EFFECT OF VAGOTOMY ON PERMEABILITY PROCESSES IN STRUCTURAL COMPONENTS OF THE RAT LIVER

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By intravital fluorescence microscopy the permeability of structural components of the rat liver for fluorescein sodium was studied 7, 21, and 60 days after bilateral subdiaphragmatic vagotomy. It was shown that vagotomy causes increased permeability both of the microvessels of the liver and of the plasma membrane of the hepatocytes. In the later stages the times of appearance of fluorescein in the liver cells and of its elimination therefrom return to the initial levels.

KEY WORDS: vagotomy; liver; permeability; intravital microscopy.

Only a few papers have been published on the role of the nervous factor in changes in the permeability of the tissue-blood barrier [5, 6, 8]. Disturbance of innervation causes a series of morphological and functional reorganizations, and an important role in their development is played by changes in the permeability of the structural components of the organ, which can be revealed by the use of special methods of investigation.

The object of this study was to examine the effect of subdiaphragmatic vagotomy on the rate of passage of sodium fluorescein through the blood-parenchymatous barrier of the liver, by the use of intravital luminescence microscopy.

EXPERIMENTAL METHOD

Experiments were carried out on male albino rats weighing 180-230 g. Under ether anesthesia bilateral subdiaphragmatic vagotomy was performed on the experimental animals. The animals were investigated in a fasting state under pentobarbital anesthesia, 7, 21, and 60 days after the operation. Ten vagotomized and five control rats were used at each time. Autofluorescence of the liver was first tested under the MLD-1 fluorescence microscope with the aid of contact objectives, and later, after intravenous injection of sodium fluorescein (in a concentration of 2 mg/100 g body weight in 2% physiological saline) the stages of passage of the fluorescent solutions through the structures of the organ were recorded with a stopwatch. Throughout the experiment, conditions for the animal were maintained as physiological as possible. The results were subjected to statistical analysis.

EXPERIMENTAL RESULTS

The study of autofluorescence of the liver in the control animals revealed pale green fluorescence of the liver trabeculae, which were clearly outlined by the dark sinusoidal capillaries. In some animals stellate cells were seen (these gave the brightest fluorescence in the period when sodium fluorescein was found in the liver sinusoids). After intravenous injection of the fluorescent solutions its appearance could be detected initially in the interlobular vessels of the liver (Fig. 1), but later (after 4-5 sec) the sinusoidal capillaries began to fluoresce, whereas the hepatic trabeculae preserved only weak primary luminescence, so that they appeared much darker than the microvessels of the liver lobules. The liver cells began to fluoresce 40 sec after injection of the solution, whereas the blood vessels were free from the fluorescent substance. Filling of the hepatocytes in the lobule took place at different times: Cells at the periphery of the lobule began to fluoresce first, and those in the central part not until 6-8 min later. A certain number of hepatic lobules, incidentally, began to fluoresce later, so that side by side with a lobule filled with sodium fluorescein, a lobule preserving its autofluorescence could be observed. Fluorescence

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TABLE 1. Time Indices of Passage of Sodium Fluorescein Through Structural Components of Rat Liver Under Normal Conditions and After Vagotomy (M ± m)

Group of animals	No. of observations	Final appearance of sodium fluorescein in liver cells, sec	Time of elimination of sodium fluorescein from liver cells, min
Control	15	40,2±2,3	93,2±2,9
After vagotomy			
7 days	10	15,3±1,2	50,8±2,9
P		<0,001	<0,001
21 days	10	16,1±1,9	46,9±1,7
P		<0,001	<0,001
60 days	10	42,7±1,7	88,5±3,9
P		>0,05	>0,05

appeared in the bile capillaries after 8 min. Initially they appeared as brightly fluorescent dots, located along the central axial line of the hepatic trabeculae, and subsequently changing into thread-like formations. Under high power a construction resembling a honeycomb appeared (Fig. 2). The accumulation of sodium fluorescein and its excretion from the bile capillaries took place at different times. Whereas in some capillaries fluorescence became weaker so that the capillaries ceased to be visible, in other capillaries bright fluorescence appeared. The liver lobules lost their secondary luminescence 1.5 h after injection of the fluorescent solution.

Changes in the structure of the hepatic lobules appeared during autofluorescence both 7 and 21 days after the operation. The pattern of the hepatic tissue was blurred and the

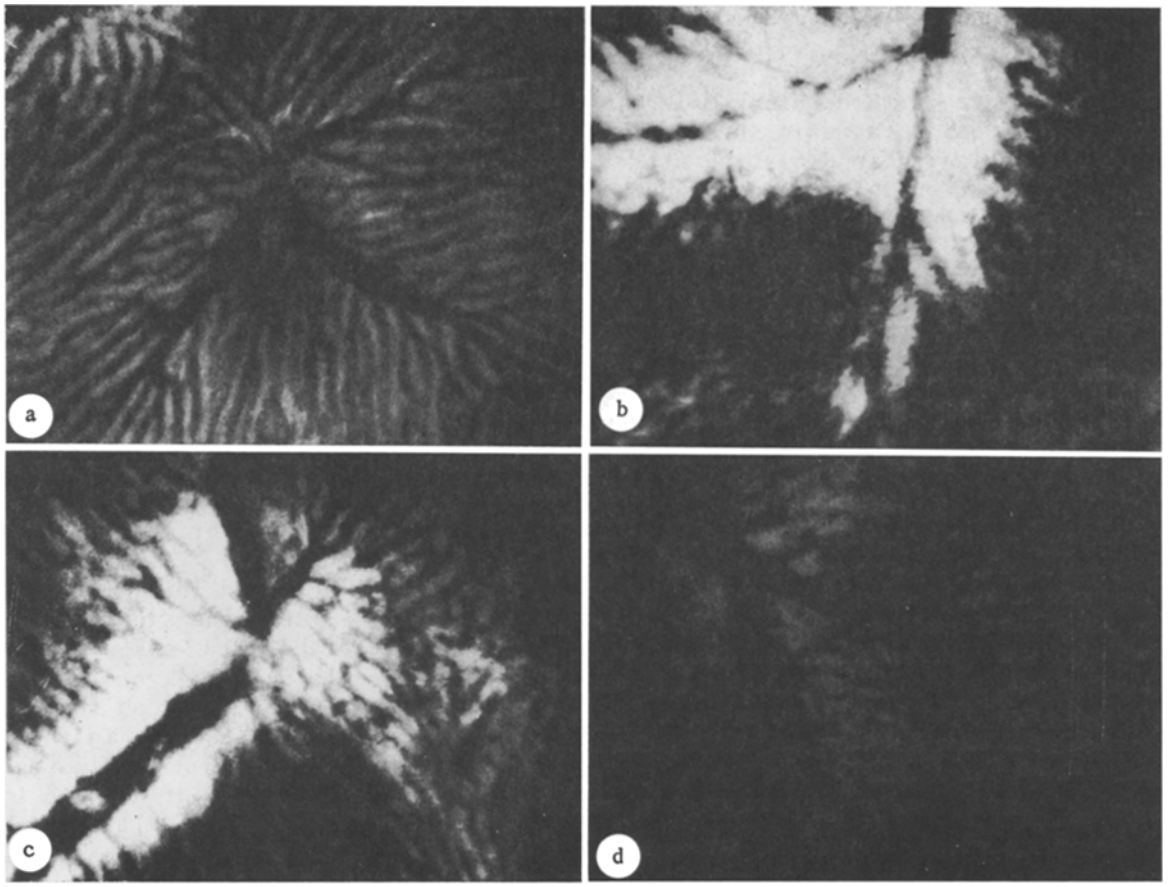

Fig. 1. Interlobular vessels of the liver (20 sec after injection of sodium fluorescein). a) Control; b, c, d) 7, 21, and 60 days respectively after vagotomy. Objective 25.

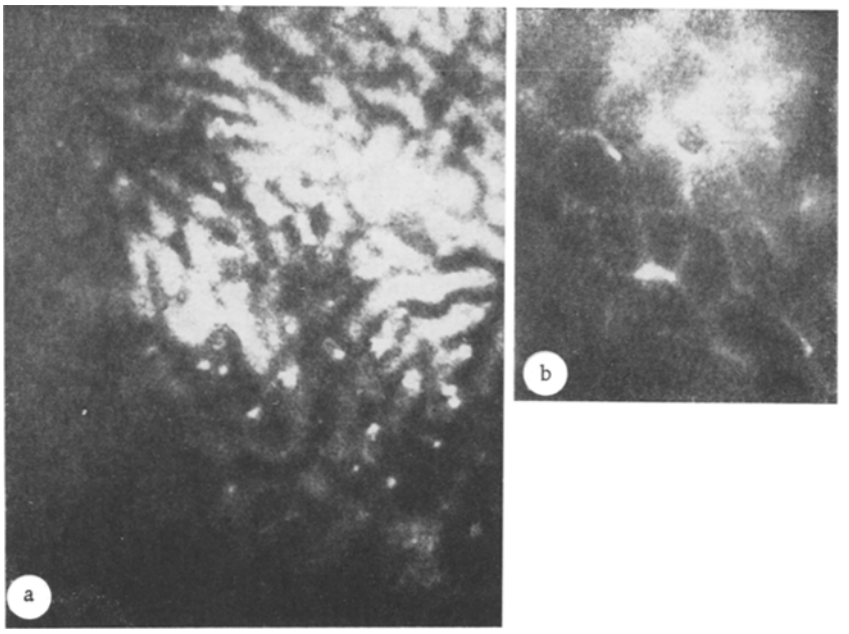

Fig. 2. Filling of bile capillaries with fluorescent material (control). a) 8 min after injection of sodium fluorescein (objective 25); b) 10 min after injection of sodium fluorescein (objective 60).

trabeculae were poorly outlined. It follows from the results given in Table 1 that the liver cells after vagotomy were filled with fluorescent solution earlier, as a result of the more rapid passage of the sodium fluorescein through the wall of the microvessels and the membrane of the hepatocytes. It must be emphasized that in the period indicated above individual areas with uneven, blurred outlines, completely without fluorescence, were seen in the liver tissue. The accumulation of sodium fluorescein in the bile capillaries of the vagotomized animals also took place sooner, and it was eliminated much faster than in the control animals. The liver lobules lost their fluorescence after 40-50 min.

The time of passage of the fluorescent solution through the structural components of the liver in the experimental animals at all stages 60 days after subdiaphragmatic vagotomy differed very little from the control.

By means of this function test it was thus possible to obtain information on the activity of the liver under normal conditions and when its innervation is disturbed. When the mechanism of the increased permeability of the tissue-blood barrier after denervation are examined, not only the direct effect of the nervous components of the structure of the liver, but also the indirect effect through physiologically active substances, whose content and activity vary considerably when nervous connections are disturbed [3, 4, 9, 10], must definitely be taken into account. It has also been shown [2, 7] that after vagotomy the blood vessels in the liver dilate and stasis develops, and this has a corresponding effect on the development of tissue hypoxia in the organ. These and other processes may probably be reflected in the permeability of the tissue-parenchymatous barrier. Under the fluorescence microscope, changes in the configuration of the sinusoidal capillaries also were found, together with the appearance of considerable fusiform dilation along the whole of their length in the liver of the vagotomized animals. Furthermore, 21 days after the operation in some cases a tortuous network of blood capillaries could be seen on the surface of the liver capsule, and its appearance can evidently be interpreted as the formation of new blood vessels. Under such conditions there is no doubt that the circulation of sodium fluorescein through the microvessels of the liver is considerably modified. At a later period (60 days after the operation) signs of compensation began to develop, as shown by the return of the time indices to their initial level. The asynchrony observed in the activity of liver lobules [1] and observed in the present experiments in the control animals was also maintained in the vagotomized animals, although it was less marked.

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THE HEMODYNAMIC COMPONENT OF COMPENSATION IN THE BRAIN AFTER UNILATERAL BLOCKING OF THE SOMATOSENSORY CORTEX

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In experiments on anesthetized and waking cats the dynamics of the cerebral blood flow was investigated by a thermoelectric method in one hemisphere during experimental injury to the somatosensory area of the opposite hemisphere. Temporary cold blocking of this area of the cortex gives rise to definite hemodynamic disturbances in the opposite hemisphere, namely a biphasic vascular response: an initial decrease in the blood supply followed by a long after-effect of an increase in the blood flow. Similar vascular responses also were observed after unilateral extirpation of the somatosensory cortex. Vascular responses of this type are evidence of increased activity of the cortical structures in the intact hemisphere and can be regarded as a compensatory response to local injury of particular areas of the cortex.

KEY WORDS: thermoelectric method; dynamics of the cerebral blood flow; somatosensory cortex.

Reactive brain changes to pathological effects arising as a result of head injuries, brain tumors, or neurosurgical operations are constantly being observed in clinical practice. Experimental and clinical observations over a period of many years have yielded convincing evidence that after injury to cortical structures the disturbed integrative activity of the brain gradually recovers [1, 4, 5, 8, 9]. To analyze the dynamics of these compensatory reactions it is useful to study interhemispheric relations in patients with lesions affecting only one hemisphere. For instance, in patients with tumors of this localization definite changes in brain function were discovered in both the affected and the intact hemispheres [2, 6, 7]. Inactivation of the cells of the affected hemisphere was shown to be accompanied by desynchronization and activation of the EEG in the symmetrical region of the opposite hemisphere. This enhancement of functional activity is regarded as a manifestation of replacement and compensatory processes. Considering the close correlation between the functions of the brain and its blood supply, it can tentatively be suggested that an essential factor in the recovery process must be hemodynamic shifts arising in response to a disturbance of brain function.

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