Data on precipitation of BGS, containing terminal fucose, by the specific lectin for fucose Eel, also are given in Table 1. It will be clear from Table 1 that BGS and Eel, in the presence of any of the amino acids used except cysteine, just as in their absence, gave a distinct precipitate. No precipitates were formed in the presence of cysteine, or in the presence of fucosyl-lactose, a specific inhibitor of fucose-specific precipitation.

Cysteine was found to inhibit the carbohydrate-binding activity of three other lectins: RCA_1, Con A, and Eel. On the one hand, this can be logically explained on the grounds that cysteine perhaps reacts chemically with certain residues of the lectins, leading to loss of carbohydrate-binding activity. However, since all the experiments were carried out at room temperature and neutral pH, this hypothesis seems unlikely [3]. On the other hand, the results can be explained by competition between cysteine and the cysteine residues of the lectins, essential for manifestation of their carbohydrate-binding activity. Considering data in the literature cited above [4, 6, 7], we regard this hypothesis as the most likely. Cysteine residues of lectins RCA_1, Con A, and Eel, just as lectin from Lima bean, are evidently essential for manifestation of carbohydrate-binding activity.

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ADENYLATE CYCLASE ACTIVITY AND cAMP CONCENTRATION IN BRAIN TISSUE OF DOGS DURING CLINICAL DEATH AND AFTER RESUSCITATION

S. I. Pylova and V. A. Tkachuk

UDC 616-036.882-08-07:616.831-008.931+616.831-008.93:577.123.3

KEY WORDS: circulatory arrest; adenylate cyclase; cAMP; gray matter of the brain; striatal system.

Neurochemical studies in the last few years have shown that cyclic nucleotides play an essential role in the pathogenesis of neurologic disorders of varied etiology [8]. The role of cyclic nucleotides in intracellular transmission of the receptor stimulus, and the connection between adenylate cyclase (AC) and synaptic sensitivity of neurons provide a firm basis for the study of these compounds in order to reveal the mechanisms of postresuscitation encephalopathy.

In the investigation described below the cAMP concentration and AC activity were investigated in tissue of the gray matter of the brain and striatum of dogs during circulatory arrest following electric shock and in the postresuscitation period.

EXPERIMENTAL METHOD

Acute and chronic experiments were carried out on 28 mongrel dogs of both sexes, weighing 10-17 kg, and anesthetized with trimeperidine (6-8 mg/kg). Circulatory arrest occurred in the animals as a result of ventricular fibrillation, induced by electric shock. Tissue of

Research 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 Byullen' Éksperimental'noi Biologii i Meditsiny, Vol. 100, No. 10, pp. 422-424, October, 1985. Original article submitted April 19, 1985.

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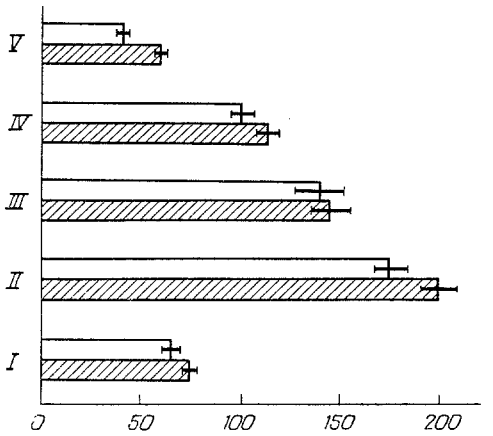

Fig. 1. cAMP concentration (in pmoles/g tissue) in cerebral cortex and striatum during circulatory arrest due to electric shock and in postresuscitation period: I) control; II) 1-2 min, III) 15 min, IV) 45 min after circulatory arrest; V) postresuscitation period (2-5 days later). Unshaded column — striatum, shaded columns — cerebral cortex.

TABLE 1. AC Activity (in pmoles cAMP/mg protein/min) in Cerebral Cortex and Striatum of Dogs during Circulatory Arrest and in Postresuscitation Period

Brain region	Control	Duration of circulatory arrest, min			Postresuscitation period
		1—2	15	45	2—5 days
Cortex	64,31±3,03 *n*=10	291,58±11,67* *n*=11	199,67±9,87* *n*=11	140,78±9,74 *n*=11	34,15±2,22* *n*=7
Striatum	35,56±3,95 *n*=100	258,19±9,03* *n*=9	160,10±6,62* *n*=9	135,43±7,65* *n*=8	88,06±8,95* *n*=7

Legend. *P_T < 0.001 compared with control; n) number of experiments.

the gray matter (parietal region) and striatum (caudate nucleus, substantia nigra) of the brain of dogs of the control group was removed immediately after trephining of the skull under thiopental anesthesia (10-20 mg/kg) in animals exposed to cardiac arrest for 15 min, again 1-2, 15, and 45 min after circulatory arrest, and on the 2nd-5th days of the postresuscitation period. Completeness of recovery of the neurologic status was asseessed according to a neurologic deficit scale [9].

AC and phosphodiesterase (PDE) activity was determined in membrane fractions obtained by centrifugation (40,000g) of homogenates of brain tissues, in isolation medium consisting of: 10 mM Tris-HCl, 0.32 M sucrose, and 2 mM EGTA (pH 7.4) [11]. The protein concentration was measured by Lowry's method. The cAMP level in brain tissue homogenates was determined by means of kits from Amersham Corporation (England). The results were subjected to statistical analysis by Wilcoxon's P_T test [1].

EXPERIMENTAL RESULTS

Circulatory arrest had a characteristic and considerable effect on the cAMP level in brain tissues (Fig. 1). During the first minutes of total cerebral ischemia the cyclic nucleotide level was 250% of the control, faling to 180% after 15 min and 140% after 45 min. These results are in agreement with those of investigations of cyclic nucleotides in the brain tissue during hypoxia of different genesis (bilateral compression of both carotid arteries, decapitation etc.) [7, 10]. Determination of AC activity in the period of systemic circulatory arrest also revealed marked activation — activity of the enzyme was increased more than fivefold after 1-2 min of ischemia, but later after cirulatory arrest (15 and 45 min) it fell, although it remained significantly higher than in the control (Table 1).

Elevation of the cAMP level during the first few minutes of circulatory arrest was probably connected with rapid and considerable release of catecholamines and other biologically active compounds, activating AC and stimulating cyclic nucleotide production [5]. The high cAMP level considerably modified cell metabolism and directed it toward maintenance of hemo-

stasis, disturbed by hypoxia. Under conditions of hypoxia elevation of the cAMP level is known to be one mechanism which activates processes of glycolysis [4].

In the postresuscitation period, in animals subjected to systemic circulatory arrest for 15 min, in which the neurologic deficit on the 2nd-5th day was 12-20 points, the increased muscle tone, ataxia, and changes in cyclic nucleotide metabolism were not restored to normal. The cAMP level in the cerebral cortex and striatum of these animals was below the control values by 20 and 40% respectively ($P < 0.05$). However, changes in activity of the enzymes responsible for cAMP synthesis and hydrolysis, namely AC and PDE, in brain regions studied were opposite in character: In the cortex AC activity was more than 50% lower than the control values, whereas in the striatum it was twice as high. PDE activity in the striatum of these animals was 584.99 ± 12.70 pmoles/mg protein (in the control 359.75 ± 8.73 pmoles/mg protein/min); in the gray matter of the brain 260.66 ± 9.68 pmoles/mg protein/min (373.12 ± 11.59 pmoles/mg protein/min). Since the cyclic nucleotide level reflects the relations between their biosynthesis and degradation, the changes discovered evidently suggest that disturbances reducing sensitivity of the adenylate cyclase system in this brain region by a greater degree than in the striatum are formed in the cerebral cortex. This fact is to some degree in harmony with the character of the neurologic disorders: Considerable disturbances of motor functions were observed in the experimental animals in the postresuscitation period.

The fall in the cAMP level in the brain tissues during the recovery period was evidently due to several causes. Foremost among these causes were disturbances of monoamine metabolism and, as a result, a fall in their effective concentration, a reduction of sensitivity of receptors coupled with AC to catechoalmines, and also disturbances of permeability of cell membranes of brain tissue [2, 6]. It has been shown that the biological effect of cAMP is connected with regulation of mediator secretion, and with processes of phosphorylation of proteins which participate in the regulation of membrane permeability [3].

The results of this investigation thus shed light on one mechanism of the disturbances of synaptic transmission linked with cyclic nucleotides, in the brain tissues of animals in the postresuscitation period, recovering from clincial death. Disturbances discovered in cyclic nucleotide metabolism, in addition to other elements of the postresuscitation process, may play an essential role in the pathogenesis of postresuscitation encephalopathy.

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