EFFECT OF SOME NEUROTROPIC DRUGS ON DIFFERENTIAL ENZYME SECRETION BY THE PANCREAS

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The basal secretion of the pancreas and the secretion stimulated by duodenal perfusion were investigated in chronic experiments on dogs. A protein digest stimulated pancreatic enzyme secretion to a greater degree than protein itself. Amobarbital, chlorpromazine, and benactyzine inhibit both basal and stimulated pancreatic secretion. The differential character of pancreatic secretion was disturbed most by chlorpromazine and benactyzine; this is evidence of the essential role of central adrenergic and cholinergic structures in the adaptation of pancreatic secretion to food stimuli.

KEY WORDS: pancreas; enzymes; periodic adaptation; neurotropic drugs.

Pavlov's concept of periodic adaptation of the enzyme-secretory function of the pancreas to the type of food stimulus has recently been confirmed experimentally [4-6, 8, 11, 12]. Analysis of the degree of differentiation of the pancreatic-secretory response to various food stimuli or to perfusion of the duodenum with various solutions has shown that the enzyme-secretory function of the pancreas depends on the qualitative composition of protein added to the hydrochloric acid solution in the duodenum or perfused through it under chronic experimental conditions [7, 8]. Indices of pancreatic secretion following administration of hydrochloric acid alone were significantly lower than those following administration of products of protein hydrolysis. The greatest differences in pancreatic secretion were observed in response to perfusion of the duodenum with protein and a polypeptide digest. This fact confirms the role of initial gastric hydrolysis of protein in the stimulation of pancreatic secretion and subsequent proteolysis [6] and it points to the existence of mechanisms for "comparing" substances entering the duodenum that ensure the fine differentiation of the pancreatic-secretory response.

In this investigation an attempt was made to analyze the central mechanisms of the differential response of the pancreas to perfusion of the duodenum with protein and with a polypeptide digest.

EXPERIMENTAL METHOD

Altogether 102 chronic experiments were carried out on 5 dogs with a duodenopancreatic fistula [9] and a jejunal fistula formed beyond Treitz's ligament. After determination of the half-hourly basal pancreatic (fasting) secretion, the duodenum was perfused for 2.5 h with a 3% solution of egg albumin or a polypeptide digest from it (in 0.2% hydrochloric acid) at the constant speed of 12 drops per minute (100 ml in 2.5 h). The polypeptide digest was obtained by adding 500 mg medicinal pepsin to 100 ml of a 3% solution of egg albumin and incubating the mixture for 18 h at 37°C. The content of amylase [11], and trypsin and chymotrypsin (from the results of spectrophotometric determination of amino acids formed during hydrolysis of casein) was investigated in the pancreatic juice, the volume of which was determined every 30 min in the course of 5 periods when the degree of differentiation of the pancreatic response to these stimuli had been established in control experiments, the effects of amobarbital (80 mg/kg, subcutaneously), chlorpromazine (2 mg/kg, intramuscularly), and benactyzine (0.3 mg/kg, intramuscularly), drugs with marked selectivity with respect to particular central synaptic contacts [1-3], were investigated. The basal secretion was

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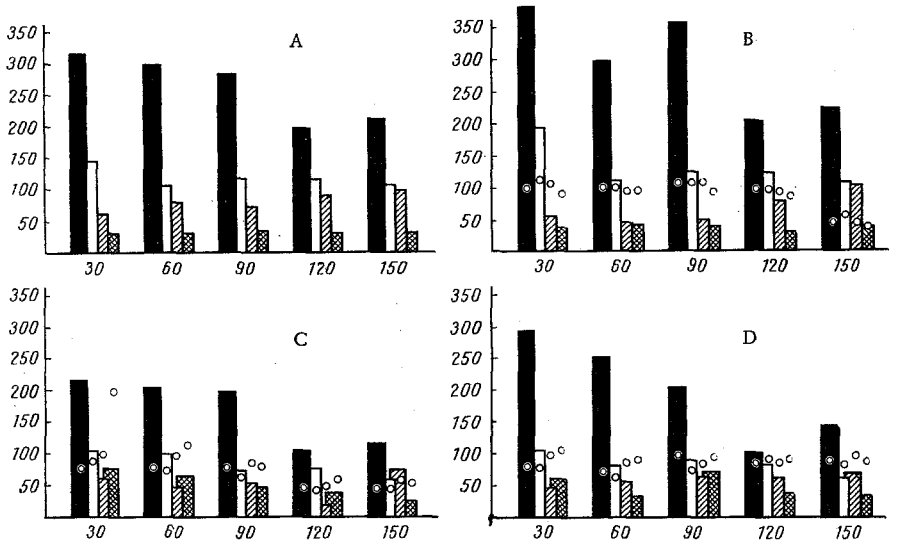

Fig. 1. Effect of amobarbital on pancreatic secretion stimulated by duodenal perfusion (dogs Ryzhik and Strelka). A) Volume of pancreatic secretion; B-D) content (circles) and secretion (columns) of amylase, trypsin, and chymotrypsin, respectively. Black and horizontally shaded columns show indices of pancreatic secretion during perfusion with polypeptide solution before and after administration of amobarbital, respectively. Abscissa, 30-min periods of experiment; ordinate, indices of pancreatic secretion (in % of basal secretion).

TABLE 1. Basal Pancreatic Secretion (in %) and Effect of Central Neurotropic Drugs on It (M ± m)

Drug	Number of experiments	Volume of secretion	Amylase		Trypsin		Chymotrypsin	
			1	2	1	2	1	2
Amobarbital	24	17,4±2,2	85,9±5,3	15,8±2,0	93,2±12,7	16,3±3,4	87,7±13,2	14,9±3,1
Chlorpromazine	44	50,5±5,3	92,2±7,0	54,1±9,7	97,6±10,2	50,5±9,6	97,1±9,6	60,4±8,6
Benactyzine	34	44,3±5,1	79,4±7,0	35,0±6,0	76,7±7,1	34,3±7,0	82,7±7,1	38,2±6,1

Note. Indices of basal secretion before administration of drugs taken as 100%; 1) mean content of enzyme in 1 ml secretion; 2) mean excretion of enzyme in 30 min.

determined again 30 min after administration of the drugs, and the duodenum was then perfused with a solution of egg albumin or a digest of it.

EXPERIMENTAL RESULTS

The volume of perfusion fluid flowing from the intestine (irrespective of the solution injected) was reduced by amobarbital, chlorpromazine, and benactyzine approximately by half. All the neurotropic drugs used reduced the basal secretion of the pancreas on account of a sharp decrease in the volume of juice secreted; the enzyme content in the secretion was virtually unchanged (Table 1).

Under the influence of amobarbital the external secretory activity of the pancreas stimulated by both food stimuli decreased sharply (Fig. 1). Although in some periods the differentiation of enzyme secretion was reduced, in others differentiation between the stimuli with respect to volumes of secretion and amylase production was preserved. At the end of the experiments differentiation between stimuli for excretion of trypsin and chymotrypsin was restored.

The external secretory activity of the pancreas, when stimulated by duodenal perfusion with polypeptide digest, was significantly reduced by chlorpromazine. The differential response of pancreatic secretion to the action of the two stimuli was completely disturbed in this series of experiments and it was often paradoxical in character (Fig. 2). This was shown by the greater secretion of enzymes in response to the action of the weaker stimulus (protein).

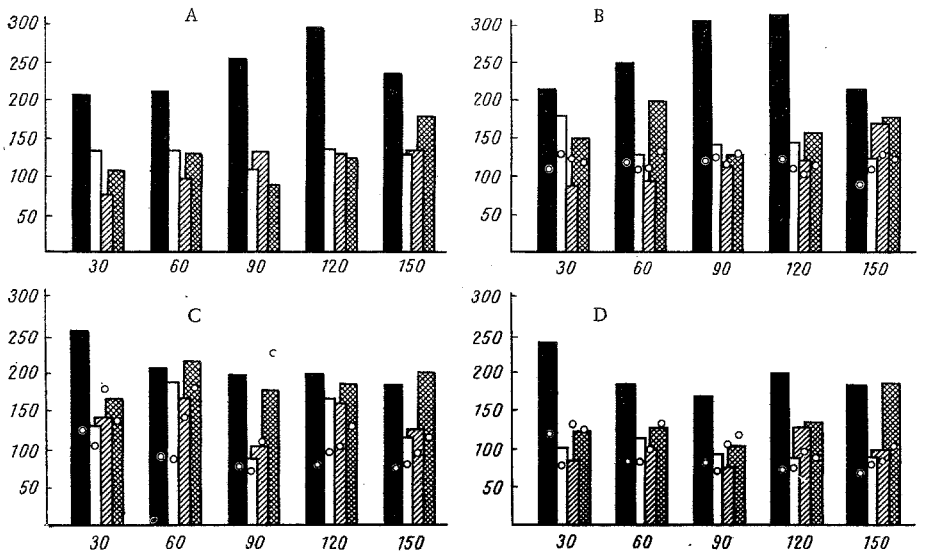

Fig. 2. Effect of chlorpromazine on pancreatic secretion stimulated by duodenal perfusion (dogs Ryzhik, Kutsyi, Dzhek). Legend as in Fig. 1.

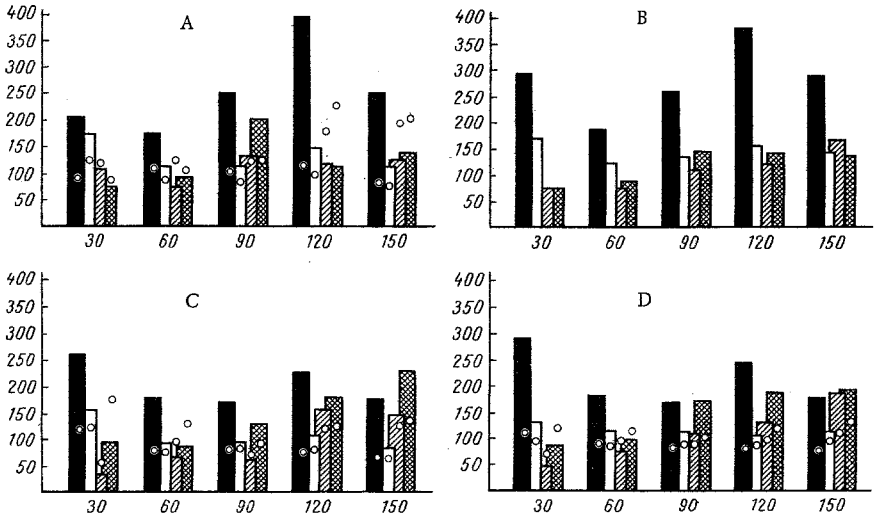

Fig. 3. Effect of benactyzine on pancreatic secretion stimulated by duodenal perfusion (dogs Laska and Kutsyi). A) Content (circles) and secretion (columns) of amylase, trypsin, and chymotrypsin, respectively. Remainder of legend as in Fig. 1.

Benactyzine disturbed the differential character of external secretory activity of the pancreas similarly to the result observed in the experiments with chlorpromazine (Fig. 3).

Central neurotropic drugs thus significantly affect the external secretory function of the pancreas and reduce secretion of both juice and enzymes. Disturbance of the differential character of enzyme secretion in response to perfusion of the duodenum with protein and polypeptide digest under the influence of chlorpromazine and benactyzine demonstrates the important role of central adrenergic and cholinergic structures in the regulation of the effectiveness of hydrolysis of nutrient substances and of the activity of the pancreas.

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