

Electroacupuncture improves impaired gastric motility and slow waves induced by rectal distension in dogs

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Submitted 4 May 2008; accepted in final form 20 July 2008

Chen J, Song G-Q, Yin J, Koothan T, Chen JD. Electroacupuncture improves impaired gastric motility and slow waves induced by rectal distension in dogs. *Am J Physiol Gastrointest Liver Physiol* 295: G614–G620, 2008. First published July 24, 2008; doi:10.1152/ajpgi.90322.2008.—Rectal distension (RD) is known to induce upper gastrointestinal (GI) symptoms. The aim of this study was to investigate the effects and underlying mechanisms of RD on gastric slow waves (GSW) and motor activity and furthermore to investigate the effects and mechanisms of electroacupuncture (EA) on GSW and motor activity. Eight female hound dogs chronically implanted with gastric serosal electrodes and a gastric fistula were studied in six separate sessions. Antral motility, GSW, heart rate variability, and rectal pressure were evaluated for the above purposes. 1) RD at a volume of 120 ml suppressed antral motility significantly. Guanethidine blocked the inhibitory effect of RD. EA at ST36 was able to restore the suppressed antral contractions induced by RD (16.6 ± 1.7 vs. 8.0 ± 1.4 , $P < 0.001$). Naloxone partially blocked the effect of EA on antral contractions. 2) RD reduced the percentage of normal GSW from $98.8 \pm 0.8\%$ at baseline to $76.1 \pm 8.6\%$ ($P < 0.05$) that was increased to $91.8 \pm 3.0\%$ with EA. The effects of EA on the GSW were nullified by the presence of naloxone. 3) EA did not show any significant effect on rectal pressure, suggesting that the ameliorating effects of EA on RD-induced impaired gastric motility were not due to a decrease in rectal pressure. 4) EA increased the vagal activity suppressed by RD. In conclusion, RD inhibits postprandial gastric motility and impairs GSW in dogs, and the inhibitory effects are mediated via the adrenergic pathways. EA at ST36 is able to restore the RD-induced impaired GSW and motor activities, possibly by enhancing vagal activity, and is partially mediated via the opioid pathway. EA may have therapeutic potential for functional gastrointestinal disorders.

adrenergic pathway; gastric slow waves; naloxone

CHRONIC, IDIOPATHIC, slow-transit constipation and constipation-dominant irritable bowel syndrome (IBS) are commonly observed in clinical practice. These patients frequently complain of upper abdominal symptoms such as bloating, upper abdominal discomfort or pain, and vomiting. The symptoms overlap with lower abdominal symptoms and are resistant to dietary and pharmacological treatments because of the constipation issues; they are related to the presence of impaired gastrointestinal myoelectrical activity and reduced upper gastrointestinal motor activity (1, 4, 13, 31, 33, 37). This phenomenon has led to the hypothesis that rectal distension (RD) with fecal stasis in the colorectal region directly causes reflexive inhibition of proximal gastrointestinal motility (5, 7, 9, 22, 32, 50).

A number of investigations have indicated that RD induces upper gastrointestinal symptoms, inhibits gastric tone and accommodation, and delays gastric emptying (3, 14, 20–21, 24, 34–35, 50). However, little information about the effects of RD on gastric contractions is available, although gastric contractions play an important role in functional gastrointestinal disorders. Also, the mechanism of how RD impairs gastric motility is unclear. It may be mediated via the neural reflex, and either the nociceptive or nonnociceptive afferent pathway is involved, which is correlated with distension volumes and visceral sensation (19). More recent studies showed that sympathovagal balance was altered in IBS patients (23, 41, 45), but it is not clear whether these activities are altered with RD.

Acupuncture is a traditional Chinese medicine involving stimulation of the acupoints in the skin by thin, metallic needles that are manipulated manually or combined with electrical stimulation, a procedure referred to as electroacupuncture (EA). Acupressure is a noninvasive medical technique conducted by pressing on the acupoints with the fingers or by an embedded stud over the acupoints. EA is commonly used in clinical research since it is more reproducible than manual acupuncture, and it has been applied to treat gastrointestinal disorders (11). Our previous studies have shown that EA at ST36 accelerated gastric emptying in both dogs and patients with gastroparesis and restored vagotomy-induced impaired gastric accommodation in dogs (29, 30). However, its precise mechanism remains unclear, although the analgesic effect of acupuncture is known to be mediated via the opioid pathway (11). It is also unknown whether EA has an excitatory effect on antral contractions. If EA is capable of restoring impaired gastric motor activity that was induced by RD, it may be used to treat patients with upper abdominal symptoms or impaired motility related to constipation or other colorectal disorders.

The aims of this study were to investigate the effects and underlying mechanisms of RD on gastric motility and slow waves and furthermore to study the effects and mechanisms of EA on RD-induced impairment in gastric motor activities and slow waves in conscious dogs.

MATERIALS AND METHODS

Animal Preparation

A total of eight healthy female hound dogs (22–26 kg) were used in this study. After an overnight fast, the dogs were anesthetized with an initial intravenous infusion of sodium thiopental (5 mg/kg; Abbott Laboratories, North Chicago, IL) and maintained on IsoFlo (1.5%

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isoflurane, inhalation anesthesia; Abbott) in oxygen-nitrous oxide (1:1) carrier gases delivered from a ventilator following endotracheal intubation. A midline laparotomy was performed. One pair of wires was implanted in the distal antrum (6 cm above pylorus) near the greater curvature. The two electrodes were arranged circumferentially at a distance of ~ 1.0 cm. The electrodes were penetrated into the subserosal layer and were affixed to the serosa by nonabsorbable sutures. The connecting wires of the electrodes were tunneled through the anterior abdominal wall subcutaneously along the right side of the trunk and placed outside the skin around the right hypochondrium for the attachment to the electromyographic recorder. In addition, a cannula was placed in the stomach 10 cm above the pylorus. The dogs were transferred to a recovery cage after receiving medications for postoperative pain control.

The study was initiated after the dogs were completely recovered from the surgery (usually 2 wk after the surgery). On the study day, one bottle of enema liquid (Fleet enema; C.B. Fleet Lynchburg, VA) was given to each dog at 8:00 AM. After clearance of the rectum, the experiment was performed in the laboratory with the animal slightly restrained with a sling. Consecutive sessions were performed on separate days with an interval of 3 days or more. The female canine menstrual cycle is different from that of humans, since it usually lasts 1–3 wk and happens only once or twice a year. During the cycle, a small amount of bleeding may be noticed. In this study, none of the experiments were performed during the menstrual period. The study was approved by the Institutional Animal Care and Use Committees of the University of Texas Medical Branch at Galveston and the Veterans Affairs Medical Center at Oklahoma City.

Experimental Protocol

The experiment involved six separate sessions on separate days described as follows.

Sessions 1 and 2 were performed to study the effects of RD at different volumes on gastric slow waves (GSW) and gastric motor activity. It entailed a 30-min baseline recording and a 30-min recording during rectal balloon distension at a volume of 20 ml or 120 ml; distention volume was chosen randomly for each dog. *Session 3* was performed to investigate the involvement of the sympathetic pathway in the RD-induced suppression of GSW and gastric motor activity. It included a 30-min baseline recording and a 30-min recording after intravenous infusion of guanethidine (3 mg/kg), and another 30-min recording during rectal balloon distension at a volume of 120 ml. *Sessions 4 and 5* were designed to determine the possible role of EA in RD-induced impairment of GSW and gastric motor activity. It included a 30-min baseline recording, a 30-min recording during EA at bilateral acupoints ST36 or BL21 with RD of 120 ml. *Session 6* was performed to explore the possibility of the opioid pathway of EA improving RD-induced impaired GSW and gastric motor activity. It consisted of a 30-min baseline recording, a 30-min recording after intravenous infusion of naloxone (1 mg/kg iv), and another 30-min recording with EA and RD at a volume of 120 ml.

These sessions were performed in the postprandial state in a randomized order. After an overnight fast, dogs were transferred to the laboratory for study. Each session was initiated immediately after a solid test meal consisting of 375 g beef. Antral contractions, GSW and electrocardiogram readings were simultaneously recorded in all these sessions. The rectal balloon pressure was measured in RD sessions (*sessions 1 and 2*) and EA at the ST36 session (*session 4*).

Rectal Distension and Measurement of Rectal Tone

A balloon attached to the tip of a manometric catheter was inserted into the rectum and positioned so that the caudal pole of the balloon lay 6 cm from the anal verge. The balloon was inflated with different volumes of air via a 60-ml syringe. The distension volume of 120 ml was the largest volume the dogs could tolerate without adverse behaviors suggestive of pain and discomfort as noted in previous

studies (24, 34). The intraballloon pressure, reflecting rectal tone, was measured by connecting the balloon to a manometric system (PC polygraf HR system, Synectics Medical, Stockholm, Sweden).

Electroacupuncture

Bilateral acupoints, ST36 (stomach-36 or Zusanli), were used in this study (8, 47). The location of ST36 is at the proximal one-fifth of the cranialateral surface of the rear leg distal to the head of the tibia in a depression between the muscles of the cranial tibia and the long digital extensor. ST36 is one of the most frequently used acupuncture points for the treatment of gastric diseases and has been used in our previous studies in both humans and dogs (26, 30, 36). EA at acupoints located on the back [bladder-21 (BL21)] were used for sham acupuncture. BL21 is located 1 cm lateral of the spinous process of the 12th thoracic vertebrae (45).

The electrical current for EA was generated by a commercial electroeedling instrument (electrotherapeutic apparatus, model D-860; Jinshan Electronic Device, Shanghai, China). The electrical stimuli consisted of pulse trains. The frequency of the pulse trains was 12 trains/min, the duration of each train was 2 s, and the pulse amplitude was 10 mA. The frequency of pulses in each train was 25 Hz. Electrical stimulation was applied via the needles inserted into the acupoints.

Recording and Analysis of GSW

A multi-channel recorder (Acknowledge III, EOG 100A; Biopac Systems, Santa Barbara, CA) was used to record gastric myoelectrical activity throughout the study. All signals were displayed on a computer monitor and saved on the computer's hard disk. The low and high cutoff frequencies of the amplifiers were 0.05 and 35 Hz, respectively. The signals were initially sampled at a frequency of 100 Hz and then downsampled to 2 Hz after low-pass filtering with a cutoff frequency of 1 Hz. The parameters assessed were percentage normal intestinal slow waves, dominant frequency, and dominant power.

Dominant frequency and power of the slow wave. The frequency at which the power spectrum of an entire recording had a peak power was defined as the dominant frequency. The power at the dominant frequency in the power spectrum was defined as the EGG dominant power. These two parameters were calculated by the smooth-power spectral analysis method. Decibel units were used to represent the power of the gastric slow wave.

Percentage of normal GSW. The percentage of normal GSW was defined as the percentage of time during which regular 4–6 cpm (cycles/min) slow waves were present over the entire recording period. It was computed by the adaptive spectral analysis method. In this method, each recording was divided into blocks of 1 min without overlap. The power spectrum of each 1-min recording was calculated and examined to see whether the peak power was within the range of 4–6 cpm. The 1-min recording was categorized as normal if the peak power was within the 4–6 cpm range; otherwise it was categorized as dysrhythmia. The definition of the normal frequency range of 4–6 cpm in the stomach was based on our previous study (40).

Recording and Analysis of Antral Motility

Antral contractile activity was recorded from four pressure sensors 1 cm apart from each other that were attached to the manometric catheter. The recording was done by a PC polygraf HR system (Synectics Medical) and a microcapillary infusion system (Medtronic Synectics, Stockholm, Sweden). The catheter was inserted into the distal antrum via the gastric cannula. All recordings were displayed on a computer monitor. Motor activity of the stomach was assessed by using the mean area under the curve (AUC) per second, which was computed with the Polygram Function Testing Software (Medtronic) (52). The data presented in this study were obtained from channel 3, which had the highest quality recording.

Recording and Analysis of HRV

The ECG was recorded via a special one-channel amplifier with a cutoff frequency of 100 Hz (model 2283 Fti Universal Fetrote Amplifier, UFI, Morro Bay, CA) from two separate leads and one ground electrode. The two leads were attached to the left and right supraclavicular fossas of the subjects and the ground to the left leg. The data were digitized online at 1,000 Hz via a PC and a data-acquisition package (Alice 3, Healthdyne Technologies, Marietta, GA). The heart rate variability (HRV) signal was derived from the ECG recording by using a special program developed and validated in our laboratory (48) by identifying R peaks, calculating R-R intervals, interpolating the R-R intervals so that the time interval between consecutive samples was equal and finally downsampling the interpolated data to a frequency of 1 Hz.

Overall power spectral analysis was applied to the HRV signal and the power in each frequency subband was calculated by a previously validated method (30). It has been well established that the power in the low-frequency band (0.04–0.15 Hz), LF, represents mainly sympathetic activity, and the power in the high-frequency band (0.15–0.50 Hz), HF, stands purely for parasympathetic or vagal activity (48). LF was defined as the AUC in the frequency range of 0.04–0.15 Hz, and HF was defined as the AUC in the frequency range of 0.15–0.50 Hz. The ratio LF/HF reflects the balance between sympathetic activity and vagal activity.

Statistical Analysis

Results are reported as means \pm SE. Paired Student's *t*-test was used to investigate the differences between any two periods if the ANOVA revealed a significant difference among the three sessions/periods or more.

RESULTS

All eight dogs tolerated the procedures well. A distension volume of 120 ml was the largest volume the dogs could tolerate without adverse behaviors indicative of pain or discomfort, such as gasping for breath and writhing.

Effects and Mechanisms of RD and EA on Antral Contractions

RD suppressed gastric antral motility. At the mild distension volume of 20 ml, the antral contraction AUC was marginally reduced (13.6 ± 1.5 at baseline vs. 12.8 ± 1.5 , $P = 0.054$). When RD of 120 ml was applied, antral contractions were decreased immediately. At the distension volume of 120 ml, the antral contraction AUC was significantly reduced by $42.7 \pm 6.2\%$ from 13.6 ± 1.5 at baseline to 8.0 ± 1.4 during distension ($P < 0.001$), and the AUC recovered to 13.0 ± 1.4 within a couple of minutes after distension was stopped, which was comparable with its baseline of 13.6 ± 1.5 ($P = 0.12$). Guanethidine blocked the inhibitory effect of RD on antral contractions (16.5 ± 1.6 during RD with guanethidine vs. 15.9 ± 1.9 at baseline $P > 0.05$), suggesting that the RD-induced effect involves the adrenergic pathways (Fig. 1).

EA at ST36 normalized the impaired antral motility induced by RD (Figs. 1 and 2). The AUC during RD with EA at ST36 was 16.6 ± 1.7 , which was significantly higher than during RD without EA (8.0 ± 1.4 ; $P < 0.001$) and comparable with baseline without RD (14.4 ± 1.7). However, the ameliorative effect was not observed during RD with sham EA (BL21). The AUC during RD with sham EA was 8.5 ± 1.3 , which was significantly lower than the session with EA (16.6 ± 1.7 ; $P < 0.001$) and comparable with the session during RD without EA

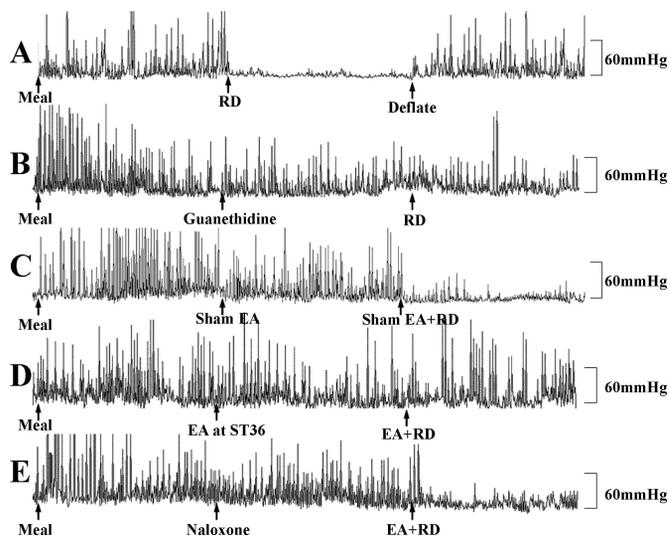


Fig. 1. Typical tracing of gastric antral contractions. A: antral contraction decreased immediately after rectal distension (RD) at a volume of 120 ml and recovered quickly. B: guanethidine blocked the inhibitory effect of RD. C and D: electroacupuncture (EA) at ST36 normalizing the impaired antral motility induced by RD, but the sham stimulation did not show the effect. E: when naloxone was applied, EA could not restore the RD-induced impaired antral motility to its baseline level suggesting that the effect of EA was partially mediated via the opioid pathway.

(8.0 ± 1.4 ; $P = 0.24$). Naloxone partially blocked the effect of EA on antral contractions. The AUC during RD with EA after naloxone was 12.1 ± 1.4 , which was significantly lower than the AUC without naloxone (16.6 ± 1.7 , $P = 0.001$) but still significantly higher than the AUC during RD ($P = 0.01$), suggesting that the effect of EA was partially mediated via the opioid pathway (Fig. 2).

Effects of EA on GSW

The percentage of normal 4–6 cpm GSW was not significantly altered during RD at a volume of 20 ml compared with baseline ($92.7 \pm 3.6\%$ during distension vs. $97.6 \pm 0.8\%$ at baseline, $P > 0.15$). However, RD at a volume of 120 ml significantly reduced the percentage of normal GSW immediately from $98.8 \pm 0.8\%$ at baseline to $76.1 \pm 8.6\%$ during distension ($P < 0.03$) but did not affect the dominant frequency or dominant power of the slow waves. The percentage of normal GSW recovered to $97.2 \pm 2.0\%$ quickly after distension was stopped, which was comparable with the baseline of $98.8 \pm 0.8\%$ ($P = 0.43$). The decrease in the percentage of normal GSW during RD was attributed to a significant increase in tachyarrhythmia ($0.36 \pm 0.12\%$ to $15.41 \pm 3.60\%$, $P < 0.01$, Fig. 3). Guanethidine blocked the inhibitory effect of RD on GSW. The percentage of normal slow waves was $97.0 \pm 1.6\%$ at baseline and $91.8 \pm 2.5\%$ during RD of 120 ml with guanethidine ($P > 0.05$).

EA at ST36 improved the impaired GSW induced by RD. The percentage of normal slow waves was $76.1 \pm 8.6\%$ during RD of 120 ml and increased to $91.8 \pm 3.0\%$ during RD of 120 ml when EA at ST36 was applied ($P < 0.05$ vs. RD without EA). This was comparable to the baseline without RD level ($93.4 \pm 3.6\%$, $P = 0.72$). The percentage of normal slow waves was $76.6 \pm 7.0\%$ during RD of 120 ml with sham EA, which was significantly lower than during RD with EA ($91.8 \pm$

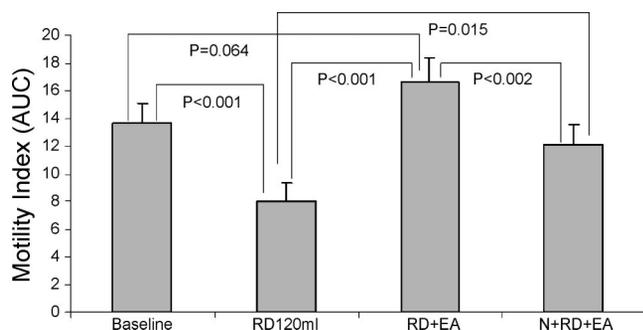


Fig. 2. EA normalized impaired antral motility induced by RD ($P \leq 0.001$ vs. RD without EA). Naloxone diminished the effect of EA on antral motility. The area under the curve (AUC) during RD with EA after naloxone (N) was 12.1 ± 1.4 that was significantly lower than EA without naloxone 16.6 ± 1.7 ($P = 0.001$), but still significantly higher than that during RD without EA ($P = 0.01$), indicating that the effect of EA was partially mediated via the opioid pathway. The data shown in the figure are means \pm SE.

3.0%; $P < 0.03$) and comparable with GSW levels during RD without EA ($76.1 \pm 8.6\%$; $P = 0.44$). However, with the presence of naloxone, the ameliorating effect of EA on RD-induced dysrhythmic slow waves was no longer observed, and the percentage of normal slow waves remained comparable to what was observed during RD of 120 ml without EA (70.1 ± 6.0 vs. $76.1 \pm 8.6\%$; $P = 0.18$) (Fig. 4).

Effects of EA on Rectal Pressure

The effects of EA on rectal pressure were studied to understand whether the ameliorating effects of EA on gastric motility were attributed to a reduction in rectal pressure during EA. Accordingly, rectal balloon pressure was measured at baseline and during EA. The intraballoon pressure (in mmHg) was higher during RD of 120 ml than RD of 20 ml (18.9 ± 0.45 vs. 8.2 ± 0.32 ; $P = 1.49 \times 10^{-6}$). EA did not change the intraballoon pressure at RD of 120 ml (19.1 ± 0.51 during RD with EA and 18.9 ± 0.46 during RD without EA, $P = 0.65$), suggesting that the ameliorating effects of EA on RD-induced gastric motility were not due to a decrease in RD pressure.

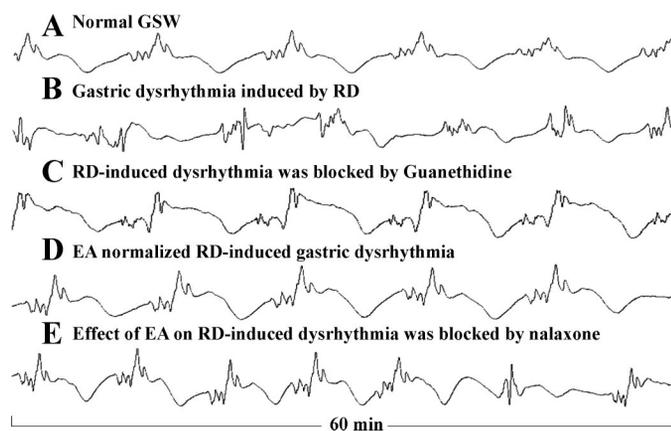


Fig. 3. Typical gastric slow wave tracings. A: normal gastric slow waves (GSW) at baseline. B: GSW dysrhythmia during RD. C: RD-induced dysrhythmia was blocked by guanethidine. D: EA normalized the RD-induced gastric dysrhythmia. E: in the presence of naloxone, the ameliorating effect of EA on RD-induced gastric dysrhythmic was no longer observed.

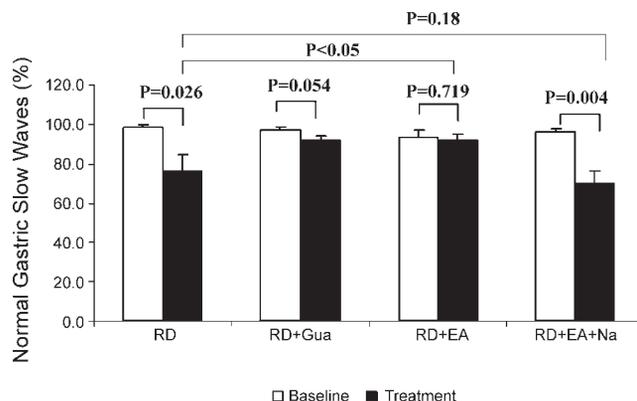


Fig. 4. Percentages of normal gastric slow waves in different sessions. RD reduced the percentage of normal gastric slow waves; guanethidine (Gua) blocked the inhibitory effect of RD on gastric slow waves; the percentage of normal slow waves remained unchanged with RD during EA; and the ameliorating effect of EA on gastric slow waves was blocked by naloxone (Na).

Effects of EA on HRV

The sympathetic activity (LF) assessed by the spectral analysis of the HRV showed no difference among baseline, RD at different volumes, EA, and other periods (ANOVA, $P = 0.53$). RD at a volume of 120 ml decreased the vagal activity (HF) from 1.47 ± 0.29 at baseline to 0.70 ± 0.14 during distension ($P = 0.03$), and this effect was blocked by guanethidine (1.68 ± 0.35 , $P < 0.03$ vs. distension only). EA restored the vagal activity that was decreased by RD (1.32 ± 0.20 with EA during RD vs. 0.70 ± 0.14 without EA during RD; $P < 0.02$) (Fig. 5A). RD at a volume of 120 ml significantly increased the sympathovagal ratio (LF/HF) compared with baseline (0.57 ± 0.054 vs. 0.37 ± 0.067 , $P < 0.01$). Guanethidine blocked the distension-induced increase in the sympathovagal ratio (0.21 ± 0.035 during distension with guanethidine vs. 0.57 ± 0.054

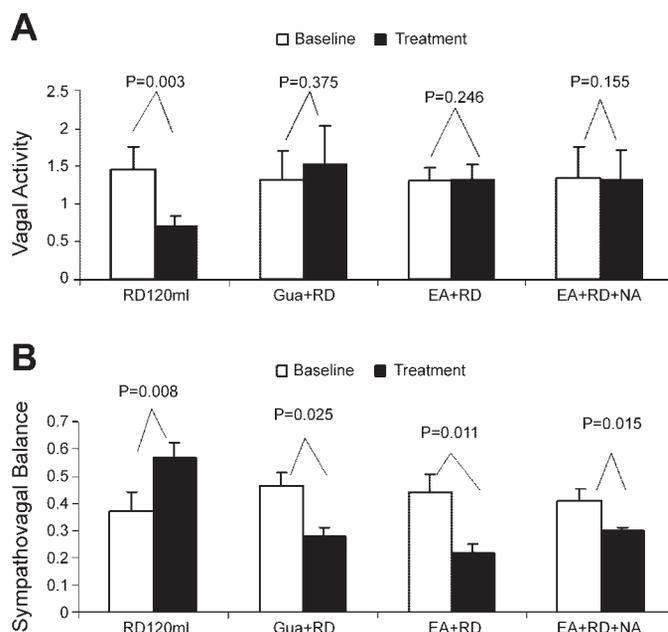


Fig. 5. Vagal activity (A) and sympathovagal ratio (B) in different sessions (RD of 120 ml, infusion of guanethidine during RD, EA during distension without naloxone and with naloxone).

during distension only, $P < 0.01$). EA decreased the sympathovagal ratio that was increased by RD (0.22 ± 0.03 during EA and distension vs. 0.57 ± 0.05 during distension, $P < 0.01$), and this effect was not affected by naloxone (0.30 ± 0.01 with naloxone vs. 0.22 ± 0.03 without naloxone during EA and RD, $P = 0.08$) (Fig. 5B).

DISCUSSION

In the present study we demonstrated the following: 1) Rectal distension at a volume of 120 ml resulted in an inhibition of postprandial antral motor activity and impairment of GSW in dogs and the inhibition was mediated via the adrenergic pathway. 2) EA was able to restore the impaired antral motor activities and dysrhythmic slow waves induced by RD, possibly by enhancing vagal activity and mediated via the opioid pathway.

Overlapping Syndrome and Constipation

Chronic idiopathic slow-transit constipation and constipation-dominant IBS are common in clinical practice, and upper gastrointestinal dyspepsia symptoms are commonly present in these disorders. However, the pathophysiological mechanisms of the overlapping symptoms between IBS and dyspepsia are not clear. Studies have reported that 30–50% of patients with functional gastrointestinal disorders had both functional dyspepsia and IBS (16–17, 28). On the other hand, overlapping dyspepsia was found in 55–87% of patients with IBS (2, 42). Minocha et al.'s (28) data suggested that almost every patient with IBS suffered from symptoms suggestive of dyspepsia. Talley et al. (43) reported that upper gastrointestinal symptoms consistent with functional dyspepsia were more frequent in constipation-dominant IBS. Bouin et al. (6) reported that 91% patients with overlapping symptoms exhibited rectal intolerance to distension. Therefore, we hypothesized that fecal or gas distension might be a major pathophysiological mechanism of overlapping symptoms between IBS and dyspepsia.

Effects and Mechanisms of RD on Gastrointestinal Motility

Rectal balloon distension mimicking fecal or gas stasis in the colorectal region is one of the constipation models commonly used in the study of upper gastrointestinal motor activity. A number of investigations have indicated that RD induces upper gastrointestinal symptoms, inhibits gastric tone and accommodation, and delays gastric emptying in humans and animals (3, 14, 20, 21, 24, 34, 35). Similar studies were also performed on the RD-induced inhibition in small intestinal motor activity in humans and animals (22, 35). More recently, Iwa et al. (19) studied the effects of EA on the nociceptive pathway using the RD model. However, little information is available on the effects and mechanisms of RD on gastric contractions. In this study, we found that RD inhibited antral contractions and the inhibitory effect was mediated via the sympathetic pathway since the blockage of the sympathetic pathway by guanethidine abolished this inhibitory effect. Since no animal behaviors suggestive of pain were noted in the study, we speculate that the RD-induced inhibition on antral contractions involves the nonnociceptive afferent pathway instead of the nociceptive pathway.

EA Improves Antral Motility Impaired by RD

Clinically, overlapping symptoms between IBS and functional dyspepsia were difficult to be treated because of the lack of effective drugs or because of side effects. EA has been applied for the treatment of gastrointestinal disorders (11). Our previous studies showed that EA at ST36 could accelerate gastric empty and restore impaired gastric accommodation in canine models (29, 30). The present study was designed to investigate the effects of EA on RD-induced impairment in gastric antral contraction and GSW.

One previous study showed that RD induced upper gastrointestinal symptoms and inhibited gastric tone and accommodation in dogs (24). This RD-induced proximal stomach inhibition is indicative of the existence of a “rectogastric” reflex, and the activation of this reflex causes inhibitory effects on gastric motility (5). Visceral hypersensitivity may enhance the afferent signal of rectal stretching to the central nervous system and thus potentially heightens the activation of the rectogastric reflex (6). This theory may help explain why constipation-dominant IBS patients tend to have overlapping symptoms with dyspepsia. Furthermore, studies showed that the inhibitory reflex in the proximal stomach was mediated by cholinergic and nitrenergic efferent nerves (10, 25). Our finding that RD decreased antral contractions demonstrated the existence of the inhibition reflex from the rectum to the distal stomach. However, to elicit this reflex efficiently, the distention volume should be sufficient in normal conscious dogs. This finding was consistent with the previous report that RD inhibited distal gastric motor activity and delayed gastric emptying in humans (22). As discussed previously, the physiological mechanism of the reflex is complicated. In this study, we found that RD of 120 ml decreased the vagal activity, and the RD-induced inhibitory effects were blocked by guanethidine, an adrenergic blocker preventing the release of norepinephrine. These findings suggest that the inhibitory reflex was mediated via the sympathovagal balance. However, the exact mechanism of RD-induced inhibition on antral motility is still unclear; it may involve peripheral, sensory, and intrinsic nerves, the prevertebral ganglion, the spinal cord, and many signal intermediaries.

EA at ST36 was reported to enhance gastric contractions in rats, and the effect was found to be mediated via the vagal pathway (44). In our laboratory's previous study, EA at both ST36 and PC6 accelerated gastric emptying of liquid in dogs (30). EA at ST36 stimulated the parasympathetic pathway and accelerated colonic transit in rats (18). The stimulatory effects of EA at ST36 on both gastric motility and colonic motility were anticipated to be beneficial for the overlapping symptoms of constipation-dominant IBS and dyspepsia. On the other hand, most patients with functional GI disorders appear to have visceral hypersensitivity and altered reflex responses in different gut regions (27). If EA could reverse the hypersensitivity at the same time, it may be possible to use it as a new treatment for some subgroup of functional GI disorders. Recently, Xing et al. (49) found that EA at ST36 and PC6 significantly increased the threshold of rectal sensations induced by RD in IBS patients, suggesting that EA at ST36 and PC6 was capable of reducing visceral perception in IBS patients. Several reports have supported a positive effect of acupuncture on constipation. One clinical study showed that acupuncture was successful in treating 80% of patients with constipation (12). However,

it remained unknown whether acupuncture could improve the RD-induced impaired gastric motor activity. The present study, for the first time, demonstrated that EA was able to restore the impaired gastric motor activities induced by RD. The ameliorating effects of EA on RD-induced impairment in gastric motility was not attributed to a decrease in rectal pressure, but possibly to enhanced vagal activity, and was partially mediated via the opioid pathway.

EA Normalized the GSW Impaired by RD

In a previous study, GSW activity was severely impaired by RD in the fasting state in dogs (1). The dominant power and the percentage of normal GSW were significantly decreased, and the instability coefficient of the dominant frequency was increased during distension. In another study in humans, RD significantly reduced the regularity of GSW in the fed state, but not in the fasting state (35). This postprandial change was attributed to a significant increase in bradygastria and a marginal increase in tachygastria. However, the present postprandial data showed a decrease only in the percentage of normal GSW and no changes in other parameters. These different results might be attributed to the different species and different experimental settings (such as fasting and fed states). The mechanism of RD-induced impairment in GSW is complex, involving both neural and humoral components (15, 39, 51). In this study, a concurrent decrease in vagal activity was noted with the reduced percentage of GSW during RD, and the inhibitory effect of RD on GSW was blocked by guanethidine. These data suggested that the sympathovagal balance plays an important role in the communication between the upper gut and the lower gut.

EA at ST36 and PC6 enhanced the gastric migrating motor complex by reducing the length of phase I and increasing the lengths of phases II and III. EA at ST36 and PC6 increased the regularity of GSW in both the proximal and distal stomach and accelerated gastric emptying of liquid in conscious dogs (30, 36). Lin et al. (26) performed EA at the same acupuncture points and reported a significant increase in the percentage of normal GSW in healthy volunteers. In a duodenal distention-induced delayed gastric emptying model of dogs, EA at PC6 and ST36 was found to significantly accelerate gastric emptying of liquid by improving GSW rhythmicity and increasing spike activity (30). In another study, EA was shown to restore impaired gastric accommodation in vagotomized dogs, suggesting that the effects of EA, besides the vagal pathway, may also be mediated via nonvagal pathways (29). The different effects of EA between PC6 and ST36 on GSW have been compared in healthy humans. EA at PC6 reduces dominant power of the GSW, whereas EA at ST36 increases it. Since dominant power of the GSW is associated with the amplitude of gastric contractions, these findings suggest that EA at these two acupoints may have different excitatory or inhibitory effects on gastric motility (38). Our present study showed that EA at ST36 normalized RD-induced slow wave dysrhythmia and increased the vagal tone. In the presence of naloxone, this ameliorating effect of EA on GSW was no longer observed. These findings suggested the involvement of the vagal pathway as well as the opioid pathway.

Potential of EA and Strength and Weakness of the Study

The findings of the present study suggest the potential of EA as a new treatment for patients with upper gastrointestinal symptoms related to constipation or other colorectal disorders. Clinically, overlapping symptoms between IBS and dyspepsia are difficult to treat because of poor understanding of the pathophysiology and the lack of effective medications. The findings of the present study suggest that the RD-induced impairment in distal gastric motor activity and the RD-induced alteration in sympathovagal ratio may be parts of pathophysiological mechanisms involving overlapping symptoms between dyspepsia and constipation-dominant IBS. Accordingly, EA may have a potential for treating these overlapping symptoms. However, it should also be noted that the RD used in this study may not well represent constipation or fecal stasis that are seen in patients with IBS or other patients with overlapping syndromes. Clinical studies are needed to establish the therapeutic role of EA in the treatment of upper gastrointestinal symptoms or impaired gastric motility attributed to the disorders of the lower gastrointestinal tract.

Conclusions

In conclusion, EA is able to restore RD-induced impairment in antral motility and GSW by possibly enhancing vagal activity and is partially mediated via the opioid pathway. EA may have a therapeutic potential for functional gastrointestinal disorders.

REFERENCES

1. Abo M, Kono T, Wang Z, Chen JDZ. Impairment of gastric and jejunal myoelectrical activity during rectal distension in dogs. *Dig Dis Sci* 45: 1731–1736, 2000.
2. Agreus L, Svarsdudd K, Nyren O, Tibblin G. Irritable bowel syndrome and dyspepsia in the general population: overlap and lack of stability over time. *Gastroenterology* 109: 671–680, 1995.
3. Azpiroz F, Malagelada JR. Perception and reflex relaxation of the stomach in response to gut distention. *Gastroenterology* 98: 1193–1198, 1990.
4. Bassotti G, Stanghellini V, Chiarioni G, Germani U, De Giorgio R, Vantini I, Morelli A, Corinaldesi R. Upper gastrointestinal motor activity in patients with slow-transit constipation. Further evidence for an enteric neuropathy. *Dig Dis Sci* 41: 1999–2005, 1996.
5. Bojo L, Cassuto J. Gastric reflex relaxation by colonic distension. *J Auton Nerv Syst* 38: 57–64, 1992.
6. Bouin M, Lupien F, Riberdy M, Boivin M, Plourde V, Poitras P. Intolerance to visceral distension in functional dyspepsia or irritable bowel syndrome: an organ specific defect or a pan intestinal dysregulation? *Neurogastroenterol Motil* 16: 311–314, 2004.
7. Cannon WB, Murphy FT. Physiological observations on experimentally produced ileus. *JAMA* 49: 840–843, 1907.
8. Cheng X. *Chinese Acupuncture and Moxibustion* (rev. ed.). Beijing: Foreign Language Press, 1999.
9. Coremans G, Geypens B, Vos R, Tack J, Margaritis V, Ghooys Y, Janssens J. Influence of continuous isobaric rectal distension on gastric emptying and small bowel transit in young healthy women. *Neurogastroenterol Motil* 16: 107–111, 2004.
10. Coulie B, Tack J, Sifrim D, Andrioli A, Janssens J. Role of nitric oxide in fasting gastric fundus tone and in 5-hydroxytryptamine-1 receptor-mediated relaxation of the gastric fundus. *Am J Physiol Gastrointest Liver Physiol* 276: G373–G377, 1999.
11. Diehl DL. Acupuncture for gastrointestinal and hepatobiliary disorders. *J Altern Complement Med* 5: 27–45, 1999.
12. Fischer MV. Acupuncture therapy in the outpatients department of the University Clinic Heidelberg. *Anaesthesist* 31: 25–32, 1982.
13. Glia A, Lindberg G. Antroduodenal manometry findings in patients with slow transit constipation. *Scand J Gastroenterol* 33: 55–62, 1998.

14. **Glise G, Abrahamsson H.** Reflex vagal inhibition of gastric motility by intestinal nociceptive stimulation in the cat. *Scand J Gastroenterol* 15: 769–744, 1980.
15. **Grundy D, Scratcherd T.** A splanchno-vagal component of the inhibition of gastric motility by distention of the intestine. In: *Motility of the Digestive Tract*, edited by Weinbeck M. New York: Raven, 1982, p. 39–43.
16. **Halder SL, Locke GR 3rd, Talley NJ, Fett SL, Zinsmeister AR, Melton LJ 3rd.** Impact of functional gastrointestinal disorders on health-related quality of life: a population-based case-control study. *Aliment Pharmacol Ther* 1519: 233–242, 2004.
17. **Holtmann G, Goebell H, Talley NJ.** Functional dyspepsia and irritable bowel syndrome: is there a common pathophysiological basis? *Am J Gastroenterol* 92: 954–959, 1997.
18. **Iwa M, Nakade Y, Matsushima M, Pappas T, Fujimiya M, Takahashi T.** Electroacupuncture at ST-36 accelerates colonic motility and transit in freely moving conscious rats. *Am J Physiol Gastrointest Liver Physiol* 290: G285–G292, 2006.
19. **Iwa M, Strickland C, Nakade Y, Pappas T, Takahashi T.** Electroacupuncture reduces rectal distension-induced blood pressure changes in conscious dogs. *Dig Dis Sci* 50: 1264–1270, 2005.
20. **Jansson G.** Vagovagal reflex relaxation of the stomach in the cat. *Acta Physiol Scand* 75: 245–252, 1969.
21. **Julia V, Su X, Bueno L, Gebhart GF.** Role of neurokinin 3 receptors on responses to colorectal distention in the rats: electrophysiological and behavioral studies. *Gastroenterology* 116: 1124–1131, 1999.
22. **Kellow JE, Gill RC, Wingate DL.** Modulation of human upper gastrointestinal motility by rectal distension. *Gut* 28: 864–868, 1987.
23. **Lee CT, Chuang TY, Lu CL, Chen CY, Zhang FY, Lee SD.** Abnormal vagal cholinergic function and psychological behaviors in irritable bowel syndrome patients: a hospital-based Oriental study. *Dig Dis Sci* 43: 1794–1799, 1998.
24. **Lei Y, Zhu H, Xing J, Chen JDZ.** Rectal distension modulates canine gastric tone and accommodation. *Dig Dis Sci* 50: 2134–2140, 2005.
25. **Lidums I, Hebbard GS, Holloway RH.** Effect of atropine on proximal gastric motor and sensory function in normal subjects. *Gut* 47: 30–36, 2000.
26. **Lin X, Liang J, Ren J, Mu F, Zhang M, Chen JD.** Electrical stimulation of acupuncture points enhances gastric myoelectrical activity in humans. *Am J Gastroenterol* 92: 1527–1530, 1997.
27. **Mayer E, Gebhart G.** Basic and clinical aspects of visceral hyperalgesia. *Gastroenterology* 107: 271–293, 1994.
28. **Minocha A, Chad W, Do W, Johnson WD.** Racial differences in epidemiology of irritable bowel syndrome alone, uninvestigated dyspepsia alone, and “overlap syndrome” among african americans compared with Caucasians: a population-based study. *Dig Dis Sci* 51: 218–226, 2006.
29. **Ouyang H, Xing J, Chen JDZ.** Electroacupuncture restores impaired gastric accommodation in vagotomized dogs. *Dig Dis Sci* 49: 1418–1424, 2004.
30. **Ouyang H, Yin J, Wang Z, Pasricha PJ, Chen JDZ.** Electroacupuncture accelerates gastric emptying in association with changes in vagal activity. *Am J Physiol Gastrointest Liver Physiol* 282: G390–G396, 2002.
31. **Pallotta N, Pezzotti P, Calabrese E, Baccini F, Corazziari E.** Relationship between gastrointestinal and extra-gastrointestinal symptoms and delayed gastric emptying in functional dyspeptic patients. *World J Gastroenterol* 11: 4375–4381, 2005.
32. **Pearcy JF, Van Liere EJ.** Studies on the visceral nervous system XVII. Reflex from the colon. *Am J Physiol* 78: 64–73, 1926.
33. **Preston DM, Lennard-Jones JE.** Severe chronic constipation of young women: idiopathic slow transit constipation. *Gut* 27: 4–8, 1986.
34. **Qi H, Brining D, Chen JDZ.** Rectal distension inhibits postprandial small intestinal motor activity partially via the adrenergic pathway in dogs. *Scand J Gastroenterol* 42: 807–813, 2007.
35. **Qian L, Orr WC, Chen JDZ.** Inhibitory reflexive effect of rectal distension on postprandial gastric myoelectrical activity. *Dig Dis Sci* 47: 2473–2479, 2002.
36. **Qian L, Peters LJ, Chen JDZ.** Effects of electroacupuncture on gastric migrating myoelectrical complex in dogs. *Dig Dis Sci* 44: 56–62, 1999.
37. **Reynolds JC, Ouyang A, Lee CA, Baker L, Sunshine AG, Cohen S.** Chronic severe constipation. *Gastroenterology* 92: 414–420, 1987.
38. **Shiotani A, Tatewaki M, Hoshino E, Takahashi T.** Effects of electroacupuncture on gastric myoelectrical activity in healthy humans. *Neurogastroenterol Motil* 16: 293–298, 2004.
39. **Sims MA, Hasler WL, Chey WD, Kim MS, Ouyang C.** Hyperglycemia inhibits mechanoreceptor-mediated gastriocolonic response and colonic peristaltic reflex in healthy humans. *Gastroenterology* 108: 350–359, 1995.
40. **Song G, Hou X, Yang B, Liu J, Qian W, Chen JD.** Two-channel gastric electrical stimulation accelerates delayed gastric emptying induced by vasopressin. *Dig Dis Sci* 50: 662–668, 2005.
41. **Spiller RC.** Disturbances in large bowel motility. *Baillieres Clin Gastroenterol* 13: 397–413, 1999.
42. **Stanghellini V, Tosetti C, Barbara G, De Giorgio R, Cogliandro L, Cogliandro R, Corinaldesi R.** Dyspeptic symptoms and gastric emptying in the irritable bowel syndrome. *Am J Gastroenterol* 97: 2738–2743, 2002.
43. **Talley NJ, Dennis EH, Schettler-Duncan VA, Lacy BE, Olden KW, Crowell MD.** Overlapping upper and lower gastrointestinal symptoms in irritable bowel syndrome patients with constipation or diarrhea. *Am J Gastroenterol* 98: 2454–2459, 2003.
44. **Tatewaki M, Harris M, Uemura K, Ueno T, Hoshino E, Shiotani A, Pappas TN, Takahashi T.** Dual effects of acupuncture on gastric motility in conscious rats. *Am J Physiol Regul Integr Comp Physiol* 285: R862–R872, 2003.
45. **Tatewaki M, Strickland C, Fukuda H, Tsuchino D, Hoshino E, Pappas TN, Takahashi T.** Effects of acupuncture on vasopressin-induced emesis in conscious dogs. *Am J Physiol Regul Integr Comp Physiol* 288: R401–R408, 2005.
46. **Walter S, Bodemar G, Hallbook O, Thorell LH.** Sympathetic (electrodermal) activity during repeated maximal rectal distensions in patients with irritable bowel syndrome and constipation. *Neurogastroenterol Motil* 20: 43–52, 2008.
47. **Wang YC.** Canine acupuncture atlas. In: *Veterinary Acupuncture*, edited by Schoen AM. New York: Mosby, 1994, p. 107–140.
48. **Wang ZS, Chen JDZ.** Robust ECG R-R wave detection using evolutionary-programming-based fuzzy inference system (EPFIS) and its application to assessing brain-gut interaction. *IEEE Proc Sci Meas Technol* 147: 351–356, 2000.
49. **Xing J, Laeive B, Mekhail N, Soffer E.** Transcutaneous electrical acustimulation can reduce visceral perception in patients with irritable bowel syndrome: a pilot study. *Altern Ther Health Med* 10: 38–42, 2003.
50. **Youle MS, Read NW.** Effect of painless rectal distension on gastrointestinal transit of solid meal. *Dig Dis Sci* 29: 902–906, 1984.
51. **Youmans WM, Meak WJ.** Reflex and humoral gastrointestinal inhibition in Unanesthetized dogs during rectal stimulation. *Am J Physiol* 120: 750–755, 1937.
52. **Zhu H, Chen JD.** Implantable gastric stimulation inhibits gastric motility via sympathetic pathway in dogs. *Obes Surg* 15: 95–100, 2005.