Inhibitory Effects and Mechanisms of Intestinal Electrical Stimulation on Gastric Tone, Antral Contractions, Pyloric Tone and Gastric Emptying in Dogs

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Short Title: IES and gastric emptying

Abbreviations: IES: intestinal electrical stimulation, GES: gastric electrical stimulation, AUC: area under curve; NO: nitric oxide

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Abstract

The aim of this study was to investigate the effects and mechanisms of intestinal electrical stimulation (IES) on gastric tone, antral and pyloric contractions, and gastric emptying in dogs. Female hound dogs were equipped with a duodenal or gastric cannula and implanted with one pair of serosal electrodes at the small intestine. The study was composed of 5 different experiments. A test of liquid gastric emptying was performed in a number of sessions with and without IES, and with and without L-NNA (L-nitro-N-arginine). Gastric emptying was assessed by collecting the chyme from the duodenal cannula. Postprandial antral and pyloric contractions were measured by placing a manometric catheter into the antrum and the pylorus via the duodenal cannula. The measurements were taken at the absence/presence of IES and absence/presence of L-NNA or phentolamine. Gastric tone was assessed by the measurement of gastric volume at a constant pressure. It was found that gastric emptying was substantially and significantly delayed with IES or L-NNA in comparison with the control session. The IES-induced delayed gastric emptying became normal when L-NNA was added to IES. IES reduced gastric tone, that was blocked by L-NNA. IES also inhibited antral contractions (both frequency and amplitude) and this inhibitory effect was not blocked by L-NNA but by phentolamine. IES alone showed no effects on pyloric tone or resistance but decreased pyloric tone at the presence of L-NNA. In conclusion, IES reduces gastric tone via the nitrergic mechanism, inhibits antral contractions via the adrenergic pathway, exerts no effects on pyloric tone, and delays liquid gastric emptying. The IES-induced delay in gastric emptying is attributed to its inhibitory effects on gastric motility.

Key words: Gastric emptying; Gastrointestinal motility; Intestinal electrical stimulation; Gastric pacing.
INTRODUCTION

Electrical stimulation as a potential modality for treatment of morbid obesity is gaining more and more attention (15,16) since there is a lack of long-term efficacy with the conventional behavior modifications and pharmacotherapies (12, 29) and a high rate of mortality and morbidity with the surgical interventions (4, 9, 21, 42, 46). Gastric electrical stimulation (GES) has been under clinical investigations for the treatment of morbid obesity and preliminary data have been encouraging but inconclusive about the GES effects on food intake and weight loss (15, 16).

The proximal small intestine plays an important role in regulating gastric emptying (30), optimizing nutrient absorption (26) and signaling satiety in the central nervous system (CNS) (20). Intestinal electrical stimulation (IES) may have multiple effects on gastrointestinal functions including gastric emptying, small bowel transit, nutrient absorption and feedback signaling of satiety to the CNS. This makes IES a very attractive alternative option for obesity treatment. In 1977, Kelly showed that distal duodenal pacing caused duodenal-gastric reflux of BaSO$_4$ in dogs and the rate of liquid gastric emptying was slowed by 25% (28). However, there has been a lack of follow-up studies investigating the inhibitory effects of IES on gastrointestinal motility and related mechanisms.

While it may not be conclusive, a number of studies have showed that the obesity patients have accelerated gastric emptying (5, 6, 49, 52). The accelerated gastric emptying is believed to shorten the satiety period, i.e. the shorter time to the ingestion to the next meal. The critical factors that control gastric emptying are gastric tone, antral peristalsis, pyloric resistance, and duodenal feedback control. Dysfunction of any of these factors results in impairment of gastric emptying (13, 19, 22, 23, 25, 27, 36, 37, 45, 47, 48). Effective peristaltic antral contractions play a major role in solid gastric emptying (13, 27). The coordination of the antro-pyloro-duodenal region is another key factor that controls solid and liquid gastric emptying (2, 3, 17, 25), and any factors that affect the coordination of the antro-pyloro-duodenal region will result in delayed gastric emptying (28, 52). While few previous studies reported the inhibitory effect of IES on gastric emptying, the underlying mechanisms are unknown. It is not clear whether the IES-induced delay in gastric emptying is attributed to a reduction in gastric tone and/or antral contractions. It is unknown whether the pylorus is also involved in the IES-induced delay in
gastric emptying. Nitric oxide, released from the non-adrenergic non-cholinergic nerve, is known to be involved in the relaxation of gastric fundus. Gastric electrical stimulation was previously reported to inhibit gastric tone via the nitrergic pathway and decrease antral contractility via the sympathetic pathway (both alpha- and beta-adrenergic pathways). We believed that IES might have similar effects and mechanisms on fundic tone and antral contractions as gastric electrical stimulation. Accordingly, we hypothesized that IES would inhibit gastric motility via the nitrergic and adrenergic pathways.

Therefore, the aim of this study was to systematically and comprehensively investigate the effects and mechanisms of IES on gastric motility, including gastric tone, antral contractions, pyloric tone and gastric emptying in dogs.

**MATERIALS AND METHODS**

**Animal Preparation**

The procedures used in this study were approved by the Institutional Animal Care and Use Committee at the University of Texas Medical Branch at Galveston, Texas, USA. Fourteen healthy female hound dogs (17.4~25.2 Kg) were included in the study. The operation was performed under general anesthesia after an overnight fast. Seven of the dogs were surgically prepared with a chronic duodenal fistula located 20 cm beyond the pylorus (Figure 1). The cannula was brought out through the abdominal wall and fixed to prevent rotation. The other seven dogs were placed with a chronic gastric cannula 10 cm above the pylorus and these dogs were used for the study of gastric tone (Figure 1). In all dogs, two 28-guage cardiac pacing electrodes (A & E Medical, Farmingdale, NJ) were implanted 1 cm apart on the serosal surface of small intestine 30 cm distal to the duodenal cannula. The electrode wires were subcutaneously tunneled through the anterior abdominal wall along the right side of the trunk and were placed outside the skin around the right hypochondrium for attachment to the electrical stimulator. The study was initialized after the dogs were completely recovered from the surgery, usually after 2 weeks.

**Experimental Protocols**

The first experiment was designed to study the effects and mechanisms of IES on gastric emptying of liquid in 7 dogs with the duodenal fistula. Each dog was studied randomly in 4
sessions on 2 separated days (a minimum of 2 days apart) after a 12-h fast. During each study session, the dog was fed with a liquid meal composed of 237ml Ensure (Ross, Products Division Abbott Laboratories, Columbus, OH, USA) mixed with 100 mg of phenol red. The meal had 250 calories (fat, 6 g; carbohydrate, 40 g; and protein, 9 g). Gastric emptying was assessed using an established method (41). Four sessions were performed including 1) control without IES; 2) IES for the entire 90 min; 3) Continuously infusion of L-nitro-N-arginine with the dose of 2.5 mg/kg/h (Sigma, St. Louis, MO); 4) IES together with infusing of L-NNA.

The second experiment was designed to study the effects and mechanisms of IES on antral contractions and pyloric tone after a solid meal and performed on the 7 dogs with the duodenal cannula. It was composed of 3 randomized sessions (control, L-NNA and phentolamine). At the beginning of each study session, the dog was fed with 375 g of standard canned dog food. A manometric catheter with a sleeve (Dentsleeve) was placed into the stomach and pylorus to assess antral contractions and pyloric tonic pressure during four consecutive 20-min postprandial periods called baseline (baseline period without intervention), treatment (drug/vehicle was given during this period), IES (IES was performed continuously during this entire 20-min period), and recovery (without IES or medication) respectively. In study session 1, intravenous normal saline was continuously infused during the second 20-min period and third 20-min period. Session 2 was the same as the session 1 except the replacement of saline with L-NNA (2.5 mg/kg/h). In session 3, phentolamine (Sigma, St. Louis, MO) was given (bolus injection of 1 mg kg$^{-1}$ followed by perfusion of 1 mg kg$^{-1}$ h$^{-1}$, IV). Antral contractions were measured in all 3 sessions, whereas, pyloric tone was measured only in sessions 1 and 2.

The third experiment was designed to study the effect of IES on antral contractions after a liquid meal in the 7 dogs with the duodenal cannula. The procedure was the same as the second experiment except that the solid meal was replaced with the same liquid meal used in the experiment 1. Antral contractions were measured for 20 min immediately after the test meal, followed with another 20 min with IES.

The fourth experiment was designed to investigate the effects and mechanism of IES on gastric tone and performed in 7 dogs with the gastric cannula. It was composed of 3 randomized sessions (control, IES and IES with L-NNA). Gastric volume was measured by barostat using an established method previously published (50). Fasting gastric volume was recorded at an operating pressure of 2 mmHg higher than the minimal distending pressure for 20-minute at
baseline and 20-minute with IES. The L-NNA session was the same expect that L-NNA was infused for 40 minutes after the 20-min baseline and IES was performed during the entire L-NNA infusion. Gastric volume was calculated by the mean value during each 20 min period. Gastric tone was determined by the gastric volume, that is, an increase in gastric volume represented a decrease in gastric tone, vice versa.

**Intestinal Electrical Stimulation**

IES was composed of a series of pulses (square waves) with a frequency of 20 cycles/pulses per min (cpm), pulse amplitude of 10 mA and pulse width of 200 ms. These stimulation parameters were previously shown to inhibit intestinal contractions in the fed state (33). An electrical stimulator (Model A310, World Precision Instruments, Sarasota, FL. USA) was connected to the connection wires of the electrodes in the small intestine with a constant current mode.

**Gastric emptying**

The liquid test meal contained 237ml of Ensure mixed with 100 mg of phenol red as a mark, and gastric emptying was determined by assessing the amount of phenol red in each collection of gastric effluent using an established method published previously (41). During the study, the volume of each collection was recorded every 15 min for 90 min. A spectrophotometer was used to detect the amount of phenol red in each sample. Gastric emptying was assessed by calculating the amount of phenol red recovered from each collection of gastric content.

**Measurement of contractile activity and tone of the antrum and pylorus**

The measurements of the antral and pyloric contractions were made using the manometric catheter which contained a 4-cm-long sleeve sensor, one sensor (or side-hole) at the distal end and two sensors at the proximal side at an interval of 2cm (Synectics Medical AB, Stockholm, Sweden). The catheter was inserted via the duodenal cannula into the pylorus and antrum immediately after the test meal. The position of the sleeve portion astride the pylorus was confirmed by the pull-through technique by assessing the waveform of the antral contractions (at a frequency of 5 cpm) measured by the sensor distal to the sleeve and the waveform of the
duodenal contractions (at a frequency of 10-15 cpm) measured from the two sensors located proximal to the sleeve.

**Analysis of contractile active and tonic pressure of the antrum and the pylorus**

The manometric tracing of each 20-min period was composed of two parts: the baseline level of the tracing and the phasic oscillation of tracing above the baseline level. The phasic oscillations above the baseline level were called contractions, whereas the baseline level of the tracing was called tone pressure. A phasic contraction was defined as an increase in pressure over the baseline level of >10 mmHg. This threshold of 10 mmHg was used to exclude possible pressure changes attributed to respiration artifacts. The area under curve (AUC) was used to represent the summation of contractile activities a given period. It was calculated by summing all contractile points over each of the four 20-min period. The sum was then divided by 1200 (seconds) to avoid large values. The number of contractions of each 20-min period was visually counted.

The tonic pressures were calculated from the baseline level of the manometric recording. The average of pressure values during the absence of phasic contractions and the lowest pressures of each phasic contraction was considered as the tonic pressure.

**Statistics**

Data are reported as mean ± SD. Analysis of variance was used to compare data among three or more different interventions or periods. Student’s paired t-test was used to investigate the differences between pairs when p value of ANOVA was less than 0.05. A p value less than 0.05 was considered statistically significant.

**RESULTS**

**Effects and nitrergic mechanism of IES on gastric tone**

Gastric tone was reduced with IES, reflected as an increase in gastric volume. There was a significant difference among the control, IES and IES plus L-NNA sessions (one way ANOVA, P< 0.001). The gastric volume was 90.9 ± 22.4ml in the control session and substantially increased to 263.6 ± 98.0 ml during IES ( P = 0.001), suggesting a reduction of gastric tone. At
the presence of L-NNA, IES was failed to increase gastric volume (113.9 ± 49.5ml, P = 0.2 vs. control and P = 0.003 vs. IES), suggesting the involvement of the nitrergic pathway in the IES-induced gastric relaxation (Fig.2).

**Effects and mechanism of IES on antral contractions**

IES significantly inhibited phasic contractions after the solid meal in the distal antrum (see Figure 4A for typical manometric recordings in the control session with saline). As shown in Figure 3A, the total number of contractions in the antrum during the 20-min IES period was significantly different regardless of the test conditions (saline infusion vs. iv L-NNA) (p < 0.0001, two-way ANOVA tests across four experimental periods; baseline vs. treatment vs. IES, vs. recovery and two study sessions: saline infusion as control vs. iv L-NNA). Specifically, the number of contractions in the distal antrum was significantly inhibited during the IES periods compared to the 20-min period immediately before or after IES (“treatment” period or recovery period), regardless of test conditions (saline infusion vs. iv L-NNA) (p < 0.05 paired t test). These data also indicated that L-NNA did not block the inhibitory effects of IES on the number of contractions in the antrum. Similar results were noted with the AUC of the contractile activity (see table). The data obtained from the session with phentolamine is also presented in table and Fig.3A. It is seen that the inhibitory effect of IES on the postprandial contractions was blocked by phentolamine, suggesting a sympathetic pathway (Fig.3A). Similar findings on the effects of IES on pyloric contractions was noted and presented in Figure 3B.

The liquid meal did not induce obvious antral contractions. The AUC of the postprandial antral contractions was 1.9±0.5 that was not different from the fasting data. Accordingly, the inhibitory effect of IES could not be determined due to the absence of antral contractions.

**Effects and nitrergic mechanism of IES on pyloric tone**

The effects of IES and L-NNA are presented in Figure 5. In the control session (absence of L-NNA), IES showed no effects on pyloric tone which was 31.7 ± 7.7 mmHg at baseline, 30.4 ± 6.6 mmHg during saline infusion, 32.4 ± 9.4 mmHg during IES and 35.6 ± 7.9 mmHg during the recovery period (P>0.05). No significant difference was noted. In another session, the pyloric tonic pressure was 30.4 ± 6.6 mmHg at baseline, increased to 44.6 ± 12.4 mmHg during L-NNA (P<0.05 vs the same period in saline session), reduced to 24.3 ± 5.8 mmHg when IES was
performed (P<0.05 vs L-NNA infusion period or IES without L-NNA) and recovered to 38.9 ± 13.9 mmHg during the recovery period.

These data indicated that while IES had no effects on pyloric tone at the absence of L-NNA but significantly reduced pyloric tone at the presence of L-NNA.

**Effects and mechanisms of IES on gastric emptying**

IES significantly delayed gastric emptying and this inhibitory effect was blocked by L-NNA. As shown in Fig.6. IES alone or L-NNA alone delayed gastric emptying, whereas, in the session with IES and L-NNA, gastric emptying was almost normal compared with the control session and significantly faster than the IES only session. The percentage of gastric emptying at 90 min was 72.9 ± 10.9% in the control session, 22.4 ±9.1% with IES (P<0.001 vs. control), 24.4 ±17.2% (P<0.01 vs. control) with L-NNA and 64.6 ± 16.8% with IES plus L-NNA (P=0.4 vs. control, P < 0.01 vs. IES)

**DISCUSSION**

In this study, we found that IES reduced gastric tone, inhibited antral contractions, had no effects on pyloric tone and delayed liquid gastric emptying. The mechanistic studies indicated that the inhibitory effects of IES on gastric tone, antral contractions and gastric emptying were blocked by L-NNA, phentolamine and L-NNA, respectively. These data suggested that the inhibitory effect of IES on gastric tone was medicated via the nitrergic pathway, on antral contractions was mediated through the sympathetic mechanisms and on gastric emptying was attributed to the reduced gastric tone.

Electrical stimulation of the duodenum was first reported to delay gastric emptying of non-nutrient liquid meals in dogs by Kelly et al in 1977 (28). The liquid gastric emptying was delayed by 25% during electrical stimulation of the small intestine. Subsequently, IES was successfully used to treat dumping syndrome after gastrectomy by slowing gastric emptying (18, 34, 35). However, the mechanism of IES-induced delayed gastric emptying had not been previously investigated. In this study, we confirmed the previous findings on IES-induced delayed gastric emptying and also found that L-NNA restored the IES-induced delayed gastric
emptying. This suggested that the reduced gastric tone with IES played a major role in the IES-induced delayed gastric emptying: IES reduced gastric tone and led to a delay in gastric emptying, whereas, L-NNA blocked the inhibitory effect of IES on gastric tone and therefore gastric emptying was not delayed any more.

Nitric oxide is a well-known inhibitory neurotransmitter on gastrointestinal motility. It has been shown that nitric oxide synthase is present in the enteric nervous system (3, 10, 11). Electric field stimulation induced the release of nitric oxide in muscle strips of the small intestine in vitro (1). This leads to the logical assumption that electric stimulation of the small intestine induces the production of nitric oxide, which might be responsible for suppressed gastric motility and delayed gastric emptying. Furthermore, previous studies showed that L-NNA increased contractile activity and tonic pressure in the antrum (38), pylorus (7) and duodenum (8). However, both liquid and solid gastric emptying was delayed by L-NNA (24, 44). It has been postulated that delayed gastric emptying by L-NNA is due to the action of L-NNA blockage of the relaxation effect on the pylorus, which results in increased pyloric resistance. In addition, it abolishes the inhibitory effects on duodenal contractions, which results in increased duodenal brake. An increase in pyloric tone was noted with L-NNA compared with the administration of saline. Surprisingly, however, the pyloric tone was significantly reduced when IES was performed at the presence of L-NNA. This phenomenon has never been reported in the literature and deserves further investigation.

Gastric emptying is controlled by various motility components working in concert including the propulsive components for gastric emptying—fundic tone, antral contractions vs. the resistive components—pyloric tone and duodenal resistive contractions. However, studying motility in the antro-pyloro-duodenal region is a technical challenge. In our unique dog model, the catheter with a 4-cm long sleeve was inserted into the pylorus via the duodenal cannula with a known fixed length. Using the push-through technique, we were able to accurately position the sleeve astride the pylorus. Only about 20 cm of the catheter were inserted. The catheter was fixed to the cannula to prevent dislocation of the sleeve from the pylorus. New findings were reported in this study on IES and are illustrated in Fig7. From this figure, we can see that the inhibitory effect of IES on gastric emptying was mediated via (see Fig.7A) 1) inhibition of fundic tone via the nitrergic pathway; 2) inhibition of antral contractions via the sympathetic pathway; 3) inhibition of duodenal contractions via the sympathetic pathway as shown in a previous study (33).
reduction in duodenal motility slows intestinal transit and therefore increases duodenal resistance, contributing to delayed gastric emptying. The role of L-NNA in preventing IES-induced delay in gastric emptying is illustrated in Fig.7B: 1) L-NNA blocks the nitrergic pathway and therefore blocks the inhibitory effect of IES on gastric tone; 2) L-NNA plus IES reduces pyloric tone (resistance). Regarding the sympathetic mechanisms of IES on antral contractions, it should be noted that in a previous study, gastric electrical stimulation was found to inhibit antral contractions mediated through both $\alpha$- and $\beta$- adrenergic pathways (39). Although it was not investigated, the involvement of the $\beta$- adrenergic pathway could not be ruled out. It is reasonable to speculate the same mechanisms involved in the IES with the GES.

The physiological observations and mechanistic findings in the study are of great clinical importance. In a previous clinical study in healthy volunteers (32), IES applied via ring electrodes attached to the tip of a naso-jejunal feeding tube placed in the duodenum resulted in a decrease in water intake and delayed gastric emptying of solid. Based on the findings of the present study, the decreased water intake with IES might be attributed to a decrease in gastric tone or an increase in gastric volume with IES as the increase in gastric volume was reported to be correlated with a decrease in food intake in dogs (40). Whereas, the delay in gastric emptying of solid with IES might be caused by a decrease in antral contractions according to the findings of the current study.

The inhibitory effects of IES on various gastric functions observed in this study support the concept of the IES therapy for obesity although no direct data were given in this study. Limiting food intake and reducing absorption are two major goals in the development of obesity treatment modalities. The induction of gastric distention (or reduced gastric tone) and delay in gastric emptying have been reported to reduce food intake (51). In addition, a few recent animal and human studies have shown an inhibitory effect of IES on fat absorption. In a rodent study, IES accelerated intestinal transit and reduced fat absorption (43). Similar acceleration in intestinal transit and reduction in fat absorption were noted in a clinical study in healthy volunteers (31). Taken together, IES might be a better therapy for obesity than gastric electrical stimulation that has been shown to delay gastric emptying and reduce food intake but has no effects on intestinal transit or nutrient absorption. However, systematic studies are needed to compare the efficacy in treating obesity between gastric electrical stimulation and intestinal electrical stimulation.
In conclusion, IES reduces gastric tone via the nitrergic mechanism, inhibits antral contractions via the adrenergic pathway, exerts no effects on pyloric tone, and delays liquid gastric emptying. The IES-induced delay in gastric emptying is attributed to its inhibitory effects on gastric motility.

**Perspectives and Significance**

The current study was designed to investigate the effects of IES on gastric motility including gastric tone, antral contractions, pyloric tone, liquid gastric emptying and possible mechanisms. We have found that IES reduced gastric tone via the nitrergic pathway, inhibited postprandial antral contractions via the sympathetic pathway and delayed liquid gastric emptying.

**Acknowledgement**

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Legends of figures

Figure 1. Surgical preparation: In 7 of the dogs, a gastric cannula was placed 10 cm proximal to the pylorus for the assessment of gastric tone; in the other 7 dogs, a duodenal cannula was placed 20 cm distal to the pylorus for the assessment of antral contractions, pyloric tone and gastric emptying. In addition, each dog was implanted with one pair of electrodes on the small intestine 30 cm distal to the pylorus.

Figure 2. Effect of IES on gastric volume. IES significantly increased gastric volume, represented a decreased gastric tone (P = 0.001) and its inhibitory effect was blocked by L-NNA (P = 0.2 vs. control and P = 0.003 vs. IES).

Figure 3. Effect of IES on antral and pyloric contractions to a solid meal. A: IES significantly inhibited antral contractions (P < 0.05), this inhibition was not blocked by L-NNA, it was blocked by phentolamine instead, suggesting the involvement of sympathetic pathway. B: IES significantly inhibited pyloric contractions (P < 0.05) and this inhibition was not blocked by L-NNA.

Figure 4. Typical antral manometric tracings after a solid meal. A: control with infusion of saline. B. Infusion of L-NNA. C. Infusion of phentolamine.

Figure 5. Effects of IES on tonic pressure of the pylorus in the sessions with and without presence of L-NNA. Saline had no effect on pyloric tone, nor did IES. However, L-NNA increased pyloric tone whereas, IES reduced pyloric tone compared with the period right before IES in the same
session and the same period in the control session, suggesting an inhibitory effect of IES on pyloric tone at the presence of L-NNA.

Figure 6: Effect of IES on liquid gastric emptying at different time points. Both IES and L-NNA delayed gastric emptying at all time points (P < 0.01), however, at the presence of L-NNA, IES was failed to delay gastric emptying (P < 0.01 vs. IES + L-NNA), suggesting the involvement of the nitrergic pathway on the inhibitory effect of IES on gastric emptying.

Figure 7: Mechanisms involved in the inhibitory effect of IES on gastric emptying. a). Effects of IES. IES reduced fundic tone via the nitrergic pathway; reduced antral contractions via the sympathetic pathway; had no effects on pyloric tone and reduced duodenal contractions via sympathetic pathway (reported from previous study). All these inhibitory effects resulted in delayed gastric emptying. b). Roles of L-NNA in restoring gastric emptying. L-NNA blocked the inhibitory effect of IES on gastric tone, reduced pyloric tone and almost restored gastric emptying. “Via NO”: via the nitric oxide pathway; “Via sym.”: via the sympathetic pathway.
Table. Effects of IES on the AUC of contractions during 4 consecutive 20-min periods after a solid meal in antro-pyloro-duodenal region. Saline or L-NNA was given during the second 20-min period called “Treatment”. IES was performed during the 3rd period called “IES”.

<table>
<thead>
<tr>
<th>Location/Session</th>
<th>AUC (mmHg/sec) of the contractions during each 20-min period</th>
<th></th>
<th></th>
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<tbody>
<tr>
<td>Baseline</td>
<td>Treatment</td>
<td>IES</td>
<td>Recovery</td>
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<td>Antrum</td>
<td></td>
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<td></td>
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<tr>
<td>Control</td>
<td>6.7 ± 3.4</td>
<td>6.8 ± 2.9</td>
<td>4.8 ± 2.3</td>
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<tr>
<td>L-NNA iv</td>
<td>10.9 ± 5.8</td>
<td>11.9 ± 5.4</td>
<td>5.5 ± 1.0</td>
<td>11.4 ± 11.7</td>
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<tr>
<td>Phentolamine</td>
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<td>12.3 ± 1.6</td>
<td>12.2 ± 1.5</td>
<td>10.3 ± 3.1</td>
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<tr>
<td>Pylorus</td>
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<td></td>
<td></td>
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</tr>
<tr>
<td>Control</td>
<td>7.1 ± 4.2</td>
<td>11.31 ± 6.4</td>
<td>4.7 ± 3.7*</td>
<td>11.3 ± 8.7</td>
</tr>
<tr>
<td>L-NNA iv</td>
<td>10.5 ± 5.0</td>
<td>32.3 ± 3.5‡</td>
<td>4.0 ± 2.0*</td>
<td>33.6 ± 15.0‡</td>
</tr>
</tbody>
</table>

* p < 0.05, compared to treatment or recovery period;
‡ p < 0.05, compared to control session
Figure 1

Duodenal cannula for measuring antro-pyloro-duodenal contractions and assessing gastric emptying

Gastric cannula for measuring gastric volume

Electrodes for IES
Figure 2

The graph shows the gastric volume (ml) for different groups: Control, IES, and IES+L-NNA. The y-axis represents gastric volume in milliliters ranging from 0 to 400. The x-axis represents the different groups. The IES group shows a significantly higher gastric volume compared to the Control and IES+L-NNA groups, indicated by the asterisks (* and **) on the graph.
Figure 4

A

Baseline  Saline  IES  Recovery

B

Baseline  L-NNA  IES  Recovery

C

Baseline  Phentolamine  IES  Recovery
Figure 5

Baseline Treatment IES Recovery

Tonic Pressure (mmHg)

Control
L-NNA iv

Experimental Periods (20-min)

p < 0.05
Figure 6

[Graph showing the percentage of gastric emptying over time for different conditions. The graph includes lines for Control, IES, L-NNA, and IES+L-NNA, with asterisks indicating statistical significance.]
Figure 7

(a). Inhibitory effects of IES

IES

Fundic Tone

Antral Contractions

Pyloric Tone (no effect)

Duodenal Contractions

Gastric Emptying

IES + L-NNA

Fundic Tone

Antral Contractions

Pyloric Tone

Duodenal Contractions

Gastric Emptying Back to "Normal"

(b). Roles of L-NNA in restoring gastric emptying