Ameliorating effects and mechanisms of electroacupuncture on gastric dysrhythmia, delayed emptying, and impaired accommodation in diabetic rats

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Yin J, Chen J, Chen JDZ. Ameliorating effects and mechanisms of electroacupuncture on gastric dysrhythmia, delayed emptying, and impaired accommodation in diabetic rats. Am J Physiol Gastrointest Liver Physiol 298: G563–G570, 2010. First published January 21, 2010; doi:10.1152/ajpgi.00252.2009.—The aim of this study was to investigate the effects and mechanisms of electroacupuncture (EA) on gastric accommodation, gastric dysrhythmia, and gastric emptying (GE) in streptozotocin (STZ)-induced diabetic rats. Five experiments were performed in five groups of STZ-induced diabetic rats to study the effects of EA at ST-36 (Zusanli) on gastric slow-wave dysrhythmia, delayed GE and intestinal transit, impaired gastric accommodation, and the mechanisms of EA involving the autonomic and opioidergic pathways. We found the following: 1) EA improved gastric dysrhythmia in the diabetic rats. The normal percentage of slow waves was 55.4 ± 2.9% at baseline and significantly increased to 69.2 ± 2.2% with EA (P = 0.01); this effect was blocked by naloxone. 2) EA resulted in a 21.4% increase in GE and 18.2% increase in small intestinal transit in the diabetic rats. 3) EA restored diabetes-induced impairment in gastric accommodation. Gastric accommodation was 0.98 ± 0.13 ml with sham EA and significantly increased to 1.21 ± 0.15 ml with EA (P = 0.01), and this effect was blocked by naloxone. 4) EA increased vagal activity assessed by the spectral analysis of the heart rate variability. We concluded that EA at ST-36 improves gastric dysrhythmia, delayed GE and intestinal transit, and impaired accommodation in STZ-induced diabetic rats, and the improvement seems to be mainly mediated via the vagal pathway. EA may have a promising therapeutic potential for diabetic gastroparesis.

gastrointestinal motility; gastric emptying; gastric accommodation; diabetes

EPIDEMIOLOGICAL studies have indicated the complication of gastroparesis in 30–50% of patients with type I or type II diabetes (12, 13). Autonomic dysfunctions in diabetes may result in impaired gastric accommodation (GA), gastric dysrhythmia, antral hypomotility, and/or delayed gastric emptying (GE) (10, 46), causing symptoms of gastroparesis.

Acupuncture is a traditional Chinese medicinal treatment performed by inserting the tips of needles on specific points (called acupoints) through the skin. Electroacupuncture (EA) is a modification of this technique that stimulates acupoints with electrical current instead of manual manipulations and appears to have more consistently reproducible results in both clinical and research settings (20, 27). Both conventional and EA have been used for a variety of ailments, particularly for the relief of pain (35). It has been confirmed that acupuncture or EA has a modification of this technique that stimulates acupoints with electrical current instead of manual manipulations and appears to have more consistently reproducible results in both clinical and research settings (20, 27). Both conventional and EA have been used for a variety of ailments, particularly for the relief of pain (35). It has been confirmed that acupuncture or EA has therapeutic effects for the treatment of postoperative dental pain and postoperative and chemotherapy-induced nausea and vomiting (30). During the last decade, a considerable number of studies have been performed in examining the efficacy of EA for the treatment of functional gastrointestinal disorders (32). Clinical and animal studies were conducted to explore the effects of EA on gastrointestinal secretion, sensation, motility, and gastric myoelectrical activity (6, 15, 20, 22, 32, 34, 47). However, there is lack of comprehensive studies to explore the effects of EA on gastrointestinal motility in diabetic gastroparesis.

Treatment options for diabetic gastroparesis are limited and unsatisfactory. Medical treatment is the first choice of therapies (1, 17, 28). Prokinetic agents are mainstays of the medical therapy. Although a number of prokinetic agents are able to accelerate GE and improve antral contractions, their therapeutic benefits are limited, probably attributed to the fact that prokinetics do not improve or even impair GA (8, 45). Impaired GA has been well recognized as one of the major contributing factors causing gastroparetic symptoms (18, 44, 46).

The site-specific effects of EA on gastric motility have been reported. It is well established that acupuncture to the lower limbs elicits gastric contractions, whereas acupuncture to the abdomen elicits gastric relaxation (16). In animal models, EA at ST-36 has been reported to have ameliorating effects on gastric motility, such as acceleration of delayed GE (34), restoration of impaired GA in vagotomized dogs (33), and relaxation of the gastric fundus in rats (47). The excitatory effect of EA at ST-36 was reported to be mediated via the parasympathetic pathway (38, 51), whereas the relaxative or inhibitory effect of EA at the right lower abdomen was theorized to be attributed to the sympathetic pathway (47). The involvement of the opioidergic pathway has also been frequently reported (35, 51). However, there have been no studies investigating the effects of EA on both GE and GA simultaneously in an animal model of diabetic gastroparesis; moreover, the mechanisms involved in possible ameliorating effects of EA on gastric motility in diabetic gastroparesis have not yet been clarified.

The aim of this study was therefore to investigate the effects and mechanisms of EA at ST-36 on GE, GA, gastric slow waves (GSW), and intestinal transit in streptozotocin (STZ)-induced diabetic rats, a previously validated model of diabetic gastroparesis (21, 24).

MATERIALS AND METHODS

Subjects

Sixty-three Sprague-Dawley rats (male, 300–350 g; Charles River Laboratory, Wilmington, MA) were randomly divided into five groups (see Fig. 1). The rats were housed in the microisolator cage equipped with filter hoods under controlled temperature (20°C) and with a 12-h:12-h light/dark cycle and free access to water and solid food. The experimental protocol was approved by the Institutional
Animal Care and Use Committee, University of Texas Medical Branch at Galveston, Texas.

Surgical Procedure

Ten rats in group A were implanted with one pair of serosal electrodes for recording GSW 1 wk before the injection of STZ. After an overnight fast, the rats were operated under anesthesia with the inhalation of 1.5–2.0% isoflurane (Forane; Abbott Laboratories, Abbott Park, IL). A midline laparotomy was performed, and one pair of 28-gauge cardiac pacing wires (A&E Medical, Farmingdale, NJ) was implanted on the gastric serosal surface 0.5 cm proximal to the pylorus. The electrode-connecting wires were tunneled subcutaneously through the anterior abdominal wall and externalized at the back of the neck. No surgical procedures were performed on group B rats.

In groups C and D rats, an intragastric balloon was placed for the measurement of GA using a barostat device. Under the same method of anesthesia, a midline laparotomy was performed and a small abdominal electrodes for 30 min at baseline and 30 min during EA at ST-36. The EA + naloxone session included a 30-min baseline, intraperitoneal injection of naloxone (3 mg/kg), a 20-min waiting period for naloxone to take effects, and a 30-min period with EA.

After an overnight fast, each rat was fed with 1.5 ml phenol red (0.5 mg/ml) mixed with 1.5% methylcellulose by gavage. EA or sham EA was performed during the following 30 min. The rat was then euthanized for the measurement of GE and small intestinal transit (SIT).

Fig. 1. Animals used in different experiments. STZ, streptozotocin.

Experimental Protocols

Experiment 1: effects and mechanisms of EA on GSW. This experiment was performed in the 10 group A rats 6 wk after the STZ injection in two randomized sessions (EA and EA + naloxone). After an overnight fast, GSW were recorded via the serosal electrodes for 30 min at baseline and 30 min during EA at ST-36. The EA + naloxone session included a 30-min baseline, intraperitoneal injection of naloxone (3 mg/kg), a 20-min waiting period for naloxone to take effects, and a 30-min period with EA.

Experiment 2: effects of EA on GE and small intestinal transit. This experiment was performed in group B rats 6 wk after the STZ injection. The rats were randomly divided into two subgroups (group B1 for EA, N = 11, and group B2 for sham EA, N = 10). After an overnight fast, each rat was fed with 1.5 ml phenol red (0.5 mg/ml) mixed with 1.5% methylcellulose by gavage. EA or sham EA was performed during the following 30 min. The rat was then euthanized for the measurement of GE and small intestinal transit (SIT).

Experiment 3: effects of diabetes on GA. This experiment was designed to investigate the effects of the progression of diabetes on GA. The GA test was performed in the group C rats 1 wk before and once weekly during 4 wk after the STZ injection. The method for assessing GA was validated in previous studies (25, 29) and described as follows: after an overnight fast, the gastric volume was recorded via the intragastric balloon for 10 min at a pressure of 1 mmHg (baseline), 10 min with the pressure increased by 1 mmHg per minute up to a maximum of 10 mmHg (ramp phase), 10 min at a pressure of 10 mmHg (tonic phase), and 10 min at a pressure of 1 mmHg (recovery phase). GA was defined as the mean volume during the ramp distention. A computerized barostat device (Distender Series IIR; G & J Electronics, Willowdale, ON, Canada) was used to ensure that the intragastric balloon was maintained at the specified operating pressure. The barostat device is considered a gold standard for the assessment of gastric accommodation (46).

Experiment 4: effects and mechanisms of EA on GA. This experiment was performed in group D rats 6 wk after the STZ injection in two randomized sessions (EA and EA + naloxone). The protocol of the EA session included a 40-min GA test without EA (baseline test), a 30-min recovery period, and a second 40-min GA test with EA. The EA (baseline test), a 30-min recovery period, and a second 40-min GA test after the injection of STZ (consistent with other studies), whereas the implanted intragastric balloon and the connecting tube in group C could not be maintained until 6 wk after the STZ injection. The rats were randomly divided into two subgroups (group D1 for EA, N = 11, and group D2 for sham EA, N = 10). After an overnight fast, each rat was fed with 1.5 ml phenol red (0.5 mg/ml) mixed with 1.5% methylcellulose by gavage. EA or sham EA was performed during the following 30 min. The rat was then euthanized for the measurement of GE and small intestinal transit (SIT).

Animals were injected intraperitoneally with STZ (65 mg/kg; Sigma, St. Louis, MO) dissolved in a 1.5-ml citrate buffer (pH 4.5, Sigma) (24). The blood glucose was then measured weekly using a commercially available glucometer (Accu-Check Aviva; Roche Diagnostics, Indianapolis, IN). Diabetes was defined as a blood glucose concentration of 350 mg/dl or higher. The rats not meeting this criterion by the time of the experiments were excluded from the study.

EA

EA was performed at ST-36 (Zusanli) bilaterally, which is located 5 mm below the head of the fibula under the knee joint and 2 mm lateral to the anterior tubercle of the tibia. An L-shaped needle was inserted into each ST-36 with a depth of 3–5 mm. The pair of the

Induction of Diabetes

All rats were injected intraperitoneally with STZ (65 mg/kg; Sigma, St. Louis, MO) dissolved in a 1.5-ml citrate buffer (pH 4.5, Sigma) (24). The blood glucose was then measured weekly using a commercially available glucometer (Accu-Check Aviva; Roche Diagnostics, Indianapolis, IN). Diabetes was defined as a blood glucose concentration of 350 mg/dl or higher. The rats not meeting this criterion by the time of the experiments were excluded from the study.
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needles was connected to an EA device (Model D-860; Jinshan Electronic Device, Shanghai, China). Stimulation parameters shown in a previous study to accelerate GE in dogs were used and set as a train of on time of 2 s, off time of 3 s, pulse frequency of 25 Hz, and amplitude of 10 mA (34). For sham EA, the same needles were inserted into nonacupuncture points at the hypochondrium on bilateral sides with the electrical stimulator turned off.

Measurements and Data Analyses

Recording and analysis of GSW. The GSW were recorded using a Biopac system (EEG 100A; Biopac Systems, Santa Barbara, CA) as described previously (24). The percentage of normal GSW was defined as the percentage of time during which regular 4–6-cycle/min (cpm) waves were presented and computed using a previously validated method (24).

Recording and analysis of GE and SIT. A previously established method was used for the measurement of GE and SIT (37) and is described as follows. After an overnight fast, the rat was gavage fed with a 1.5 ml phenol red solution (0.5 mg/ml) mixed with 1.5% methylcellulose. Thirty minutes after the feeding, the rat was rapidly euthanized by inhalation of overdose of isoflurane (5%). The entire stomach and small intestine were carefully isolated and removed. The small intestine was divided into 10 equal segments. The amount of phenol red in the stomach and each of the intestinal segments was measured by a spectrophotometer (39). The percentage of GE was defined as the ratio between the amount of phenol red recovered from the stomach and the amount of phenol red ingested into the stomach. The intestinal transit was determined by the geometric center (GC) defined as follows: GC = \( \frac{1}{n} \sum (P_n \cdot n) \) for \( n = 1, 2, 3, \ldots 10 \), where, \( P_n \) is the percentage of phenol red in segment \( n \) and \( n \) is the number of the segment. Any phenol red found in the colon was included in segment 10.

Recording of ECG and analysis of heart rate variability. The ECG signal was recorded using a special amplifier (UFI, Morro Bay, CA) with a recording range of 1.5 to 100 Hz. The heart rate variability (HRV) signal was derived from the original ECG recording by identifying R waves, interpolating R-R interval data at 100 Hz, and finally downsampling the interpolated HRV data at 8 Hz suitable for analysis using a previously validated software (23). Spectral powers of the HRV at two frequency ranges were calculated (19) as follows: 1) a high-frequency band (HF; 0.8–4.0 Hz) reflecting cardiac vagal efferent activity and 2) a low-frequency band (LF; 0.3–0.8 Hz) reflecting mainly sympathetic efferent activity.

Statistical Analysis

All data are presented as means ± SE. Paired Student’s t-test was applied to investigate the difference in each of the measurements/parameters between EA and sham EA or between baseline and EA. ANOVA was applied before the paired t-test if the comparison was made among three sets of data or more. A P value of <0.05 was considered statistically significant.

RESULTS

Induction of Diabetes

All except two rats were confirmed with diabetes 1 wk after the injection of STZ, and hyperglycemia was maintained during the entire course of the study. The two nondiabetic rats were found in group A, excluded from the study and not counted in the number of rats presented in Fig. 1. The animals recovered well from the surgical procedures because most of the procedures for the chronic implantation of gastric electrodes or intragastric balloon were performed before the induction of diabetes.

Effects and Mechanisms of EA on GSW

EA at ST-36 improved gastric dysrhythmia in diabetic rats (experiment 1, \( n = 10 \), group A). In the EA session, the percentage of normal slow waves was 55.4 ± 2.9% at baseline and significantly increased to 69.2 ± 2.2% during EA (\( P = 0.01 \), Fig. 2). Naloxone blocked the improvement of gastric dysrhythmia by EA. In the EA + naloxone session, the percentage of normal slow waves was 53.7 ± 2.9% at baseline and maintained at 55.6 ± 3.3% during the EA application (\( P = 0.2 \) vs. baseline without EA; \( P = 0.02 \) vs. the corresponding EA period in the EA session). These data indicated that the ameliorating effect of EA on GSW was blocked by naloxone. Figure 3 shows typical GSW recordings before and during EA.

Effects of EA on GE and SIT

Experiment 2 in the group B rats revealed that EA resulted in a 21.4% increase in GE in diabetic rats. Thirty minutes after the test meal, the GE was found to be significantly faster in the rats treated with EA (group B1) than in the rats treated with sham EA (group B2) (91.2 ± 1.5% vs. 75.1 ± 5.0%, \( P = 0.01 \), Fig. 4A). Concurrently, the SIT was increased by 18.2% with EA compared with sham EA. The GC was 4.4 ± 0.2 in the sham EA group and 5.2 ± 0.2 in the EA group (\( P = 0.01 \), Fig. 4B). Figure 4C shows the amount of phenol red in each small intestinal segment in the EA-treated rats and sham EA-treated rats; a higher amount of phenol red was observed in more distal segments in the EA-treated rats compared with the sham EA-treated rats.

Effects and Mechanisms of EA on GA

The findings of experiment 3 in the group C rats showed impaired GA associated with diabetes, and the impairment was observed 1 wk after the injection of STZ and maintained until 4 wk after the injection of STZ. Compared with the baseline value before the injection of STZ, the gastric volume during the ramp distention was significantly decreased by 35.1% 1 wk after and by 30.9% 4 wk after the injection of STZ.

Experiment 4 in the group D rats demonstrated the ameliorating effect of EA on diabetes-induced impairment in GA, and the effect was mediated via the opioidergic pathway. As shown

![Fig. 2. Effects and mechanism of EA on gastric dysrhythmia](http://apjpi.physiology.org/content/doi/10.2093/ajpgi/G565.full)
in Fig. 5A, the gastric volume during ramp distention was $0.98 \pm 0.13 \text{ ml}$ at baseline and significantly increased to $1.21 \pm 0.15 \text{ ml}$ with EA ($23.5\%$ increase, $P = 0.01$). A consistent increase in gastric volume was noted at all pressure levels above 3 mmHg (see Fig. 5B). Naloxone had no effects on GA, as the baseline gastric volume values were similar between the session without naloxone and the session with naloxone ($P = 0.2$) but blocked the effect of EA on GA; in the session with naloxone, EA failed to increase the gastric volume during ramp distention (Fig. 5A, right). The gastric volume during ramp distention was $0.97 \pm 0.12 \text{ ml}$ when EA was applied at the presence of naloxone, which was similar to the baseline value but significantly lower than that when EA was applied at the absence of naloxone ($P = 0.01$ vs. EA).

**Effects of EA on Vagal Activity**

The spectral analysis of the HRV data obtained from experiment 5 in the group E rats indicated that EA significantly increased vagal activity and sympathovagal balance in diabetic rats. Six weeks after the injection of STZ, the HF, suggestive of the vagal component, was $0.55 \pm 0.05$ at baseline and increased to $0.61 \pm 0.03$ during EA ($P = 0.03$); the LF/HF, indicative of the sympathovagal balance, was $0.85 \pm 0.13$ at baseline and significantly decreased to $0.67 \pm 0.08$ during EA (Fig. 6). These findings suggested involvement of the vagal pathway with EA.

**DISCUSSION**

In the present study, we have found that EA at ST-36 improved gastric dysrhythmia and accelerated GE and SIT in the diabetic rats. Surprisingly, however, unlike most of the prokinetic agents that impair GA, EA was also able to improve impaired GA in the diabetic rats. The ameliorating effects of EA on gastric motility and GA were mediated by the opioi-
dergic and vagal pathways.

To the best of our knowledge, this was the first comprehensive study systematically investigating the effects and mechanisms of EA on gastrointestinal motility, including GSW, GE, intestinal transit, and GA in a rodent model of diabetes. Although a number of previous studies investigated the effects and mechanisms of EA on gastric motility in animals and patients, none of them were as comprehensive as the present study. Because GSW dysrhythmia and delayed GE were previously reported in STZ-induced diabetic rats, the focus of the present study on these two measurements was on the treatment effects and mechanisms of EA. Because none of the previous studies investigated the effect of diabetes on GA in STZ-induced diabetic rats, the present study was designed to investigate both the effect of the progression of diabetes and the effect of EA on GA. It is known that the diabetes-induced impairment in gastric motility is related to the progression or duration of diabetes. Accordingly, for the sake of consistency, all experiments investigating the therapeutic effects of EA were performed 6 wk after the injection of STZ. The methodologies used in the present study for measuring GSW, GE, and intestinal transit have been well established (24, 37). The method used in this study for assessment of GA in rats was different from that used in humans but was well validated (25, 29).

Gastric dysrhythmia, impaired GA, and delayed GE are common in patients with gastroparesis (5, 9, 43) and are major contributing factors to the symptoms of gastroparesis or functional dyspepsia. It has been reported that GSW are abnormal in about 50–75% of patients with gastroparesis and that the major slow-wave dysrhythmia is tachygastria and/or tachyar-rhythmia, attributed to ectopic tachygastric pacemaking in the distal antrum (5). In a rodent model of diabetes induced by STZ, GSW were found to be impaired 4 wk after the injection of STZ, and GE of liquid was delayed 6 wk after the induction of diabetes (24, 42). Similar abnormalities in GE and slow waves were reported in nonobese diabetic mice (24, 42). Although impaired GA has been frequently reported in patients with gastroparesis, the present study was the first to report the impairment in GA in STZ-induced diabetic rats. The findings of this study showed an approximate 30% decrease in GA during the first 4 wk after the injection of STZ compared with that before the injection of STZ (group C rats), and a similar impairment was also noted 6 wk after the injection of STZ (group D rats).

During the past decades, a number of studies have investigated the effect of acupuncture or EA on gastrointestinal motility (20, 40, 52, 56). In animal models, EA was reported to improve GSW impaired by rectal distension and accelerate GE in dogs (34) and reduce gastric tone in rats and vagotomized dogs (33, 47). In humans, EA has been shown to accelerate GE in patients with gastroparesis (54, 55), modulate
GSW in healthy volunteers (22, 41), and improve slow-wave
dysrhythmia in diabetic patients (4). However, each of these
previous studies was focused on one or two elements of gastric
motility. In clinical settings, a comprehensive and systematic
approach is often needed to treat patients with gastric motility
disorders. One typical example is the use of prokinetic agents;
a prokinetic agent may accelerate GE but is often unable to
improve symptoms of gastroparesis because of its detrimental
effect on GA. In this present study, the effects of EA on GE
and GA were studied in the same animal model of diabetic
gastroparesis. Most interestingly, EA was able to accelerate GE
and also improve GA in diabetic gastroparetic rats.

Delayed GE is a feature of gastroparesis. In healthy humans,
more than 90% of ingested food is emptied from the stomach
4 h after the meal (53). In patients with gastroparesis, however,
GE is delayed, which is attributed to antral hypomotility.
Traditionally, delayed GE is considered the major pathophysi-
ological mechanism underlying the symptoms of gastropa-
resis. Recently, it has been clear that impaired GA plays an
important role in the generation of certain symptoms of gas-

troparesis. GA is a consistent physiological response that
allows the stomach to accommodate the ingested food without
increasing intragastric pressure or inducing discomfort. This
accommodation reflex is mediated by the vagal pathway, and
the impairment of GA in diabetes results from impaired au-

tonomic nervous system. Although GE was commonly consid-

ered to be the important mechanism of symptoms in gastropa-

eresis, a number of studies have shown a poor correlation
between GE and symptoms (2, 3, 46, 49, 50). Recently a study
by Karamanolis et al. (18) revealed that, in patients with
idiopathic gastroparesis, the symptom pattern is determined by
the proximal stomach dysfunction rather than by the severity of
delayed GE. The prokinetic therapy enhances GE but, at the
same time, fails to improve impaired GA in patients with
gastroparesis (8, 45); this may explain the reason why certain
prokinetics, such as erythromycin, are able to improve gastric
motility and GE but not symptoms of dyspepsia. In the present
study, we showed that EA at ST-36 enhanced GE by about

Fig. 4. Effects of EA on GE and SIT. A: EA significantly accelerated GE (P = 0.01). B: EA
significantly accelerated SIT, determined by the
geometric center (P = 0.01). C: amount of phenol
red in each segment in sham EA group and EA
group. EA significantly accelerated SIT (P < 0.05).
21% and accelerated SIT by about 18% in diabetic rats; at the same time it also improved impaired GA. Accordingly, the EA therapy may be more beneficial to patients with gastroparesis than the prokinetic therapy. Clinical studies are needed to validate these findings.

A number of studies by Takahashi and colleagues (15, 16, 41, 47, 48) have strongly demonstrated the site-specific effects EA on gastric motility. Whereas EA at ST-36 (lower limb) has been consistently shown to have an excitatory effect on gastric motility via the vagal pathway, EA at the abdomen or ST-25 has been reported to induce gastric relaxation via the sympathetic pathway. Tada et al. (47) reported a relaxative effect of EA on the stomach that was abolished by guanethidine, propranolol, splanchnic ganglionectomy, spinal cord transection, and spinomedullary transaction, suggesting the involvement of the sympathetic pathway. Takahashi and colleagues investigated the c-Fos expression in the nucleus tractus solitarius (NTS), the dorsal motor nucleus of the vagus (DMV), and the rostral ventrolateral medulla (RVLM) following acupuncture. They reported that EA at the lower limbs (ST-36) significantly increased c-Fos-positive cells in both the caudal NTS and the DMV, whereas acupuncture at the abdomen (ST-25) increased c-Fos-positive cells in both the medio-caudal NTS and the RVLM. They concluded that acupuncture at ST-36 stimulates the DMV through the caudal NTS, causing gastric contractions, whereas acupuncture at the ST-25 stimulates the RVLM through the medio-caudal NTS, causing gastric relaxation in rats (16).

The vagal mechanism of EA at ST-36 has also been explored in a number of studies using the spectral analysis of the HRV. Concurrent with improved gastric motility, enhanced vagal activity assessed by the spectral analysis of HRV has been consistently reported in humans (26, 36), dogs (6, 32), and rats.
(14) in response to EA at ST-36. In this study, a significant increase in HF of the HRV signal representing vagal activity and a decrease in LF/HF representing sympathovagal balance were also reported. These findings suggest that the improvement in gastric motility is at least partially attributed to the enhancement of vagal efferent activity or improvement in the sympathovagal balance.

In the present study, we have found that, in the diabetic rats, the EA at ST-36 induced improvement in both GSW and GA which was blocked by the presence of naloxone, suggesting the involvement of the opioidergic pathway. Similar opioid mechanisms were also reported in the EA at ST-36-induced improvement in GSW and antral contractions in dogs with rectal distention (6). In control nondiabetic rats, the effect of acupuncture on gastric motility was also reported to involve the opioidergic mechanism (47, 51). Opioids are known to inhibit distention (6). In control nondiabetic rats, the effect of acupuncture on gastric motility is at least partially attributed to the involvement of the opioidergic pathway. Similar opioid mechanisms were also reported in the EA at ST-36-induced improvement in both GSW and GA.

It should be mentioned that the mechanisms of impaired gastric motor functions in diabetes are complex and that the effects of EA on gastric motility in diabetes may involve mechanisms other than those discussed above. For example, several recent studies have shown a loss of interstitial cells of Cajal (ICC) associated with diabetes, and this loss may lead to abnormal slow waves and gastric motility (7, 11, 31). Further studies are needed to investigate whether the effects of EA on gastric motility are also mediated via the modulation of the ICC network.

In conclusion, EA at ST-36 improves GSW dysrhythmia, enhances delayed GE and intestinal transit, and ameliorates impaired GA in STZ-induced diabetic rats. These ameliorating effects seem to be mainly mediated via the vagal pathway. EA may have a therapeutic potential for treating diabetic gastroparesis.

DISCLOSURES

No conflicts of interest are declared by the authors.

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