3. G. I. Kositskii, S. D. Mikhailova, S. V. Putygin, et al., Patol. Fiziol., No. 6, 31 (1980).
4. B. I. Tkachenko, Kardiologiya, No. 4, 16 (1964).
5. J. A. Bennett, C. Groodchild, C. Kidd, et al., J. Physiol. (London), 310, 64 (1981).
6. N. Mei, Exp. Brain Res., 11, 465 (1970).
7. N. Mei, Exp. Brain Res., 11, 480 (1970).
8. A. S. Paintal, Physiol. Rev., 53, 159 (1973).

CHANGES IN THE HEART RATE DURING HYPERACTIVATION OF THE ANTERIOR AMYGDALOID NUCLEUS

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If a pathological process involves the limbic system it disturbs the cardiac rhythm [1-3, 5-11]. These disturbances may vary in character but their particular features and the conditions determining their origin are still largely unexplained. In the investigation described below this problem was studied in the light of views on the role of hyperactive determinant structures in disturbances of regulation of physiological systems and their conversion into pathological [4]. For this purpose a generator of pathologically enhanced excitation (GPEE) was created in the anterior amygdaloid nucleus (AAN), a formation belonging to the limbic system.

Stimulation of different zones of the amygdala is known to induce a predominantly bradycardic effect [15]. It must therefore be expected that hyperactivation of AAN as a result of the formation of a GPEE would cause changes in the cardiac rhythm.

EXPERIMENTAL METHOD

Experiments were carried out on 55 male rats weighing 150-200 g. Preparations for the experiment (tracheotomy, catheterization of the subclavian vein, fixation of the animal in a stereotaxic apparatus, and exposure of the cranium) were carried out under superficial pentobarbital sodium anesthesia (2.5 mg/100 g). After recovery from anesthesia the rats were immobilized with succinylcholine and artifically ventilated. The GPEE was created by microinjection of penicillin, which interferes with GABA-ergic control [12, 13, 16]. For this purpose penicillin in a dose of 100 i.u. in a volume of 0.2 µl was injected by means of a microinjector through a micropipet into one AAN of the animals (27 rats) taking coordinates from the stereotaxic atlas [14]: A = 6.5, L = 3.5, H = 7. In 10 animals of this group the ECG alone was recorded, in 17 rats the ECG together with electrical activity of AAN before and after injection of penicillin. Nichrome electrodes (150 µ), coated with enamel, with tips 50 µ in diameter uninsulated for a distance of 0.5 mm, were used. On the side of injection of penicillin the electrodes were inserted at an angle of 21° to the vertical axis (A = 3.5, L = 3, H = 7.7). In some experiments electrical activity also was recorded in the intact nucleus. In control experiments on seven animals physiological saline was injected into AAN in the same volumes as penicillin. To depress or eliminate the GPEE, cerebral hypothermia and electrical coagulation respectively were used. Cerebral hypothermia was created

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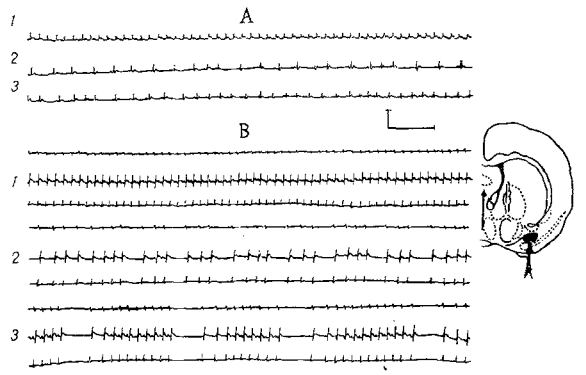

Fig. 1. Effect of AS(A) and injection of penicillin (B) into AAN on the ECG. A: 1) Initial ECG (lead I), 2) during stimulation, 3) immediately after stimulation; B): 1) initial ECG (leads I, II, and III), 2) 25 min, 3) 60 min after injection of penicillin. Arrows indicate location of stimulating electrodes and site of injection of penicillin. Calibration: 1 mV, 1 sec.

by applying ice to the animal's exposed cranium and electrical coagulation was carried out by passing an anodal current (50 mA) through the active electrode for 10-15 sec.

In 10 animals, besides electrical activity of AAN and the ECG, electrical activity also was recorded in efferent fibers of the ipsilateral vagus nerve on the side of injection of penicillin into AAN at the height of development of GPEE. For this purpose the animals were released from the stereotaxic apparatus and fixed in the supine position. The previously dissected nerve was divided and its central end placed on platinum electrodes (interelectrode distance 4 mm). Electrical activity of the nerve was recorded by means of a cathode-ray oscilloscope and FOR-2 camera. Signals were led in parallel from one output of the UBP2-03 amplifier to an integrator, the voltage at the input of which was proportional to the discharge frequency (integration time 1 sec). The results of averaging were recorded on an ELKAR-4 electrocardiograph through its amplifier tube simultaneously with electrical activity in AAN (signals from which were led to the electrocardiograph from the second output of the UBP2-03 amplifier) and the ECG; the winding speeds of the photographic film and squared paper tape were equal.

Disturbances of the cardiac rhythm arising under the influence of GPEE in AAN were compared with its changes during electrical stimulation (ES) of the same nucleus, for which glass electrodes filled with 2.5M NaCl, with a tip 20-35 μ in diameter, were used. Stimuli were generated by an ESU-2 stimulator (300 Hz, 1.5-4 V, duration 1 msec) for 20-30 sec (experiments on 11 animals).

The ECG was recorded from standard leads. The location of the micropipets and electrodes after each experiment was verified histologically in sections cut on a freezing microtome.

EXPERIMENTAL RESULTS

Electrical stimulation of AAN as a rule evoked sinus bradyarrhythmia (Fig. 1A). The arrhythmia usually appeared 3-5 sec after the beginning of ES and lasted throughout the period of stimulation. The normal cardiac rhythm was restored after the end of stimulation. The arrhythmias were most clearly observed after ES of the anteromedial part of the nucleus. During stimulation of other zones of AAN rapid adaptation of the heart developed and the normal rhythm was restored actually during stimulation. Injection of penicillin into one AAN evoked similar changes in the cardiac rhythm as in the experiments with ES (Fig. 1B). They usually began 15-20 min after injection of penicillin and lasted 1.5-2 h; they reached a maximum toward the end of the first hour.

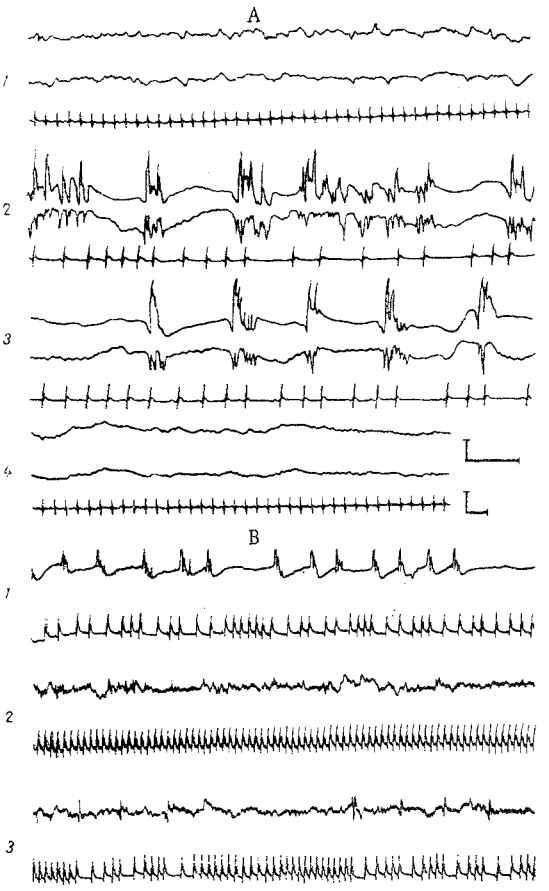

Fig. 2. Effect of hyperactivation of AAN caused by injection of penicillin into nucleus, coagulation of hyperactivated nucleus (A), and cooling of the brain (B) on electrical activity in AAN and on the ECG. A: 1) Initial background, 2) at end of episode of seizure activity in AAN, 3) immediately after episode of seizure activity in AAN, 4) after coagulation of left AAN. In each fragment from top to bottom: electrical activity of left AAN, electrical activity of right AAN, ECG in lead I; B: 1) 20 min after injection of penicillin into AAN, 2) 10 min after application of ice to animal's cranium, 3) 15 min after removal of ice. In each fragment, top — electrical activity of AAN, bottom — ECG in lead II. Calibration: 250 μV, 1 sec (top for A, bottom for B).

Simultaneous recording of the ECG and electrical activity of the nucleus revealed correlation between activity of the generator and disturbance of the cardiac rhythm (Fig. 2A, 2). The experiments showed that the arrhythmias did not occur before two episodes of seizure activity in AAN; they occurred, moreover, during the first 20-30 min and the duration of each episode was not less than 1 min. Later cardiac arrhythmias appeared also in association with single epileptic discharges (Fig. 2A, 3). Electrical coagulation of AAN into which penicillin was injected immediately restored the normal cardiac rhythm (Fig. 2A, 4).

A similar effect was obtained in the other series of experiments with cerebral hypothermia. Epileptic discharges in AAN disappeared 10 min after application of ice to the cranium, and the normal cardiac rhythm was restored at the same time. After removal of ice from the cranium, as the brain temperature was restored, these cardiac arrhythmias developed once again (Fig. 2B, 3).

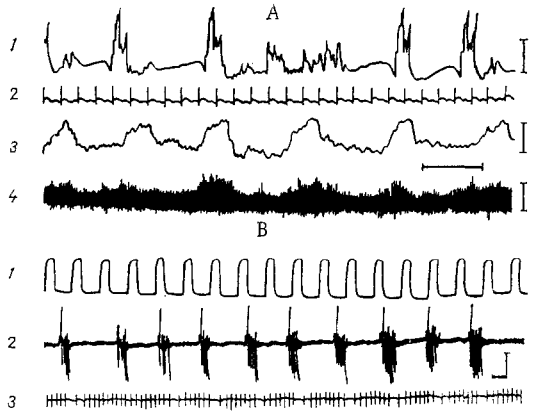

Fig. 3. Correlation between electrical activity in AAN and some parameters of cardiac activity after division of the vagus nerve and with artificial respiration. A) Correlation between electrical activity in central end of divided vagus nerve (4) and electrical activity in AAN (1) 15 min after injection of penicillin, 2) ECG (lead I), 4) electrical activity in vagus nerve recorded by pulse integrator. Calibration, from top to bottom: 250 μV, 25 Hz, 25 μV, time 1 sec. B) Correlation between seizure discharges in AAN after injection of penicillin (2), ECG changes (3), and frequency of artificial respiration (1). Calibration: 250 μV, time 1 sec; respiration rate 40 cycles/min.

Experiments with simultaneous recording of electrical activity in AAN and in the central end of the divided ipsilateral nerve after injection of penicillin into AAN (Fig. 3A) showed that bursts of epileptic activity in AAN were accompanied by bursts of electrical activity in the vagus nerve; strong correlation was observed between the times of the two processes. It is important to note that division of the vagus nerve prevented the development of cardiac arrhythmias.

Simultaneous recording of seizure discharges in AAN, the ECG, and the rhythm of artificial respiration (Fig. 3B) showed no correlation between the times of onset of discharges in AAN when hyperactivated by penicillin and the rhythm of artificial respiration, although correlation was found between the times of bursts of epileptic activity and changes in the cardiac rhythm.

The experiments showed that a GPEE created with the aid of penicillin in one AAN is manifested by characteristic episodes of prolonged seizure activity and by single high-amplitude seizure discharges.

The onset of hyperactivity in AAN led to disturbance of the cardiac rhythm. This disturbance evidently did not develop immediately, but when some time had elapsed after the appearance of epileptic activity in AAN; this activity, moreover, had to be strong enough (at least two long episodes). It was only after this that disturbances of the cardiac rhythm appeared in response to single epileptic discharges. This fact is evidence that a disturbance of the mechanisms of regulation of cardiac activity is an important condition for the development of cardiac arrhythmias in the presence of hyperactivity of AAN. Evidence that these arrhythmias are central in genesis and are connected with activity of GPEE in AAN was given by experiments with coagulation of the region of the generator, which abolished the epileptic activity in the nucleus and, at the same time, restored the cardiac rhythm. This conclusion also was confirmed by the experiments with cerebral hypothermia.

The cardiac arrhythmias observed in these experiments were parasympathetic in type. The onset of epileptic activity in AAN led to bradycardia, accompanied by bursts of increased electrical activity in the central end of the divided ipsilateral vagus nerve that coincided in time with bursts of epileptic activity in AAN.

Hyperactivation of AAN by the creation of a GPEE in it thus leads to hyperactivation of the vagus nerve nuclei, resulting in a disturbance of the cardiac rhythm of bradycardic

type. In this case the AAN in which the GPEE is created plays the role of determinant structure in the genesis of the pathological system, for which the vagus centers constitute the intermediate stage.

LITERATURE CITED

1. E. A. Andrikyan and O. D. Gaske, Fiziol. Zh. SSSR, No. 1, 13 (1967).
2. A. D. Becheka and A. F. Koseko, in: Problems in the Physiology of the Hypothalamus (Interinstitute Scientific Reports) [in Russian], No. 11, Kiev (1977), p. 61.
3. M. Ya. Buryak, in: Current Problems in the Pharmacology of the Reticular Formation and Synaptic Transmission [in Russian], Leningrad (1963), p. 266.
4. G. N. Kryzhanovskii, Determinant Structures in the Pathology of the Nervous System [in Russian], Moscow (1980).
5. A. A. Ul'yaninskii, E. I. Stepanyan, É. I. Agapova, et al., Kardiologiya, No. 4, 94 (1978).
6. L. S. Ul'yaninskii, A. I. Balashov, A. V. Grishak, et al., Byull. Eksp. Biol. Med., No. 12, 1288 (1979).
7. B. M. Fedorov, The Mechanisms of Disturbance and Recovery of Cardiac Activity [in Russian], Moscow (1968).
8. B. M. Fedorov, Fiziol. Zh. SSSR, No. 6, 948 (1974).
9. B. M. Fedorov, Emotions and Cardiac Activity [in Russian], Moscow (1977).
10. F. R. Calaresu, A. Faiers, and G. Mogenson, Prog. Neurobiol., 5, 1 (1975).
11. F. R. Calaresu and M. Thomas, Brain Res., 2-3, 235 (1975).
12. D. R. Curtis, C. J. A. Game, and G. A. R. Johnston, Brain Res., 43, 242 (1972).
13. R. A. Davidoff, Brain Res., 45, 638 (1972).
14. J. F. R. Koning and R. A. Klippel, The Rat Brain, Baltimore (1963).
15. D. J. Reis and M. C. Oliphant, J. Neurophysiol., 27, 893 (1964).
16. N. M. Van Gelder, J. Neurochem., 16, 1355 (1969).

TIME COURSE OF THE LOCAL CORTICAL BLOOD FLOW IN EXPERIMENTAL CEREBRAL ISCHEMIA

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Local cerebral ischemia is accompanied not only by disturbances of the local cerebral circulation, but also by considerable hemodynamic changes at a distance from the ischemized focus [1-6]. However, the time course of the blood flow in different parts of the brain after local ischemia still remains virtually unstudied. The investigation described below accordingly was carried out to study changes in the cerebral blood flow in different parts of the cortex and some mechanisms of its regulation at different times after the formation of a focus of cerebral ischemia.

EXPERIMENTAL METHOD

Experiments were carried out on 98 cats of both sexes weighing 2.5-4 kg. The animals were prepared for the experiments under general halothane anesthesia. To create an ischemic

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