Influence of duodenal acidification on the sensorimotor function of the proximal stomach in humans

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Influence of duodenal acidification on the sensorimotor function of the proximal stomach in humans. Am J Physiol Gastrointest Liver Physiol 286: G278–G284, 2004. First published May 21, 2003; 10.1152/ajpgi.00086.2003.—Decreased acid clearance and increased exposure to acid of the duodenum have been reported in a subset of functional dyspepsia patients. However, the mechanism by which increased duodenal acid exposure may affect symptoms is unclear. The aim of the present study was to investigate the effects of duodenal acidification on proximal gastric tone and mechanosensitivity in humans. An infusion tube with a pH electrode attached was positioned in the second part of the duodenum, and a barostat bag was located in the gastric fundus. In 12 healthy subjects, fundic tone and sensitivity to distensions were assessed before and during duodenal infusion of 0.1 N hydrochloric acid or saline in a randomized, double-blind design. In 10 healthy subjects, meal-induced accommodation was measured during duodenal infusion of acid or saline. Acid infusion in the duodenum significantly increased fundic compliance and decreased fasting fundic tone. This was accompanied by a significant decrease in the pressures and the corresponding wall tensions at the thresholds for discomfort. During infusion of acid, significantly higher perception and symptom scores were obtained for the same distending pressures. The meal-induced fundic relaxation was significantly smaller during acid infusion compared with saline infusion. In conclusion, duodenal acidification induces proximal gastric relaxation, increases sensitivity to gastric distension, and inhibits gastric accommodation to a meal. Through these mechanisms, increased duodenal acid exposure may be involved in the pathogenesis of dyspeptic symptoms.

Functional dyspepsia; duodenal acid exposure; gastric accommodation; mechanosensitivity

Functional dyspepsia (FD) is a clinical syndrome defined by recurrent or persistent pain or discomfort centered in the upper abdomen without evidence of organic disease likely to explain the symptoms (28). A variety of symptoms presented by FD patients reflects the multifactorial nature of this syndrome. Different pathophysiological mechanisms have been suggested to be involved. These include delayed gastric emptying, gastric hypersensitivity to distension, impaired gastric accommodation to a meal, abnormal duodenal motility, or a central nervous system dysfunction (4, 14, 24, 25, 27, 29).

In a subset of FD patients, but not in healthy controls, intraduodenal infusion of hydrochloric acid (HCl) was found to induce nausea, suggesting duodenal hypersensitivity to acid (18). Furthermore, a decreased duodenal motor response to acid, resulting in reduced duodenal clearance of exogenous acid, has been shown in a group of FD patients (10, 21, 22). Recently, we confirmed that spontaneous duodenal exposure to endogenous acid was increased in a subset of FD patients who displayed reduced clearance of exogenous acid in the duodenum (10). Our previous study also showed that increased spontaneous duodenal acid exposure was associated with higher dyspeptic symptom severity, although a direct relationship between duodenal acid exposure and symptom severity was lacking (10). Thus the mechanism by which increased duodenal acid exposure may affect symptoms warrants investigation.

Duodenal acidification was found to affect gastric emptying and interdigestive gastric motility (8, 30). However, the influence of duodenal acidification on the sensorimotor function of the proximal stomach is unknown. Therefore, the aim of the present study was to assess the effects of duodenal acidification on proximal gastric tone and mechanosensitivity in a group of healthy volunteers.

Materials and Methods

Subjects. Twenty-two healthy volunteers (10 men and 12 women; mean age 25 yr, range 22–35 yr) participated in this study. None of the subjects had symptoms or a history of gastrointestinal disease or drug allergies, nor were they taking any medication. Written, informed consent was obtained from each participant, and the study protocol had been approved by the Ethics Committee of the University Hospital.

Techniques of a barostat study. After an overnight fast of at least 12 h, a double-lumen polyvinyl tube (14-Ch Salem suction tube; Sherwood Medical, Petit Rechain, Belgium) with an adherent plastic bag (1,200-ml capacity; 17-cm maximal diameter), finely folded, was introduced through the mouth and secured to the subject’s chin with adhesive tape. The position of the bag in the gastric fundus was checked fluoroscopically.

The polyvinyl tube was then connected to a computer-driven, programmable, volume-displacement barostat device (Synectics Visceral Stimulator; Synectics Medical, Stockholm, Sweden). The barostat device can deliver volume ramps or pressure steps at different rates while simultaneously monitoring pressure and volume at a sampling rate of 8 samples/s. To unfold the intragastric bag, it was inflated with a fixed volume of 300 ml of air for 2 min with the study subject in a recumbent position and again deflated completely. After a 10-min equilibration period, the subjects were positioned in a comfortable sitting position with the knees slightly bent (80°) in a bed specifically designed for that purpose.

Experimental design. This study consisted of two separate protocols. In the first protocol, the effects of duodenal infusion of either acid or saline on the fasting fundic tone and the sensitivity to isobaric fundic distensions were studied in 12 subjects (4 men and 8 women; mean age, 25.2 ± 1.0 yr, range 22–35 yr). On the morning after an overnight fast, the assembly including a pH electrode with an anti-
mony pH sensor and a thin infusion tube (2-mm OD) was introduced through the mouth. Subsequently, a barostat tube was inserted through the mouth. The pH electrode was calibrated by using commercial buffer solutions at pH 7.0 and pH 1.0 before insertion and checked after removal. A reference electrode was attached to the upper chest.

After a 30-min accommodation period, minimal intragastric distending pressure (MDP) was first determined as the lowest pressure level that provided an intrabag volume of 30 ml or more (17). This pressure level equilibrates the intra-abdominal pressure. With each subject in a sitting position, MDP, determined by increasing intrabag pressure by 1 mmHg every 3 min, was 8.0 ± 0.3 mmHg. Subsequently, sequential isobaric distensions were performed in stepwise increments of 2 mmHg, starting from MDP, and each lasting for 2 min while the corresponding intragastric volume was recorded. Subjects were instructed to score their perception of upper abdominal sensations at the end of every distending step by using both a graphic rating scale that combined verbal descriptors on a scale graded 0–10 (17) and the VAS. Thereafter, a sequence of stepwise isobaric distensions with the assessment of sensations was repeated during duodenal infusion of either 0.1 N HCl or 0.9% saline. Perception threshold was defined as the first level of pressure that provoked a perception score of 5 or more during isobaric distensions. Discomfort threshold was defined as the first level of pressure that had evoked a perception score of 1 or more during isobaric distensions.

Gastric tone was measured by calculating the mean intrabag volume for consecutive 5-min intervals during the long distending periods at MDP + 2 mmHg. The effect of duodenal infusions or the meal on fundic tone was evaluated by the comparison of these volumes. In addition, changes induced by duodenal infusions were also quantified by calculating the differences between the mean intrabag volume during 5 min immediately before duodenal infusion or ingestion of the meal and during the defined periods. To evaluate the effect of duodenal infusion on the phasic contractility of the fundus, which corresponds to slow changes in baseline volume after filtering out respiratory artefact, a baseline reconstruction was performed according to a computerized algorithm (2). Consistently, a motility index (MI) was calculated as the area between the signal and the baseline normalized over time (26). MI values were calculated for consecutive 5-min intervals during the distending periods at MDP + 2 mmHg. Changes in the phasic contractile activities of the fundus by duodenal infusions or the meal were assessed by calculating the differences between the mean MI during 5 min immediately before duodenal infusion or ingestion of the meal and during the defined periods.

Statistical analysis. ANOVA for repeated measures was used for the comparison of the first three steps in the pressure-perception or pressure-symptom curve, which all of the subjects have taken. In addition, the area under the curve for the same pressure steps in the pressure-perception curve and pressure-symptom curve was compared before and during infusion by paired *t*-test, using, on average, the first 4.2 steps. Paired comparisons of gastric tone and MI were performed by using ANOVA for repeated measures. Paired Student’s *t*-test was used for the comparison of the average values of intrabag volumes and MI during the defined periods, thresholds for perception and discomfort, and the compliance. All statistical analysis was performed with SPSS version 10.0 for Microsoft Windows. *P* < 0.05 was considered statistically significant. Data are presented as means ± SE.

RESULTS

Oral intubation with subsequent positioning of the barostat bag and the assembly including a pH electrode and an infusion tube was well tolerated by all subjects. A single volunteer complained of severe nausea within 5 min after the start of acid infusion, which spontaneously improved without interruption of infusion. The mean MDP was 8.1 ± 0.4 mmHg in the acid experiment and 7.8 ± 0.4 mmHg in the placebo experiment (nonsignificant [NS]). The mean pH of the duodenum significantly decreased by acid infusion (5.5 ± 0.4 before infusion vs. 1.7 ± 0.2 during infusion; *P* < 0.001), whereas saline infusion
did not affect intraduodenal pH (5.5 ± 0.4 before infusion vs. 5.4 ± 0.4 during infusion; NS).

Compliance of the fundus. Compliance of the fundus obtained in the pressure-volume curve remained unaltered during saline infusion (52.8 ± 7.0 before infusion vs. 58.2 ± 7.0 ml/mmHg during infusion; NS) (Fig. 2A). In contrast, acid infusion in the duodenum significantly increased the compliance of the proximal stomach (55.9 ± 5.3 before infusion vs. 69.6 ± 8.1 ml/mmHg during infusion; P < 0.05) (Fig. 2B).

Sensitivity to gastric distension. During stepwise isobaric distensions, saline infusion had no significant influence on the pressures, the corresponding volumes, and the corresponding wall tensions inducing first perception (Table 1). Similarly, the pressures, the corresponding volumes, and the corresponding wall tensions inducing discomfort were not affected by saline infusion (Table 2).

During acid infusion, the pressures, the corresponding volumes, and the corresponding wall tensions at the thresholds for first perception remained unchanged (Table 1). However, in contrast to saline, acid infusion significantly decreased the pressures and the corresponding wall needed to induce discomfort, but not the corresponding volumes (Table 2).

Saline infusion did not affect the perception scores and the severity scores for different symptoms during stepwise distensions (Fig. 3A). In contrast, during acid infusion, significantly higher perception scores were obtained for the same distending pressures compared with scores before acid infusion (P < 0.05) (Fig. 3B). During acid infusion, the severity scores of discomfort, fullness, bloating, nausea, satiety, and epigastric pain were significantly higher at the same distending pressures than those before infusion.

Similarly, the area under the pressure-perception curve for the same pressure steps was significantly higher during acid infusion than that before acid infusion (5.8 ± 0.2 vs. 3.8 ± 0.2; P = 0.001), whereas it was not affected by saline infusion (5.2 ± 0.2 vs. 8.0 ± 2.6; NS). In keeping with this observation, the area under the curve for the same pressure steps in pressure-symptom curves such as discomfort (P < 0.01), fullness (P < 0.005), bloating (P < 0.005), nausea (P < 0.05), satiety (P < 0.05), and epigastric pain (P < 0.05) was significantly higher during acid infusion than that before infusion. However, these values remained unaltered during saline infusion (Table 3).

Fasting tone of the fundus. Two representative tracings are shown in Fig. 4. The mean intrabag volumes for consecutive 5-min-interval saline infusion were not significantly different from the basal value for 5 min immediately before infusion (Fig. 5A). Intrabag volume 15 min after infusion did not differ from the basal value 5 min immediately before infusion (189.3 ± 21.9 vs. 170.4 ± 18.1 ml; NS). During acid infusion, an immediate and significant increase of the intrabag volume occurred, reflecting relaxation of the proximal stomach, and this significant relaxation was maintained throughout the acid infusion period compared with the basal value just before infusion (Fig. 5B). The intrabag volume 15 min after acid infusion was significantly increased compared with 5 min before infusion (310.3 ± 19.0 vs. 201.3 ± 38.7 ml; P < 0.001). Average fasting intrabag volume during acid infusion was significantly higher than that during saline infusion (310.3 ± 19.0 vs. 189.3 ± 21.9 ml; P < 0.001), and the average increase of the intrabag volume by acid infusion was significantly greater compared with the increase induced by saline infusion (109.8 ± 9.7 vs. 15.3 ± 7.1 ml; P < 0.001).

Table 1. Comparison of perception thresholds during stepwise isobaric distensions between saline and acid infusion

<table>
<thead>
<tr>
<th></th>
<th>Saline Before infusion</th>
<th>Saline During infusion</th>
<th>Acid Before infusion</th>
<th>Acid During infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressure, mmHg</td>
<td>2.7±0.5</td>
<td>2.5±0.4</td>
<td>3.7±0.8</td>
<td>2.8±0.5</td>
</tr>
<tr>
<td>Volume, ml</td>
<td>186.7±28.7</td>
<td>209.9±43.8</td>
<td>232.6±3.2</td>
<td>304.9±40.7</td>
</tr>
<tr>
<td>Tension, cm × mmHg</td>
<td>50.5±7.4</td>
<td>49.5±8.2</td>
<td>58.8±9.4</td>
<td>58.5±6.4</td>
</tr>
</tbody>
</table>

Data are means ± SE.

discomfort, fullness, bloating, nausea, satiety, and epigastric pain were significantly higher at the same distending pressures than those before infusion.

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Table 2. Comparison of discomfort thresholds during stepwise isobaric distensions between saline and acid infusion

<table>
<thead>
<tr>
<th></th>
<th>Saline Before infusion</th>
<th>Saline During infusion</th>
<th>Acid Before infusion</th>
<th>Acid During infusion</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pressure, mmHg</td>
<td>10.0±1.0</td>
<td>10.3±0.8</td>
<td>11.3±1.2</td>
<td>7.8±0.5*</td>
</tr>
<tr>
<td>Volume, ml</td>
<td>571.1±63.7</td>
<td>596.5±46.8</td>
<td>634.7±53.0</td>
<td>648.5±40.5</td>
</tr>
<tr>
<td>Tension, cm × mmHg</td>
<td>119.3±12.1</td>
<td>120.2±8.1</td>
<td>132.0±12.7</td>
<td>101.5±6.9*</td>
</tr>
</tbody>
</table>

Data are means ± SE. *P < 0.05 vs. before infusion using paired t-test.
Fig. 3. The pressure-perception curve. Perception scores at the same distending pressures did not differ before and during saline infusion (A). During acid infusion, significantly higher perception scores were obtained for the same distending pressures compared with those before infusion (*P < 0.05, ANOVA for repeated measures) (B).

Fig. 4. Representative tracing of intraballoon volume at MDP + 2 mmHg with administration of a meal. After a 15-min basal recording, duodenal infusion of saline (A) or acid (B) started in a randomized, double-blind manner. A mixed liquid meal was administered at 15 min after the start of infusion. Measurement continued during 60 min after the meal, with the end of duodenal infusion at 30 min.

Table 3. Comparison of the area under the pressure symptom curve for the same pressure steps before and during duodenal infusion

<table>
<thead>
<tr>
<th></th>
<th>Area Under the Curve, mm × mmHg</th>
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<tbody>
<tr>
<td></td>
<td>Before infusion</td>
</tr>
<tr>
<td>Discomfort</td>
<td>39.8 ± 5.7</td>
</tr>
<tr>
<td>Fullness</td>
<td>35.6 ± 5.1</td>
</tr>
<tr>
<td>Bloating</td>
<td>38.6 ± 5.6</td>
</tr>
<tr>
<td>Nausea</td>
<td>32.4 ± 2.3</td>
</tr>
<tr>
<td>Belching</td>
<td>18.6 ± 2.7</td>
</tr>
<tr>
<td>Burning sense</td>
<td>22.3 ± 3.3</td>
</tr>
<tr>
<td>Satiety</td>
<td>35.8 ± 5.2</td>
</tr>
<tr>
<td>Epigastric pain</td>
<td>17.6 ± 2.5</td>
</tr>
</tbody>
</table>

Data are means ± SE. *P < 0.05 vs. before infusion using paired t-test.

Fig. 5. The tone of the fundus. A: during duodenal saline infusion, fundic tone remained unchanged, but it was significantly decreased after a meal (*P < 0.05, ANOVA for repeated measures). B: during duodenal acid infusion, fundic tone was significantly decreased (*P < 0.05, ANOVA for repeated measures), but significant postprandial decrease of the tone was observed only during the first 10 min after the stop of acid infusion, compared with the basal value immediately before a meal (*P < 0.05, ANOVA for repeated measures).
**Postprandial tone of the fundus.** Mean intrabag volumes for consecutive 5-min intervals during the distending periods at MDP + 2 mmHg were significantly increased after the meal during saline infusion compared with the basal value for 5 min immediately before the meal (Fig. 5A). This significant postprandial increase of intrabag volumes was continuous during saline infusion, whereas it was not observed during acid infusion. During saline infusion, ingestion of the meal induced a significant increase of the intrabag volume compared with the basal value 5 min before the meal both during the first and second 30 min after the meal (193.1 ± 27.4 vs. 370.6 ± 44.9 ml, P ≤ 0.001, and vs. 335.5 ± 43.3 ml, P = 0.001). During acid infusion, the intrabag volume during the first and second 30-min period after the meal did not differ from the preprandial value (289.0 ± 32.6 vs. 335.4 ± 34.5 ml, NS, and vs. 342.4 ± 62 ml, NS). During the first 10 min after the end of acid infusion, intrabag volumes significantly increased compared with the basal value just before the meal (P < 0.05), but this was not maintained for the rest of the study (Fig. 5B).

Average intrabag volume during the postprandial period did not differ between acid and saline infusion (335.4 ± 34.5 vs. 370.6 ± 44.9, NS, during the first postprandial 30 min and 342.4 ± 62.2 vs. 335.5 ± 43.3, NS, during the second postprandial 30 min). However, the average increase of the intrabag volume by meal ingestion was significantly lower during the first postprandial 30 min in the acid studies than in the saline studies (46.5 ± 28.4 vs. 177.5 ± 28.6; P = 0.05).

**Phasic contractility of the fundus.** The mean MI of the proximal stomach for consecutive 5-min intervals during the fasting period were not altered by saline infusion, compared with the basal value for 5 min immediately before infusion. The mean MI during 15-min saline infusion in the fasting state remained unchanged compared with the basal value for 5 min immediately before infusion (25.3 ± 2.3 vs. 26.1 ± 2.6 ml × s; NS). During saline infusion, the MI of the fundus significantly decreased from 10 min until 30 min after the meal, compared with the basal value immediately before the meal (Fig. 6A).

Acid infusion caused a significant decrease of the MI in the fasting period compared with the basal value immediately before infusion, but no significant postprandial decrease was observed during acid infusion (Fig. 6B). The mean MI during 15-min acid infusion in the fasting state was significantly decreased compared with the basal value (21.2 ± 3.4 vs. 27.5 ± 2.5 ml × s; P ≤ 0.001). During saline infusion, ingestion of the meal was accompanied by a significant decrease in the average MI during the first 30 min postprandially, compared with the basal value just before the meal (22.5 ± 2.6 vs. 29.1 ± 2.7 ml × s; P = 0.005). During acid infusion, ingestion of the meal did not significantly affect the MI of the proximal stomach (21.2 ± 1.9 vs. 21.2 ± 3.4 ml × s; NS).

Decrease of fasting MI during acid infusion was significantly greater compared with that during saline infusion (6.5 ± 1.5 vs. 0.9 ± 1.3 ml × s; P ≤ 0.01). Decrease in the MI by the ingestion of the meal during acid infusion was significantly lower than that during saline infusion (0.1 ± 2.8 vs. 6.7 ± 1.8 ml × s; P ≤ 0.05).

**DISCUSSION**

In this study, we have shown that acid infusion in the duodenum 1) increases compliance of the proximal stomach; 2) enhances mechanosensitivity of the proximal stomach; 3) decreases the tone and phasic contractile activities of the proximal stomach; and 4) seems to inhibit postprandial fundic relaxation.

The pathogenesis of FD has remained obscure, but it has been suggested that FD is a heterogenous disorder associated with diverse underlying mechanisms. Recent studies indicate possible implication of altered duodenal responses to acid in the pathophysiology of FD (10, 18, 20, 21). Decreased duodenal clearance of exogenous acid, impaired duodenal motor response to acid, and duodenal hypersensitivity to acid have all been observed in FD patients (18, 20, 21). In line with these studies, we have recently demonstrated that spontaneous duodenal acid exposure is increased in a subset of FD patients compared with healthy controls, suggesting impaired duodenal clearance of endogenous acid. However, the relevance of increased duodenal acid exposure to symptoms still remains unknown. Previous studies showed that infusion of 5 ml of 0.1 N HCl in the duodenum induced nausea in a subset of FD patients during duodenal saline infusion, the motility index (MI) of the fundus was not altered, but it was significantly decreased from 10 min until 30 min after a meal (\( ^{*}P < 0.05, \text{ANOVA for repeated measures} \)). B: during duodenal acid infusion, the MI of the fundus was significantly decreased (\( ^{*}P < 0.05, \text{ANOVA for repeated measures} \)), but no significant decrease of the MI was observed after a meal, compared with the basal value immediately before a meal (B).
patients, which was regarded as duodenal hypersensitivity to acid (10). However, in our previous study, infusion of an acid bolus did not induce any symptoms in a group of FD patients with prominent nausea and increased spontaneous duodenal acid exposure. These data indicate that the role of duodenal hypersensitivity to acid in symptom generation of FD patients is unclear.

Duodenal acidification is known to play a major role in the regulation of gastric emptying. It has been shown that the greater the concentration of acid in the duodenum, the greater the inhibition of gastric emptying (8). This action may be important in protecting the duodenum from excessive amounts of acid. Actually, the motor response to duodenal acid infusion in healthy controls includes an enterogastric feedback causing a marked suppression of propagated waves from the antrum and stimulation of isolated pyloric pressure waves (20, 21). In addition, duodenal pH influences interdigestive gastric motility in humans, and lowering of duodenal pH prevents the occurrence of gastric phase III (30). Furthermore, duodenal acidification was found to induce gastric relaxation by an inhibitory effect on the stomach in animals (11). Through these pathways, increased duodenal acid exposure might contribute to the occurrence of delayed gastric emptying, antral hypomotility, or impaired interdigestive motility, all of which have been reported to occur in FD (3, 9, 12, 24, 29).

Mechanisms known to be linked to symptoms in FD include impaired gastric accommodation to a meal and hypersensitivity to gastric distension as well as delayed gastric emptying (4, 14, 24, 25, 27). However, little is known about the effect of duodenal acidification on proximal gastric motor and sensory function in humans. Results of the present study have shown that duodenal acidification may affect proximal gastric motor function including gastric accommodation to a meal. In the fasting period, duodenal acid infusion increased fundic compliance and decreased the tone and phasic contractile activities of the fundus. However, during duodenal acid infusion, no significant postprandial decrease of the fundus tone was observed. Preprandial fundic relaxation induced by duodenal acid infusion might be responsible for this apparent decrease of accommodation, because the absolute intrabag volume during the first 30 min after a meal did not differ between acid and saline infusion. Nevertheless, considering the occurrence of significant relaxation after the stop of acid infusion, it is tempting to speculate that proximal gastric relaxation in response to meal ingestion may be inhibited under the circumstances of increased duodenal acid exposure. Insufficient adaptive relaxation of the proximal stomach during and after the ingestion of a meal may be accompanied by increased intragastric pressure and activation of mechanoreceptors in the gastric walls, thus inducing symptoms. Rapid changes in intrabag volume during constant intrabag pressure at MDP + 2 mmHg may reflect phasic contractions of the proximal stomach. Our results showed that duodenal acidification also inhibited the phasic contractile activities of the proximal stomach. However, it is difficult to determine its pathophysiological relevance, because the role of phasic contractile activities of the fundus in symptom generation is not yet fully understood.

Our results have also shown that acid infusion in the duodenum increases sensitivity to gastric distension and the severity of symptoms during isobaric gastric distensions. In this study, duodenal acid increased compliance of the fundus, leading to increased corresponding volumes and wall tensions at the same pressures. This may contribute to increased sensitivity and more severe symptoms during stepwise isobaric distensions. On the other hand, pressures and corresponding wall tensions needed to induce discomfort were significantly decreased during acid infusion, indicating that duodenal acidification enhances gastric mechanosensitivity. In line with this finding, duodenal acid infusion increased the intensity of perception or individual symptoms during isobaric gastric distensions. These observations suggest that chemical stimulation of intestinal afferents by acid exerts a sensitizing effect on the stomach and increases perception of well-tolerated gastric distensions up to levels of discomfort. This suggestion is supported by previous animal studies showing that chemical stimulation is able to induce sensitization at the peripheral or the central level (6, 13, 16). Such sensitization manifests as increased background activity of sensory neurons, the lowering of nociceptive thresholds, changes in stimulus response curves, and enlargements of receptive fields (1, 6). In keeping with these studies, acid perfusion in the esophagus, stomach, or duodenum was found to result in enhanced mechanosensitivity of the same region (5, 15, 23). Furthermore, it has been shown that acid perfusion in the distal esophagus is associated with the development of mechanical hyperalgesia in the proximal esophagus, which has not been exposed to acid (19). Accordingly, chemical irritation with acid appears to increase sensory input to interneurons and/or projection neurons in the dorsal horn of the spinal cord, resulting in a secondary hyperalgesia in adjacent, undamaged visceral tissue and a central hyperexcitability (13). Through these mechanisms, duodenal acidification may increase gastric mechanosensitivity. Thus increased duodenal acid exposure presented in a subset of FD patients might potentiate perception of a different concurrent stimulus, leading to dyspeptic symptoms.

In conclusion, duodenal acidification increases proximal gastric mechanosensitivity, induces proximal gastric relaxation, and seems to inhibit the proximal gastric accommodation to a meal. Through these mechanisms, increased duodenal acid exposure may affect dyspeptic symptoms.

REFERENCES


