CHANGES IN AXONAL PROTEIN TRANSPORT PRODUCED BY INCREASED PHYSIOLOGICAL ACTIVITY OF NEURONS

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An increase in the physiological activity of the nervous system is manifested by changes in energy metabolism of the neurons. Axonal transport (AT) plays an important role in the maintenance of physiological activity by supplying substances essential for nerve endings and synaptic processes, and the distribution of substances along the course of the fiber [4, 9]. However, the character of changes in AT during physiological activity of neurons is not absolutely clear.

In the present investigation the effect of physical exercise of varied intensity on AT of proteins was studied in sensory and motor fibers of the rat sciatic nerve.

EXPERIMENTAL METHOD

Experiments were carried out on male albino rats weighing 280-320 g. The intensity of the physical exercise varied, rats being compelled to swim in water at a temperature of 33-35°C for 12 ± 2 h without a load or for 60 ± 10 min with a load, amounting to 1/11 of the animal's body weight. Swimming was stopped when it was replaced by diving, i.e., when the animals periodically rose to the surface of the water to breathe [3]. Next, under pentobarbital anesthesia (30 mg/kg), and using a micromanipulator, ^{14}C-glycine (specific activity 1.85 GBq/mmole) was injected into the 5th lumbar spinel ganglion (8-16 kBq) or into the anterior horns of the spinal cord of the same segment (20-32 kBq). After definite time intervals (1 and 2 h for determining the velocity of the fast component of AT, or 14 or 28 days, for determining the slow component of AT) after the microinjection of the labeled amino acid the ganglion, the segment of the spinal cork, and the sciatic nerve with its roots were excised. The anterior or posterior roots and the nerve were cut into fragments each 3 mm long. The origin of the anterior root (transport along motor fibers) or the 5th lumbar spinal ganglion (transport along sensory fibers) was taken as the zero point. Analysis of the TCA-insoluble radioactivity of the spinal ganglia, nerve fragments, and spinal cord was carried out in Dray's dioxan scintillator on and SL-30 scintillation counter. The results were expressed in conventional units:

The average velocity of movement of labeled proteins was calculated from the position of the radioactivity front [15].

EXPERIMENTAL RESULTS

The data in Fig. 1 and Table 1 show that the velocities of the fast and slow components of TT in central and peripheral processes of sensory nerve cells of rats after swimming for 12 ± 2 h did not differ significantly from those in the control animals. The level of radioactivity of the transported material also did not differ significantly in the control and experiment.

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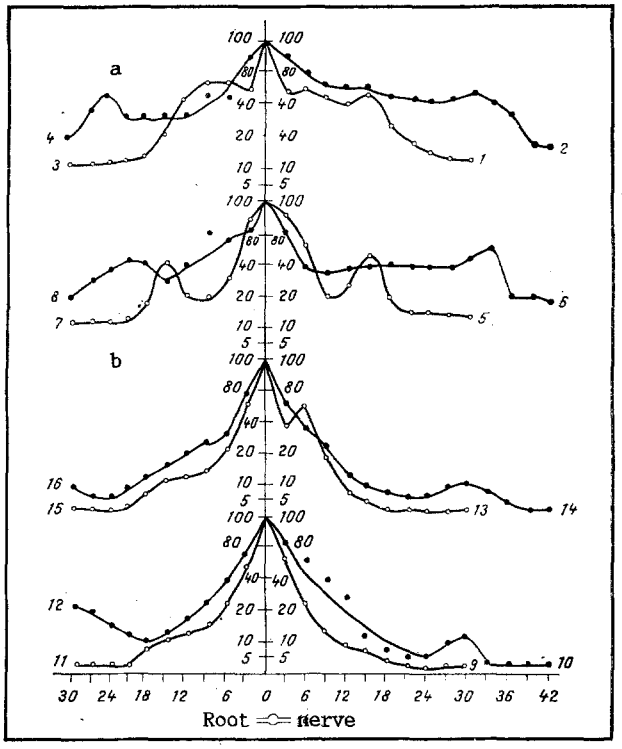

Fig. 1. Transport of slow (a) and fast (b) components of labeled proteins along central and peripheral processes of sensory nerve cells. abscissa, distance (in mm) from ganglion; ordinate, radioactivity (in conventional units). Control: 1, 3) sacrifice after 14 days; 2, 4) after 28 days; 9, 11) after 1 h; 10-12) after 2 h. Swimming (12 ± 2 h: 5, 7) sacrifice 14 days; 6, 8) 28 days; 13, 15) 1 h, 14, 16) 2 h after microinjection.

The velocity of movement of the fast component of AT along motor fibers of the sciatic nerve of rats after swimming for 12 ± 2 h fell by 18% below the control level, but the amount of protein transported by the axons was reduced by more than half (Fig. 2, Table 1). With respect the slow component of AT, with a load of the same intensity, only a very small decrease (by 1.9 times) in the volume of protein transported was recorded, and the velocity of the front of spread of radioactivity was unchanged. If the animals rested for 6 h, these parameters returned to normal (Fig. 2, Table 1).

It thus follows from the data described above that changes in anterograde AT under the influence of a relatively light, but prolonged load, differed for different components of the axonal flow, and depended on the type of nerve cells. These conclusions are confirmed indirectly in the literature [6]: under the influence of physical exercise the RNA concentration in motoneurons of the rat spinal cord showed considerable changes, but in nerve cells of the spinal ganglia it remained at its initial level.

According to data in the literature [2, 7, 11] during excessively long and intensive stimulation, leading to fatigue and exhaustion of the nervous system, the protein-synthesizing apparatus of the neuron cannot cope with the increased metabolic demands, whereas relatively brief stimulation induces activation of protein synthesis. Accordingly, the effect of more intensive, but relatively brief exercise (swimming for 60 ± 10 min with a weight of 1/11 of body weight) was studied. It follows from Table 1 and Fig. 3 that the velocity of transport of the fast component along motor fibers of the sciatic nerve of the rats rose by 10%, whereas the level of radioactivity of the transported material also rose to a level more than twice higher. These parameters returned to normal after 6 h of rest. The results are in agreement with those of other workers who found an increase in the velocity of AT and the volume of material transported in response to relatively brief electrical stimulation [1, 12, 13, 14].

A decrease in the velocity of the fact component of AT during prolonged (4 h) electrical stimulation of the sciatic nerve was observed by Ochs [15].

TABLE 1. Transport of Fast and Slow Components of Labeled Protein along Motor and Sensory Fibers of Sciactic Nerve of Rats Subjected to Different Schedules of Physical Exercise

Test object	Velocity of transport, mm/day			Level of radioactivity of transported material (conventional units)		
	control	swimming without load 12 ± 2 h	swimming with load 60 ± 10 min (1/11 of body weight)	control	swimming without load 12 ± 2 h	swimming with load 60 ± 10 min (1/11 of body weight)
Fast component						
in sensory central fibers	401,11±21,11	414,0±18,0	—	17,43±1,32	15,18±1,28	—
in sensory peripheral fibers	398,51±17,91	414,63±17,41	—	11,14±1,95	8,28±1,06	—
in motor fibers	392,42±10,23	322,0±8,71*	431,5±9,58*	3,93±0,29	1,92±0,20*	8,08±0,41*
during resting after swimming for 6 h	—	396,91±11,71	382,0±16,19	—	4.62±0,31	3,91±0,39
Slow component						
in sensory central fibers	0,89±0,03	0,95±0,03	—	7,65±0,2	7,31±0,19	—
in sensory peripheral fibers	1,28±0,04	1,22±0,04	—	5,95±0,18	7,11±0,29	—
in motor fibers	1,34±0,05	1,31±0,05	—	7,39±0,32	3,85±0,21*	—
during resting after swimming for 6 h	—	1,36±0,04	—	—	9,32±0,35	—

Legend. *$p < 0.05$, Differences compared with group of control rats are significant; each value obtained by testing 10-12 animals.

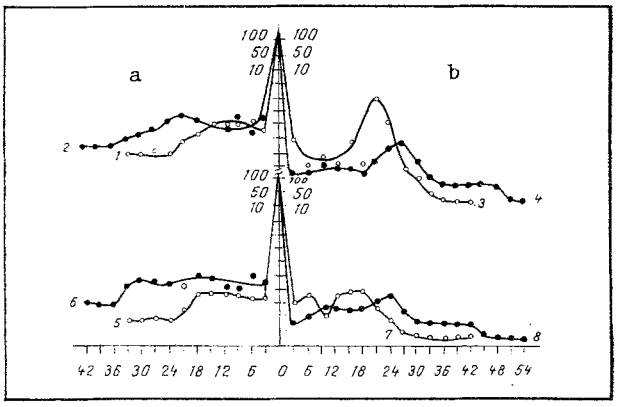

Fig. 2. Transport of slow (a) and fast (b) components of labeled proteins along axons of motoneurons. Abscissa, distance (in mm) from anterior horns of spinal cord; ordinate, radioactivity (in conventional units). Control: 1, 2) sacrifice after 14 and 28 days; 3, 4) after 2 and g h. Swimming (12 ± 2 h); 5, 6) sacrifice after 14 and 28 days; 7, 8) after 2 and 3 h.

In all probability the velocity of the fast component of AT is a more variable parameter than that of the slow component [4], and it evidently depends more on certain functional states of the cell. The energy supply for AT is provided by a combination of processes of oxidative phosphorylation and glycolysis in the axoplasm; it is slowed if the necessary concentrations of ATP and oxygen cannot be maintained in the axon [15]. Meanwhile, excitation is accompanied by marked changes in the concentration of high-energy phosphates and the ionic balance in nerve fibers [5].

The quantity of material transported by the axons may evidently depend on synthesis and degradation or a change in the ratio of proteins supplied to the transport systems [10]. Relations between these processes probably change during increased physiological activity of the neurons, and this is reflected in the level of proteins transported.

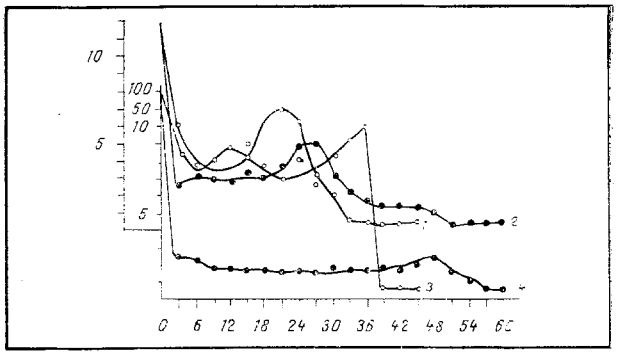

Fig. 3. Transport of fast component of labeled proteins of rat motoneurons during intensive but brief exercise. Abscissa, distance (in mm) from anterior horns of spinal cord; ordinate, radioactivity (conventional units). Control: 1, 2) sacrifice after 2 and 3 h. Swimming (60 ± 10 min) with load of 1/11 of body weight; 3, 4) sacrifice after 2 and 3 h.

Transport of materials from the bodies of neurons into the axons and nerve endings is thus an important mechanism for the existence and functioning of nerve cells. Changes in the velocity of transport and the amount of protein transported when physiological activity of the neurons is increased can be regarded as evidence in support of dependence of enterograde transport of materials in nerve fibers on the functional state of the neurons and their processes.

LITERATURE CITED

1. T. A. Alzhimolaev, S. M. Bezruchko, and N. I. Vozhenina, Biofizika, **17**, No. 1, 77 (1972).
2. V. Ya. Brodskii, Cell Nutrition [in Russian], Moscow (1966).
3. Yu. Ya. Genisman, Structural and Metabolic Manifestations of Neuron Function [in Russian], Moscow (1974).
4. R. N. Glebov and G. N. Kryzhanovskii, Usp. Sov. Biol., **82**, No. 3, 417 (1976).
5. O. R. Kol's and G. V. Maksimov, Rhythmic Excitation in Somatic Nerves: Physicochemical Aspects [in Russian], Moscow (1987).
6. L. Z. Pevzner and S. Kh. Khaidarliu, Tsitologiya, **9**, No. 7, 840 (1967).
7. N. E. Yarygin and V. N. Yarygin, Pathological and Adaptive Changes in the Neuron [in Russian], Moscow (1973).
8. G. G. Badr and W. G. McDean, J. Neurochem., **25**, 921 (1975).
9. D. S. Forman, Trends Neurosci., **7**, 112 (1984).
10. B. Grafstein and D. L. Edwards, Axoplasmic Transport in Physiology and Pathology, D. G. Weiss and A. Gorio (eds.), Berlin (1982), p. 21.
11. H. Hyden, in: The Cell (ed. by J. Brachet and A. Mirsky), Vol. 4, New York (1960), p. 215.
12. P. Keen and W. G. McLean, Brit. J. Pharmacol., **52**, 527 (1974).
13. G. A. Kerkut, Growth of the Neurons System, London (1968), p. 220.
14. J. Kiss, E. Lang, and J. Hamori, J. Neural. Transmiss., **95**, Suppl. 11, 125 (1974).
15. S. Ochs, Fed. Proc., **33**, 1049 (1974).