MORPHOLOGICAL AND FUNCTIONAL STATE OF THE CHOLINERGIC INNERVATION OF THE RAT PANCREAS AFTER VAGOTOMY

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The cholinergic innervation of the pancreas was studied in normal albino rats and after bilateral subdiaphragmatic vagotomy (1, 3, 7, and 21 days and 2 months after the operation). Cholinergic nerve fibers in the control rats were found in all structures of the organ, in both the vascular system and the system of glands and ducts. Vagotomy led to a brief increase in the number of detectable nerve fibers toward the end of the first day, followed by a decrease on the seventh day. After 2 months the number of detectable nerve fibers was close to its initial level.

KEY WORDS: pancreas; cholinergic nerve fibers; vagotomy.

Disconnection of organs from the CNS does not result in the cessation of their function. For instance, a disturbance of innervation of the pancreas does not change the ability of that organ to respond to a specific (food) stimulus and does not render the organ incapable of regeneration. However, the marked disturbances of metabolism of the acinar cells that arise under those conditions, accompanied by destructive changes in their organelles, disturb the normal functioning of the organ [2, 3]. Nevertheless, there is little information in the literature about the relative morphological and functional state of the nervous structures of the pancreas when its innervation is disturbed, although this apsect of the problem is of undoubted interest as a method of obtaining a closer insight into the pathology of the changes arising in organs on denervation.

With the above considerations in mind it was decided to study the degree of participation of the parasympathetic component of the autonomic nervous system in the innervation of the pancreas in albino rats under normal conditions and also to study the response of the nervous structures of the pancreas to a disturbance of vagal innervation.

EXPERIMENTAL METHOD

Male albino rats were used. Series I consisted of animals kept under ordinary conditions (control), series II of rats studied 1, 3, 7, and 21 days and 2 months after bilateral subdiaphragmatic vagotomy (experiment). Six animals were chosen at each time. Cholinesterase activity was detected in the pancreas of both series of animals by means of Karnovsky's thiocholine method. For quantitative analysis the number of nerve fibers in 1 mm^2 was counted. The results were subjected to statistical analysis by the Fisher–Student method.

EXPERIMENTAL RESULTS

Cholinergic nerve fibers were discovered in all structures of the pancreas. As components of large and small nerve trunks they were found in the interlobular connective tissue. Nerve fibers were fairly numerous in the walls of the interlobular ducts. In the ducts of small diameter they penetrated into all layers

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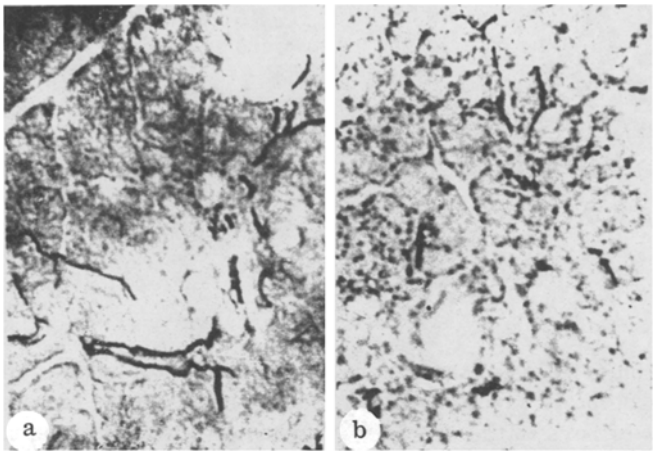

Fig. 1. Cholinergic nerve fibers in parenchyma of lobule of rat pancreas: a) cholinergic nerve fibers in parenchyma of lobule of control rat; b) fewer cholinergic nerve fibers can be seen in parenchyma of pancreatic lobule of rat 7 days after vagotomy.

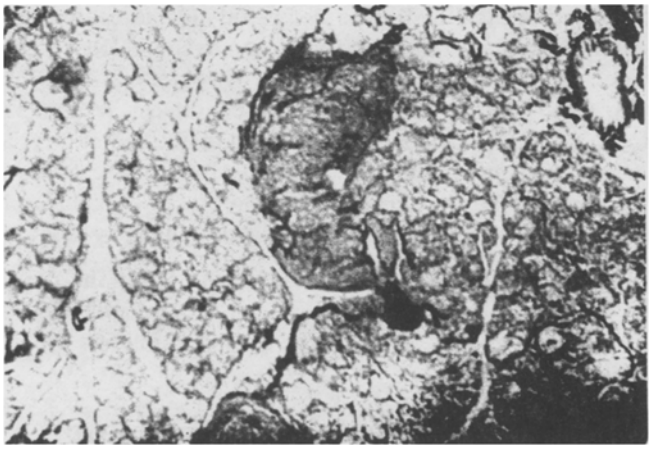

Fig. 2. Cholinergic nerve fibers surrounding pancreatic islet of control rat. Karnovsky's method, 140×.

of the wall as far as the epithelium, but in large nerve fibers they were arranged as a network mainly in the outer coat, penetrating deeply into the muscular coat. Nerve fibers in the walls of blood vessels formed plexuses on the boundary between the outer and inner layers. In the interacinar space, in the immediate vicinity of the gland cells, only solitary, thin nerve filaments with uneven edges were detected (Fig. 1a). A very frequent finding was for a single fiber to surround an acinus, and then to leave it, continuing thus along a series of acini located side by side.

Highest enzyme activity was discovered in the intramural nerve ganglia; in nerve trunks surrounding a ganglion it was higher than in the nerve cell bodies. Depending on the functional state of the nerve cells, activity of the enzyme in them varied. The number of neurons in the intramural ganglia varied from two to eight to ten. Nerve ganglia were located in the interlobular connective tissue, less frequently in the parenchyma. Around the pancreatic islands nerve fibers formed a peripheral plexus and they penetrated along with blood vessels into the interior of the islet (Fig. 2).

Analysis of the state of the pancreatic nervous system of rats after bilateral subdiaphragmatic vagotomy showed that initially (first day after the operation) the number of nerve fibers detected in the parenchyma of the lobule increased appreciably (normal 23.0 ± 3.4, experiment 44.0 ± 3.1; $P < 0.002$), but after the third and, in particular, by the seventh day after the operation, it was reduced (normal 23.0 ± 3.4, seventh day of experiment 13.0 ± 1.1; $P < 0.001$) (Fig. 1b). By the 21st day and, in particular, toward the 2nd month the number of nerve fibers discovered returned to normal (Fig. 3).

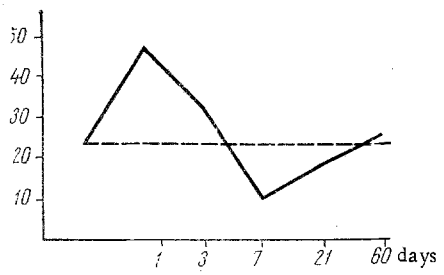

Fig. 3. Dynamics of changes in number of nerve fibers discovered at different times after operation. Abscissa, time after operation; ordinate, number of cholinergic nerve fibers, expressed in absolute units.

The results of this investigation thus showed that the pancreas in rats has a well-marked cholinergic innervation of all its structural components, both in the system of glands and ducts, and in the vascular system. In this respect the results agree fully with data in the literature. As regards innervation of the pancreatic islets, there is no general agreement regarding innervation of the A and B cells. According to some observations, the A cells have an adrenergic innervation and the B cells cholinergic [5, 10]. Other workers consider that both A and B cells are innervated by cholinergic nerve fibers [9].

It can be concluded from the observation of a network of cholinergic nerve fibers at the periphery and in the center of the pancreatic islet in these experiments that, considering the topography of the A and B cells, cholinergic nerve fibers innervate not only the B cells.

Changes in the number of cholinergic nerve fibers discovered at different times (from 1 day to 2 months) after bilateral subdiaphragmatic vagotomy are of the utmost interest. The increase found in the number of functionally active nerve fibers 24 h after the operation can perhaps be regarded as the response of the pancreatic nervous system to an increasing quantity of acetylcholine. The increase in the quantity of mediator can be explained, first, by the stress reaction during which large quantities of acetylcholine enter the tissue from the nerve endings and, second, by destruction of cholinergic synapses [1]. Side by side with the increased quantity of acetylcholine, activity of cholinesterase, the enzyme hydrolyzing it, also increases.

There is no general agreement on the character of the changes in cholinesterase activity during the first days after denervation. There is some evidence [7] of a decrease in activity of the enzyme after parasympathetic denervation, but more recent investigations, on the other hand, revealed an increase in its activity [1, 6].

The decrease in the number of detectable nerve fibers started on the third day and intensified toward the seventh day. This could be in consequence of a reduction in cholinesterase activity in the nerve fibers associated both with degeneration of the preganglionic fibers following their division [6, 8], and a decrease in the quantity of acetylcholine in the postganglionic elements of the intramural apparatus of the gland. The quantity of acetylcholine present in the postganglionic elements is known to depend on the degree of its accumulation in the preganglionic structures [8]. It has also been found that labeled protein is transported across synapses in the CNS [4]. On the basis of these observations, it has been suggested [8] that preganglionic elements have a constant trophic action on postganglionic structures, controlling their metabolism. It can accordingly be concluded that vagotomy leads to a disturbance of the trophic influence of the preganglionic nerve fibers on nerve cells of the intramural ganglia of the pancreas. This disturbance is expressed as the development of transneuronal degeneration. This state is manifested as a change in metabolism of the nerve cell, which is probably reflected in the synthesis of acetylcholine and the activity of the enzymes of its synthesis and hydrolysis.

The decrease in the number of nerve fibers detectable on the seventh day after vagotomy can thus be regarded not only as the result of degeneration of the preganglionic nerve fibers, but also as the result of a decrease in enzyme activity in the intramural nervous structures of the gland.

The increase in the number of detectable nerve fibers observed after the 21st day, however, suggests, first, the development of compensatory or adaptive structural changes in the preserved intramural apparatus of the pancreas and, second, the possibility of regeneration of preganglionic nerve fibers. At the same time, the presence of other sources of cholinergic innervation of the pancreas cannot be ruled out.

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