Mechanism of Enhanced Gastric Contractions in Response to Stimulation of the Sympathetic Trunk

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Stimulation of the sympathetic trunk in the thoracic cavity of dogs was found to result, as a rule, in increased gastric contractions. The stimulatory effect was better defined in the presence of the drug Ornid but could be greatly decreased or completely eliminated by Promedol. It is suggested that the sympathetic trunk contains preganglionic serotoninergic nerve fibers which enhance gastric contractions.

Key Words: *gastric contractions; sympathetic trunk; regulation*

It has been known for a long time that the splanchnic nerves can not only inhibit but also stimulate gastrointestinal motoricity [1,2,8,12]. The stimulatory phenomenon was discovered as far back as 1857 by Pfluger, yet its mechanism remains uncertain to this day, although many hypotheses have been offered.

Tonic gastric contractions arising in response to stimulation of the splanchnic or periarterial nerves are presumed to result from activation of cholinergic mechanisms and α-adrenergic receptors [11] or from excitation of parasympathetic fibers originating in the posterior nerve roots [3,10]. Other investigators [9], having found that the stimulatory effects of the greater splanchnic nerve can be abolished by atropine but not by hexamethonium or guanethidine, while its inhibitory effects in intact animals can be transformed into stimulatory effects with both hexamethonium and guanethidine, have come to the conclusion that the latter effects are due to activation of fine afferent fibers by an axon-reflex mechanism.

It has also been suggested [6] that the enhancement of gastric contractions seen to occur upon stimulation of the greater splanchnic nerve is mediated by the serotoninergic nerve fibers running within sympathetic nerves and exerting a powerful enhancing influence on gastric contractions. This conclusion is based on the observation that the stimulatory effect of the splanchnic nerve is abolished by atropine, a blocker of M-serotoninergic receptors on sympathetic ganglia, but not by benzohexonium, which blocks H-cholinergic receptors. It should be noted that atropine blocks not only the M-serotoninergic receptors of sympathetic ganglia, but also the M-cholinergic receptors of gastrointestinal smooth muscles. For this reason, a more specific blocker of M-serotoninergic receptors should be used instead of atropine in further studies [6].

Thus, highly conflicting views have been expressed by different scientists regarding the mechanisms by which the splanchnic nerves enhance gastric contractions. The purpose of the present study was to investigate this effect further so as to gain a deeper insight into the mechanisms regulating gastrointestinal tract activity and into the functional organization of the autonomic nervous system.

MATERIALS AND METHODS

The experiments were conducted on mongrel dogs (body weight 7-10 kg) in the surgical stage of Nem-

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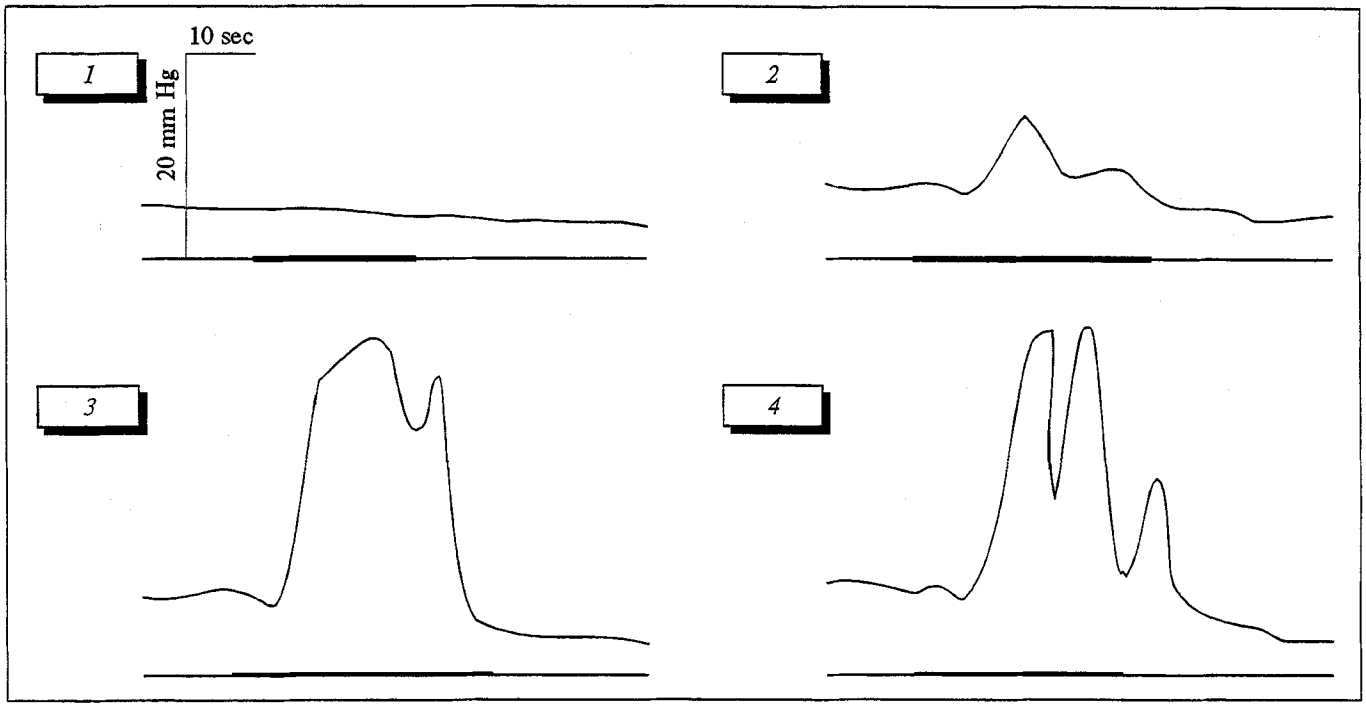

Fig. 1. Increases in gastric contractions in a dog with increasing intensity of ST stimulation in the thoracic cavity. *1*, *2*, *3*, and *4*: stimulation with 1, 5, 10, and 15 V, respectively. Here and in Figs. 3 and 5, the straight line on each fragment is the zero line whose bold segment indicates the duration of stimulation.

butal narcosis (60 mg/kg, intramuscularly). Mechanical gastric activity was evaluated by recording alterations in intragastric pressure with a P6Ch01 polygraph using a d-c amplifier unit, an H30301-6 automatic recorder, and an external EMT-35 electronic pressure sensor of high sensitivity connected to a small balloon of 50-70 ml capacity introduced into the dog's stomach. The balloon was filled 2/3 full with warm (38°C) distilled water and connected to the electronic pressure sensor by means of a polyethylene tube which was also filled with water. A pursestring suture was placed around this tube at the site of its exit from the stomach and the gastric wall was then either sutured or clamped.

In this study, in contrast to those reported by other workers [3,7,9,11], gastric contractions were enhanced by stimulation of the sympathetic trunk (ST), which does not carry parasympathetic fibers, rather than of the splanchnic or periarterial nerves, which contain not only sympathetic but also parasympathetic fibers - a factor that complicates interpretation of the results. For a stimulatory effect (enhanced gastric contractions) to be achieved, the ST had to be stimulated in the area of origin of the greater splanchnic nerve, i.e., in the thoracic cavity. When the peripheral portion of this nerve was stimulated, impulses were able to reach the abdominal organs and stomach along efferent fibers of both splanchnic nerves and of the ST, which was divided at the level of thoracic vertebrae IX and X. Although this technique made the experiment more difficult to perform (it was necessary to open the chest and ventilate the dogs artificially), it did provide reliable results, as only the ST devoid of parasympathetic fibers was stimulated. Stimulation of the ST proved to be more convenient than stimulation of the greater splanchnic nerve because

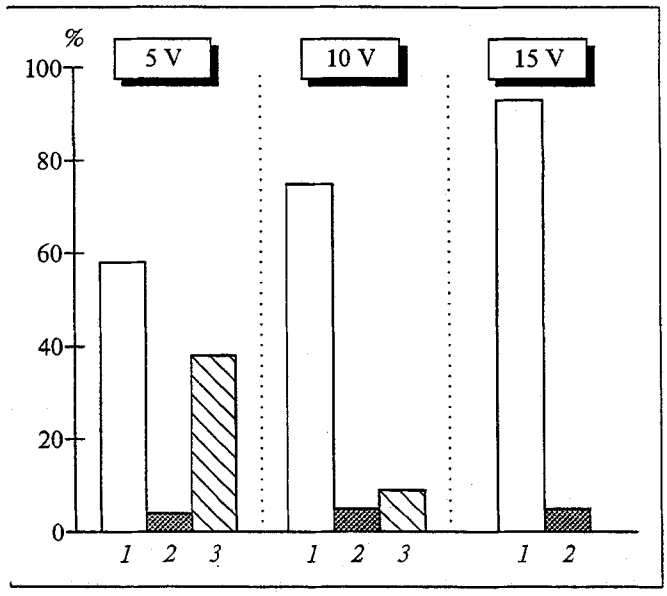

Fig. 2. Percentage ratios of dogs showing stimulatory and inhibitory gastric responses to ST stimulation of three different intensities. *1*) Enhanced gastric contractions; *2*) inhibited contractions; *3*) no response because the inhibitory and stimulatory influences on the stomach were equal.

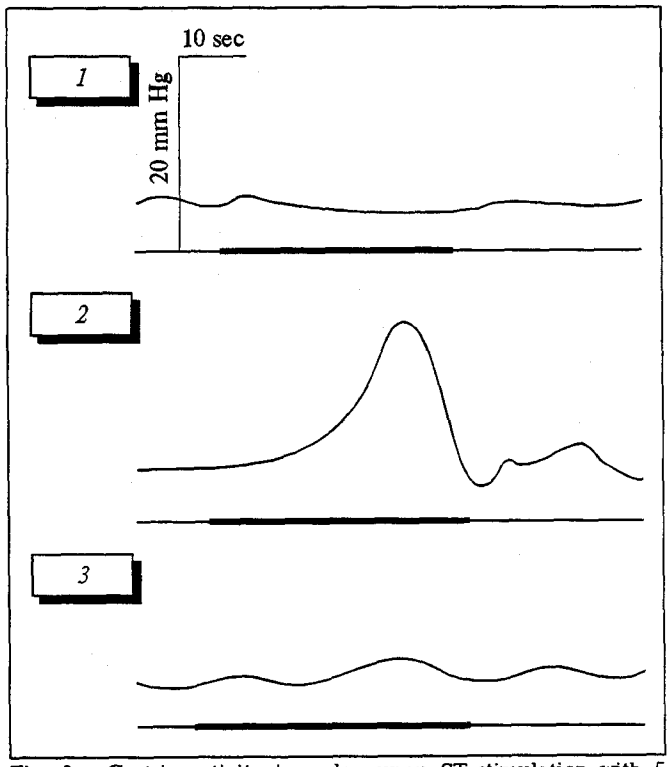

Fig. 3. Gastric activity in a dog upon ST stimulation with 5 V under different conditions. *1*) slight inhibition before injection of pharmacological agents; *2*) strikingly enhanced contractions after Ornid injection; *3*) enhanced contractions eliminated after the injection of both Ornid (blocker of adrenergic nerve endings) and Promedol (blocker of M–serotoninergic receptors on sympathetic ganglia).

the latter is made up of several small branches which become damaged much more rapidly.

These features of the technique we used led to the discovery of new and quite unexpected facts about the mechanisms of gastrointestinal tract regulation and the functional organization of the autonomic nervous system.

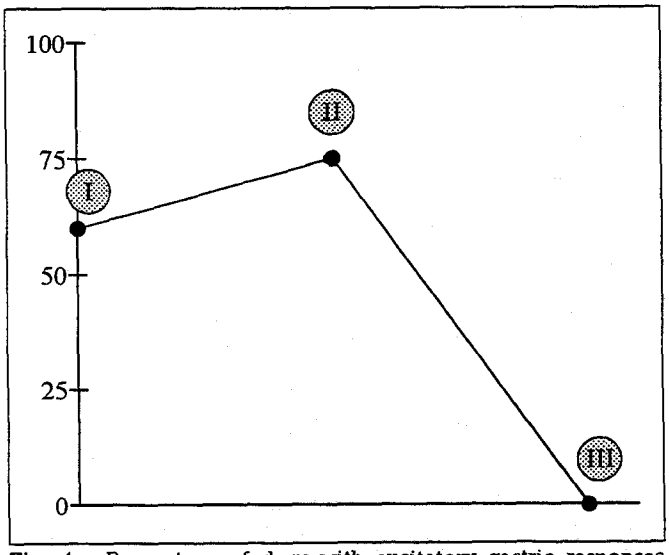

Fig. 4. Percentage of dogs with excitatory gastric responses to ST stimulation with 5 V under different conditions. *I*) before injection of pharmacological agents; *II*) after Ornid injection; *III*) after injection of both Ornid and Promedol.

The thoracic cavity was reached through a skin incision and blunt dissection of muscles in the ninth intercostal space on the right. The peripheral portion of the ST was stimulated by square pulses of different intensities using an ESL-2 electrostimulator and bipolar gold-plated electrodes spaced 2 mm apart.

Blood pressure was also recorded, using a cannula inserted into the femoral artery and connected by a polyethylene tube to the electronic pressure sensor and the polygraph. The cannula and tube were filled with physiological saline. The dogs were artificially ventilated with an RO-6 apparatus.

The sympathetic part of the autonomic nervous system was blocked with Ornid (bretylium tosylate) (20 mg/kg, intravenously) which prevents the release of catecholamines from postganglionic sympathetic nerve fibers. M-serotoninergic receptors of sympathetic ganglia were blocked with Promedol (10 mg/kg, also intravenously).

RESULTS

Gastric contractile responses to stimulation of the peripheral portion of the right ST in the thoracic cavity were first studied in 28 dogs without the use of any pharmacological agents except for the anesthetic. In three series of tests a total of 77 gastric responses to ST stimulation of three different intensities - 5, 10, and 15 V, respectively (pulse frequency 20 Hz, pulse duration 1.5 msec) - were recorded; each stimulation lasted 30 sec.

In these tests ST stimulation elicited either inhibitory or stimulatory responses, or else no response at all. The number and magnitude of responses depended on stimulus intensity (Fig. 1). With the stimulus intensity of 5 V, increased gastric contractions were recorded in 16 of the 28 dogs (57.1%) (intragastric hydrostatic pressure rose from 7.1±1.0 to 16.4±2.1 mm Hg; $p<0.01$), inhibition of contractions in 2 (7.1%), and no response in 10 (35.7%) (Fig. 2). When the ST was stimulated with 10 V, gastric contractions were increased in 18 of 24 dogs (75%) (hydrostatic pressure rose from 7.1±0.7 to 20.4±2.4 mm Hg; $p<0.001$) and decreased in 2 (8.3%); the remaining 4 dogs (16.6%) failed to respond.

The stimulatory effect was still greater at the stimulus intensity of 15 V: gastric contractions were enhanced in 23 of 25 dogs (92%) (hydrostatic pressure rose from 6.0±0.7 to 21.5±2.6 mm Hg; $p<0.001$) and weakened only in 2 (8%) (Fig. 2).

Thus, the proportion of animals with a stimulatory response increased from 57% to 92% (gastric contractions increased by 228% and 309%, respectively) with the increase in stimulus intensity from 5 to 15 V. In such tests, as we have shown earlier [6], neither bilateral vagotomy nor blockade of H-cholinergic receptors on sympathetic ganglia will abolish the sympathetic stimulatory effect.

The results presented above indicate that stimulation of a peripheral ST segment in the thoracic cavity, instead of eliciting inhibition of gastric contractions as one would expect on the basis of generally accepted data [2,4], was found to enhance them in a large majority of instances. It should be mentioned that spontaneous gastric contractions (i.e., those without nerve stimulation) were, as a rule, absent, but hydrostatic pressure in the gastric cavity usually ranged from 8 to 10 mm Hg, indicating that the tonus of the gastric smooth musculature was good.

In the next test series on 26 dogs, we also recorded a total of 77 gastric responses and found that blockade of the sympathetic nervous system with Ornid even increased the stimulatory effect markedly instead of depressing it (Fig. 3). Another unexpected finding was "sympathetic" enhancement of gastric contractions without any participation of the sympathetic nervous system. When the ST was stimulated with 5 V in the presence of Ornid, enhanced gastric contractions were recorded in 19 of 25 dogs (76%) (Fig. 4), with a rise from 5.9±0.8 to 17.1±2.8 mm Hg ($p<0.01$) in intragastric hydrostatic pressure; the remaining 6 dogs (24%) failed to respond. With the stimulus intensity of 10 V, gastric contractions were increased in 24 of 26 dogs (92.3%) (hydrostatic pressure rose from 6.5±0.9 to 19.9±2.9 mm Hg; $p<0.001$) and remained unchanged in 2 animals (7.7%). Stimulation with 15 V also led to enhanced gastric contractions in 92.3% of the dogs (24 out of 26), with a rise of hydrostatic pressure from 5.8±0.6 to 21.8±2.0 mm Hg ($p<0.001$); an inhibitory response was observed in 1 dog (3.84%) and no response in another one.

The results of this study point to the presence in the ST of noncholinergic and nonadrenergic nerve fibers exerting a strong excitatory influence on gastric contractility. This conclusion is based on the observations that enhancement of gastric contractions occurs upon stimulation of the sympathetic nerve devoid of parasympathetic fibers and is not abolished by bilateral vagotomy, blockade of H-cholinergic receptors on sympathetic ganglia, or blockade of adrenergic nerve endings.

Of particular interest are the stimulations in our experiments which neither enhanced nor depressed gastric contractions prior to Ornid injection. They indicate that inhibitory and stimulatory nerve fibers influenced gastric contraction to equal degrees. Further evidence that the ST contains nerve fibers enhancing gastric contraction is provided by the observed strong tonic contraction of the stomach in response to ST stimulation when adrenergic fibers were blocked.

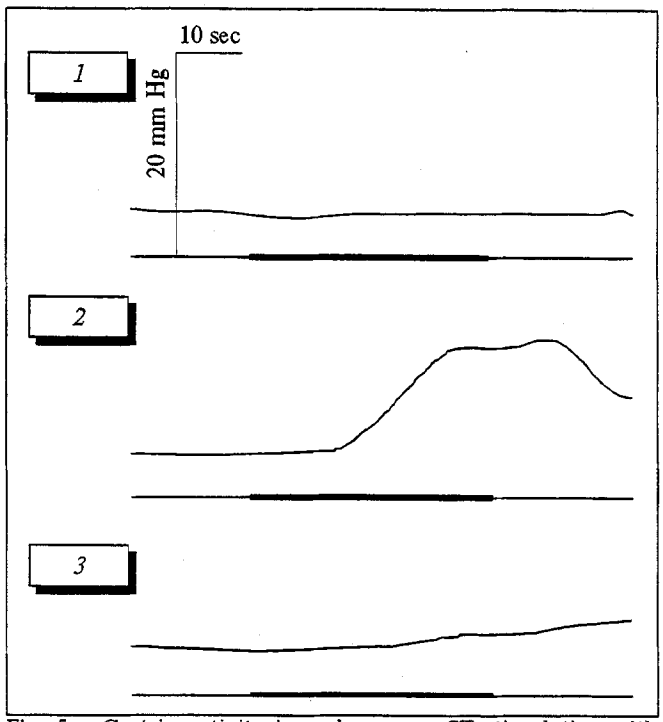

Fig. 5. Gastric activity in a dog upon ST stimulation with 10 V under different conditions. *1*) no response; *2*) greatly enhanced contractions after Ornid injection; *3*) greatly reduced stimulatory effect after injection of both Ornid and Promedol.

The results of our earlier study [6] led us to believe that the ST nerve fibers promoting gastric contractions are serotoninergic. This view was supported by the reported presence of serotoninergic neurons in the intramural neural apparatus of the gastrointestinal tract [5,7], and it received further support in the present study from tests using Promedol. This blocker of M-serotoninergic receptors on sympathetic ganglia was injected into 17 dogs when the previously injected Ornid was still active. In these dogs we studied 35 gastric responses to ST stimulation with 5, 10, or 15 V and found that Promedol eliminated (Fig. 3) or greatly diminished the magnitude of stimulatory responses in the animals.

Gastric contractions were not increased in any of the 7 dogs whose ST was stimulated with 5 V (Fig. 4). With the stimulus intensity of 10 V, no enhancement of contractions was recorded for 4 dogs out of 11 (36.4%), while the stimulatory effect in the remaining dogs was markedly weakened

by Promedol (Fig. 5): intragastric pressure increased only from 8.3±2.8 to 15.8±5.6 mm Hg (+90.9% *vs.* +205.6% when the nerve was stimulated in the presence of Ornid prior to Promedol injection). Similar weakening of the stimulatory effect occurred in 9 dogs of 17 (52.9%) upon ST stimulation with 15 V: intragastric pressure rose from 10.1±2.5 to 19.5±4.4 mm Hg (+93.4% *vs.* +271.6% before Promedol injection); of the remaining 17 dogs, ST stimulation was without effect in 6 (35%) and resulted in inhibition in 2 (11.8%). The failure of Promedol to abolish the stimulatory effect completely in some animals is attributed to incomplete blockade of M-serotoninergic receptors on sympathetic ganglia by the Promedol dose used (10 mg/kg).

To summarize, the present results strongly suggest that the sympathetic trunk contains nonadrenergic and noncholinergic nerve fibers capable of acting as powerful stimulators of gastric contractions whose mediator appears to be serotonin. The currently prevailing view that the splanchnic (sympathetic) nerves exert inhibitory influences on gastric activity will probably have to be revised since the major influence of these nerves on the stomach is most likely to be excitatory. However, this view is not at odds with the well-known fact that adrenergic nerves have inhibitory effects on gastric activity.

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