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# A tale of gastric layering and sieving: Gastric emptying of a liquid meal with water blended in or consumed separately

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ABSTRACT

*Background:* The process of gastric emptying determines how fast gastric content is delivered to the small intestine. It has been shown that solids empty slower than liquids and that a blended soup empties slower than the same soup as broth and chunks, due to the liquid fraction emptying more quickly. This process of 'gastric sieving' has not been investigated for liquid foods.

*Objective:* To determine whether gastric sieving of water can also occur for liquid foods.

*Method:* Two groups of men participated in a parallel design ($n$ = 15, age 22.6 ± 2.4 y, BMI 22.6 ± 1.8 kg/m$^2$, and $n$ = 19, age 22.2 ± 2.5 y, BMI 21.8 ± 1.5 kg/m$^2$) and consumed an isocaloric shake (2093 kJ, CARBOHYDRATES: 71 g, FAT: 18 g, PROTEIN: 34 g), either in a 500-mL version (MIXED) or as a 150-mL shake followed by 350 mL water (SEPARATE). Participants provided appetite ratings and were scanned using MRI to determine gastric emptying rate and volume at three time-points within 35 min post ingestion.

*Results:* Gastric emptying the percentage emptied in 35 min was significantly smaller for MIXED (29 ± 19%) than for SEPARATE (57 ± 11%, $p$ < 0.001).

*Conclusion:* In the present study we show that gastric sieving can occur for liquid foods; water is able to drain from the stomach while a layer of nutrient rich liquid is retained. In indirect gastric emptying measurements, the behavior of labelling agents may be affected by the layering and confound emptying measurements.

## 1. Introduction

Gastric emptying is an important part of digestion, as the stomach acts as a gatekeeper distributing nutrients to the small intestine, in order to optimize digestion. The dynamics of stomach content flow and passage are still not completely understood. Gastric emptying was studied in relation to food qualities in animals, namely canines, in the seventies. This work showed that solids empty slower than liquids [1,2].

Subsequent work from the nineties showed congruent results in humans; the liquid fraction of the gastric content was dispersed quickly and drained quickly as well, with solid pieces being retained for longer periods in the stomach [3]. Additionally, Collins et al. showed differences in gastric content in the proximal and distal parts of the stomach. A subsequent study compared a solid meal given together with water versus a homogenized soup-like stimulus made out of the same ingredients [4]. In this study, the homogenized version yielded significantly higher feelings of fullness and slower gastric emptying. The authors attributed this to greater distension of the antral region by the homogenized version in combination with the slower emptying. Rolls et al. extended this by showing that subsequent intake can be reduced by incorporating water into a food dish, instead of serving water concurrently with the dish [5].

In 2012 it was shown - using MRI - that a possible mechanism for this greater satiety resulting from incorporated water is caused by the fact that when the solid and water fractions are not homogenized, the water sieves from the gastric content and empties quickly [6]. This gastric sieving can be prevented by blending the two fractions together to create a homogeneous caloric food. Additionally, emulsifiers have been used to manipulate the dispersion of fats throughout the gastric content and thereby manipulate gastric emptying [7].

Many commercial meal replacements in liquid form are currently available. Liquid meals are also often used in studies because they offer practical benefits over solid meals, for example when feeding must take place at standardised rates or through a tube. Although gastric sieving of water has been shown with solid and semi-solid foods, it has to our knowledge never been investigated using a liquid meal. MRI is optimal measurement method understanding gastric passage of liquid meals and

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**Table 1**
Energy content and nutrient composition of the shakes.

| | MIXED | SEPARATE |
|---|---|---|
| **Ingredients, per 100 g shake** | | |
| Protein powder, g | 5.1 | 12.4 |
| Cream, g | 8.5 | 20.8 |
| Dextrin-maltose, g | 8.9 | 21.9 |
| Vanilla sugar, g | 1.3 | 3.3 |
| Water, g | 76.2 | 41.6 |
| Total, g | 100 | 100 |
| **Nutrients, 100 g shake** | | |
| Energy[a], kJ | 418 | 1393 |
| Carbohydrates, g | 12 | 40 |
| Of which mono- and disacharides | 2.1 | 7 |
| Fat, g | 3 | 10 |
| Of saturated | 2.1 | 7 |
| Protein, g | 6 | 20 |
| Fiber, g | 0.5 | 1.7 |
| **Total ingested** | | |
| Shake weight, g | 591 | 241 |
| Amount of water served after shake, g | 0 | 350 |
| Shake energy, kJ (kcal) | 2093 (500) | 2093 (500) |
| Total volume, mL | 500 | 500 |

[a] Nutrient composition of the shake resembles a mixed meal, with 50% of the energy load coming from carbohydrates, 30% from fats and 20% from protein.

the interaction with water consumption. Understanding this passage will help create novel experimental designs in the future.

In this research we sought to determine whether gastric sieving of water can also occur with liquid meals. We hypothesized that the stomach empties more quickly when water is consumed separate from a liquid meal, as compared to when water is consumed as part of a liquid meal (mixed in). We also hypothesized that mixed consumption will suppress appetite more.

## 2. Materials and methods

### 2.1. Design

The design for this analysis is a two sample comparison between two treatments. Participants participated in one of two larger trials (Dutch Trial Register (NTR4573 (published: [8]) and NTR5507)).

### 2.2. Test products

An overview of the nutrient content of the test products can be found in Table 1.

The shake consisted of 50 g cream (Albert Heijn B·V, Zaandam, The Netherlands), 53 g Fantomalt (Nutricia®, Cuijk, The Netherlands), 30 g whey powder (Whey Delicious Vanilla, XXL Nutrition, Helmond, The Netherlands) and 8 g vanilla-sugar (Dr. Oetker®, Bielefeld, Germany). These ingredients were used to create a liquid shake either with 100 g of water or with 450 g of water (SEPARATE or MIXED). The shakes were mixed by adding the ingredients into a closed 600-mL beaker and whisking with an internal spherical whisk (diameter 3.5 cm). In case of the smaller shake, 350 g of water was consumed directly after finishing the shake.

### 2.3. Participants

Two groups of healthy men, SEPARATE ($n = 15$, age 22.6 ± 2.4 y, BMI 22.6 ± 1.8 kg/m$^2$) and MIXED ($n = 19$, age 22.2 ± 2.5 y, BMI 21.8 ± 1.5 kg/m$^2$), participated. There were no participants partaking in both trials. Participants were recruited via email. To be eligible, participants had to be male, healthy and 18–35 years old. Potential participants were screened to be of normal weight (BMI 18.5–25.0 kg/m$^2$) and willing to comply with the study procedures. By use of a questionnaire, potential participants were excluded if they had a self-reported hypersensitivity for any components which were present in the test products, if they were on a diet or had unexplained weight loss or gain in the past months, or if they reported any MRI contraindications. The procedures were approved by the Medical Ethical Committee of Wageningen University in accordance with the Helsinki Declaration of 1975 as revised in 2013. Written informed consent was obtained from all participants.

### 2.4. Study procedures

Participants were instructed to have a light meal the night before the session and not do any rigorous exercise or strenuous activities that day. Participants were instructed to fast for at least 3 h, only drinking water in that time and nothing during the last hour before each session. After arrival participants provided baseline appetite ratings, that is ratings of hunger, fullness, prospective consumption, desire to eat and thirst. These were orally scored from 1 to 100 points [9].

Subsequently participants were scanned for baseline stomach content (to confirm it was empty). After this, participants exited the scanner and consumed the shake (MIXED) or shake and water (SEPERATE).

Each participant consumed the shake within 2 min as instructed. After that, they were positioned in the scanner and provided appetite ratings via the intercom and underwent gastric MRI scans up to 40 min after ingestion. For MIXED scans and scores were obtained directly after ingestion, at 10, 20, 30 and 40 min. Data for 30 and 40 min were interpolated. For SEPARATE scans and scores were obtained directly after ingestion and at 15 and 35 min.

### 2.5. MRI

Participants were scanned with the use of a 3-Tesla Siemens Verio (Siemens AG, Munich, Germany) MRI scanner using a $T_2$-weighted spin echo sequence (HASTE, 24 6-mm slices, 2.4 mm gap, 1.19 × 1.19 mm in-plane resolution, effective TE of 87 ms with parallel imaging (grappa, factor 2), with breath hold command on expiration to fixate the position of the diaphragm and the stomach. The duration of one scan was approximately 19 s. Syngo fastView MRI software (Siemens AG, Munich, Germany, http://www.healthcare.siemens.com/medical-imaging-it/syngo-special-topics/syngo-fastview) was used to manually delineate gastric content on every slice. Gastric volume on each time point was calculated by multiplying surface area of gastric content per slice with slice thickness including gap distance, summed over the total slices showing gastric content.

### 2.6. Statistical analyses

AUC over 35 min was calculated for subjective ratings and gastric content using Graphpad Prism 5 (Graphpad Software, La Jolla, USA), following the trapezoidal rule. Change in appetite ratings was tested using an ANOVA with time, treatment and the interaction as fixed factors and subject as random factor and baseline measurement as a covariate. Post hoc LSD corrected test were performed in case of significant effects.

Differences between the AUC values were tested using a *t*-test. Emptying percentage of the gastric content in 35 min was calculated by correcting for baseline and dividing the content at 35 min by the starting volume. The difference between percentage emptied in this period was tested using a *t*-test. Significance level was set at $p = 0.05$. Data are expressed as mean ± SD. All tests were performed using IBM SPSS 22.0 (IBM, Armonk, USA).

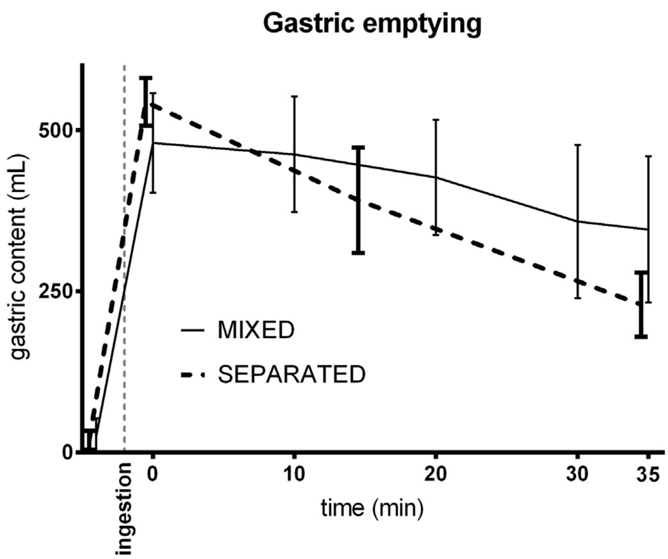


**Fig. 1.** Gastric emptying curves for both treatments are shown over 35 min. SEPARATE empties significantly more quickly over 35 min. In Supplemental Fig. 1 separate curves are shown for the emptying of the shake and water fraction in the SEPARATE condition.

## 3. Results

### 3.1. Gastric content

Gastric emptying curves for both treatments of the meal can be found in Fig. 1. Fig. 2 shows example MRI images from both treatments. Percentage emptied in 35 min was significantly smaller for MIXED (29 ± 19%) compared to SEPARATE (57 ± 11%, $p < 0.001$). Table 2 shows the gastric content and percentage at each timepoint.

MIXED AUC (18,813 ± 3170 mL·min$^{-1}$) was significantly greater than SEPARATE AUC (13,170 ± 1708 mL·min$^{-1}$, $p = 0.035$).

### 3.2. Subjective ratings

None of the subjective ratings were significantly different between treatments when comparing AUCs.

Appetite curves for both treatments can be found in Fig. 3.

## 4. Discussion

### 4.1. Summary of results

In the current analyses we aimed to show gastric sieving of water with liquid gastric food content. We found that a liquid meal followed by a drink of water empties about twice as fast in the first 35 min compared to the same amount of water incorporated within the liquid meal. Despite dissimilar emptying rates we found similar changes in appetite feelings.

### 4.2. General

Our results show, in line with our hypothesis, that 'gastric sieving' can also occur with a liquid food. It has been shown recently that a nutrient rich filling of the stomach which absorbs water (bread), leads to a greater delay in gastric emptying than one which does not absorb water as readily (rice) [10]. We observed that if liquid food and water do not mix in the stomach, a layer rich in nutrients including fat, can remain separate. That watery, low nutrient layer can subsequently drain from the stomach. This prevents the nutrient content from entering the duodenum and delaying gastric emptying, thereby creating a relative increase in gastric emptying when compared to the mixed shake. Gastric MRI images taken after ingestion allow us to clearly discern the layer of water beneath the nutrient rich liquid in the stomach (Fig. 2). This finding strongly resembles research from 2013 in which different gastric layers were observed for an isocaloric liquid and semi-solid meal [11].

SEPARATE had a higher post ingestive volume than MIXED. We attribute this to the fact that the smaller shake volume is thicker and thereby contains more air bubbles, which yields a slightly larger starting volume. The volume increase for SEPARATE was 24 ± 22 mL air, which corresponds to a ratio of 0 to 25%. This larger volume may have stimulated gastric emptying. However, this difference in starting volume is relatively small and further research is necessary

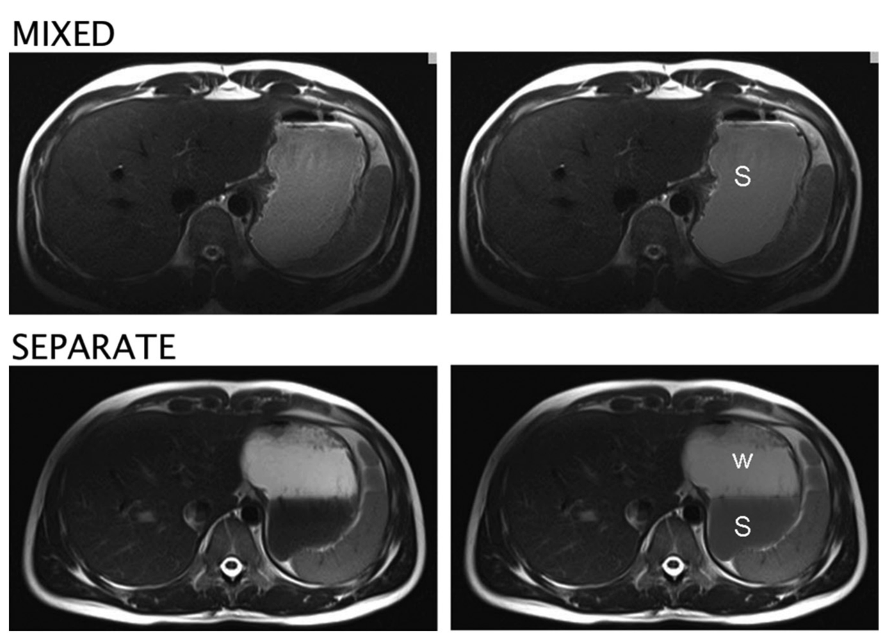


**Fig. 2.** Example gastric MRI images. Shown are transverse slices at the height of the liver, directly after ingestion. Left: original images. Right: the same slices as shown on the left but with the gastric content highlighted manually based on signal strength as indicated by colorization. S: shake fraction. W: water fraction.Water yields high signal in a $T_2$-weighted scan, and therefore appears bright. In the MIXED condition a uniform coloration of the gastric content can be observed. In the SEPARATE condition, owing to the watery content, a whiter layer can be observed on top of the shake layer. In Supplemental Fig. 2 an in vitro example of the SEPARATE condition is shown.

**Table 2**
Gastric content per timepoint.

| Time | MIXED, mL ± SD | % emptied | SEPARATE, mL ± SD | % emptied |
|---|---|---|---|---|
| Baseline | 26 ± 27 | | 18 ± 15 | |
| 2 | 480 ± 77 | 0 | 543 ± 37 | 0 |
| 10 | 463 ± 89 | 4% | | |
| 15 | | | 391 ± 82 | 28% |
| 20 | 427 ± 89 | 11% | | |
| 30 | 358 ± 119 | 25% | | |
| 35 | | | 229 ± 50 | 58% |
| 40 | 346 ± 113 | 28% | | |

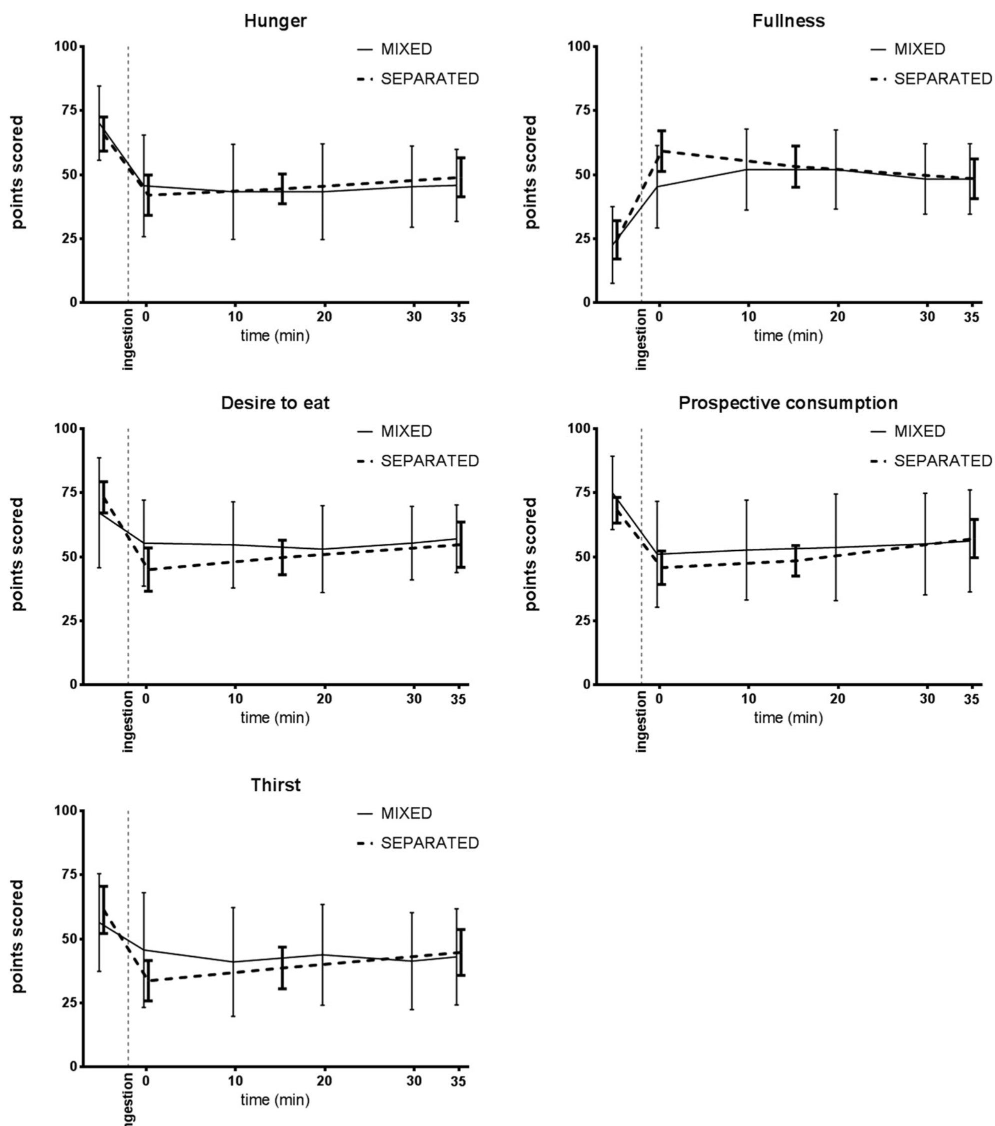


**Fig. 3.** Appetite curves for both treatments are shown over 35 min. There were no significant differences between treatments.

to determine whether this could explain the observed difference in emptying.

For SEPARATE there was a larger variance of gastric content than for MIXED. This could be due differences in stomach anatomy between participants. Stimulation of the antral region of the stomach by the nutrient rich layer may be more or less pronounced depending on the anatomical shape of the stomach. This would be an interesting avenue for further research.

We did not find any significant differences in appetite ratings between the two treatments, with the exception that if water is consumed separately it quenches thirst more than when incorporated within a shake. The lack of appetite suppression may be due to there not being an effect, or to the fact that significant differences will only occur at a later moment and that our measurement window was simply too short to observe these differences. The latter seems plausible as effects on satiety have been reported in other work with longer measurement windows [6]. Alternatively, the fact that we did not find any difference might be due to the fact that both stimuli were liquid, yielding smaller differences.

### 4.3. Limitations

These results show significant differences in the emptying time between the treatments when comparing two groups in a parallel design. However, a limitation of this work is that we compare between different groups. Differences between the individual participants may have confounded the results.

Ideally, the work would have been carried to using one sample and a crossover design, making MRI scans at the exact same time. In future work, the data collection period should be lengthened, as this will give more insight in the complete emptying curve. Though the studied period was long enough to find very significant differences, additional measurement points will allow better analysis of the emptying curve.

Gastric content at different time points has been used in other publications to fit an emptying curve and thereby estimate the gastric emptying $t^{50}$ [12]. In this study the number of data points was not sufficient to do curve fitting. However, we feel that using the AUC of the emptying curve for this specific comparison is justifiable since in similar studies the largest differences in emptying occur within the first 35 min [6,11].

Participants were scanned while remaining in a supine position. Therefore, gastric emptying rate may have been slower than in a standing or sitting position [13]. However, we conject that relative differences will be similar, although the overall emptying may be slower than that in an upright position.

Additionally, in other experiments positioning of the subject in a supine position was accompanied with adjustments with a pillow to manipulate the pyloric and antrum location. This prevents a delivery of the rich top fatty layer into the duodenum or stimulating the antrum leading to slowed gastric emptying [14–16]. In our experiment both treatments had the same completely supine position, and the position was not adjusted using a pillow, which may increase the effect of the layering.

### 4.4. Implications and suggestions for further research

In the design for SEPERATE we purposefully had the participants drink the calorie rich shake first, because we feared that if water was consumed first it may seep through the stomach as gastric emptying is mainly determined by nutrient load [17,18]. The sensing of calories in the duodenum will retard emptying and thereby make sure that the following water does not directly pass.

We conject that because the shake is different in density and viscosity as compared to water, it stays separated from the water fraction. This is potentially mitigated by the emulsification of the cream in the shake and its additives. It would be possible that if the two fractions are more similar in composition the layers would not stay separated.

The gastric layering with fluid we and others have observed may explain differences between gastric emptying measuring methods [19]. Indirect gastric emptying measurement methods such as isotope labelling and acetaminophen plasma levels can be confounded if the measured agent is in either layer: underestimation of emptying time if it is in the water fraction, and overestimation of emptying time if it is in the nutrient rich layer. This implies that if a research paradigm includes both nutrient ingestion and drinking water or there is a potential for post-ingestive gastric layering, MRI measures or MRI piloting is advisable. MRI allows us very detailed insights of the emptying process, which may lead to new avenues for strategies to influence appetite.

## 5. Conclusion

We showed using MRI that gastric sieving, which has been demonstrated for solid and semi-solid foods, can also occur in liquids. We attribute this to gastric sieving of water from the stomach, by water draining from above a layer of nutrient rich liquid. This can have large effects on gastric emptying rate, even when the total nutrient content of the gastric load is the same. Also, this suggests that indirect gastric emptying measurements may be affected by gastric layering.

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GC, MM, CdG and PAMS designed the study, GC conducted the research, GC performed statistical analysis; GC, MM, CdG and PAMS wrote the paper, PAMS had primary responsibility for final content.

## Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.physbeh.2017.03.029.

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