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ACTIVATION OF METABOLISM OF THE GABA SYSTEM IN THE CEREBRAL HEMISPHERES BY STRESS FACTORS

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Emotional and pain-induced stress (EPIS) is known to regularly cause activation of metabolism of the brain GABA system, which is expressed as a two-threefold increase in glutamate decarboxylase (GDC) and GABA transaminase (GABA-T) activity, and also as increased incorporation of labeled precursors into glutamate and GABA [3].

The study of the biological significance of this activation revealed that administration of γ-hydroxybutyric acid (GHBA), an end product of GABA, before EPIS largely prevents activation of the hypophyseo-adrenal system [6], the development of gastric ulcers [3-5], and disturbance of myocardial metabolism [4], which usually develop after severe EPIS.

On the basis of these observations it can be postulated that activation of brain GABA metabolism is a nonspecific mechanism which is realized during the action of various extremal stimuli on the body, and which by limiting the stress syndrome, prevents stress-induced injuries. To test this hypothesis, the basic indices of GABA metabolism were compared in this investigation in four groups (series) of animals.

The experiments of series I were conducted on Wistar rats weighing 180-200 g. EPIS was produced by the method of Desiderato et al. [4, 10], described previously, in the form of an anxiety neurosis, with a duration of 6 h. In the experiments of series II, conducted on similar rats, 2% formalin solution in a dose of 1 ml was injected subcutaneously into the region of the spine at intervals of 24 h for 2 days. Rats not subjected to any procedure served as the control to these two series. The experiments of series III were carried out on rabbits in which the descending branch of the left coronary artery was ligated by the usual method [1, 7]. The development of necrosis was confirmed by the ECG and the results of morphological investigations. The experiments of series IV were conducted on rabbits in which experimental aortic stenosis was created by the method described previously [2], resulting in a reduction of two-thirds in the area of cross section of the aortic orifice and leading to the development of compensatory hyperfunction of the heart. Animals on which thoracotomy was performed without ligation of the coronary artery and aorta served as the control for series III and IV.

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TABLE 1. Activity of GABA-ergic System in Cerebral Hemispheres of Animals Two Days after Exposure to Various Kinds of Stress

Animals	Series of experiments	Glutamate, mg %	GABA, mg %	GDC, μmoles GABA formed/h/g	GABA-T, μmoles GABA hydrolyzed/h/g
Rats	Control (n = 10)	104,8±2,1	14,3±0,2	13,08±0,8	13,0±0,7
	I – emotional and pain-induced stress (n = 10)	68,1±2,0*	10,6±0,6†	31,6±1,2†	35,4±1,0†
	II – injection of formalin (n = 10)	70,0±0,6†	11,14±0,4*	20,0±0,8†	47,7±0,84†
Rabbits	Control (n = 6)	62,5±2,0	15,25±1,2	9,5±0,6	9,25±0,3
	III – ischemic necrosis of myocardium (n = 6)	25,5±1,7†	14,75±1,1*	18,0±2,0†	45,0±2,4‡
	IV – creation of aortic stenosis (n = 6)	26,5±1,9†	14,0±2,0	20,0±2,2†	33,75±2,3‡

*P < 0.05.

†P < 0.01.

‡P < 0.001.

The animals of all four series were killed 2 days after the beginning of exposure to stress. To assess the state of the GABA system in the cerebral hemispheres the concentration of glutamate, from which GABA is formed, and of GABA itself was determined by chromatography on paper as described by Shatunova and Sytinskii [9]. At the same time, activity of GDC, an enzyme involved in the formation of GABA from glutamate, and of GABA-T, which destroys GABA, was determined by the method described by Sytinskii and Shang K'o-tsin [8]. Activity of the enzyme was expressed in micromoles of substrate hydrolyzed per hour in 1 g of tissue.

It will be clear from Table 1 that after exposure to all kinds of stress used, GDC activity increased approximately twofold, and the glutamate concentration in the brain tissues fell correspondingly by 30-60%. GABA-T activity rose after exposure to all kinds of stress used by a somewhat greater degree – namely threefourfold, and there was a corresponding tendency for the GABA concentration to fall.

On the whole these facts show unequivocally that the GABA-ergic system of the brain is activated as a result of exposure to different kinds of stress and they must be evaluated in conjunction with data already mentioned, showing that GABA, an end product of GABA metabolism, prevents excessive stimulation of the function of the hypophyseo-adrenal system and the increase in damage to the internal organs during stress. This suggests that the GABA-ergic system may in fact play the role of a nonspecific mechanism limiting the stress syndrome and preventing damage during exposure of the organism to various kinds of stress.

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