a special type of adaptation to the gradual increase of resistance in the arterial system. Compensatory hyperfunction of the myocardium of rabbits with arterial hypertension was homeometric in its type of development. The rapid rise of pressure in the ventricles enabled the cardiac frequency to be increased without impairment of filling of the heart with blood during systole. However, the reserve capacity of the hypertrophied myocardium was found to be limited, as shown by experiments with compression of the animals' aorta. Under isometric conditions of work of the myocardium, the "ladder of fatigue" [5] developed faster in the animals with a hypertrophied myocardium. Compression of the aorta evoked much less excitation of the sympathetic nervous system [2, 5] in animals with arterial hypertension than in intact animals. Constant and prolonged hyperfunction of the myocardium evidently led to partial exhaustion of the reserves of the sympathico-adrenal system.

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PREVENTION OF DISTURBANCES OF MYOCARDIAL CONTRACTILITY ARISING AFTER EMOTIONAL PAIN STRESS BY γ-HYDROXYBUTYRIC ACID AND THE ANTIOXIDANT IONOL

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KEY WORDS: rat heart; stress; γ-hydroxybutyric acid; ionol; peroxidation of lipids.

The excess of catecholamines in the blood arising under the influence of emotional pain stress leads to activation of lipid peroxidation and to the accumulation of lipid hydroperoxides in the heart muscle and other organs [5]. The harmful action of these peroxidation products leads to increased outflow of enzymes from the heart muscle [4] and to the development of focal lesions of contracture type in the myocardium [1].

It has also been shown that these stress-induced lesions in the heart can be completely prevented, first, by inhibition of the response to stress itself with the aid of the inhibitory metabolite γ-hydroxybutyric acid (GHBA), which acts at the brain level [1, 2] and, second, with the aid of the antioxidant ionol, an inhibitor of peroxidation, which acts mainly at the level of the heart and of other target organs [4]. Besides the disturbances of cardiac metabolism mentioned above in animals exposed to emotional pain stress (EPS),

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TABLE 1. Disturbance of Contractile Function of Heart Muscles under the Influence of Emotional Pain Stress and Its Prevention by Ionol and GHBA (M ± m)

Series of experiments and number	Amplitude of contraction, percent of initial	P	Velocity of contraction, metric units/sec	P	Velocity of relaxation, metric units/sec	P	Index of contraction, sec^{-1}	Index of relaxation, sec^{-1}
I (10)	6,99±0,81		1,086±0,049		0,891±0,062		0,156	0,118
II	17,33±3,24	P_{I-II} <0,001	3,463±0,327	P_{I-II} <0,01	3,655±0,377	P_{I-II} <0,01	0,194	0,207
III	9,83±1,09	P_{I-III} <0,05	1,126±0,047	P_{I-III} <0,05	1,273±0,118	P_{I-III} <0,05	0,127	0,118
IV	4,72±0,44	P_{I-IV} <0,01	0,518±0,060	P_{I-IV} <0,01	0,474±0,068	P_{I-IV} <0,01	0,109	0,107
V	15,03±1,28	P_{IV-V} <0,01	2,076±0,316	P_{IV-V} <0,01	2,184±0,318	P_{IV-V} <0,01	0,138	0,128
VI	9,00±0,83	P_{IV-VI} <0,01	1,362±0,344	P_{IV-VI} <0,01	1,312±0,293	P_{IV-VI} <0,01	0,151	0,122

disturbances of the contractile function of the heart regularly develop, as has been shown in the intact organism [6], on the isolated working heart [7], and on papillary muscle [3].

The possibility of preventing these poststressor disturbances of cardiac function with the aid of GHBA and ionol was studied in the present investigation.

EXPERIMENTAL METHOD

Male Wistar rats weighing 180-230 g were used. The animals were divided into six series, with 10 or 11 rats in each series. The animals of series I were the control, rats of series II and III were not exposed to stress or other procedures but received GHBA or ionol, respectively, the rats of series IV were exposed to emotional pain stress, the animals of series V were given GHBA before and during exposure to stress, and finally, the animals of series VI received ionol before exposure to stress.

EPS was applied in the form of an anxiety neurosis [9], for which the exposure to stress, which was accompanied by a long period of expectation of randomly applied painful blows, lasted 5-6 h.

GHBA was given by mouth in a dose of 100 mg/kg in 40% glucose solution through a catheter, the first dose 10 min before the beginning of EPS, the second, similar dose 3 h after the beginning of EPS.

Ionol [2,6-di(tert-butyl)-4-methylphenol] was injected intraperitoneally in a sessional dose of 100 mg/kg daily for 3 days before EPS; a suspension of the compound in physiological saline was prepared beforehand with the aid of the detergent Tween.

Under urethane anesthesia, 2 h after the end of exposure of the animals to stress, the heart and other organs were removed. The harmful effect of EPS was regularly manifested by this time as the development of gastric ulcers in all the rats exposed to stress; the mean length of the ulcers, calculated for one stomach, was 8-9 mm. The prophylactic effect of the two chemical agents used, as in previous investigations [1, 4], was manifested as a sharp decrease in ulceration of the gastric mucosa: In one-third of the rats these lesions were absent altogether, and in the rest the mean length of the ulcers was 2-3 mm per stomach.

The contractile function of the lateral papillary muscle of the left ventricle was investigated in animals of all series [10].

EXPERIMENTAL RESULTS

Data on disturbances of contraction and relaxation of the papillary muscle of the heart after EPS and on the prevention of these disturbances by GHBA and ionol are given in Table 1. They show, first, that as a result of administration of GHBA to intact animals (series II) the amplitude of contraction, the velocity of contraction, and the velocity of relaxation of the papillary muscles were increased 3-4-fold. After injection of ionol into the intact animals (series III) the same effect was observed but was weaker: The parameters were increased by about 1.5 times compared with the control. This effect of GHBA and ionol, unexpected in our opinion, on the contractile function of the heart of control animals was reproduced with complete constancy in many repeated experiments. This effect can be explained on the grounds that administration of the natural inhibitory metabolite GHBA and of the synthetic antioxidant ionol protected the organism as a whole and the heart muscle in particular against two noxious influences, namely: against "the stress of beating" and

"dissection hypoxia." The reason why the effect of GHBA was stronger than that of ionol is that GHBA has both an antistressor [2, 3] and an antihypoxic action [8], whereas ionol has no appreciable antihypoxic action.

Although a more detailed analysis of this phenomenon must await a future investigation, it can be said that the results now obtained provides a basis for the use of GHBA and ionol to protect the myocardium in all experiments with the isolated heart and papillary muscle, and also during operations associated with mechanical injury or ischemic traumatization of the heart.

Second, the data in Table 1 show that in animals which did not receive GHBA or ionol, the amplitude of contraction, velocity of contraction, velocity of relaxation, and index of contraction were reduced by 30-35% under the influence of EPS (as was observed previously [3, 6, 7]). In other words, disturbances of the contractile function were quite distinctly observed under the influence of EPS.

Finally, the main result of this investigation is that administration of GHBA before EPS increased the parameters of the contractile function of the papillary muscle by about the same degree as in intact animals: The amplitude of contraction, and also the velocity of contraction and relaxation of the papillary muscle of animals exposed to EPS after administration of GHBA were more than twice as high as in control animals not exposed to stress, whereas the indices of contraction and relaxation did not differ significantly from the control.

Preliminary administration of GHBA thus prevented the lowering of the parameters of the contractile function of the papillary muscle to those very low values which are usually observed in animals exposed to stress, and in this sense the prophylactic effect of GHBA is not in dispute. However, a closer analysis of the data in Table 1 shows that the reduction of the main parameters of contractile function of the papillary muscle caused by EPS in animals receiving GHBA was equal in absolute values to those not receiving GHBA before stress, or was even higher than in the latter. In fact, the amplitude of contraction was reduced under the influence of EPS in the animals of both series (IV and V) by about two units (compared with the corresponding control). The velocity of contraction was reduced by 0.5 units in animals not receiving GHBA, but by one unit in animals protected with GHBA, and so on. Consequently, preliminary administration of GHBA did not abolish the disturbances of contractile function, but it made these disturbances not significant, so that the original prestress contractile function of the papillary muscle was significantly higher in the animals receiving GHBA.

Ionol had a different effect. Its injection completely abolished the disturbances of contractile function that usually arose under the influence of EPS. The data given in Table 1 in fact show that all parameters of the contractile function of the papillary muscle of animals exposed to EPS after preliminary treatment with ionol were completely indistinguishable from these parameters in intact animals receiving ionol.

It can thus be concluded that under the experimental conditions used GHBA prevented disturbances of myocardial contractile function induced chiefly by hypoxic damage, but that ionol, an inhibitor of peroxidation, prevented disturbances of contractile function caused mainly by stress injury.

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EFFECT OF ELECTRICAL STIMULATION OF NUCLEUS CAUDALIS RETICULARIS PONTIS ON FOCI OF EPILEPTIC ACTIVITY IN THE CORTEX

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KEY WORDS: epileptic focus; epileptic complex; pathological system; antiepileptic system; "antisystem"; neocortex; nucleus caudalis reticularis pontis.

Stimulation of nucleus caudalis reticularis pontis (NCRP) has been shown to depress epileptic activity [6, 7]. To elucidate the special nature of this effect it was decided to study it in the presence of different forms of epileptic activity in the cerebral cortex: a single epileptic focus and a complex of foci of epileptic activity [4, 5], constituting a unique form of pathological system [2, 3], which arises under the influence of a hyperactive determinant structure [1-3] or determinant epileptic focus [4].

EXPERIMENTAL METHOD

Acute experiments were carried out on cats. Under ether anesthesia bipolar constantan electrodes, 120 μ in diameter with interpolar distance of 0.5 mm, were inserted into NCRP, and a monopolar electrode 250 mm in diameter was inserted into the central periaqueductal gray matter in accordance with coordinates of a stereotaxic atlas [7, 8]. The central periaqueductal gray matter was destroyed by coagulation (2-4 mA, 15-20 sec). The eye was then drained and the bones of the calvaria and orbit were removed, to provide wide access to different parts of the frontal region of the neocortex of one hemisphere. Scattered foci of epileptic activity were created by application of a piece of filter paper (2 mm^2) soaked in 0.1-0.5% strychnine nitrate solution. Foci of this sort were created in different parts of the coronal and anterior, posterior, and middle sigmoid gyri. A focus of more powerful epileptic activity was created in the orbital or coronal gyrus by application of a 1-3% solution or a crystal of strychnine. After the appearance of the foci the application of strychnine ended and the filter paper with strychnine was removed. Potentials were derived by a monopolar technique; the reference electrode was fixed in the nasal bones, and cotton threads soaked in Ringer's solution served as active electrodes. Potentials were recorded on the 4-ÉÉG-3 ink-writing electroencephalograph. Electrical stimulation (ES) of NCRP was carried out with series of square pulses (0.5 msec, 220 Hz, 3-5 V), in sessions 10-20 sec in duration, separated by intervals of 2 min. The locations of the electrode tip in the subcortical structures were determined histologically.

EXPERIMENTAL RESULTS

In the experiments of series I the effect of stimulation and destruction of NCRP on activity of a single epileptic focus was studied. An epileptic focus (Fig. 1A) was created in the cortex of the posterior sigmoid gyrus with the aid of a 1% solution of strychnine (Fig. 1A). ES of NCRP was shown to completely suppress epileptic discharges in the focus;

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