differed in degree. Significant inhibition of synthesis of water-insoluble proteins, to the greatest degree, was observed in the hypothalamus, and in the other structures it was less marked. Incorporation of ^{35}S-methionine into water-soluble proteins of the experimental animals was significantly reduced in the hippocampus, subcortical formations and the medulla, and it was reduced by a lesser degree in the cerebral cortex and cerebellum. Some degree of activation of protein synthesis was observed in the hypothalamus. Comparison of the results with data on the action of ethanol administered in the antenatal period on brain protein synthesis [1, 2] reveals definite similarity: inhibition of incorporation of precursors into brain proteins. Some differences were found in the effect of ethanol during each of these periods. Whereas with intrauterine exposure to ethanol synthesis of water-insoluble proteins was disturbed by a greater degree, mainly in the hippocampus and neocortex, postnatal administration of ethanol was accompanied in late ontogeny by marked inhibition of synthesis of water-soluble proteins in several brain structures. Meanwhile, changes of this kind in water-insoluble proteins were observed mainly in the hippocampus.

Disturbances of metabolism of individual groups of proteins in certain brain structures may lie at the basis of changes in behavioral responses and may be reflected in integrative activity of the brain. As was shown above, the action of ethanol in the early postnatal period led to disturbances of certain forms of learning (CPAR) but had no significant effect on CAAR, i.e., it was selective in character. Antenatal alcoholization gave rise to more marked changes in various forms of behavioral reactions than exposure to ethanol in the lactation period. These results are evidently linked both with the action of ethyl alcohol on different stages of ontogenetic maturation of the CNS and with its smaller doses transmitted with maternal milk.

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STAGE OF INHIBITION OF LIPID PEROXIDATION DURING STRESS

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KEY WORDS: stress; pain syndrome; lipid peroxidation.

One result of exposure of the body to stress is activation of free-radical lipid peroxidation (LPO), leading to damage to cell membrane structures [2, 7]. However, the question of the pathogenetic role of different stages of stress and of their particular features remains unexplained; in particular, it is not clear what changes in LPO take place during the little-studied early stage of stress.

The aim of this investigation was to study the state of LPO in the brain and blood of rats during exposure to acute stress and to compare it with changes in the parameters of LPO during a pain syndrome.

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TABLE 1. Parameters of LPO in Brain and Blood of Rats Exposed to Immobilization Stress for 2 h (M ± m)

Parameters	Test object	Control	Immobilization in tubes	Immobilization in supine position
TBA-active products	Brain	100,0±3,4	80,6±3,0**	23,4±5,1**
The same	Serum	100,0±3,1	100,0±3,4	21,4±6,0**
Conjugated dienes	Brain	100,0±5,5	93,1±5,3	86,0±4,6**
The same	Serum	100,0±7,1	95,9±5,4	107,0±7,6
Schiff bases	Brain	100,0±2,2	93,1±2,3**	94,6±2,2**
Superoxide dismutase activity	Brain	100±5	99±3	144±7**
Nonenzymic superoxide scavenging activity	Serum	100±5	96±3	106±3*
Total PL concentration	Lipid extracts of brain	100,0±3,2	87,3±2,3**	92,4±2,5*
Ch concentration		100,0±2,7	89,2±3,3**	85,2±3,0**
Ch/PL		100	102,2	79,5*
Readily oxidized PL/not so readily oxidized PL		100	103,1	117,5**

Legend. 1. Parameters calculated in percent of corresponding values for control group, taken as 100%. 2. Readily oxidized PL: phosphatidylserine + phosphatidylethanolamine + phosphatidylinositol + cardiolipin; not so easily oxidized PL: phosphatidylcholine + sphingomyelin. 3. *$p < 0.05$, **$p < 0.01$ for comparison with control.

EXPERIMENTAL METHOD

Experiments were carried out on 100 noninbred albino rats weighing 150-180 g. The following procedures were used to induce stress: immobilization in Plexiglass tubes for 2 h, strict immobilization in the supine position with the paws fixed for 2 h, painful electrical stimulation in a special chamber with electrically conducting floor, by a current of 3-4 mA; frequency of electrical stimulation 1-2 pulses/sec, duration 0.25-2 h. After the end of the procedure the animals were decapitated, a homogenate of the cerebral cortex was obtained together with blood serum, in which the concentration of material reacting with 2-thiobarbituric acid (TBA) [12], conjugated dienes [6], and superoxide dismutase activity [11] were determined. Lipids were extracted from the homogenate by means of a mixture of chloroform and methanol by Folch's method [13], fluorescent products of LPO (Schiff bases) were determined in the lipid extracts [4], and the concentrations of phospholipids (PL) and cholesterol (Ch) were determined by thin-layer chromatography. Parameters of LPO also were investigated in venous blood plasma from 44 women with dysmenorrhea, in the midlutein phase of the menstrual cycle, at the height of the pain, during the first 12 h and 12-24 h after the beginning of the pain syndrome during menstruation. The concentration of Schiff's bases were determined as in [4], lipid hydroperoxides were estimated by chemiluminescence induced by Fe^{++} ions [5], peroxide chemiluminescence was measured in a system induced by H_2O_2 [8].

EXPERIMENTAL RESULTS

Parameters of LPO in the brain and blood serum of rats subjected to immobilization stress are given in Table 1. Activation of LPO did not take place under these conditions; moreover, in the case of immobilization in the supine position for 2 h significant inhibition of LPO was observed in the brain, accompanied by accumulation of readily oxidized PL and by an increase in superoxide dismutase activity. Since data indicating activation of LPO during stress were obtained as a rule during the long-term action of stressors, it was logical to suggest that activation of LPO is preceded by a stage of its inhibition.

To test this hypothesis changes in parameters of LPO during severe stress caused by the action of the electric current were investigated (Table 2). During continuation of the action of stress all the parameters underwent phasic changes. The content of LPO products in the brain and blood serum fell sharply after 15 min, then rose, to approach the corresponding initial values, and to exceed them after 30 min and 1 h. Maximal activation of LPO was observed after 2 h of continuous action of the electric current, and it lasted at least 4-5 h after discontinuation. The corresponding stages also were characteristic of brain lipids: The concentration of Ch and the Ch/PL ratio fell to minimal values after 15 min, then rose, to reach a maximum after 2 h of exposure to stress. The PL concentration and the ratio of readily oxidized to not so readily oxidized forms of PL showed reciprocal changes relative to those of the Ch level. Changes in superoxide dismutase activity in the brain and blood serum also were phasic in character, rising during inhibition of LPO and falling in the phase of its activation.

TABLE 2. Parameters of LPO in the Brain and Blood of Rats Exposed to Stress due to Painful Electrical Stimulation (M ± m)

Parameters	Test object	Duration of exposure to stress, min							
		0	15	30	60	120	120[a]	120[b]	120[c]
TBA-active products	Brain	100,0±3,4	21,5±2,6**	30,0±6,8**	130,8±15,6**	251,7±13,7**	192,3±11,3**	200,0±12,1**	257,7±13,6
The same	Serum	100,0±3,1	20,1±1,9**	28,1±2,3**	108,9±5,9**	224,4±9,3**	174,9±8,2**	165,0±8,3**	209,7±10,7**
Conjugated dienes	Brain	100,0±5,5	61,1±8,3**	110,0±9,7	121,8±9,4*	156,3±10,1**	143,1±10,5**	150,5±9,9**	161,2±9,9**
The same	Serum	100,0±7,1	52,3±8,4**	90,8±9,0	100,0±8,9	128,4±10,1*	133,3±10,4**	131,7±10,1**	136,8±10,8**
Schiff bases	Brain	100,0±2,2	61,1±2,4**	68,0±2,1**	94,2±2,6*	133,3±3,8**	133,3±3,7**	129,0±3,2**	133,3±3,6**
Superoxide dismutase activity	Brain	100±5	165±7**	125±5**	105±5**	95±4**	85±4**	75±4**	70±3**
Nonenzymic superoxide scavenging activity	Serum	100±5	250±8**	200±6**	150±6**	140±6**	80±4**	60±3**	50±3**
Total PL concentration	Lipid extracts of brain	100,0±3,2	108,6±2,9*	106,4±2,7*	104,0±3,0	92,4±2,8*	93,4±2,7*	90,0±2,5*	92,2±2,5*
Ch concentration		100,0±2,7	76,2±3,1**	87,0±3,0**	100,4±3,6	111,7±3,3**	110,1±3,3**	102,8±3,4	116,4±3,7**
Ch/PL		100,0	70,4**	81,8*	96,5	121,3**	122,7**	114,2*	126,3**
Readily oxidized PL/not so readily oxidized PL		100,0	119,6**	108,7*	100,0	101,7	103,9	104,3	105,2

Legend. [a], [b], [c]) Investigations conducted 90, 180, and 270 min respectively after end of a session of stress lasting 120 min. Remainder of legend the same as to Table 1.

TABLE 3. Dynamics of Parameters of LPO at Different Periods of the Pain Syndrome in Patients with Dysmenorrhea (in % of value of LPO parameters in midlutein phase, taken as 100%; M ± m)

Parameter	Control (C)	First 12 h after beginning of pain (I)	13-24 h from beginning of pain (II)	P_{C-I}	P_{C-II}	P_{I-II}
Schiff's bases	141,1 (n=14) / 109,4—177,2	50,98 (n=15) / 7,92—101,16	260,07 (n=14) / 19,17—642,58	<0,001	>0,05	<0,001
Peroxide chemiluminescence	259,8 (n=15) / 87,8—700,0	460,2 (n=8) / 1,7—1550,4	15117,3 (n=7) / 999,9—68263,4	<0,05	<0,001	<0,005
Hydroperoxides (induced chemiluminescence)	105,6 (n=14) / 93,0—114,6	102,1 (n=16) / 30,3—238,9	172,8 (n=8) / 47,4—518,5	>0,05	>0,05	>0,05

Legend. 1. Numerator shows mean value, denominator shows limits of variations. 2. Significance of difference calculated by Mann—Whitney U test.

In women with dysmenorrhea the plasma concentration of Schiff's bases 12 h after the beginning of pain was reduced by almost two-thirds, whereas after 12-24 h it was raised to almost twice the corresponding control values (Table 3). In the early stage of pain stress no increase was found in the levels of hydroperoxides or of peroxide chemiluminescence, which was observed in the later period.

The results are evidence that in different forms of stress there is a primary stage of inhibition of LPO, which is followed by its activation; the times of onset of the phases of inhibition and activation of LPO, moreover, depend on the nature of the stress and the state of the organism. Inhibition of LPO is accompanied by an increase in the fraction of readily oxidized PL, a decrease in the Ch concentration and the Ch/PL ratio, whereas on the change from inhibition of LPO to its activation, the shift of these parameters also changes. The results of correlation agree with the regulatory scheme suggested by Burlakova [1]. The increase in superoxide dismutase activity in the brain and blood serum corresponded to inhibition of LPO, a decrease to its activation. All changes appearing in homogenates of the cerebral cortex corresponded to changes observed in fractions of glia, neurons, and synaptosomes, evidence of generalized changes in these parameters.

The question of the causes and physiological significance of the biphasic changes in LPO in the body under the influence of stress is of great theoretical and practical importance. Since we know that catecholamines and certain steroid compounds have the ability to act as "traps" of superoxide radicals [9], it can be postulated that these hormones, secreted intensively by the adrenals in response to the action of stress factors [14], take part in the inhibition of LPO in the initial period of stress. Activation of scavenging of superoxide radicals in the brain and, in particular, in the blood serum takes place predominantly through an increase in the contribution of the nonprotein, cyanide-resistant component, indirect evidence in support of this hypothesis.

What is the cause of the subsequent rapid replacement of inhibition of LPO by its activation? Probably a predisposition to activation of LPO is created actually in the period of its inhibition: readily oxidized PL accumulate, the Ch level falls, and the lipids become less resistant to LPO. Disturbances of the microcirculation observed during stress [3] lead to increased radical formation [10], loosening of the structure of the membranes, and in the presence of an excess of radicals, catecholamines undergo autooxidation, and are converted from "traps" into generators of additional radicals. All these phenomena create conditions favorable for activation of LPO.

On the basis of all the facts described above, the two sequences of events, whose realization leads to inhibition, followed by activation, of LPO can be represented schematically. The first: stress—catecholamine release—lowering of the Ch concentration, the Ch/PL ratio, and the antioxidative activity of membrane lipids, while the second stage is realized simultaneously: the sequence of stress—catecholamine release—disturbances of the microcirculation—radical formation—activation of LPO. The state of LPO at each moment of time depends on the contribution of both processes. For instance, initially the excess of radicals does not initiate LPO because of the sufficient quantity of antioxidants and because of the elevated level of hormones, which are scavengers of radicals. Later, when the total antioxidative capacity is exhausted, radical and lipids with low antioxidative activity accumulate because of the first group of processes and they are rapidly oxidized. LPO products inhibit superoxide dismutase, which leads to a further decrease in the antiradical protection of the body and to intensification of LPO.

The results also deserve attention from the general biological point of view: The first phase, in which LPO is inhibited, is the stage of mobilization of protective mechanisms and activation of antistressor systems; the second phase develops as a result of overcoming of the activity of the antistressor system due to the continued exposure to stress.

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EFFECT OF DIFFERENT REPERFUSION SCHEDULES ON RESTORATION OF MYOCARDIAL CONTRACTILITY AFTER TOTAL ISCHEMIA

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KEY WORDS: heart; ischemia; reperfusion; contractility.

Reperfusion of the ischemic myocardium often causes additional disturbances of its structure and metabolism [6, 10] accompanied by arrhythmias, the development of contracture, and incomplete recovery of its contractile function (CF) [7, 9, 11]. Excessive reoxygenation of the myocardium and accumulation of intracellular calcium [4] play an important role in the onset and development of reperfusion disturbances, and for that reason the use of antioxidants [7], of Ca^{++}-antagonists [8, 13], and of reperfusion hemodilution [12] diminishes the damaging action of reperfusion. These data suggest that delayed recovery of CF of the ischemic myocardium, determining the intensity of energy expenditure in the initial period of reperfusion, may improve the restoration of CF at the end of reperfusion. In this investigation energy expenditure in the initial period of reperfusion was reduced by the use of a reperfusion solution with modified ionic composition or the initial rate of perfusion was limited.

EXPERIMENTAL METHOD

Experiments were carried out on guinea pigs weighing 200-300 g, anesthetized with urethane (1.25-1.50 g/kg). The isolated hearts were perfused in the retrograde direction through

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