Tonic and phasic motor activity in the proximal and distal colon of healthy humans

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In studies of human colonic motor function, the stimulating effect of eating is one of the most consistent findings. However, the colonic response to food has been mainly studied in the rectosigmoid colon using manometric and myoelectrical techniques (6, 25) and, more recently, the electronic barostat (26). Due to their inaccessibility, little is known about the motor effect of eating in more proximal colonic areas.

The proximal colon differs from the distal colon anatomically in its embryological origin, blood supply, innervation, and morphology (saccular vs. tubular); functionally in its capacities of absorption and fermentation (7); and pharmacologically in its response to drugs (8). Such regional differences associated with the absence of coordination between the motor activity of the proximal and distal colon (8, 15) could have, as a consequence, a different motor response to food. Indeed, scintigraphic studies have demonstrated that the proximal colon acts as a reservoir, whereas distal colonic segments mainly act as a conduit (21). Moreover, the proximal colon is able to adapt its capacity during a direct infusion of isotonic saline into the cecum (13). In the terminal ileum of healthy humans, a postprandial reservoir function has also been evidenced during scintigraphy (4, 12), which may be explained by the prolonged tonic relaxation that follows the brief and immediate tonic and phasic contractions triggered by meal ingestion (5). Therefore, we hypothesized that, in contrast to the distal colon, the proximal colon would relax in response to eating to accommodate the postprandial increase in ileal flow.

Recording of colonic motor activity is usually done by introducing a probe into the colon over a guide wire by means of a colonoscope that is then removed. The drawbacks of this technique are the necessity to empty the colon of its contents and the difficulty in recording the proximal colon due to the distal migration of the probe during or after removal of the colonoscope. Fos-sati-Marchal et al. (10) and Lémann et al. (16) described a different technique to record the proximal colonic motor phasic and tonic activity using a long probe introduced by mouth that migrates to the proximal colon. This probe, consisting of perfused catheters and a barostat bag, allows the simultaneous recording of phasic and tonic motor activity in the unprepared colon. In the present study, by using this method, we compared the phasic and tonic activity in the proximal and distal colon of healthy humans in the fasting and postprandial states.

SUBJECTS AND METHODS

Participants

Twelve healthy volunteers (7 men and 5 women aged 21–37 yr) were included after they gave informed consent to the protocol, which has been approved by the Ethics Committee of Lariboisière-Saint Louis Hospitals. All were required to have no gastrointestinal symptoms, a normal bowel habit, a normal physical examination, and no previous gastrointestinal surgery (except for appendectomy), and none was taking medications other than oral contraceptives.

Recording Assembly

The barostat maintains a constant pressure within an air-filled bag using a feedback mechanism, which consists of a strain gauge linked by an electronic relay to an air injection and aspiration system. Both the strain gauge and the injection-aspiration system are connected by a separate lumen to a cylindrical noncompliant bag (10-cm longitudinal axis, 9.4-cm diameter, 450-ml capacity) made of ultrathin polyethylene. A dial in the electronic system allows selection of the pressure level. The barostat can respond to a change in pressure in the bag of 0.4 mmHg above or below the preset value by withdrawing or injecting air, respectively. The volume of air inside the bag is determined electronically by the computer from the known excursion of the bellows within the reservoir system.
We used a multilumen tube assembly (1-cm OD, 3.5 m long) with six manometric catheters and a latex balloon in addition to the barostat bag. Validation experiments were performed in vitro to demonstrate that the length of the tube did not modify the technical properties of the electronic barostat (5). The barostat bag was mounted over and sealed airtight to the tube; it was connected to the strain gauge and the air pump by two vinyl tubes. One latex balloon (5-cm axis) was placed at the tip of the tube 24 cm caudad to the bag of the barostat. It contained 25 g of mercury and could be filled with air to facilitate the progression of the tube. The six manometric ports were located 2, 7, and 12 cm distal from and proximal to the barostat bag. Manometric catheters were connected to a low-compliance perfusion system (0.1 ml/min flow rate), and phasic activity was recorded by external pressure transducers connected to a data-processing system as was pressure and volume of the barostat (Synetics, ABS, Saint-Dié, France). For each experiment, the minimal distending pressure needed to overcome the intra-abdominal pressure was determined (1, 24). Then, basal pressure to record intrabag volume variations was defined as a pressure level 2 mmHg above the minimal distending pressure (24).

Experimental Procedure

The participants were intubated by mouth. The progression of the tube through the small bowel and colon was aided by inflating the distal balloon and was monitored by fluoroscopy. When the bag of the barostat was located in the desired colonic site, the distal balloon was deflated. The duration of the progression was 24–48 h. The exact location of the bag was checked by fluoroscopy before and after each experiment. Recordings were performed once the tube had reached the desired colonic site. The barostat bag was located in the ascending colon or at the hepatic flexure in six volunteers and in the descending colon between the splenic flexure and the sigmoid area in the other six volunteers. On the experimental day, the barostat bag was unfolded by inflation with 100 ml of air and thereafter was completely deflated and connected to the barostat.

Basal colonic intrabag volume and phasic activity were recorded for 1 h in the fasting state. Then the participants ingested within 10 min a 1,000-kcal liquid meal (50% fat, 30% carbohydrate, and 20% protein; Respalis, Sopharga, Sèvres, France). Volume variations and phasic activity were continuously recorded for 3 h after meal ingestion. During the recording period, the subjects were asked to avoid any movement and not to sleep.

Data Analysis

Phasic pressure activity is expressed as a motility index (area under the curve of phasic contractions) calculated for 30-min periods. We calculated the mean motility index for the catheters proximal to the barostat bag (proximal motility index), for the catheters distal from the barostat bag (distal motility index), and for all catheters (overall motility index). The mean maximal motility index was calculated using the highest postprandial motility index for each volunteer. The mean motility index of the two 30-min periods recorded during the fasting state represented the basal motility index, and postprandial variations in motility indexes are expressed as a percentage of this value. High-amplitude propagated contractions (HAPCs) were defined as single pressure waves with an amplitude of at least 60 mmHg that rapidly propagated through the colon on at least three ports (3, 18).

Intrabag volume variations were visually analyzed. After motion artifacts were deleted, phasic volume events, defined as rapid changes in the baseline volume of ≥10% occurring at a frequency of 1–4/min, were excluded from the barostat volume analysis according to von der Ohe et al. (29). Ten-minute baseline volumes were averaged over 30-min periods. In each subject, the mean baseline volume during the two 30-min fasting periods represented the basal volume of the colonic segment occupied by the barostat bag. The mean intrabag volumes for the six successive 30-min periods after the meal are expressed as a percentage of the 1-h basal value to correct for interindividual variations in baseline volumes reflecting differences in colonic diameters. The greatest volume change in the barostat bag recorded for at least 10 min after the meal was defined as the maximal tonic response. We also calculated the mean postprandial intrabag volume for the first 90 min after the meal according to the study by Ford et al. (9) for subsequent comparison. Using the actual recorded values of motility indexes and barostat volumes instead of values expressed as percentages of the basal values, we calculated the gradient of phasic and tonic activity between the distal and proximal colon for each 30-min period.

Statistical Analysis

Results are expressed as means ± SE. In the proximal and distal colon, analysis of variance was used to compare changes induced by the meal in the colonic volume and motility index. The Newman-Keuls test was used for multiple comparisons. The nonparametric Spearman correlation test was used to study the relationship between motility indexes and intrabag volumes. Comparisons of means between the proximal and distal colon were made with the nonparametric Mann-Whitney test. A P value < 0.05 was considered to be significant.

RESULTS

Phasic Motor Activity

During the fasting state, the motility index of the proximal colon was not significantly different from that of the distal colon (14,659 ± 1,921/30 min vs. 11,141 ± 2,970/30 min; P = 0.2). The 1,000-kcal meal produced an increase in the overall motility index in the proximal and distal colon, which was maximal during the first 30 min after the meal at both sites (Fig. 1). Compared with the basal value, this increase was not significant in the proximal colon (138 ± 25% of the basal value; P = 0.2), whereas it was in the distal colon (230 ± 46% of the basal value; P < 0.05). There was no significant difference between the proximal and distal colon in the mean maximal motility index (158 ± 21 vs. 235 ± 44% of the basal value; P = 0.24) and the mean area under the curve of the overall motility index (700 ± 86 vs. 901 ± 128; P = 0.3). At both sites, the postprandial increase in the motility index during the first 30-min period was not significantly different in the catheters proximal and distal to the barostat bag (148 ± 30 vs. 127 ± 25%, P = 0.60 in the proximal colon and 287 ± 62 vs. 186 ± 30%, P = 0.16 in the distal colon, respectively). During the 12 h of fasting-state recordings, 4 HAPCs were recorded in 2 of the 12 participants (mean frequency 0.33 ± 0.3/h). During the 36 h of postprandial recordings, a total of 30 HAPCs were recorded in 6 of the 12 participants (range 0–14 HAPCs; mean frequency 0.84 ± 0.4/h). The postprandial increase in
HAPC frequency was statistically significant compared with the fasting period ($P = 0.03$). Figure 2 shows examples of phasic motor activity recordings in the proximal and distal colon.

**Tonic Motor Activity**

During the fasting state, the mean volumes of the barostat bag were $199 \pm 18$ and $163 \pm 18$ ml in the proximal and distal colon, respectively ($P = 0.2$). The mean value of the minimal distending pressure was $10.8 \pm 0.7$ mmHg in the proximal colon and $9.1 \pm 1.6$ mmHg in the distal colon ($P = 0.7$).

The meal produced a decrease in intrabag volume in both the proximal and distal colon (Fig. 1). This decrease occurred within 10 min after the beginning of the meal in all cases, reaching its maximal value $22 \pm 10$ (range 6–60) and $13 \pm 4$ min (range 6–34) after the beginning of the meal in the proximal and distal colon, respectively ($P = 0.4$). The minimal intrabag volumes recorded for at least 10 min were significantly different between the proximal and distal colon ($50 \pm 9$ and $26 \pm 11\%$ of the basal value in the proximal and distal colon, respectively; $P = 0.04$). The mean intrabag volumes for the first 90-min postprandial period were $76 \pm 3$ and $36 \pm 11\%$ of the basal value in the proximal and distal colon, respectively. The intrabag volume returned to its basal value $103 \pm 31$ and $146 \pm 21$ min after the end of the meal in the proximal and distal colon, respectively ($P = 0.1$). The areas under the curve of volume variations were significantly lower in the proximal colon than in the distal colon ($253 \pm 63$ and $460 \pm 15$, respectively; $P = 0.04$). Figure 2 shows examples of tonic motor activity recordings in the proximal and distal colon.

No significant correlation was found between the areas under the curve of volume variations and those of the overall motility indexes in the proximal colon ($r = 0.49; P = 0.36$), whereas a significant correlation was found in the distal colon ($r = 0.94; P = 0.02$).

**Gradient of Phasic and Tonic Pressure Between the Proximal and Distal Colon**

For each 30-min period, we calculated the difference between the proximal and distal colon. During the

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**Fig. 1.** Effects of ingestion of the meal on phasic motor activity recorded from perfused catheters (motility index) and on intrabag volume recorded from barostat located in proximal ($n = 6$ subjects; A) and distal colon ($n = 6$ subjects; B). Values are means ± SE of percentages of basal values. Note that the meal significantly decreased intrabag volume (increase in tone) in proximal and distal colon and significantly increased motility indexes in distal colon but not in proximal colon. *$P < 0.05$ vs. basal period by analysis of variance and Newman-Keuls test.

**Fig. 2.** Recordings of intrabag volume (tonic activity) and perfused catheters (phasic activity) in proximal (A) and distal (B) colon before and after a 1,000-kcal meal. Tracings 1–6, perfused catheters located 2, 7, and 12 cm proximal to (1–3) and distal from (4–6) barostat bag. Tracing 7, barostat bag volume recording.
fasting state, the mean motility index was lower in the distal than in the proximal colon but became higher during the first 30 min after the meal (Fig. 3). The barostat bag volume was higher in the proximal than in the distal colon during the fasting state, and the magnitude of this difference increased after the meal (Fig. 3). Thus the meal increased the gradient of phasic and tonic pressure between the distal and proximal colon. The change in gradient of phasic activity was brief, whereas it was more prolonged for tonic activity.

DISCUSSION

Due to its inaccessibility in humans, little is known about the motor activity of the proximal colon. Our method allows regular access to the proximal colon and simultaneous recording of colonic phasic and tonic motor activity in healthy subjects without prior colonic cleansing, premedication, air insufflation, and colonoscopy. Cleansing the colon leads to an increase in the number of HAPCs without affecting the fundamental pattern of phasic motor activity (16). Effects of cleansing and other factors required for retrograde tube placement on colonic tone are unknown. In the present study performed in the unprepared colon of healthy humans, we confirmed that the ingestion of a meal increased the phasic and tonic motor activity and showed that this effect was less pronounced in the proximal than in the distal colon.

Motor Activity in the Fasting State

As in the previous study by Lémann et al. (16), the motility indexes in the fasting state were not significantly different between the proximal and distal colon. These results did not agree with those of Dapoigny et al. (6), who found that myoelectrical colonic activity was different between the proximal and distal colon, with a significantly higher number of long spike bursts in the latter. The difference in the methods used could explain such discrepancies. The intrabag volume was slightly higher in the proximal than in the distal colon, confirming previous results found by Steadman et al. (26). This difference actually reflects a small difference in colonic diameter because if we consider that the bag has a cylindrical shape in the colonic lumen, the mean calculated diameters are 5.0 and 4.6 cm in the proximal and distal colon, respectively, which does not affect the sensitivity of manometry (see below). Thus, during the fasting state, the phasic and tonic motor activity of the proximal colon does not appear markedly different from that of the distal colon, although we cannot exclude a type II error due to the limited number of subjects studied.

Motor Activity in the Postprandial State

Phasic motor activity. We found that the meal produced a nonsignificant increase in the phasic motor activity of the proximal colon. Kerlin et al. (15) also found no response to a 600-kcal no-residue liquid meal in the proximal colon, whereas the motility index was enhanced by solid-liquid meals.

In the distal colon, the meal produced an immediate increase in phasic motor activity, which was significantly different from the fasting value during the first 30 min after the meal. Duration of the distal colonic response to the meal differs from one study to another depending on the meal tested, duration of postprandial recording, and method of recording used (6, 11, 15). A motor pattern similar to ours was evidenced by Moreno-Osset et al. (17) in healthy humans receiving a meal containing a similar amount of fat and calories, but contrary to other studies (26, 27), we did not find a late increase in the motility index. This increase, possibly related to the arrival of nutrients into the colon (27), could be absent in our study because our meal did not contain residue.

The sensitivity of open-tipped manometric techniques to detect phasic contractions is decreased if the colonic diameter is >5.6 cm (i.e., a barostat bag volume > 250 ml) (30). In our study, all subjects but one had a basal barostat bag volume < 250 ml, and the barostat bag volume decreased after the meal in all subjects. Thus a difference in the sensitivity of manometry cannot explain the regional difference in the motility index. The postprandial change in phasic...
activity was similar in catheters proximal from and distal to the barostat bag. Thus the presence of the bag did not appear to affect the phasic motor activity. This is in agreement with previous studies showing that the bag has no effect on the transit of colonic contents (26) and on the characteristics of HAPCs (30). Finally, we found a great individual variation in the number of HAPCs stimulated by the meal, as previously described (3, 16, 17, 28).

Tonic motor activity. The meal produced an immediate tonic contraction in the proximal and distal colon. The mean postprandial maximal reduction in barostat volume was more pronounced in the distal than in the proximal colon (74 vs. 50% of the basal value). Furthermore, the mean reduction in the barostat volume for the first 90-min after the meal was 24 and 64% of the basal value in the proximal and distal colon, respectively. These figures can be compared with the 24 and 13% reductions found by Ford et al. (9) in the cleansed human transverse and sigmoid colon, respectively, after a 1,000-kcal liquid meal. This discrepancy with our study appears, therefore, to be less related to the different method but rather is explained by the different location of the barostat bag (sigmoid colon vs. descending colon) or by the possible inhibitory effect of the barostat bag located in the transverse colon on the sigmoid tone. Steadman et al. (26) did not find any difference in the magnitude of the tonic response between the ascending and descending colon to a 1,000-kcal liquid meal, but this could be explained by the very few number of subjects (three and two, respectively) studied at each site.

Contrary to our hypothesis, we did not find any relaxation in the proximal colon. We used a low-residue liquid meal, and it cannot be ruled out that a meal containing residues would have induced a different response in colonic tone. Indeed, in scintigraphic studies, Kamath et al. (13) have shown the ability of the human proximal colon to accommodate different volumes depending on the nature of its contents. However, in dogs, the response of the proximal colon to food ingestion was also a tonic contraction that was further increased by the arrival of nutrients into the colon (2).

Moreover, we have shown in healthy humans that the same low-residue meal as used in the present study was able to produce a sustained tonic relaxation in the terminal ileum (5). Thus the occurrence of a postprandial relaxation in the proximal colon of healthy humans is unlikely.

Passage of food or chyme along the gut requires that distal segments be programmed to accept contents occurring from more proximal loci. From our results, if we consider that tonic activity reflects the capacitance of the gut lumen, the absence of tonic relaxation reduces the capacity of the colon to store contents after a meal. This capacity appears to be supported by the terminal ileum, where ingestion of the same meal triggers a transient tonic contraction followed by a prolonged (>120-min) relaxation (5). Our results do not, however, rule out that the proximal colon is able to accommodate bolus entries of chyme. In the canine proximal colon, Neri et al. (19) also showed a decrease in barostat volume in the 10 min after the ingestion of a meal, followed by a return to the fasting value. In addition, they showed that the proximal colon may relax transiently during the occurrence in the terminal ileum of prolonged propagations contractions, which are propulsive waves occasionally recorded only in fasting conditions in both canine and human ileum (5, 14, 19, 22, 23).

Picon et al. (20) have previously shown, using scintigraphic studies performed in healthy humans, that the same meal induced a linear emptying of the proximal colon, whereas it triggered retrograde movements of the colonic contents from the descending colon, a finding previously observed by Moreno-Osset et al. (17). Because retrograde contractions have never been described in manometric studies, these authors (17) suggested that the overall retrograde movement of the colonic contents evidenced by scintigraphy could be due to a pressure gradient induced by the higher phasic motor activity of the descending colon relative to the transverse colon. In our study, we found a distal-to-proximal phasic pressure gradient during the first 30 min after the meal that was associated with a distal-to-proximal tonic pressure gradient lasting for at least 3 h after the meal. This suggests that regional differences in tonic activity may amplify the phasic pressure gradient between the proximal and distal colon and may be involved in postprandial retrograde movements of the colonic contents. Furthermore, the persistency of this tonic pressure gradient for 3 h after the meal could explain the absence of movement of the proximal colonic contents toward the descending colon found in scintigraphic studies (20).

We conclude that, in healthy humans, a tonic relaxation does not occur in the proximal colon after eating. The prominent postprandial tonic response of the distal colon may allow retrograde movements and mixing of intraluminal contents and limit the risk of overloading the rectosigmoid area.

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