Aerated drinks increase gastric volume and reduce appetite as assessed by MRI: a randomized, balanced, crossover trial\(^1\)–\(^5\)


ABSTRACT

Background: Compared with nonaerated, isocaloric controls, aerated foods can reduce appetite throughout an entire dieting day. Increased gastric volumes and delayed emptying are possible but unexplored mechanisms.

Objective: We tested the hypothesis that aerated drinks (foams) of differing gastric stability would increase gastric distension and reduce appetite compared with a control drink.

Design: In a randomized, balanced, crossover trial, 18 healthy male participants consumed the following 3 skimmed-milk–based test products (all 110 kcal): 2 drinks aerated to foams by whipping (to 490 mL), one drink that was stable in the stomach [stable foam (SF)], and one drink that was less stable in the stomach [less-stable foam (LSF)], and a nonaerated drink [liquid control (LC); 140 mL]. Over 4 h, stomach contents (foam, air, and liquid) were imaged using magnetic resonance imaging (MRI), and self-reported appetite ratings were collected and quantified by the area under the curve or time to return to baseline (TTRTB).

Results: Compared with the LC, both foams caused significantly increased gastric volumes and reduced hunger (all \(P < 0.001\)). Compared with the LSF, SF further produced a significantly slower decrease in the total gastric content (\(P < 0.05\)) and foam volume (\(P < 0.0001\)) and a longer TTRTB (197 compared with 248 min, respectively; \(P < 0.05\)), although the hunger AUC was not statistically different. Results for other appetite scales were similar.

Conclusions: With this MRI trial, we provide novel insights on the gastrointestinal behavior of aerated drinks by measuring separate volumes of foam, liquid, and air layers in the stomach. Appetite suppression induced by foams could largely be explained by effects on gastric volumes and emptying, which may be further enhanced by foam stability. This trial was registered at clinicaltrials.gov as NCT01690182. Am J Clin Nutr 2015;101:270–8.

Keywords MRI, emptying, foam, hunger, stomach

INTRODUCTION

The global obesity epidemic is a result of many coexistent factors, but an overabundant supply of pleasurable, energy-dense foods and beverages with a low appetite value could be a major contributor. A decrease in subsequent appetite of these products might reduce snacking and daily food intake. In addition, the appetite value of foods designed for inclusion in weight-management programs is an important determinant of consumer compliance to such programs. Physical and chemical properties of the food such as the volume, whether it is liquid or solid, and its energy density and palatability, all influence appetite (1).

The entrapment of large volumes of water or air into a food may be an alternative approach to designing products that have an increased ability to satiate but reduced caloric density (2). A previous study has shown that the consumption of 500 or 1000 mL aerated meal-replacement shake significantly reduced appetite compared with consumption of the original shake (3). A recent study also showed that a 200 mL low-energy aerated drink consumed 3 times/d in the context of a reduced-energy diet reduced appetite throughout the entire dieting day (4). The possible benefit of aeration was built on established evidence of the acute satiety effects of entrapped air in foods. In these experiments, it was shown that aerated foods reduced hunger and increased satiety more than did nonaerated foods (5, 6).

However, little evidence is available to show mechanisms whereby aerated drinks may affect appetite ratings. An increased total gastric content (inducing gastric distension) and delayed...

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4Supplemental Figures 1 and 2 and Supplemental Table 1 are available from the “Supplemental data” link in the online posting of the article and from the same link in the online table of contents at http://ajcn.nutrition.org.

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gastric emptying are likely to be involved, but this relation is difficult to assess without noninvasive abdominal imaging. MRI is ideally suited to measure intragastric volumes of liquid- and gas-containing products serially and noninvasively (7). The technique has been previously validated, it has been used by different groups to measure gastric volumes, and the measurement is widely accepted (7–11). MRI visualizes different meal components such as gas, liquids, particulate phases, and fat (12, 13), and it has been previously used to investigate alginate rafts in vivo (14, 15) and foams in vitro (16–18). However, to our knowledge, the technique has never been applied to visualize foams in the human stomach.

On the basis of these considerations, we designed a randomized, balanced, crossover MRI trial in healthy humans to investigate the hypotheses that 1) an aerated drink will generate more gastric distension than a nonaerated isocaloric control; 2) an aerated drink that is stable in the stomach will generate more or longer gastric distension than an aerated drink that is less stable in the stomach; 3) an aerated drink will reduce appetite more than a nonaerated isocaloric control; and 4) an aerated drink that is stable in the stomach will reduce appetite more than an aerated drink that is less stable in the stomach.

SUBJECTS AND METHODS

Test products

The 3 test products were isocaloric (110 kcal) and comprised of skimmed-milk powder (Lactoland), xanthan gum (Keltrol RD), and water and lemon syrup (Karvan Cevitam) for flavoring. The products were a nonaerated beverage termed liquid control (LC),6 an aerated beverage that was expected to be stable in the stomach termed stable foam (SF), and an aerated beverage that was expected to be less stable in the stomach than SF termed less-stable foam (LSF).

The nutritional content and characteristics are shown in Table 1. The expected gastric stability was based on prior in vitro testing whereby the SF was a strong foam shown to be stable in vitro at an ambient temperature (for ≥2 h) and also in vitro in a simulated stomach after undergoing a simulated oral step. The LSF was also stable at an ambient temperature for ≥2 h, but it was less stable under simulated gastric conditions (almost none of the foam remained after 30 min) because of the lower concentration of xanthan gum. The aerated drinks were produced individually by aerating a larger amount of the drink base by using a Kenwood Chef Classic KM336 kitchen mixer (Kenwood Ltd.) and weighing out the correct amount for the serving. The SF was prepared by using 815 g 0.5% xanthan test product with 91 g lemon syrup, whereas the LSF was prepared by using 905 g 0.1% xanthan test product with 101 g lemon syrup. Both aerated drinks were produced by blending for 2 min at a low speed and whipping for 5 min at a high speed. In the final serving, 350 mL air was added to the 140 mL control beverage, resulting in 490-mL aerated drinks. The LC was prepared by using 135 g 0.5% xanthan test product with 15 g lemon syrup. This LC was mixed gently with a spoon to ensure a minimal incorporation of air.

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6 Abbreviations used: AUC 2h, AUC for 2 h; AUC 4h, AUC for 4 h; EVAS, electronic visual analog scale; LC, liquid control; LSF, less-stable foam; SF, stable foam; TTRTB, time to return to baseline; T50%VOL, time taken for a 50% reduction in total stomach volume post–drink ingestion.

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The measure of the amount of air incorporated in an aerated drink was termed the overrun and defined as

\[
100\% \times \left(\frac{\rho_1 - \rho_f}{\rho_f}\right) - 1
\]

where \(\rho_1\) is the density of the nonaerated product and \(\rho_f\) is the density of the aerated product (i.e., an aerated product with 100% overrun contained a 50% air phase). The overrun of each aerated solution used was determined by knowing the density of the nonaerated test product and calculating the density of the aerated drink by measuring the mass of a known volume of each aerated drink batch.

Experimental design

This trial used a single-center, randomized, balanced, crossover design that consisted of a screening visit and 3 test days, each of which were 1 wk apart. The trial was carried out at the 1.5T MRI unit of the Sir Peter Mansfield Magnetic Resonance Centre located at the University Park campus of the University of Nottingham. On each test day, volunteers were scanned at baseline to ensure that they were fasted. Subjects received 150 g of one of the 3 isocaloric drinks (i.e., the LC, SF, or LSF) according to a computer-generated randomization sequence generated by EAHS. Subjects were asked to finish the test product within 10 min after which MRI measurements and appetite assessment were carried out for ≤4 h postconsumption (Table 2). Before the main trial, the experimental protocol and imaging were refined by using a separate group of 5 healthy volunteers.

The primary outcome was the time taken for a 50% reduction in total stomach volume post–drink ingestion (T50%VOL; in min). Secondary outcomes were gastric volumes (in mL), appetite [in electronic visual analog scale (EVAS) scores], and their respective AUCs (in L/min). Another outcome measure was the relation between the intragastric behavior of test products and appetite. The trial was registered on clinicaltrials.gov as NCT01690182. The trial flow diagram is shown in Supplemental Figure 1.

For the primary outcome, we calculated that a gastric emptying MRI trial with a paired design and \(n = 18\) volunteers would have enough power to detect a difference between products in the gastric half emptying time (T50%VOL) of 30 min with \(\alpha = 0.05\) and a power of 0.90 by using an SD of 30 min (8). The outcome assessor was blinded to the treatment allocation, and subjects were also kept blinded to the intervention although the nonaerated drink was clearly different from the 2 indistinguishable aerated...
drinks. The blind code was broken only after a blind data review was conducted. The trial was formally monitored.

### Trial participants

Twenty healthy male volunteers were initially assessed for eligibility. The entry criteria were age between 18 and 60 y, BMI (in kg/m²) between 20 and 35, nonsmoker, no history of gastrointestinal disorders, and not taking any medication that could interfere with the trial measurements. Only normal and low-restraint eaters (anorexia nervosa or bulimia) were excluded (21). One participant was not eligible, and another individual declined to participate. Therefore, 18 participants were randomly assigned to take part. These subjects had a mean (±SEM) age of 25 ± 1 y (range: 19–38 y) with BMI of 23.8 ± 0.6 (range: 20.3–29.5). Of these subjects, one participant withdrew after the first study day because of a change in the subject’s diary commitments, and another participant was withdrawn by the investigators on the third study day because the subject did not fast at baseline as required.

Participants were asked to minimize changes in their physical activities and not to allow to follow a weight-loss diet for 1 mo before and during the test period. Subjects were instructed not to use alcohol or play sports on the day before each test day. Each volunteer was asked to refrain from eating from 2200 the night before, and only water was allowed before arrival at the test facility. During the test day, subjects were asked to minimize activity and not allowed to eat or drink anything other than the test drinks. Participants were enrolled by EP and KM who also allocated the treatment.

The trial, including the initial optimization phase, was approved by the local Medical School Research Ethics Committee and was carried out in accordance with the Helsinki Declaration of 1975 as revised in 1983. Informed written consent was obtained from each volunteer before experiments. Subjects also completed an MRI safety questionnaire to ensure there were no contraindications for scanning. A site master file and case report forms were kept according to good clinical practice. There were no adverse events during the trial.

### MRI

MRI scanning was performed on a research-dedicated 1.5 T Philips Achieva MRI (Philips Healthcare) scanner. Each volunteer was positioned supine with a 16-element parallel imaging receiver coil wrapped around the abdomen. Gastric contents and emptying were assessed by using a single-shot balanced-gradient echo sequence (80° flip angle; repetition time: 2.8 ms; echo time: 1.40 ms; reconstructed resolution: 1.56 × 1.57 × 10 mm³), which acquired 30 contiguous axial slices across the abdomen under a 12-s expiration breath hold. During imaging, subjects were kept tilted with their left sides slightly raised by using padding on the scanner bed. This simple procedure was comfortable for the volunteers and reduced risk that, in the supine position, floating layers could fill the antrum, reach the pylorus, and empty first, which does not happen during normal upright digestion. The MRI acquisition at each time point lasted ~5 min including the positioning of the participant on the scanner bed, set up, and imaging. Participants were instructed to sit up in a quiet volunteer lounge next to the scanner room between MRI scans so that they spent most of the time upright to minimize possible posture effects on the digestion of test products. Each time participants were about to enter the scanner room, they recorded appetite ratings. Timings of all MRI and questionnaire data points are detailed in Table 2.

### Appetite ratings

Self-reported ratings of appetite measures were collected at baseline, immediately postconsumption, and at intervals thereafter before entering the scanner room (Table 2). Ratings of appetite feelings were scored using reproducible and valid scales (22, 23) by means of a mark on 64-mm scales by using and EVAS on a HP iPAQ pocket personal computer (hx2190b; Hewlett-Packard) (24). Scales were anchored at the low end with the most-negative or lowest-intensity feelings (e.g., not at all) with the opposite term at the high end (e.g., very high). Participants were asked to indicate on a line which place of the scale best reflected their feelings at that moment. The questions related to fullness (How full are you?); hunger (How hungry are you?); desire to eat a snack (How strong is your desire to eat a snack?); desire to eat a meal (How strong is your desire to eat a meal?); thirst (How thirsty are you?), and prospective food consumption (How much do you think you could eat right now?). Ratings of product taste and liking (mouth feel, overall liking, smell, and taste) were also recorded on an EVAS after each test product was consumed. In addition, ratings on physical discomfort (headache, stomach discomfort, bloating, heartburn, nausea, and belching) were recorded on the iPAQ personal computer on a 4-point scale (0 = not, 1 = little, 2 = moderate, and 3 = much) at 2 time points (Table 2).

### Data and statistical analysis

Analyses were carried out by using both intention-to-treat and per-protocol populations as planned. Both populations had similar results.
and conclusions, and hence, only intention-to-treat results were used, which had the advantage of including all available data in the mixed-model analysis with the subject included as a random factor.

Volumes of bulk liquid layer, foam layer, and air layer in the stomach were measured by a single experienced operator by tracing manually a region of interest around each area as shown in Figure 1 with Analyze 9.0 software (Biomedical Imaging Resource, Mayo Foundation) and summing the volume across slices. Plots of volume against time were created and used to determine the time taken for the $T_{50\%\text{VOL}}$, which was computed using a regression analysis. The AUC for 2 and 4 h (AUC 2h and AUC 4h, respectively) were means weighted by time differences between sequential time points and calculated by using the trapezoid method. In the literature, $T_{50\%}$ normally refers to the gastric emptying half time, which is defined as the time needed for the stomach to empty 50% of the meal. Note that, from these images, it was not possible to discriminate between the actual emptying of the foam from the stomach and collapse of the foam in the stomach (whereby part of the foam might drain to liquid and another part of the foam might escape as air via, for instance, belching); hence, the distinction made in this study by using $T_{50\%\text{VOL}}$. The interoperator variability for total gastric volume measurements was evaluated for 3 subjects between 2 operators. This variability was shown to be <7%. The intraoperator variability was shown to be <5% for 3 subjects evaluated 4 times.

For appetite questionnaires, the time course of the mean score for each of the 5 appetite-related questions (fullness, hunger, desire for a meal or snack, and prospective food consumption) and thirst was plotted, and the AUC was calculated. The 64-mm appetite EVAS scores were transformed and expressed on a 100-mm basis. The time to return to baseline (TTRTB) was also calculated for appetite scores for all 3 test products. The TTRTB was calculated by using the Weibull modeling technique, which allowed for the quantitative estimation of the duration of appetite responses. A formal statistical hypothesis testing was technically not possible, and therefore, differences between aerated and nonaerated products were considered to be statistically significant ($P < 0.05$) if their CIs did not overlap (25).

An exploratory, semiquantitative foam-breakdown index was also calculated post hoc because it could provide novel insights into the time courses of foam characteristics in vivo. This index was the mean signal intensity of the foam layer divided by the volume of the foam layer in arbitrary units. Values were calculated up to $t = 90$ min after which the foams had mostly emptied.

All data were analyzed with JMP 9.0 software (SAS Institute Inc.). MRI data were analyzed per time point and per calculated variables ($T_{50\%\text{VOL}}$, AUC 2h, and AUC 4h) by using an ANCOVA with the treatment, visit, and treatment × visit interaction as fixed variables and the subject as a random variable. Covariates used were baseline stomach volume and normalized foam overrun. Liking scores were added as covariates. Appetite data were analyzed per time point and per calculated variables by using an ANCOVA with the treatment, visit, and treatment × visit interaction as fixed variables and the subject as a random variable. Baseline values were used as covariates in the ANCOVA, which is recommended practice in appetite research and corrects well for baseline differences (26). Appetite AUCs were expressed as the average score of a time frame. Similar to the MRI-data treatment, the baseline stomach volume and normalized foam overrun were covariates. Liking scores were also added as covariates to investigate if product liking would influence the outcome. Tukey’s post hoc test was used to compare treatments. Differences were considered significant at $P < 0.05$. All data are reported as means (±SEM).

**RESULTS**

Measured overrun values of the SF (247% ± 7%) and LSF (254% ± 3%) did not differ significantly ($P < 0.4$). All 3 test products were well tolerated by volunteers and finished within the requested 10 min, indicating 100% test product compliance. All 3 layers in the stomach: liquid, foam, and air were clearly distinguished on the MRI images. A representative example is shown in Figure 1. On the T2-weighted images of the stomach, liquids appeared bright white and formed a layer at the bottom of the stomach. Foams appeared as a middle layer darker than fluid because of their lower water proton density and the air bubble matrix that affected the signal. As such, the intensity display scale of images was globally increased for better display of the foams for the analysis. Air appeared as a thin black layer at the top of the stomach.

**Total gastric volumes**

Total gastric volumes rose on consumption and declined with time as shown in Figure 2A. The SF induced a higher total gastric volume than the LSF at all postprandial time points up to $t = 90$ min ($P < 0.05$) and a higher total gastric volume than the LC at all postprandial time points up to $t = 120$ min ($P < 0.05$) except for the first postprandial time point at $t = 10$ min where there was no difference between the SF and LSF. More-pronounced differences were seen in the first 70 min after ingestion. Both aerated drinks decayed to form air and liquid, but the LSF broke down at a faster rate with mostly air and liquid remaining after 65 min. Table 3 shows variables calculated from

![Figure 1](https://academic.oup.com/ajcn/article-abstract/101/2/270/4494382/1)

"FIGURE 1" Representative example of axial MRI images through the same location in the abdomen of a volunteer who ingested a stable foam aerated drink. The images were acquired (A) 10 min and (B) 90 min after ingestion. Anatomical landmarks such as the liver, spine, and spleen are indicated by white arrows. Panel A shows the contour of the stomach in blue. On such T2-weighted MRI images, liquids appear bright white with a layer at the bottom of the stomach clearly visible (green arrow). The foam appears in a middle layer (red arrow) darker than fluid because of the lower water proton density and air-bubble matrix affecting the signal. Air appears as a thin black layer at the top of the stomach (yellow arrow). Panel B shows examples of the regions of interest drawn to measure separately the intra-gastric layers color-coded as in panel A with yellow for the upper air layer, red for the middle foam layer, and green for the bottom liquid layer. Note that the foam layer at this later time point appears brighter than in panel A.
MRI images. The SF had a total gastric volume half emptying time ($T_{50\%VOL}$) that was significantly greater than that for the LSF ($P < 0.02$). In keeping with the smaller initial volume, the rate of emptying of the LC was significantly slower than for the larger aerated drinks. The AUC 4h of the SF was significantly greater than that for both the LSF ($P < 0.001$) and LC ($P < 0.0001$). The AUC 4h of the LSF was also significantly higher than that of the LC ($P < 0.0001$). AUC 2h values showed similar significant differences.

Intragastric foam layer volume

The SF induced a higher intragastric volume of foam than the LSF did at all postprandial time points up to $t = 70$ min ($P < 0.05$) and a higher intragastric volume of foam than the LC did at all postprandial time points up to $t = 90$ min ($P < 0.05$) (Figure 2B). The SF had 5.6 times the volume of foam than that of the LSF at $t = 50$ min, and this difference was significant ($P < 0.0001$). The foam $T_{50\%VOL}$ was significantly longer for the SF than LSF (Table 3, $P < 0.01$). Similarly, the AUC 4h and AUC 2h for foam volume were significantly higher for the SF than for the LSF ($P < 0.0001$).

Intragastric liquid layer volume

The LC had a significantly higher liquid volume in the stomach than that of the SF up to $t = 50$ min (Figure 2C). During this time, the volume of liquid in the stomach after the LSF was significantly greater than that for the SF. Similarly the AUC 4h and AUC 2h showed a higher volume of intragastric liquid for the LC than for the LSF and the SF (Table 3).

Intragastric air layer volume

The change of intragastric air volumes with time is shown in Figure 2D. Initially the LSF produced a higher postprandial
volume of air in the stomach than did both the LC and SF ($P < 0.0001$ at $t = 30$ min compared with both). There was no significant difference after $t = 30$ min. The intragastric air layer volumes of AUC 4h and AUC 2h for both the SF and LSF were higher than for the LC. The difference was small but significant ($P < 0.05$; Table 3).

Appetite

Both the SF and the LSF significantly and positively affected all appetite scores relative to the LC ($P < 0.001$). An example of the time course for hunger scores is shown in Figure 3. All other appetite scales showed similar patterns and differences (Supplemental Figure 2, Table 4). There was no significant overall difference in appetite effects between the SF and LSF for any of the scales as represented by the AUC. At the time points $t = 180$, 210, and 240 min, there were differences of $6$–$12$ mm between the 2 aerated drinks for most of the questions with the difference being significant for fullness at $t = 240$ min ($P < 0.05$). However, a post hoc calculation of the AUCs from $t = 180$ to 240 min showed no different trends to the AUC 2h.

TTRTB calculations that were based on the Weibull modeling technique (25) indicated that the SF had a significantly longer mean TTRTB value than that of LSF, and 95% CIs did not overlap for all appetite questions of fullness, hunger, desire to eat a snack, desire to eat a meal, and prospective food consumption. The LSF, in turn, had a longer mean TTRTB relative to that for the LC again for all appetite questions (Figure 4). Correlations between appetite and total gastric behavior were based on plots of scores for all time points against the total gastric volume. There was a modest but significant correlation with appetite ratings ($r = 0.4$ to 0.5, $P < 0.0001$; Supplemental Table 1).

There were no significant differences in subjects’ scores for mouth feel, smell, or taste between the 3 products. Scores for overall liking were not significantly different apart from a difference between the LC and SF ($P < 0.05$). Because some studies suggested that product liking might affect appetite [although these effects are mostly short lasting; see, e.g., reference 27], liking scores were included as a covariate in the analysis. This analysis showed that product liking had no significant effect on appetite ratings.

Physical discomfort scores confirmed the generally very good acceptance of the 3 test products with only a limited number of subjects (4 subjects) scoring mild abdominal symptoms and fewer subjects (2 subjects) scoring a moderate symptom with approximately one-half of scores on the LC.

Foam-breakdown index

The time course of the foam-breakdown index of SF and LSF foam layers are plotted in Figure 5. This exploratory variable showed a general increase with time with the LSF increasing faster, but because of differences in the baseline signal intensity between visit days, significant differences could not be assessed reliably.

DISCUSSION

MRI allowed both aerated test products to be visualized as foams in the stomach after oral ingestion. It was possible to measure separate volumes of intragastric foam, liquid, and air layers serially and, in turn, total gastric volumes. The presence of a high concentration of proteins and hydrocolloids in the composition of these products was expected to provide sufficient amounts of foaming and stability, thereby preventing rapid disintegration during mastication and gastric steps. Compared with other semisolid food foams, such as whipped cream, the loss of foam from these test products under simulated oral conditions

Figure 3 Mean (±SEM) perceived hunger electronic VAS scores throughout testing days from an intention-to-treat analysis in 18 healthy adult subjects. Line graphs display time courses of changes throughout the 4-h testing day for the SF, LSF, and LC test products. Arrows below x axes denote feeding times. Where indicated, means that do not share a common letter were significantly different at that time point at $P < 0.05$ (Tukey’s test). LC, liquid control; LSF, less-stable foam; SF, stable foam; VAS, visual analog scale.

### Table 3

Scores for postprandial intragastric variables for all trial products

<table>
<thead>
<tr>
<th></th>
<th>SF</th>
<th>LSF</th>
<th>LC</th>
<th>$P^2$</th>
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</thead>
<tbody>
<tr>
<td><strong>Total gastric volume</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$T_{50%VOL}$, min</td>
<td>$48 \pm 4^a$</td>
<td>$39 \pm 4^a$</td>
<td>$63 \pm 4^b$</td>
<td>$&lt;0.0001$</td>
</tr>
<tr>
<td><em>At t = 50 min (mL)</em></td>
<td>$271 \pm 17^c$</td>
<td>$185 \pm 17^b$</td>
<td>$140 \pm 17^b$</td>
<td>$&lt;0.0001$</td>
</tr>
<tr>
<td><strong>AUC 2h, L/min</strong></td>
<td>$34 \pm 2^c$</td>
<td>$28 \pm 2^b$</td>
<td>$18 \pm 2^b$</td>
<td>$&lt;0.0001$</td>
</tr>
<tr>
<td><strong>AUC 4h, L/min</strong></td>
<td>$40 \pm 2^c$</td>
<td>$34 \pm 2^c$</td>
<td>$23 \pm 2^c$</td>
<td>$&lt;0.0001$</td>
</tr>
<tr>
<td><strong>Foam layer volume</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>$T_{50%VOL}$, min</td>
<td>$38 \pm 2^b$</td>
<td>$27 \pm 2^a$</td>
<td>—</td>
<td>$&lt;0.01$</td>
</tr>
<tr>
<td><strong>AUC 2h, L/min</strong></td>
<td>$21 \pm 1^b$</td>
<td>$11 \pm 1^a$</td>
<td>—</td>
<td>$&lt;0.0001$</td>
</tr>
<tr>
<td><strong>AUC 4h, L/min</strong></td>
<td>$21 \pm 1^b$</td>
<td>$11 \pm 1^a$</td>
<td>—</td>
<td>$&lt;0.0001$</td>
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<tr>
<td><strong>Liquid layer volume, L/min</strong></td>
<td></td>
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<td></td>
</tr>
<tr>
<td><strong>AUC 2h</strong></td>
<td>$5.4 \pm 0.7^c$</td>
<td>$8.4 \pm 0.7^b$</td>
<td>$13.6 \pm 0.7^a$</td>
<td>$&lt;0.0001$</td>
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<tr>
<td><strong>AUC 4h</strong></td>
<td>$8.7 \pm 0.8^c$</td>
<td>$12.1 \pm 0.9^c$</td>
<td>$16.8 \pm 0.9^c$</td>
<td>$&lt;0.0001$</td>
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<tr>
<td><strong>Air layer volume, L/min</strong></td>
<td></td>
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<td></td>
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<tr>
<td><strong>AUC 2h</strong></td>
<td>$7.3 \pm 0.8^b$</td>
<td>$8.6 \pm 0.8^b$</td>
<td>$4.4 \pm 0.9^a$</td>
<td>$&lt;0.01$</td>
</tr>
<tr>
<td><strong>AUC 4h</strong></td>
<td>$10 \pm 1^b$</td>
<td>$11 \pm 1^b$</td>
<td>$7 \pm 1^a$</td>
<td>$&lt;0.01$</td>
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</table>

$^2$All values are means ± SEMs. Where indicated, means that do not share a common superscript letter were significantly different at that time point at $P < 0.05$ (Tukey’s test). LC, liquid control; LSF, less-stable foam; SF, stable foam; V AS, visual analog scale.
It has also been shown that significant gastric distension signaling has previously been shown to be fast acting and short lived with effects observed only during balloon inflation (30, 35). This result was consistent with the third hypothesis of the trial. This finding had been expected because increasing the total gastric volume will mostly clear from the stomach. This result indicated that there may be some advantage of using a SF instead of LSF. The foam phase of the LSF was shown to degrade faster than that of the SF. However, even with this lower intragastric stability, the LSF achieved a significant change in appetite scores compared with those with the LC at the tested intakes. Gastric distension alone could not fully explain what effect the aerated drinks had on appetite scores because the correlation between gastric volumes and appetite ratings were relatively weak, and effects on appetite were of longer duration than were volume effects. Other mechanisms responsible may include preingestive and oral stimulation signals (36), gut hormones (37), or the stimulation of an intestinal appetite mechanism (38). In other studies [e.g., see references 39 and 40], the correlation reported was much higher possibly because of a higher energy content (including increased fat) inducing slower gastric emptying and possibly enhanced small bowel feedback (41–43).

The overall appetite was not significantly changed by the SF compared with LSF; hence, the data were not consistent with the fourth hypothesis, although there was a tendency for a difference in the final hour of the experiment after the aerated drinks had mostly cleared from the stomach. This result indicated that there may be some advantage of using a SF instead of LSF. The foam phase of the LSF was shown to degrade faster than that of the SF. However, even with this lower intragastric stability, the LSF achieved a significant change in appetite scores compared with those with the LC at the tested intakes. Gastric distension alone could not fully explain what effect the aerated drinks had on appetite scores because the correlation between gastric volumes and appetite ratings were relatively weak, and effects on appetite were of longer duration than were volume effects. Other mechanisms responsible may include preingestive and oral stimulation signals (36), gut hormones (37), or the stimulation of an intestinal appetite mechanism (38). In other studies [e.g., see references 39 and 40], the correlation reported was much higher possibly because of a higher energy content (including increased fat) inducing slower gastric emptying and possibly enhanced small bowel feedback (41–43).

## TABLE 4

### Appetite scores by question

<table>
<thead>
<tr>
<th></th>
<th>SF</th>
<th>LSF</th>
<th>LC</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fullness</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC 2h</td>
<td>$51 \pm 4^b$</td>
<td>$51 \pm 4^b$</td>
<td>$32 \pm 4^*$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AUC 4h</td>
<td>$43 \pm 3^b$</td>
<td>$40 \pm 3^b$</td>
<td>$26 \pm 3^*$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hunger</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC 2h</td>
<td>$38 \pm 4^b$</td>
<td>$37 \pm 4^b$</td>
<td>$56 \pm 4^*$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AUC 4h</td>
<td>$47 \pm 4^b$</td>
<td>$49 \pm 4^b$</td>
<td>$65 \pm 4^*$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Desire to eat a snack</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC 2h</td>
<td>$40 \pm 4^b$</td>
<td>$43 \pm 4^b$</td>
<td>$60 \pm 4^*$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AUC 4h</td>
<td>$49 \pm 4^b$</td>
<td>$53 \pm 4^b$</td>
<td>$66 \pm 4^*$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Desire to eat a meal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC 2h</td>
<td>$34 \pm 4^b$</td>
<td>$35 \pm 4^b$</td>
<td>$57 \pm 4^*$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AUC 4h</td>
<td>$44 \pm 4^b$</td>
<td>$48 \pm 4^b$</td>
<td>$65 \pm 4^*$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Prospective food consumption</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC 2h</td>
<td>$39 \pm 4^b$</td>
<td>$41 \pm 4^b$</td>
<td>$59 \pm 4^*$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AUC 4h</td>
<td>$47 \pm 4^b$</td>
<td>$52 \pm 4^b$</td>
<td>$66 \pm 4^*$</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Thirst</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>AUC 2h</td>
<td>$55 \pm 4$</td>
<td>$50 \pm 4$</td>
<td>$55 \pm 4$</td>
<td>&lt;0.2</td>
</tr>
<tr>
<td>AUC 4h</td>
<td>$58 \pm 4$</td>
<td>$54 \pm 4$</td>
<td>$58 \pm 4$</td>
<td>&lt;0.2</td>
</tr>
<tr>
<td>Mouth feel</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Overall liking</td>
<td>$44 \pm 6$</td>
<td>$50 \pm 6$</td>
<td>$58 \pm 6$</td>
<td>&lt;0.2</td>
</tr>
<tr>
<td>Overall liking</td>
<td>$40 \pm 6^b$</td>
<td>$47 \pm 6^b$</td>
<td>$55 \pm 6^e$</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Smell</td>
<td>$60 \pm 4$</td>
<td>$64 \pm 5$</td>
<td>$60 \pm 5$</td>
<td>&lt;0.6</td>
</tr>
<tr>
<td>Taste</td>
<td>$49 \pm 6$</td>
<td>$49 \pm 6$</td>
<td>$55 \pm 6$</td>
<td>&lt;0.4</td>
</tr>
</tbody>
</table>

1All values are means ± SEMs. Where indicated, means that do not share a common superscript letter were significantly different at that time point at $P < 0.05$ (Tukey’s test). AUC 2h, AUC from $t = 0$ to 120 min expressed as the average score of a time frame; AUC 4h, AUC from $t = 0$ to 240 min expressed as the average score of a time frame; LC, liquid control; LSF, less-stable foam; SF, stable foam.

2Overall P value. Comparison test: Tukey’s test with $n = 18$.

was negligible (3). Aerated beverages were prepared immediately before consumption, and drinks volumes and overrun were checked before ingestion. This method showed that there were no differences in aerated product volumes before ingestion. The first imaging point at $t = 10$ min after ingestion also showed that SF and LSF total gastric volumes were the same.

Both aerated products caused greater gastric distension than did the LC. This result was consistent with the first hypothesis of the trial. The decrease in the total gastric volume and foam layer volume was slower after ingestion of the SF than LSF. This result was consistent with the second hypothesis of the trial. The SF was more stable than the LSF because of the increased xanthan gum concentration (28). The aerated products significantly reduced the appetite scores compared with those with the isocaloric, nonaerated control, which confirmed result of earlier studies even though the type of aerated drinks (and presumably their gastric stability) used in the current study differed (3–6). This result was consistent with the third hypothesis of the trial. This finding had been expected because increasing the total gastric volume will progressively distend the stomach, and distension has an inverse relation on appetite as shown previously by using intragastric balloons (29, 30) and meals of different viscosities (31). This relation is assumed to be attributable to the activation of mechanoreceptors in the stomach wall (32–34), which likely trigger vagal discharges leading to the activation of hypothalamic neurons and the modulation of feelings of appetite. The gastric distension signaling has previously been shown to be fast acting and short lived (30, 35) with effects observed only during balloon inflation (30, 35). It has also been shown that significant changes in appetite scores occur only at higher intragastric volumes [400 mL (30) and 600 mL (35)]. The starting aerated drink volumes used in this trial (490 mL) were within this range, and indeed, a significant decrease in appetite compared with the LC was observed. What would happen intragastrically at lower initial aerated drink volumes remains to be evaluated, although previous studies showed beneficial appetite effects for volumes between 150 and 250 mL and a volume of 200 mL after repeated daily consumption (4).

The overall appetite was not significantly changed by the SF compared with LSF; hence, the data were not consistent with the fourth hypothesis, although there was a tendency for a difference in the final hour of the experiment after the aerated drinks had mostly cleared from the stomach. This result indicated that there may be some advantage of using a SF instead of LSF. The foam phase of the LSF was shown to degrade faster than that of the SF. However, even with this lower intragastric stability, the LSF achieved a significant change in appetite scores compared with those with the LC at the tested intakes. Gastric distension alone could not fully explain what effect the aerated drinks had on appetite scores because the correlation between gastric volumes and appetite ratings were relatively weak, and effects on appetite were of longer duration than were volume effects. Other mechanisms responsible may include preingestive and oral stimulation signals (36), gut hormones (37), or the stimulation of an intestinal appetite mechanism (38). In other studies [e.g., see references 39 and 40], the correlation reported was much higher possibly because of a higher energy content (including increased fat) inducing slower gastric emptying and possibly enhanced small bowel feedback (41–43). The TTRTB for appetite scores...
also showed that the aerated drinks reduced appetite more than did the LC and particularly the SF. During this late postprandial time window, the stomach was already empty, which suggested the possible stimulation of an intestinal appetite mechanism. The concept of intestinal appetite beyond a gastric volumetric appetite is not new (41) because it is well known that the arrival of nutrients in the duodenum is a major source of feedback signaling and a determinant of appetite (44). The aerated drinks seemed to act to create a 2-phase system in the stomach, and it would be interesting to evaluate whether the emptying of foam in the duodenum occurs and investigate how this alters the nutrient delivery.

The observed increase in the foam signal intensity with time was greater for the LSF, probably reflecting an increase in air-bubble size within the foam with time, which is a process known as disproportionation (17, 45). This effect was also reflected in the changes along the signal-intensity line profiles. This relatively easy, semiquantitative measurement could help to assess the status of foam in the gastric lumen and differences in performance between alternative formulations.

Subjects were kept blinded to intervention although the appearance and volume of the nonaerated LC were necessarily different from the volume of both indistinguishable aerated products. The LC difference in volume and consistency compared with those of the aerated products could have stimulated cognitive effects on ingestion. For instance, there might have been an expectation that larger volumes would be more filling. Brunstrom et al. (46) showed that the amount of expected satiety and satisfaction are related to the perceived volume of a meal, whereas other authors also hypothesized that volume might affect beliefs of the satiating capacity of foods (47, 48).

The difference in initial volumes was also expected to have some impact on the rate of gastric emptying of the LC relative to the aerated drinks. It has been previously reported that increased gastric filling increases intragastric pressure as well as the gastric emptying rate (49, 50). The initial volume difference also explained why the $T_{50\% VOL}$ for the LC appeared artificially long (49).

In conclusion, this trial provides novel insights, to our knowledge, of the intragastric behavior of aerated drinks. MRI makes it possible to measure separate volumes of foam, liquid, and air layers in the stomach. The data suggest that the hunger suppression induced by aerated drinks could largely be explained by effects on gastric volumes and emptying, which may be further enhanced by foam stability. Such knowledge and methods could be useful to aid the manufacture of aerated products by providing an objective assessment of in vivo performance and improved understanding of mechanisms affecting gastrointestinal physiology and appetite.

We are grateful for support from the National Institute for Health Research Nottingham Digestive Diseases Biomedical Research Unit. The Consolidated Standards of Reporting Trials flow diagram and checklist are available in the Supplemental Material.

The authors’ responsibilities were as follows—LM and HPFP: designed the research; KM, EP, and LM: conducted the research; PAG and RCS: supervised the study; LNA, SDS, and WK: were involved in all (in vitro and in vivo) work for the selection and preparation of foams; CLH: designed the MRI sequences; SEP: analyzed data; KM: analyzed data and had primary responsibility for the writing of the manuscript; WAMB: assisted with data discussion; EAHS: performed the statistical analysis; LM: had primary responsibility for the final content of the manuscript; and all authors: substantially contributed to the completion of the manuscript and read and approved the final version of the manuscript. EAH, WK, LNA, WAMB, SDS, and HPFP were Unilever employees. KM, EP, CLH, SEP, PAG, RCS, and LM had no conflicts of interest.

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