EFFECT OF ACETYLCHOLINE, HISTAMINE, AND SEROTONIN ON MYOELECTRICAL ACTIVITY OF THE STOMACH AND SMALL INTESTINE IN WAKING DOGS

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Myoelectrical activity of the gastrointestinal tract, which lies at the basis of its motor function, is characterized by a proximal—distal gradient, which is manifested as the stronger activity of the proximal portions of the digestive tube compared with distal [2-5, 9]. A proximal—distal gradient of the distribution of physiologically active substances also has recently been found in the digestive tract. According to data in the literature [6, 7], for instance, acetylcholine (ACh) is present in highest concentrations in the jejunum, but serotonin (5-HT) in the duodenum and ileum; the distribution of histamine (HA) occupies an intermediate position between ACh and 5-HT. The effect of these physiologically active substances on the muscles of the gastrointestinal tract has been studied chiefly in isolated smooth-muscle strips [10-12].

The object of this investigation was to study the effect of ACh, HA, and 5-HT on myoelectrical activity of the different regions of the digestive tube in waking dogs.

EXPERIMENTAL METHOD

Altogether 72 experiments were carried out on four unanesthetized dogs weighing 18-24 kg. Silver loop electrodes (interelectrode distance 5-10 mm) were implanted into the smooth-muscle layer of the fundal and antral portions of the stomach, and the duodenum, jejunum, and ileum by the method described previously [8, 9]. The myoelectrical activity of the stomach and intestine was recorded on an Orion encephalograph. The catheter for introducing the substances was inserted into the external jugular vein. Acetylcholine chloride, histamine dihydrochloride, and serotonin creatinine-sulfate (from Gee Lawson Chemicals Ltd.), dissolved in 1 ml physiological saline, were injected intravenously. The doses of the drugs were calculated as weight of the compound. The substances were injected when no action potentials (APs) were being recorded. The number of evoked volleys of APs, their amplitude, the duration of the response, and the period of the basic electrical rhythm (BER) were analyzed. The statistical significance of differences between the means was determined according to the range of their variation at a 95% level [1].

EXPERIMENTAL RESULTS

Intravenous injection of each of the substances, ACh (0.1 mg/kg), HA (5 μg/kg), or 5-HT (5 μg/kg), caused the appearance of APs and an increase in the period of BER both in the stomach and in the intestine. The results are shown in Table 1 (fundal and antral portions of the stomach) and Table 2 (duodenum, jejunum, and ileum). It will be clear from Table 1 that the number of volleys of APs arising under the influence of ACh, HA, and 5-HT, and their amplitude were greater in the antral portion of the stomach than in the fundal portion. The duration of the responses and the period of BER also were greater in the antral portion. These differences were manifested more clearly after injection of HA and 5-HT. The number of volleys of APs, the duration of the reactions, and the period of BER all differed statistically significantly in the antral and fundal portions. The period of BER as a rule was the

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TABLE 1. Changes in Electrical Activity of Smooth Muscles of Fundal and Antral Portions of Stomach after Intravenous Injection of ACh, HA, and 5-HT into Waking Dogs (M ± m; n = 24)

Substance	Dose	Portion of stomach	Number of AP volleys	Amplitude of AP volleys, mV	Duration of response, sec	Period of BER, sec
ACh	0,1 mg/kg	Fundal	2,6±1,2	0,4±0,2	36,8±20,3	15,8±0,9
		Antral	3,3±1,3	0,8±0,4	56,6±16,4	21,9±1,4*
HA	5 μg/kg	Fundal	3,3±2,7	0,2±0,1	49,3±19,6	16,6±0,5
		Antral	8,8±3,6*	1,1±0,2*	144,0±35,2*	18,3±1,0*
5-HT	5 μg/kg	Fundal	3,7±0,7	0,4±0,1	80,5±16,8	17,2±0,5
		Antral	8,2±2,8*	0,6±0,3	140,7±10,8*	20,5±0,9*

*Differences statistically significant ($P < 0.05$) compared with values obtained when studying fundal portion.

TABLE 2. Changes in Electrical Activity of Smooth Muscles of Three Portions of Small Intestine after Intravenous Injection of ACh, HA, and 5-HT into Waking Dogs (M ± m; n = 24)

Substance	Dose	Portion of stomach	Number of AP volleys	Amplitude of AP volleys, mV	Duration of response, sec	Period of BER, sec
Ach	0,1 μg/kg	Duodenum	6,4±0,8	0,6±0,2	26,6±6,3	3,3±0,1
		Jejunum	4,8±0,7*	0,4±0,1	22,4±6,5	3,6±0,2
		Ileum	2,9±0,5*	0,3±0,1*	18,5±3,5	4,0±0,2*
HA	5 μg/kg	Duodenum	9,6±0,4	0,6±0,1	83,4±24,9	3,4±0,2
		Jejunum	13,0±1,1*	0,7±0,2	111,8±37,4	3,2±0,3
		Ileum	18,3±0,4*	0,6±0,1	169,6±53,5*	3,9±0,2*
5-HT	5 μg/kg	Duodenum	19,0±0,6	0,5±0,1	109,0±13,2	3,5±0,1
		Jejunum	15,3±1,2*	0,6±0,1	102,0±13,9	3,6±0,3
		Ileum	13,1±1,1*	0,2±0,1*	31,2±18,5*	4,3±0,2*

*Differences statistically significant ($P < 0.05$) compared with values obtained when studying duodenum.

same for the different parts of the stomach during periodic activity before administration of the drugs, and varied from 4 to 39 sec. Statistically significant differences between the fundal and antral portions of the stomach with respect to amplitude of AP volleys were observed in the experiments with HA.

The results indicate that the action of HA and 5-HT and, to a lesser degree, that of ACh on electrical activity of the muscles of the stomach, is more effective in its distal than in its proximal portion.

Table 2 shows that the number of AP volleys arising under the influence of ACh, HA, and 5-HT in the jejunum and ileum differed significantly from the number in the duodenum. In the experiments with ACh and 5-HT there was a decrease, but in the experiments with HA an increase in the value of this parameter in the proximal–distal direction. After administration of each drug the value of BER was greater in the ileum than in the duodenum, i.e., the proximal–distal gradient characteristic of periodic activity of the intestine was preserved when the period of BER in the ileum was greater (3.9-5.0 sec) than that in the duodenum (2.8-3.5 sec). Under the influence of HA and 5-HT the duration of the response of the ileum differed statistically significantly ($P < 0.05$) from this parameter for the duodenum. However, after administration of HA an increase was observed in the value of this parameter in the proximal–distal direction, but a decrease after administration of 5-HT.

The results indicate that ACh and 5-HT stimulate the proximal portion of the small intestine more actively, whereas HA activates its distal portion more strongly.

The difference observed between the effects of ACh, HA, and 5-HT in the proximal and distal portions of the stomach and intestine can be compared with the proximal–distal gradient of spontaneous muscular activity of these organs. This gradient is manifested [2-5] by the stronger activity of the proximal portions of the small intestine than of the distal portions. The effects of ACh and 5-HT in the experiments described above corresponded to the proximal–distal gradient of spontaneous activity of the small intestine: Responses of the small intestine to these drugs were stronger in its proximal portion. However, the action of ACh, HA, and 5-HT on electrical activity of the gastric muscles was stronger in the distal part of the stomach. The effect of HA on the smooth muscles both of the stomach and

of the intestine was greater in their distal portions. The selectivity of action of the drugs tested, with respect to myoelectrical activity in the proximal and distal portions of the stomach and intestine, revealed by these experiments may evidently be determined by the proximal–distal gradient of distribution of physiologically active substances [6, 7] in the digestive tract.

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