



Effects of small-intestinal fat and carbohydrate infusions on appetite and food intake in obese and nonobese men¹⁻³

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ABSTRACT To determine whether the satiating effects of nutrients in the small intestine are lower in obese than in nonobese people, 9 healthy, obese men [age: 18–33 y; body mass index (BMI; in kg/m²) 30.4–40.8] and 11 healthy, nonobese men (age: 18–33 y; BMI: 19.1–26.4) received an intraduodenal infusion of saline (control), lipid (11.97 kJ/min, or 2.86 kcal/min), or glucose (11.97 kJ/min) for 120 min on separate days. Fullness, hunger, and nausea were assessed by visual analogue scales. After the infusions, a meal was offered and food intake was quantified. There was no difference in appetite ratings between the obese and nonobese subjects during the infusions, in the amount or macronutrient composition of food eaten after the infusions, or in the time taken to eat the meals. Both the lipid and glucose infusions were associated with greater fullness than the control infusion. The energy content of the food eaten was less after the lipid infusion than after either the control or glucose infusion ($P < 0.01$); lipid infusion suppressed energy intake by 22% compared with the control infusion and by 15% compared with the glucose infusion. Suppression of energy intake after intraduodenal nutrient infusions was due to slower eating ($P < 0.01$). Intraduodenal infusions of fat suppressed appetite and food intake more than did equienergetic infusions of carbohydrate in both obese and nonobese young men, and the responses to intraduodenal fat and glucose were not affected by obesity. The latter observation suggests that established obesity is not associated with reduced small-intestinal responses to dietary fat or carbohydrate. *Am J Clin Nutr* 1999;69:6–12.

KEY WORDS Appetite, hunger, fat, carbohydrate, small intestine, duodenum, satiety, obesity, men

INTRODUCTION

Although numerous environmental and genetic factors contribute to the development of obesity, it is implicit that energy intake must exceed energy expenditure for a significant time during the development of obesity and closely match it during the maintenance of an increased body weight. Obese people usually expend more energy than do lean people in absolute terms and similar amounts when corrected for differences in total body weight and fat-free mass (1, 2). In large part this is both because basal metabolic rate, which accounts for approximately two-thirds of total energy expenditure, and the energy expended in performing physical activities increase in response to the

requirements of increasing body weight (3). Therefore, of necessity, most stable-weight, obese people have a greater energy (food) intake than do lean people.

Consumption of high-fat diets favors the development of obesity in several species, including humans (4–7). This is mainly due to an increase in energy intake because high-fat foods are more energy dense and are generally highly palatable and so are easily consumed in excess (8). Consumption of high-fat foods may also lead to greater weight gain than does the equienergetic consumption of high-carbohydrate foods (9). Obese people express an increased preference for high-fat foods (10) and there is evidence that their diets contain a higher proportion of fat than those of nonobese people (11, 12). This finding is consistent with evidence that dietary fat is less satiating in obese than in nonobese people (13, 14).

The above-mentioned observations can be interpreted to indicate that obesity is, at least in part, a disorder of appetite control associated with impaired defenses against overeating (15), particularly overconsumption of fat. The regulation of appetite is complex and is thought to depend on a central feeding drive, originating mainly in the hypothalamus, which is counteracted by peripheral satiety signals (16). Powerful satiety signals arise from the gastrointestinal tract in response to eating. They include those produced by orosensory stimulation (17, 18), gastric distension (19), and perhaps most importantly, the interaction of nutrients with receptors in the lumen of the small intestine (16). The small intestine is an important source of satiety signals and it has been well documented that infusion of nutrients into the small intestine is associated with suppression of food intake in humans, to a much greater extent than when nutrients are given intravenously (20, 21). The interaction of nutrients in the small intestine stimulates the release of putative satiety hormones,

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²Supported by a Pharmacia Research Fellowship of the Royal Australasian College of Physicians and an Establishment Grant for Clinical Investigators from the Sylvia and Charles Viertel Charitable Foundation (to IMC).

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Received January 29, 1998.

Accepted for publication May 29, 1998.

such as cholecystokinin (22), glucagon-like peptide 1 (23), and amylin (24); slows gastric emptying, thereby prolonging postprandial gastric distension (16, 25); and modulates the sensations arising from gastric distension so that they are perceived more as a physiologic fullness than as discomfort (26, 27). Nutrients in the small intestine also delay the passage of food through the small intestine (28, 29), thus prolonging the time available for absorption and giving rise to early postabsorptive effects such as the reversal of hunger-inducing hypoglycemia (23, 30).

We showed recently in normal subjects that the effects of intraduodenal nutrient infusions on satiety vary between nutrient classes. Fat, in the form of a triacylglycerol emulsion, suppresses short-term hunger ratings and food intake more than does an equienergetic infusion of carbohydrate (25% glucose) in normal-weight men (31, 32). This finding contrasts with reports that fat is, if anything, less satiating than is carbohydrate when administered orally or intragastrically (5, 13, 14, 33–35) and highlights the importance of the small intestine in mediating the satiety response to fat. Impairment of the satiating effects of small-intestinal nutrients, particularly fat, would favor the development and maintenance of obesity. In view of the greater food intake by obese people, associated with a possible reduction in the satiating effects of fat (13, 14), we hypothesized that obese people have a reduced small-intestinal satiety response to nutrients, particularly fat. The present study was designed to test this hypothesis.

SUBJECTS AND METHODS

Subjects

Eleven healthy, nonobese, young men with a mean body mass index (BMI; in kg/m^2) of 22.6 ± 0.6 (range: 19.1–26.4) and a mean age of 24.1 y (range: 18–33 y), and 9 healthy, obese, young men with a BMI >30 (\bar{x} : 34.9 ± 1.3 ; range: 30.4–40.8; $P < 0.01$ compared with nonobese men) and a mean age of 23.8 y (range: 18–33; $P > 0.05$ compared with nonobese men) were recruited by advertisement. All subjects were nonsmokers who consumed <20 g alcohol/d. None of the subjects were dieting in an attempt to lose or gain weight, had experienced a loss or gain of $>5\%$ of body weight in the 3 mo before enrollment, had a history of gastrointestinal disease or surgery, or were taking medication at the time of the study. The protocol was approved by the Human Ethics Committee of the Royal Adelaide Hospital, and each subject gave written, informed consent.

Protocol

Subjects completed a 5-d diet diary before the first study day to assess baseline eating habits and were instructed to maintain their normal diet between study days. Subjects also completed a questionnaire to assess dietary restraint (36). Subjects underwent 3 studies in a single-blind, randomized manner during which intraduodenal infusions of glucose, lipid, or saline (control) were administered. The 3 studies were separated by ≥ 7 d. At a screening visit ≤ 2 wk before the first study day, body fat was measured by bioelectrical impedance (Bodystat 1500; Bodystat Ltd, Isle of Man, United Kingdom) and the subjects were familiarized with the questionnaires and the technique of intraduodenal nutrient administration (by having the tube inserted into the stomach and then withdrawn).

On each study day, subjects arrived at the laboratory at 0800 after an 11-h fast from food and all fluid except water and from

water after 0630. On arrival, subjects were weighed, an intravenous cannula was placed in their right arm vein for blood sampling, and a silicone rubber manometric assembly (4 mm external diameter) was inserted into their stomach via an anesthetized nostril. The tip of the tube was allowed to pass into the duodenum by peristalsis. A subcutaneous saline-filled reference electrode (20-gauge intravenous cannula) was inserted into the subjects' left forearms to measure antroduodenal transmucosal potential difference, so that the position of the tube could be monitored continuously (31, 37). All subjects recorded their ratings of appetite on visual analogue scales at 0 min (the time at which the tube passed into the duodenum), then every 20 min to 140 min, and then at 170 and 200 min; venous blood was collected at these same times for measurement of glucose concentrations with a portable blood glucose meter (Medisense Companion 2 Blood Glucose System; Medisense, Waltham, MA). At 20 min, an infusion of 0.9% saline (control) at a rate of 3 mL/min, 25% glucose (3989 kJ/L; Baxter Healthcare, Old Toongabbie, Australia) at a rate of 3 mL/min, or 10% Intralipid (triacylglycerol emulsion, 4602 kJ/L; Kabi Pharmacia Ltd, Milton Keynes, United Kingdom) at a rate of 2.6 mL/min plus 0.9% saline at a rate of 0.4 mL/min was started and continued for 120 min. Each subject therefore received the same volume (3 mL/min) during all infusions and the same energy load [11.97 kJ/min (2.86 kcal/min); total: 1436 kJ] during the glucose and triacylglycerol emulsion infusions. At 140 min, the intraduodenal infusions were stopped and the tube removed. Subjects were then presented with a cold buffet meal, prepared in excess of what they would normally be expected to eat, and invited to eat as much as they wanted in the next 30 min. The meal consisted of 8 slices of bread (4 white and 4 whole meal), 20 g nondairy spread, 20 g mayonnaise, 4 slices of shoulder ham, 4 slices of chicken, 4 slices of cheddar cheese, sliced tomato and cucumber, lettuce, 300 mL full-fat milk, 300 mL unsweetened orange juice, 200 g low-fat strawberry yogurt, 200 g chocolate custard, 50 g vanilla ice cream, an apple, a pear, and a banana. The total energy content of the food offered was ≈ 10050 kJ. The rate and duration of ingestion and the total amount of food eaten was recorded. The DIET4/NUTRIENT CALCULATION software package (Xyris Software, Highgate Hill, Australia) was used to determine energy intakes and the macronutrient composition (percentage protein, carbohydrate, and fat) of the meal (31).

Assessment of appetite

Appetite was assessed with 10-cm linear scales (38). Hunger, fullness, and nausea were quantified; other questions related to drowsiness, happiness, anxiety, and strength. Subjects were asked to make a single vertical mark on each scale somewhere between the 0- and 10-cm extremes (eg, full to not full) to indicate their feelings at that time point. The 0- and 20-min values were averaged to produce a baseline value and the change in ratings from baseline was quantified (31).

Statistical analyses

Comparisons of baseline values between the obese and nonobese groups were performed by using Student's unpaired t tests because these data were normally distributed. Similarly, comparisons between values at the beginning and end of the study (eg, body weight) within each weight group were performed by using Student's paired t tests. Relations between variables were determined by linear regression analysis. Energy and

macronutrient intakes from the test meal, blood glucose concentrations during intraduodenal infusions, and the effects of the intraduodenal infusions on ratings of hunger, fullness, and nausea during the treatment infusions (baseline to 140 min) were analyzed by using two- and three-factor repeated-measures analysis of variance (ANOVA) with the SUPERANOVA program (version 1.11; Abacus Concepts, Berkeley CA). When the P value of the ANOVA was <0.05 , multiple pairwise comparisons of all groups were performed by using the Student-Neuman-Keuls test. Because the percentage of each macronutrient (protein, carbohydrate, and fat) eaten in the test meal was dependent on that of the other macronutrients, in the post-ANOVA analyses of percentage macronutrient intakes an adjustment was made for multiple comparisons by using the Sidak method (39). Data are presented as means \pm SEs. A P value <0.05 was considered significant in all analyses.

RESULTS

Subjects

The percentage body fat in the obese subjects was more than double that in the nonobese subjects, as assessed by bioelectrical impedance: $31.7 \pm 1.4\%$ (range: 28.6–38.8%) compared with $14.9 \pm 1.1\%$ (9.5–20.2%) ($P < 0.001$). As assessed by the questionnaire of Stunkard and Messick (36), the obese subjects had higher measures of restrained eating (6.3 ± 0.7 compared with 3.7 ± 0.6 , $P = 0.013$) and nonsignificantly higher measures of disinhibition (7.3 ± 1.3 compared with 4.6 ± 1 , $P = 0.11$) than the nonobese subjects, and similar ratings of hunger (5.3 ± 1.1 compared with 5.1 ± 0.8 , respectively). Two of the obese subjects did not complete a 5-d diet diary before the study. In the other 7 obese subjects, self-reported energy intake was nonsignificantly less than in the nonobese subjects (7435 ± 460 kJ/d compared with 9046 ± 540 kJ/d, $P = 0.053$); energy intake per kilogram lean body mass was significantly less than in the nonobese subjects (106 ± 4.6 kJ/d compared with 150 ± 7.9 kJ/d, $P < 0.001$). There was no significant difference in the macronutrient composition of the food eaten by the 2 groups (data not shown).

The tube entered the duodenum after 5–160 min (mean: 42 ± 4 min) and this time did not differ between the study conditions or weight groups. The study protocol and intraduodenal infusions were well tolerated. Body weights on days 1 and 3 were 106.03 ± 4.9 and 106.06 ± 5.2 kg for the obese and 71.4 ± 2.3 and 70.9 ± 2.2 kg for the nonobese subjects, respectively.

Appetite ratings

Before the intraduodenal infusions started, hunger was greater in the obese (5.2 ± 0.4 cm) than in the nonobese (4 ± 0.25 cm) subjects ($P = 0.008$; mean of 0- and 20-min values). There were no significant differences between the obese and nonobese groups in ratings of fullness (3.95 ± 0.4 cm and 3.37 ± 0.12 cm, respectively) or nausea (1.54 ± 0.3 and 1.53 ± 0.3 cm, respectively).

During the intraduodenal infusions (20–140 min), hunger ratings were not significantly different between the obese and nonobese subjects or between different treatments, but were affected by time ($P = 0.03$) (Figure 1); subjects rated themselves as significantly more hungry at the end (140 min) than at the beginning (20 min, $P = 0.004$) of the infusions. There were no interactions between the effects of treatment, body weight, or time.

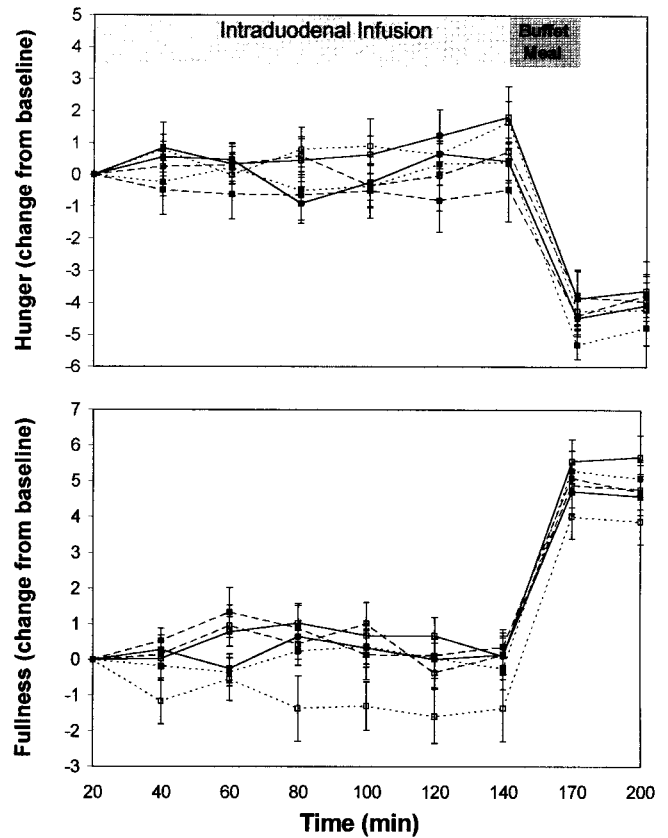


FIGURE 1. Mean (\pm SE) changes from baseline (mean of 0- and 20-min values) in subjective sensations of hunger and fullness in nonobese (■) and obese (□) subjects receiving intraduodenal infusions of saline (control; ····), glucose (---), and lipid (—) administered from 20 to 140 min. There were no significant differences in hunger or fullness ratings between nonobese and obese subjects during any treatment. Fullness ratings were greater after glucose ($P = 0.004$) and lipid ($P = 0.01$) infusions than after saline.

During the infusions, fullness ratings were not significantly different between the obese and nonobese subjects (Figure 1), but were affected by the type of infusion ($P = 0.008$); both glucose ($P = 0.004$) and lipid ($P = 0.01$) infusions were associated with greater fullness than the saline infusion. There was no significant difference between the effects on fullness of the 2 nutrients. There was no effect of time on fullness ($P = 0.08$) nor were there any interactions between the effects of treatment, body weight, or time (data not shown).

During the infusions, nausea ratings were not significantly different between the obese and nonobese subjects nor between the different treatments, but were affected by time ($P = 0.008$); subjects rated themselves as significantly more nauseated at the end than at the beginning of the infusions (20 compared with 120 and 140 min, 40 compared with 120 and 140 min). There were no interactions between the effects of treatment, body weight, or time.

Food intake

None of the subjects ate all the food offered and none ate for the full 30 min allotted. Energy intakes from the test meals on the 3 study days are shown in Figure 2; the mean energy intake was 3636 ± 170 kJ (869 ± 41 kcal).

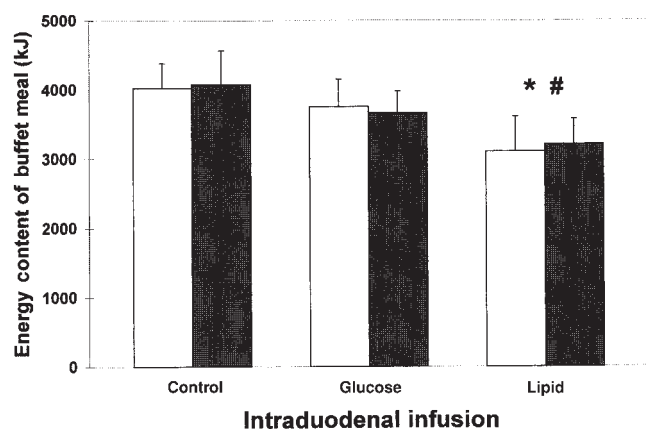


FIGURE 2. Mean (\pm SE) energy content of the buffet meal consumed after intraduodenal infusions of saline (control) or isoenergetic infusions of glucose and lipid in nonobese (\square) and obese (\blacksquare) subjects. *Significantly different from control, $P < 0.05$. #Significantly different from glucose, $P < 0.05$. There were no significant differences between obese and nonobese subjects.

Effect of intraduodenal infusion type

Characteristics of the meals eaten after the 3 different intraduodenal infusions by the obese and nonobese subjects are shown in **Table 1**. The weight ($P = 0.01$) and energy ($P = 0.006$) contents of the food eaten were less after lipid infusion than after either the control or glucose infusion. Lipid infusion suppressed energy intake by 22% compared with the control (saline) infusion ($P < 0.05$) and by 15% compared with the glucose infusion ($P < 0.05$), whereas glucose infusion was associated with a nonsignificant 9% suppression of intake compared with the control infusion. The suppressive effect of intraduodenal nutrient infusions on subsequent food intake was due to a reduction in the rate of energy ingestion ($P = 0.005$), without any effect on the duration of eating. Subjects ate 11% and 15% more slowly (fewer kJ/min) after glucose and lipid infusions, respectively, than after the control infusion. The ANOVA indicated that the intraduodenal nutrient infusions increased the relative carbohydrate content ($P = 0.03$) and decreased the relative fat content ($P = 0.02$) of the food eaten, but had no effect on the protein content (Table 1). However, after adjustment for multiple comparisons, these effects on relative carbohydrate and fat intakes were not significant.

Effect of body weight

The obese subjects did not differ from the nonobese subjects in any aspect of their test meal consumption. There was no effect of body weight on the weight or energy content of the food eaten during the test meal; the mean energy intake per study day was only 0.5% different between the obese (3648 ± 230 kJ) and nonobese (3628 ± 247 kJ) subjects. There was no interaction between infusion type and body weight in the effect on energy intake or weight of the food eaten. The macronutrient composition of the food eaten was also not significantly different between obese and nonobese subjects (Table 1) and there was no interaction between body weight and infusion type for any macronutrient (data not shown). There was a nonsignificant trend for the obese subjects to eat faster ($P = 0.25$) and for less time ($P = 0.25$) than the nonobese subjects (Table 1), but no interaction between body weight and infusion type for either rate or duration of energy ingestion.

TABLE 1

Characteristics related to the test meals eaten by 9 obese and 11 non-obese men after 2-h intraduodenal infusions of saline (control), glucose, and lipid¹

Characteristics related to the test meal	Control	Glucose	Lipid
Weight of food eaten (g)			
Obese	921 \pm 104	866 \pm 81	773 \pm 81
Nonobese	961 \pm 75	926 \pm 65	735 \pm 113
Mean	943 \pm 61	899 \pm 50	752 \pm 70 ^{2,3}
Energy intake (kJ)			
Obese	4074 \pm 491	3659 \pm 317	3211 \pm 367
Nonobese	4020 \pm 358	3755 \pm 396	3109 \pm 506
Mean	4044 \pm 288	3712 \pm 254	3155 \pm 316 ^{2,3}
Duration of eating (min)			
Obese	16.5 \pm 1.6	18.7 \pm 2	16.1 \pm 1.2
Nonobese	19.3 \pm 1.3	20.1 \pm 0.9	17.7 \pm 1.8
Mean	18 \pm 1.1	19.4 \pm 1	17 \pm 1.1
Rate of energy ingestion (kJ/min)			
Obese	247 \pm 16	204 \pm 19	200 \pm 22
Nonobese	208 \pm 15	186 \pm 16 ³	177 \pm 22
Mean	226 \pm 12	193 \pm 12	187 \pm 15 ³
Protein (% of energy)			
Obese	18.8 \pm 1.6	18.2 \pm 1.4	16.7 \pm 1.4
Nonobese	19.2 \pm 1	17.9 \pm 0.5	19.3 \pm 1.1
Mean	19 \pm 0.9	18.1 \pm 0.7	18 \pm 0.9
Fat (% of energy)			
Obese	34.1 \pm 4.3	33.3 \pm 3.7	31.2 \pm 4.1
Nonobese	32.5 \pm 4.2	30.1 \pm 2.5	28.6 \pm 2.5
Mean	33.2 \pm 2	31.6 \pm 2.1	29.9 \pm 2.3 ³
Carbohydrate (% of energy)			
Obese	47.1 \pm 4.2	48.2 \pm 3.6	52.1 \pm 4.1
Nonobese	48.5 \pm 1.6	52 \pm 2.7	52 \pm 2.3
Mean	47.9 \pm 2	50.3 \pm 2.2	52.1 \pm 2.2 ³

¹ $\bar{x} \pm$ SE. There were no significant differences between obese and nonobese subjects and there was no significant interaction between body type and treatment for any index.

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

³Significantly different from control, $P < 0.05$.

Relation between appetite ratings and food intake

Changes (Δ) in hunger and fullness ratings (mean of 120- and 140-min values minus the mean of 0- and 20-min values) on the 10-cm visual analogue scales during the intraduodenal infusions were inversely related in all subjects (Δ hunger: 0.52 ± 0.31 cm; Δ fullness: -0.12 ± 0.22 cm; $r = -0.54$, $P < 0.0001$) and for the lean (Δ hunger: 0.1 ± 0.4 cm; Δ fullness: 0.11 ± 0.23 cm; $r = -0.53$, $P = 0.0015$) and obese (Δ hunger: 1.02 ± 0.42 cm; Δ fullness: -0.4 ± 0.37 cm; $r = -0.54$, $P = 0.0045$) subjects alone. There was no significant relation between the ratings of hunger before the meal, either the absolute change or the change from baseline, and the amount of energy consumed during the meal (data not shown). In contrast, analysis of all subjects indicated a significant inverse relation between energy consumption (3636 ± 170 kJ) and perception of fullness immediately before the meal, both for the absolute change (3.5 ± 0.25 cm; $r = -0.36$, $P = 0.005$) and the change from baseline (-0.12 ± 0.22 cm; $r = -0.29$, $P = 0.03$).

Blood glucose concentrations

Baseline venous glucose concentrations did not differ significantly between obese (5.1 ± 0.2 mmol/L) and nonobese

(5.0 ± 0.3 mmol/L) subjects. Venous glucose was unaffected by intraduodenal lipid or saline in both obese and nonobese subjects (data not shown), but rose ($P < 0.001$) during intraduodenal glucose infusion in both groups. The rise in blood glucose was greater in the obese subjects than in the nonobese subjects (9.3 ± 0.5 compared with 7.1 ± 0.4 mmol/L at 100 min, $P < 0.05$) and their blood glucose concentrations remained higher at the beginning of the test meal (8.8 ± 0.6 compared with 6.1 ± 0.2 mmol/L, $P < 0.05$).

DISCUSSION

Our study was the first to evaluate the small-intestinal regulation of appetite in obesity. The major observation was that obese subjects did not differ from nonobese subjects in any of their responses to equienergetic, intraduodenal fat and carbohydrate infusions. Despite the obese subjects rating themselves as more hungry immediately before the infusions, there were no significant differences between the obese and nonobese groups in appetite or nausea ratings during the infusions, in weight or energy or macronutrient composition of the test meals eaten after the infusions, or in the time taken to eat the test meals. We therefore found no evidence to support our hypothesis that obesity is associated with a reduction in the satiating effects of small-intestinal nutrients. If the satiating effects of dietary fat are diminished in obesity, the effect is likely to be mediated elsewhere in the complex pathways that control feeding.

We confirmed our previous finding that nonobese, young men eat less after intraduodenal lipid infusions than after equienergetic carbohydrate infusions (31, 32) and showed that this was also true for obese, young men. In dogs, intraduodenal fat infusions are also more satiating than are equienergetic infusions of either carbohydrate or protein (40). In our previous studies (31, 32), intraduodenal lipid infusion increased ratings of fullness and decreased hunger when compared with a glucose infusion, consistent with the effects of these infusions on subsequent food intake. It is therefore somewhat surprising that in the present study there was no significant difference between the 2 nutrients in their effects on these ratings. Although there is no apparent explanation for this discrepancy, a control infusion permitted demonstration of a significant absolute suppressive effect of duodenal lipid infusion on food intake and an increase in feelings of fullness. The latter observation is consistent with previous reports that small-intestinal fat infusions suppress food intake in a variety of nonhuman species (40–42) and that ileal and jejunal lipid infusions suppress food intake in humans (20, 43). Lieverse et al (44) reported suppression of food intake by intraduodenal lipid infusion, which, although quantitatively similar to the suppression in this study (23% compared with 22%), was not significant. Intraduodenal glucose also suppressed appetite and food intake in the present study, although to a lesser extent than did fat and not significantly so. Intraduodenal infusions of both lipid and carbohydrate were associated with a reduction in the rate of eating (kJ eaten per minute), but not in the amount of time spent eating the test meal. This contrasts with the finding by Welch et al (20) that intrajejunal and ileal lipid infusions reduce the duration of subsequent eating.

We do not know why intraduodenal fat is more satiating than carbohydrate. The difference appears to be due to a specific, nonaversive effect because there was no difference between nausea ratings on the 2 d of nutrient infusion in this or previous stud-

ies (31, 32) and both infusions were equally well tolerated. Possible causes include the satiating effects of cholecystokinin, which is secreted in greater amounts after oral and intraduodenal fat infusions than after carbohydrate infusions (45).

The greater suppression of food intake by intraduodenal fat than by carbohydrate contrasts with the results of studies that compared the effects of fat and carbohydrate administered orally and intragastrically. These studies showed either no difference in the satiating effects of the 2 nutrients—particularly when lean, eating-unrestrained young men were studied (13, 14, 33)—or a greater satiating effect of carbohydrate (5, 34, 35). The reason for this discrepancy is unclear. It is unlikely that it was due to differences in subject characteristics. We have shown greater satiating effects of intraduodenal fat than of carbohydrate in lean, young, eating-unrestrained men in 3 studies and in obese men in 1 study. In contrast, lean, young men were reported to experience equal appetite suppression after oral and intragastric fat and carbohydrate in other studies (13, 14) and dietary carbohydrate was reportedly more satiating than was fat in obese subjects in the study by Rolls et al (14). It is possible that direct infusion of nutrients into the duodenum bypasses several suprapyloric mechanisms that increase the satiating effects of carbohydrates or reduce the intraduodenal satiating effects of lipid. These mechanisms could include a nutrient-specific effect on the rate of gastric emptying. Ingestion of both fat and carbohydrate delays gastric emptying, largely because of feedback signals arising from the contact of nutrients with small-intestinal receptors (46–49). There is considerable evidence, albeit disputed (45), that fat ingestion delays gastric emptying more than does carbohydrate ingestion (49). Thus, after oral ingestion, entry of fat into the small intestine may occur more slowly than that of carbohydrate, which would have the effect of masking the greater intraduodenal satiating effect of fat.

There are several potential limitations of the present study and of our 2 previous studies in which we investigated the satiating effects of intraduodenal fat and carbohydrate (31, 32). We studied 9 obese men in the present study. Because of this small sample size, we do not know how widely our findings can be generalized to other people with obesity or whether our findings necessarily apply to women, who are less tolerant of intraduodenal nutrient infusions at this rate than are men. Nevertheless, preliminary studies with lower nutrient infusion rates than we used suggest that food intake in women is also suppressed more by intraduodenal fat than by carbohydrate. In all 3 studies, nutrients were infused at a rate (11.97 kJ/min, or 2.86 kcal/min) that is slightly greater than the usually quoted mean rate of gastric emptying (≈ 8.4 kJ/min, or 2 kcal/min) (50). We do not know whether the satiety responses to these nutrients would differ between obese and nonobese subjects if the intraduodenal infusions were given more slowly. Fat and carbohydrate were each administered in one form only and we did not infuse protein or combinations of fat and carbohydrate. There is evidence from animal studies that the effects of macronutrients, particularly fat, on the small intestine depend on the form in which they are administered (41, 51). For example, in pigs, satiety produced by intraduodenal infusion of monoacylglycerols can be inhibited by a cholecystokinin antagonist, but satiety produced by infusion of the fatty acid oleic acid is not (41). Therefore, it is possible that we may have found differences between obese and nonobese subjects if we had combined fat and carbohydrate, infused protein, or administered the nutrients in different forms or at differ-




ent rates. In addition, the osmolality of intraduodenal nutrient solutions may be an independent determinant of their satiating effects; increasing osmolality increases satiety to the degree that it exceeds isotonicity (52, 53). Although the osmolality of the glucose and lipid infusions differed greatly, it did not explain the greater satiating effect of the triacylglycerol emulsion than of glucose because glucose has the higher osmolality of the 2 (1390 compared with 300 mosmol/kg).

We matched the subjects for age because we found previously that intraduodenal nutrient infusions had different effects on appetite, food intake, and gastric motility in elderly than in young men (31). Nevertheless, subjects in the 2 weight groups differed in several respects other than body weight and these differences may have affected our results. First, the obese subjects scored higher than the lean subjects on the restraint section of the eating questionnaire (36), which is designed to quantify a person's tendency to override hunger and other drives to eat. This difference was statistically but probably not biologically significant. The maximum score possible on this questionnaire is 21; a higher score indicates more restrained eating. None of the obese or nonobese subjects scored >9 on this scale; therefore, none were classified as restrained eaters according to accepted criteria (14). If the obese subjects were more restrained, it might have been expected that they would consume less fat during the test meal than would the nonobese subjects (54), which they did not. Furthermore, it might have been expected that the suppressive effects of the nutrient (in particular lipid) infusions would have been comparatively less in the obese than in the nonobese subjects, mainly because of the restrained intake on the control day. Consequently, there would have been smaller differences between the test meal intakes on the 3 study days in the obese than in the nonobese subjects; this was not the case.

Another potentially confounding factor was possible differences between the background diets of the 2 groups. Sustained changes in energy intake can affect gastrointestinal function and the satiating effect of nutrients. For example, a prolonged fast retards gastric emptying (55), dietary supplementation with glucose for 3–7 d accelerates the gastric emptying of glucose and fructose but not protein (56, 57), and supplementation with large amounts of glucose (1600 kcal/d) for 1 wk reduces the satiating effect of an intraduodenal fat infusion in lean, young men (32). Presumably, therefore, chronic reductions in energy intake might have the opposite effect and enhance the satiating effect of a nutrient, although as far as we know this has not been studied. The obese subjects recorded a lower food intake in their food diaries than did the nonobese subjects: 18% less energy in absolute terms and 29% less when corrected for lean body mass. Because we did not measure energy expenditure, we cannot exclude the possibility that the obese subjects had a lower energy intake as a response to lower energy expenditure, particularly as physical activity. This was unlikely, however, because the obese subjects were active, healthy volunteers and none of the nonobese subjects reported particularly high levels of physical activity. Moreover, physical activity accounts for only ≈ 15 –30% of total energy expenditure in moderately active individuals (3), and studies in which total energy expenditure was accurately measured showed it to be increased, on average, in obesity (*see* Introduction). Alternatively, the obese subjects may have knowingly or otherwise reduced their food intake in response to being in the study, despite instructions to maintain their usual diet. However, neither the obese subjects nor the nonobese subjects

lost weight during the study, suggesting that they did not substantially reduce their energy intake during this time. Most likely, the lower reported food intake by the obese subjects was due to underreporting, which is a well-documented tendency among overweight people (1, 9, 58).

In summary, intraduodenal infusions of fat suppressed appetite and food intake more than did equienergetic infusions of carbohydrate in both obese and nonobese young men. There were no differences between the obese and nonobese subjects in any response to the nutrient infusions. This finding suggests that small-intestinal regulation of appetite is not disordered in obesity and that reduced small-intestinal satiety responses to dietary fat or carbohydrate are unlikely to play a role in the maintenance of obesity. 

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