Synergism of Sympathetic and Parasympathetic Systems in the Regulation of Gastric Motility

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We studied the mechanisms of opposite effects of sympathetic and parasympathetic nervous systems on gastric motility. The involvement of serotoninergic structures in the realization of the stimulatory effect of the sympathetic trunk on gastric motility and the role of adrenergic intramural ganglia in vagal inhibition of electrical and motor activities of the antrum were demonstrated.

Key Words: *stomach; regulation, autonomic nervous system; serotonin*

Regulation of internal organs by the autonomic nervous system (ANS) is still an important problem of experimental and clinical physiology, because the mechanisms of possible synergism of the sympathetic and parasympathetic systems in this regulation are not studied in detail.

Sympathetic and parasympathetic nerves produce inhibitory or stimulatory effects on gastrointestinal motility [11]. Sympathetic innervation can attenuate or enhance vagal inhibition of cardiac activity [3,6,9]. The stimulatory effect of sympathetic nerves on gastrointestinal motility can be revealed after treatment with sympatholytics [5] or at rest [10]. The stimulatory effects of the sympathetic trunk and vagus on gastrointestinal motility attest to their synergistic interactions [1,2,4,7,8].

The purpose of the present study was to examine the transmitter mechanisms of sympathetic stimulation and parasympathetic inhibition of the gastric motility.

MATERIALS AND METHODS

The experiments (n=23) were performed on male and female mongrel dogs weighing 4-10 kg anesthetized with hexanal or sodium thiopental. The experiment was carried out for 5-7 h; narcosis, preparation, and tuning of recording devices took 3-4 h. The peripheral segment of the right sympathetic nerve was stimulated in the thorax, where this nerve is presented by only sympathetic fibers (abdominal portion of this nerve contains also parasympathetic vagal fibers). For obtaining more reliable results, 9 animals were subjected to right-sided vagotomy in the cervical region 1.5-3 weeks before the experiment. Preliminary vagoctomy caused degeneration of the main trunk and anastomoses between vagal fibers and sympathetic trunk. However, the results of acute and chronic experiments were similar, which pointed to the absence of these anastomoses in the thorax. Therefore, in the next 15 experiments acute vagotomy was used, which allowed to exclude vagus reflex effects on the gastrointestinal motility.

The mechanisms of inhibition of electrical activity and motility of the antrum caused by vagus stimulation were examined using platinum needle bipolar electrodes (diameter 0.3 mm, length 0.5 mm, distance between tips 1.5 mm) for extracellular recordings. The amplitude and frequency of recorded slow electrical waves, baseline rhythm, and total fast potentials were expressed in mV and the number of fast potentials per 100 slow basic waves, respectively.

Myorelaxation of the antrum was caused by relatively weak stimulation (0.5-5.0 V, 5 Hz, 2 msec) of the peripheral vagus segment. The degree of myo-

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relaxation was evaluated by the decrease in the frequency and amplitude of the total fast potentials.

The obtained results were processed using Student's *t* test.

RESULTS

The effect of the digestion phase on the studied phenomenon was examined in two animal groups. Group 1 (n=12) and group II (n=11) dogs received food 2.5-3.5 h and 7-8 h before the experiment, respectively. Control stimulation of the sympathetic trunk enhanced stomach contractions. This stimulatory effect developing against the background of nerve stimulation with 3-10-min intervals was stable and observed more frequently (in 73% animals) than the inhibitory one (11% animals). No response was recorded in 16% animals. Inhibition and the absence of response were most frequently observed during weak stimulation (0.5-5.0 V).

Control stimulation also showed that weak background peristalsis and low initial gastric pressure (6-12 mm Hg) promoted the development of the stimulatory effect, while active peristalsis facilitated the inhibitory effect. Enhanced stomach activity was manifested as single tonic contractions in response to series of stimuli during 30-60 sec.

Thus, these experiments showed that, in most cases, stimulation of the sympathetic trunk in the thorax increased stomach activity, while active peristalsis facilitated the inhibitory reactions.

The role of catecholamines in the mechanism of enhancement of stomach contractions by the sympathetic trunk was examined in 11 experiments using presynaptic sympatholytic bretylium (20 mg/kg intravenously). In these experiments, bretylium promoted the development of the stimulatory sympathetic effects in animals showing no excitation before bretylium application. The inhibitory effect caused by sympathetic nerve stimulation before bretylium injections was transformed into stimulatory in 10 of 11 animals (95 *vs*. 73% in the control) against the background of bretylium. This effect persisted during subsequent nerve stimulation independently on the background peristalsis, but significantly increased after bretylium injections. Stimulation of the thoracic sympathetic nerve in intact dogs enhanced tonic pressure in the stomach from 8.4±1.4 to 17.6±3.4 mm Hg (by 129%, p<0.02), but the same stimulation applied against the background of bretylium increased this parameter from 9.2±2.0 to 28.4±4.6 mm Hg (by 209%, p<0.01).

The experiments with bretylium showed that stomach contractions induced by sympathetic trunk stimulation were not mediated by catecholamines, because the inhibition of their release into the synaptic cleft not blocked, but even promoted the stimulatory effect.

The role of pre- and postganglionic sympathetic fibers in the realization of the stimulatory effect was examined using ganglionic blockers (5-10 mg/kg hexamethonium or 1-3 mg/kg arfonad, intravenously) against the background of bretylium. These experiments showed that the blockade of nicotinic cholinergic receptors in autonomic ganglia did not prevent the development of the stimulatory effect. Stimulation of thoracic segment of sympathetic nerve combined with injections of bretylium and hexamethonium or its analogues cause the same tonic stomach contractions as those observed during bretylium action before application of ganglionic blockers. This was associated with an increase in gastric pressure from 9.0±1.7 to 27.7±3.9 mm Hg (by 208%, p<0.01).

We assumed that stomach contractions were mediated by postganglionic nerve fibers, because their stimulatory effect was not inhibited by ganglionic blockers. However, these fibers were not adreno- or cholinergic ones, because their effect was not blocked by sympathetic and parasympathetic blocker hexamethonium or sympatholytic bretylium.

In 6 experiments on 12 dogs, this stimulatory effect was inhibited by the blockade of autonomic ganglionic 5HT3(S3)-receptors with 0.05 mg/kg morphine or 2 mg/kg promedol.

The last experimental series with the blocker of muscular 5HT1,2(S1,2)-receptors promethazine hydrochloride (5 mg/kg) confirmed the participation of serotoninergic structures in the mechanism of the examined effect. The stimulatory effect of sympathetic nerve stimulation of gastric motility was completely blocked by promethazine. Subsequent more strong stimulation against the background of bretylium, hexamethonium, and promethazine, or bretylium and promethazine caused no stomach contractions.

Thus, enhanced stomach contractions induced by sympathetic nerve stimulation were mediated by preganglionic serotoninergic fibers synaptically connected with serotoninergic neurons of intramural ganglia. The stimulatory action of sympathetic nerve can occur more frequently than the inhibitory one. Our data allow us to conclude that the sympathetic trunk contains

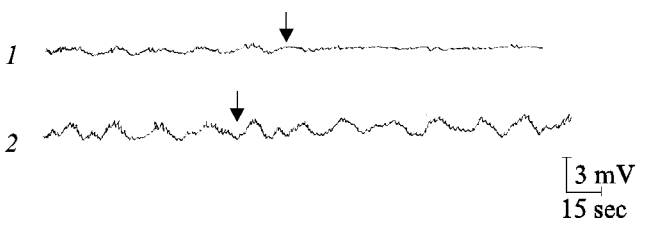

Fig. 1. Effect of vagal stimulation on electrical activity and motility of the antrum. *1*) inhibition after weak vagal stimulation, *2*) absence of inhibition against the background of propranolol and dihydroergotoxine. Arrows indicate the moment of stimulation.

serotoninergic fibers synergistically interacting with the vagus and stimulating gastric motility.

Synergistic effect of the vagus and sympathetic trunk on gastric motility was studied in experiments on rabbits. Electrical activity and motility of the antrum was recorded in intact animals and during pharmacological blockade of various ANS regions.

Stimulation of the peripheral vagus segment by medium intensity current increased the frequency and amplitude of slow electrical waves in the antrum (from 0.93±0.15 to 1.93±0.48 mV, by 108%, $p<0.02$), the amplitude of total fast potentials and their number in the bursts. Weak stimulation of peripheral vagus segment caused inhibitory response: the amplitude of slow electrical waves reduced from 1.27±0.24 to 0.88±0.15 mV (by 31%, $p<0.01$). This inhibition could be blocked by ganglionic blocker hexamethonium, which pointed to the role of intramural ganglia in the realization of this phenomenon.

Studies of the mechanisms of vagus inhibition of electrical activity and motility of the antrum showed that the examined phenomenon could be blocked by combined, but not separate action of α- and β-adrenoblockers (Fig. 1). Thus, this effect was realized via intramural adrenergic neurons synaptically connected with preganglionic parasympathetic vagus fibers.

Thus, we showed that serotoninergic fibers in sympathetic trunk and the vagus nerve stimulate motility of the stomach. The vagus nerve can stimulate and inhibit motility of the antrum. This can be regarded as synergistic interactions between the sympathetic and parasympathetic systems.

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