Effect of glucose supplementation on appetite and the pyloric motor response to intraduodenal glucose and lipid

JANE M. ANDREWS, SELENA DORAN, GEOFFREY S. HEBBARD, GEORGINA RASSIAS, WEI-MING SUN, AND MICHAEL HOROWITZ
Departments of Medicine and Gastrointestinal Medicine, Royal Adelaide Hospital, Adelaide, South Australia 5000, Australia

Andrews, J. M., Selena Doran, Geoffrey S. Hebbard, Georgina Rassias, Wei-Ming Sun, and Michael Horowitz. Effect of glucose supplementation on appetite and the pyloric motor response to intraduodenal glucose and lipid. Am. J. Physiol. 274 (Gastrointest. Liver Physiol. 37): G645–G652, 1998.—The effects of different macronutrients on appetite and pyloric motility and the impact of short-term dietary glucose supplementation on these responses were evaluated. Ten males (aged 19–38 yr) received isocaloric (2.9 kcal/min) intraduodenal infusions of glucose and lipid while antropyloroduodenal motility and appetite were assessed by manometry and visual analog scales, respectively. Effects of each intraduodenal nutrient on appetite and motility were evaluated before and after 7 days of dietary supplementation with glucose (400 g daily). Initially, both nutrients caused a similar rise in pyloric tone, but intraduodenal lipid was a more potent stimulus of phasic pyloric motility (P = 0.05) and suppressed appetite more (P = 0.013) than intraduodenal glucose. After dietary glucose supplementation, the increase in pyloric tone during intraduodenal glucose was attenuated. Although intraduodenal lipid remained a more potent stimulant of phasic pyloric motility (P = 0.016), it no longer decreased appetite. We conclude that in healthy young males 1) intraduodenal infusion of lipid is a more potent stimulus of phasic pyloric motility and suppresses appetite more than intraduodenal glucose and 2) dietary glucose supplementation alters both the appetite suppressant effect of intraduodenal lipid and the pyloric motor response to intraduodenal glucose infusion.

pylorus; small intestinal nutrients; adaptation

THE REGULATION OF APPETITE in humans is poorly understood. Although other mechanisms undoubtedly play a role in the long-term maintenance of body weight, signals from the gut, including gastric distension and small intestinal nutrient exposure, are important in the short-term regulation of food intake, particularly the induction of satiation (18, 32, 33, 39). Exposure of the small intestine to nutrients may be the more important of these mechanisms as it both decreases appetite (26, 45) and slows gastric emptying (19, 27). The presence of nutrients in the small intestine also modulates the way in which gastric distension is perceived (10). There is limited information about the mechanisms by which small intestinal nutrients signal satiation in humans. However, the stimulation of pyloric motility is likely to play a crucial role in the slowing of gastric emptying as the occurrence of tonic and phasic increases in pyloric pressure is associated with cessation of transpyloric flow (19, 44).

It has been established that males of normal body weight have the capacity to compensate accurately for covert dietary manipulations achieved by varying either the fat or carbohydrate content of enteraly presented nutrients (11, 12, 41, 38). However, there is conflict as to whether the effects of food on satiation are nutrient specific (2, 37). For example, it has been suggested that oral carbohydrate has a greater satiating effect than fat (2), although there is anecdotal evidence that high-fat foods are more likely to result in gastrointestinal symptoms such as bloating and the termination of a meal. These discrepant observations (2, 37) may relate to differences in taste or preferences among nutrients or to variations in the rate of gastric emptying. In particular, previous studies have not controlled for these factors by infusing nutrients directly into the small intestine. There is also little information as to whether nutrient class, as opposed to caloric content, influences gastric or pyloric motility.

Recent dietary intake is known to modify the motor response of the gut to food (5–7, 22, 34–36). In healthy volunteers, we have shown that supplementation of the diet with glucose accelerates gastric emptying of both glucose and fructose (7, 22) and that dietary fat supplementation accelerates gastric emptying of fat (6). Although our earlier study (7) suggested that this acceleration of gastric emptying may be nutrient specific, a relatively insensitive technique was used to evaluate gastric emptying and the nutrients tested were not matched for caloric content. Studies of gastric emptying in the obese are contradictory, with some showing accelerated (23, 49) and others slower (31) emptying rates. This may be attributable to the lack of standardization of dietary habits (e.g., calorie restricted vs. calorie excess) immediately preceding the studies (5).

In patients with anorexia nervosa, delayed gastric emptying improves within days of commencing refeeding and before attainment of normal body weight (34, 35). In these human (5–7, 22, 23, 31, 49) and animal studies (36), appetite was not evaluated, but it has been suggested that acceleration of gastric emptying may reduce the satiating effect of a meal if the duration of exposure of small intestinal receptors to nutrients is reduced (40). It has also been suggested that the effects of recent dietary intake on gastric emptying reflect a change in the magnitude of negative feedback from nutrient receptors in the small intestine (6, 7, 22), but this hypothesis has not been formally tested.

We have now evaluated the effects of intraduodenal (ID) administration of two macronutrients of different classes, glucose and triglyceride, on appetite and antropyloroduodenal (APD) motility. To determine whether dietary intake modifies the effect of ID nutrients on appetite and to define the pyloric motor correlates of...
the previously documented acceleration of gastric emptying by dietary glucose supplementation (7, 22), each subject was studied before and after supplementation of the diet with glucose for 1 wk.

MATERIALS AND METHODS

Subjects

We studied 10 healthy male volunteers [mean age, 26 yr (range 19–38 yr), and body mass index, 25 kg/m² (range 21.7–26.9 kg/m²)]. No subject had any history of eating disorder, chronic gastrointestinal disease, or gastrointestinal surgery, and none were on medication. Subjects were recruited by advertisement and were predominantly university students. Before entering the study, all volunteers completed a 5-day diet diary to ensure that their usual diet approximated the “standard” Australian diet (34% fat, 21% protein, and 44% carbohydrate), but no attempt was made to standardize the subjects’ diets.

This study was approved by the Human Research Ethics Committee of the Royal Adelaide Hospital, and each subject gave written informed consent.

Experimental Design

The protocol is shown in Fig. 1. In brief, after satisfying entry criteria (stated in Subjects), subjects were scheduled for the 2 study days on which isocaloric ID nutrient infusions of glucose and lipid were given, henceforth referred to as day 1 (presupplementation) and day 2 (postsupplementation). At the completion of the day 1 study, subjects were instructed in the consumption of a preweighed glucose supplement [glucose polymer (Poly-Joule); Sharp Laboratories, Ermington, New South Wales, Australia] and asked to take five sachets (80 g each) daily (total 400 g daily) for 7 days immediately preceding study. On day 2, subjects were provided with 35 sachets, and compliance was assessed by weighing of unused sachets on the return visit. All subjects were weighed on enrollment and on study days 1 and 2.

In 9 of the 10 subjects, the 2 study days were completed within 10 days. In one subject the interval was 35 days; this delay resulted from a minor back injury sustained after enrollment and on study days 1 and 2.

The protocol is shown in Fig. 1. In brief, after satisfying entry criteria (stated in Subjects), subjects were scheduled for the 2 study days on which isocaloric ID nutrient infusions of glucose and lipid were given, henceforth referred to as day 1 (presupplementation) and day 2 (postsupplementation). At the completion of the day 1 study, subjects were instructed in the consumption of a preweighed glucose supplement [glucose polymer (Poly-Joule); Sharp Laboratories, Ermington, New South Wales, Australia] and asked to take five sachets (80 g each) daily (total 400 g daily) for 7 days immediately preceding study. On day 2, subjects were provided with 35 sachets, and compliance was assessed by weighing of unused sachets on the return visit. All subjects were weighed on enrollment and on study days 1 and 2.

In 9 of the 10 subjects, the 2 study days were completed within 10 days. In one subject the interval was 35 days; this delay resulted from a minor back injury sustained after enrollment and on study days 1 and 2.

On the 2 study days, each subject attended the laboratory at 9:00 AM after an overnight fast. The manometric assembly, incorporating a pyloric sleeve sensor, was passed into the stomach through an anesthetized nostril. The tip of the assembly was allowed to pass into the duodenum by peristalsis. The correct position of the sleeve was verified by measurement of the antrroduodenal transmucosal potential difference (TMPD) gradient across the pylorus (21). Fasting motility was observed until the occurrence of phase III of the interdigestive migrating motor complex (MMC). Immediately after cessation of phase III MMC activity, an intravenous cannula was placed in the left antecubital vein for blood sampling. The subject then rested quietly for a further 10–15 min before the baseline blood sampling and visual analog scales (VAS) to evaluate appetite were administered (40).

At time 0 an isocaloric ID infusion of either 10% lipid (Intralipid, Kabi Pharmacia) or 25% glucose (Baxter Healthcare, Old Toongabbie, New South Wales, Australia) was commenced at 2.9 kcal/min for 90 min (2.6 ml/min lipid; 3 ml/min glucose). Blood samples were taken, and VAS were administered throughout the ID nutrient infusions at −5, 0, 5, 10, 20, 30, 40, 50, 60, 75, and 90 min. After 90 min the first ID nutrient infusion was ceased, and ID saline (0.9%, 3 ml/min) was given for 90 min (“washout”). After this, each subject received the alternate nutrient for a final 90-min period. APD motility was monitored during each of these three 90-min periods. The administration of ID nutrient infusions was randomized and single-blind (so that 5 subjects received ID lipid first and 5 ID glucose). Each subject, however, received the ID nutrients in the same order on the two study days (i.e., day 2 was not randomized) to enable a direct comparison of the effects of ID nutrients on days 1 and 2.

Outcome Measures

Plasma glucose and insulin. Venous blood was taken concurrently with the VAS. Plasma glucose was measured using the hexokinase enzymatic reagent (Trace Scientific, Baulkham Hills, New South Wales, Australia), and plasma insulin was measured by RIA (Phadesph insulin RIA, Pharmacia Diagnostics).

Appetite was assessed using previously described 100-mm linear VAS (40). Fullness and desire to eat were quantified. Subjects were familiarized with these scales at the commencement of each study day and instructed to make a single mark on the VAS corresponding to their own assessment of their current feelings. The –5 and 0 mm values were averaged to provide a baseline, and the change in ratings from baseline during the nutrient infusions was quantified.

APD pressures. APD pressures were assessed with manometry, using an 11-lumen water-perfused silicone rubber sleeve-side hole assembly (Dentsleeve, Belair, South Australia, Australia). The 4.5-cm long sleeve (channel 7) was positioned across the pylorus using TMPD, as described previously (21). Two sideholes located on the back of the sleeve 1.5 and 3 cm from its orad end (channels 8 and 9) are designated P1 and P2 respectively. Five channels (channels 1–5) were positioned proximal to the sleeve at 1.5-cm intervals. ID nutrient infusions were administered through a channel 10 cm distal to the pylorus. A computer-based recording system was used (Powermac 7100/75, Apple Computer, Cupertino, CA), running software (MAD) written by Professor C. H. Malbert (Rennes, France) in Labview 3.0.1 (National Instruments). Manometric pressures were digitized using an NBM1016H data acquisition board, recorded direct to disk at a frequency of 10 Hz, and stored for later analysis.

APD pressures were only analyzed when the sleeve sensor was positioned correctly across the pylorus. Variables that were quantified included 1) the total number, frequency, and amplitude of isolated pyloric pressure waves (IPPW) during ID nutrient infusions and 2) pyloric tone during ID nutrient infusions. An IPPW was defined as a pressure wave of >10 mmHg recorded by the sleeve sensor, with or without a concurrent pressure wave in either P1 or P2, in the absence of

<table>
<thead>
<tr>
<th>Positioning tube</th>
<th>Intraduodenal Infusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intubation ~9am</td>
<td>Glucose Lipid Saline Lipid Glucose</td>
</tr>
<tr>
<td>30–180 min</td>
<td>90 min 90 min 90 min</td>
</tr>
</tbody>
</table>

Blood samples & Visual Analog Scales

Fig. 1. Protocol for 2 study days on which intraduodenal (ID) infusions were administered. See text for detailed explanation.
an antral or duodenal pressure wave with an onset within 5 s of the IPPW onset (21). The frequency and amplitude of IPPW were assessed in two ways: 1) in 10-min segments during the ID nutrient infusions and 2) comparing the “early” response (IPPW per 10 min), defined as that between 20 and 50 min of the ID nutrient infusion, which was with the “late” response between 50 and 90 min.

Pyloric tone was calculated each minute by in-house software (MAD). The mean pressure (excluding phasic pressure waves) in the antral channel 1.5 cm proximal to the sleeve sensor was subtracted from the mean pressure in the sleeve channel. Tone was then averaged over 5-min intervals. We only included 5-min blocks in the analysis if the sleeve was correctly positioned for 3 or more of the 5 min.

**Statistical Analyses**

Differences between nutrients between the two study days and between the early and late responses were evaluated using mixed model analysis of variance (ANOVA), a model with a mixture of fixed and random effects (SAS Institute, Carey, NC). Paired comparisons were done using tests of simple effects (slices of interactions) (47). Missing data points were left as blanks in the analysis. Data are presented as means ± SE, unless otherwise stated. \( P < 0.05 \) was considered significant.

**RESULTS**

The study was well tolerated, with all volunteers completing the protocol. As assessed by the 5-day diet diary, usual macronutrient intake was 16.7% protein (range 14–20%), 36% fat (31–47%), and 45% carbohydrate (35–52%). Compliance with the glucose supplement was excellent, with volunteers consuming 84–96% of the dispensed supplement. There was no significant weight gain between studies (81.02 ± 3.29 vs. 81.48 ± 3.25 kg). Two subjects vomited during the ID lipid infusion on both study days; both had already completed both the ID glucose and ID saline infusions. On day 1 they vomited 30 and 40 min after commencement of ID lipid. On day 2 both tolerated the infusion for a longer period, vomiting at 60 and 50 min. The onset of nausea was only 3–5 min before emesis. In these subjects VAS from the first time point at which nausea was reported were not included in the analysis. No other subjects reported nausea.

**Plasma Glucose and Insulin Concentrations**

During ID glucose plasma glucose increased on both days, whereas there was no change during ID lipid. There was no significant difference in the magnitude or the time course of the rise in plasma glucose during ID glucose between day 1 and day 2 (day 1, baseline 4.6 ± 0.4 mmol/l, peak 8.9 ± 0.4 mmol/l; day 2, baseline 4.8 ± 0.4 mmol/l, peak 8.6 ± 0.4 mmol/l). Plasma insulin also increased during ID glucose on both days and did not change during ID lipid. Although there was no significant difference in the magnitude or the time course of the rise in plasma insulin between the two study days (day 1, baseline 6.8 ± 9.5 µU/ml, peak 112.6 ± 9.6 µU/ml; day 2, baseline 6.8 ± 9.5 µU/ml, peak 90.8 ± 9.6 µU/ml), there was a trend for plasma insulin at 90 min to be higher on day 1 compared with day 2 (day 1 vs. day 2, 112.6 vs. 85.7 µU/ml, respectively, \( P = 0.066 \) by ANOVA).

**Appetite**

On day 1 ID lipid was associated with a reduction in desire to eat (\( P < 0.05 \)) and increase in fullness (\( P < 0.05 \)). In contrast, on both days 1 and 2 appetite ratings did not change from baseline during ID glucose. On day 1 ID lipid was more potent at suppressing appetite than ID glucose, as evidenced by an overall reduction in desire to eat during ID lipid compared with ID glucose (\( P = 0.016 \)) and increase in fullness during ID lipid after 40 min (\( P < 0.05 \)). The greater satiating effect of ID lipid compared with ID glucose on day 1 was not evident on day 2 (desire to eat on day 2, lipid vs. glucose, \( P > 0.05 \); fullness on day 2, lipid vs. glucose, \( P > 0.05 \)). The difference between the responses on days 1 and 2 reflected a decrease in the suppression of appetite by ID lipid (desire to eat, day 1 lipid vs. day 2 lipid, \( P = 0.006 \)), as there was no difference in the response to ID glucose between days 1 and 2 (\( P = 0.9 \)) (Fig. 2).

![Fig. 2. Change from baseline in desire to eat and fullness during ID lipid and glucose, presented as means ± SE, both before (A) and after (B) dietary glucose supplementation. On day 1 ID lipid reduced desire to eat (\( P < 0.05 \)) and increased fullness (\( P < 0.05 \)), whereas there was no change in appetite ratings during ID glucose cf. baseline. Desire to eat was less during ID lipid than during ID glucose (\( P = 0.013 \) by ANOVA for whole curves), and fullness was greater from 40 min on during ID lipid (*\( P < 0.05 \) cf. baseline). After dietary glucose supplementation neither ID nutrient had a significant effect on appetite ratings compared with baseline and there was no difference between nutrients.](http://ajpgi.physiology.org/Downloadedfrom)
APD Pressures

No antral pressure waves were seen during the ID nutrient infusions. The total number of IPPW during the 90-min ID infusions was greater with ID lipid than ID glucose (day 1: lipid vs. glucose, 86.6 ± 16.0 vs. 59.6 ± 14.6, P = 0.048; day 2: lipid vs. glucose, 95.5 ± 21.3 vs. 62.2 ± 11.7, P = 0.06). There was no significant difference between the total number of IPPW induced by each nutrient on days 1 and 2 (day 1 lipid vs. day 2 lipid, P = 0.74; day 1 glucose vs. day 2 glucose, P = 0.89). The temporal patterning of IPPW varied between nutrients (Fig. 3), so that the maximum rate of IPPW was greater during ID lipid than ID glucose on both days 1 and 2 (day 1, P = 0.05; day 2, P = 0.059 by ANOVA for whole curves). Comparison of early (20–50 min) and late (60–90 min) responses demonstrated attenuation of the IPPW response during both ID nutrient infusions on day 1 (day 1 lipid: early vs. late response, 15.78 ± 2.12 vs. 8.40 ± 2.28 IPPW/10 min, P < 0.002; day 1 glucose: early vs. late response, 9.8 ± 2.12 vs. 4.67 ± 2.12 IPPW/10 min, P < 0.02). After supplementation, attenuation of the frequency of the IPPW response was still evident for ID glucose (day 2 glucose: early vs. late response, 9.40 ± 2.12 vs. 4.70 ± 2.12 IPPW/10 min, P < 0.02) but not in response to ID lipid (day 2 lipid, early vs. late response, 11.10 ± 2.12 vs. 11.02 ± 3.57 IPPW/10 min, P = 0.98).

Before dietary glucose supplementation, there was no difference in the temporal patterning of the amplitude of IPPW (Fig. 4) between the two nutrients (P = 0.25). In contrast, on day 2 the mean amplitude of IPPW was greater during ID lipid (day 2 lipid vs. day 2 glucose, P = 0.016 by ANOVA for whole curves). Attenuation of the amplitude of IPPW was evident during ID glucose on day 1 (day 1 glucose: early vs. late response, 25.73 ± 3.67 vs. 17.66 ± 3.93 mmHg, P = 0.038). There was no significant difference in the amplitude of IPPW between 20 and 50 min compared with 60–90 min during ID lipid on day 1 (P = 0.23) or for either nutrient on day 2 (P > 0.36 for both). For both ID nutrients the amplitude of IPPW was greater on day 2 compared with day 1 (day 1 lipid vs. day 2 lipid and day 1 glucose vs. day 2 glucose, P < 0.001 by ANOVA for whole curves).
On day 1, the increase in pyloric tone in response to both ID lipid and ID glucose was not significantly different; both were higher than baseline (P < 0.05) after 10 min of infusion and remained elevated up to 90 min (P < 0.05). Although there was no overall difference in the tonic responses to the two ID nutrients on day 2, the curves were clearly divergent from 10 to 40 min, with tone slower to rise and reaching a lower peak value in response to ID glucose compared with ID lipid (Fig. 5).

**DISCUSSION**

We have established that there are substantial differences in the effects of ID infusion of two nutrients of different macronutrient classes on appetite and pyloric motility in healthy male volunteers. The major novel observations are that ID lipid compared with an isocaloric glucose load 1) suppressed appetite more, 2) stimulated a higher frequency, but similar amplitude, of phasic pyloric pressure waves (IPPW), and 3) stimulated a similar increase in tonic pyloric pressure. Moreover, we have shown that short-term alteration in diet has the capacity to modify the effects of ID nutrients on both appetite and pyloric motility. In particular, after dietary supplementation with glucose for 1 wk, 1) ID lipid no longer had a differential effect on appetite compared with an isocaloric ID glucose load, and 2) the tonic pyloric pressure response to ID glucose was attenuated.

In interpreting these observations, the potential limitations of the study should be considered. The studies were not randomized (and hence no sham supplementa-

![Fig. 5. Change in pyloric tone during both ID lipid and ID glucose.](https://example.com/image.png)

**Fig. 5.** Change in pyloric tone during both ID lipid and ID glucose, presented as means ± SE in 5-min blocks both before (A) and after (B) dietary glucose supplementation. On day 1 both ID nutrients stimulated a similar rise in pyloric tone, which began within 15 min of commencing the nutrient infusion. On day 2, pyloric tone in response to ID glucose failed to rise above baseline until 45 min. The response to ID lipid is unchanged. (*P < 0.05 cf. baseline).*
important satiety mechanism, gastric distension is now thought to play a lesser role in modulating intake than stimulation of small intestinal nutrient receptors (39, 40). The observation that intravenous nutrient loads have little, if any, effect on appetite (26, 41, 45) suggests that postabsorptive signals play only a minor role in the short-term regulation of appetite.

It is controversial as to whether fat and carbohydrate exert different effects on appetite. For example, Blundell et al. (2) have reported a greater degree of appetite suppression by fat in one study and by carbohydrate in another, although the subjects studied appear similar. In young, unrestrained eaters of normal weight, acutely administered, isocaloric, enteral (oral and intragastric) loads of fat and carbohydrate appear to suppress hunger to a similar degree (see Ref. 37 for review). It may be that any differences between fat and carbohydrate are time dependent, so that the time interval between intake and evaluation of appetite is critical. In the obese there is evidence that fat is less satiating than carbohydrate; this conclusion is based on both acute clinical studies, longitudinal studies, and diet surveys (reviewed in Refs. 2 and 37). However, it should be recognized that convenience, taste, and social situations are likely to confound some of these results. In this study we have clearly demonstrated a greater immediate satiating effect of ID lipid (a triglyceride emulsion) compared with ID carbohydrate before dietary alteration.

After dietary glucose supplementation the effects of ID fat on satiation were diminished, so that there was no difference from ID glucose. This observation is important as current hypotheses of the mechanisms of satiation tend to invoke relatively nutrient-specific signals, e.g., release of insulin in response to glucose (32, 35) and CCK release in response to fat (39). In studies that have examined the effects of dietary supplementation on gastric emptying (4, 6, 7, 22), gastric emptying is increased in response to the macronutrient that had been given as a supplement, but the nutrient specificity of this adaptation was not adequately examined nor was appetite evaluated. In patients with anorexia nervosa gastric emptying is generally delayed while they have inadequate caloric intake but improves once refeeding commences and before normal body weight is obtained (34, 35, 43), suggesting that the caloric load presented to the small intestine, rather than its specific nutrient composition, is the major factor modulating gastric emptying. Although appetite was not formally evaluated in these latter studies, there is anecdotal evidence that symptoms of bloating and early satiety usually diminish in patients with anorexia nervosa once an adequate enteral intake is maintained, supporting the concept that the rate of nutrient entry into the small intestine has the capacity to alter appetite signals, as well as motor function. These effects may be mediated by changes in receptor sensitivity, receptor number, length of intestine exposed to nutrients, or the central response to a given satiety signal. Taking the above observations and the results of our study together, it is likely that in the regulation of appetite, “nutrient-general” (rather than nutrient-specific) small intestinal mechanisms are involved.

Pyloric Motility

The presence of nutrients within the small intestine retards gastric emptying (19, 27–30, 45, 46), and this is associated with suppression of antral motility and elevation of tonic and phasic pressures in the pylorus (13, 19, 20, 44). Our study demonstrates for the first time that ID lipid is a more potent stimulus of phasic pyloric activity (IPPW) than ID glucose, both before and after dietary glucose supplementation, with a higher frequency and amplitude of IPPW and less attenuation in the response over time. This was not completely unexpected given that intestinal lipid has also been shown to cause greater proximal gastric relaxation than carbohydrate in dogs (1). Although there was no statistically significant difference between the two nutrients, the stimulation of pyloric tone by ID lipid appeared to be greater than with ID glucose before supplementation. Furthermore, on day 2 the initial effect of ID glucose on pyloric tone was diminished, despite preservation of the frequency, and an increase in the amplitude, of IPPW. The major significance of these findings lies in the notion that pyloric tone and IPPW are not all or none phenomena and that different nutrient receptors may act via discrete pathways to influence pyloric motor patterns or generate quantitatively differing signals. A discrepancy between the tonic and phasic pyloric motility has been reported in humans (9, 15–17), for example in response to ID infusions of D- and L-tryptophan (9), acute hyperglycemia (16), and intravenous CCK-8 (35). In our study this discrepancy may reflect mediation of phasic and tonic pyloric pressures via different neural or humoral signals or different sensitivities to stimuli or may possibly indicate that we had reached a “ceiling” for pyloric tone (but not IPPW) by delivering nutrients at a relatively high caloric rate. Previous studies of pyloric motility in humans with ID lipid infusions used caloric rates one- or two-thirds of those we chose (14, 20, 46); however, others have given ID dextrose at higher caloric rates (13). Because the two nutrients were not directly compared in these previous studies and because ID infusions were performed at only one caloric rate in our study, the question regarding dose cannot be answered. Both the tonic and phasic pyloric responses to ID dextrose and ID lipid have been shown to be sensitive to atropine, perhaps reducing the likelihood that they are mediated by entirely separate mechanisms (13, 14).

Before dietary glucose supplementation, both the tonic and the phasic pyloric pressures remained above baseline throughout the ID lipid and ID glucose infusions, although there was attenuation of the phasic response (both frequency and amplitude) to ID glucose over the last 30 min, as reported previously (8). A previous study reported attenuation in the tonic pyloric motor response to ID lipid infusion (14); this attenuation was not seen during any ID nutrient infusion in
our study. However, the low caloric rate of delivery of lipid in the previous study (1.1 kcal/min compared with 2.9 kcal/min) may account for this difference.

IPPW are associated with the slowing of gastric emptying caused by nutrients in the small intestine (19, 20, 44). However, it is unlikely that IPPW are primarily responsible for retarding transpyloric flow. Even at their peak frequency of ~3/min, IPPW occupy only a fraction (less than one-third) of the time course during which flow is stopped (44). A sustained rise in pressure is likely to contribute to the retardation of gastric emptying, as increases in pyloric tone of as little as 3–4 mmHg are likely to be mechanically significant (48).

Our observation of altered pyloric motor responses after dietary supplementation with glucose extends earlier observations that modification of intake of a nutrient affects gastric emptying, the usual response being that increasing the intake of a substance accelerates its subsequent gastric emptying and decreasing intake retards it (4, 6, 7, 22). Gastric emptying was not evaluated in this study. However, it should be noted that the glucose supplement we used was similar to that previously documented to accelerate gastric emptying of a subsequent load of both glucose and fructose (7, 22). Therefore, the fact that there was attenuation of the tonic pyloric response to glucose after dietary glucose supplementation (with the phasic pyloric response to glucose being unaltered) leads us to hypothesize that this may be responsible for the acceleration of gastric emptying reported in these studies (7, 22). We did not evaluate proximal gastric motor mechanisms and therefore cannot exclude the possibility that changes in fundal tone contributed to acceleration in gastric emptying (1). However, pyloric tone is likely to be the final arbiter in gastric emptying of a liquid, as emptying cannot occur against a closed sphincter (44). Unlike the effect on appetite, this adaptation of pyloric tone to ID nutrients was nutrient specific, with no modification in the response to ID lipid, suggesting that motor and sensory adaptation to dietary manipulation may be mediated by different mechanisms.

In summary, we have demonstrated a differential response in terms of appetite regulation and motor function of the pylorus to ID delivery of two macronutrients of different classes. In addition, it has been established that both the appetite signals generated by and motor responses to these nutrients can be altered by dietary manipulation. The adaptation of the appetite signals occurred across macronutrient class, whereas the adaptation of the motor response was more nutrient specific.

We gratefully acknowledge the assistance of K. Wilson, biostatistician, in data analysis and S. Suter for secretarial assistance.

This work was supported by a project grant from the National Health and Medical Research Council of Australia. J. M. Andrews and G. S. Hebbard are both recipients of National Health and Medical Research Council Postgraduate Research Scholarships.

Address for reprint requests: M. Horowitz, Dept. of Medicine, Royal Adelaide Hospital, North Terrace, Adelaide, South Australia 5000, Australia.

Received 25 J. June 1997; accepted in final form 17 December 1997.

REFERENCES


17. Fraser, R., T. Shearer, J. Fuller, M. Horowitz, and J. Dent. Intravenous erythromycin overcomes small intestinal feedback inhibition caused by nutrients in the small intestine (19, 20, 44). However, it is unlikely that IPPW are primarily responsible for retarding transpyloric flow. Even at their peak frequency of ~3/min, IPPW occupy only a fraction (less than one-third) of the time course during which flow is stopped (44). A sustained rise in pressure is likely to contribute to the retardation of gastric emptying, as increases in pyloric tone of as little as 3–4 mmHg are likely to be mechanically significant (48).

Our observation of altered pyloric motor responses after dietary supplementation with glucose extends earlier observations that modification of intake of a nutrient affects gastric emptying, the usual response being that increasing the intake of a substance accelerates its subsequent gastric emptying and decreasing intake retards it (4, 6, 7, 22). Gastric emptying was not evaluated in this study. However, it should be noted that the glucose supplement we used was similar to that previously documented to accelerate gastric emptying of a subsequent load of both glucose and fructose (7, 22). Therefore, the fact that there was attenuation of the tonic pyloric response to glucose after dietary glucose supplementation (with the phasic pyloric response to glucose being unaltered) leads us to hypothesize that this may be responsible for the acceleration of gastric emptying reported in these studies (7, 22). We did not evaluate proximal gastric motor mechanisms and therefore cannot exclude the possibility that changes in fundal tone contributed to acceleration in gastric emptying (1). However, pyloric tone is likely to be the final arbiter in gastric emptying of a liquid, as emptying cannot occur against a closed sphincter (44). Unlike the effect on appetite, this adaptation of pyloric tone to ID nutrients was nutrient specific, with no modification in the response to ID lipid, suggesting that motor and sensory adaptation to dietary manipulation may be mediated by different mechanisms.

In summary, we have demonstrated a differential response in terms of appetite regulation and motor function of the pylorus to ID delivery of two macronutrients of different classes. In addition, it has been established that both the appetite signals generated by and motor responses to these nutrients can be altered by dietary manipulation. The adaptation of the appetite signals occurred across macronutrient class, whereas the adaptation of the motor response was more nutrient specific.
GLUCOSE SUPPLEMENTATION ALTERS APPETITE AND MOTILITY