PRINCIPLES OF REORGANIZATION OF THE NEOCORTICAL SYNAPTOARCHITECTONICS AFTER RESUSCITATION

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Irrespective of the cause of the terminal state, processes which take place after resuscitation have many features in common with those characteristic of the revived organism. The general principle of extinction and recovery of function in the postresuscitation period are characteristic of the CNS [2]. However, the structural basis of these changes has not been adequeately studied. The state of interneuronal contacts as one of the most important stages in the integrative function of the brain is particularly interesting [1, 3, 4].

EXPERIMENTAL METHOD

Clinical death from massive blood loss through the external iliac artery (series I) and from mechanical asphyxia for 6 min (series II) was used as the model. Experiments were carried out on 50 albino rats weighing 190-210 g under ether anesthesia. Material was taken 1, 3, 7, 14, and 30 days after resuscitation. The brain was fixed by perfusion with a mixture of 4% paraform and 1% glutaraldehyde in 0.1 M phosphate buffer (pH 7.4) with the addition of sucrose through the ascending aorta. Part of the material was postfixed in 1% OsO_4 solution, whereas the rest was stained during dehydration in 5% phosphotungstic acid (PTA) solution. The material was embedded in a mixture of Epon and Araldite [5]; sections were cut in a plane tangential with the molecular layer of the neocortex. Selective staining of paramembranous neurofilaments combined with general staining with PTA enabled the synaptic pool to be estimated quantitatively [3, 5]. The total number of synpases, the number of symmetrical and asymmetrical compositions of the contact, and the length of synaptic contacts were determined per unit area of the molecular layer of the cortex. Photomicrographs were taken under a standard magnification of 15,000 on the EMV-100LM electron microscope. The material was analyzed on negatives (9 × 12 cm) enlarged twofold by a photographic enlarger, and using a control grid with a 3-mm step. The results of the quantitative analysis were processed by statistical methods.

EXPERIMENTAL RESULTS

On the first day after resuscitation a marked decrease was found in the total number of interneuronal contacts in the case of asphyxia (by 41.9%, $P < 0.001$) and blood loss (by 27.2%, $P < 0.001$) on account of a decrease in the number of symmetrical (by 42.3% in asphyxia, by 26.9% in blood loss) and asymmetrical (by 39,8 and 27.3% respectively) contacts (Table 1). The number of synapses in the cerebral cortex of both series of animals on the 3rd day of the recovery period remained at about the same level, with a tendency for the number to increase on the 7th day (Table 1). Complete recovery of the number of interneuronal contacts in the neocortex was not observed on the 30th day after resuscitation, and this was particularly marked in the case of resuscitation after asphyxia (the deficiency of synapses was 19%). Characteristically destruction of synapses in the cortex in the postresuscitation period was of the pale type, as described previously in other hypoxic states [1], in both series of experiments. Occasionally focal disorganization of synapses and other types of destruction were found. According to data in the literature [5] PTA-positive symmetrical contacts are intermediate, immature forms of synapses, whereas asymmetrical contacts are functionally mature. Consequently, in the postresuscitation period both groups of synapses were damaged to an equal degree in the cerebral cortex. Destruction of many functionally active interneuronal contacts leads to disturbance of integrative-investigative brain activity.

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TABLE 1. Number of Synapses in Molecular Layer of Rat Cerebral Cortex in Postresuscitation Period (M ± m)

Parameter	Series of experiments	Control	Time of investigation, days				
			1	3	7	14	30
Total number of synapses	I	11,4±0,01	8,3±0,16	7,8±0,07	8,1±0,02	7,2±0,02	11,0±0,10
	II		6,8±0,07	7,2±0,08	7,6±0,19	8,2±0,05	9,5±0,10
Number of symmetrical synapses	I	2,6±0,02	1,9±0,01	1,4±0,04	1,6±0,03	1,5±0,01	2,3±0,04
	II		1,5±0,13	1,4±0,07	2,4±0,12	1,2±0,03	2,0±0,10
Number of asymmetrical synapses	I	8,8±0,03	6,4±0,17	6,3±0,11	6,6±0,02	5,7±0,02	8,7±0,07
	II		5,4±0,06	6,2±0,01	5,3±0,06	7,0±0,01	7,5±0,10

Legend. Here and in Table 2, $P < 0.001$ compared with control.

TABLE 2. Length of Synaptic Contacts in Molecular Layer of Rat Cerebral Cortex in Postresuscitation Period (M ± m)

Time of investigation, days	Series of experiments	Number of intersections with control grid				
		1–2	3–4	5–6	7–8	9–16
Control	—	1,9±0,03	5,8±0,06	3,2±0,01	0,5±0,01	0,2±0,01
1	I	1,0±0,01	3,4±0,01	1,6±0,06	0,5±0,01	0,2±0,01
	II	1,0±0,04	4,3±0,01	2,8±0,02	0,9±0,01	0,4±0,01
3	I	0,8±0,01	2,4±0,01	2,4±0,01	1,4±0,03	0,3±0,03
	II	0,6±0,01	3,0±0,05	3,4±0,05	0,7±0,01	0,2±0,01
7	I	0,9±0,05	3,3±0,04	2,3±0,02	1,3±0,04	0,2±0,01
	II	1,7±0,10	4,5±0,05	3,0±0,01	0,8±0,01	0,2±0,01
14	I	0,9±0,01	2,9±0,01	2,4±0,01	0,9±0,01	0,3±0,03
	II	0,6±0,02	3,7±0,01	3,0±0,04	1,4±0,02	0,7±0,01
30	I	1,6±0,05	5,7±0,05	3,0±0,01	0,5±0,01	0,1±0,01
	II	2,7±0,10	5,3±0,10	3,0±0,10	1,2±0,10	0,3±0,01

Against the background of destructive changes in the cerebral cortical synapses, processes of compensation and repair were activated. On the first day after resuscitation, for instance, a tendency was observed for the length of the synaptic contacts to increase. After 3 days the volume of the presynpatic zone increased significantly, the relative number of synapses with a long zone of contact increased (Table 2), as also did the number of active zones of the synapse, the structural reflection of increased informativeness of the residual contacts. On the 7th day the number of small symmetrical synapses increased in the cortex of both groups of animals, and this can be regarded as the appearance of new functionally immature synapses. A similar increase in the number of these types of synapses in the brain was observed [5] during postnatal development and the formation of the synaptic apparatus.

The following basic changes in synaptoarchitectonics were thus observed in the cerebral cortex in the postresuscitation period: 1) a sharp decrease in the number of synapses; 2) the pale type of destruction — the predominant form of destruction of synapses; 3) compensation in the early stages after resuscitation (1-3 days) chiefly on account of hypertrophy of synapses; 4) activation of the formation of new interneuronal contacts at later stages (7 days); presence of both forms (hypertrophy of existing and formation of new synapses) of structural restoration of the synaptic pool to a marked degree in the late period (1 month).

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