CHARACTER OF SPIKE DISCHARGES OF LIVER MECHANORECEPTORS ON CESSATION OF VENOUS OUTFLOW FROM THE HEPATIC VEINS

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The role of the liver receptors in the regulation of the volume of the body fluids has never been specially studied, although clinical [1] and experimental [5-7] investigations established the influence of the liver on water diuresis and on kidney function a long time ago. Liang [5], for instance, showed that elevation of the venous pressure in the portal vein of the liver soon causes an increase in diuresis in dogs, and he suggested that the response is by nature a nervous reflex. This suggestion was confirmed in experiments by another worker [7], who observed a decrease in the frequency of efferent impulses in fibers of the renal and adrenal nerves in rabbits in response to an increase in mesenteric venous pressure and during occlusion of the portal vein. The present writer found [3, 4] that many mechanoreceptors, differing both in the pattern of their spontaneous spike activity and in the specific nature of their responses to an increase in the volume of the portal blood flow, are present in the cat liver and may play an important role in the regulation of the extracellular fluid volume. Besides physiological fluctuations in the intravascular fluid volume of the liver, associated with the intake of food and water, when the venous inflow is increased, a considerable increase in its intravascular volume also is observed when the venous outflow from the liver is retarded or stopped, as may often be found in various forms of pathology.

The pathogenesis of disturbances of water and electrolyte homeostasis in such pathological situations has not been adequately explained. The study of spike discharges of liver mechanoreceptors when the outflow of blood from the hepatic veins has ceased is accordingly of considerable interest.

EXPERIMENTAL METHOD

Characteristics of 15 mechanoreceptor units of the liver in 10 cats anesthetized by intravenous injection of pentobarbital (30-40 mg/kg), were studied before and after complete interruption of the blood flow from the hepatic vein. Besides introduction of a catheter into the portal vein and separation of the trunks of the hepatic nerve plexus into thin branches, the preparatory operation also included superdiaphragmatic thoracotomy to obtain access to the hepatic vein. After thoracotomy the animals were artificially ventilated.

To record spike activity bipolar platinum electrodes and the necessary combination of amplifiers and recording system were used. Primary recording of spikes during the experiment was carried out on magnetic tape and motion picture film. The records on magnetic tape were analyzed after the experiment (for details of the method see [2-4]). The modality of the fiber was first determined experimentally. If the fiber conveyed impulses from mechanoreceptors, its spontaneous activity and its response to an increase in intraportal volume were recorded, after which a flexible clip was applied to the hepatic veins so that the outflow of blood was completely stopped. The clip was kept in situ for 7-21 min in different experiments. Throughout this time and after removal of the clip until the original level of unit activity had been restored, the spike discharges were recorded continuously.

EXPERIMENTAL RESULTS

Seven of the 15 units studied had no initial spontaneous activity; the rest had an irregular discharge with a frequency of 0.5-3 spikes/10 sec (Fig. 1a) to 51-72 spikes/10 sec (Fig. 2a). During infusion of physiological

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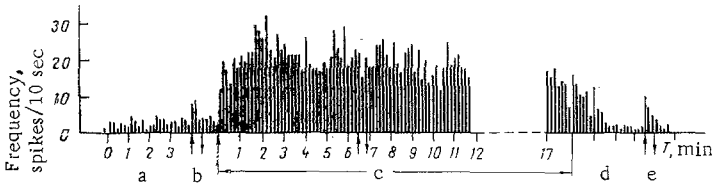

Fig. 1. Activity of a mechanoreceptor unit before and after cessation of venous outflow from liver. a) Initial spontaneous activity; b) response to injection of 3 ml physiological saline into portal vein at the rate of 0.14 ml/sec (here and subsequently small arrows indicate beginning and end of infusion); c) increase in activity after interruption of outflow of blood from hepatic veins (large arrows here and in Fig. 2 indicate times of application and removal of clip) and absence of response to injection of same volume of physiological saline (indicated by small arrows); d) restoration of initial level of spontaneous activity after removal of clip; e) response to injection of physiological saline.

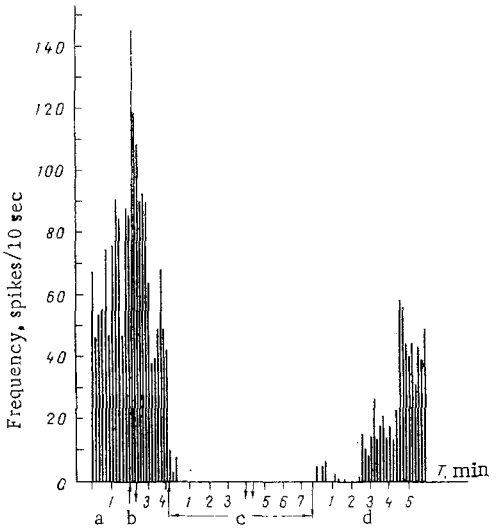

Fig. 2. Activity of a mechanoreceptor unit with higher initial activity before and after interruption of venous outflow from liver. a) Initial spontaneous activity; b) response to injection of 2.5 ml physiological saline into portal circulation at the rate of 0.12 ml/sec; c) inhibition of activity after application of clip to hepatic veins and absence of response to injection of the same volume of physiological saline; d) restoration of initial level of activity after removal of clip.

saline into the portal circulation at the rate of over 0.1 ml/sec all these units generated a steady discharge, the frequency of which depended directly on the rate of injection of the solution (Figs. 1b and 2b). As regards the character of their responses these units did not differ from those investigated previously [3], which belonged both to the spontaneously "silent" group and to the group with irregular activity.

For several seconds after application of the clip to the hepatic veins, the spontaneous activity changed in up to 10 units. These changes were not all of the same type: In five units which had no initial spontaneous activity, discharges appeared immediately – in two of them with maximal frequency (24.44 spikes/10 sec), but

in the rest the discharge frequency increased gradually and reached a peak 2-6 min after application of the clip. A similar increase in spontaneous discharge frequency occurred also in two units with low initial activity (Fig. 1c). In three units with higher initial activity (51-72 spikes/10 sec) changes of an opposite kind were observed in the discharge. The discharge frequency of these units fell sharply immediately after interruption of the outflow of blood to between 7 and 3 spikes/10 sec, and after 0.5-1 min they completely stopped generating spikes (Fig. 2c). The remaining five units changed their firing pattern not immediately, but 2-4 min after application of the clip. Their discharge frequency increased gradually to reach a maximum after 6-8 min. The changes in unit activity described above continued throughout the period of interruption of blood flow.

However, in five experiments the discharge frequency fell a little after reaching its maximum. Longer observations (18-21 min) showed that the decrease in discharge frequency was not due to worsening of the functional state of the receptors, but rather was connected with their adaptation to the action of steady stretching, for after this decrease, the discharge remained at a constant level for as long as desired (Fig. 1c). It can also be concluded from these observations that receptor units responding to interruption of the blood flow by an increase in spike activity belong to the slowly adapting type. Meanwhile the response to injection of physiological saline into the portal vein after interruption of the outflow of blood was absent in all units (Figs. 1 and 2).

After removal of the clip, discharges of the units returned to their initial level (Figs. 1d and 2d). It is interesting to note that five units responded to removal of the clips by a considerable increase in discharge frequency; in two units this increase was observed for only a short time (1-2 min), but in the rest it continued for 8 min, after which the firing pattern of these units resumed its initial spontaneous level which existed at the beginning of the experiment. After recovery of their initial activity the units began to respond to an increase in volume of the portal blood flow (Fig. 1e).

These experiments thus showed that when the outflow of blood from the hepatic veins is interrupted and the intravascular fluid volume in the liver rises sharply, the discharge from mechanoreceptors changes significantly and the response to an increase in fluid volume in the system of the portal vein disappears. Such changes in liver mechanoreceptor activity may probably also take place under pathological conditions causing a disturbance of the normal venous outflow from the organ, and such considerable changes in afferent impulsation may in turn lead to a disturbance of regulatory processes in the system of water and electrolyte homeostasis. Clinical observations [1], showing a decrease in sodium excretion, in the osmolarity of the urine, and in the clearance of osmotically free water during cirrhosis of the liver accompanied by considerable portal hypertension, confirms this suggestion.

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