 4</td>
<td>32 ± 4</td>
</tr>
<tr>
<td>Duodenal pressure waves</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No.</td>
<td>451 ± 83</td>
<td>339 ± 53</td>
<td>300 ± 55</td>
</tr>
<tr>
<td>Amplitude (mm Hg)</td>
<td>29 ± 2</td>
<td>25 ± 2</td>
<td>24 ± 1</td>
</tr>
</tbody>
</table>

1 All values are $\bar{x} \pm$ SEM; $n = 13$. There were no significant differences between C12 and C18.

2 Significantly different from control, $P < 0.05$.

Plasma hormone concentrations

Plasma CCK

Baseline plasma CCK concentrations did not differ among study days. A significant treatment \times time interaction was observed for plasma CCK concentrations ($P < 0.001$) (Figure 2). C12 and C18 both increased plasma CCK between $t = 10$ and 60 min compared with control ($P < 0.001$), with a slightly greater effect of C18 compared with C12 between $t = 10$ and 20 min ($P < 0.05$). The rise in plasma CCK in response to both C12 and C18 occurred rapidly, ie, in the first 10 min, and thereafter concentrations plateaued until the end of the infusion. Plasma CCK

![Figure 1](https://academic.oup.com/ajcn/article-abstract/87/5/1181/4650862)

![Figure 2](https://academic.oup.com/ajcn/article-abstract/87/5/1181/4650862)
immediately before the meal, ie, at t = 60 min, did not differ between C12 and C18.

**Plasma PYY**

Baseline plasma concentrations of PYY were (inexplicably) slightly higher on the control day compared with both C12 and C18 (P < 0.001), with no difference between C12 and C18. A significant treatment x time interaction was observed for plasma PYY (P < 0.001) (Figure 2). C12 and C18 both increased plasma PYY, between t = 40 and 60 min and t = 30 and 60 min, respectively, compared with control (P < 0.001). The increase in plasma PYY in response to both C12 and C18 was progressive and evident from ≈30 min. The effect of C18 was greater than that of C12 between t = 30 and 60 min (P < 0.001).

**Appetite perceptions and energy intake**

No effect of treatment was observed on perceptions of hunger, fullness, nausea, or bloating (data not shown). Scores did not change significantly from baseline during the 60-min infusion period.

A significant effect of treatment was observed on energy intake (P < 0.05) (Table 2). Energy intake after C12 was lower than after control and C18 by ≈10% (P < 0.05), with no difference between control and C18. A trend (P = 0.06) was observed for C12 to reduce the amount (in g) of food ingested compared with both control and C18 (Table 2). No difference was observed in the percentage of fat, carbohydrate, or protein ingested between treatments (Table 2).

**Relations between antropyloroduodenal pressures, plasma hormone concentrations, and appetite perceptions with energy intake**

No significant relations were observed between antropyloroduodenal pressures, plasma hormone concentrations, or appetite perceptions with energy intake (data not shown).

**DISCUSSION**

The present study compared the effects of equicaloric intraduodenal infusions of C12 and C18 on antropyloroduodenal motility, gastrointestinal hormone secretion, and energy intake and established that, at the load given, C12 and C18 both 1) reduced the number and amplitude of antral pressure waves and reduced the amplitude of duodenal pressure waves, 2) increased the number and amplitude of phasic pyloric pressure waves and basal pyloric pressure, and 3) stimulated plasma concentrations of CCK and PYY. Arguably of most interest is that the stimulation of basal pyloric pressure by C12 was substantially greater than that of C18, and that C12, but not C18, reduced energy intake. These differential effects were not apparently attributable to effects on CCK and PYY secretion; in fact, the stimulation of PYY by C18 was clearly greater than that induced by C12.

In rats, infusion of C12 into the colon suppressed energy intake more than an equicaloric infusion of C18, whereas equimolar intraduodenal infusions of C12 and C18 suppressed energy intake to the same extent (14), suggesting that, when given at equicaloric loads, C12 might suppress energy intake more than C18. Therefore, we hypothesized in our study that in humans intraduodenal C12 would suppress energy intake to a greater extent than C18, when administered at the same energy load. Indeed, C12 suppressed energy intake by ≈550 kJ, or ≈10%, compared with control, whereas C18 was ineffective.

In contrast, our hypothesis that specific changes in gastrointestinal function would underlie the greater suppression of energy intake by C12 proved incorrect. We expected the suppression of energy intake to be associated with a greater modulation of antropyloroduodenal motility, particularly the stimulation of isolated pyloric pressure waves (Brennan IM, Little TJ, Feltrin KL et al, unpublished observations, 2008) (27) and hormone secretion (28, 29); however, C12 and C18 both stimulated isolated pyloric pressures and plasma CCK comparably, and, although C12 increased basal pyloric pressure more than C18, C18 increased PYY concentrations slightly more than C12. In relation to the latter, it should be recognized that our assay did not specifically measure PYY-3–36, the form that has been implicated particularly in feeding inhibition (28). In dogs, electrical stimulation of the pylorus, increasing both tonic and phasic pressures, is associated with suppression of energy intake (27). A recent study from our laboratory established that there is an inverse relation between energy intake and the number of isolated pyloric pressure waves in humans; ie, the stimulation of pyloric motility is associated with the suppression of energy intake (Brennan et al, unpublished observations, 2008). The administration of a CCK receptor antagonist in humans (29, 30) and PYY receptor antagonist in animals (28) abolishes the suppressive effect of fat on energy intake, showing that CCK and PYY, at least in part, mediate the effects of fat on energy intake. Hence, we postulated that a greater suppression of energy intake by C12 would be associated with greater stimulation of isolated pyloric pressure waves, greater hormone secretion, or both compared with C18, neither of which proved to be the case.

Several other possibilities may explain the differences, or discrepancies, in effects between C12 and C18 on energy intake. 1) Interestingly, basal pyloric pressures were markedly greater during the C12 infusion, despite comparable plasma CCK concentrations between C12 and C18, although the difference in energy intake between C12 and C18 was not related to changes in basal pyloric pressure. Similarly, equimolar amounts of C12 were reported to stimulate much higher outputs of pancreatic bicarbonate per output of pancreatic protein secretion than did C18 (7). These 2 observations suggest important, qualitative differences in how the gastrointestinal tract senses and responds to C12 compared with C18, the reasons for which are currently undefined. 2) Shorter-chain fatty acids (including C12) are absorbed 10 times more rapidly than longer-chain fatty acids (including C18) (31). In rats, when maltose or lactose is confined to a fixed segment of proximal small intestine, so that the slowly absorbed

---

**TABLE 2**

Energy intake from the buffet meal, and macronutrient distribution, after 60-min intraduodenal infusion of lauric acid (C12), oleic acid (C18), or control (0.9% saline)1

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>C12</th>
<th>C18</th>
</tr>
</thead>
<tbody>
<tr>
<td>Energy intake (kcal)</td>
<td>1265 ± 92</td>
<td>1134 ± 80</td>
<td>1249 ± 72</td>
</tr>
<tr>
<td>Amount consumed (g)</td>
<td>1206 ± 127</td>
<td>1062 ± 120</td>
<td>1200 ± 113</td>
</tr>
<tr>
<td>Energy (%)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fat</td>
<td>34 ± 2</td>
<td>35 ± 3</td>
<td>34 ± 2</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>43 ± 3</td>
<td>43 ± 3</td>
<td>45 ± 3</td>
</tr>
<tr>
<td>Protein</td>
<td>22 ± 1</td>
<td>23 ± 1</td>
<td>22 ± 1</td>
</tr>
</tbody>
</table>

1 All values are x ± SEM; n = 13.
2 Significantly different from control and C18, P < 0.05.
lactose cannot activate feedback from the ileum, maltose suppresses energy intake more than lactose, which is known to be absorbed ≈10% as fast as maltose (32). This observation with carbohydrates suggests that the rate of flux across enterocytes within a fixed length of small intestine determines the magnitude of the effect on energy intake that is generated by that intestinal segment. No comparable experiments have been performed with C12 compared with C18 to confirm or refute this idea with fatty acids. 3) Shorter-chain fatty acids are oxidized more extensively in the liver to anorexigenic ketone bodies than are longer-chain fatty acids (33) and undergo a more extensive conversion to malonyl-coA. Malonyl-coA is believed by some to be an important intracellular signal of energy stores in the hypothalamus that modulates feeding behavior (34). Thus, a third possibility to explain the greater inhibition of energy intake by C12 than by C18 is a significant difference in postabsorptive metabolism that leads acutely to a cascade of anorexigenic signals. Differences in saturation between C12 (saturated) and C18 (monounsaturated) are unlikely to be responsible for the observed effects on energy intake, considering that increasing unsaturation of fatty acids was reported to be associated with greater suppression of energy intake in humans (35, 36).

As discussed, fatty acids empty from the stomach into the small intestine at rates between 0.2 and 0.4 kcal/min (9), and we have established that the maximum load of intraduodenal C12 that suppresses energy intake in the absence of gastrointestinal adverse effects is 0.4 kcal/min, at concentrations between 56 and 72 mmol/L (10, 16, 17). Therefore, in our study C18 was also infused at 0.4 kcal/min to match this maximal load of C12, which was probably insufficient for an effect on energy intake, despite effects on gastrointestinal function. The latter is supported by the findings from one study, in which C18 suppressed subsequent energy intake when infused at the reported rate of 0.77 kcal/min for 60 min (13). Nevertheless, it is also possible that in our study both C12 and C18 may have maximally suppressed antral pressures and stimulated isolated pyloric pressures [eg, the mean number of isolated pyloric pressure waves during C12 and C18 infusions was ≈2/min, which is close to the maximum of ≈3/min (2), and there were virtually no antral waves], precluding quantification of potential differences between C12 and C18. Accordingly, further studies that determine the effects of increasing doses of C18 on energy intake and their relation with gastrointestinal function in humans would be of interest.

In conclusion, this study has shown that, at the load administered, C12, but not C18, suppresses energy intake and that C12 is a more potent stimulant of pyloric tone. This suppression of energy intake could not be related directly to changes in gastrointestinal function, considering that both C12 and C18 suppressed antral pressure waves, stimulated isolated pyloric pressures, and increased plasma CCK concentrations to the same extent, whereas C18 increased PYY concentrations more than C12. Taken together, our data confirm the potent appetite-suppressant effects of intraduodenal C12, but also they suggest that this may not be accounted for entirely by the actions of C12 on gastrointestinal function.

The author’s responsibilities were as follows—KLF: was involved in study design and coordination, subject recruitment, study performance, data and statistical analyses, data interpretation, and drafting of the manuscript; TJL: was involved in study design and performance, subject recruitment, data analysis and interpretation, and drafting of the manuscript; JHM: was involved in the study concept, data interpretation, and drafting of the manuscript; MH: was involved in the study concept, data interpretation, and drafting of the manuscript; TR: was involved in the study concept and design; CF-B: was involved in the study concept and design, data analysis and interpretation, and drafting of the manuscript and had overall responsibility for the study; JW: performed the radioimmunoassays. None of the authors had a personal or financial conflict of interest.

REFERENCES


