EFFECT OF SCOPOLAMINE AND AMINAZINE ON THE ELECTRICAL ACTIVITY OF THE CORTEX, HYPOTHALAMUS, AND RETICULAR FORMATION OF THE MIDBRAIN IN RABBITS WITH A FOOD-SEARCH CONDITIONED REFLEX

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In our previous investigation, it was shown that the administration of aminazine gives rise to a disappearance of the protective response of the animal, with simultaneous inhibition of the electrical activity of the ventro-medial nucleus of the hypothalamus, while the administration of scopolamine does not inhibit the activity of the latter formation of the hypothalamus and does not lead to disappearance of the protective reflex.

It was of interest to trace the influence of these same substances upon the electrical activity of the cortex, reticular formation of the midbrain, lateral and ventro-medial nucleus of the hypothalamus in the presence of a food reflex, since this reflex is related to excitation of the lateral nucleus of the hypothalamus [6, 8, 9], as the structure belonging to the cholinergic system [5, 10].

EXPERIMENTAL METHOD

The experiments were conducted on 5 rabbits in a sound-insulated chamber; the biopotentials were recorded during free movement of these animals (according to the method of B. I. Kotlyar [7]). The recording was performed on the 16-channel electroencephalograph produced by the Biofizpribor [Biophysical instrument] factory, with take-offs from the optical-auditory cortex, reticular formation of the midbrain, ventro-medial and lateral nuclei of the hypothalamus, while in certain animals, instead of the ventro-medial nucleus of the hypothalamus, we investigated the dorsal hippocampus. The conditioned food reflex was developed to sound or light according to the food search method [1]. In individual rabbits, a conditioned defensive reflex was developed before the development of the food reflex according to an avoidance procedure [4]. Scopolamine (0.1-0.2 mg/kg) and aminazine (1-2 mg/kg) were injected intramuscularly directly before the experiment. The control animals received physiological saline. The histological investigation was conducted according to Nissl.

EXPERIMENTAL RESULTS

After reinforcement of the food conditioned reflex in all the rabbits in response to the appearance of the signal, a flare-up of synchronized fluctuations of the biopotentials (frequency 8-10 per second) was observed in the cortex, reticular formation of the midbrain, in the lateral nucleus of the hypothalamus (Fig. 1a), and in the hippocampus (Fig. 2a); however, there was no such flare-up or it was less pronounced in the ventro-medial nucleus of the hypothalamus.

When scopolamine was administered, the following general principles were noted in the change in the conditioned reflex food activity and electrical activity of the regions indicated above. Slow waves with a frequency of 2 to 3 oscillations per second and an amplitude up to 100-150 μV appeared in all the divisions during the intervals between signals 10-15 min after injection of the preparation. The conditioned and unconditioned food

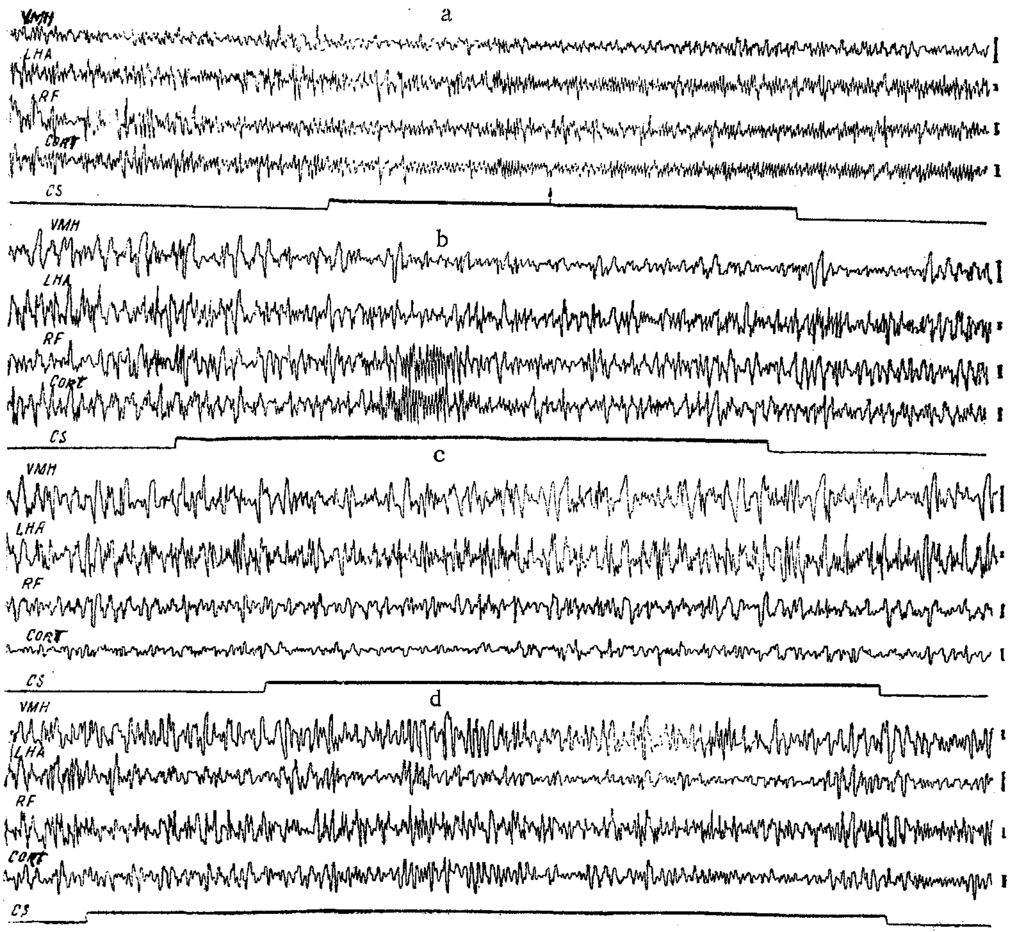

Fig. 1. Changes in the electrical activity after injection of scopolamine. a) Before injection (in response to conditioned food stimulus); b) 20-30 min after injection; c) after 30-40 min; d) after 30-40 min. Reaction to conditioned defensive stimulus. Explanation in text. VMH) ventro-medial nucleus of the hypothalamus; LHA) lateral nucleus of the hypothalamus; RF) reticular formation of the midbrain; CORT) optical cortex; CS) mark of action of conditioned stimulus. The arrow denotes the moment of pressing on the pedal.

reflex disappeared after 20-30 min following the injection: the rabbit did not twitch the lever and it did not eat the offered food. At the same time, in individual combinations, the conditioned food signal gave rise to a motor reaction of the animal: it approached the manipulator but did not complete the reaction. In this case, synchronized oscillations of the biopotentials, with a frequency of 8-10 per second, were recorded only on the EEG of the cortex and reticular formation of the midbrain, and were absent in the lateral nucleus of the hypothalamus (Fig. 1b).

During the following 5-10 min, the conditioned stimulus did not yet induce any appreciable behaviorable reaction or change in the EEG: the animal sat fixedly in one position, while slow waves with a frequency of 2 to 3 oscillations per second and high amplitude were reported in all the divisions, with the exception of the takeoff from the cortex, where the wave rhythmics were more frequent (Fig. 1c). However, the conditioned defensive signal, which was never used in this situation, as a rule gave rise to a motor reaction of the animal to the defensive manipulator and simultaneously synchronized oscillations of the biopotentials, with a frequency of 8-10 per second, appeared. It is characteristic that this synchronized activity appeared in the cortex and ventro-medial nucleus of the hypothalamus, being absent in the lateral nucleus of the latter (Fig. 1d).

A gradual restoration of the conditioned food reflex was observed 40-50 min after injection of scopolamine; this process passed through all the stages indicated above, but in reverse order: at first the conditioned signal induced only a motor reaction with the appearance of synchronized oscillations of the biopotentials, with a frequency of 8-10 per second in the cortex and reticular formation of the midbrain, with their absence in the lateral hypo-

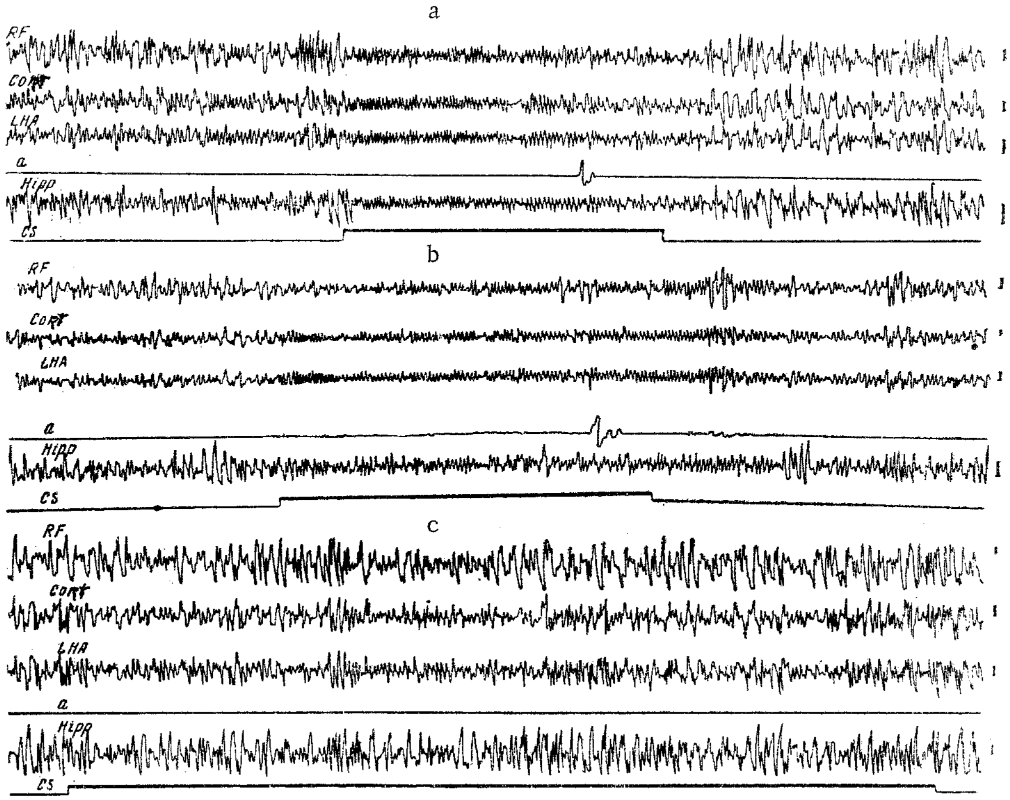

Fig. 2. Changes in the electrical activity upon the administration of aminazine. a) Before injection (in response to conditioned food stimulus); b) 10-20 min after injection; c) 30-40 min after injection. Explanation in text. a) Mark of clamp on pedal; Hipp) dorsal hippocampus. Remaining notations the same as in Fig. 1.

thalamus; then the food unconditioned reflex was restored, and finally the conditioned reflex; moreover, the rhythmics were synthesized on the EEG of the cortex, reticular formation of the midbrain, and lateral nucleus of the hypothalamus.

After the injection of aminazine, the following general principles of variation of the conditioned food activity and electrical activity were observed. Before injection of the substance, the conditioned signal induced a flare-up of synchronized vibrations of the biopotentials in the cortex, reticular formation of the midbrain, hippocampus, and later nucleus of the hypothalamus (Fig. 2a). Ten to twenty minutes after its injection and in the presence of a conditioned food reflex, changes in the EEG were noted in the form of flare-ups of synchronized vibrations of the biopotentials, with a frequency of 8-10 per second, which were recorded only in the lateral nucleus of the hypothalamus and cortex, but were absent or appeared less distinctly in the reticular formation of the midbrain and hippocampus (Fig. 2b). The conditioned reflex and waking reaction on the EEG disappear simultaneously 30-40 min after the injection of aminazine (Fig. 2c). The animal was immobile in this case. It is characteristic that the waking reaction on the EEG was absent for any external stimulus. At the same time, in contrast to the analogous stage of the action of scopolamine, the unconditioned food reflex was preserved.

During the following 10-15 min, the conditioned food reflex was gradually restored, and the electrical activity was normalized, passing through all the stages indicated above in reverse order: synchronized vibrations of the biopotentials, with frequency 8-10 per second, are at first reported in the lateral nucleus of the hypothalamus and cortex and are still absent in the reticular formation of the midbrain and hippocampus; then they are restored in these structures.

Thus, in the case of injection of scopolamine, at first the unconditioned food reflex of the animal disappears, although some portion of the conditioned reflex component in the form of the motor reaction of the rabbit in response to the signal is still retained. It is characteristic that in this case, synchronized activity with a frequency of 8-10 oscillations per second is recorded in the cortex and reticular formation of the midbrain, but it is absent in the lateral nucleus of the hypothalamus. Evidently at this stage of the action of scopolamine there is a blockage only of this structure of the hypothalamus, while the nonspecific activating system of the reticular formation of the midbrain continues to function. Also unblocked at this point is the excitability of the ventro-medial nucleus of the hypothalamus, which is evidenced by the appearance of synchronized activity in it with a frequency of 8-10 vibrations per second, in response to the defensive signal. Later the nonspecific activating system is also blocked, as a result of which the conditioned reflex component of the food reflex disappears, and a waking reaction is not recorded on the EEG, which is explained by a drop in the tone of the cerebral cortex and by a decrease in the "level of awakening." Since the appearance of food reactions of the animals is related to the functioning of the lateral nucleus of the hypothalamus [6, 8, 9], which belongs to the cholinergic system [12], the injection of a cholinolytic—scopolamine — induces a blockage of this formation, which also leads to the disappearance of the unconditioned food reflex. At the same time, scopolamine does not block the defensive reaction, the manifestation of which is related to the functioning of the adrenergic ventro-medial nucleus of the hypothalamus [5, 6, 13].

Aminazine, in contrast to scopolamine, induces a decrease in the frequency of the electrical activity in the hippocampus and reticular formation of the midbrain, but does not disturb the appearance of the conditioned food reflex, retaining a synchronized rhythm of 8-10 oscillations per second in the lateral nucleus of the hypothalamus and in the cerebral cortex. This is evidence that, as a result of its adrenolytic properties, at this phase of its action aminazine inhibits the activity of the nonspecific activating system, thereby lowering the "level of awakening," but does not affect the function of the cholinergic lateral nucleus of the hypothalamus and thereby the food reaction of the animal. Later, blocking the reticular formation of the midbrain and thereby reducing the tone of the cerebral cortex, aminazine blocks the waking reaction on the EEG in response to the signal and causes a disappearance of the conditioned reflex component of the food reflex. It is characteristic that in this case, in contrast to the action of scopolamine, the unconditioned food reflex is retained.

The disappearance of a food reaction, simultaneously with the decrease in the electrical activity in the lateral nucleus of the hypothalamus under the influence of scopolamine and the conservation of the unconditioned food reflex under the action of aminazine indicate that the food activity of the animal is related to the functioning of the lateral nucleus of the hypothalamus, which evidently belongs to the cholinergic system.

SUMMARY

Rabbits with food search conditioned reflex in response to a signal from the cortex, hippocampus, and the lateral nucleus of the hypothalamus showed an outbreak of synchronized biopotential oscillations at a rate of 8-10 osc/sec, which, however, was absent in the reticular formation of the midbrain and the ventro-medial nucleus of the hypothalamus. Scopolamine injection caused disappearance of the conditioned and unconditioned food reflex with a simultaneous cessation of the rhythm of 8-10 osc/sec at first in the hypothalamus and then in the other leads. Aminazine injection caused the disappearance only of the conditioned component of the reflex whereas the unconditioned component was retained. Disappearance of the conditioned component of the reflex was noted at the moment of cessation of the rhythm of 9-10 osc/sec in the lateral nucleus of the hypothalamus, which belongs to the cholinergic system.

LITERATURE CITED

1. L. G. Voronin, Lectures on the Comparative Physiology of the Higher Nervous Activity, Moscow (1957).
2. L. G. Voronin and B. I. Kotlyar, Zh. Vyssh. Nerv. Deyat., Vol. 13, No. 3 (1962), p. 547.
3. L. G. Voronin and B. I. Kotlyar, Ibid., Vol. 13, No. 5 (1963), p. 917.
4. L. V. Kalyuzhnyi, Transactions of the Institute of Higher Nervous Activity, Academy of Sciences USSR, Physiological Series [in Russian], Vol. 7 (1962), p. 271.
5. L. V. Kalyuzhnyi, Summaries and Abstracts of the Conference on Problems of Higher Nervous Activity [in Russian], Leningrad (1963), p. 118.
6. L. V. Kalyuzhnyi, Uspekhi Sovr. Biol., Vol. 57, No. 2 (1964), p. 232.
7. B. I. Kotlyar, Fiziol. Zh. SSSR, No. 9 (1963), p. 1115.
8. N. N. Lyubimov, Zh. Vyssh. Nerv. Deyat., Vol. 8, No. 4 (1958), p. 560.
9. B. Anand, S. Dua, and K. Shornberg, J. Physiol., London, Vol. 127 (1955), p. 143.
10. T. Kurotsu, C. Kuritani, and J. Ban, Med. J., Osaka University, Vol. 8 (1957), p. 111.
11. B. Sadowsky and V. G. Longo, Electroenceph. Clin. Neurophysiol., Vol. 14 (1962), p. 455.
12. C. C. D. Shute and P. R. Lewis, Nature, Vol. 199 (1963), p. 1160.
13. W. Wyrwizsak and C. Dobrzeska, Science, Vol. 131 (1960), p. 3430.