Effect of meal viscosity and nutrients on satiety, intragastric dilution, and emptying assessed by MRI

LUCA MARCIANI,1 PENNY A. GOWLAND,1 ROBIN C. SPILLER,2 PRETIMA MANOJ,3 RACHEL J. MOORE,1 PAUL YOUNG,1 AND ANNETTE J. FILLERY-TRAVIS3

1Magnetic Resonance Centre, School of Physics and Astronomy, Nottingham NG7 2RD; 2Division of Gastroenterology, Queen’s Medical Centre, University Hospital, Nottingham NG7 2UH; and 3Institute of Food Research, Colney, Norwich NR4 7UA, United Kingdom

Received 2 August 2000; accepted in final form 30 January 2001

Marciani, Luca, Penny A. Gowland, Robin C. Spiller, Pretima Manoj, Rachel J. Moore, Paul Young, and Annette J. Fillery-Travis. Effect of meal viscosity and nutrients on satiety, intragastric dilution, and emptying assessed by MRI. Am J Physiol Gastrointest Liver Physiol 280: G1227–G1233, 2001.—The relationship between the intragastric distribution, dilution, and emptying of meals and satiety was studied using noninvasive magnetic resonance imaging techniques in 12 healthy subjects with four polysaccharide concentration (15, 16). It can also accurately map in three dimensions the intragastric distribution of a physically heterogeneous food mass.

The present study investigated the interaction between meal viscosity and nutrient content on the intragastric distribution, dilution, and emptying of meals and the sense of satiety in normal subjects with noninvasive EPI techniques. In particular, this study sought to test the hypothesis that high meal viscosity increases the rate of meal dilution and also increases satiety. We also measured antral and proximal gastric volumes to evaluate the intragastric distribution of the meals to determine whether this could explain the differences in sense of fullness induced by the different meals.

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.

Address for reprint requests and other correspondence: R. C. Spiller, Div. of Gastroenterology, Queen’s Medical Centre, University Hospital, Nottingham NG7 2UH, UK (E-mail: Robin.Spiller@nottingham.ac.uk).

http://www.ajpgi.org 0193-1857/01 $5.00 Copyright © 2001 the American Physiological Society G1227
**MATERIALS AND METHODS**

**Volunteers and Study Design**

Twelve healthy volunteers (7 male and 5 female, age 18–30 yr, body mass index 19–25 kg/m²) with no history of gastrointestinal disorders and taking no regular medication took part in this study. Subjects attended four morning sessions (>1 day and <7 days apart), having fasted overnight. At each session, they ingested 500 ml of a low- or high-viscosity locust bean gum (LBG) test meal either containing nutrients or being a nonnutrient control, according to a four-way crossover design

<table>
<thead>
<tr>
<th>LVC</th>
<th>HVC</th>
</tr>
</thead>
<tbody>
<tr>
<td>LVN</td>
<td>HVN</td>
</tr>
</tbody>
</table>

with low-viscosity nonnutrient control (LVC), high-viscosity nonnutrient control (HVC), low-viscosity nutrient (LVN), and high-viscosity nutrient (HVN) meals.

At the beginning of their first experimental session, subjects were familiarized with self-assessment satiety questionnaires and instructed on how to hold their breath before each image acquisition to minimize diaphragmatic displacement. Subjects were then asked to ingest the meals within 10 min. The meals were given according to a Latin square randomization design to avoid order effects.

The following measurements were made every 12 min. First, the subjects were asked to fill in the satiety questionnaire and were positioned in the scanner. Serial volume sets of images were then acquired from the heart to the kidneys to determine the position and measure the volume of the gastric lumen. Finally, T2 data sets were acquired on the gastric contents using a spin-echo EPI sequence to measure meal dilution. These measurements were repeated for the whole experimental session, which lasted 1.5 h. Between scans, subjects sat upright on the scanning bed, lying down only for the short time necessary to acquire the images. T2 was also calibrated against meal dilution in vitro for each meal. This study was approved by the University Medical School Ethics Committee, and subjects gave informed written consent before experiments.

**Test Meals**

Test meals were prepared by adding appropriate amounts of LBG (food-grade *Ceratonia siliqua*; Lucas Meyer Colloids, Chester, UK) powder to hot water. Nutrient meals contained a total of 1,350 kJ, 37% as lipids (olive oil emulsified with sorbitan monostearate, Crillet 3 VEG, and Vykamol 83 G; Croda Food Services, Oldham, UK) and 63% as carbohydrates. Control meals contained only the LBG and 16 g of dextrose to equalize its osmolality to the 200 mosmol/kg H₂O of the nutrient meals. Concentrated banana flavoring was added using a food mixer and were then kept at 90°C for 1 h before being allowed to cool down slowly to 37°C in a water bath. The viscosity, measured with a Bohlin VO rheometer (Bohlin Instruments, Cirencester, UK), was 0.06 Pa·s (water) for LVC and LVN and 29.5 Pa·s (barely pourable) for HVC and HVN meals.

**Echo-Planar Imaging**

Single-shot EPI (11) images were acquired on a whole body 0.5-T purpose-built EPI scanner equipped with actively shielded gradients and a 50-cm-diameter birdcage coil. The in-plane resolution was 3.5 mm × 2.5 mm, and a slice thickness of 1 cm was used throughout the experiments. Each image was acquired in 130 ms using a 128 × 128 matrix with an effective echo time of 40 ms. Transverse multislice volume sets of images were acquired rapidly to measure gastric volumes (total acquisition time 4 s). T2 data sets were acquired in vitro at 37°C on the four test meals and in vivo on the gastric contents using a single spin-echo EPI measurement with eight echo times varying from 60 to 700 ms repeated once (total acquisition time 2.7 min).

**Data Analysis**

**Gastric emptying.** Gastric volumes were calculated by drawing a region of interest around the stomach contents on each image of a multislice set (using Analyze software, Biomedical Imaging Resource, Mayo Foundation, Rochester, MN) and summing the areas across the slices. Data were then averaged across subjects for each time point, and the average gastric emptying curves were plotted for each meal. The time needed to empty one-half of the initial gastric volume (T½ (prox)) was also calculated from the volume-time curve for each subject and averaged per meal.

**Intragastric distribution: antral-to-proximal ratios.** Antral-to-proximal distribution ratios were assessed on the first volume image sets acquired after meal ingestion at time (t) = 12 min, when differences in gastric emptying were minimized, because these might have affected the comparison of antral volumes between meals. The boundary of the antral region was defined by drawing a 45° line at the incisura in a coronal three-dimensional reconstruction of the volume image set, and antral volumes were measured as described in *Gastric emptying* using Analyze software. The remaining volume was designated as the proximal stomach, and antral-to-proximal ratios were calculated.

**Meal dilution calibrations in vitro.** The nuclear magnetic relaxation of LBG water solutions depends mainly on polysaccharide concentration. Therefore, it is possible to calibrate in vitro the dilution of a LBG water solution against the inverse of its T2 as described previously (15, 16). The calibration curve can then be used to predict the dilution of a LBG test meal by simply measuring its T2. T2 data sets were therefore acquired in vitro at 37°C using the same experimental setup as for the experiments in vivo, at four different dilution fractions F = 1, 0.66, 0.50 and 0.33, where F is defined as

\[
F = \frac{\text{initial volume}}{\text{initial volume}} + \text{added volume of 0.1 M HCl} \quad (1)
\]

for six different samples for each meal. Because gastric secretions are strongly acidic, the effect of acidification was accounted for by diluting the solutions with a 0.1 M HCl stock solution. The fit of these data yielded a calibration curve for T2 against acid dilution for each meal.

**Meal dilution calculations in vivo.** The in vitro calibration curves made it possible to translate the T2(t) measurements made in vivo on the stomach contents to a dilution fraction F(t) of the test meal within the gastric lumen. Knowledge of the gastric volume V(t) at the same time point made it possible to obtain the volume M(t) of the initial meal present in the digesta at time t simply as

\[
M(t) = F(t) \cdot V(t) \quad (2)
\]

The volume of the secretion S(t) added to the initial test meal was then calculated as

\[
S(t) = V(t) - M(t) \quad (3)
\]
The counteracting effects of secretion rate and gastric emptying rate suggested that it would be important to be able to calculate the total volume of gastric secretions produced for a meal. We used a simple model of gastric emptying and secretion, which is reported in the APPENDIX. Table 2 reports the integrated values of total gastric secretion produced by the stomach at \( t = 80 \) min obtained with gastric emptying and secretion data from this study. Pixel-by-pixel T2 maps of the stomach contents were also calculated and translated into color-coded meal dilution maps using the in vitro calibrations described above.

Satiety. A self-report scale technique was used to assess the volunteers’ subjective feelings of satiety. They were instructed to give a number between 1 and 10 to indicate their feeling of fullness, hunger, and appetite every 12 min. The satiety scores were then plotted against time for each experiment, and the area under the curve was calculated and averaged for each meal. Satiety data were also plotted against gastric volume by grouping the data by measuring time points for each meal.

Statistics. Results are expressed as means \( \pm SE \). The hypothesis of a normal data distribution was rejected using Shapiro-Wilk’s test. Hence statistical analysis was performed using the nonparametric Friedman two-way analysis of variance by ranks followed by Wilcoxon signed-rank test for paired comparisons, using the Bonferroni correction to adjust the significance obtained for multiple comparisons (24).

RESULTS

Gastric Emptying

All meals were well tolerated by subjects and ingested within the requested 10 min, although the less viscous meals were finished more rapidly. All meals provided good contrast in EPI images in vivo without the need for contrast enhancers. Gastric emptying was significantly delayed by meal viscosity (Table 1), but the presence of nutrients had a more powerful effect and almost doubled the \( T_{50\%} \) with respect to the control meals of equal initial viscosity. The form of gastric emptying curves (Fig. 1) changed from exponential for the nonnutrient control meals (\( R^2 = 0.95 \) for LVC and \( R^2 = 0.98 \) for HVN) to linear for the nutrient meals (\( R^2 = 0.99 \) for both LVN and HVN). Antral volumes and antral-to-proximal ratios at \( t = 12 \) min are also reported in Table 1. Antral volumes for the HVN meal were significantly higher than for the control LVC meal (\( P < 0.05 \)). Furthermore, the antral-to-proximal ratio was significantly influenced by viscosity and nutrient content (\( P < 0.003 \)). The antral-to-proximal ratio for the nutrient meal was significantly increased by increasing the viscosity (HVN > LVN, \( P < 0.05 \)).

Meal Dilution In Vitro

The calibration curves of the transverse relaxation rate (\( T_2^{-1} \)) versus the dilution fraction \( F \) are shown in Fig. 2. \( T_2^{-1} \) depended linearly on \( F \) for the LVC

\[
\begin{align*}
\text{Table 1. EPI and satiety measurements of meal viscosity and nutrient effect on gastric emptying, satiety, and meal dilution} \\
&\text{LVC} & \text{HVC} & \text{LVN} & \text{HVN} \\
T_{50\%}, \text{ min} & 32 \pm 7 & 46 \pm 9^* & 67 \pm 9^* & 76 \pm 6^† \\
\text{Total emptying rate, ml/min} & 6.1 \pm 0.6 & 4.7 \pm 0.3^† & 4.1 \pm 0.3^* & 3.3 \pm 0.2^† \\
\text{Antral volume at} & 55 \pm 9 & 58 \pm 6 & 51 \pm 6 & 74 \pm 5^§ \\
\text{Antral-to-proximal ratio} & 0.15 \pm 0.02 & 0.16 \pm 0.02 & 0.11 \pm 0.01 & 0.19 \pm 0.02^§ \\
\text{Fullness, scores} & 419 \pm 54 & 535 \pm 48^* & 475 \pm 50 & 567 \pm 37^* \\
\text{Hunger, scores} & 483 \pm 45 & 470 \pm 47 & 530 \pm 47 & 458 \pm 54 \\
\text{Appetite, scores} & 516 \pm 49 & 491 \pm 56 & 557 \pm 53 & 484 \pm 61 \\
\text{Secretion volume} & 51 \pm 23 & 75 \pm 13 & 60 \pm 10 & 73 \pm 24^a \\
& \text{at} t = 60 \text{ min, ml} & & & \\
\end{align*}
\]

Values are means \( \pm SE \) from 12 subjects. LVC, low-viscosity nonnutrient control meal; HVC, high-viscosity nonnutrient control meal; LVN, low-viscosity nutrient meal; HVN, high-viscosity nutrient meal; \( T_{50\%} \), half-emptying time for total gastric volume. \( *P < 0.05, ^†P < 0.001, \) and \( §P < 0.001 \) significant difference from LVC; \( ^*P < 0.05 \) vs. LVN. Fullness, hunger, and satiety scores are based on area under the curve of the self-assessment satiety questionnaires.

Fig. 1. Gastric emptying curves for the 4 locust bean gum meals: low-viscosity nonnutrient control (LVC), high-viscosity nonnutrient control (HVC), low-viscosity nutrient (LVN), and high-viscosity nutrient (HVN). Meal viscosity and nutrients significantly delayed gastric emptying and modified the form of the emptying curves from exponential (\( n = 12 \) subjects; \( R^2 = 0.95 \) for LVC and \( R^2 = 0.98 \) for HVN) to linear (\( n = 12; R^2 = 0.99 \) for both LVN and HVN).

Fig. 2. In vitro 37°C calibrations of the transverse relaxation rate (\( T_2^{-1} \)) vs. the dilution fraction \( F \) for all locust bean gum meals. The dependence is linear for LVC (\( n = 6 \) subjects; \( R^2 = 0.98 \)), LVN (\( n = 6; R^2 = 0.91 \)), and HVN (\( n = 6; R^2 = 0.98 \)) meals and logarithmic for HVN meals (\( n = 12; R^2 = 0.99 \)). These calibrations were used to calculate dilution of the stomach contents in vivo.
0.98), LVN ($R^2 = 0.91$), and HVC ($R^2 = 0.98$) meals, and linearity was independent of acidification. The HVN meal showed instead an initial effect of acidification on $T_2^{-1}$. It was then decided to further investigate this dependence by diluting six batches of HVN meal with neutral pH water and six batches with 0.1 M HCl water solution. A logarithmic dependence of $T_2^{-1}$ on the dilution fraction $F$ ($R^2 = 0.99$) was found. Considering a dilution fraction $F = 0.666$, the standard deviation error introduced by meal acidification on $T_2^{-1}$ was 8%. This acidification error was much lower than the 21% error on $T_2^{-1}$ measured in vivo at the same dilution fraction $F = 0.666$. This higher data scatter detected in vivo could be introduced either by individual variability between subjects or higher noise of in vivo data, and it masked the 8% error on the calibration data in vitro.

**Meal Dilution In Vivo**

Figure 3 shows the dilution fraction $F$ curves for all meals. The volume of secretion present in the stomach at $t = 60$ min, calculated using the dilution fraction $F$ curves and the corresponding time point gastric volume, is reported in Table 1. The data for the HVN meal were significantly higher than for the control ($P < 0.04$). Nutrient meals contained more secretions than controls, but this effect was not as large as the viscosity effect. When the model of gastric secretions was integrated to calculate the total gastric secretions produced in the presence of each meal, taking into account the variable emptying rates, similar effects were found (Table 2), with viscosity having a more dramatic effect than nutrient content. In fact, the LVN meal caused fewer secretions than the LVC meal.

A typical example of dilution map images of the stomach contents at different times is shown in Fig. 4 for a high-viscosity meal. Initial images showed that the outer part of the viscous meal was more dilute (coded in red), reflecting dilution by gastric and salivary secretions, whereas the inner meal bolus remained more viscous (coded in green). Meal dilution then slowly increased from the outer region toward the core of the meal, showing the process of mixing. Analogous dilution maps for the low-viscosity meals showed a more homogeneous, progressive dilution of the meal by gastric secretion.

**Satiety**

The integrated sense of fullness induced by the more viscous meals with time was significantly higher than that induced by the presence of nutrients ($P < 0.02$; Table 1). Similarly, the integrated sense of hunger and appetite decreased more with high meal viscosity than with the presence of nutrients, although this difference was not significant (Table 1).

An unexpected finding was the correlation observed between satiety and gastric volumes for all meals, as shown for the sense of fullness in Fig. 5A for the nutrient meals and in Fig. 5B for the control meals. The sense of fullness increased linearly with gastric volumes ($R^2 = 0.98$ for HVN and 0.99 for LVN), whereas hunger ($R^2 = 0.98$ for HVN and 0.99 for LVN) and appetite ($R^2 = 0.95$ for HVN and 0.99 for LVN) decreased linearly for the nutrient meals. The sense of fullness increased logarithmically with gastric volumes ($R^2 = 0.97$ for HVC and 0.96 for LVC), whereas hunger ($R^2 = 0.96$ for HVC and 0.97 for LVC) and appetite ($R^2 = 0.98$ for HVC and 0.92 for LVC) decreased exponentially for the control meals. Figure 5 also shows that changes in integrated satiety scores for different meal types do not simply reflect changes in gastric emptying rates: for a given gastric volume,
meals of higher viscosity induce a higher sense of fullness.

DISCUSSION

We hypothesized that there would be an interaction between the effect of meal viscosity and nutrient content on emptying, secretion, and satiety, and we designed this four-way crossover study to investigate the relationships between these parameters using noninvasive EPI techniques.

Our results clearly show that calorie content and viscosity have an additive effect in delaying gastric emptying and increasing the sense of satiety during meal consumption and gastric emptying. We found that, with the test meals used, the high calorie content was more effective in delaying gastric emptying, whereas high meal viscosity had a greater effect on the sense of satiety, a key factor in eating behavior. However, a dose-response study is required to establish whether this is generally true for other levels of calories or viscosity. The effect of fat entering the duodenum, releasing cholecystokinin, and inducing satiety is well recognized, as is its powerful effect in delaying gastric emptying [5, 18, 20]. However, we found that high viscosity had the power to further increase satiety after the fat-containing nutrient meal. This agrees with the frequently reported finding that at least some of the metabolic benefits of high-fiber diets arise because they reduce overall calorie intake [3, 19, 23].

We found a good correlation between gastric volumes and satiety. This presumably reflects the activation of mechanoreceptors in the gastric body and fundus that others have shown using guar gum [6] or balloon distension to induce the sensations of fullness and satiety [12, 26]. Importantly, we also found that the volume versus fullness curve was shifted to the left for the high-viscosity meals compared with the low-viscosity meals. This increased satiety for the same gastric volume suggests that there is another mechanism whereby viscosity influences satiety beyond simply delaying gastric emptying. The increase in fullness early on may reflect the increased tactile stimulation of the oropharynx during ingestion of the more viscous meal; however, the effect continued until the meal was emptied from the stomach, making it likely that this explanation is at best incomplete. We found that the antral volumes were increased with the high-viscosity nutrient meal compared with the low-viscosity nutrient meal, and we suggest that this may induce a sense of fullness. Others have also reported increased antral distension with more viscous meals, possibly because such meals may reduce the amplitude of antral contractions [21], which normally keep the antral volumes small. There is good evidence that the normal gastric body undergoes “receptive relaxation” after meal ingestion, and balloon distension rarely produces discomfort until >400 ml is instilled [26]. The antral wall may be less distensible, and hence distension may be more likely to lead to a sensation of discomfort. This is clearly seen in patients with non-ulcer dyspepsia who fail to show normal postprandial relaxation [26] and experience postprandial discomfort associated with an abnormally dilated antrum [9, 17]. This may be caused by associated antral hypomotility or, more likely, by failure of proximal gastric relaxation forcing the meal to enter and distend the antrum [28].

If the stretch receptors responsible for the sensation of fullness are in series with antral muscle as some experiments have suggested [26], then they might be stimulated by more forceful contractions induced by the stimulus of greater viscosity. As we previously reported [16], the stomach does respond to increased...
viscosity because gastric emptying rates are only increased by a few percent in spite of 1,000-fold increases in meal viscosity. Gastric emptying is also strongly influenced by pyloric contractions that are induced by fat in the duodenum (10, 27). Our nutrient meal may well have induced pylorospasm, but reliable measurement of the pylorus is beyond the resolution used in these MRI experiments so we cannot assess that response.

Our color-coded dilution maps provided a new insight on the mechanism of meal dilution by gastric secretions because they allowed monitoring of the process of dilution and mixing of viscous meals. Contrary to the traditional idea of rapid and complete homogenization of a meal, gastric contents seem to be rather poorly mixed. Long after ingestion the meal remains heterogeneous, with gastric secretions only poorly penetrating the center of the food bolus. This was observed with a barely pourable test meal. Many real meals are more viscous than this and would be expected to show this effect to a much more striking degree. This is important because there are several buccal enzymes such as lingual lipase that are inactivated at low pH but that are able to continue working for perhaps an hour in the center of a bolus. This may also explain why ~10% of dietary fat is found to be hydrolyzed in the stomach because the buccal lipases are able to continue acting for up to an hour after the bolus enters the stomach. Furthermore, in vitro models of digestion are often carried out by rapid exposure of finely ground food to a very acidic environment. Our findings suggest instead that the center of the meal bolus is not diluted by secretions for an appreciable time. The color coding also suggested that the stomach selectively emptied the more dilute, peripheral components of the meal bolus, which are closest to the contractile activity. This suggests that food leaves the bolus by a process of elution.

We also observed that the volume of secretions present in the digesta increased with high meal viscosity. This is indeed confirmed by the calculations based on the model described in the APPENDIX, according to which the more viscous and nutrient meals showed the higher total volume of secretion produced. The model is based on simple assumptions and could be improved by modeling different kinds of gastric emptying and secretion curves. The mechanism underlying this increase in secretions is again unclear, but early experiments indicated that salivary flow increases under the food stimulus (22). Also, physical distension of the stomach induces gastric secretion (7), so it may be a response to increased distending forces due to the increased resistance to flow of the more viscous meal. We recognize that gastric secretion is determined by cephalic, gastric, and intestinal factors, most of which have not been quantified in this study. We used a heuristic model in which secretion is proportional to the volume of the stomach without implying a causal relationship.

Although our technique is expensive at present, MRI scanners with ultra-fast imaging capability such as EPI are likely to be found in local hospitals within the next few years, raising the possibility that this will become the preferred method of assessing gastric function in clinical practice. Using EPI, we have shown that the intragastric processing of the physically complex meals that we habitually consume is far from simple. The intragastric distribution of meals is influenced by viscosity, with more viscous meals increasing antral distension and satiety. Gastric secretion may also play a role by increasing gastric volumes in response to increased viscosity.

APPENDIX

This APPENDIX presents the simple model used to calculate total gastric secretion. The model assumes that for all meals gastric emptying was exponential in form so that

$$\frac{dv_m}{dt} = -v_m(t) p$$

where $v_m(t)$ is the volume of meal present in the stomach at time $t$ and $p$ is the gastric emptying rate. The model also assumes that the rate of secretion increased linearly with the volume of meal present in the stomach (constant of propor-
tionality $k$) while never falling below $d_{s_0} = 60 \text{ ml/h}$, the assumed basal secretion rate, i.e.,
\[
\frac{dv_s}{dt} = v_u(t)k + d_{s_0} - v_s(t)p
\]
the last term taking account of emptying of the secretion present in the stomach.

At any given time, with EPI we can measure the total volume of meal and secretion present in the stomach $[v_i(t)]$ and the volume of secretion $[v_s(t)]$. The measured curves of $v_i$ and $v_s$ were then fitted to the above model, assuming that the initial volume of secretion present in the stomach was $10 \text{ ml}$. This yielded values of $p$ and $k$, the constants describing the rate of gastric emptying and the rate of secretion induced by a meal. The model equation for $v_s(t)$ was then integrated from $t = 0$ up to $t = 80 \text{ min}$ to calculate the total volume of secretion produced in the presence of the meal. The resulting calculations are presented in Table 2. When the model of gastric secretion produced in the presence of each meal was integrated, taking into account the variable emptying rates, similar effects were found, with viscosity having a greater effect than nutrients.

We gratefully acknowledge Dr. P. Boulby for helpful discussions, Dr. Ron Coxon and Paul Clark for technical assistance, and the Biotechnology and Biological Sciences Research Council (Swindon, UK) for funding this work.

REFERENCES