NEUROCHEMICAL MECHANISMS OF ASCENDING ACTIVATION OF THE CEREBRAL CORTEX IN STARVING ANIMALS

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A number of studies [1, 14, 21] have established a definite significance of the adrenergic substances in the mechanism of ascending activating influences of the reticular formation of the brain stem. In addition, it has been shown that cholinergic mechanisms may also operate in the reticular formation [3, 6-9, 15, 16, 18-20]. Analyzing the studies of the authors indicated above, we can see that they all did not consider the important criterion of ascending activating influences of the subcortical formations, namely, their biological modality. It is known that the concept of specific mechanisms of the ascending activating influences on the cerbral cortex in reactions of various biological types was advanced and experimentally substantiated by P. K. Anokhin [2]. The further development of these concepts has shown that various systems of ascending activation of the cerebral cortex in reactions of biological types are selectively and specifically sensitive at the subcortical level to various pharmacological agents, in particular, to narcotics. Thus, it has been established that aminazine, which selectively blocks the mechanisms of ascending activation of the cortex during pain stimulation and defensive reactions, in the same doses does not affect the manifestation of food activation [4, 5, 10, 11, 13]. All this has permitted us to believe that the subcortical mechanisms of the ascending activating influences on the cerebral cortex in reactions of different biological types, such as food and defensive, are of different neurochemical natures. Since it is known that aminazine selectively acts on the adrenergic apparatus of the reticular formation [1, 4], it was possible to assume that the activation of the cerebral cortex in a state of physiological starvation, maintained after the injection of aminazine, was determined by some other, nonadrenergic neurochemical mechanisms.

On the basis of the literature data, it might be assumed that a significant role in the maintenance of the activation of the cerebral cortex during a state of starvation, i. e., activation known to be of food biological modality, is played by the cholinergic mechanisms. The purpose of this investigation was an experimental verification of this hypothesis.

EXPERIMENTAL

The experiments were conducted on 40 cats under urethan narcosis. Urethan was injected in a 15% solution intravenously in a dose of 1.5 g/kg. Animals after 24 hours of starvation were usually used for the experiments. In most of the experiments the EEG was recorded from the surface of the cranium with the aid of needle electrodes. However, in a number of experiments for the direct application of chemical substances to the cerebral cortex, the skull was trepanned over the anterior pole of one of the hemispheres. The dura mater was locally opened through the trepanned opening (diameter 10 mm). In these cases the electrocorticogram was recorded directly from the cerebral cortex with the aid of wick electrodes moistened with physiologic saline. The EEG was recorded by a unipolar method. The indifferent electrode was applied along the mid-line above the frontal sinus.

In a number of experiments, the potentials induced in response to a single stimulation of the sciatic nerve were recorded from the surface of g. cruciatus anterior. In certain experiments, the frontal sinus was opened for this

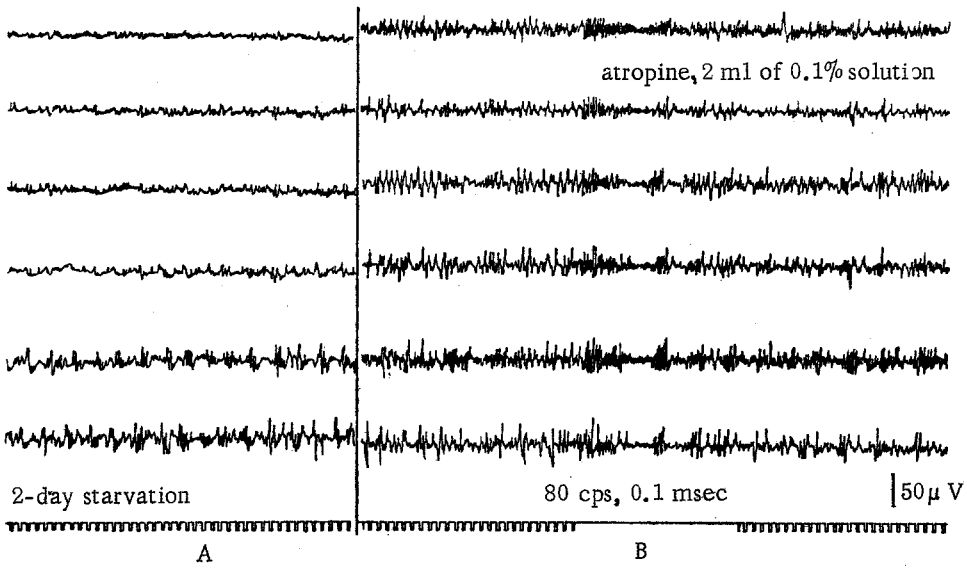

Fig. 1. Variation of the electrical activity of the cerebral cortex in starving animals under urethan narcosis, after intramuscular injection of atropine. Stimulation of the sciatic nerve by electric current under these conditions leads to generalized desynchronization of the EEG in all divisions of the cortex. A) Initial activity of the cerebral cortex of the animal after 2-day starvation; B) electrical activity of the brain of the same animal 30 min after injection of atropine. Significance of the curves (top to bottom): temporal right regions; temporal left; sensomotor right; sensomotor left; occipital right; occipital left; time marking (1 sec).

purpose, and a needle electrode was set up on the inner bony plate, covering the anterior portions of the brain, above the corresponding region of the brain. In other experiments, the induced potential was recorded directly from the cerebral cortex. The sciatic nerve was stimulated with rectangular pulses, using "Fiziovar" stimulator. The stimulus was applied with bipolar electrodes, which were applied to the sciatic nerve.

Solutions of 0.1% atropine and amizil were used as the substances applied to the cortex. Filter paper (0.3 × 0.3 cm), which was applied to the exposed surface of the cortex in direct proximity to the take-off electrode, was soaked with these solutions. The EEG was recorded on a 10-channel electroencephalograph, produced by Alvar Electronic Company. A four-channel "Biophase" amplifier, produced by the same company, with transmission band 0.5 cps to 10 kc/sec, was used to record the induced potentials.

RESULTS

In the first series of investigations we studied the changes in the EEG of starving animals, kept under urethan narcosis after intramuscular injection of cholinolytic substances. As has already been reported [10], the state of physiological starvation in such animals is manifested in the form of a selective activation of the EEG in the anterior portions of the cerebral cortex, while in the parietal-occipital divisions the slow high-amplitude electrical activity characteristic of the state of narcotic sleep is registered in this case. In conducting this series of experiments, we were interested primarily in whether the "starvation" activation of the cerebral cortex can be selectively blocked by the introduction of cholinolytic substances into the organism. Our experiments indicated that the intramuscular injection of 0.1% atropine or 1% amizil (0.3-0.5 mg/kg) in the overwhelming majority of cases led after 2-5 min to replacement of desynchronization in the anterior divisions of the cerebral cortex by a slow high-amplitude activity, similar to that which was recorded in the parietal-occipital divisions. Moreover, in a number of experiments, stimulation of the sciatic nerve was used as a control (3V, 80 cps, 0.5 msec). Such stimulation, just as before, induced a generalized reaction of activation in all the divisions of the cerebral cortex (Fig. 1).

The effect described above indicated that cholinolytic substances selectively blocked only the mechanisms of food activation of the cerebral cortex, leaving relatively intact the mechanisms of pain activation. On the basis of these experiments, of course, we could say nothing definite of what mechanisms of ascending activation of the cortex during starvation are affected by the cholinolytic substance—the cortical or subcortical mechanisms.

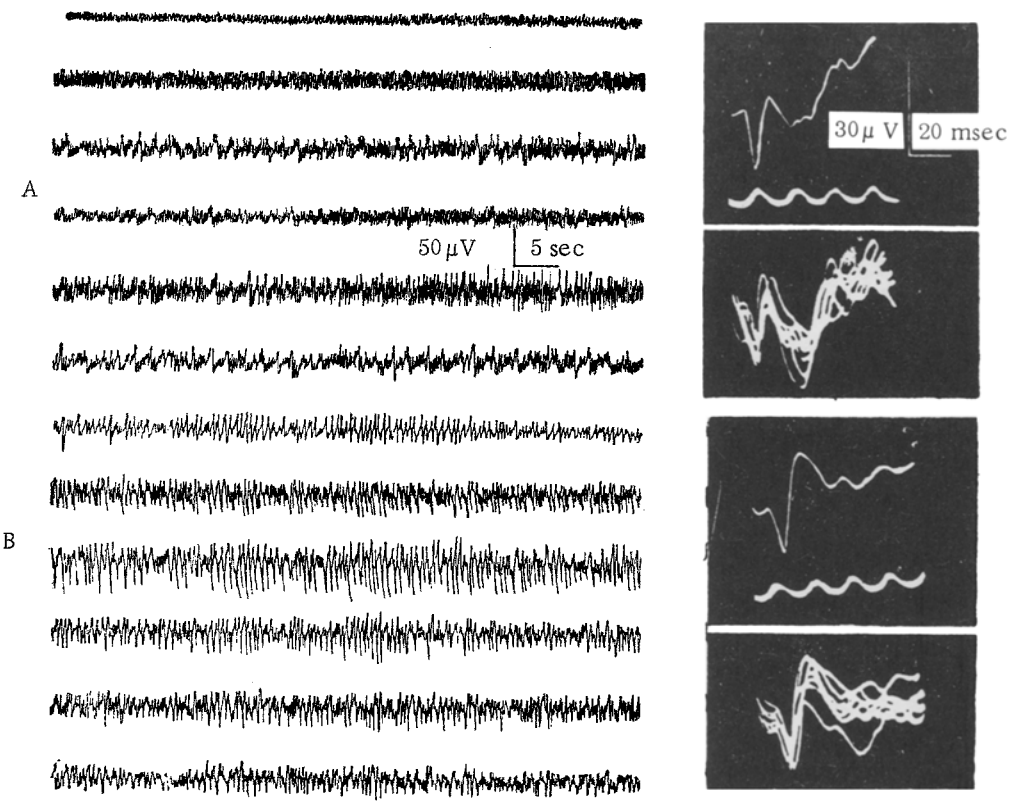

Fig. 2. Variation of the EEG and nature of the cortical induced potential in response to stimulation of the sciatic nerve after intramuscular injection of aminazine. A) EEG and induced potential arising in response to stimulation of the sciatic nerve in the sensomotor region of the cortex in an animal after 24-hour starvation; B) EEG and induced potential to stimulation of sciatic nerve in the same animal after intramuscular injection of amizil (0.2-0.3 mg/kg). Remaining notations the same as in Fig. 1.

Considering all the complexity of this question, we limited ourselves in further experiments only to a study of the cortical chemical mechanisms of food activation.

As our previous investigations have shown [12], local application of cholinolytic substances to the anterior divisions of the cerebral cortex of starving animals eliminated the original activation of the anterior divisions of the cerbral cortex and did not affect the manifestation of pain activation, which arose upon stimulation of the sciatic nerve. Thus, one of the possible points of application of the action of cholinolytic substances, inducing an elimination of the "starvation" cortical activation after their introduction into the organism, may be the synaptic formations of the cerebral cortex.

To investigate the neurochemical mechanisms of the synaptic formations of the cortex, participating in the food excitation, in our following experiments we studied the changes in the induced potential arising in response to stimulation of the sciatic nerve, both against a background of "starvation" activation of the anterior divisions of the cerebral cortex, and after elimination of this activation with cholinolytic substances.

In our previous investigations [10], it was established that after 24-hour starvation, the induced potential in the anterior divisions of the cerebral cortex (g. cruciatus anterior) in response to a single stimulation of the sciatic nerve is poorly detected or is recorded primarily in the form of its positive phase. In animals fed before the experiment, in response to the same stimulation of the sciatic nerve, as a rule, all the components of the induced potential are recorded, i. e., the positive and negative phases of the primary response and the secondary positive phase. This indicates that the system of hypothalamic "starvation" excitation, forming cortical activation, involves the axodendritic synaptic formations of the cortex, which prevents the formation of induced potentials arising after pain stimulation. Consequently, it is quite logical to assume that if the cholinoreactive synaptic formations of the cortex participate

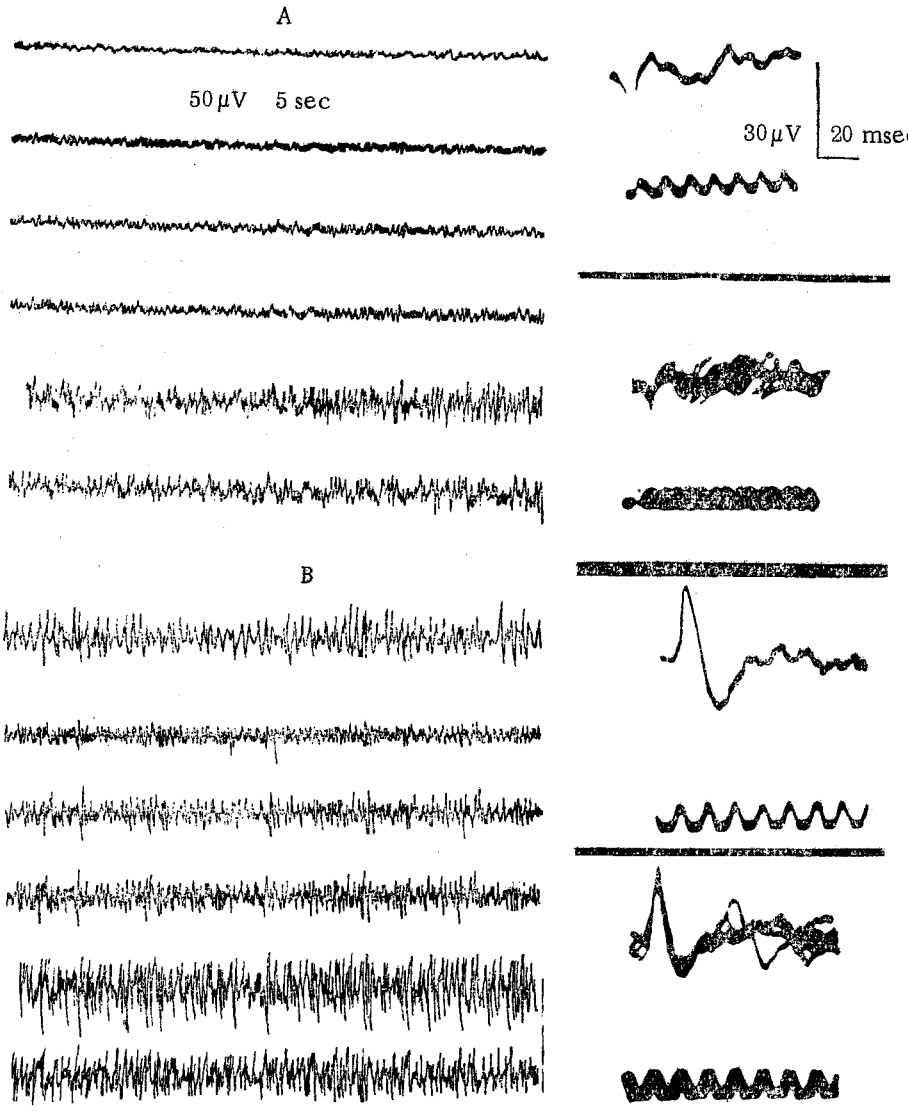

Fig. 3. Variation of the EEG and cortical induced potential in response to stimulation of the sciatic nerve after application of a 1% solution of amizil to the anterior divisions of the right hemisphere. A sharp increase in the negative phase of the induced potential is observed in the zone of application of amizil. A) Nature of the EEG and induced potential in the sensomotor region of the cortex during stimulation of the sciatic nerve in an animal after 1.5-day starvation; B) EEG after application of 1% solution of amizil to the anterior divisions of the cerebral cortex of the right hemisphere. Remaining notations the same as in Figs. 1 and 2.

in the excitation of the hypothalamus in the state of starvation, then the administration of cholinolytic substances to starving animals should lead to the same external effect as natural food saturation, i. e., should permit the pain excitation to form the characteristic cortical potentials.

The experiments indicated that after intramuscular administration of cholinolytic substances (atropine or amizil) to starving animals and the appearance of a slow high-amplitude electrical activity in all divisions of the cerebral cortex, the negative phase of the induced potential, arising in response to stimulation of the sciatic nerve, increased (Fig. 2). Moreover, secondary potentials also were frequently recorded. We also observed analogous results after application of cholinolytic substances to the cerebral cortex (Fig. 3).

However, the results of these experiments, in spite of the complete external analogy to the data of experiments in which good saturation was imposed, were caused by other physiological mechanisms. Actually, although in the case of food saturation there is an elimination of the ascending activating influences of the hypothalamus on the cerebral cortex on account of the reduction of the excitability of its food centers, in the case of the application of cholinolytic substances to the cortex in starving animals, the ascending activating influences of the hypothalamus are preserved and only a local block of the cholinergic synaptic formations of the cerebral cortex arises. Nonetheless, in both cases pain excitation proves capable of activating the axodendritic synapses and forming the negative phase of the induced potential. All this indicates that the ascending activating influences of the hypothalamus in the state of starvation actually selectively utilize the cholinolytic synaptic formations of the cerebral cortex. Evidently the adrenergic apparatus also take part in the mechanism of "starvation" activation of the cerbral cortex. We have no basis for believing that the adrenergic systems of the brain are included to a greater and greater degree in the mechanism of ascending activation of the cerebral cortex as the periods of starvation are lengthened. In this case, probably physiological mechanisms purely of food excitation are supplemented by mechanisms of general sympathico-adrenal stress of the organism.

Our experiments studying the changes in the cortical induced potential arising in response to stimulation of the sciatic nerve after application of cholinolytic substances to this cortical zone indicate that in the cortical axodendritic synaptic formations, in reactions of different biological types, the chemical specifics are distinctly expressed. There is no doubt that the same chemical specifics are also inherent in the subcortical apparatus in reactions of different biological types. However, the question of the degree to which these chemical specifics are expressed at the subcortical level will be the subject of our further investigations.

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