THE INFLUENCE OF THE PESSIMUM ON THE RECOVERY OF CONTRACTILITY OF SKELETAL MUSCLE

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N. E. Wedensky in his treatise (The Relationship between Stimulus and Excitation in Tetanus) paid special attention to the relationship of pessimal inhibition (which he himself discovered) to the recovery of muscular contractility. He concluded that "during the pessimum condition, vigorous recovery processes occur in the muscle, and during this time it can recover from fatigue" [3]. However, in another part, he writes: "No matter how manifest the condition of pessimum may be, and although the external effect may be equivalent to a cessation of the stimulus, it is in no way associated with any reduction of the ability of the muscle to perform further work, and there is no fatigue" [3].

We therefore find that N. E. Wedensky described two ways in which the pessimum condition was related to the recovery of contractility. Here too there is some indication that in the ultimate stages of fatigue the muscle suffers the pessimum condition at a greater cost than in the earlier stages.

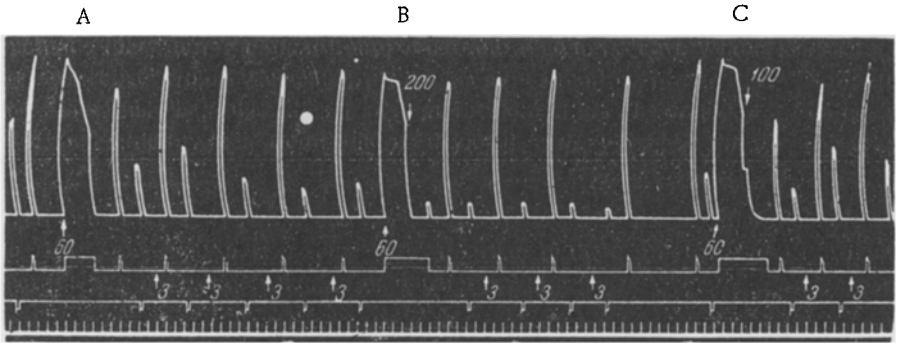

Fig. 1. Different influences of the pessimum condition on recovery of muscle contractility in response to indirect and direct stimulation. A) Control; B) second type of recovery; C) first type of recovery. Curves, from above downwards: contractions of the m. sartorius; stimulation of the sciatic nerve (stimulus to induce fatigue continued for 15 seconds, pessimal stimulation for 10 seconds); marker representing direct stimulation of muscle; time marker (5 seconds). The figures with arrows over the stimulus marker indicate the frequency of stimulation applied to the nerve; the figures beneath the stimulus marker indicate the time for which the electromyograph drum was stopped. Experiment on frog.

In later studies, these problems were exhaustively investigated. A. N. Magnitskii and his co-workers [8] showed that during the pessimum condition, the neuromuscular apparatus consumes approximately half the glycogen, and that four times less lactic acid is formed than during the optimum condition. I. A. Arshavskii and M. N. Kondrasheva [1] determined in situ a number of physiological and biochemical changes during the pessimum, and compared them with the corresponding quantities in the symmetrically opposite resting muscle. They showed that during a pessimum imposed by comparatively infrequent stimulation, there is a positive change in the current of rest, i.e., an electropositivity with an increased excitability of the muscle to direct stimulation, and the content of inorganic phosphorus

and of lactic acid is reduced. They referred to such a condition as a true pessimum to distinguish it from the false pessimum which arises at higher frequencies of stimulation and is characterized by an electronegativity, a reduction of the excitability of the muscle, and an increased content of lactic acid and inorganic phosphorus (as compared with the control muscle). It should be noted that according to A. G. Ginetsinskii and N. I. Michelson [5], the non-phasic electronegativity is thought to be an integral part of the pessimum, and in contrast to the results reported above, is susceptible to exhaustion when the stimulus rate is increased.

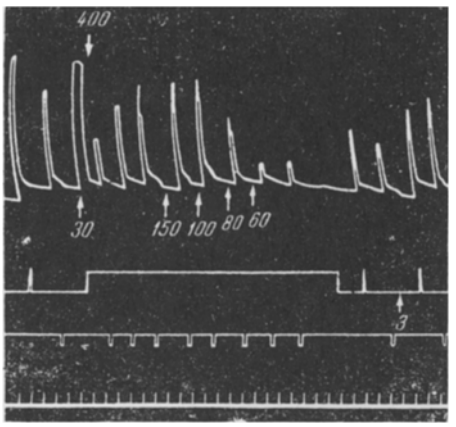

Fig. 2. Change of excitability of a muscle during the pessimum condition and its relation to the frequency of stimulation applied to the nerve. Curves, from above downwards: contractions of the m. soleus; remaining indications as in Fig. 1. Experiment on rat.

Here we report a number of facts and theoretical considerations which indicate the importance of certain features of the development of a pessimum condition during recovery of the contractile power of skeletal muscle.

METHOD

The experiments were carried out on frog and rat nerve-muscle preparations. In the frog, we used the sciatic nerve and sartorius muscle, and in the rat the m. soleus.

Squarewave stimuli from a ISÉ-01, or stimuli from an induction coil were applied to the peripheral end of the ligatured sciatic nerve. Direct stimulation to the muscle was supplied from a second induction coil. In the experiments on the frog, the electrodes for the direct muscular stimulation were fastened to the denervated portion of the sartorius muscle. In the experiments on rats, to stimulate the muscle fibers only, we caused a local block of synaptic transmission of excitation by means of diplacin. An injection of 0.1 ml of a 2% solution of diplacin was injected beneath the layer of fascia at the distal end of the muscle at the site to which the stimulating electrodes were applied. With this arrangement we could determine changes in the excitability of muscle itself during the pessimum condition, and could follow the recovery of contractile power. The injection of the amount of diplacin described above caused no appreciable changes in muscle excitability to indirect stimulation, but greatly reduced the effect of a direct stimulus.* We therefore had to determine the new threshold of excitation, in order to be able to apply test stimuli 5-10% above threshold.

The investigations were carried out in the following sequence. First of all some degree of fatigue was induced in the nerve-muscle preparation by stimulation of the nerve at an optimal frequency and a strength 20% above threshold. After the fatiguing stimulation had been discontinued, we determined a time for the muscular contraction to recover until a contraction of the initial amplitude was given in response to both direct and indirect stimulation. To determine the effect of the pessimum on the recovery of the contractile power of the muscle, we discontinued the fatiguing stimulus applied at the pessimal rhythm, which had been maintained for 15 seconds to 1 minute, and then studied the recovery process.

RESULTS

We found three ways in which the pessimum influenced the recovery of the contractile part of the muscle when tested with direct and indirect stimulation. The first was the case when after the pessimum condition recovery was more rapid to direct than to indirect stimulation, and took place considerably earlier than in the control muscle.

As can be seen from Fig. 1C, the amplitude of the muscular contraction in response to direct stimulation applied three minutes 45 seconds after the pessimum was far greater than the original value. With indirect stimulation it did not attain its original value until the seventh minute. In a control experiment in which no pessimum condition had occurred (Fig. 1A) even after 10 minutes, complete recovery was not attained whether the stimulus was direct or indirect.

The second type of recovery occurred in cases in which the pessimum condition greatly retarded the recovery of the contractile power in response to direct stimulation. However, an indirect stimulation of the muscle induced

*Diplacin is a curare-like preparation, and reduces or eliminates neuro-muscular transmission. Presumably the author means that the injection of the dose described causes no appreciable changes of excitability of the muscle to direct stimulation, but greatly reduces its sensitivity to indirect stimulation (stimulation of the nerve) – Publisher's note.

a large contraction, which in many cases was equal to the original amplitude (Fig. 1B). In the third kind of recovery process, the contractile powers in response to both direct and indirect stimulation were regained approximately in the same manner.

Such wide differences in the recovery processes after a pessimum condition must evidently be ascribed to the simultaneous involvement of several structures.

Long ago N. E. Wedensky [3] wrote that the pessimum condition could develop either in a muscle, or, at the appropriate frequencies, in the nerve endings, or even in a nerve. This conclusion was confirmed by I. S. Beritov [2], by A. G. Ginetsinskii and N. I. Michelson [5], by L. V. Latmanizova [7] and others, and recently in a number of investigations [10, 11, 13] where potentials were led off from an intracellular microelectrode. N. M. Shamarin [10] showed that blocking of the spike potential occurs at frequencies (100-120 cycles) below those which caused transformation of the local synaptic potential (200 cycles). From this result she argues that pessimal inhibition uncomplicated by fatigue, and developing in response to short-term stimulation is not due to block of the impulse in the terminal nerve branches.

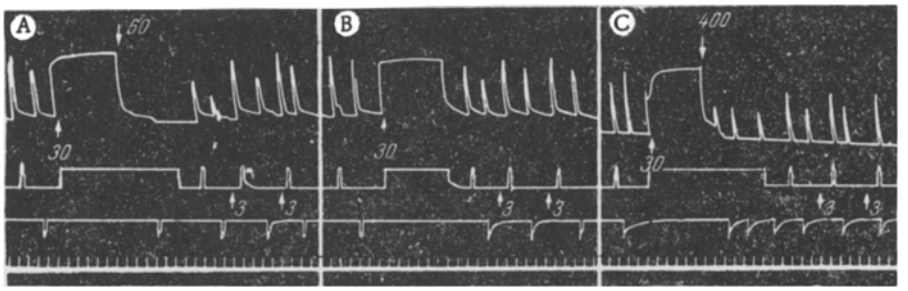

Fig. 3. Relationship between the excitation of muscle during the pessimum condition and the subsequent recovery of its contractile power. Indications as in Fig. 2. Experiment on rat. A) Frequency of stimulation 60 per second; B) control; C) frequency of stimulation 400 per second.

Besides the works referred to above, we must also note studies when it has been proposed that pessimal inhibition is of presynaptic origin [4, 6, 9, 12].

Thus at present a number of investigators admit in principle that the changes underlying the pessimum condition occur in various parts of the neuro-muscular apparatus.

Because the point at which the pessimum develops depends on the lability of various parts of the neuro-muscular apparatus, it is evident for a given functional state, that the principal condition determining its localization is the frequency of stimulation applied to the nerve trunk. We have shown that in a single experiment, by changing the frequency of the pessimal stimulation, the excitability of the muscle to direct stimulation may be markedly depressed, or greatly enhanced. To show that this is so, during pessimal inhibition, stimulation was applied to the muscle from a second electrode. When this was done, reducing the rate of pessimal stimulation led to a reduction in the excitability of the muscle, and an increase in the frequency caused the excitability to rise, often above the original level.

The fact that the excitability could rise to above the original level during a pessimal condition induced by high frequency stimulation indicated that the muscle was in an active condition.

The results of Fig. 2 illustrating the change of muscular excitability in relation to stimulus frequency of the nerve can be attributed to the different localization of the pessimum (whether pre- or postsynaptic). It should be noted that the change of the localization of the pessimum may be brought about not only by altering the stimulus frequency, but also by changing the functional condition of the neuro-muscular apparatus (for example by fatigue). We think that muscular excitability increases during a presynaptic and falls during a postsynaptic pessimum condition.

It was important to investigate the relationship between the localization of the pessimum and the course of recovery of contractile power.

Fig. 3 illustrates the influence on the recovery of contractility in response to direct and indirect stimulation of a pessimum condition evoked by different stimulus frequencies. When the pessimum condition was induced by stimulation at a low frequency of 60 per second, recovery of muscular contractility in response to direct stimulation

proceeded more rapidly than when the stimulation was indirect, so that the pessimum condition showed up as a considerable reduction of muscular excitability (Fig. 3A). In this case recovery of muscular excitability in response to direct stimulation occurred at the seventh minute, and when the stimulation was indirect it failed to regain the original level. In a control test (Fig. 3B) in which fatigue was induced without any subsequent pessimum condition, recovery occurred much later. Recovery of the contractility of skeletal muscle occurred quite differently immediately after a pessimum condition induced by stimulation at a frequency of 400 per second, during which time muscular excitability was increased (Fig. 3C).

In this case, immediately after the pessimum condition, the muscle responded to indirect stimulation with a contraction almost equal in amplitude to the original contraction, and subsequently the amplitude was somewhat reduced. With direct stimulation, the amplitude of the contraction was much less than it was in the original test, and decreased considerably.

Thus, after a pessimum condition induced by low frequency stimulation the recovery of muscular contractility is most rapid in response to direct stimulation, but when the pessimum condition is elicited by high frequency stimulation, it is the recovery of contractility in response to indirect stimulation which is the more rapid. Evidently this difference of influence of the pessimum on the recovery of muscular contractility after a short period of fatigue depends on whether the pessimum is localized pre- or postsynaptically.

The relationships we have described are not constant: when a pessimum condition is induced repeatedly by means of high frequency stimulation, recovery of contractility in response to both direct and indirect stimulation is impaired.

In exhausted preparations, the development of the pessimum condition in the presynaptic structures is greatly facilitated. Even a frequency of 60-80 per second induced a pessimum state in which muscle excitability was high although subsequent recovery of the muscular contractions in response to either direct or indirect stimulation was slowed down. It should be noted that in the exhausted preparations, as judged by muscular excitability, the pessimum condition localized in the muscle often becomes inert and incapable of recovery.

Thus, the influence of a pessimum condition on recovery processes in skeletal muscle depends largely on its localization in the neuro-muscular junction. According to its position, the pessimum may be induced by various frequencies or by a change of the functional condition of the neuro-muscular apparatus. When the pessimum is postsynaptic, recovery is more rapid in response to direct than to indirect stimulation; when however it occurs in the nerve endings, recovery to direct stimulation is greatly slowed, although in response to indirect stimulation the muscle responds by contractions which are almost of the original amplitude.

On these grounds we may conclude that the pessimum condition enhances the recovery process at the point at which it occurs.

SUMMARY

Experiments were carried out on frogs and rats, and a study was made of the effect of the pessimum condition on the recovery of contractility of a fatigued muscle subjected to direct and indirect stimulation. When the pessimum condition was induced by high frequency stimuli, muscular excitability increased, and with low frequency stimulation it fell. When in the pessimum condition muscular excitability is reduced, the contractility of a fatigued muscle in response to a direct stimulus is accelerated; however, a pessimum state in which excitability is augmented is followed by a delayed restoration of contractility elicited by a direct stimulus, though there is no delay when the stimulus is indirect.

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