EFFECT OF HYPERACTIVATION OF THE ANTERIOR AMYGADLOID NUCLEUS ON ACTIVITY OF THE REACTIVELY CHANGED HEART

Yu. I. Pivovarov and G. N. Kryzhanovskii*

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Hyperactivation of the anterior amygdaloid nucleus (AAN), a formation of the limbic system, accompanying the creation of a generator of pathologically enhanced excitation (GPEE) in it [6], has been shown [7] to lead to a parasympathetic type of disturbance of the cardiac rhythm, namely the development of bradyarrhythmias. The arrhythmias correlated with activity of the GPEE and with the onset of periods of enhanced discharges in the vagus nerves, which disappeared on removal of the GPEE or when its influence on the heart was blocked by vagotomy. The fact that these changes did not appear immediately after the formation of the GPEE, but only after several paroxysms of seizure activity of sufficient strength and duration, suggested that an important pathogenetic condition for the onset of these changes in the cardiac rhythm is overcoming the mechanisms of intrinsic regulation by the heart of the pathologically enhanced efferent impulsation.

In the investigation described below disturbances of the cardiac rhythm arising after creation of a GPEE in the AAN were studied when the reactivity of the heart was modified by various drugs and by acute myocardial ischemia.

EXPERIMENTAL METHOD

Experiments were carried out on 92 noninbred male rats weighing 150-200 g. The animals were first immobilized (with succinylcholine), artificially ventilated, and fixed in a stereotaxic apparatus, after which a GPEE was created in the left AAN by microinjection of 0.2 μl of the sodium salt of penicillin (100 units). Coordinates were taken from the stereotaxic atlas [15]: A = 6.5, L = 3.5, H = 7. Changes in reactivity of the heart were produced by intravenous injection of strophanthin K (25 animals) or KCl (10 animals), intraperitoneal injection of rausedil 5 mg/kg (11 animals), subcutaneous injection of adrenaline 7 mg/kg (16 animals), and ligation of the anterior (15 animals) and posterior (15 animals) coronary arteries. Rausedil and adrenaline were injected 24 h before the experiment. The doses of strophanthin and KCl were chosen beforehand so that they caused no changes in the ECG. Because of the variability of the effect of these drugs, before each experiment threshold doses of them, injection of which was found just to affect the cardiac rhythm, were determined in control animals with the same body weight as the experimental cats. These doses were reduced to one-tenth for the experimental animals: These did not disturb the cardiac rhythm and amounted to 460 ± 1.5 μg/kg for strophanthin and 5 ± 0.7 mg/kg for KCl. Intravenous injection of strophanthin and KCl was given at a time when the cardiac rhythm was still undisturbed. The coronary arteries (left anterior and posterior) were ligated in their lower third 10-15 min before injection of penicillin into AAN. Electrical activity in AAN was recorded by means of glass electrodes filled with 4M NaCl, with a tip 20-25 μ in diameter; the UBP2-03 amplifier and Elkar-4 electrocardiograph were used. Parallel recordings were made of the ECG in three standard leads.

EXPERIMENTAL RESULTS

If strophanthin was injected at a time of very small increases in the RR intervals associated with periodic episodes of paroxysmal activity in the nucleus (Fig. 1A, 1), it sub-

*Corresponding Member of the Academy of Medical Sciences of the USSR.

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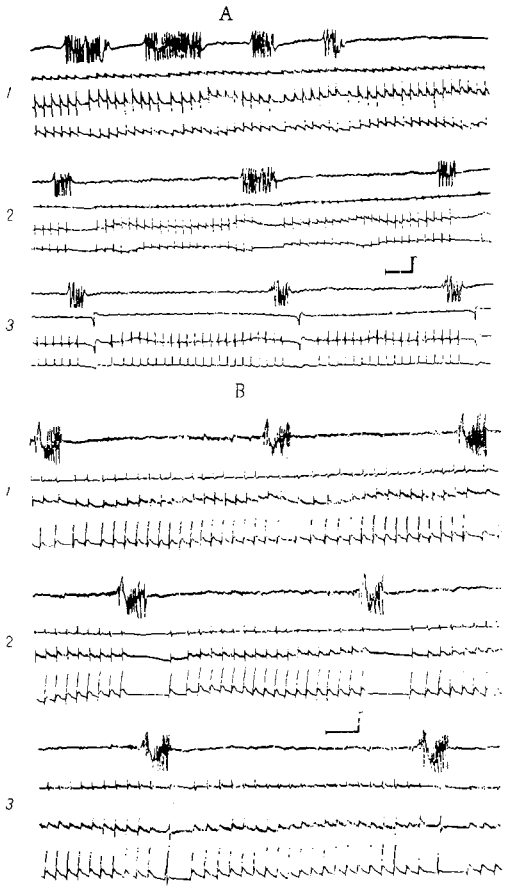

Fig. 1. Effect of hyperactivation of AAN on cardiac rhythm following intravenous injection of strophanthin K (A) and KCl (B). A: 1) 10 min after injection of penicillin into AAN, 2, 3) 15 and 25 min, respectively, after injection of strophanthin K; B: 1) 10 min after injection of penicillin into AAN, 2, 3) 10 and 15 min, respectively, after injection of KCl. Here and in Figs. 2 and 3, electrical activity in AAN and ECG leads I, II, and III are recorded in that order from top to bottom in each fragment. Calibration: 250 μV, time 1 sec.

stantially altered the ECG picture. In the overwhelming majority of experiments (20 animals) 10-15 min after injection of strophanthin discharges of the GPEE evoked a transient block of the atrioventricular node, expressed by omission of 1-3 QRS complexes (Fig. 1A, 2). Changes of rhythm of this sort were usually observed for 60-90 min and their duration depended on the level of activity of the GPEE and the duration of action of strophanthin on the heart.

Intravenous injection of KCl under conditions similar to those in the experiments with strophanthin caused well-marked asystoles as early as during the first 10 min (Fig. 1B, 2); each discharge of GPEE caused the total omission of four or five PQRST complexes. After 10-15 min these asystoles were replaced by left-ventricular beats (Fig. 1B, 3). These disturbances of the cardiac rhythm were observed for 30-40 min and they disappeared toward the end of the first hour after injection of KCl, despite continuing activity of the GPEE in AAN. This effect was evidently connected with a fall in the KCl concentration.

Opposite changes were observed on the ECG 24 h after preliminary injection of adrenalin and rausedil into the animals. They were manifested primarily as smoothing of the T wave, displacement of the S–T interval below the isoelectric line, tachysystole (500 ± 0.2 beats/min) in response to injection of adrenaline (Fig. 2A, 1) and enlargement of the T wave, and by displacement of the S–T interval above the isoelectric line and slowing of the heart rate to 200 ± 0.5 beats/min in response to injection of rausedil (Fig. 2B, 1). The effect of GPEE in AAN on the cardiac rhythm also differed under these conditions. In the initial stages of GPEE formation (5-10 min after injection of penicillin) grouped ventricular extrasystoles

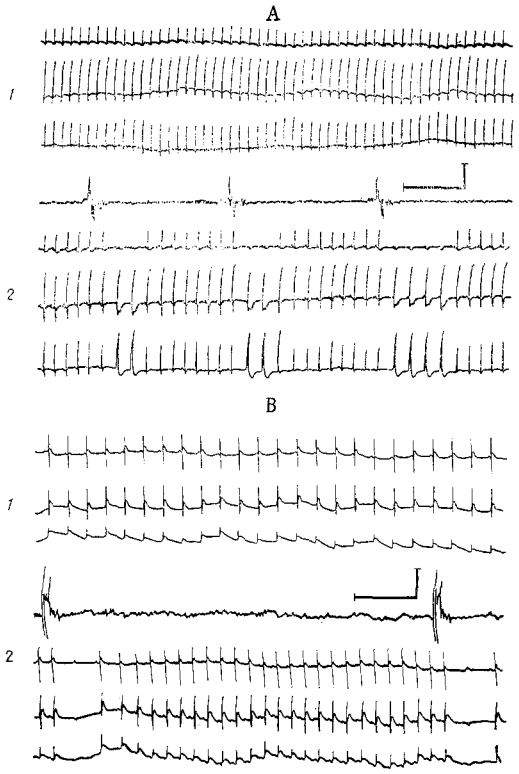

Fig. 2. Effect of hyperactivation of AAN on cardiac rhythm in animals receiving adrenaline (A) and rausedil (B) 24 h previously. A: 1) 24 h after injection of adrenaline, 2) 15 min after injection of penicillin into AAN; B: 1) 24 h after injection of rausedil, 2) 15 min after injection of penicillin into AAN.

appeared in the animals receiving adrenaline, even against the background of single discharges of GPEE (Fig. 2A, 2); they were observed throughout the period of activity of the generator. Meanwhile, in animals receiving a preliminary injection of rausedil, discharges of the GPEE in AAN (10-15 min after injection of penicillin) caused omission of the QRS complex (Fig. 2B, 2). In periods of "silence" of the GPEE the heart rate in these animals was increased by 1.5 times above the initial level. This effect was not observed in the other series of experiments described above.

Preliminary ligation of the posterior or anterior coronary artery was accompanied by features characteristic of acute myocardial ischemia on the ECG: displacement of ST above the isoelectric line, sinus tachycardia, inversion of waves in leads I and III, and the appearance of Pardee's waves. These features were most marked after ligation of the descending branch of the anterior coronary artery. Hyperactivation of AAN against this background, caused by microinjection of penicillin, led after 10-15 min to the appearance of cardiac arrhythmias, which corresponded exactly to discharges of the generator. Under these circumstances its discharges gave rise in the overwhelming majority of cases (in 10 of 15 experiments) to right-ventricular ectopic beats after ligation of the posterior coronary artery (Fig. 3A) and to an atrioventricular rhythm (in 14 of 15 experiments) after ligation of the anterior coronary artery (Fig. 3B).

The experiments showed that changes in reactivity of the heart considerably modify the effects of hyperactivation of the limbic system and, in particular, of one of its structures, the AAN. In the first place the sensitivity of the heart is increased or the resistance of its regulatory system to pathologically enhanced extracardial influences is weakened. Whereas in animals with an intact heart a disturbance of the rhythm of cardiac activity was observed following the creation of a GPEE in AAN only after several episodes of sufficiently strong and prolonged paroxysmal activity had occurred, in animals with modified reactivity of the heart arrhythmias were already appearing in the early stages of formation of the GPEE, accompanied by single paroxysmal discharges in AAN. In addition, qualitative differences in the character of disturbances of cardiac activity provoked by bursts of hyperactivity in AAN also were observed, depending on the nature of the factors acting on the heart.

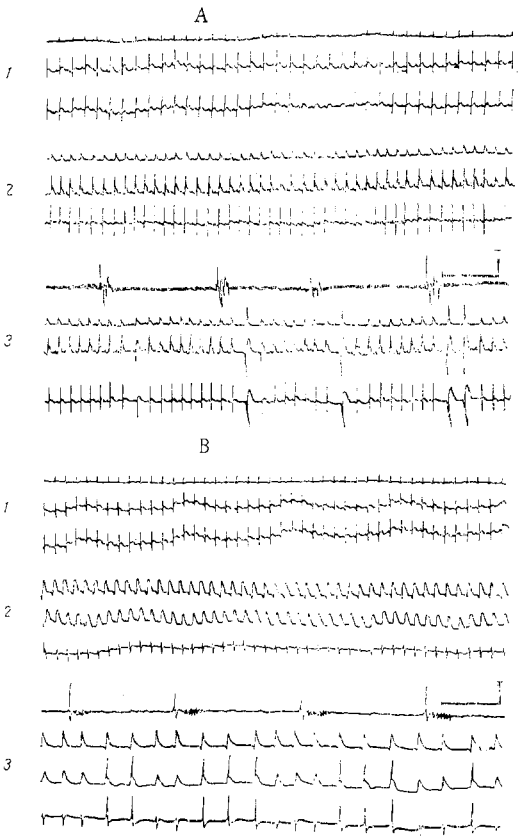

Fig. 3. Effect of hyperactivation of AAN on cardiac rhythm after ligation of posterior (A) and anterior (B) left coronary arteries. A: 1) initial ECG, 2) 10 min after ligation of descending posterior artery, 3) 15 min after injection of penicillin into AAN; B: 1) initial ECG, 2) 10 min after ligation of descending anterior artery, 3) 15 min after injection of penicillin into AAN.

As the results showed, the ECG changes were not of the same kind in animals receiving different drugs or in which different coronary arteries were ligated. This fact is all the more interesting because hyperactivity of AAN in animals with an intact heart always causes a similar effect — a similar disturbance of the cardiac rhythm (bradyarrhythmia). In the presence of the same pathologically enhanced activation, and with the same character of involvement of the limbic system in the pathological process, its effects on cardiac activity may thus be determined by the level of reactivity of the heart. The importance of this factor is emphasized by the results of the experiments with KCl, which showed that when the influence of K^+ ceases the disturbances of the cardiac rhythm disappear, despite continuing activity of the GPEE in AAN.

These results can explain the familiar clinical and experimental observations that in apparently similar situations in the emotional sphere (electrical stimulation, stress, neuroses, and other states), when the limbic system becomes involved in the process different ECG changes arise [1-5, 8-14].

The results of the investigations described above are evidence that hyperactivation of limbic structures and, in particular, of AAN may be a provocative factor in the presence of latent changes in heart, as is shown by the experiments using subthreshold doses of strophanthin and KCl. The experimental data illustrate the role of the functional state of the target organ (the effector component) in determining the fate and character of pathological processes evoked by hyperactive structures of the CNS, and they are of special interest for the study of diseases of regulation [6].

LITERATURE CITED

1. A. A. Abinder, in: Disturbances of Cardiac Rhythm [in Russian], Moscow (1967), p. 21.
2. S. V. Andreev and Yu. S. Chechulin, Outlines of Reactivity of the Cardiovascular System [in Russian], Moscow (1965).
3. D. A. Brusilovskaya, Patol. Fiziol., No. 2, 254 (1957).
4. P. V. Glazyrina, "On cortical regulation of cardiac activity following sensitization with a protein antigen," Candidate's Dissertation, Chelyabinsk (1957).
5. L. M. Gol'ber, V. I. Kandror, and I. V. Kryukova, Patol. Fiziol., No. 2, 9 (1975).
6. G. N. Kryzhanovskii, Determinant Structures in Pathology of the Nervous System [in Russian], Moscow (1980)
7. G. N. Kryzhanovskii and Yu. I. Pivovarov, Byull. Eksp. Biol. Med., No. 5 (1982).
8. B. M. Fedorov, Mechanisms of Disturbance and Restoration of Cardiac Activity [in Russian], Moscow (1968).
9. B. M. Fedorov, Emotions and Cardiac Activity [in Russian], Moscow (1977).
10. E. I. Chazov and V. M. Bogolyubov, Disturbances of Cardiac Rhythm [in Russian], Moscow, (1972).
11. S. V. Shestakov, Atrial Fibrillation and Flutter [in Russian], Moscow (1961).
12. L. M. Fogel'son, Clinical Electrocardiography [in Russian], Moscow (1957).
13. E. Corday and D. V. Irving, Disturbances of Heart Rate, Rhythm and Conduction, Philadelphia (1961).
14. M. Masasada, M. Ishada, and M. Suzuki, in: Proceedings of the Third Asian-Pacific Congress of Cardiology, Vol. 2, Kyoto (1964), p. 1089.
15. J. F. R. Köning and R. A. Klippel, The Rat Brain, Baltimore (1963).

PREVENTION OF POSTISCHEMIC REOXYGENATION DISTURBANCES OF CARDIAC FUNCTION BY ADAPTATION BY HIGH-ALTITUDE HYPOXIA

L. M. Belkina, V. A. Saltykova,
E. E. Ustinova, and F. Z. Meerson

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Preliminary adaptation to periodic and high-altitude hypoxia increases the resistance of the heart to ischemic injury and, in particular, reduces the size of the focus of ischemic necrosis [2, 8]. It has recently been shown that serious injuries to cardiomyocytes may arise not only in ischemia, but also during reperfusion of the myocardium, under the influence of the restored inflow of oxygen — reoxygenation [9, 10]. The importance of reoxygenation injuries is very great, for they may arise immediately after the transient ischemia associated with any coronary episode, as the result of reperfusion caused by the development of collaterals [1]. Meanwhile the effect of preliminary adaptation to high-altitude hypoxia on the resistance of the myocardium to reoxygenation injury has not hitherto been investigated.

The aim of the present investigation was to study the effect of preliminary adaptation of animals to high-altitude hypoxia at medium altitudes in the mountains on reoxygenation disturbances of cardiac contractile function, which regularly arise after transient ischemia caused by temporary occlusion of the coronary artery.

EXPERIMENTAL METHOD

Two series of experiments (eight or nine animals in each series) were carried out on male Wistar rats weighing 270-290 g: Series I was the control, series II consisted of animals adapted for 32-35 days in the mountains at an altitude of 2100 m at the Priél'brus'e Medical-

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