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Review

Mechanism of Reflex Regulation of the Gastroduodenal Function by Acupuncture

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Many clinical studies focus on the effects of acupuncture on digestive disorders. However, few studies describe the mechanism by which these effects are produced. We present some recent experimental work on the mechanism of acupuncture for reflex regulation of gastroduodenal function in anesthetized rats. In anesthetized rats, it has been proven that acupuncture to the abdomen excites sympathetic nerves via spinal reflexes causing inhibition of motilities while acupuncture of limbs excites vagus nerves via supraspinal reflexes causing an increase in the motilities. It has also been shown that in order to inhibit gastric motilities, acupuncture stimulation of the abdomen must be strong enough to excite group VI fibers of the afferent intercostal nerves. To increase gastric motilities, acupuncture stimulation to hind limbs must be strong enough to excite the high-threshold group III fibers of tibial nerves. It has also been shown that the neural mechanism of duodenal motility stimulation by acupuncture involves the same body regions and intensity of stimulation as that of gastric motilities. Theories regarding the underlying mechanism have proposed somato-autonomic reflexes and responses via endogenous opioids, etc., but without definitive conclusions.

Keywords: gastric motility – duodenal motility – gastric-acid secretion – somato-autonomic reflex – rat

Introduction

Recently, acupuncture treatment as a complementary and alternative medicine (CAM) has been the focus of studies from advanced basic research (1) to clinical reports (2) on pain. Although much more clinical work has centered on the effects of acupuncture on the digestive tract than for other organs (3–5), far less work has been done on the mechanism of these effects. Japan has a long history of research on acupuncture for the digestive function. In 1912, the Japanese government asked Miura, a professor at Tokyo University, to study acupuncture treatment. He observed and reported changes in the abdominal wall for the gastrointestinal motility of rabbits caused by acupuncture (6). His work, however, only encompassed physical responses to acupuncture, and until recently there have been no studies on the mechanisms by which these responses are produced.

Basic studies on somato-visceral reflexes found a high association with acupuncture mechanisms, showing that somato-sensory stimulations to the skin or muscles changed the gastrointestinal reflex function in anesthetized animals (7,8). Recent studies have explored changes in gastrointestinal motilities of the gastropyloric region and duodenum via somato-autonomic reflexes. In 1975, Sato *et al*. observed that pinching the abdomen of anesthetized rats decreased intragastric pressure. Because the decrease of intragastric pressure occurred on spinalized rats, but disappeared when the splanchnic nerves on both sides of the rats were severed, they concluded that the decrease was a reflex response that originated in the spine and was expressed via gastric sympathetic nerves (9).

In more detailed investigations of intragastric pressure decrease, Kametani *et al*. pinched anesthetized rats in

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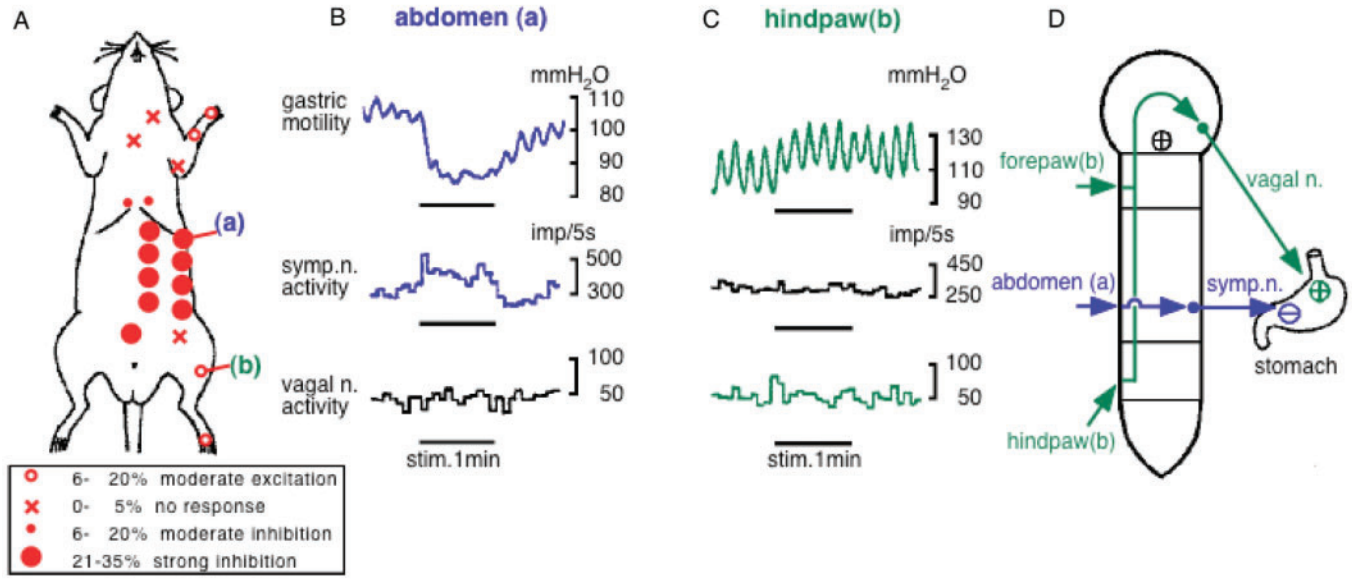

Figure 1. Changes in gastric motility caused by acupuncture. (**A**) A frame format showing gastric motilities caused by acupuncture in each dermatome. Open or closed circles showed regions of the excitatory or inhibitory gastric motilities. Circle size indicates the levels of each response shown in the figures. (**B**, **C**) Effects of acupuncture stimulation of the abdomen (B) and hind paw (C). Gastric motilities (upper traces), efferent gastric sympathetic nerve activity (middle trace) and efferent vagus nerve activity (lowest trace) after acupuncture. Activity of each nerve was continuously measured and level of acupuncture stimulation/minute is expressed with horizontal bars. (**D**) Pathway for reflex regulation of the gastric motilities of anesthetized rats. [Quoted from Sato with modification (10)].

various regions of the body and observed that stimulating the body trunk inhibited gastric motilities, while stimulating the limbs excited responses in the motilities. In the inhibitory response, the gastric sympathetic nerves were more active than normal while with an excitatory response, the gastric vagus nerves were more active than normal. Since only the inhibitory response was observed in spinalized animals, they discovered that the excitatory response to acupuncture of the limbs occurred through the excitation of vagus nerves via supraspinal reflexes (10).

We present recent basic studies mainly by our group on the mechanism of acupuncture by somato-autonomic reflexes and on the acupuncture mechanism of reflex regulation of the gastroduodenal function in anesthetized rats.

Gastroduodenal Motility

Acupuncture Stimulation

When Mori *et al*. observed gastric motility in anesthetized rabbits by the balloon method, when they were stimulated by tapping on acupuncture point ST36 in 1978, they discovered that intragastric pressure increased by acupuncture stimulation and that the response disappeared when the central side of the sciatic nerves, which govern the nerves at point ST36, were severed (11). In 1991, Kudo *et al*. observed by electrogastrogram that electro-acupuncture to anesthetized dogs on acupuncture point BL19, which is on the back, delayed kinetic rhythms of the stomach and inhibited electric activity of the stomach wall (12). These reports suggest that acupuncture changes gastric motilities in anesthetized animals, as somato-sensory stimulation does with pinching.

In 1993, Sato *et al*. observed the effect of manual acupuncture stimulation to anesthetized rats through continuous measurement of the intragastric pressure by means of a balloon inserted into the gastropyrolic region. They discovered that when they inserted a needle (with a diameter of 340 μm) about 4–5 mm deep into the subcutaneous muscular layer at many points on the whole body and gave the tested rats acupuncture by twisting the needle for 60 seconds, gastric motilities either decreased or increased.

Acupuncture inhibited gastric motilities when the abdomen was stimulated as a result of increased activity of the efferent fibers of the gastric sympathetic nerves. Increase of gastric motilities in the case of acupuncture stimulations to limbs resulted from increased activity of the efferent fibers of the gastric vagus nerves. These inhibitory or excitatory responses were induced by acupuncture to both the skin and the muscle, the skin only and the subcutaneous muscles only.

Acupuncture to the abdomen increased the activity of afferent fibers of the spinal nerves in the lower chest and, when the spinal nerves in the chest were severed, the inhibition of gastric motilities disappeared even when the

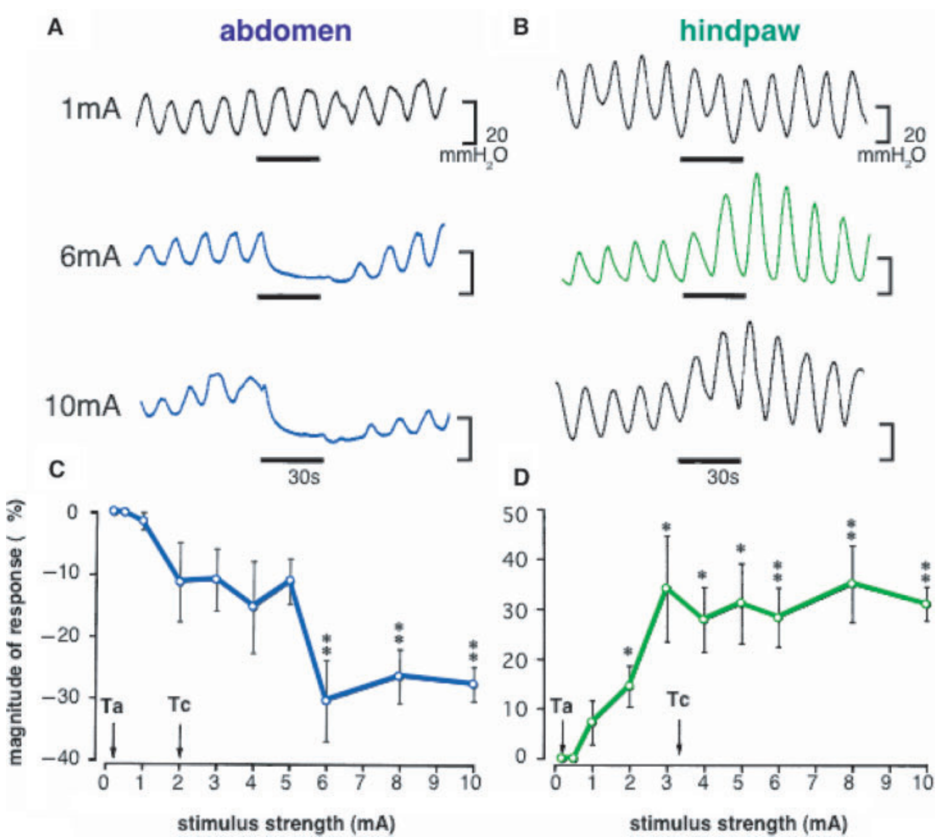

Figure 2. Changes in gastric motilities with electro-acupuncture. Measurements of gastric motilities were the same as in Fig. 1. (**A**) Inhibitory changes of gastric motilities from abdominal stimulation with electro-acupuncture. (**B**) Excitatory changes of gastric motilities by stimulation of hind limb with electro-acupuncture. (**C**) Comparison between the intensity of abdominal stimulation with electro-acupuncture and the rates of gastric motility changes. As shown with arrows, Ta and Tc indicate the average intensity of threshold of group A and B fibers in the afferent intercostal nerve activity. Significant inhibitory changes were induced by intense stimulation above the threshold of group C fibers. (**D**) Comparison between the intensity of hind paw stimulation with electro-acupuncture and the rates of gastric motility change. As shown with arrows, Ta and Tc indicate the average intensity of threshold of group A and B fibers of the tibial nerves, respectively. Significant increase was induced by intense stimulation of group A fibers with high thresholds. Changes in average intragastric pressure are expressed as a percentage before stimulation. $*P<0.05$ ($**P<0.01$) indicates significant differences in reference to prestimulatory values with paired *t*-test analysis. [Cited from Yamaguchi with modification (14)].

abdomen was stimulated. Similarly, acupuncture to the hind paw increased the activity of the thigh and the afferent fibers of the sciatic nerves and, when the thigh and sciatic nerves were severed, the response to increase gastric motilities disappeared even when the hind paw was stimulated.

Gastric motilities were inhibited by acupuncture to the abdomen in spinalized rats but acupuncture to the hind paw did not excite gastric motilities proving that inhibitory or excitatory responses to gastric motilities by acupuncture to the abdomen or the hind paw were spinal or supraspinal reflex responses. Furthermore the responses did not disappear when naloxone was given, suggesting that responses occur through a different mechanism from acupuncture analgesia (13).

Electro-acupuncture Stimulation

Yamaguchi *et al*., in the same study group, confirmed that electro-acupuncture of various intensities to the abdomen or hind limbs caused excitatory or inhibitory responses in gastric motilities. They further recorded the activity of afferent fibers from intercostal nerves or tibial nerves when the abdomen or hind paw were stimulated and examined the relationship of the intensity of the stimulation to response in gastric motilities. They identified the nerves through which the electro-acupuncture stimulations worked, observing that the responses occurred above the threshold level of electro-acupuncture stimulation intensity at which C fibers are excited in the abdomen, but above the threshold level at which Aδ and C fibers are excited in the hind paw. Accordingly, the stimulation of body trunk and hind limbs were transmitted through different nerve fibers (14).

For duodenal motilities, Sato *et al*. measured motilities caused by pinching stimulation and reported that noxious stimulation to the abdomen produced an inhibitory response by spinal reflexes. In 2003, Noguchi *et al*. measured duodenal motilities by a

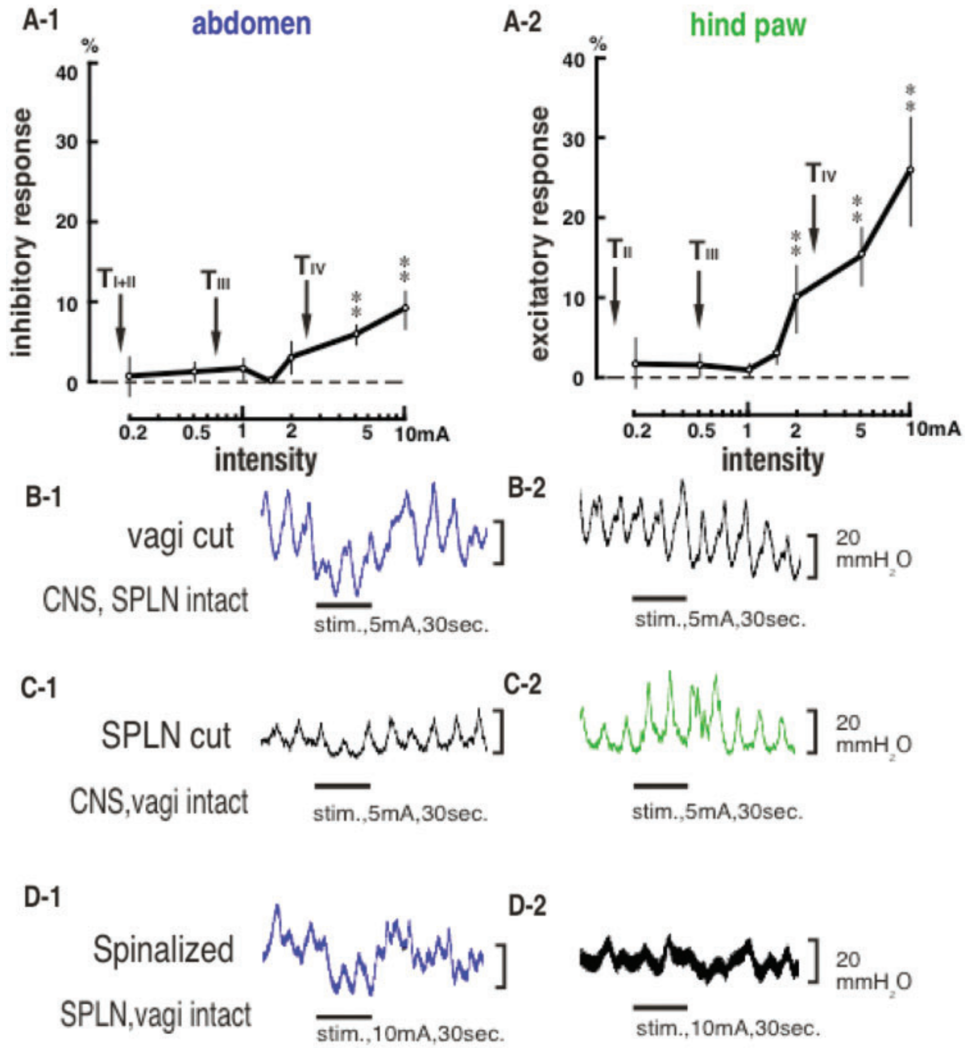

Figure 3. Changes in duodenal motilities stimulated by electric acupuncture. (**A**) Intensity of electro-acupuncture to the abdomen and hind paw and the rate of changes in duodenal motilities. (**A-1**) The threshold of afferent intercostal nerve activity innervating the stimulated abdominal region, and the inhibitory change rates of duodenal motilities. $T_{I–IV}$ arrows indicate the threshold of afferent intercostal nerve activity of each nerve. A significant inhibitory response appeared with stimulation above the intensity that excited group IV fibers. (**A-2**) The threshold of afferent tibial nerve activity innervating the stimulated hind paw region, and the inhibitory change rates of duodenal motilities. $T_{II–IV}$ arrows indicate the threshold of afferent tibial nerve activity for each nerve. A significant inhibitory response appeared with stimulation above the intensity threshold of group III or IV fibers with high thresholds. Particulars of the statistical analysis are the same as Fig. 2. (**B**) Effects of the vagotomy. (**B-1**) No inhibitory response of the duodenal motilities, (**B-2**) disappearance of excitatory response. (**C**) Effects of the splanchnic nerve section. (**C-1**) Disappearance of inhibitory response of duodenal motilities, (**C-2**): no effect on excitatory response. (**D**) Effects of the spinal cord section. (**D-1**) No effect on inhibitory response of duodenal motilities, (**D-2**) disappearance of excitatory response (Cited from Noguchi with modification [15]).

method similar to that used to measure gastric motilities, and examined the relationship between intensities of electro-acupuncture to changes in duodenal motilities. Their results revealed that to decrease duodenal motilities, electro-acupuncture stimulation to the abdomen needed to be strong enough to excite group IV fibers of intercostal nerves. To increase motilities, electro-acupuncture stimulation to the abdomen needs to be strong enough to excite the higher-threshold group III fibers of tibial nerves. They also proved that the responses occur through a path similar to that of gastric motilities (15).

Gastric-acid Secretion

The first paper given at a conference in the west to relate acupuncture treatment with gastric-acid secretion was given by Sodipo *et al.* at the University of Lagos in Nigeria in 1979 (16). They treated a group of duodenal ulcer (DU) cases and a group of non-ulcer dyspepsia (NUD) cases by various acupuncture regimens for 6 weeks. They reported that treatment relieved stomach pain, and that stimulated maximal acid output (MAO) decreased in the DU group. They concluded that acupuncture treatment was based on decreasing gastric-acid secretion.

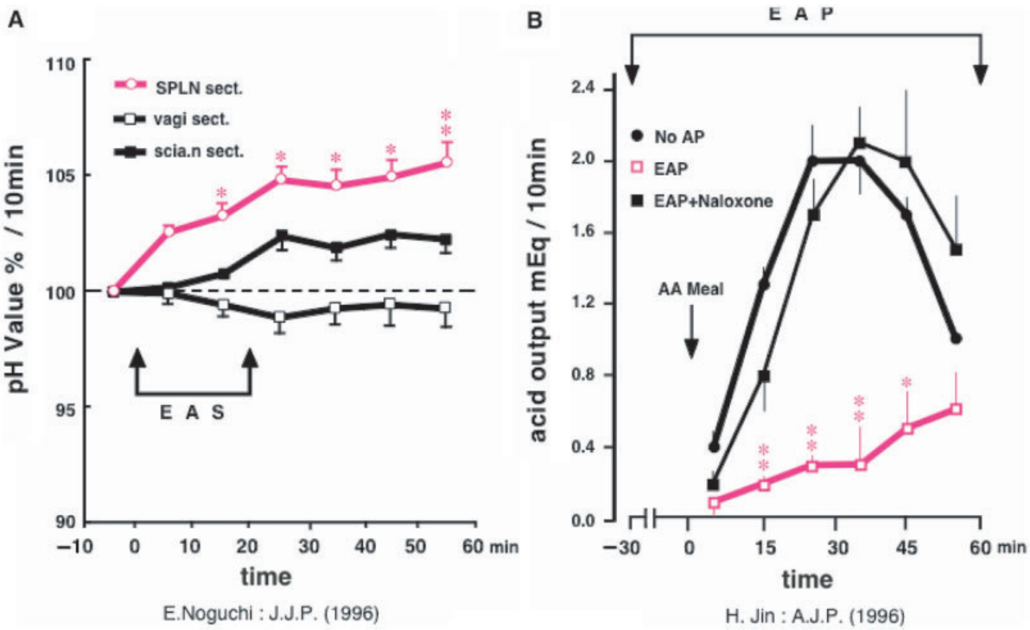

Figure 4. Changes in gastric acid secretion with electro-acupuncture. (**A**) Effects of severing the splanchnic nerve and vagus nerve on excitatory response of gastric acid secretion with electro-acupuncture of the hind paw of the anesthetized rats at acupuncture point S-36 Excitatory response of gastric acid secretion with electro-acupuncture disappeared after vagotomy (open squares) and ischiadic nerve section (closed squares), while that after the splanchnic nerve section did not disappear. Horizontal lines (EAS) indicate the period of acupuncture stimulation. [Cited from Noguchi with modification (20)]. (**B**) Effects of electro-acupuncture stimulation on gastric acid secretion after amino acid intake in conscious dogs. No AP: control without stimulation, EAP: electro-acupuncture, EAP + Naloxone: acupuncture stimulation + Naloxone ($40\,g/kg^{-1}/h^{-1}$), AAMeal: amino acid intake (given in all experiments). Horizontal lines (EAS) indicate the period of acupuncture stimulation. Electro-acupuncture inhibited gastric acid secretion after amino acid intake (open squares). However, this suppressive response was inhibited by naloxone administration (closed squares). [Cited from Jin *et al.* with modification (18)].

In the field of basic acupuncture studies, Zhou *et al.* observed in 1984 that gastric-acid secretion was inhibited in conscious dogs with a Pavlov pouch when they gave them electro-acupuncture to acupuncture points ST36, PC6 and BL20 for 2 hours. This response disappeared when they gave the dogs a vagus nerve blocker (atropine) or local anesthetic (procaine) to the regions that received acupuncture. They then concluded that gastric-acid secretion was inhibited by somato-autonomoic reflexes (17).

In 1996, Jin *et al.* observed that electro-acupuncture of conscious dogs inhibited rises in gastric-acid secretion that should have occurred when they ingested amino acid foods. This inhibition of gastric-acid secretion disappeared when they were given naloxone. They proposed that the mechanism involved endogenous opioids such as occurs in acupuncture analgesia (18).

Hang *et al.* in Shanghai, observed gastric-acid secretion through changes in the pH value of physiologic saline circulated in the stomach of anesthetized rats (Ghosh & Schild method), and observed an increase in secretion by electro-acupuncture to acupuncture point ST36 with no effect from severing the ischiadic and vagus nerves or the administration of naloxone (19).

When Noguchi *et al.* observed gastric-acid secretion in anesthetized rats, using a similar gastric circulation, they discovered that the response to increasing gastric-acid secretion occurred by electro-acupuncture stimulations to acupuncture point ST36, and that it disappeared when the ischiadic nerves or vagus nerves were severed, but did not disappear when the splanchnic nerves were severed. They concluded that the excitatory response occurred through somato-autonomic nervous reflexes (20). Although many scientists have reported on the responses of gastric-acid secretion to acupuncture stimulations, the results were not definitive and the underlying mechanism remains unknown.

Pomeranz pointed out in his paper (21), that the greatest difference between Noguchi's (1996) and Jin's (1996) reports was whether the animals were anesthetized or not. In order to observe the response to acupuncture in conscious animals, the problem of stress caused by acupuncture needed to be solved. In the study of gastric-acid secretion, there are many factors apart from anesthetization such as emotions and hormones. Accordingly many concerns must be solved to clarify the effect of acupuncture stimulations on gastric-acid secretion.

Conclusion

The following mechanisms for acupuncture stimulation to anesthetized rats have been proven to exert effects on gastric motilities. Acupuncture to the abdomen of anesthetized rats increases gastric motilities by exciting sympathetic nerves via spinal reflexes. Stimulating the limbs of rats caused an increase in gastric motilities by exciting vagus nerves via supraspinal reflexes. In addition, acupuncture simulation of the abdomen must be strong enough to excite group VI fibers of the afferent fibers of intercostal nerves in order to produce an inhibitory response. Stimulation of hind limbs should be strong enough to excite the high-threshold group III fibers of the tibial nerves in order to produce the excitatory response. As for duodenal motilities, acupuncture works through a neural mechanism similar to that of gastric motilities in terms of stimulated regions and intensity of stimulation.

Reports on inhibitory and excitatory effects of acupuncture on gastric-acid secretion are mixed. For the neural mechanism, somato-autonomic reflexes and responses of intervening endogenous opioids have also been reported with no definitive conclusion.

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