EFFECTS OF CHANGES IN THE FUNCTIONAL STATE OF THE CEREBRAL CORTEX ON SECRETION OF BILE

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It has been shown by a number of authors that the bile-secreting function of the liver is affected by changes in the functional state of the cerebral cortex. This observation is supported by the findings of a number of workers [2, 4], showing the existence of conditioned reflex stimulation of secretion of bile. According to the findings of other authors [1, 3, 5], alterations in bile secretion may be encountered during elaboration of conditioned salivary reflexes in animals, by Pavlov's classical procedures.

In all the above researches, however, only the amount of bile secreted was measured. Insufficient work has been done on alterations in its chemical composition.

The present paper deals chiefly with the effects of alterations in the functional state of the cerebral cortex on biliary secretion of bilirubin.

EXPERIMENTAL METHODS

Our experiments were performed on three dogs with gall bladder fistulae, and with parotid gland fistulae opening to the outside. In addition, the common bile duct of one of the dogs was ligated.

The conditioned reflex activity of the dogs was studied by Pavlov's classical methods, parallel with the study of bile secretion. Before proceeding to the elaboration of conditioned reflexes in the dogs, we investigated the effect on bile secretion in two dogs of introducing hydrochloric acid into the mouth. After this, we developed a conditioned defensive reflex to acid, and followed this by differentiation to it. The conditioned reflex stimulus (the sound of a metronome in one case, and of a siren in the others) was applied during the first half-hour of each experiment.

After these experiments had been completed, we investigated the effects of perturbations of higher nervous activity. These were produced: a) by evoking "confusion," by applying a positive stimulus immediately after a negative one; b) by considerable prolongation of the time of isolated action of the conditioning stimulus; c) by changing the signal significiance of the stimuli.

In each 4-hour portion of bile collected we determined the dry content and the bilirubin content (by the van den Bergh method). In addition, we calculated the total bilirubin content of the bile and of its dry content. Fasting animals were used in all the experiments.

EXPERIMENTAL RESULTS

We could not find any sufficiently noteworthy differences between the results of the experiments in which we determined the background levels and of those in which we tested the effect of hydrochloric acid. The results showed that considerable random fluctuations in the magnitudes of the volumes of bile secreted and in its bilirubin content took place, both during the course of a single experiment, and from experiment to experiment. Thus, the bilirubin content found during an experiment varied by over 100 mg% (Figure 1). In a considerable proportion of the experiments diminution in secretion of bile coincided with increase in its bilirubin concentration, and with diminution in the absolute amount of bilirubin secreted. Only by comparing the mean values derived for each series were we able to note a certain fall in the volume of bile secreted, with a corresponding rise in its bilirubin content, for the "acid" series. Thus, in the dog Sharik, the amount of bile fell during an experiment from 30.3 to 25.5 ml, and in Glazun from 23.4 to 18.5 ml.

The process of elaboration of a conditioned reflex was associated with increased production of bile, in all the animals. In contrast to the preceding experiments, the amount of bile secreted by Kutsyi rose by an average

of 6.4 ml, by Sharik by 8.4 ml, and by Glazun by 10 ml. There was at the same time a pronounced fall in the concentration of bilirubin in the bile. The most significant result of this series of experiments is, in our view, the considerable change in the course of secretion of bile. There was a marked fall in the amplitude of the variations in the volume of bile secreted and in its bilirubin content, and this applied not only to a given experiment, but also to the whole series. The effect noted was thus of the nature of a stabilization of biliary secretion (Figure 2).

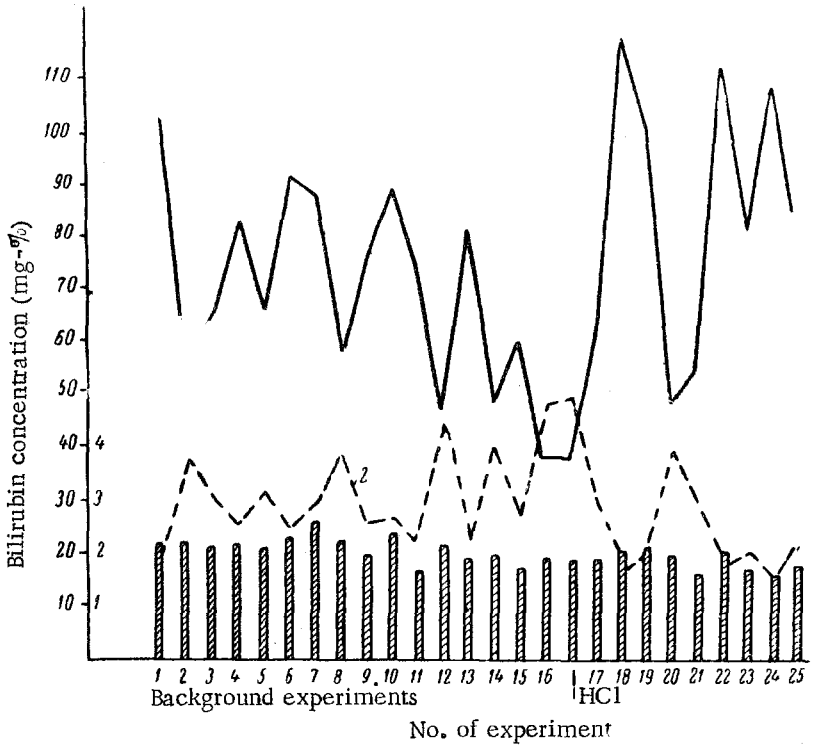

Fig. 1. Absolute amount of bilirubin, and its concentration in bile secreted by the dog Sharik (background experiments, and experiments on the action of hydrochloric acid by itself). 1) Concentration of bilirubin; 2) volume of bile secreted during the experiment; vertical columns: amount of bilirubin, in mg for each experiment.

We consider the increase in the amount of bile secreted, as well as the alteration in the nature of the process, to be results of the formation of a stable temporal link in the cerebral cortex. This view is supported by the observation that these changes in the magnitude and the nature of the biliary secretion become evident only after the given reflex has become firmly established. Moreover, the stabilization of bile secretion persists only as long as the conditioned stimuli are systematically applied. Interruption of the experiments was followed by violent and disorderly fluctuations in the volume of bile secreted, and in its bilirubin concentration, such as were observed in the "background" experiments.

The elaboration and establishment of differentiation of already existing conditioned reflexes had no perceptible effect on secretion of bile. Only during the first days of application of differentiating stimuli did we observe any more pronounced fluctuations in the volume of bile secreted, and in its bilirubin concentration. As the differentiations became more firmly established these fluctuations became much smaller, so that the "stabilization" of the bile-secreting process found in the previous series, during establishment of the conditioned reflexes, was even more marked in this series of experiments. Apart from this, the establishment of differentiation in our animals was associated with a fall in the amount of bile secreted (the average fall amounted to 0.5 ml for Kutsyi, and to 7.3 ml for Glazun), and with a certain increase in the bilirubin concentration of the bile.

Derangements of higher nervous activity, which were observed in all the animals subjected to the treatments described above, caused well-defined alterations in bile secretion. The stabilization in the amount of bile secreted and in its bilirubin concentration, which were characteristic of the phases of elaboration and firm establishment of the conditioned reflexes, and of their differentiation, disappeared. Chaotic fluctuations in the

amount secreted reappeared, both in a single experiment, and from experiment to experiment. The bilirubin content of the bile suffered a similar disturbance. These alterations in the nature of the secretion of bile proceeded against a background of general, although slight, diminution in the amount of bile secreted.

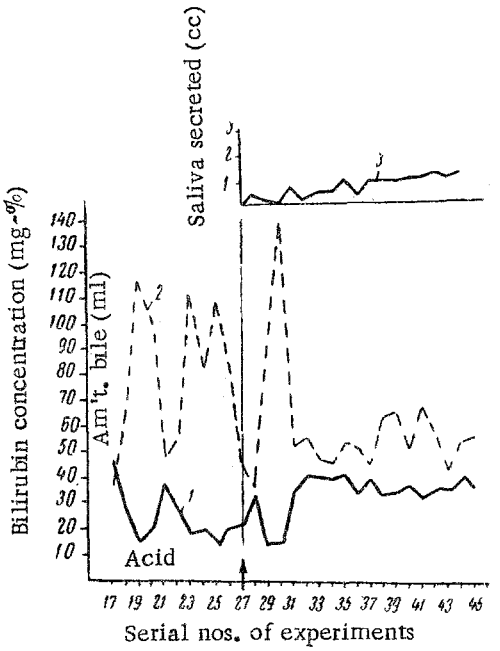

Fig. 2. Amount of bile secreted in each experiment by the dog Sharik, and its bilirubin concentration, after establishment of a conditioned reflex (beginning with the 27th experiment). 1) Amount of bile secreted, in ml per experiment; 2) its bilirubin concentration, in mg %; 3) amount of conditioned reflex salivation, in cm of the manometer scale.

We may conclude from our experiments that the variations in the functional state of the cerebral cortex which were present were of sufficient magnitude to bring about changes in the nature of bile secretion, and in its bilirubin concentration. We may suppose these changes to be caused by induction processes which arise in the cerebral cortex during the formation of the conditioned reflexes or of their differentiation.

In distinction to the amount of bile and to its bilirubin concentration, we could find no significant variations in the absolute amounts of bilirubin secreted. The variations in these values, from experiment to experiment over the whole period of the research, were of an undulant nature, and were inconsiderable. It is evident that they are not related to our interference with cortical processes (Fig. 3).

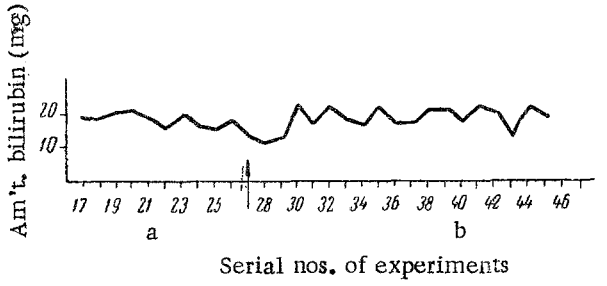

Fig. 3. Absolute amounts of bilirubin secreted with the bile of the dog Sharik. a) In background experiments; b) during formation of a conditioned reflex.

The relatively small range of variations in the absolute amount of bilirubin secreted with the bile may be explained as being due to its being a degradation product of hemoglobin, a relatively constant level of which is essential for the proper functioning of the organism. It is known that a certain parallellism exists between the amount of hemoglobin in the blood and the amount of bilirubin secreted with the bile [6]. This relative constancy is apparently a consequence of the role of bilirubin in hemopoiesis, since it has been found that one of the conditions for the proper functioning of the hemopoietic process is the normal secretion of bilirubin into the intestine [7]. It is evident that the process of formation of the bile pigments depends on complex biochemical processes, which proceed continually, chiefly in the liver. It may be thought that the changes in the functional state of the cerebral cortex produced in our experiments were of insufficient magnitude to influence the formation of bile pigments. Were such relatively slight changes in cortical function as are associated with the elaboration of a conditioned reflex, or with its differentiation, to be able significantly to affect the course of complex metabolic processes in the organism, we would expect there to be continual and violent fluctuations in the composition of the internal medium of the organism. We know, however, that organisms maintain the constancy of their internal medium with great precision.

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BILE SECRETION AFTER PARTIAL RESECTION OF THE LIVER OF DOGS WITH AN EXTERIORIZED COMMON BILE DUCT

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Structural changes taking place in the liver during the process of its regeneration following traumatic injury have been studied in a number of mammalian species [3, 5, 6, 8, 9, 10]. During reparative regeneration of the mammalian liver the resected portion of the organ is not restored, although the final weight and size of the liver are the same as initially, as a result of intensive proliferation of the surviving tissue. This mode of regeneration has been termed regenerative hypertrophy by M. A. Vorontsova [1].

While the histogenesis of hepatic regeneration has been the subject of numerous researches, only a very few papers have been devoted to the study of alterations in the functional activity of the liver after its traumatization and during the subsequent regenerative process [7]. This problem is, however, of considerable current interest, in particular for surgical practice [2, 4]. A study of the functional changes parallel with the morphological ones encountered during regeneration of the liver would permit of a correlated morphophysiological treatment of the process.

We investigated the alterations in the bile secreting function of the liver during regeneration following traumatic injury. The experiments were performed on 1-2 year-old dogs.

* In Russian.