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**Original article**

# Proximal gastric distension modifies ingestion rate in pigs

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**Summary** — Control of food ingestion related to proximal gastric distension has never been demonstrated in pigs. The aim of this study was to demonstrate its existence. Meal duration, food intake rate and characteristics of non-ingestion periods were evaluated during the ingestion of a 500 g meal with simultaneous balloon distension of the proximal stomach. Distensions were performed either at fixed pressure levels or at fixed volume levels. Five pressure levels and five volume levels were tested in duplicate experiments in random order and on different days in each animal. Pressures equal or above 11 mmHg increased meal duration (656 ± 12 vs 562 ± 30 s, 11 mmHg vs control) because of a lower rate of food intake and longer periods of non-ingestion. On the contrary, irrespective of the gastric bag volume, isovolumic distensions did not alter feeding behaviour. We concluded that a short term control of food intake exists in pigs.

**gastric compliance / barostat / food intake / gastric distension / gastric tone**

**Résumé — La distension de l'estomac proximal modifie la vitesse d'ingestion chez le porc.** Un contrôle à court terme de la prise de nourriture par l'état de distension de l'estomac proximal n'a jamais été démontré chez le porc et prête encore à controverse chez les autres espèces. En effet, la réduction de la prise alimentaire liée à l'introduction de masses non alimentaires dans l'estomac est variable. Le but de cette étude est de démontrer la réalité de ce contrôle chez le porc en utilisant une méthode de distension qui supprime l'influence de l'accommodation gastrique. La durée du repas, la vitesse d'ingestion et les caractéristiques des périodes de non ingestion ont été évaluées au cours d'un repas solide de 500 g. Les distensions de l'estomac sont effectuées selon un mode isovolumique ou isobarique. Les pressions supérieures ou égales à 11 mmHg augmentent significativement la durée du repas car la vitesse d'ingestion est réduite et la durée de l'ingestion accrue. A l'inverse, et quel que soit le volume du ballon, les distensions isovolumiques sont incapables de modifier le comportement alimentaire. Il existe donc bien un contrôle à court terme de l'ingestion chez le porc.

**compliance de l'estomac / barostat / prise alimentaire / distension de l'estomac / tonus de l'estomac**

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The contribution of gastrointestinal segments to meal termination has been extensively debated. In rats, during pyloric occlusion, inhibitory signals from the stomach generate premature meal termination (Seeley et al, 1995; Phillips and Powley, 1996), hence reduced ingestion. Similarly, balloons occupying about 30% of the rat gastric capacity (Geliebter et al, 1986) had a relatively large impact on food intake, reducing it by more than 25% (Geliebter et al, 1987). Surprisingly, in man, a 400 mL balloon occupying 30% of the stomach was unable to trigger a significant reduction in food intake (Geliebter et al, 1990). Similar inconclusive data have been obtained in dogs (Share et al, 1952). Therefore, non-alimentary mass might not represent an optimal tool to evaluate the possible role of gastric distension as meal termination signal. Use of alimentary loads is equally unsatisfactory (Kaplan et al, 1994) because, without pyloric occlusion, the chemical compounds are transferred to the small intestine. Finally, pyloric occlusion inhibits antral motility while stimulating duodenal contractions (Edelbroek et al, 1993).

In the last decade, gastroenterologists have demonstrated that the stomach does not behave like a balloon stretched by the arrival of food. Indeed, ingestion reduces temporarily gastric wall tension; a phenomenon primarily described in dogs and humans (Azpiroz and Malagelada, 1985, 1986) then later in pigs (Houpt, 1994) and defined as gastric accommodation. Therefore, if a non-alimentary mass is present in the stomach before the meal, it is likely that the afferent information from the stomach to the brain reflects a combination of an increased wall tension (by the non-alimentary mass) together with a decrease in the same wall tension (induced by gastric accommodation). For the gastric mecanoreceptors, the net effect of these conflicting changes might be null depending on the ratio between the volume of the non-alimentary mass and the amplitude of gastric accommodation (Gregersen and Kassab, 1996). Our hypothesis is that the relative inefficacy of non-alimentary loads to reduce ingestion relates to this nullification. Nevertheless, non-alimentary loads might represent a powerful tool to evaluate the relationship between food intake and gastric distension provided the consequences of gastric accomodation could be cancelled.

The aim of this study was to evaluate the influences of proximal gastric distension on food intake in pigs. Gastric distension will be performed using a barostat that maintains a steady pressure within the stomach to cancel gastric accomodation. These distensions will be compared to constant volume distensions during which the influences of gastric accomodation are preserved. To allow comparisons between distension methods, proximal gastric compliance will be evaluated first to obtain pressure–volume pairs used for distension experiments.

## MATERIALS AND METHODS

### Animals

Studies were performed on eight Large White female pigs aged 4–6 months (43 ± 5 kg). Animals were preanesthetized with Ketamine (5 $mg.kg^{-1}$, intramuscularly, Rhône Merieux). Under aseptic conditions and general anaesthesia (Halothane 5% v/v), a silicon cannula (ID 10 mm) was inserted into the fundus, 20 cm proximal to the pylorus. The cannula was exteriorized through the left flank taking care to respect the anatomical topography of the abdominal viscera. Animals were allowed to recover for 7 days before the experiments.

### Measurement of feeding behaviour

Food intake was measured by continuous weighing of the trough during the meal. A load cell (LOC30KG, Phimesure, France) was placed under the trough and secured to the bottom of the cage. The cell was connected to a specially built amplifier (1B31, Analog Devices, USA).

A low pass filter (0.6 Hz, –3 dB) was used to minimize the artifacts generated by movements of the animal. The recording bench was linear from 0 to 3 kg (± 0.01%) and its sensitivity was ± 3 g full scale.

## Fundic distension device

Fundic distensions were performed by inflating a polyurethane bag (500 mL) inserted extemporaneously in the fundus through the cannula. The bag was connected to the inflation device by a double lumen polyvinyl tube (14 French, Vygon, France).

The distension device (Synectics, Sweden) consisted of a computer controlled pump (sensitivity 0.15 mL) allowing the injection or retrieval of known volumes of air at a rate of 40 $mL.s^{-1}$ minimum. For isovolumic studies, the system behaved as a constant speed air injector. For isobaric studies, the pressure within the bag (equal to the proximal gastric pressure) was monitored constantly by the computer using a high sensitivity air pressure transducer (0.01 mmHg, Switch, USA) and the computer software controlled the retrieval or injection of air so that the bag pressure was held at a fixed value (set pressure). To minimize artefacts caused by rapid intra-abdominal pressure changes, the pressure signal was filtered (1 Hz, –3 dB) and a pressure window set at 0.2 mmHg was used by the software as previously described (Whitehead et al, 1997).

For proximal gastric compliance measurements, the computer behaved as a pressure clamp system, every 2 min the set pressure being automatically incremented by 2 mmHg. A total of 12 steps, corresponding to a pressure range of 0 to 22 mmHg was tested.

## Signal recording

During each distension modality, pressure and volume within the intragastric bag and the weight of the meal remaining in the trough were digitized at 10 Hz (Macintosh, Apple, Cupertino and NB-MIO16, National Instrument, Houston, USA) and stored on a hard drive for later analysis. Volume measurements were corrected for air compressibility using the Boyle's law ($P_1V_1 = P_2V_2$).

## Experimental protocol

All studies were performed during the ingestion of a 500 g solid meal (11.5% proteins, 63.5% carbohydrates, 2.6% lipids, 3.3% fibers) supplying 1815 kcal net energy. Experiments were performed between 10 h 00 and 11 h 00 am and after 12 h fasting. After the experiments, the animals were fed a regular (1500 g) meal.

One hour before the experiment, the stomach was cleared of any food residues and the polyurethane bag was inserted into the fundus. The bag was secured in position and was then inflated up to 250 mL to remove the folds. Afterwards, air was automatically withdrawn until the bag pressure was permanently less than –1 mmHg. Correct positioning of the bag in the fundus was checked once in each experiment using lateral X-ray imaging of the stomach.

## Experimental design

Pressure and volume used for isobaric versus isovolumic proximal gastric distensions were determined from proximal gastric compliance values. Proximal gastric compliance was measured twice on different days in each animal during the ingestion of the test meal. Pressure–volume pairs were selected along the compliance curve before, during and after the high compliance area (greater slope): 4–50, 7–150, 11–300, 16–400 and 21–450 mmHg–mL (fig 1).

Isobaric versus isovolumic distensions were performed at random on a daily basis except when proximal gastric compliance was measured. Each distension step was performed at least twice per animal. An additional distension with a bag volume set to zero mL was also performed twice on each animal and served as a control. Distensions were started 10 min before the meal and maintained for 30 min.

## Data analysis

The weight of food remaining in the trough during ingestion was processed off line to remove artefactual increases in weight related to the search for food. These periods during which the weight was higher than for periods occurring immediately before were not taken into account later in the analysis. Since removal of some data

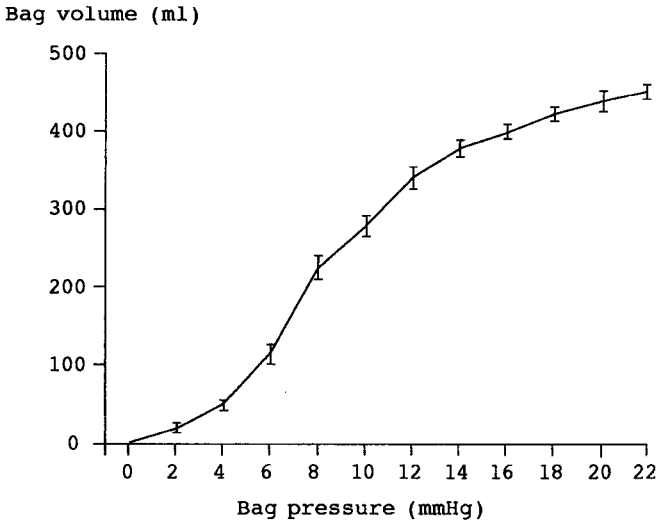



**Fig 1.** Per-prandial pressure-volume relationship (compliance) during step inflation (2 mmHg increments, each step lasting 2 min) of the proximal stomach.

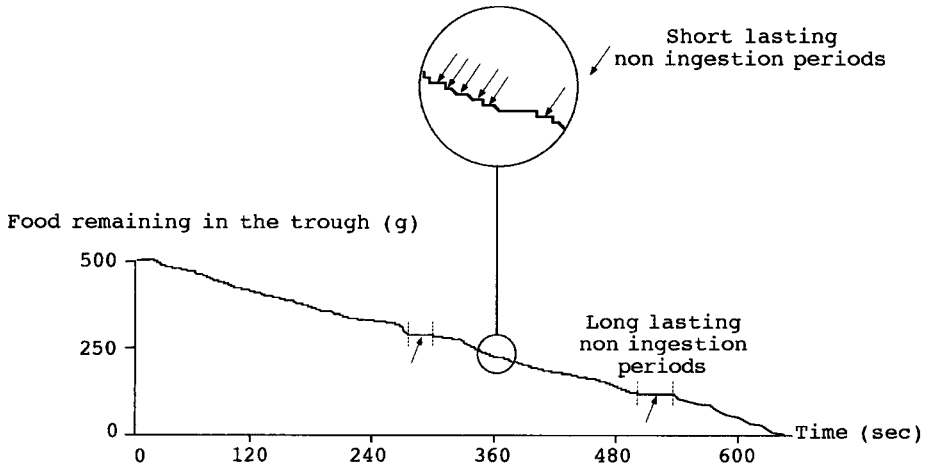



**Fig 2.** Ingestion profile obtained by weighing the food remaining in the trough. Short and long lasting non-ingestion periods (food intake rate < 0.5 $g.s^{-1}$) were present during the meal.

points would modify the accuracy of the final analysis, the error induced by this suppression was calculated over the duration of the whole meal. Experiments with an error above 10% were not included in the analysis. As a result, less than 5% of the experiments were rejected for final analysis according to these criteria.

The characteristics of non-ingestion periods and food intake rate were obtained from the filtered meal data and used to characterize ingestion

profiles. Visual inspection of filtered meal data revealed periods lasting from 2 to about 100 s during which the ingestion was less than 0.5 $g.s^{-1}$ (fig 2). Non-ingestion periods did not coincide with removed artefacts. These periods corresponded either to long lasting chewing and insalivation or to a temporary break in ingestion unrelated to chewing. They were called thereafter non-ingestion periods and their overall individual durations as well as numbers were computed. Food intake rate was derived from the meal ingested minus the duration of non-ingestion episodes.

### Statistical analysis

Data were presented as mean values ± SEM. Statistical significance was tested by one-way or two-way analysis of variance. A $P$ value $< 0.05$ was considered significant.

**Table I.** Intragastric volumes and pressures recorded during isobaric and isovolumic distension of the proximal stomach during a meal.

| *Distension* | *Pressure (mmHg)* | *Volume (mL)* |
|---|---|---|
| Isobaric | 4 | 53 ± 0.4 |
| | 7 | 148 ± 1.5 |
| | 11 | 297 ± 2.1 |
| | 16 | 412 ± 0.5 |
| | 21 | 463 · 0.2 |
| Isovolumic | 4 ± 0.5 | 50 |
| | 7 ± 0.1 | 150 |
| | 11 ± 0.1 | 300 |
| | 16 ± 1.1 | 400 |
| | 20 ± 0.1 | 450 |

Mean ± SEM for $n = 16$ experiments.

## RESULTS

The 500 g meal was entirely ingested by all animals irrespective of the distension procedures within the allowed time window (30 min).

### Proximal gastric compliance

Post-prandial gastric compliance was S-shaped. Maximal compliance indicated by the larger pressure–volume slope (34 ± 2.9 $mmHg.mL^{-1}$) was observed between 4–50 and 14–375 mmHg–mL. Below and above these values, a minute volume increase generated a large increase in proximal gastric pressure level (pressure-volume slope = 11 ± 1.3 $mmHg.mL^{-1}$).

### Effects of proximal gastric pressure

Intragastric pressures equal or higher than 11 mmHg induced significantly longer meal duration than control (656 ± 12 vs 562 ± 30 s, 11 mmHg vs control, fig 3a). Further, meal duration increased linearly with proximal gastric pressure level. A reduced food intake rate together with an increased non-ingestion duration were causative factors for this longer meal duration (fig 3b). The larger distension pressure levels only (ie, 16 and 17 mmHg) increased significantly the duration of non-ingestion periods. On the contrary, for distention pressure equal to 11 mmHg, the increased meal duration was related to a decreased food intake rate only. For distension pressures effective to increase meal duration, food intake rate was not linearly related to proximal gastric pressure whereas the duration of non-ingestion episodes was (fig 3c).

The increased duration of non-ingestion periods was related to the longer duration of each episode (12 ± 0.9 and 12 ± 0.5 vs 10 ± 0.8 s, 16 and 21 mmHg vs control, $P < 0.05$) rather than to an increase in their number (table II). Despite the similar number of non-ingestion periods, the proportion of periods lasting more than 30 s was significantly higher for distensions at 16 and 21 mmHg than at the control pressure (9.5 and 6.1% vs 3.3%, respectively).

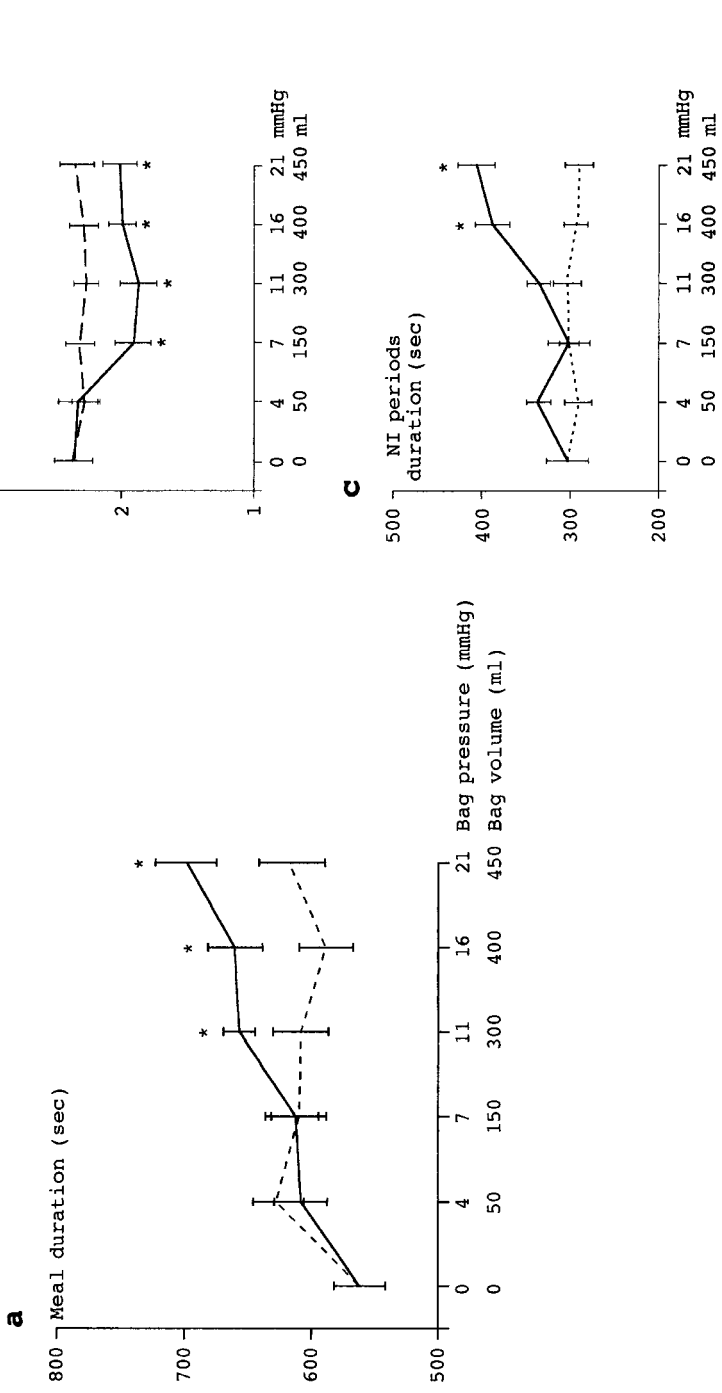



**Fig 3.** Effects of isobaric (solid line) and isovolumic (dashed line) distension of the proximal stomach on meal duration for a 500 g meal. Meal duration (a) was significantly lengthened only for the intragastric pressures equal or higher than 11 mmHg compared to control (*$P < 0.05$). The food intake rate (b) decreased significantly for pressures equal or higher than 7 mmHg whereas the duration of non-ingestion increased linearly with the intragastric pressure. The 0–0 pair corresponds to control, ie, no distension.

**Table II.** Effects of proximal stomach pressure on the duration and number of non-ingestion (NI) periods.

| *Intragastric pressure (mmHg)* | *Duration of NI periods (seconds)* | *Number of NI periods* |
|---|---|---|
| 0 | 9.9 ± 0.84 | 31 ± 3 |
| 4 | 9.9 ± 0.52 | 31 ± 6 |
| 7 | 8.4 ± 0.78 | 38 ± 4 |
| 11 | 9.2 ± 0.19 | 33 ± 5 |
| 16 | 12.4 ± 0.91* | 34 ± 3 |
| 21 | 12.2 ± 0.53* | 38 ± 5 |

Mean ± SEM for $n$ = 16 experiments. * Indicates a significant difference compared to control (0 mmHg).

### Effects of proximal gastric volume

Isovolumic proximal stomach distension did not significantly modify meal duration compared to control (see fig 3) irrespective of the volume present within the bag. Similarly, no significant changes in non-ingestion period duration or food intake rate were observed for the tested distension volumes.

### Pressure versus volume gastric distensions

Comparisons between pressure versus volume distension showed a significantly longer meal duration during isobaric mode than during isovolumic mode for pressure–volume pairs equal to or above 16 mmHg. A similar difference also exists for food intake rate and duration of non-ingestion periods. Furthermore, food intake rate was also significantly less during isobaric distension than during isovolumic distension for pressure–volume pairs equal to 7–150 and 11–300 mmHg–mL.

## DISCUSSION

This study demonstrates for the first time a short term control of food intake in pigs related to the distension of the proximal stomach. Furthermore, food intake behaviour differs for proximal stomach isovolumic versus isobaric distension.

Several lines of evidence have suggested, in various mammalian species, a short term control of food intake related to the arrival and storage of the meal in the proximal part of the stomach (Wirth and McHugh, 1983; Phillips and Powley, 1996). Balloon distension in canine and human stomachs depresses food intake (Share et al, 1952; Rigaud et al, 1995). Conversely, in rats, withdrawal of gastric contents prior to ingestion increases food intake (Kaplan et al, 1994). Finally, if ingested food is not allowed to accumulate in the stomach, dogs and rats carry on eating for longer than normal (Seeley et al, 1995). The present study is the first of its kind to demonstrate that the situation is somewhat similar in pigs. Indeed, during proximal gastric distension, food intake rate is decreased. This lengthening of the meal duration is reminiscent of the results observed in pigs for meals containing large amounts of alimentary fibres (Robert et al, 1992). A purely physical effect of these compounds on satiety has been reported whereas the nutritive needs remained unsatisfied. Lengthening of the meal in this situation relates to increased chewing time, ie, longer duration of non-ingestion periods as described in our study for intragastric pressures equal to or above 11 mmHg.

Despite the similarities mentioned above, the short term control of food intake in pigs might differ slightly from that described in other species. Irrespective of the applied proximal stomach distension, a reduction in food intake was never experienced. This deficiency might be related to the small meal size (500 g) compared to standard meal

(1200 g for 40 kg pigs fed once daily). However, in our study, the selected size for the meal was close to that spontaneously eaten by pigs fed ad libitum (Auffray and Marcilloux, 1980). Recent studies show that, in this situation, food intake occurs mainly during two major meals accounting for 500 and 350 g (Labroue, 1996). Each of these meals was intermingled with minor ingestion incidents (less than 100 g total). Therefore, in the present experiment, the size of the test meal is similar to those in pigs fed ad libitum.

Another and more important difference in the short term control of food intake, observed in pigs but not in other mammalian species, corresponded to the inefficacy of isovolumic distension on food intake patterns. Previous experiments in rats, dogs, sheep and humans demonstrate a significant reduction in food intake after the insertion of a non-alimentary volume in the stomach (Share et al, 1952; Geliebter et al, 1986, 1988). Both air and water containing balloons produce significant effects with indiscernible differences between the distension methods. The possibility of an insufficient bag volume in our experiment can be ruled out. Volumes representing about 25% of the stomach volume induce a significant effect on food intake in rats but a ratio as large as 50% seemed ineffective in pigs.

The differential effect of isovolumic versus isobaric distension represents a major finding of our study. In man, isobaric distension was also more effective than isovolumic distension to trigger post-prandial discomfort (Notivol et al, 1995). This difference also persists in the fasting state but only after administration of the gastric relaxant compound, glucagon. Therefore, it is likely that the observed difference between food intake rate was related to gastric accommodation that was effective during isovolumic distension only.

To our knowledge, per prandial analysis of ingestion profiles have only been made with ruminants. With this limitation in mind, the detailed analysis of the time course of food ingestion showed that pigs might regulate their eating behaviour differently. In pigs, an increase in eating time is the consequence of (i) decreased food intake rate and (ii) longer duration of non-ingestion periods. On the contrary, in ruminants, increased meal duration, such as those observed with fibrous forages, is always related to reduced food intake rate (Faverdin, 1985) and non-ingestion periods within the meal have never been described. It cannot be excluded that non-ingestion periods not related to chewing may represent a behavioural consequence of a sensation of fullness and, for the higher pressures, a sensation of discomfort. Indeed, similar temporary breaks during ingestion of the meal have been reported in humans after a gastrectomy (Mathias et al, 1985) and were experienced by the patients as discomfort episodes (Coffin, 1996).

In conclusion, this study demonstrates a short term control of food intake in pigs related to proximal stomach distension. Since intragastric loads were able to increase meal duration when the influences of gastric accomodation were cancelled, this suggested that physiological changes in gastric tone might modulate food intake.

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