INFORMATIVENESS OF CEREBRAL CORTICAL INTERNEURONAL SYNAPSES IN RATS AFTER ASPHYXIA

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KEY WORDS: cerebral cortex, synapses, postresuscitation period.

The intensity of specific interneuronal exchange depends on the number and size of the active zones of synaptic contact (AZC) which, according to Bogolepov [1], determine the informativeness of the synapse. It has been shown that AZC of different types of synapses differ in their functional role in the mechanism of trans-synaptic transmission [4, 5]. This difference is based on the unequal degree of maturity of the system of subsynaptic units (SSU), formed by paramembranous microfilaments of the cytoskeleton of the synapses. Many investigations have been devoted to the analysis of changes in synapses in the developing and mature brain under normal and pathological conditions, including in the postresuscitation period [1-3, 6, 7]. However, there has been no research aimed at explaining the principles governing the change in informativeness of interneuronal synapses and the synaptic pool in the brain, taking account of synapses differing in their functional maturity, in the course of the recovery period after a terminal state.

The aim of this investigation was to study the structural mechanisms of the change in informativeness of single interneuronal synapses and of the synaptic pool as a whole in the cerebral cortex in the period after recovery from asphyxia.

EXPERIMENTAL METHODS

Experiments were carried out on 20 male albino rats weighing 190-210 g, under ether anesthesia. Lethal asphyxia for 6 min was induced by compressing the intubation tube. The animals were resuscitated by artificial ventilation of the lungs and indirect cardiac massage. The sensomotor cortex was extirpated for investigation after 6 h and 1, 3, 7, and 14 days. The technique of processing of the material was published previously [3]. The numerical density of the synapses with different organization of their SSU (types A, B, C, and D) [4] was determined, the length of the active zone of contact measured, and the total length of AZC of different types of synapses per 100 μ^2 of neuropil was calculated.

EXPERIMENTAL RESULTS

The total length of AZC of type A synapses in the molecular layer of the cerebral cortex of the control animals was greater than its length for other types of synapses (Table 1). Synapses of this type are responsible for the main part of the informativeness of the synaptic pool of the molecular layer of the cortex. Synapses of types B and C have a shorter total length of AZC. The minimal total length of AZC is a feature of the D synapses (immature symmetrical SSU). Despite differences in total length of AZC, the relative content of synapses of types A, B, C, and D was the same.

The length of AZC of all synapses 6 h after asphyxia was reduced by 35.7% due to reduction of the density of the synapses by 41.1%. The total length of AZC of the type A synapses was reduced as a result of a decrease in their density (by 47.8%) and by a decrease in the length of AZC of synapses of this type. Meanwhile the contribution of B synapses to the total informativeness of the synaptic pool was increased. The total length of their AZC was increased and exceeded the control value by 22.9%. This became possible due to an increase in the length of AZC and an increase in the numerical density of synapses of this type by 13.4% compared with the control. The contribution of synapses of types C and D to the total informativeness of the synaptic pool was very small at this period (Table 1).

Department of Histology and Central Research Laboratory, Omsk Medical Institute. (Presented by Academician of the Academy of Medical Sciences of the USSR V. A. Negovskii.) Translated from Byulleten' Éksperimental'noi Biologii i Meditsiny, Vol. 105, No. 6, pp. 728-730, June, 1988. Original article submitted May 29, 1987.

 0007-4888/88/0006-0866$12.50

TABLE 1. Numerical Density (number of synapses per 100 μ^2 of neuropil) and Total Length of AZC (in nm) of Different Types of Synapses in Molecular Layer of Cerebral Cortex of Albino Rats during Recovery from Asphyxia (M ± m)

Parameter studied	Control	Time after asphyxia				
		6 h	1 day	3 days	7 days	14 days
Synapses of type A						
density	6,7±0,8	3,5±0,4*	3,1±0,2*	4,0±0,6*	4,9±0,5	6,0±0,7
length	4020±200	2030±140*	1550±150*	2160±160*	2940±167*	3660±300
Synapses of type B						
density	6,7±0,4	7,6±0,4	6,1±0,6	5,8±0,4	5,6±0,6	6,0±0,6
length	3480±280	4180±300*	3600±180	3250±250	2970±158*	3840±240
Synapses of type C						
density	5,5±0,3	0,7±0,2*	1,9±0,4*	4,1±0,3*	1,3±0,1*	2,7±0,3*
length	2370±220	390±30*	1030±90*	2130±120	2130±172	1510±160*
Synapses of type D						
density	5,7±0,7	2,7±0,4*	3,2±0,6*	4,0±0,5*	6,1±0,7	2,5±0,2*
length	1650±140	810±75*	990±80*	1040±95*	1650±86	700±25*
Total density of synapses	24,6±1,0	14,5±0,6*	14,3±0,6*	17,9±1,0*	17,9±2,0*	17,2±1,1*
Total length of contacts	11520±1200	7410±240*	7170±460*	8580±800*	9690±720	9710±565

Legend. *$p < 0.05$ Compared with control.

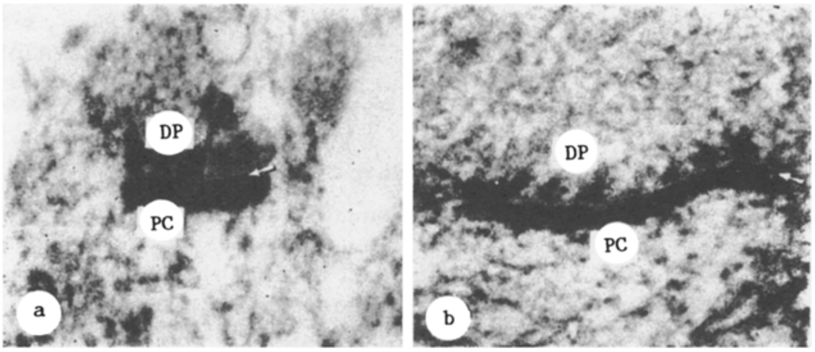

Fig. 1. Hypertrophy of SSU of interneuronal synapse in molecular layer of cerebral cortex 14 days after asphyxia. a) Type A synapse, control; b) increase in number of dense projections (DP), in length of synaptic cleft (arrow), and in postsynaptic condensation (PC) of type A synapse. Stained with phosphotungstic acid. 43,000×.

The total length of all contacts 24 h after asphyxia was reduced by 37.8%, the number of A synapses was reduced by 53.7%, and the total length of their AZC by 61.4% compared with the control. However, there was a tendency for the total length of AZC of the type C synapses to be restored.

After 3 days, compared with the results for the previous time, the total length of AZC of the synaptic pool was increased as a result of partial recovery of the density and length of AZC of the A and C synapses. The deficiency in the number of synapses 7 days after asphyxia, just as 3 days after asphyxia, was 27.2%, but the total length of AZC of the synaptic pool was increased up to the lower limits of the control level. This took place as the result of an increase in the density of functionally immature type D synapses. Under these conditions the informativeness of the synaptic pool remained at the level of the previous period, for the total length of functionally mature contacts was unchanged in this case.

The total length of the most informative synapses (types A and B) was restored to the control level 14 days after asphyxia. The mechanism of compensatory hypertrophy of the active zones of the interneuronal synapses (Fig. 1) was operative most completely in this case. As Table 1 shows, a considerable deficit of the numerical density of the synapses still remained (30.1%).

Thus to assess the informativeness of the synaptic pool, besides the length and number of AZC of the synapses, it is necessary to take account of the degree of maturity and development of the system of subsynaptic units of interneuronal synapses and, in particular, of its highly labile part, namely the dense projections (DP). Synapses with mature and maximally developed SSU, with a considerable area of contact, and with numerous AZC are the most informative. The importance of an increase in the number of AZC in increasing the informativeness of hypertrophied neocortical synapses in the postresuscitation period was demonstrated by the writers previously [3]. Informativeness of synapses differing in the number and length of their AZC increases in the order D → C → B → A, i.e., with the formation of functionally mature AZC with developed dense projections, facilitating trans-synaptic exchange. The important role of DP in trans-synaptic transmission and their high lability has been proved [4-7]. The informativeness of the synaptic pool of the neuropil of the molecular layer of the rat cerebral cortex is the sum of the informativeness of single functionally and structurally heterogeneous synapses, of which the most mature are the type A synapses [4]. Hence it follows that synapses of types C and D make a negligible contribution to the total informativeness of the synaptic pool and it is almost entirely dependent on synapses of types A and B.

In the postasphyxia period the informativeness of the synaptic pool of the molecular layer of the sensomotor cortex underwent regular changes. Reduction of the total length of AZC of the type A synapses led after 1 and 3 days to reduction of the informativeness of the synaptic pool as a whole. During this period synapses with lower DP (types C and B) underwent hypertrophy, with only partial preservation of the informativeness of the synaptic pool. The total length of AZC of interneuronal connections reached the control value 7 and 14 days after asphyxia. However, after 7 days the informativeness of the synaptic pool was not yet fully restored, for the increase in the total length of AZC took place on account of functionally immature, relatively uninformative synapses. Not until the 14th day, as a result of hypertrophy of synapses of types A and B, was the informativeness of the synaptic pool of the molecular layer of the neocortex substantially restored, despite the marked deficiency of synaptic density.

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