for the timely removal of calcium from the myofibrils and realization of diastolic relaxation, whereas ionol prevents these manifestations of injury.

Preliminary injection of ionol thus limits overactivation of LPO and abolishes postresuscitation injury to the heart, estimated on the basis of release of enzymes from cardiomyocytes and disturbance of contractility of the heart.

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ACTIVE ADJUSTMENT OF THE ARCHITECTONICS (STRUCTURE) OF MOTOR UNITS

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KEY WORDS: neuromuscular diseases; motor unit; muscle fibers; denervation-reinnervation process.

The principles governing the distribution of muscle fibers forming the motor units (MU) of normal muscles [4, 7], and also of muscles in different stages of recovery of function after denervation, have been studied in detail in investigations by electrophysiological, morphological, and histochemical methods. The principles and ability of preserved axons of motor nerves to undertake compensatory innervation by branching, to which the name sprouting has been given [2, 8], have also been studied. It has also been shown that the intensity of sprouting rises with a decrease in the number of preserved neurons, and this is reflected in the well-known phenomenon of grouping of muscle fibers of the same histochemical type [5].

Meanwhile the character of distribution of preserved nerve fibers has not yet been adequately analyzed. The data given below suggest that in the course of reinnervation the motoneuron concentrates the zone of distribution of its own axons in a narrower region than normally, and actively deprives muscle fibers located in the areas of MU remotest from the center, of its influences.

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TABLE 1. Density of Muscle Fibers in MU of Muscles at Different Stages of Development of Denervation-Reinnervation Process ($M \pm \sigma$)

Stage of process	Level of lesion							
	motoneurons and axons of motor nerves				terminal ramifications of axons and neuromuscular transmission			
	number of muscles	mean density of muscle fibers in MU	mean interspike interval of complex	mean duration of complex	number of muscles	mean density of muscle fibers in MU	mean interspike interval of complex	mean duration of complex
Normal	8	2,21±0,4*	0,81±0,07*	1,31±0,22	3	3,0±1,1	0,98±0,22	2,0±1,19
I—II	5	2,66±0,71**	1,03±0,29**	2,15±1,39	9	2,33±0,44	0,84±0,24	1,3±0,37
III	17	2,63±0,42***	0,98±0,3**	1,65±0,71	6	2,65±1,08	0,86±0,28	1,81±1,71
IV—V	5	4,4±1,95***	1,41±0,53***	4,05±2,34	—	—	—	—
Control		1,45±0,1	0,4±0,17	—	—	—	—	—

Legend. Normal — clinically intact muscles of patients with traumatic neuropathies, in whom distribution of APs of MU did not differ from that in muscles of normal persons. Control — results of investigation of muscles of normal persons from data in [7]. Significance of differences from control values: *P > 0.05, **P < 0.05, ***P < 0.01.

TABLE 2. Characteristics of Number and Volume of Groups and Diameter of Muscle Fibers of Types I and II at Different Stages of Development of Denervation-Reinnervation Process ($M \pm m$)

Stage of process	Number of muscles tested	Type I muscle fibers		Type II muscle fibers		% of fibers with diameter outside the normal limits			
		number of groups	volume of groups	number of groups	volume of groups	type I fibers		type II fibers	
						below normal	above normal	below normal	above normal
Normal	10	0,1±0,31	7,0±0	0,6±0,94	7,5±0,69	0	7,8±8,96	0,74±1,8	2,5±5,1
I	6	1,85±0,84*	8,9±2,1*	1,57±0,73*	8,6±1,5*	0,34±0,83*	0,42±1,0*	1,8±2,8*	4,8±6,24*
II	13	2,0±0,87**	9,95±2,32*	2,0±0,21*	9,6±1,7*	1,2±1,3*	9,8±21,6*	19,4±21,6*	5,4±9,4*
III	4	2,5±0,56***	23,8±4,32***	2,75±0,94**	20,9±2,4***	13,1±4,3	22,3±25,6*	57,16±24,2***	0
IV—V	3	3,2±0,46***	32,6±6,1***	3,3±0,43**	27,3±4,5***	29,0±3,9***	33,6±15,0*	72,3±9,5***	0

Legend. Normal — clinically intact muscles of patients with neuromuscular diseases, whose character of distribution of APs of MU did not differ from that in muscles of normal subjects. Significance of differences from normal values: *P > 0.05, **P < 0.05, ***P < 0.01.

EXPERIMENTAL METHOD

The density of muscle fibers in MU was determined by the number of action potentials (AP) of fibers recorded at 20 different points of a muscle by means of a microelectrode (from Medelec), with recording surface of 0.0005 mm^2, on an electromyograph (from Disa) [6]. The type of fibers in biopsied areas of the muscles was determined from histochemical activity of the enzymes myofibrillary ATPase, at pH 9.4, and mitochondrial succinate dehydrogenase. The structure of MU and the stage of development of the denervation-reinnervation process were determined by a method developed and described by the writers previously [1], based on a study of the distribution of APs of MU of different durations in human muscles.

Altogether 137 muscles in 124 patients aged from 11 to 62 years, with lesions of spinal motoneurons (23), axons of motor nerves (29), terminal ramifications (35), and neuromuscular transmission (52) were studied. The density of muscle fibers was determined in 88 patients (101 muscles), diagnostic biopsy was performed on 28 patients, and in eight patients the density of muscle fibers was determined and biopsy material investigated in the same muscle.

EXPERIMENTAL RESULTS

It will be clear from Table 1 that the density of the muscle fibers, and also values of average interspike intervals and durations of complexes characterizing the distribution of muscle fibers in MU of muscles at different stages of the denervation-reinnervation process, varied within wide limits, but the mean values of these parameters differed significantly from

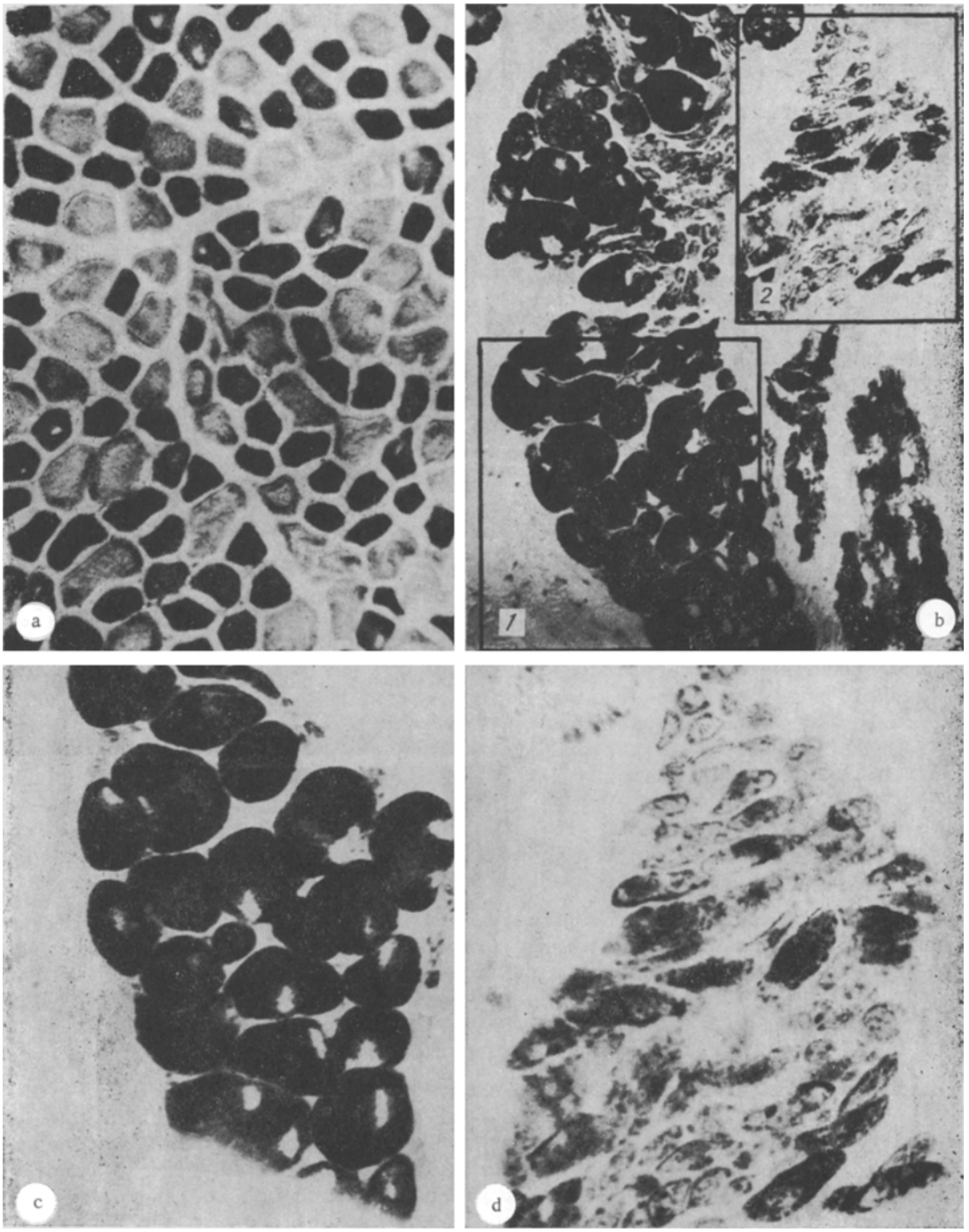

Fig. 1. Architectonics of distribution of type I and II muscle fibers in biopsy material taken from regions of human muscles: a) muscle of a person without neuromuscular disease. 40 ×; b) muscle from patient with amyotrophic lateral sclerosis, 40 ×; c, d) fragments 1 and 2 of Fig. 1b, 120 ×. Stained for succinate dehydrogenase activity.

those in normal subjects. In the context of this description the increase in density of muscle fibers in MU in which no electromyographic evidence of reinnervation could be seen, i.e., in muscles at the stage of the denervation process characterized exclusively by AP of MU of shorter duration, evidence that the MU have lost many of their muscle fibers, was particularly interesting.

This observation suggested that in the earliest stages of the denervation process, besides loss of muscle fibers located in regions remote from the center of MU, there was an in-

TABLE 3. Number of Groups with Different Numbers of Muscle Fibers in Preparations of Three Muscles from Patients with Amyotrophic Lateral Sclerosis at Stage IV of Development of the Denervation-Reinnervation Process

Preparation No.	Type of muscle fibers	Number of muscle fibers in group									Total number of muscle fibers
		7—14	15—21	22—28	29—35	36—42	43—49	50—56	57—63	64—70	
1	I	4	9	4	1	3	2	2	—	—	1283
	II	2	5	5	—	2	2	4	1	1	
2	I	17	2	2	1	—	—	—	—	—	883
	II	11	9	4	2	—	—	—	—	—	
3	I	6	2	4	4	4	—	—	—	—	1035
	II	5	2	6	4	2	—	—	—	—	

crease in the number of muscle fibers located in the center of MU, i.e., concentration of the fibers of this MU in a narrower zone of the muscle.

Subsequent analysis of this phenomenon was carried out on the basis of comparison of the number of muscle fibers lying side by side (the phenomenon of grouping of muscle fibers of the same type at the same stages of the denervation-reinnervation process), with simultaneous counting of the number and diameters of muscle fibers of types I and II, and also the number of groups (Table 2).

It will be clear from Table 2 that at all stages of development of the denervation-reinnervation process groups of muscle fibers of types I and II could be seen. At stages I and II of the denervation-reinnervation process groups were single, and their volume, i.e., the number of fibers of the same type present in them, was 8-9 (normally not more than five or six, or sometimes seven muscle fibers of the same type lie side by side, touching one another). In the next stages of the denervation-reinnervation process the number of groups increased, as also did the number of fibers in the group. Irrespective of continued death of type II motoneurons, the number of groups in the preparation and the number of muscle fibers in the group were practically the same. The only difference was in the diameter of the different types of muscle fibers: The diameter of type I fibers remained normal or was reduced in a few fibers. The diameter of the type II fibers was reduced; moreover, the number of muscle fibers whose diameter was smaller than the lower limits of normal was significantly greater and increased with an advance in the stage of the denervation-reinnervation process.

Since the calculation was done on 200 fibers, and with a considerable increase in the volume of the group the number of fibers varied from one to three, the total number of groups, total number of fibers, and number of muscle fibers of types I and II were counted in three muscle preparations obtained at biopsy, and in stage IV of the denervation-reinnervation process (Table 3). The results are evidence that the principles described above are confirmed by investigation of all muscle fibers of the preparation.

It is a particularly interesting fact that among groups of both type II and type I no muscle fibers of the opposite type were seen (Fig. 1). Whereas the absence of type II muscle fibers in type I groups can be explained by progressive death of the type II motoneurons, it is not yet clear why type I muscle fibers with normal diameter, normal function and, in the existing view [9], less affected in the forms of pathology which we studied, were not preserved in the type II groups. Evidently these observations also confirm the hypothesis noted above, that a motoneuron, even if preserving its normal functions, in the case of reinnervation of the population of muscle fibers determined by it, excludes one zone of the muscle from its innervation or actively sends muscle fibers into other zones of the muscle, i.e., concentration of influence of the motoneuron in a particular zone is observed.

It must also be noted that muscle fibers innervated by type II motoneurons were sharply reduced in diameter in zones of considerable grouping, i.e., they were subjected to atrophy unlike type I muscle fibers, which remain normal or very slightly reduced, or in some cases even slightly increased in diameter.

The above observations are evidence that the ability of a motoneuron to undergo sprouting is preserved even in cases when other functions defined as trophic are disturbed or at an end.

An increase in density of muscle fibers also was observed in clinically intact muscles of persons with peripheral nerve injury. This suggests that the adjustment of MU takes place also in muscles remote from the zone of denervation.

There is indirect evidence to suggest that adjustment of the architectonics of the motoneuron takes place within a fairly short time. For instance, in patients with a disturbance of neuromuscular transmission, when an electromyographic investigation of the muscles must invariably be performed before biopsy, as a rule we did not observe any denervation electrophysiological phenomena — fibrillation potentials (FP) and positive pointed waves in muscles in which considerable degrees of grouping were found. Since we know that FP appear in response to disturbance of contact of the muscle fiber with the corresponding motoneuron in the course of 7-14 days [3, 10], this suggests that the adjustment takes place earlier.

These results demonstate that besides branching of a motoneuron, in one zone of innervation (most probably the central) muscle fibers located at the periphery of MU are excluded from the zone of its innervation, and that the motoneuron actively adjusts its structure in order to create optimal conditions for innervation of a certain population of muscle fibers located in the zone of its innervation.

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FORMATION OF GENERALIZED SEIZURE ACTIVITY IN MICE AFTER DAILY INJECTION OF METRAZOL IN SUBTHRESHOLD DOSES

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KEY WORDS: metrazol; seizures; "kindling" phenomenon.

A method of inducing seizure activity by repeated subthreshold electrical stimulation of brain structures has been described and is known as the "kindling" phenomenon [3, 5, 6, 13]. Inducing seizure activity by repeated stimulation with chemical agents (convulsants) appeared interesting as a potential model. To study the pathogenesis of the epileptic syndrome and screening of antiepileptic drugs, a model of generalized seizures induced by systematic injection of metrazol is widely used [9, 12].

The object of this investigation was to study whether a seizure syndrome can develop in response to repeated injections of subthreshold doses of metrazol.

EXPERIMENTAL METHOD

Experiments were carried out on inbred (CBA × C57BL/6, BALC/C)F_1 hybrid mice and noninbred albino mice weighing 18-22 g. Each group consisted of at least 15 animals. Metrazol

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