METHODS

Model of Motor and Secretory Activities of the Gastrointestinal Tract

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The model of motor and secretory activity was created using modified rheographer, and pharmacological analysis of the mechanisms activating alimentary motility of the gastrointestinal tract was carried out.

Key Words: *gastrointestinal tract; alimentary motility; model*

Activity of gastrointestinal organs can be simulated by creation of an artificial entry into the stomach or by esophagotomy and fistula of the corresponding compartment of the gastrointestinal tract [3]. However these methods cannot be used in the studies of autonomic regulation of motor and secretory activity of the gastrointestinal tract (GIT), because motor activity cannot be recorded under these conditions and pharmacological analysis of activation of the motor and secretory activities is impossible.

We created a model of motor and secretory activities of GIT.

MATERIALS AND METHODS

Motor and secretory functions of GIT were modeled on 4 rats.

Electrical and motor activity (EMA) was studied without preliminary esophagotomy. One week before the experiment transducers for EMA and impedansogram recordings were fixed to the serous membrane of the antrum and duodenum. Labeled conductors were brought through skin incision. Alimentary motor activity was studied in chronic experiments.

Impedance was recorded using modified electrodes: 2 insulated PEL-12 electrodes were fixed at a distance of 2.5-3.0 mm from each other on one support plate; the insulation was removed from the electrode at a length of 2.5-3.0 mm at a distance of 2 mm from the site of fixation. The area of active surface of the electrodes was 0.9-1.0 mm^2, which allowed rheographer adjustment with a lesser distance between the electrodes (in comparison with the previous method of electrode fixation). This modification of the electrode design ruled out distortions of impedance recording caused by friction of the supporting plates.

A RG4-01 rheograph was modified in order to extend its functional potentialities: a TG1-2 switch was inserted in the channel circuit, due to which the capacities could be "shortened" and the working mode of the device could be changed at any moment. If the contacts of the switch were disconnected, the rheograph operated in the common mode and recorded only rapid impedance fluctuations. If the contacts were connected, the rheograph recorded both slow and rapid impedance fluctuations and impedance of the substrate at a new stable level.

Modification of the RG4-01 rheograph improved its sensitivity and allowed fixation of changes in the impedance of a muscle portion between the recording electrodes, which depended on tissue blood content and on impedance changes resultant from changed distance between the recording electrodes during muscle contraction. The amplitude of impedance oscillations during change of distance between the electrodes resultant from muscle contractions was by 2 orders of

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magnitude greater than the amplitude of changes resultant from changes in blood content in the examined muscle portion. Alteration of impedance due to changes in blood content is negligible, and therefore the impedance of the GIT contracting muscle is recorded.

Modified RG4-01 rheograph is intended for recording of rapid and slow changes in impedance and impedance stabilized at a new level. In this latter case the device records rapid changes at a new stable level, *i.e.* the constant constituent is recorded in parallel with the rapid impedance fluctuations. Such impedance changes are most incident in the smooth-muscle organs of GIT, when rapid and slow contractions of smooth muscles occur and the muscular tone increases. This shortened the distance between the recording electrodes and the impedance of this portion of the stomach or intestine decreases.

The rats were narcotized with hexenal. Median section of the abdomen was made under aseptic conditions during surgical stage of narcosis, and fistulas of the stomach and duodenum were created. Transducers for EMA and impedance recording were fixed to the serous membrane of the antrum and duodenum. Labeled conductors were brought out through skin incision. One week after surgery activation of motility during feeding was recorded.

Pharmacological analysis of motility stimulation was carried out using intramuscular injections of ganglioblocker benzohexonium (0.7-2.0 mg/kg), purine blocker theophylline (20 mg/kg), 5-$HT_{1,2}$($S_{1,2}$)-receptor blockers sumatryptane (0.5-1.0 mg/kg) and spiperone (0.5-1.0 mg/kg) and 5-HT_3(S_3)-receptor blockers morphine (0.1-0.3 mg/kg), promedole (1-2 mg/kg), and droperidol (0.5-1.0 mg/kg) [1,2,4]. The involvement of ganglion and receptor formations in the realization of stimulation of the GIT motor activity was evaluated by the secretory and motor responses of GIT to the test drugs.

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

RESULTS

The duration of gastric motility activation after a single test feeding was 1.5 h. Pharmacological analysis (test feeding plus administration of one drug) took 30-40 min.

Feeding stimulated gastric EMA: the frequency and amplitude of the slow component increased.

Benzohexonium injection led to a negligible decrease of food-activated motility of the stomach (Table 1), while 1.5 h postinjection gastric EMA returned to the fasting level. Subsequent test feeding increased again the slow frequency component and EMA amplitude.

Injection of droperidol (5-HT_3-receptor blocker) completely blocked the studied phenomenon (Table 1).

Hence, injection of benzohexonium (ganglionic blocker) only slightly reduced food-stimulated moti-

TABLE 1. Gastric EMA after Alimentary Motility Activation in Rats under Conditions of Blocked Formations and Autonomic Nervous System Receptors (*M*±*m*)

Drug	Slow frequency component, per min		Amplitude, mV	
	without drugs	injection of test drug	without drugs	injection of test drug
Benzohexonium	6.2±0.9*	4.9±0.1$^+$	1.05±0.15*	0.60±0.13$^+$
Droperidol	6.00±1.12*	3.8±0.9$^+$	0.95±0.15*	0.5±0.1$^+$
Sumatryptine	6.6±1.4*	4.3±1.0$^+$	0.60±0.07	0.30±0.05$^+$
Spiperone	6.0±1.3	4.1±1.2	0.90±0.07	0.4±0.1$^+$

Note. Basal fasting level: frequency 4.2±1.1/min, amplitude 0.5±0.1 mV. Here and in Table 2: $p<0.05$: *compared to fasting level, $^+$compared to the corresponding parameter without treatment.

TABLE 2. Duodenal EMA during Food-Dependent Motility Activation in Rats under after Blockade of Autonomic Ganglia and Receptors (*M*±*m*)

Drug	Slow frequency component, per min		Fast potentials frequency, per min	
	without drugs	after injection	without drugs	after injection
Benzohexonium	35.9±2.2*	33.0±1.2	0.85±0.07*	0.60±0.09$^+$
Droperidol	36.9±1.3*	29.0±3.1$^+$	0.80±0.05*	0.14±0.01$^+$
Spiperone	36.5±1.4*	29.5±1.2$^+$	0.86±0.09*	0.57±0.05$^+$

Note. Fasting parameters: frequency 30.5±2.5/min, amplitude 0.57±0.10 mV.

lity, while droperidol (5-HT_3-receptor blocker) arrested it completely, but preserved basal EMA.

Possible involvement of 5-$HT_{1,2}$-receptors was studied in 12 experiments.

Sumatryptane (5-HT_1-receptor blocker) completely prevented the stimulating effect of food on gastric motility (Table 1). This means that activation of 5-HT_1-receptors plays the key role in activation of gastric alimentary motor activity.

Spiperone reduced slow frequency component of food-activated gastric EMA (Table 1). These data indicate that 5-HT_2-receptors of gastric smooth muscles play a less important role in activation of motor activity.

Feeding stimulated duodenal EMA: frequencies of both the slow component and fast potentials increased (Table 2).

Injection of benzohexonium slightly attenuated food-stimulated motility of the duodenum (Table 2). Duodenal EMA returned to the fasting level 1.5 h after injection of this drug. Subsequent test feeding again stimulated the slow component of duodenal EMA to 36.9±1.3/min. Subsequent injection of droperidol blocked the studied phenomenon: the frequency of the slow component and fast potentials decreased below the basal fasting level.

Hence, injection of benzohexonium only slightly reduced food-induced motility, while droperidol completely inhibited it without affecting basal EMA.

Sumatryptane completely abolished the effect of stimulation of duodenal motility. This indicates that activation of 5-HT_1-receptors plays the key role in activation of alimentary motility.

Spiperone decreased the frequency of the slow component of food-activated duodenal EMA to a fasting level (Table 2). These data indicate that 5-HT_2-receptors of duodenal smooth muscles play a less important role in activation of duodenal motility.

Hence, our results showed that neurons of autonomic ganglia carrying nicotinic and 5-HT_3-receptors are involved in the realization of stimulation of antral and duodenal food-activated motility. Serotoninergic neurons transmit the stimulating signal to 5-HT_2-receptors on effector cell. Hence, serotoninergic structures stimulate food-dependent activity of GIT, which is synergistic to the vagus nerve. Serotoninergic nerve fibers play the key role in this process, and 5-HT_1-receptors play the key role among effector serotonin receptors.

These data confirm the concept of V. M. Smirnov and S. F. Volyntseva (1995) that in addition to the sympathetic (adrenergic) and parasympathetic (cholinergic) compartments, the autonomic nervous system has a serotoninergic compartment, which exerts a potent stimulatory effect on the GIT motor activity.

Hence, our model based on the use a modified RG4-01 rheograph and drugs detects fine physiological mechanisms of the effects of autonomic nervous system compartments on the gastroduodenal contractile function during feeding.

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