Cross-talk along gastrointestinal tract during electrical stimulation: effects and mechanisms of gastric/colonic stimulation on rectal tone in dogs

Shi Liu,1 Lijie Wang,1 and J. D. Z. Chen1,2
1Division of Gastroenterology, University of Texas Medical Branch, Galveston, Texas; and 2Transneuronix, Mt. Arlington, New Jersey

Submitted 16 December 2004; accepted in final form 26 January 2005

Liu, Shi, Lijie Wang, and J. D. Z. Chen. Cross-talk along gastrointestinal tract during electrical stimulation: effects and mechanisms of gastric/colonic stimulation on rectal tone in dogs. Am J Physiol Gastrointest Liver Physiol 288: G1195–G1198, 2005. First published February 3, 2005; doi:10.1152/ajpgi.00554.2004.—Gastric electrical stimulation (GES) has been shown to alter motor and sensory functions of the stomach. However, its effects on other organs of the gut have rarely been investigated. The study was performed in 12 dogs implanted with two pairs of electrodes, one on the serosa of the stomach and the other on the colon. The study was composed of two experiments, Experiment 1 was designed to study the effects of GES on rectal tone and compliance in nine dogs compared with colonic electrical stimulation (CES). Rectal tone and compliance were assessed before and after GES or CES. Experiment 2 was performed to study the involvement of sympathetic pathway in 8 of the 12 dogs. The rectal tone was recorded for 30–40 min at baseline and 20 min after intravenous guanethidine. GES or CES was given for 20 min before the initiation of the infusion. It was found that both GES and CES reduced rectal tone with comparable potency. Rectal compliance was altered neither with GES, nor with CES. The inhibitory effect of GES but not CES on rectal tone was abolished by an adrenergic blockade, guanethidine. GES inhibited rectal tone with a comparable potency with CES but did not alter rectal compliance. The inhibitory effect of GES on rectal tone is mediated by the sympathetic pathway. It should be noted that electrical stimulation of one organ of the gut may have a beneficial or adverse effect on another organ of the gut.

Preparation of Animals

Twelve healthy female hound dogs (21–28 kg) were selected for the study. After an overnight fast, a surgical procedure was performed on the dogs under anesthesia. Anesthesia was induced with pentothal (sodium thiopental, 5 mg/kg iv, Abbott Laboratories, North Chicago, IL) and maintained on IsoFlo (isoflurane 1.5%, halothane anesthesia, Abbott). A midline laparotomy was performed. One pair of 28-gauge stainless steel cardiac pacing wires (A&E Medical, Farmingdale, NJ) were implanted on the serosal surface of the stomach along the greater curvature 2 cm above the pylorus. Another pair of electrodes was implanted on the descending colon ~15 cm proximal to the anus. The electrodes in each pair were 1 cm apart and were affixed to the seromuscular layer of the stomach or colon. The connecting wires of the electrodes were subcutaneously tunneled through the anterior abdominal wall along the right side of the trunk and placed outside the skin caudal to the left scapula for the attachment to an electrical stimulator. The protocol was approved by the Institutional Animal Care and Use Committee at the University of Texas Medical Branch at Galveston, TX.

Experimental Protocol

The study was initiated 2 wk after the surgery when the dogs had completely recovered. After an overnight fast, the dog was brought to the laboratory for the study. Enema was administered 2 h before the study to void the rectum. The study was composed of two experiments.

Experiment 1 was designed to study the effects of GES on rectal tone and compliance in 9 of the 12 dogs. The experiment was performed in two randomized sessions (GES and CES) on separate days.

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
days at an interval of at least 3 days. The aim of each session was to study the effects of GES or CES on rectal tone and rectal compliance. In the first part of the session, rectal tone was recorded for 30–40 min at baseline, 20 min during electrical stimulation and 20 min after the cessation of stimulation (recovery period). Then, the intrarectal balloon was deflated and maintained deflated for a period of 30 min or more to ensure that the rectal tone was recovered to baseline. The second part of the session was designed to test rectal compliance and was composed of two identical sequences (control without stimulation followed with GES or CES). In each sequence, the rectal volume was measured continuously while the balloon was distended at various pressures in a stepwise fashion without (control sequence) or with stimulation (GES or CES sequence). GES or CES was performed with a frequency 12 cycles per minute (cpm), a pulse width of 300 ms, and an amplitude of 10 mA. These parameters were selected based on preliminary experiments performed in our lab, which showed consistent inhibition of gastric and intestinal motility, respectively (27, 29).

An adjustable electrical stimulator (model A301; World Precision Instruments, Sarasota, FL) was used for stimulation. In preliminary experiments performed in our lab, which showed consistent inhibition of gastric and intestinal motility, respectively (27, 29). An adjustable electrical stimulator (model A301; World Precision Instruments, Sarasota, FL) was used for stimulation.

Experiment 2 was performed in 8 of the 12 dogs after the completion of experiment 1, when the effects of GES/CES on rectal tone were known, to study the involvement of possible sympathetic mechanisms. It was performed in two randomized sessions (GES and CES) on separate days at an interval of 7 days. In each session, rectal tone was sequentially recorded for 30–40 min at baseline, 20 min after intravenous infusion of guanethidine (3 mg/kg for 5 min, Sigma, St. Louis, MO), 20 min during GES or CES, and 20 min after the termination of GES or CES.

Measurement and Analysis of Rectal Tone and Compliance

An electronic barostat (Synetics Visceral Stimulator, Synetics Medical, Stockholm, Sweden) was used to measure rectal tone. A catheter, with a polyethylene balloon (600-ml maximum capacity) on its tip connected to the barostat, was inserted through the anus and positioned with the caudal end of the attached balloon 5 cm from the anal verge. Rectal tone and rectal compliance were measured as follows.

Rectal tone. After the determination of the minimal distending pressure (MDP; a pressure level needed to overcome intra-abdominal pressure), a constant pressure procedure was initiated at a pressure of 2 mmHg above MDP. The rectal tone was calculated by averaging the rectal volume during the last 10 min of each period (baseline, stimulation, or recovery).

Rectal compliance. A stepwise pressure distension procedure was applied to test rectal compliance. Isobaric distensions were performed in 2-mmHg steps every 60 s from 2 mmHg to a maximum of 12 mmHg. The rectal intraballooon volume was constantly measured, and the average value over the last 30 s of each pressure level was analyzed. A volume-pressure curve was generated for each subject. Rectal compliance was defined as the linear slope of the volume-pressure curve (13, 19).

Statistical Analysis

The results are expressed as means ± SE. ANOVA was used to compare the data among three or more different periods, and the Student’s t-test was used to assess the effect of stimulation compared with the baseline or control. P values <0.05 were considered statistically significant.

RESULTS

Effects of GES on Rectal Tone

Both GES and CES significantly reduced rectal tone, reflected as an increase in rectal volume. Figure 1 shows typical rectal barostat tracings before and after electrical stimulation. The rectal intraballooon volume was significantly increased from 79.4 ± 10.3 ml at baseline to 118.9 ± 18.8 ml with GES (P = 0.008; Fig. 2A) and from 97.2 ± 11.6 ml at baseline to 154.1 ± 19.8 ml with CES (P < 0.001; Fig. 2B).

Effects of GES on Rectal Compliance

Neither GES nor CES altered rectal compliance. Figure 3A shows the volume-pressure curve during GES. The rectal compliance expressed as the slope of the volume-pressure curve was not significantly altered by GES (7.6 ± 1.1 vs. 9.1 ± 1.3 ml/mmHg, P > 0.05). During CES, a higher intraballooon volume was noted at each distending pressure compared with the control. The volume-pressure curve was shifted to the left (Fig. 3B) but remained parallel to the volume-pressure curve obtained without stimulation; the slope was not changed by CES (10.9 ± 1.2 vs. 11.2 ± 1.9 ml/mmHg, P > 0.05).

Efficacy of GES Compared with CES

GES was as effective as CES in inhibiting rectal tone, although GES was performed using the electrodes at the stomach, far away from the rectum, whereas CES was applied via the electrodes at the descending colon, very close to the rectum. The mean increase in rectal volume was 39.6 ± 10.6

![Image](http://ajpgi.physiology.org/Downloadedfrom http://ajpgi.physiology.org/)
ml in the GES session and 56.8 ± 10.6 ml in the CES session ($P > 0.05$).

**Involvement of Sympathetic Pathway with GES**

Guanethidine blocked the inhibitory effect of GES on rectal tone. After the infusion of guanethidine, the intraballoon volume remained unchanged when GES was applied ($P > 0.05$; Fig. 4). However, the inhibitory effect of CES on rectal tone was not abolished by guanethidine; the intra-balloon volume was still increased when CES was applied, compared with the value after guanethidine infusion without CES ($P < 0.004$; Fig. 4).

**DISCUSSION**

The present study demonstrated that GES decreased rectal tone but did not alter rectal compliance. GES was as effective as CES in inhibiting rectal tone. The inhibitory effect on rectal tone induced by GES was abolished by guanethidine.

Currently, there is a growing interest in the application of gastrointestinal electrical stimulation for the treatment of various clinical conditions. GES has been investigated as a therapeutic option in the management of refractory gastroparesis (1, 12, 15, 18, 20) and morbid obesity (6 – 8). A number of reports is available in the literature on GES with long pulses, demonstrating beneficial effects of this approach on gastric motor and sensory functions (3, 9, 16, 18, 20, 22, 28). However, little is known on the effects of GES on other organs of the gut. The inhibitory effect of GES on rectal tone observed in this study demonstrates that GES may affect the motility of other organs of the gut.

Colonic electrical stimulation with long pulses was reported to induce electrical activity in patients with total colonic inertia (26), improve colonic transit in a cat model with spinal cord injury (4), and normalize tachyarrhythmia and reduce symptoms of irritable bowel syndrome (25). On the basis of these preliminary data, CES might have a therapeutic potential for...
the treatment of colonic functional disorders. However, little is known about the effect of CES with long pulses on rectal motor function. To the best of our knowledge, this was the first study showing the effect of CES on an organ other than the colon.

In addition to studying the effect of electrical stimulation of one organ on another organ, the experiment was also tuned to investigate whether the efficacy was associated with the distance between the stimulation organ and the measurement organ. Accordingly, two stimulation locations were chosen, with one closest to the rectum and the other farthest from the rectum. Surprisingly, electrical stimulation of both the descending colon and the stomach had inhibitory effects on rectal tone, and the effects were comparable. To our knowledge, this was the first experiment to show that rectal tone could be altered or regulated by electrical stimulation of the other part of the gut.

The rectum serves as a reservoir for feces until defecation becomes socially convenient (17a). In some patients with fecal incontinence, the rectum was reported to be unable to fulfill its duty as a reservoir and act more like a conduit (23). The inhibitory effect of GES and CES on rectal tone observed in this study suggests that GES and CES may have a therapeutic potential in the treatment of fecal incontinence, because the inhibition in rectal tone may increase the reservoir capacity of the rectum. However, more studies are needed to further explore this potential.

The sympathetic nerves of the gut are primarily involved in the inhibition of gastrointestinal motility (14). Therefore, we studied the involvement of the sympathetic mechanism in the GES/CES-induced rectal relaxation. The effect of GES on rectal tone was expected to be a neural reflex phenomenon, because the rectum (measurement) is far away from the stomach (stimulation). Indeed, it was abolished by guanethidine, suggesting the involvement of the sympathetic pathway. Surprisingly, however, the CES effect was not blocked by guanethidine, excluding the involvement of the sympathetic pathway. We speculate that CES may activate local inhibitory mechanisms, because the rectum (measurement) is far away from the stomach (stimulation).

In conclusion, GES with long pulses inhibits rectal tone but does not alter rectal compliance. GES is as effective as CES in inhibiting rectal tone. The GES-induced inhibitory effect on rectal tone is mediated, at least in part, via the neural sympathetic pathway. However, the sympathetic pathway may not be involved in the rectal relaxation induced by CES. These results suggest that electrical stimulation of one organ of the gut may have a beneficial or adverse effect on another organ of the gut.

REFERENCES


28. Xing JH, Brody F, Brodsky J, Larive B, Ponsky J, and Soffer E. Gastric electrical stimulation at proximal stomach induces gastric relax-