CIRCULATORY AND RESPIRATORY CHANGES ASSOCIATED WITH THE ACTION OF SOME CHEMICAL SUBSTANCES ON CEREBRAL MENINGES

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Many observations have been accumulated in the practice of neurosurgery which attest to the possibility of serious impairment of circulation and respiration associated with trauma of the cerebral meninges. Reflex changes of blood pressure and respiration have been described in a number of research papers dealing with experimental mechanical stimulation of the cerebral meninges [2, 3, 6, 7, 9].

Investigation of the sensitivity of the meninges to chemical stimuli is of particular interest since many medicinal substances possessing certain chemical structures are introduced into the CSF and therefore come in contact with the cerebral meninges. It is also known that the relatively constant chemical composition of the cerebrospinal fluid is ensured by special physiologic adaptations which prevent the passage of a number of substances into the CSF. However, under certain conditions such as pathologic states, changes in the permeability of biologic barriers may lead to disturbances of the chemical composition and biologic properties of the cerebrospinal fluid. It may be supposed that sensitive elements are present in the meninges which react to changes in the composition of the cerebral milieu interieur, viz. the cerebrospinal fluid [4].

EXPERIMENTAL METHODS

Experiments were performed on 50 dogs under short-term and long-term conditions. Free access to the dura was achieved by operative means. Trephining was carried out under morphine-ether anesthesia. Part of the cranial bone was removed in such a way as to leave the dura intact. The edges of the bone defect were smoothed down with nippers, continuous catgut sutures were placed in the soft tissues and a colloid dressing applied to the defect. A "window" was thus made in the skull to be used for observations under long-term conditions. In short-term experiments the same operation was carried out under urethane anesthesia but the trephining was more extensive. Stimulation of the cerebral meninges was performed under a depth of anesthesia at which the corneal reflexes were preserved.

The following substances were used as chemical stimuli: acetylcholine and nicotine in dilutions of 1 : :10,000, adrenalin 1 : 1,000, 4% solution of pyramidon, 40% solution of glucose, lobeline 1 : 250. All these substances were introduced in small amounts (0.2-0.5 ml) under the dura at various sites. Some of the observations were made after preliminary introduction of 0.5% solution of novocain or cocaine into the subdural space. The other group of control experiments was made up of observations with subdural administration of 0.9% sodium chloride solution.

Reflex reactions were assessed by recording the electrocardiogram, blood pressure (mercury manometer), rate of blood flow (lobeline test) and respiration.

EXPERIMENTAL RESULTS

The results obtained may be summarized briefly as follows: the effect of adrenalin (36 stimulations) was expressed in acceleration of the blood flow, a pressor-depressor reaction of the blood pressure and changes in the electrocardiogram indicating increased contractile power of the heart muscle (Fig. 1).

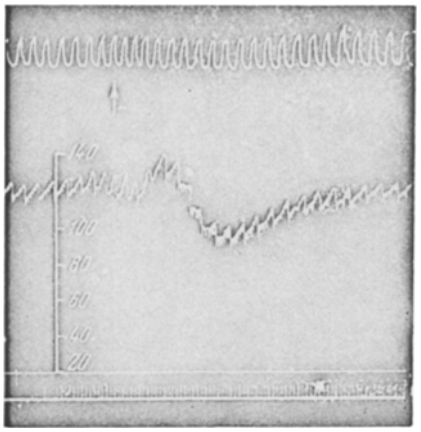


Fig. 1. Changes in respiration (top trace) and blood pressure (middle trace) following subdural introduction of 0.3 ml 1 : 1,000 solution of adrenalin in the fronto-parietal area (moment of injection denoted by arrow).
The two bottom traces are blood pressure base line and time marker (1 second). Short-term experiment, December 22, 1955. Female dog No. 24 weighing 9.7 kg.

The action of pyramidon on the meninges (36 stimulations) led to slowing of the blood flow and some fall in blood pressure; the electrocardiogram indicated impairment of coronary circulation and weakening of cardiac contractions (Fig. 2 and 2,a).

Stimulation of the cerebral meninges by solutions of acetylcholine and nicotine under short-term experimental conditions (43 stimulations) was accompanied by a rise of blood pressure. As a rule, parallel to the rise of blood pressure, changes also occurred in respiration shown on the kymogram as increased respiratory rate and increased amplitude. The electrocardiographic changes were characterized by tachycardia, shortening of the S-T interval and increased T-wave. In isolated experiments with subdural introduction of nicotine, paroxysmal tachycardia was noted (Fig. 3 and 3,a). No characteristic changes in the rate of blood flow were seen in this series of experiments.

Subdural introduction of glucose (42 trials) led to no substantial changes of circulation or respiration either in short-term or prolonged experiments. The recorded indices remained unchanged when larger amounts of glucose were given subdurally.

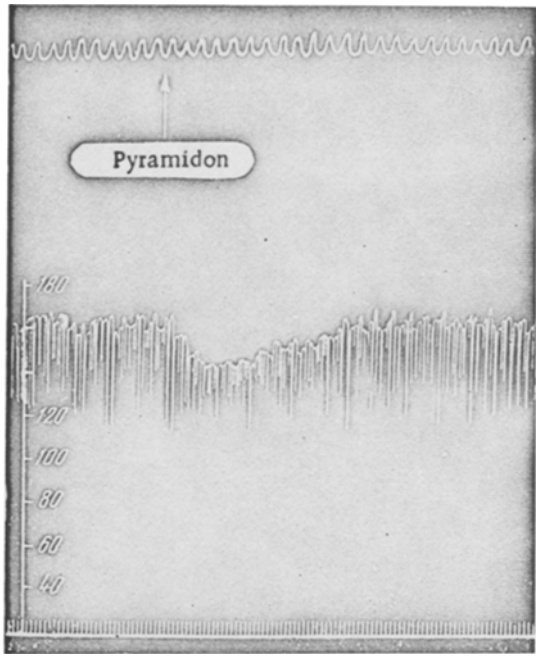
In the case of some of the chemical substances tested (pyramidon, lobeline) increasing the amount of solution given subdurally led to the development of convulsive paroxysms with an acute onset and relatively rapid termination. This phenomenon was noted only in the prolonged experiments in the case of lobeline.

The experiments thus show that more or less pronounced changes in circulation and respiration occur in response to chemical stimulation of the cerebral meninges. The intensity of the effects produced by similar stimuli in different experiments was different, but the character and direction of the ensuing changes remained the same.

We are inclined to the view, based on our observations, that the changes occurring upon chemical stimulation of the cerebral meninges are reflex and arise as the result of stimulation of the meningeal receptor apparatus. This view is supported by the fact that novocain or cocaine anesthesia of peripheral receptor elements followed by the action of chemical stimuli was accompanied by extremely slight reactions or no changes at all. The rapid onset and short duration of the changes also favor their reflex character. Finally, this view is also confirmed by experiments in which acetylcholine and nicotine stimulation was followed by a rise of blood pressure. It is well known that resorptive action of these substances leads to lowering of blood pressure.

It was noticed in the course of the experiments that application of the various chemical substances to the surface of the dura and the pia did not produce the described effects while sub-meningeal introduction of the same substances led to definite changes. This demonstrates that the receptors are situated predominantly on inferior surface of the dura.

In order to effect stimulation of the inner surface of the dura a dural flap was turned and the chemical substances being tested were applied to its inner surface. This led to effects similar to those obtained on subdural introduction of the substances but less marked. This considerable diminution in the intensity of response reaction is, in our opinion, connected with interruption of nervous conductors during the turning of the flap. The possibility is not excluded that the more pronounced effects observed on subdural administration of the chemical substances is determined by the complex action exerted when this method of introduction is used (large area, increase in pressure, absence of lowering of sensitivity produced by preliminary deprivation of the dura of its usual environment etc).



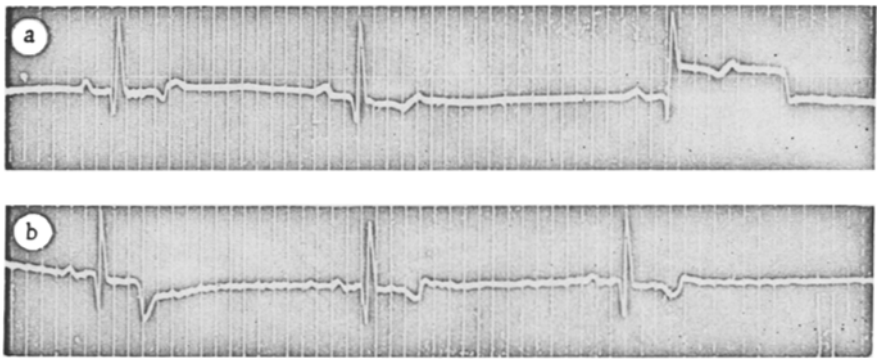


Fig. 2. Changes in respiration (top trace) and blood pressure (middle trace) following subdural introduction of 0.5 ml 4% solution of pyramidon in the occipital area (moment of injection denoted by arrow).
Bottom trace – time marker (1 second). Short-term experiment, December 12, 1955. Male dog, No. 4 weighing 17.5 kg. Electrocardiograms: a) before pyramidon injection; b) after injection. Lead II.

The meningeal sensory elements which can be considered as mechanoreceptors on morphological grounds can, under certain conditions, respond to chemical stimuli also. The fact that the observed changes which follow the action of chemical substances on the cerebral meninges are connected with stimulation of nervous elements situated predominantly on the inner surface of the dura is in accord with the modern concepts [1, 5] which stress the barrier role of the pia and selective permeability of chemical substances from the subdural space into the cerebrospinal fluid. It is quite possible that the described properties of the meningeal receptor elements assist the reflex regulation of the chemical composition of the cerebrospinal fluid. The view that reactions to chemical stimuli might result from sensitivity of nonspecific chemoreceptors was expressed before us by V. N. Chernigovskii [3] with respect to sensory nervous elements of other receptor zones.

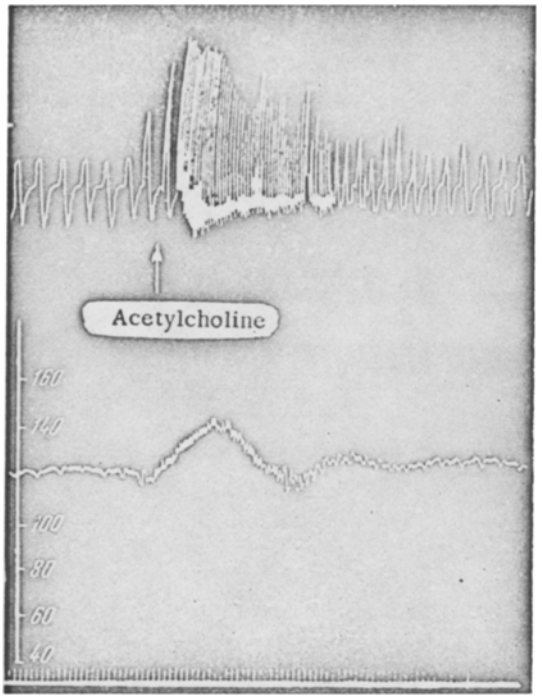


Fig. 3. Changes in respiration (top tracing) and blood pressure (middle tracing) following subdural introduction of 0.5 ml 1 : 10,000 solution of acetylcholine in the temporal area (moment of injection denoted by arrow).
Bottom tracing – time marker (1 second). Short-term experiment, July 27, 1955. Male dog, No. 9 weighing 18.5 kg.

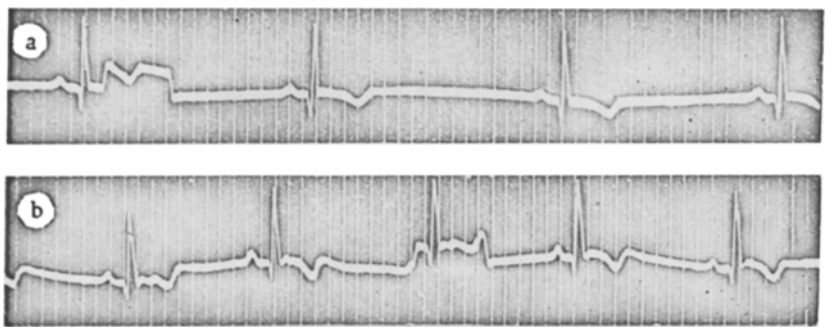


Fig. 3a. Electrocardiograms (Lead II); experiment on July 27, 1955.
a) Before acetylcholine stimulation; b) after stimulation.

SUMMARY

Excitation of brain meninges by chemical substances was carried out in 50 dogs in short-term and prolonged experiments. The following solutions were used: acetylcholine and nicotine – 1 : 10,000, lobeline – 1 : 250 adrenalin – 1 : 1,000, 4% pyramidon solution and 40% solution of glucose. These solutions were introduced into various areas of the dura mater in the dose of 0.2-0.5 cc. Electrocardiogram tracings were taken, blood pressure, the velocity of blood flow and respiration were recorded. Adrenalin caused acceleration of the blood flow, pressor-depressor reactions of the blood pressure and changes in the electrocardiogram which denoted increased contractile

power of the heart muscle. Pyramidon diminished the velocity of blood flow and reduced the blood pressure. Electrocardiogram showed disturbance of the coronary circulation. Acetylcholine and nicotine caused increase of respiration frequency and an increased amplitude of the respiratory movements which were the result of the rise in blood pressure. The above reactions are reflexes, as they disappear following the preliminary subdural introduction of novocain.

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