the mitochondria of the polypeptide factor responsible for their "calcium capacity" [2, 3].

LITERATURE CITED

1. A. I. Marzoev and Yu. A. Vladimirov, Byull. Éksp. Biol. Med., No. 10, 426 (1977).
2. A. I. Gagel'gans, "Ion transport in mitochondria and the action of thyroid hormones," Candidate's Dissertation, Tashkent (1970).
3. Ya. Kh. Turakulov, M. Kh. Gainutdinov, A. A. Abidov, et al., Dokl. Akad. Nauk SSSR, 220, 248 (1975).
4. Ya. Kh. Turakulov, M. Kh. Gainutdinov, R. S. Salikhov, et al., Dokl. Akad. Nauk SSSR, 222, 991 (1975).
5. A. L. Lehninger and B. L. Ray, Biochim. Biophys. Acta, 26, 643 (1957).
6. M. Waite, L. L. M. Van Deenen, T. J. C. Ruigrok, et al., J. Lipid. Res., 10, 599 (1969).
7. D. F. Tapley, J. Biol. Chem., 222, 325 (1956).
8. L. Wojtczak and A. L. Lehninger, Biochim. Biophys. Acta, 51, 442 (1961).
9. W. C. Schneider, J. Biol. Chem., 176, 259 (1948).
10. M. M. Anderson and R. E. McCarty, Anal. Biochem., 45, 260 (1972).
11. A. L. Lehninger, J. Biol. Chem., 234, 2465 (1959).

CYCLIC AMP IN THE ORGANS AND TISSUES DURING ADAPTATION TO EXTREMAL FACTORS

L. A. Kozhemyakin, D. S. Korostovtsev, and T. R. Koroleva

UDC 612.014.4-063].017.2-06:612.398.145.4

Extremal factors of different nature (hypoxic hypoxia, carbon monoxide poisoning, exposure to chemicals and to noise, hypokinesia) caused similar changes in the cyclic AMP level in the organs of albino rats (liver, cerebral hemispheres, heart). A considerable increase in the cyclic AMP concentration was found in the first stages, followed by a progressive fall during subsequent exposure, especially if the intensity of the factor was high. It is suggested that the universality of this response reflects one of the central adaptive mechanisms of the cell and of the organism as a whole.

KEY WORDS: adaptation; hypoxia; cyclic AMP; extremal factors.

The discovery of cyclic adenosine-3',5'-monophosphate (cyclic AMP) as an intracellular mediator of neurohormonal regulatory influences has provided a new approach to the study of the cellular mechanism of adaptation to extremal environmental factors. A few papers describing the study of the cyclic AMP system in hypoxic states have now been published. An increase in the cyclic AMP concentration and adenylate cyclase activity has been demonstrated in brain tissue in acute hypoxia [3, 6], and a sharp increase in the cyclic AMP concentration has been found in the early stages after acute isolated ischemia of the brain [7] and myocardium [5] in dogs.

Considering the importance of the determination of the principles governing the response of the cyclic AMP system to extremal factors in order to understand the mechanisms of goal-directed changes in the resistance of the body, changes in the cyclic AMP concentration in the organs and tissues were studied during exposure to extremal factors of varied nature.

EXPERIMENTAL METHOD

Noninbred male albino rats weighing 150-180 g were used. The effect of extremal factors was studied under dynamic conditions at two levels of intensity (acute limiting – Lim. ac.) and mean lethal (LD_{50}) exposure. Hypoxic hypoxia was produced by "raising" the animals in a pressure chamber to an "altitude" of 6000-10,000 m (the mean rate of "ascent" was 150-200 m/min). Acute poisoning with carbon monoxide (CO), styrene, and

Leningrad Pediatric Medical Institute.

(Presented by Academician S. E. Severin.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 84, No. 11, pp. 567-568, November, 1977. Original article submitted May 17, 1977.

TABLE 1. Cyclic AMP Concentration (in picomoles/mg tissue) in Organs of Rats Exposed to Extremal Factors (M ± m)

Intensity of factor	Extremal factor	Brain	Liver	Heart
Lim. ac.	Hypoxic hypoxia	3,89±0,28	3,25±0,28	4,60±0,38
	CO	4,02±0,29	2,80±0,31	3,25±0,24
	ECU	3,32±0,22	3,10±0,21	2,30±0,14
	Styrene	3,65±0,21	3,48±0,23	2,10±0,14
LD_{50}	Hypoxic hypoxia	0,63±0,07	0,90±0,11	0,57±0,06
	CO	0,50±0,05	0,69±0,02	0,78±0,07
	ECH	1,05±0,13	0,25±0,06	1,00±0,10
	Styrene	0,84±0,10	0,66±0,06	1,65±0,21*
	Control	2,22±0,10	1,38±0,15	1,51±0,19

*Not statistically significant.

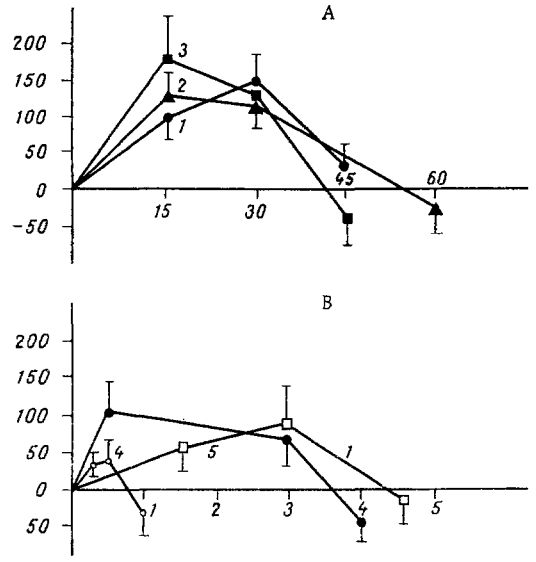

Fig. 1. Changes in cyclic AMP level in organs of rats during acute (A) and chronic (B) exposure to extremal factors. Abscissa, time: in min (A) and msec (B); ordinate, cyclic AMP concentration in tissues (in % of control). 1) Chemical action (aggregated results for exposure to ECH and styrene); 2) hypoxic hypoxia; 3) CO poisoning; 4) exposure to noise; 5) hypokinesia. Cyclic AMP concentration determined in liver, except during exposure to noise, when it was determined in brain tissue.

epichlorhydrin (ECH) was produced by the inhalation method in special chambers, with the following concentrations: CO 0.6-1.0 and 3.0-4.0 g/m^3, styrene 0.8-1.2 and 10-20 g/m^3, ECH 0.04 and 0.1-0.2 g/m^3. The length of survival of the animals during acute exposure was 20-60 min. The concentration of the chemicals during chronic poisoning was 0.1 g/m^3 for styrene and 0.001 g/m^3 for ECH. The background intensity of noise exposure was 105 dB and the pulse intensity 75 dB. Hypokinesia was simulated by the usual method [2]. The cyclic AMP concentration was determined in liver, heart, and brain homogenates by Gilman's method [4], based on competitive binding of cyclic [^{3}H]AMP and endogenous cyclic AMP by cyclic AMP-dependent protein kinases; cylic [^{3}H]AMP was from the Radiochemical Centre, Amersham, and cyclic AMP-dependent protein kinase was obtained from pig brain by the method of Severin et al. [1]. Each series of experiments involved 10-12 animals.

EXPERIMENTAL RESULTS AND DISCUSSION

The character of the changes in the cyclic AMP concentration in the tissues differed substantially depending on the intensity of the extremal factors studied (Table 1). At the acute limiting level of exposure a definite increase in the cyclic AMP concentration was found in all organs investigated; in the case of the mean lethal level of intensity the cyclic AMP concentration in the tissues fell significantly.

Investigation of the dynamics of changes in the cyclic AMP concentration during exposure to the various extremal factors showed a common pattern (Fig. 1): 1) parallel changes in the cyclic AMP concentration in the various organs and tissues during both acute and chronic exposure to extremal factors; 2) a distinct phasic character of these changes with an initial increase in the cyclic AMP concentration (up to 196-280% with acute and 131-208% with chronic exposure) followed by a progressive decline to below the original values.

Extremal factors of different nature thus caused changes of a similar character in the cyclic AMP system. The general biological significance of cyclic AMP in the mechanism of neurohumoral regulatory influences and the integration of cellular metabolism suggests that universality of this response reflects one of the central adaptive mechanisms of the cell and of the organism as a whole.

LITERATURE CITED

1. M. V. Nesterova et al., Biochim. Biophys. Acta, 377, 271 (1975).
2. I. V. Fedorov and L. A. Grishanina, Kosmich. Biol., No. 3, 43 (1967).
3. I. Benzi and R. F. Villa, J. Neurol. Neurosurg. Psychiatr., 39, 77 (1976).
4. A. Gilman, Proc. Nat. Acad. Sci. USA, 67, 305 (1970).
5. B. Rabinowitz, W. W. Parmley, M. Kligerman, et al., Chest, 68, 69 (1975).
6. R. F. Villa, Farmaco Ed. Sci., 30, 561 (1975).
7. H. Watanabe and S. Ishii, Brain Res., 102, 383 (1976).

ENERGY POTENTIAL OF THE CEREBRAL CORTEX IN THE PREAGONAL AND RESUSCITATION PERIODS AFTER ACUTE BLOOD LOSS

V. L. Kozhura

UDC 616-036.882-08-07:616.831-073.97

In experiments on dogs the ATP concentration fell (by 38%) and the ADP and AMP concentrations rose by 121 and 875%, respectively, in the cortical gray matter in the preagonal period after hypovolemic hypotension for 4 h. Reflecting these changes, the energy potential fell from 0.931 to 0.736 ($P < 0.05$). In the early and late postresuscitation period the concentrations of these metabolites and the level of the energy potential were the same as initially.

KEY WORDS: energy potential; cerebral cortex; hypovolemic hypotension; postresuscitation period.

It was shown previously that profound degenerative changes develop in the cerebral cortex in the late postresuscitation period after massive blood loss and prolonged hypotension, as the result of a disturbance of structural metabolism and proteolysis [3].

Investigation of the energy metabolism under these conditions is particularly important, for impairment of the energy supply is known to be a trigger factor in the disturbance of brain nutrition [1, 2, 8]. Meanwhile the study of the energy state of the CNS in preagonal states developing after prolonged hypotension caused by blood loss are not homogeneous and they apply mainly to acute hypoxia and not to the postresuscitation period [7, 13].

The object of this investigation was to study the energy potential of the adenine–nucleotide system of the cerebral cortex (the gray matter) in the preagonal state after hypovolemic hypotension for 4 h, and also in the early and late postresuscitation period.

EXPERIMENTAL METHOD

Experiments were carried out on 13 adult dogs of both sexes. After trimeperidine premedication (10 mg/kg) and under extensive local anesthesia rapid bleeding was carried out for a period of 3-5 min from the femoral artery, reducing the blood pressure to 40 mm Hg, at which level it was maintained for 4 h.

Toward the end of the period of hypotension the mean blood loss was 40 ± 5 ml/kg body weight. The blood pressure was restored by intraarterial reinfusion of the blood in small doses (50-150 ml) into the femor-

Laboratory of General Resuscitation, Academy of Medical Sciences of the USSR, Moscow.

(Presented by Academician of the Academy of Medical Sciences of the USSR V. A. Negovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 84, No. 11, pp. 569-570, November, 1977. Original article submitted May 3, 1977.