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Intragastric pressure as a determinant of food intake

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Abstract

Background *Different studies indicated a correlation between intragastric pressure (IGP) and satiation. Our aim was to investigate this correlation while artificially increasing the IGP.* ***Methods*** *In 12 fasted healthy volunteers an infusion catheter and a manometry probe were positioned intragastrically. Intragastric pressure was increased using a custom-made belt before or progressively during intragastric nutrient infusion. Nutrient drink (1.5 kcal mL^{-1}) was intragastrically infused at 60 mL min^{-1}. The subjects scored satiation using a 6-point Likert scale until maximum, when the infusion ended and the belt was released. Results are presented as mean ± S.E.M. and compared using a paired t-test.* ***Key Results*** *When the belt was tightened before the nutrient infusion, fasting IGP was significantly increased (13.6 ± 1.3 vs 9.6 ± 0.9 mmHg; P < 0.05) but no differences in satiation could be observed. When progressively tightening the belt during nutrient infusion the IGP increased with 0.43 ± 0.04 mmHg per minute while in control experiments this was 0.28 ± 0.05 mmHg per minute (P < 0.01). During the latter experiment satiation linearly increased with 0.35 ± 0.03 and 0.29 ± 0.02 units per minute until maximal satiation (P < 0.01) while maximum volume consumed was 926 ± 66 and 1095 ± 82 mL when progressively increasing the IGP vs control respectively (P < 0.01).* ***Conclusions & Inferences*** *These findings indicate that IGP per se does not affect satiation but that a gradual IGP increase during food intake is associated with decreased food intake, indicating that gastric accommodation is an important determinant of food intake.*

Keywords *food intake, gastric accommodation, intragastric pressure, satiation.*

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Abbreviations: BMI, body mass index; GA, gastric accommodation; HV, healthy volunteers; LES, lower esophageal sphincter; NO, nitric oxide; NS, not statistically different; IGP, intragastric pressure.

INTRODUCTION

In between meals the proximal stomach maintains a high basal muscle tone, mediated by the myoelectrical properties of the fundus[1] and by the constant cholinergic input from the vagus nerves.[2] Proximal gastric tone decreases upon food intake, a reflex relaxation that is mediated by different (para)sympathetic reflex pathways that have been shown to decrease the contractile cholinergic input and activate the release of nitric oxide (NO).[3,4] This gastric accommodation (GA) reflex increases the storage capacity of the stomach by increasing the compliance of the stomach muscles and thus keeps the intragastric pressure (IGP) low during food intake.[5,6]

A number of studies have investigated the importance of GA in relation to food intake in both healthy volunteers and patients using the barostat.[4] In a subgroup of functional dyspeptic patients for example, we demonstrated that early satiation and weight loss can be attributed to impaired GA.[7] Also in binge eating disorder, bulimia nervosa and cancer patients a possible correlation between GA and food intake or satiety has been described.[8–10] Although the barostat is considered the golden standard to assess GA, it is less suitable to use during unrestricted food intake because of the presence of an inflated intragastric balloon. We recently reported a technique that allows to assess changes in gastric tone during food intake by measuring the IGP.[11,12] Indeed, when GA is impaired, IGP is higher during food intake while a relaxation of the stomach is accompanied with an IGP decrease.[12] Using this technique we observed that the IGP during nutrient drink ingestion is significantly correlated to satiation and the nutrient volume required to induce maximal satiation.[11,12]

These findings indicate that the regulation of IGP during food intake is an important determinant of food

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intake, and that impaired GA is associated with decreased food intake. Most of the studies above report correlations between GA, IGP and nutrient tolerance, but changes in food intake could well be mediated by other mechanisms not necessarily related to changes in GA.

In this study we aimed to directly determine the effect of IGP changes on food intake in healthy volunteers by simultaneously measuring IGP and satiation during food intake in a control situation, in a situation where the IGP was constantly mechanically increased and while the IGP was gradually mechanically increased.

METHODS

Study subjects

All study procedures were approved by the Ethics Committee of the Leuven University Hospital, Belgium. Written, informed consent was obtained from all subjects. A total of 12 healthy volunteers (HVs; five men, age: 31 ± 3 years, body mass index: 22.0 ± 0.7 kg m^{-2}) participated in the studies, most volunteers participated in both protocols (see below). In each protocol, 10 HVs were included. None of the HV's had symptoms or a history of gastrointestinal disease, other significant diseases, psychological disorders or drug allergies; none were taking any medication or had any drug history. All participants participated after an overnight fast, furthermore were they asked to refrain from alcohol, tea, and coffee at least 12 h before participation, and to refrain from smoking cigarettes at least 1 h before the start of the experiment.

IGP measurement during nutrient infusion

Preparation of the volunteers A high-resolution solid-state manometer system was used (36 channels, 1 cm in between each channel, Manoscan 360, Sierra Scientific Instruments, Los Angeles, CA, USA, Manoview analysis software v2.0.1). Upon arrival in the clinic the manometer was positioned through the nose so that at least one sensor was positioned in the lower esophageal sphincter (LES; detected as a clearly elevated pressure zone compared to oral and aboral areas), while IGP was measured as the average pressure of the first five pressure channels that were clearly positioned below the LES or the pressure area influenced by the LES (approximately 3–8 cm under the LES).

A second catheter (Flocare, Nutricia, Bornem, Belgium) was positioned in the stomach through the mouth through which nutrient drink could be infused directly into the stomach. The tip of the infusion catheter was positioned approximately 5 cm under the LES and its position was verified by fluoroscopy. The catheters were fixed to the subjects chin.

General protocol After positioning of the catheters the HVs were asked to take place in a chair. Volunteers were equipped with a specially-designed belt around the abdomen that could be used to increase the pressure on a specific location on the abdomen (see below). Following a stabilization period of at least 30 min, nutrient drink (Nutridrink, Nutricia, Zoetmeer, The Netherlands; 630 KJ, 6 g proteins, 18.4 g carbohydrates, and 5.8 g lipids per 100 mL) was infused directly into the stomach at a constant speed of 60 mL min^{-1} determined by an automated system using a peristaltic pump. During nutrient infusion the HVs were asked to score their satiation at 1-min intervals, using a graphic rating scale that combines verbal descriptors on a scale graded of 0–5 (1, threshold; 5, maximum satiation). Maximum satiation was defined as the moment the HV's could not tolerate more nutrient drink. At 5-min intervals the HV's were asked to fill out a visual analogue scale for 11 epigastric symptoms (fullness, bloating, nausea, belching, epigastric burning, substernal burning, substernal cramps, abdominal cramps, pain, hunger, and appetite). The visual analogue scale was 100 mm long (0 mm: no feeling, 100 mm: the worst imaginable feeling). Intragastric infusion was stopped as soon as the HVs scored maximally on one of the 11 epigastric symptoms or when a score of 5 was reached on their satiation scores, hereafter the experiment was terminated.

Study design – regulation of IGP We previously observed that during nutrient infusion IGP decreases initially but gradually increases upon continuous nutrient infusion. The nadir pressure was defined as the lowest IGP during nutrient infusion and from previous work we know this pressure is reached 4.9 ± 0.5 min after the start of the nutrient infusion.[12] From the same study we know that the IGP increase from nadir IGP correlates very well to the corresponding satiation scores. In the present study the effect of mechanically increased IGP on satiation was studied in two different protocols (Fig. 1): in the 1st protocol the fasting IGP was increased with approximately 5 mmHg while in the 2nd protocol the IGP was progressively increased with approximately 5 mmHg during food intake after the nadir IGP was reached. Per protocol the experiments were planned with the appropriate control experiment in a randomized crossover fashion. A specially designed belt was used that allowed to increase the pressure on a specific location of the abdomen using a cylindrical plastic attachment (5 cm diameter and 15 cm long) to the belt that could be located on a specific place on the abdomen so that when tightening the belt the pressure under the attachment increased, while no pressure on the adjacent abdomen was applied.

Data analysis

The original data was imported from the recording software to excel. We were primarily interested in slow IGP changes that could reflect changes in gastric muscle tone. Therefore, and in order to avoid influence from movement artefacts as well as artefacts caused by coughing, sneezing, moving or swallowing a moving median was calculated per channel from the original data (median value over 1 min of original data). Per channel, a baseline value was calculated from the moving median data as the average pressure in the last 5 min of the stabilization period. IGP data was presented per minute as the difference of the moving median value in that minute and the baseline value as the average value of the five measurement channels that were clearly positioned below the LES as described above. Maximum IGP decrease was reported as the difference between the baseline value and the nadir IGP.

All data were presented as mean ± S.E.M. and compared with a paired, 2-tailed *t*-test; $P < 0.05$ was considered significant.

RESULTS

Increased fasting IGP

The IGP before the nutrient drink infusion start (baseline IGP) was significantly elevated when the belt was continuously tightened around the stomach (from 9.6 ± 1.6 to 13.6 ± 1.3 mmHg before and after the belt

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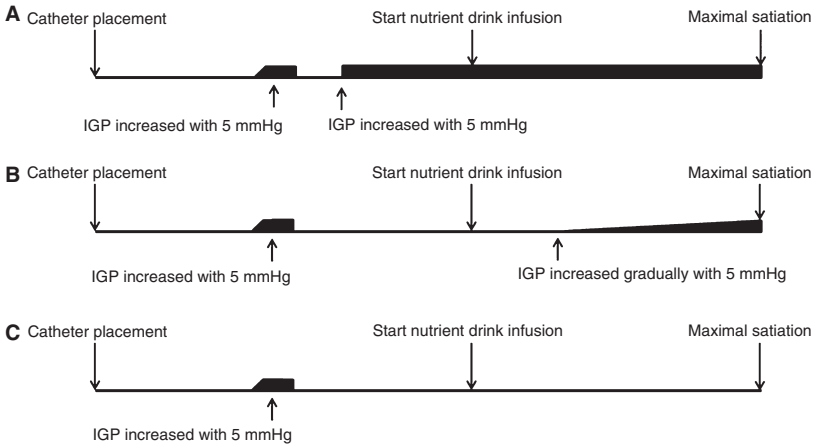

Figure 1 A schematic representation of the different protocols in the study. In all protocols a stabilization period was respected after positioning of the catheters. During the stabilisation period, a custom-made belt was positioned around the upper abdomen with an attachment between the belt and the abdomen on top of the stomach and it was determined how tight the belt had to be to increase the IGP with approximately 5 mmHg. Hereafter the belt was released and a period of at least 15 min was respected before the intragastric nutrient infusion was started. In the 1st protocol (A) the belt was tightened around the upper abdomen to increase the fasting IGP with approximately 5 mmHg 10 min before the nutrient infusion started until the end of the experiment. In the 2nd protocol (B) the IGP was progressively increased during nutrient infusion by tightening the belt gradually, starting 5 min after nutrient infusion started so that the belt was tightened maximally (as determined in the stabilisation period) 10 min after the nutrient infusion started, hence from 5 to 10 min after the nutrient infusion started the IGP was increased with an extra 1 mmHg per minute. In the control experiments (C) the belt was tightened around the lower abdomen, more specifically on the area above the right hip. No IGP increase could be measured when tightening the belt around this part of the abdomen. At maximal satiation, the nutrient drink ingestion stopped and the belt was released.

was constricted respectively; $P < 0.01$) and was significantly higher as compared to the control IGP group (9.6 ± 0.9 mmHg; $P < 0.05$). When nutrient infusion started, the IGP initially decreased but gradually increased again upon continuous infusion (Fig. 2). No significant difference between the maximal IGP decrease was observed when the fasting IGP was increased *vs* the control experiment (4.1 ± 0.6 mmHg after 5.6 ± 1.0 min and 3.2 ± 0.4 mmHg after 3.8 ± 0.7 min respectively; NS). From the nadir IGP, the pressure increased with 0.37 ± 0.1 and 0.33 ± 0.05 mmHg per minute until 2.2 ± 0.7 and 2.0 ± 0.6 mmHg above the baseline IGP at the end of the experiment with increased and control fasting IGP respectively (Fig. 2A; NS).

Satiation linearly increased from the start of the nutrient infusion with 0.30 ± 0.02 and 0.29 ± 0.02 units per minute until maximal satiation (NS); maximum volume consumed at maximal satiation was 978 ± 94 and 1072 ± 73 mL with increased and control fasting IGP respectively (Fig. 2A; NS).

No significant differences could be observed between any of the 11 epigastric symptoms at any time point before, during or after nutrient infusion.

Increased IGP during nutrient infusion

Baseline/fasting IGP was similar in both groups (9.3 ± 0.9 *vs* 10.1 ± 0.9 mmHg in the group with increased IGP *vs* control group respectively; NS). The maximal IGP decrease was 3.2 ± 0.5 mmHg after 4.0 ± 0.7 min and 2.8 ± 0.7 mmHg after 4.4 ± 0.7 min (NS). Five minutes after the start of the nutrient infusion the belt was progressively tightened over the stomach or lower abdomen. From this point IGP increased with 0.43 ± 0.04 and 0.28 ± 0.05 mmHg per minute until 2.6 ± 0.6 and 1.2 ± 0.5 mmHg above the baseline IGP at the end of the experiment when the belt was tightened over stomach area *vs* lower abdomen respectively (Fig. 2B; $P < 0.01$).

Satiation linearly increased from the start of the nutrient infusion with 0.35 ± 0.03 and 0.29 ± 0.02 units per minute until maximal satiation ($P < 0.01$); maximum volume consumed at maximal satiation was 926 ± 66 and 1095 ± 82 mL in group where the IGP was progressively increased *vs* the control group respectively (Fig. 2B; $P < 0.01$).

No significant differences could be observed between any of the 11 epigastric symptoms at any time point before, during or after nutrient infusion.

DISCUSSION

In this study we investigated the effect of increased fasting IGP and gradual IGP increase during food intake on satiation. Satiation was only affected when IGP was progressively increased during food intake while it was not affected when the fasting IGP was increased.

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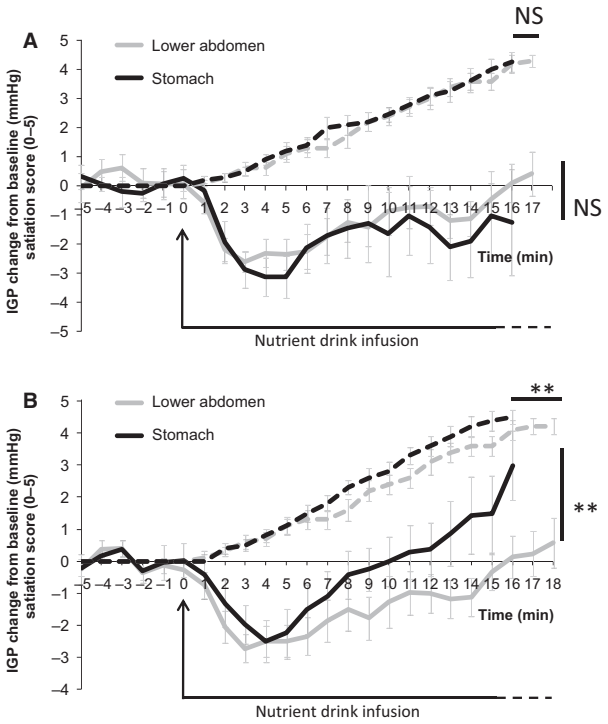

Figure 2 Average intragastric pressure (IGP; solid lines) and satiation scores (interrupted lines) before and during intragastric nutrient infusion. Data was shown until the volunteers scored maximal satiation. (A) Experiment was performed while a belt was constantly tightened around the lower abdomen (control experiment) or around the stomach. (B) Experiment was performed while progressively tightening a belt around the lower abdomen (control experiment) or around the stomach. Data was represented as mean ± S.E.M. and after subtraction of the baseline value (calculated in the 5 min before nutrient infusion) until 50% of the volunteers reached maximum satiation. $^{**}P < 0.01$.

Fasting IGP has been correlated to abdominal pressure, BMI, and waist circumference.[13,14] From the literature there is no indication that people with increased BMI eat smaller meals or that people with decreased BMI and eat larger meals. On the contrary, there appears to be a positive correlation between BMI and meal size or satiation which has been attributed in obese people to an increased stomach capacity.[15,16] In the present study we showed that when the fasting IGP is increased food intake is not affected. Our findings therefore seem to confirm the hypothesis that increased meal size in obese is caused by an increased stomach capacity and is not affected by fasting IGP.[17]

The GA reflex decreases the gastric muscle tone during food intake to provide the meal with a reservoir for ingested food while avoiding IGP increase.[5,18–20] When GA is impaired, fasting IGP is not affected; however IGP will increase more during food intake. We previously discussed that IGP can be used as an indirect measurement for GA[12] but also other groups showed that in healthy volunteers IGP increase is minor or stable during stomach distension but IGP increased during stomach distension in patients with impaired GA e.g., after vagotomy, patients with Chagas' disease and patients with functional dyspepsia.[21–24]

In the present study we mimicked this aspect of impaired GA. While constraining the belt with the attachment over the lower abdomen no changes in IGP were measurable indicating that our method allows to locally increase the pressure without carry over effect to the upper abdomen. While constraining the belt with the attachment over the stomach, IGP increased significantly and based on the comparison with the belt constricted over the lower abdomen we assume that the effect was local. When we progressively augmented the IGP, satiation was significantly increased during nutrient infusion, indicating that a higher IGP affects food intake as suggested before by our group and others.[4,5] It has to be noted that, most likely, the mechanical push of the attachment on the stomach did not alter muscle tone and consequently our model does not mimic all aspects of impaired GA. It is more likely that the mechanical push of the attachment on the belt caused redistribution of the food from the proximal stomach to the antrum as has also been shown in imaging studies with patients with impaired GA.[25,26] As the antrum is less compliant than the proximal stomach it is more sensitive to distension, and increased feelings of fullness and satiation in patients with impaired GA can originate from the antrum.[27] Furthermore, increased IGP could increase gastric emptying of liquid but also of solid food[28–30] which in turn could influence satiety and food intake.[31]

The question remains why increasing the fasting IGP did not affect satiation while gradually increasing the IGP did. One possible explanation for this might be that the mechanosensors in the stomach are sensitive to changes but can rapidly adapt to them. Indeed it has been postulated before that rapidly adapting mechanosensors in the stomach mucosa are involved in sensations during gastric distension.[32,33] Given that in the first protocol the belt was tightened 10 min before the nutrient infusion started while in the second protocol the IGP was gradually increased during food intake the existence of rapidly adapting mechanosensors might explain the different effects on satiation, although this remains speculative and further research on the involvement of rapidly adapting mechanosensors in the control of food intake is needed. Alternatively, increasing the fasting IGP *vs* gradually increasing the

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IGP might have differential effects on gastric emptying and therefore nutrient feedback. Indeed, gastric accommodation has been shown to be a parameter in the determination of gastric emptying, especially of liquids.[34]

Taken together, these findings indicate that the regulation of IGP during food intake is an important determinant of food intake, and that impaired GA is associated with decreased food intake.

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DISCLOSURE

No competing interests declared.

AUTHOR CONTRIBUTIONS

PJ and SV contributed to conception and design of the experiments, collection, analysis, and interpretation of data and drafting the article; JT contributed to conception and design of the experiments, and revising the manuscript critically for important intellectual content.

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