Disturbances of automatic activity and conductivity of the myocardium observed in some divers during exposure to an increased pressure could reflect an increase in tone of the vagus nerve arising during inhalation of the hyperoxic gas mixture. However, the appearance of these changes simultaneously with marked tachycardia suggests that other mechanisms may be responsible for their development.

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CHANGES IN ELECTROGENIC PROPERTIES OF STRIATED MUSCLE FIBERS IN EXPERIMENTAL BOTULISM

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Changes in the electrical parameters of fibers of fast and slow muscles were studied during the development of local botulism in rats. In the early stage of poisoning the membrane potential (MP) of fibers of both fast and slow muscles fell. In the late stage of poisoning, marked depolarization of the membrane was accompanied by a change in the input resistance and time constant (RC) of the membrane, rheobase currents, and amplitude of the action potentials evoked by direct intracellular stimulation. Changes in the electrical parameters were more marked in fast muscle fibers.

KEY WORDS: *striated muscle; electrical parameters; botulism.*

Botulinus toxin disturbs neuromuscular transmission by blocking liberation of the mediator from the presynaptic terminals. No significant changes are found under these circum-

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stances in the structure of the nerve fibers and motor nerve endings, or in synthesis of the mediator [1, 8, 15]. Prolonged blockade of neuromuscular transmission in botulism increases the sensitivity of the extrasynaptic muscle membrane to mediators and leads to atrophy of the muscle fibers and to changes in the concentration of potential-forming K^+ and Na^+ ions in skeletal muscle [3, 13, 15].

The investigation described below was accordingly undertaken in order to study the character of disturbance of electrogenesis and the biophysical parameters of the cytoplasmic membrane of muscle fibers in botulism.

EXPERIMENTAL METHOD

Albino rats weighing 200-250 g were used. Type C botulinus toxin (1 MLD for mice = 0.0006 mg) was injected into the leg muscles in a dose of 0.0001 mg/100 g body weight. This dose caused local paralysis to develop in the third to fourth day in the limb into which the toxin was injected. Tests were carried out in the early (4 days after injection of the toxin) and late (14 days) stages of poisoning. The rats were anesthetized with pentobarbital sodium (3-4 mg/100 g body weight). Glass microelectrodes filled with 2.5 M KCl, connected to a bridge circuit [11], were used for intracellular recording and also to polarize the muscle fibers. Potentials and polarizing currents were recorded photographically from the screen of an SI-18 dual-beam oscilloscope. The input resistance, threshold potential, time constant (RC) of the membrane, and threshold currents of direct stimulation of fibers of fast (m. extensor digitorum longus) and slow (m. soleus) skeletal muscles were investigated by the usual methods [14]. The RC of the membrane was measured at a level of 83% of the amplitude of the anelectronic potential [6]. The duration of the pulses of testing current was 50 msec.

EXPERIMENTAL RESULTS AND DISCUSSION

In the early stage of botulinus poisoning (Table 1) a sharp decrease in membrane potential (MP) was observed in the fibers of the fast muscle. Under these circumstances the number of highly polarized muscle fibers decreased and the number of fibers with a low level of polarization increased (Fig. 1). Meanwhile the duration of the action potential (AP) of the muscle fibers increased. However, the input resistance, threshold potential, and RC of the membrane, the threshold currents of direct stimulation, and the amplitude of AP were indis-

TABLE 1. Electrical Parameters of Fibers of Fast and Slow Skeletal Muscles of Rats Receiving Botulinus Toxin

Experimental conditions	Membrane potential, mV	Amplitude of AP, mV	Duration of AP, msec	Threshold potential, mV	Threshold current, mA	Input resistance, Ω	Time constant, msec
			m. extensor digitorum longus				
Control	87,3±1,5 (92)	95,5±1,9 (33)	1,21±0,05 (29)	13,3±0,55 (35)	19,9±1,5 (35)	0,398±0,038 (33)	3,17±0,13 (33)
Botulism (4 days)	71,8±1,8 (61)	91,2±3,0 (32)	1,66±0,07 (32)	14,3±0,59 (31)	21,4±1,6 (31)	0,385±0,041 (38)	3,47±0,2 (38)
P	<0,001	>0,5	<0,001	>0,2	>0,5	>0,5	>0,5
Botulism (14 days)	72,3±1,7 (54)	81,8±2,9 (28)	1,61±0,09 (26)	17,9±0,67 (28)	15,3±1,2 (28)	0,483±0,034 (32)	4,1±0,2 (31)
P	<0,001	<0,001	<0,001	<0,001	<0,05	<0,05	<0,001
			m. soleus				
Control	73,8±1,84 (53)	87,7±1,3 (51)	1,58±0,05 (50)	15,5±0,65 (51)	23,9±1,1 (51)	0,36±0,019 (39)	3,06±0,13 (38)
Botulism (4 days)	65,6±3,1 (60)	85,8±1,7 (44)	1,42±0,05 (44)	15,4±0,71 (42)	23,4±1,4 (44)	0,34±0,027 (29)	3,32±0,15 (28)
P	<0,01	>0,5	<0,05	>0,2	>0,5	>0,5	>0,5
Botulism (14 days)	61,7±2,2 (55)	81,7±1,9 (53)	1,77±0,04 (53)	15,2±0,51 (53)	12,8±0,73 (53)	0,54±0,03 (30)	4,44±0,18 (30)
P	<0,001	<0,02	<0,01	>0,5	<0,001	<0,001	<0,001

Legend. Number of fibers tested shown in parentheses.

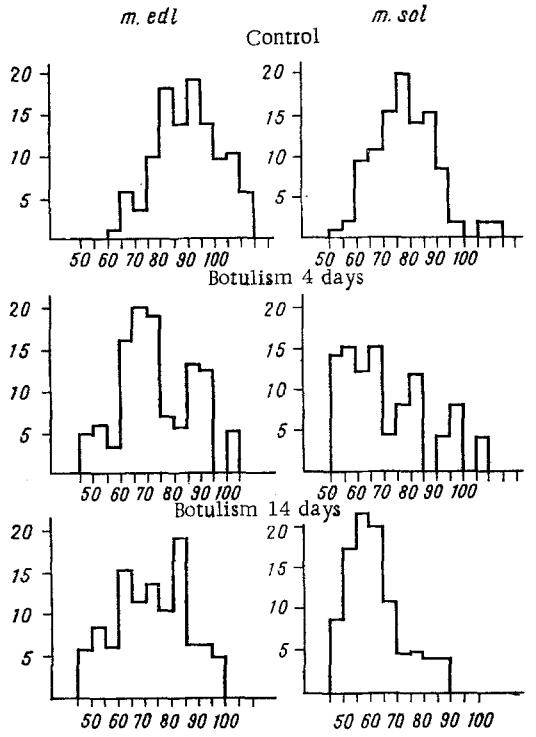

Fig. 1. Distribution of muscle fibers by level of membrane potential. Abscissa, membrane potential (in mV); ordinate, number of muscle fibers (in %).

tinguishable from the control in the early stage of botulism. At this stage of poisoning no changes in the above-mentioned electrical parameters were observed in the slow muscle except a greater fall in the MP level than in the fast muscle.

In the late stages of local botulinus poisoning, although the level of MP of the fast muscle fibers remained low, changes were observed in the passive and active properties of their surface membrane. The input resistance and RC of the membrane were considerably increased. The latter was attributed to an increase in the threshold potential and a marked decrease in amplitude of AP evoked by direct intracellular stimulation, and to a sharp increase in their duration compared with the control. Dissociation between changes in the active and passive properties of the fiber membranes was found in the slow muscles. The MP of individual muscle fibers continued to fall, whereas the levels of the input resistance and RC of the membrane were 40-50% higher than in the control. The character of the regenerative responses showed a much smaller change: The amplitude of AP fell by only 6.9% and their duration increased by 12%. The threshold currents for direct stimulation fell sharply in both muscles. The threshold potential in the fibers of m. soleus in the late stage of poisoning was indistinguishable from the control (Table 1).

During the development of local botulism the earliest disturbances of the electrical parameters of the skeletal muscle fibers was thus a sharp fall in the value of MP. Changes in the level of polarization of the muscle fibers were more marked in the fast muscle, in agreement with the greater damage by botulinus toxin observed in the neuromuscular synapses of fast muscles [9, 10]. The early and marked change in the level of polarization of the striated muscle fibers was perhaps due to weakening of the trophic effect of the motor nerve on the skeletal muscle, for in botulism axoplasmic protein transport along thick myelinated nerve fibers is severely disturbed [2, 7] and the spontaneous secretion of mediator in the myoneural junctions of the affected muscles is inhibited [7, 12, 15]. Prolonged depolarization of the muscle fibers in turn may cause an increase in the threshold potential and a decrease in the amplitude and steepness of rise of the AP [4, 5]. Atrophy developing in the skeletal muscles in botulism [13] evidently plays a role in the mechanism of the increase in the input resistance and the parallel decrease in the rheobase currents of direct stimulation. The input resistance is known to depend not only on the membrane resistance, but also on the diameter of the muscle fiber. The smaller the cell, the higher its input resistance. The rheobase strength of the current in nerve and muscle fibers is inversely proportional to the input resistance [4].

It can be concluded from these findings that changes in the electrical parameters of striated muscle fibers and, in particular, in the value of MP, in botulinus poisoning are evidently the result of weakening of neurotrophic influences on the skeletal muscle.

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RESISTANCE OF THE MYOCARDIUM TO ADRENALIN IN RATS ADAPTED TO HYPOXIA

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The intensity of the changes produced by adrenalin in the myocardium of rats adapted to hypoxia was studied after its administration to the intact animal and perfusion of the isolated heart. The changes were revealed by histochemical reactions for succinate dehydrogenase activity and staining for lipids. After intramuscular injection of a cardiotoxic dose of adrenalin (2.0 mg/kg) into adapted rats no damage to the myocardium was found, whereas perfusion of the isolated heart with adrenalin (20 µg/ml) caused the formation of micronecroses of the cardiocytes. However, their volume was statistically significantly smaller than in the isolated heart of intact rats under similar conditions. Differences in the sensitivity of the myocardium in vivo and in vitro indicate that the phenomenon of protection of the myocardium against the harmful effects of adrenalin in rats adapted to hypoxia is manifested at the level of the intact organism. The increase in the resistance of the myocardium itself is probably due to an increase in the power of the metabolic systems during adaptation.

KEY WORDS: *rat myocardium; adaptation to hypoxia; resistance to adrenalin; isolated heart.*

Adaptation to hypoxia, physical exertion, and other extremal environmental factors is accompanied by an increase in the nonspecific resistance of the organism to several pathogenic agents [2, 7]. In particular, preliminary adaptation to high-altitude hypoxia [7, 13]

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