PROTEIN METABOLISM OF RAT BRAIN SYNAPTOSOMES DURING TRAINING

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The intensity of metabolism of proteins with fast and slow turnover from cerebral cortical synaptosomes of rats trained in defensive movements, pseudotrained, and control animals was studied by determining their specific radioactivity 1 and 3 days, and 1, 3, 6, and 9 weeks after intraventricular injection of lysine-^{14}C. Three fractions of synaptosomal proteins, differing in the overall values of their half-life (τ_{50}) were found. An increase was found in the specific radioactivity of brain proteins of the trained animals compared with those of the pseudotrained and control rats. Values of τ_{50} were increased for the slowly metabolized fraction of synaptosomal protein fractions from the brain of the trained rats. The role of protein metabolism in brain synapses in the mechanisms of formation of long-term memory is discussed.

KEY WORDS: brain; memory; synapse; proteins.

One of us (V.V.D. [3]) previously suggested a neuroselective hypothesis of memory, according to one of the propositions of which the brain synapses play a key role in the mechanisms of its formation.

According to some investigators [1], the level of function of synapses during learning is very closely connected with the particular features of the structure and metabolism of their proteins. Experimental data in the literature are sometimes contradictory: An increase [11] or no change [12] in the synthesis of synaptic proteins has been found in the brain of trained animals. Furthermore, during training, changes in metabolism of proteins of different relative molecular weight may be opposite in direction [5]. The learning process may affect the ratio between the level of synthesis of synaptic proteins in the neuron body and local synthesis in nerve endings, and in particular, it may depress the latter [6]. The facts described above point to the urgency of the study of metabolism of brain synaptic proteins in animals during training.

The object of this investigation was to study the intensity of turnover of rapidly and slowly metabolized proteins of cerebral cortical synaptosomes of rats trained in defensive movements, and in pseudotrained and control rats.

EXPERIMENTAL METHOD

Experiments were carried out on male albino rats weighing about 150 g. The animals of group 1 (control) were kept under ordinary animal house conditions and received no stimulation of any kind. The animals of group 2 received the same stimuli as the trained animals, but in random order (pseudotraining). The animals of group 3 were trained in defensive movements in a Φ-shaped maze for 3 days, for 30 min daily. On the last day of training (or pseudotraining) the experimental animals (and the control animals at the same time) received an injection of 30 μCi lysine-^{14}C into the lateral ventricle.

The animals were killed by decapitation 1 and 3 days and 1, 3, 6, and 9 weeks later. Synaptosomes, isolated from the cerebral cortex of the rats [8], were processed for counting radioactivity [9], which was measured in dioxan scintillator on an Intertechnique SL-30 liquid scintillation counter.

Statistical evaluation of the rate of change of radioactivity of the test proteins with time was carried out by regression analysis [2].

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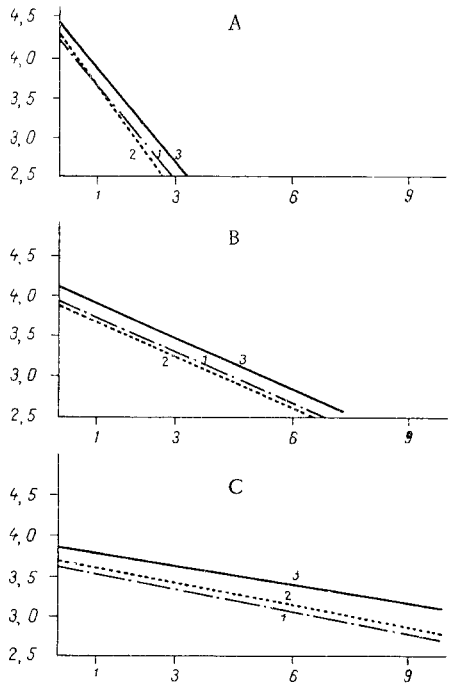

Fig. 1. Theoretical change in specific radioactivity of rat brain synaptosomal proteins depending on time elapsing after injection of lysine-^{14}C (semilogarithmic coordinates). Abscissa, time (in weeks) after injection of lysine-^{14}C; ordinate, $\log_{10}$ of specific radioactivity of proteins. 1) Control; 2) pseudotrained animals; 3) trained animals. A, B, and C) Synaptosomal protein fractions.

EXPERIMENTAL RESULTS

On the basis of values of specific radioactivity of the synaptosomal proteins (Table 1) coefficients of regression were calculated. These showed that three protein fractions with different rates of turnover — A, B, and C (Fig. 1) — were isolated from animals of all three groups (trained, pseudotrained, and control). This indicates heterogeneity of the test proteins as regards the rate of turnover, probably reflecting differences in their functions.

Values of specific radioactivity at all times of the investigation were significantly higher for the brain proteins of the trained animals than for those of the pseudotrained and control rats (Table 1).

Data in the literature do not support the view that the changes discovered are due to differences in the precursor pool [10]. It is suggested that they can be explained by an increase in the synthesis of pre-existing and(or) qualitatively new synaptosomal proteins, found

TABLE 1. Specific Radioactivity of Synaptosomal Proteins from Rat Brain (cpm/mg protein)

Group of animals	Time after injection of lysine-^{14}C (M ± m)					
	1 day	3 days	1 week	3 weeks	6 weeks	9 weeks
1—control	18 311±252	9 266±283	4 815±192	1 971±80	1 184±75	582±18
2—pseudotrained	18 690±355	9 652±300	4 647±196	2 216±130	1 310±94	649±23
P_{2-1}	>0,05	>0,05	>0,05	>0,05	>0,05	>0,05
3—trained	21 953±159	16 393±385	6 782±203	2 759±113	1 795±94	965±46
P_{3-2}	<0,05	<0,05	<0,05	<0,05	<0,05	<0,05
P_{3-1}	<0,05	<0,05	<0,05	<0,05	<0,05	<0,05

in the composition of the fractions labeled A, B, and C (Fig. 1), during training. This could take place either through synthesis in the neuron body or local synthesis in nerve endings, due on the whole, possibly, to activation of the function of the genetic apparatus of the nerve cells [7]. Changes in the velocity and(or) volume of the axon flow of these proteins in the region of the synapses likewise cannot be ruled out. It is impossible on the basis of these results to analyze the true relationship between these various causes.

An increase in the half-life of the slowly metabolized fraction C of brain proteins of the trained animals was observed in these experiments compared with the control. This could be associated with a selective increase in the intensity of synthesis or in the velocity and volume of axon flow of a certain group of slowly metabolized proteins. Conformational changes in these proteins can also be suggested, for the view is held that the breakdown velocity of a protein depends on its three-dimensional structure [13].

Dergachev [4] postulated in 1977 that imprinting of a skill requires the simultaneous and independent activation of the pre- and postsynaptic regions, which leads to structural changes and to permanent facilitation of the conduction of excitation through the given synapse. The possibility cannot be ruled out that this is connected with changes in the structure and metabolism of proteins in extrasynaptic filaments of the synaptic space, which may be responsible for the complementary character of the pre- and postsynaptic membranes. These proteins are probably not specific for the nervous system. However, they evidently participate in other processes indirectly connected with memory (electrogenesis and so on).

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