PHASES OF THE PRIMARY RESPONSE OF THE SYMPATHOADRENAL SYSTEM TO STRESS

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Virtually no information about the principles governing the response of the sympathicoadrenal system (SAS) in the earliest, initial period of formation of the stress syndrome can be found in the literature on the catecholaminergic mechanisms of stress [4, 5, 8, 9, 13].

The aim of this investigation was to make a combined assessment of changes in the concentrations of catecholamines (CA) and their precursors and metabolites in the blood and tissue of various organs immediately after exposure to stress.

EXPERIMENTAL METHOD

A state of stress was produced experimentally in 42 sexually mature mongrel dogs (males) under 10 kg in weight, by one-stage trauma to the soft tissues of the thigh, below the threshold for inducing shock, inflicted by means of a percussive mechanism (Efficiency Suggestion No. 850, 1984, Rostov Medical Institute), whereby the intensity of nociceptive action could be regulated so as not to exceed the threshold of behavioral response (Instructions of the Ministry of Health of the USSR specifying the rules of work with experimental animals). The dogs were killed by one-stage decapitation in the control (intact animals, group 1), and also 10-15 sec (group 2) and 60 sec (group 3) after exposure to stress, under pentobarbital anesthesia (10-15 mg/kg body weight). Tissue samples were placed in ice, quickly separated, and processed. Adrenalin (A), noradrenalin (NA), dopamine (DA), dopa, and free forms of metanephrine (MN) and normetanephrine (NMN) in the blood and tissues of various organs were determined fluorometrically [6, 7]. The intensity of fluorescence was measured by means of an Hitachi spectrofluorometer (Japan). Monoamine oxidase (MAO) activity in the blood and tissues was determined by the method [2] and expressed in micrograms of ammonia per milligram protein. The protein concentration was measured as in [13]. To estimate qualitative changes in CA metabolism the values of the coefficients of correlation between concentrations of their fractions were calculated by the method in [1].

EXPERIMENTAL RESULTS

Analysis of the data given in Table 1 showed that the response of SAS developing immediately (10-15 sec) after exposure to stress was characterized by an increase in the concentrations of A and DA in the tissues, accompanied by mobilization of the NA reserves, most marked in the hypothalamus, a fall of the A level and rise of the NA level in the blood, inhibition of MAO activity, and a fall of the MN and NMN levels in the blood and tissues.

Emptying of the hypothalamic NA depots during stress, as several studies have shown [9, 10], is associated with the secretion and increased utilization of NA during development of adaptive reactions at the hypothalamic level, including in the peptidergic systems responsible for the reorganization of pituitary–adrenocortical activity. On the basis of our results this mechanism can be interpreted as one of the possible factors leading to reduction of NA synthesis, accompanied by inhibition of o-methylation and oxidative deamination, and also with intensification of methylation of NA into A. The following evidence supports this conclusion: 1) depletion of the NA reserves in the tissue accompanied by a marked increase in the A and DA concentrations and a decrease in MN and NMN concentrations; 2) lowering of the NA/DA ratio, indicating a decrease in the relative activity of the conversion of DA into NA; 3) an increase in the A/NA and DA/dopa ratios, which characterizes the increase in the relative velocity of the reactions of A and DA synthesis respectively; 4) lowering of the intensity of CA degrada-

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TABLE 1. Effect of Stress on Concentrations of CA and Their Precursors and Metabolites in the Blood (in μg/liter) and Tissues (in μg/g) of Dogs (M ± m)

Tissue	Group of animals	Parameter					
		A	NA	DA	dopa	MN	NMN
Blood	1	3,88±0,14	6,56±0,31	8,05±0,41	3,30±0,22	0,67±0,03	2,00±0,10
	2	1,11±0,11*	9,16±0,49*	11,03±0,94*	4,46±0,38*	0,32±0,02*	0,35±0,02*
	3	4,91±0,37**	5,93±0,76***	20,50±1,27***	4,03±0,32	1,64±0,14***	2,36±0,23**
Adrenal	1	3395±144	346±20,6	112±7,4	203±20,6	2,98±0,30	3,90±0,25
	2	6599±422*	0*	59,4±4,1*	120±9,5*	0,79±0,06*	0,81±0,40*
	3	6043±305*	2190±147***	139±10,6**	404±30,2***	3,53±0,20**	4,19±0,24***
Hypothalamus	1	0,23±0,01	1,22±0,03	1,23±0,05	0,23±0,02	0,03±0,002	0,06±0,004
	2	2,00±0,10*	0*	1,93±0,16*	0,12±0,01*	0,02±0,001*	0,03±0,002*
	3	0,51±0,04***	1,97±0,19***	2,45±0,14***	0,16±0,01***	0,26±0,028***	0,36±0,018***
Heart	1	0,09±0,004	0,43±0,008	0,30±0,02	0,06±0,004	0,014±0,0007	0,023±0,001
	2	0,34±0,027*	0,28±0,022*	0,42±0,04*	0,04±0,003	0,005±0,0003*	0,015±0,001*
	3	0,17±0,008***	0,75±0,040***	0,35±0,04	0,04±0,002***	0,045±0,003***	0,079±0,005***
Liver	1	0,04±0,003	0,25±0,014	0,17±0,01	0,04±0,002	0,011±0,0007	0,23±0,001
	2	0,17±0,014*	0,18±0,015*	0,29±0,03*	0,05±0,003*	0,006±0,0003*	0,016±0,001*
	3	0,09±0,003***	0,48±0,028***	36±0,03*	0,04±0,003	0,040±0,004***	0,059±0,005***

Legend. *) Differences significant compared with group 1 of the corresponding series of experiments; **) the same, compared with group 2; ***) compared with groups 1 and 2.

tion via the o-methylation (a decrease in the MN/A and NMN/NA ratios) and oxidative deamination (lowering of MAO activity) pathway.

Lowering of the transmitter concentration in the peripheral organs is due to similar causes and also to probable NA release into the blood stream [10]. Evidently as a result of the rapid emptying of the central and peripheral NA depots in the initial period of stress a unique kind of deficiency of adrenergic regulation is created in the body, and it may lead to elimimation of circulating A by the tissues [14]. Increased NA utilization in the tissues behaves in many cases as a factor activating its biosynthesis. CA metabolism in the brain in all probability is no exception. It can be tentatively suggested that in the phase immediately after exposure to stress (after 60 sec) not only does the rate of synthesis of monoamines increase, but it also exceeds the rate of their utilization, as a result of which the CA concentration rises in various organs. On account of this, the fall in the NA concentration in the brain and other tissues is followed not only by its rapid and complete recovery, but also by a sharp increase in its value in the hypothalamus, the adrenal medulla, and the tissues of peripheral organs, with maintenance of high A and DA levels everywhere, and also an increase in MAO activity and in the MN and NMN concentrations in the blood and tissues. The statistically confirmed homogeneity of the numerical data for intact and stressed dogs, and also the results of similar investigations on noninbred albino rats and rabbits [3], are evidence that significant individual variations between different animals do not exist and that the changes discovered are universal in character.

Consequently, reactive changes in SAS are characterized by a definite level of activity of the processes of CA secretion, elimination, and metabolism, which differs at different times after exposure to stress, in agreement with existing views of the staggered response of SAS to acute stress situations [4, 8, 9, 10]. Accordingly we distinguish two phases in the time course of the primary response of SAS to stress, distinguished by the different direction of the changes in parameters of the hormonal and transmitter components of the system. The first phase, characterized by activation of adrenal and dopamine components and by parallel inhibition of the noradrenergic mechanism, was described as the phase of dissociation of secretory and synthetic activity of the SAS. The second stage of the response, in view of the generalized character of excitation of all levels of the system, we considered to be the phase of synchronous activation of SAS. The most important manifestations of the phase of dissociation of secretory and synthetic activity of the SAS, arising immediately after stress, are thus elevation of the A and DA levels and lowering of the NA concentration, i.e., opposite changes in the concentrations of these CA fractions with parallel inhibition of the mechanisms of their inactivation. A characteristic feature of the phase of activation of the SAS, recorded 60 sec after stress, is that changes in the A, NA, and DA concentrations take place in the same direction, for they are all sharply increased, and this is accompanied by an increase in the intensity of their metabolism along the path of oxidative deamination and o-methylation.

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EFFECT OF LIPID PEROXIDATION IN THE LUNGS ON ARTERIAL HYPOXEMIA DEVELOPMENT IN RATS SOON AFTER TRAUMA

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After injury to the lungs the residual portions undergo hyperventilation [9], and this induces the accumulation of lipid peroxides and free radicals in them [11, 13, 15]. However, the relative importance of activation of lipid peroxidation (LPO) in the lungs, which requires O_2 for it to proceed [1], in the development of post-traumatic arterial hypoxemia, which often appears in the period immediately after closed chest trauma and is responsible for its unfavorable course [7], is not yet clear. The aim of this investigation was to determine the role of these processes in the mechanism of the fall of p_aO_2 in the early post-traumatic period following contusion of the chest in rats.

EXPERIMENTAL METHOD

Experiments were carried out on 135 male Wistar rats weighing 200-250 g. Contusion of the lungs was produced by means of a spring-operated pistol. A blow of measured force was applied to the right half of the chest as described previously [5]. As a result of trauma the upper and cardiac lobes of the light lung (RL) were injured, whereas in the left lung (LL) no mechanical injury was produced. To analyze the time course of their state rats were decapitated before trauma (intact rats), 1 and 2 h after trauma, and every subsequent day until the 7th day inclusive, with 10-12 animals used at each time. Before sacrifice, the rats were bound in the prone position and their respiration rate (RR) and fO_2 value, i.e., the difference between the O_2 concentration in the inspired air (21%) and the O_2 concentration in the end-expired air, measured with a MKh-6202 gas analyzer. The parameter fO_2 was used to char-

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