THE FUNCTIONAL STATE OF THE NERVE–MUSCLE PREPARATION IN THE INTACT ORGANISM UNDER CONDITIONS OF DISTURBED CIRCULATION

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Investigation of the natural course of development of muscle ischemia due to disturbance in circulation is of considerable interest both practically and theoretically. Of parameters typifying the functional state of the nerve – muscle apparatus under conditions of ischemia those studied in greatest detail are rheobase and chronaxy [1, 2, 5, 7, 8, 9, 10, 11, 12] and also accommodation [9]. However, such important indices as refractivity and lability were not subjected to investigation. Estimation of lability based only on the threshold reaction to rhythmic stimulation [11] or on the degree of chronaxy can hardly be regarded as convincing. Chronaxy, threshold reaction [6] and even refractivity determined with the aid of two consecutive impulses cannot serve as criteria regarding capacity of nerve – muscle preparations for rhythmic stimulation and tetanic contraction. By applying the method developed in the laboratory for incomplete isolation of muscle [3], we studied the lability of the nerve – muscle preparation and its capacity for summation of two consecutive impulses upon abrupt disturbance of circulation within the muscle.

EXPERIMENTAL METHOD

Lability was determined with the aid of rhythmic stimulation with square-wave impulses of 0.2-millisecond duration and a frequency rising from 10 to 2500 impulses per second, suitability for summation – with the aid of two maximal impulses of the same duration. The interval between them was gradually increased to the duration of 3 diapasons.* During each diapason a series of tests was carried out. Interval between impulses in the first diapason for the first test was less than 0.1 millisecond, for the subsequent ones – 0.2; 0.3; 0.4; 0.6; 0.8; 1; 1.2; 1.4; 1.6 and 1.7 milliseconds; in the second diapason – for the first test – 1 millisecond, for subsequent ones – 1.5; 2; 3; 4; 5; 6; 7; 9 and 11 milliseconds, and in some instances up to 15, 18, 22 and 25 milliseconds; in the third diapason – 5, 7, 12, 17, 22, 30, 40, 50, 60, 70, 85, 100 and 110 milliseconds; in some instances 7 and 17 millisecond intervals were eliminated in which cases the third diapason consisted of 11 tests. As the interval was increased the phase of absence of summation of stimulation made its appearance (phase of absolute refractivity) and lasted 0.6-0.8 milliseconds; also the phase of increasing summation (intervals from 0.6-0.8 to 1.5-2 milliseconds), the phase of maximal summation (intervals from 1.5-2 to 18-20 milliseconds), phase of decreasing summation (intervals above 20 milliseconds) (Fig. 1). Unipolar stimulation was used in the experiments. Active platinum electrodes (epicutaneous and needle-shaped) were placed upon or into a muff which contained a motor nerve. For direct stimulation the electrodes were inserted hypodermically at the cranial and caudal ends of the muscle contained in the muff. Muscle contraction was recorded on the kymograph. Ischemia was produced by clamping (for up to 3 hours) the vascular muffs and both ends of the muscle (at the points of its attachments) with small clamps. In the course of examination of muscular contraction, this technic makes it possible to eliminate undesirable moments which are unavoidable with other technics (anesthesia and trauma in acute experiments; compression of a nerve with a tourniquet; incomplete ischemia from the use of straps, etc.). The parameters were recorded during the experiment every 2-3 minutes.

*As in original.

The total number of experiments was 23. Lability was investigated 18 times, summation capacity – 13.

EXPERIMENTAL RESULTS

The contractile effect of muscle in response to rhythmic and single impulses decreased progressively as the degree of ischemia progressed. We did not observe phases of increased excitability and contractile capacity of muscle, as described by some workers [7, 11] and not elicited by others [9, 10]. Indirect excitability of the nerve – muscle preparation disappeared 20-30 minutes following application of clamps to the vessels (first stage ischemia). Sensitivity of muscle to direct stimulation, although gradually decreasing, was preserved for $1\frac{1}{2}$ – 2 hours (second stage ischemia).

A progressing increase in the phase of absolute refractivity was observed in all experiments 3-5 minutes after clamping of the vessels. Prior to the disappearance of the neuromuscular conductivity this parameter increased from 0.6-0.8 milliseconds to $1\frac{1}{2}$ – 2 milliseconds, i.e., twice or more. The phase of increasing summation shifted in the direction of longer intervals and increased by 1 millisecond. The interval at which beginning of decreasing summation occurred did not change. The phase of maximal summation was thus shortened by $1\frac{1}{2}$ – 2 milliseconds. These phase changes took place during the first 15-20 minutes. As ischemia deepened there developed a disturbance in summation of impulses which followed one another at optimum intervals (3-16 milliseconds). Not long before the disappearance of neuromuscular conductivity the responses of the muscle to two impulses equalized regardless of the intervals between the latter, i.e., there developed a loss of capacity for summation of two indirect stimulations (see Fig. 1, e).

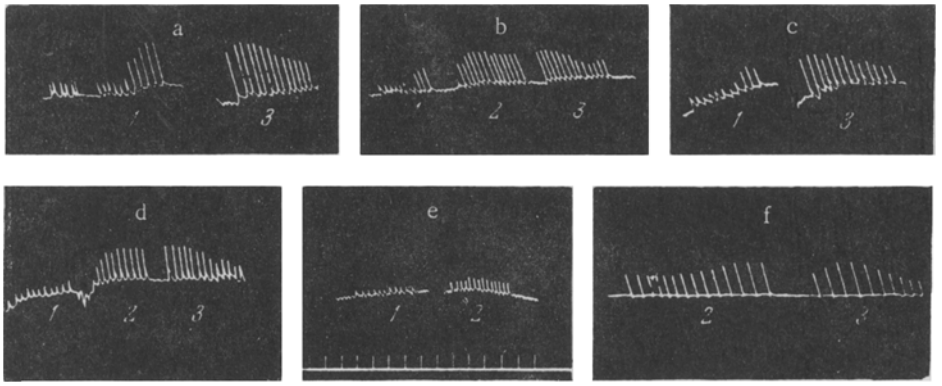

Fig. 1. Changes in capacity for summation in the nerve – muscle preparation in a state of ischemia. a) Initially, b) seven minutes after application of clamps, c) ten minutes later, d) eighteen minutes later, e) twenty minutes later, f) thirty-seven minutes later. Time – five seconds. The numbers below the contraction tracings identify the group of tests (diapason). Contractions on kymogram f were recorded by direct stimulation of muscle.

In the second stage of ischemia, during which sensitivity of the nerve – muscle preparation was preserved only to direct stimulation, increase in the refractory phase continued as brought forth now with the aid of direct stimulation. It reached 6-10 milliseconds and over. The maximal summation phase was shortened to 2-4 instead of 17-20 milliseconds, and was displaced in the direction of intervals of 20 milliseconds and over (see Fig. 1, f).

During the entire first stage of ischemia and up to the point of disappearance of indirect excitability, the lability of the nerve – muscle preparation, as far as our technic permits us to judge, did not experience any substantial changes. Optimum of muscle contraction developed at the same frequency of stimulation (Fig. 2). Only in the second stage, when even direct excitability decreased to the point that in order to obtain muscle contraction stimuli of 20-40 v were required, there developed a decrease in lability which gradually progressed. Optimum muscle contraction arose at 30-50 impulses per second instead of 70-100 (Figs. 2 and 3). Frequency gradually decreased followed by normal contraction. Thus, at first tetanic contraction followed in

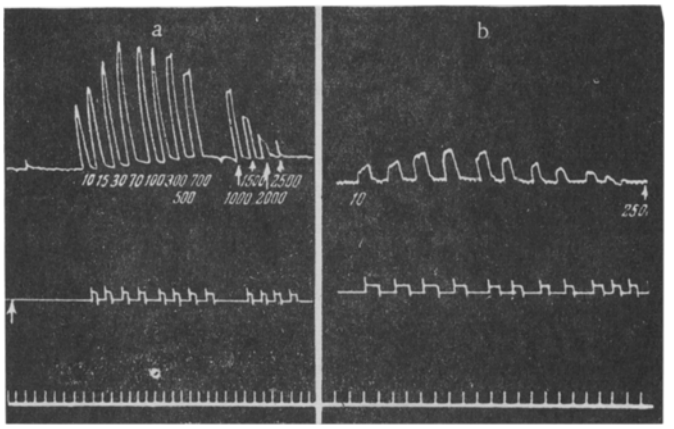

Fig. 2. Lability of a nerve – muscle preparation in the first stage of ischemia (indirect stimulation). Meaning of tracings (from above down): muscle contractions, record of stimulation, record of time (5 seconds). a) Initial lability, b) 20 minutes after cessation of circulation. The numbers beneath the contraction tracings indicate the frequency of stimulation in terms of impulses per second.

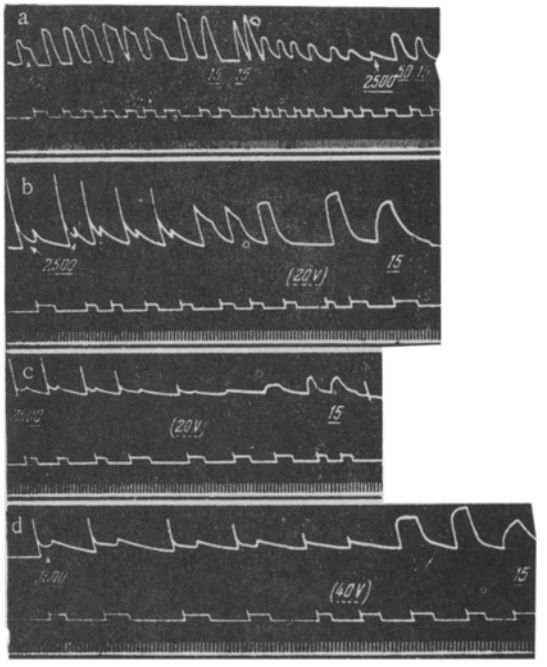

Fig. 3. Changes in lability of a nerve – muscle preparation in the second stage of ischemia (direct stimulation). a) Lability 45 minutes after onset of ischemia, b) 65 minutes later, c and d) 1 hour and 45 minutes later. Frequency of stimulation (the numbers beneath the contraction tracings) 15, 50, 100, 300, 500, 1000, 1500, 2000, 2500 impulses per second. Numbers in parentheses indicate the amplitude of stimulation in volts.

response to rhythmic stimulation at a rate as high as 1,500 impulses per second, later in response to stimulation of not more than 500 impulses per second and finally, in response to stimulation of not more than 100

impulses per second (Fig. 3). To stimulation of greater frequency the muscle reacted with an initial twitching which changed in succession first to a decreasing tonus then an increasing one when the current was disconnected and finally to a tonic contraction. Such a reaction reminds one of the response of normal muscle to the passage of a continuous current. Apparently, the ischemic muscle loses the capacity of rhythmic excitability and responds to stimulation of even moderate frqquency such as stimulation with a continuous current. It is interesting to note that the greater the frequency of stimulation the greater the contractile response of the muscle in the form of the initial twitching, i.e., the degree of contraction is determined by the quantity of electricity passing through an organ per unit time, which increases together with a rise in the frequency of the impulse. Simultaneously, other changes in the contractile reaction of muscle take place, such as slowing down of contraction and especially its weakening after a tetanic contraction or an isolated twitching (residual contracture).

In such a manner, the disappearance of neuromuscular conductivity in ischemia of the skeletal muscle of the rabbit is accompanied by a decrease in excitability of the nerve – muscle preparation and a disturbance of summation of two stimulations. Abrupt changes in lability which could be uncovered by our technic were not observed by us. After cessation of nerve – muscle conductivity, the disturbance in excitability and capacity for summation continues to deepen and in addition there is an abrupt fall in lability. A reactivity of muscle develops in $1\frac{1}{2}$ – 2 hours after complete ischemia. Changes in lability, capacity for summation, excitability and contractile capacity of a muscle in a state of ischemia differ from changes in these parameters in other forms of disturbance of the nerve – muscle preparation due, for example, to curare-like substances or anesthesia [4].

SUMMARY

Experiments were staged on rabbits with the aid of a method of incomplete separation of the muscle and placing it into a cutaneous muff with intact vascular and nervous connections. The lability and contractile property of the nerve – muscle preparation, preserved in the body, was studied in the state of ischemia. The decrease of excitability, increase of the absolute refractory phase and shortening of the phase of maximal summation were noted under the effect of ischemia. These changes progressed after development of the block of the neuromuscular transmission and an acute decrease of lability was added. Complex reactivity of the muscle appeared in 1 – $1\frac{1}{2}$ to 2 hours of ischemia.

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