MECHANISM OF DISTURBANCE OF THE FUNCTIONAL PROPERTIES OF STRIATED MUSCLE FIBERS IN POSTDIPHTHERITIC POLYNEURITIS AND EXPERIMENTAL ALLERGIC ENCEPHALOMYELITIS

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The development of the paralytic syndrome in postdiphtheritic polyneuritis was characterized by a sharp decrease in polarization of the muscle fibers, the accumulation of sodium and potassium ions and noradrenalin in them, and by a deficiency of adrenalin. In experimental allergic encephalomyelitis the polarization of the skeletal muscle fibers was not significantly changed, despite the marked increase in the concentrations of sodium, potassium, adrenalin, and noradrenalin in the muscle tissue. It is concluded that changes in the functional properties of skeletal muscle fibers in postdiphtheritic polyneuritis, unlike those in experimental allergic encephalomyelitis, are evidently due to a disturbance of regulatory nervous influences on the processes of electrogenesis in the muscle fibers.

KEY WORDS: postdiphtheritic polyneuritis; allergic encephalomyelitis; sodium; potassium; adrenalin; noradrenalin.

The paralytic syndrome in postdiphtheritic polyneuritis (PDP) is characterized by demyelination, changes in the axons of the thick myelinated nerve fibers, a progressive increase in the refractory period, and slowing of the velocity of conduction of the nervous impulse or even its total blockade. In experimental allergic encephalomyelitis (EAE) it is associated only with demyelination of the internodal segments, a moderate increase in the refractory period, and slowing of the conduction of the nervous impulse [2, 6, 7].

Because of this difference in the character of the disturbance of the nervous influence on the muscle in PDP and EAE, it was necessary to determine how the level of the membrane potential (MP), the electrolyte balance, and the catecholamine concentrations change in the affected muscles in PDP and EAE, and to what extent they can be corrected by administration of pharmacological agents acting on energy metabolism and on the sodium–potassium pump.

EXPERIMENTAL METHOD

Experiments were carried out on noninbred guinea pigs of both sexes weighing 300-500 g.

PDP was produced by Frick's method [5] by subcutaneous injection of partially inactivated diphtheria toxin (1 MLD, 0.003 ml of the liquid toxin) in a solution of medinal–veronal buffer (pH 8.5), into the lumbar region in a dose of 0.5 MLD/0.3 kg body weight. Paresis of the skeletal muscles developed on the 17th-21st day and paralysis on the 25th-45th day after injection of the toxin.

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TABLE 1. Changes in MP (M ± m) of Gastrocnemius Muscle Fibers of Guinea Pigs in the Course of PDP and EAE

	No. of fibers	MP (in mV)	P_1	P_2
Control	141	75,6±1,28		
Control + Phenylephrine	113	85,9±1,06	<0,001	
Control + ATP	103	77,5±0,93	>0,2	
Control + Pyruvate–phosphate	118	74,2±0,81	>0,2	
Control + Pyruvic acid	110	75,1±1,00	>0,5	
Control + Cysteine	107	74,2±0,94	>0,2	
Control + Methionine	101	73,7±0,78	>0,2	
PDP				
10th day after injection of toxin	100	75,7±0,97	>0,5	
15th day after injection of toxin	100	74,2±0,77	>0,2	
Early state (15th-21st day after injection of toxin)	120	63,7±0,76	<0,001	
Late stage (22nd-45th day after injection of toxin)	120	58,2±0,81	<0,001	<0,001
Late stage + artificial respiration	143	64,0±1,38		>0,5
Late stage + Phenylephrine	102	70,0±0,89	<0,001	<0,001
Late stage + ATP	94	78,4±1,46	>0,1	
Late stage + Pyruvate–phosphate	86	78,4±1,28	>0,1	
Late stage + Pyruvic acid	102	65,4±1,43		>0,2
Late stage + Cysteine	99	73,6±1,47	>0,2	
Late stage + Methionine	80	75,9±1,89	>0,5	
EAE				
Late stage (15th-22nd day)	126	75,0±0,87	>0,5	

Legend. P_1) compared with control; P_2 compared with early stage of PDP.

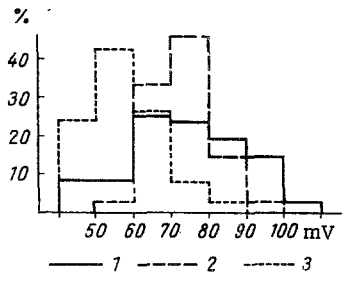

Fig. 1. Histograms of distribution of muscle fibers with various levels of MP: 1) control (n = 141); 2) PDP (15 days, n = 100); 3) PDP (late stage, n = 120). Abscissa, level of MP (in mV); ordinate, number of fibers with various levels of MP (in % of total number).

EAE was produced by the subcutaneous injection of an encephalitogenic mixture (spinal cord homogenate with Freund's complete adjuvant, 1:1.5) into the plantar pads, 0.5 ml into each pad, at intervals of 3 days.

A clinical picture of EAE (disturbance of movement coordination, paresis and paralysis of the skeletal muscles and the sphincters of the urinary bladder, and so on, developed in almost 100% of the animals after 14-20 days. The methods of recording the MP and of determination of the catecholamines and electrolytes were the same as those described earlier [3].

EXPERIMENTAL RESULTS

The results of the experiment carried out at different stages of PDP showed a well-marked dependence of changes in the functional state of the striated muscle fibers on the character of injury to the nervous system. For instance, in the preparalytic period (10th-15th day of sensitization), although the mean value of MP of the fibers of the tested muscle was still similar to the control (Table 1), an increase in the number of medium-polarized fibers could be clearly seen on the histogram (Fig. 1). The adrenalin concentration in the muscle was slightly reduced, the concentrations of potassium and sodium ions were increased, and the K/Na ratio was lowered (Table 2). With the first signs of paresis of the muscles (on the 17th-21st day) the value of MP fell appreciably and the spectrum of the histogram was shifted significantly toward a low level of polarization of the muscle fibers. This pattern was seen most clearly in the phase of development of paraplegia and tetraplegia (25th-45th day). Meanwhile the sodium, potassium, and noradrenalin concentrations in the muscle rose and the adrenalin concentration fell.

So far as the mechanisms of these changes are concerned, given the development of the general paralytic syndrome, especially in the severe cases of PDP, one of the principal pathogenetic factors could have been hypoxia. The addition of artificial ventilation of the lungs under these circumstances increased the polarization of the muscle fibers but it never reached the control level (Table 1).

TABLE 2. Changes in Concentrations of Electrolytes (in meq/g dry weight of tissue) and Catecholamines (in μg/g wet weight of tissue) in Gastrocnemius Muscle of Guinea Pigs in the Course of PDP and EAE

Parameter studied	Control		PDP						EAE		
			preparalytic stage (10-15 days)			late paralytic stage (22-45 days)			late stage (15-22 days)		
	No. of expts.	M±m	No. of expts.	M±	P	No. of expts.	M±m	P	No. of expts.	M±m	P
Potassium	9	0,359±0,007	10	0,404±0,009	<0,001	8	0,443±0,018	<0,001	11	0,398±0,012	<0.02
Sodium	9	0,059±0,004	10	0,092±0,003	<0,001	8	0,106±0,009	<0,001	11	0,084±0,002	<0,001
K/Na ratio		6,07		4,38			4,06			4,76	
Adrenalin	12	0,084±0,013	10	0,041±0,006	<0,001	9	0,033±0,006	<0,01	10	0,179±0,022	<0,01
Noradrenalin	12	0,116±0,021	10	0,113±0,011	>0,5	9	0,232±0,037	<0,02	10	0,363±0,032	<0,001

Considering the marked stimulation of phosphorylase activity by catecholamines [1] and changes in the concentration of the catecholamines in the muscles it was interesting to study the extent to which the polarization of the membranes of the muscle fibers when paralyzed in PDP could be changed by the action of the sympathomimetic drug phenylephrine. As Table 1 shows, the polarization under the influence of phenylephrine did not reach the normal level. This could be due to the insufficiency of substances utilized in the metabolic cycles of the sodium–potassium pump – high-energy compounds and thiol enzymes [6]. An attempt was therefore made to restore the normal MP of the muscle fibers paralyzed in PDP by injecting ATP, methionine, cysteine, and phosphoenolpyruvic and pyruvic acids. These experiments showed that nearly all the preparations used normalized the MP of muscle fibers paralyzed in PDP.

In comparative tests on animals with EAE no changes were found in the MP of the muscle fibers (Table 1), despite some increase in the concentrations of adrenalin, noradrenalin, potassium, and sodium in the muscle tissue and a slight decrease in the K/Na ratio (Table 2).

It can be concluded from this analysis of the results as a whole that the character of the disturbance of the influence of the nervous system on skeletal muscle differs in PDP and EAE. In the first disease, total injury to the thick myelinated nerve fibers evidently leads to changes in the polarization level and the concentrations of sodium, potassium, and catecholamines similar in magnitude to the characteristic changes after denervation [3], whereas in the second disease the internodal demyelination does not exclude their regulatory influence on processes of electrogenesis in the muscle fibers.

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