INCREASED WORK CAPACITY OF MUSCLE ON STIMULATION THROUGH THE NERVE AND THE CAUSES OF THIS PHENOMENON

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It is commonly known that gradually increasing expenditure of substances and accumulation of decomposition products such as inorganic phosphorus and lactic acid occur in the neuromuscular preparation during work; this is accompanied by a decline of work capacity. These phenomena are also noted in experiments on muscle in situ with preservation of blood supply and innervation [3, 5, 17, 18, 20].

In studying questions connected with the mechanism of neuromuscular transmission of excitation in situ [2, 7, 8, 9] we succeeded in observing such tetanic contraction of muscle under certain conditions of indirect stimulation during which the muscle tissue content of phosphorus not only did not increase in relation to the initial resting state but even diminished, and there was delay in the development of fatigue. A description of the condition requisite for the appearance of this phenomenon and an analysis of its cause are given below.

EXPERIMENTAL METHOD

Experiments were performed on white rats under ether anesthesia. The cut tendon of the gastrocnemius muscle in situ was connected to a stylus. Square-wave and saw-tooth impulses generated by an electronic stimulator GRAKh-1 were used as stimuli.

One of the symmetric muscles was stimulated through buried platinum electrodes via the nerve, the other directly through platinum needles inserted into the proximal and distal ends of the muscle.

After the experiment both the muscles were excised at the same time and frozen with liquid air. Inorganic phosphorus and lactic acid were determined in the powder obtained by triturating the muscle in a mortar with liquid air, the former by the microcolorimetric method following reduction of the phosphorus-molybdenum complex with stannous chloride in butanol extract of the trichloroacetic acid extract [21], the latter with the help of p-hydroxydiphenyl [12].

EXPERIMENTAL RESULTS

It is known that when nerve is stimulated by frequency or strength of stimulation in excess of a certain value, the muscle relaxes instead of contracting, a phenomenon referred to as pessimum [6, 8, 13].

However, in the majority of pessimal states described in the literature the action of the stimulus was not confined to the area of neuromuscular transmission but affected the muscle also, owing to which the latter showed signs of exhaustion with complete pessimal relaxation and absence of any external work [2, 8, 10, 11]. We discovered that on stimulation with square-wave and saw-tooth pulses of long duration (10 milliseconds) at frequencies of around 53-55 cps and moderate strength, complete pessimal relaxation of muscle was observed only on account of block in the intermediate link, without involving the muscle fibers. We designated this state as "true pessimum" [2, 8].

When the stimulus strength is gradually increased beginning with subthreshold, muscle being stimulated indirectly responds first, followed by response from the directly stimulated muscle also. The level of tetanus observed in the latter is lower than that given by the indirectly stimulated muscle when the strength of stimulation applied is the same. When stimulus strength is increased further the height of optimal contractions of both muscles becomes equalized.

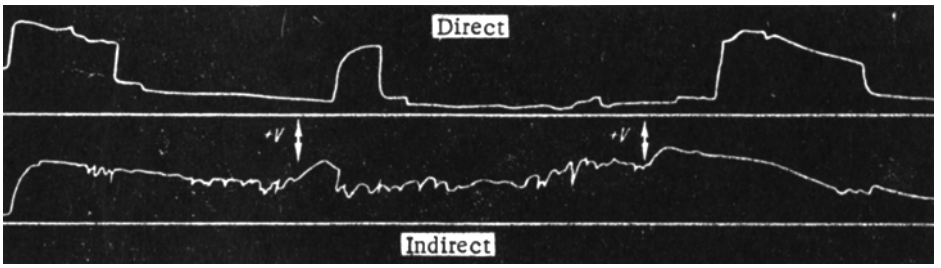

Fig. 1. Examples of investigated form of prolonged tetanus with direct and indirect stimulation (explanations in text).

When stimuli with parameter values close to the pessimal (duration 10 milliseconds, frequency 50-52 cps) but still giving optimal response are used, indirect stimulation (Fig. 1) leads to tetanus which does not pass into relaxation during continuous action but assumes an undulating course, sometimes even without appreciable lowering of the summated height of contractions. Direct stimulation under similar conditions leads to rapid relaxation with no or slight secondary rises, the most frequently observed effect being that of a sharp decline to the base line. This relaxation of the muscle to zero level during continuing direct stimulation attests to a steeper rise in stimulation threshold than in the case of similarly prolonged indirect stimulation.

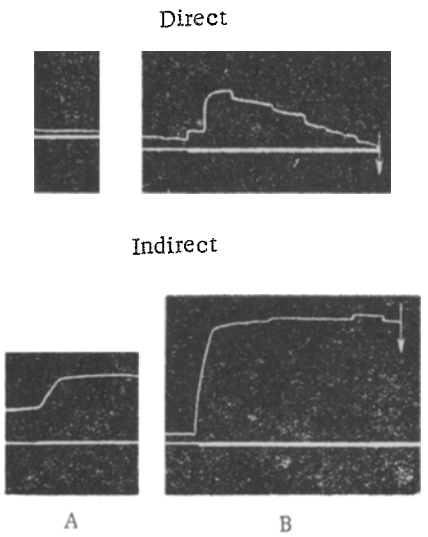

Fig. 2. Examples of investigated forms of brief tetanus during direct and indirect stimulation (explanations in text).

During direct stimulation of muscle a small increase in stimulus strength (arrows in Fig. 1) usually elicits a sharp increase in the height of contractions, following a considerable latent period, which is replaced by a sharp fall. Indirect stimulation under these conditions leads to a much more stable increment in the height of contractions.

We investigated the accumulation of inorganic phosphorus during the described simultaneous direct and indirect stimulation of symmetrical muscles in the same animal. Two stimulus strengths were investigated: one which elicited no response from the directly stimulated muscle and submaximal tetanus from the indirectly stimulated muscle (sections of myograms A in Fig. 2) and the other which elicited submaximal tetanus from the directly stimulated muscle and a higher tetanus from the indirectly stimulated muscle (myogram examples B in Fig. 2). In both cases the work performed in lifting the load was apparently greater in the case of the indirectly stimulated muscle. This would appear to require greater metabolic turnover, with greater accumulation of inorganic phosphorus resulting from the decomposition of its organic forms as compared with the directly stimulated muscle. Experimental findings, however, revealed just the opposite. During brief work (about 1 minute) the indirectly stimulated muscle invariably showed less inorganic phosphorus than the directly stimulated one.

These results are presented in the table which shows the data of several typical experiments. It demonstrates that in all cases the changes in inorganic phosphorus content compared with the mean data for the resting state are opposite for directly and indirectly stimulated muscles. This effect is also apparent on comparison with mean data obtained on different animals, but is particularly clear in experiments on symmetrical muscles of the same

animal. It would seem that under such conditions of stimulation we observe forms of activity approaching the physiologic. This is also supported by the absence of accumulation of lactic acid. The absence of differences in lactic acid content of directly and indirectly stimulated muscles is explained by the lower sensitivity of this index to changes in the functional state.

The described effect of opposite shifts in inorganic phosphorus content can only be observed during brief activity of both muscles.

More prolonged stimulation (5-7 minutes) (Fig. 1) is shown by biochemical data to be associated with much more profound shifts in the case of both the directly and indirectly stimulated muscles. Under these conditions it is no longer possible to detect any consistency in the relations of the extent of change during direct and indirect stimulation. Myograms typical for this situation (Fig. 1) show that performance of such prolonged work is associated with a rise in threshold. Therefore, in order to maintain contraction at a definite level, it was necessary to increase very slightly the amplitude of stimulation several times (arrows on the myograms).

Inorganic Phosphorus and Lactic Acid Content in Directly and Indirectly Stimulated Symmetrical Muscles During Different Forms of Activity.

Each pair of values across represents results of one experiment on symmetrical muscles The average inorganic phosphorus content at rest is 17.5 mg%, of lactic acid 144 mg%

Inorganic phosphorus				Lactic acid			
In mg % calculated on net tissue weight							
Tetanus				Tetanus			
Brief		Prolonged		Brief		Prolonged	
Stimulation				Stimulation			
direct	indirect	direct	indirect	direct	indirect	direct	indirect
19.0	15.0	45.0	41.0	130	130	250	248
17.5*	14,5	47.0	50.0	143	140	270	250
17.5	13,0	46.0	50.0	145	148	260	320
18.0*	16,5	68.0	65.0	138	140	380	365

*Examples of stimulation with the weaker stimulus strength of those investigated, when direct stimulation elicited no muscular contraction.

The data given in the table show that during prolonged stimulation the inorganic phosphorus and lactic acid content of muscle increases whether stimulation is direct or indirect.

No consistent distinction in terms of biochemical indices can be made between directly and indirectly stimulated muscles when they are briefly stimulated with current strengths which elicit maximal response from both muscles.

The described favorable shift in the state of the muscle during activity elicited by indirect stimulation cannot be explained by internal stimulation of metabolism by decomposition products arising during moderate activity [18], since analogous phenomena should have been noted during submaximal tetanic contraction of directly stimulated muscle also.

Since no such phenomena are observed, the cause of the effect under consideration must be sought in some other influences arising in muscle stimulated through the nerve.

We have already mentioned that for the given type of stimuli of long duration it is sufficient to increase the frequency very slightly (by 3-5 cps) in order to obtain pessimal relaxation instead of optimal contraction. This pessimum, unlike other forms, represents extremely selective blocking of neuromuscular transmission owing to which muscle tissue is completely untouched by the action of the stimulus ("true pessimum"). It is known that

tissue altered by a stimulus and bordering on unchanged tissue elicits in the latter, perielectrotonically, a state opposite to its own [1, 19, 20]. Therefore the occurrence of complete blocking of transmission with signs of the second phase of parabiotic process in neuromuscular transmission is responsible for the fact that the state of relaxing muscle fibers in "true pessimum" does not simply return to the initial resting level but improves on it (in "true pessimum" muscle tissue shows lowering of inorganic phosphorus content and lowering of thresholds to stimulation as compared to the resting state) [2, 3, 10, 12, 13].

Despite the sharp differences of external manifestation of pessimum and optimum reactions, the improvement in the condition of the muscle fibers in both cases is evidently due to the same mechanism of neuromuscular transmission block.

This becomes apparent on investigation of the muscular response which is intermediate between the optimal and pessimal [2, 3, 10, 12, 13]. Such a reaction consists of rhythmic alternation of muscular contraction and relaxation during continuous stimulation maintained for an indefinitely long period of time, with no signs of fatigue and even with slow but definite improvement on the initial condition. The mechanism responsible for the development of favorable changes in the muscle in this case too is the development of block in neuromuscular transmission. This block, during continuous stimulation, can appear and disappear periodically only when the frequency of stimulation is lowered compared to the pessimal [12]. It would appear that on further lowering of stimulation frequency the periodicity of appearance and disappearance of this block occurs with an even higher rhythm, which leads to a tetanic response. The similarity between the described tetanic contraction and rhythmic activity is confirmed by the coincidence of a number of conditions under which they become manifest,as well as by the fact that this form of tetanus passes into wave-like contraction approaching rhythmic contraction when stimulation is prolonged.

It is relevant to mention the work of A. I. Rappoport [13] and I. M. Bocharnikova in connection with the fact that the described increased capacity for work observed in muscle stimulated by way of the nerve disagrees with the widely held view that muscle is more vulnerable under such conditions of stimulation; these authors have shown that the latter concept is not valid for physiologic conditions. When experiments are staged under conditions closer to the natural, with constant washing away of products of activity toxic to the neuromuscular junction, it is seen that it is the nerve-stimulated muscle which preserves excitability for longer periods. There are grounds, therefore, for considering that the possibility of increasing the working capacity of muscle by its indirect stimulation,as discovered in our experiments,also occurs during natural physiologic activity.

SUMMARY

Indirect stimulation of the rat neuromuscular preparation in situ by square-wave and saw-tooth electric current impulses with the frequency of 50-52 cycles/second,10 msec duration causing submaximal or initial maximal responses gives rise to a peculiar tetanic contraction.

The usual increase of lactic acid in muscle tissue is absent in this contraction; the quantity of inorganic phosphorus in it even decreases compared with the value during the initial condition of rest, while the development of fatigue is retarded as compared to the directly stimulated muscle. The peculiarities of tetanus are connected with increased working capacity of the muscle as a result of the form of activity described above.

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