The Mechanisms of Post-Tetanic Potentiation in Cat Soleus and Gastrocnemius Muscles

FRANK G. STANDAERT

From the Department of Pharmacology, Cornell University Medical College, New York

ABSTRACT Post-tetanic potentiation of muscle contraction strength (PTP) occurs in cat soleus and gastrocnemius muscles. However, the mechanisms of potentiation are different in these two muscles. Soleus PTP is predominantly a neural event. The application of a high frequency stimulus to the soleus nerve regularly causes each subsequent response to a single stimulus to become repetitive. This post-tetanic repetitive activity (PTR) originates in the motor nerve terminal and is transmitted to the muscle. Consequently each potentiated soleus contraction is a brief tetanus. In gastrocnemius PTR occurs too infrequently to account for PTP. Furthermore, PTP occurs in curarized directly stimulated gastrocnemius muscles to the same extent as in the indirectly stimulated muscle. In this instance PTP is a muscle phenomenon.

Post-tetanic potentiation (PTP) of muscle contraction seems to be a general phenomenon of neuromuscular systems. It has been observed in almost every muscle in which it has been sought (for review, see Hughes, 1958). Curiously, this ubiquity seems to be a major factor in the failure to provide a satisfactory explanation for the phenomenon. The fact that many muscles respond similarly to a high frequency stimulus has fostered the belief that they share a common mechanism of potentiation, but to date no single mechanism has been found to reconcile the diverse observations.

Neurally stimulated cat soleus and gastrocnemius muscles develop PTP of similar appearance. However, examination of the phenomenon in these two muscles revealed two distinct mechanisms of potentiation: one residing in the motor nerve terminal, the other in the muscle. Furthermore, it was found that both mechanisms operate in both muscles, but in different degree. Soleus PTP is predominantly neural, while gastrocnemius PTP is almost wholly muscular.

METHODS

The experiments were performed on cats anesthetized with 80 mg α-chloralose per kg. Several methods were employed, each a variant of the experimental arrangement schematized in Fig. 1.

1. Whole muscle twitch tension: The sciatic nerve was cut at the sciatic notch. The popliteal fossa was dissected, and all branches of the tibial nerve except the one to the soleus or medial head of the gastrocnemius muscle were severed. Similarly, all branches of the popliteal artery except the posterior tibial were occluded. The soleus muscle was prepared by dissecting the soleus nerve free from the lateral head of the gastrocnemius and extirpating both heads of the latter. The medial gastroc-

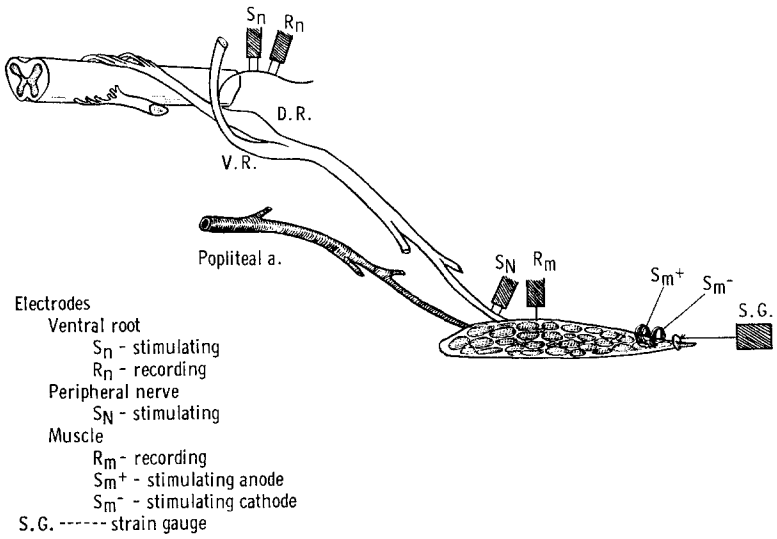

FIGURE 1. Scheme of the methods.

nemius muscle was isolated by splitting the septum and extirpating the lateral gastrocnemius. The animal was mounted in a modified Brown-Shuster myograph and the Achilles tendon was attached to an isometric electrical strain gauge. A mineral oil pool was formed in the popliteal fossa. This was kept at 37°C and continuously bubbled with 95 per cent O_2 and 5 per cent CO_2. Stimulation was applied to the peripheral nerve with a bipolar platinum electrode (S_N in Fig. 1).

2. Directly stimulated muscle tension: The soleus or medial gastrocnemius muscle was isolated as described above. Muscle electrodes were formed by sewing 33 gauge stainless steel wire in loose concentric loops across the width of the muscle. The cathode (S_m- in Fig. 1) was placed just proximal to the muscle-tendon junction and the anode (S_m+ in Fig. 1) about 2 cm proximal to the cathode. Stimuli generated by synchronized stimulators were applied alternately to the nerve and muscle electrodes (S_N and S_m+, S_m- in Fig. 1). *d*-Tubocurarine, 0.33 mg/kg, was administered intra-arterially to abolish the neurally evoked twitch. Supplemental doses were administered as necessary to maintain neuromuscular blockade. In every experiment the tension

developed by the curarized muscle in response to a supramaximal, direct stimulus closely approximated that evoked by supramaximal nerve stimulation prior to the administration of tubocurarine.

3. Single motor unit recordings: The procedure for recording from single axons and from the axon and muscles of a motor unit was described previously (Standaert, 1963). In brief, the leg was prepared as in 1 above except that the sciatic nerve was not sectioned. In addition, a lumbar laminectomy was performed. The animal was mounted in a rigid frame and a mineral oil pool formed to cover the exposed spinal cord; this was kept at 37°C and bubbled with 95 per cent O_2 and 5 per cent CO_2. Ventral root L-7 was isolated, cut close to the spinal cord, and teased apart until a filament containing a single active axon from the soleus or medial gastrocnemius nerve was obtained. This was placed across bipolar platinum stimulating and recording electrodes (S_n and R_n in Fig. 1). A stimulus was applied to the axon and the muscle was observed for activity. A glass-insulated platinum needle electrode (R_m in

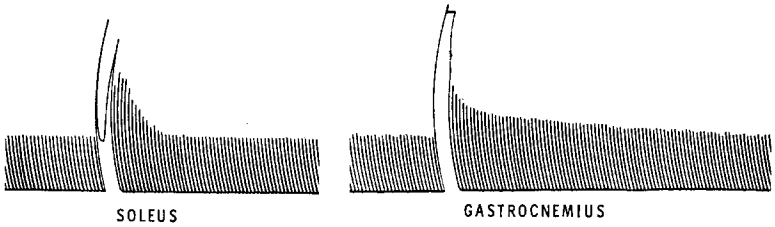

FIGURE 2. Post-tetanic potentiation (PTP) of muscle contraction tension. Peripheral nerve stimulated supramaximally once every 2.5 sec. before and after the tetanic stimulus. Indirect tetanic stimulation, soleus, 10 sec., 400 CPS; gastrocnemius, 10 sec., 200 CPS.

Fig. 1) was placed in the contracting motor unit. The axonal and muscular electrical activities were displayed simultaneously on a dual-beam oscilloscope. Twitch tension was recorded by attaching the tendon of the whole muscle to a sensitive, isometric, electrical strain gauge.

Stimulation was accomplished with rectangular pulses. The stimulus duration was 0.01 msec. for the single motor units, 0.2 msec. for peripheral nerve stimulation, and 1.0 msec. for direct muscle stimulation. The stimuli were applied continuously at a rate of 0.4 CPS except during the periods of tetanic stimulation. The frequency and the duration of the latter are specified in the text. Stimuli applied to single axons were suprathreshold; those applied to peripheral nerve or muscle were supramaximal. In the curarized muscle experiments neural stimulation was discontinued prior to the onset of high frequency stimulation and reinstituted immediately thereafter.

RESULTS

Examples of soleus and gastrocnemius PTP are shown in Fig. 2. In both cases single supramaximal stimulation of the peripheral nerve elicited a stronger contraction after high frequency stimulation than in the control period. Although the two examples of PTP are qualitatively similar, differ-

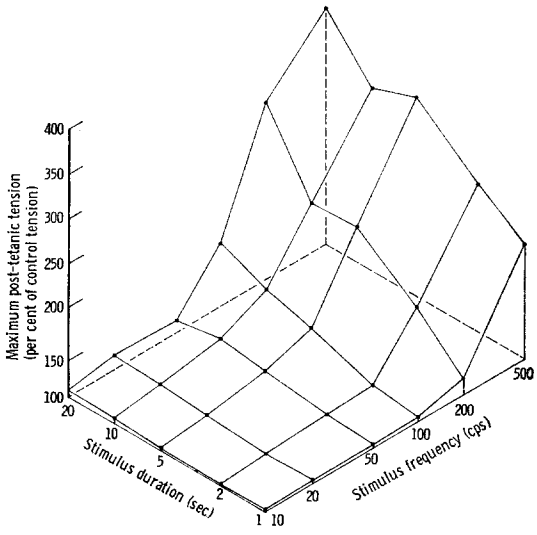

FIGURE 3*a*. Soleus

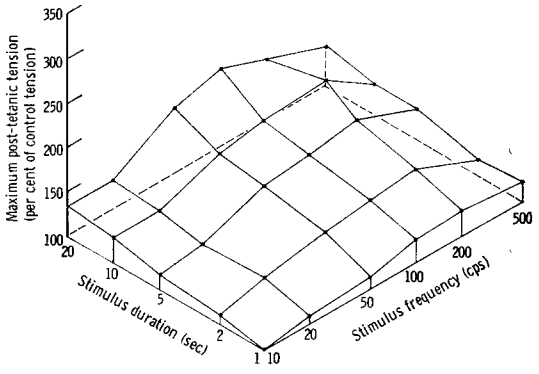

FIGURE 3*b*. Gastrocnemius

FIGURE 3. PTP of muscle tension evoked by indirect stimulation as a function of the frequency and duration of the indirect tetanic stimulus.

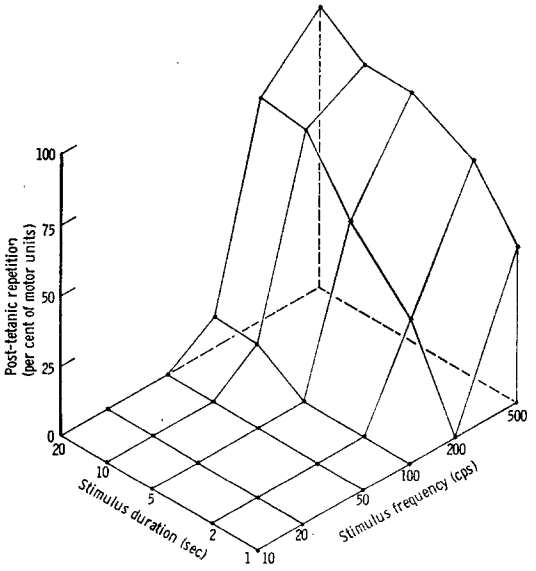

FIGURE 4*a*. Soleus

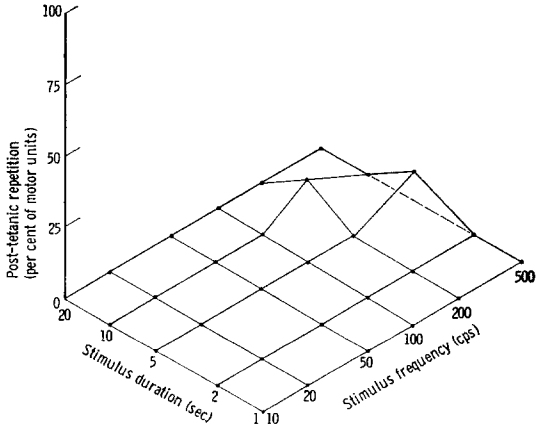

FIGURE 4*b*. Gastrocnemius

FIGURE 4. Percentage of motor units which develop muscle post-tetanic repetition (PTR) as a function of the frequency and duration of the indirect tetanic stimulus.

ences in the maximum degrees of potentiation and the time-courses of recovery are apparent. More striking is the difference in the relationship between degree of potentiation and the frequency of the preceding tetanic stimulus. A suggestion of this difference is provided by the records in Fig. 2. In both instances they represent the maximum PTP obtained in the respective experiments; for the soleus this followed a 400 CPS stimulus while for the gastrocnemius the maximum was reached after a 200 CPS stimulus.

A more complete presentation of the relationship among frequency and duration of the tetanic stimulus and PTP is given in Fig. 3. The isometric graphs in this figure were constructed by plotting the frequency and the

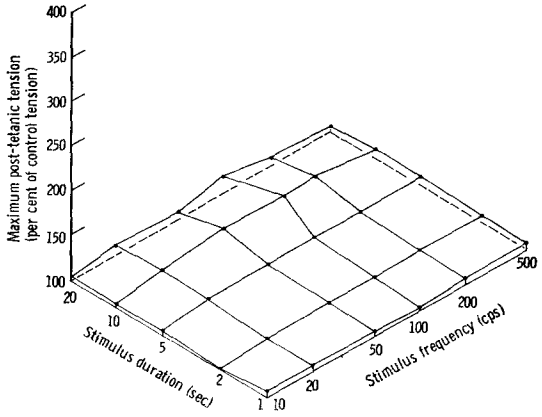

FIGURE 5*a*. Soleus

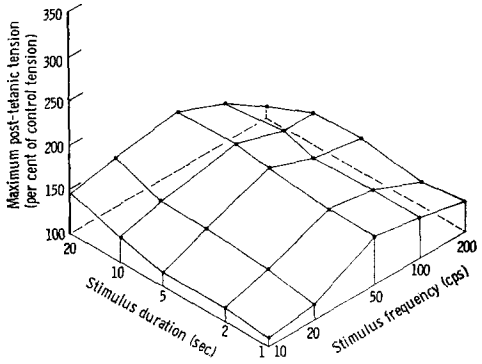

FIGURE 5*b*. Gastrocnemius

FIGURE 5. PTP of muscle tension evoked by direct stimulation of the curarized muscle as a function of the frequency and duration of the direct tetanic stimulus.

duration of the tetanic stimulus on logarithmic scales on the x and z axes, respectively, and the maximum post-tetanic twitch tension, expressed as percentage of control tension, linearly on the y axis. Maximum tension is produced usually by the first post-tetanic gastrocnemius contraction and by the first or, more commonly, by the second post-tetanic soleus contraction (Fig. 2). The muscles show a striking difference in PTP frequency dependence. The soleus is little affected by stimulation frequencies below 100 CPS. At higher stimulation frequencies, the potentiation increases rapidly with frequency and additionally with increasing duration of stimulation. The maximum potentiation occurs after the greatest frequency and duration of tetanic stimulation shown in Fig. 3 *a*. Gastrocnemius PTP, on the other hand, occurs after lower frequencies of stimulation (Fig. 3 *b*); maximum potentiation is produced by 100 to 200 CPS stimulation and higher frequencies result in less potentiation. In further contrast to the soleus, short periods of low frequency stimulation are effective in generating gastrocnemius PTP.

Fig. 3 also illustrates a remarkable difference in the degree of potentiation produced in the two muscles. Following a 20 second, 500 CPS stimulus, the soleus muscle twitch tension increases to an average of 390 per cent of control tension. In one experiment, a post-tetanic tension of 540 per cent of control was recorded. In contrast, the maximum average gastrocnemius PTP is 190 per cent of control and the maximum recorded in an individual experiment was 275 per cent of control. These average and individual maxima both occurred after 20 seconds of 100 CPS stimulation.

To investigate the mechanisms underlying these differences, attention was first turned to the occurrence of post-tetanic repetitive activity in the motor nerves supplying the two muscles. The application of a single stimulus to an axon of the soleus nerve normally results in the production of a single action potential. Following a period of high frequency stimulation, however, a single stimulus results in a train of repetitive potentials. This post-tetanic repetitive activity (PTR) is generated in the motor nerve terminal and is transmitted to the muscle (Standaert, 1963). Therefore, in the post-tetanic period the stimulus received by the soleus muscle is not single but repetitive and, consequently, the resulting contraction is not a simple twitch, but a brief tetanic contraction.

PTR is readily produced in the soleus muscle. Following an adequate stimulus, it can be recorded from virtually every motor unit. This is shown in Fig. 4 *a* which presents an isometric graph of PTR occurrence in the muscles of nine soleus motor units as a function of the frequency and duration of the preceding tetanic stimulus. The surface formed by the data in Fig. 4 *a* is remarkably similar to that formed by the soleus PTP results presented in Fig. 3 *a*, indicating an intimate relationship between PTR and PTP in this muscle. Fig. 4 *b* presents the results of a similar study of the occurrence of PTR in the muscles of ten gastrocnemius motor units. In striking contrast to the soleus, gastrocnemius PTR is a rare event. In the 300 trials represented in the figure, PTR was only seen twice. In each case it occurred as a single repetitive potential occurring shortly after the tetanic stimulation. A comparison of this graph with Fig. 3 *b* suggests that gastrocnemius PTP occurs in the absence of PTR.

Parenthetically, it should be noted that PTR is observed more frequently in the gastrocnemius nerve than in the gastrocnemius muscle; a 20 second, 500 CPS stimulus produces PTR in approximately 20 per cent of gastrocnemius axons. However, the brevity of the repetitive trains, when PTR occurs, and the proximity of the one or two repetitive spikes to the stimulus-evoked action potential do not permit reexcitation of the muscle, which is still refractory from the initial stimulus. Consequently the repetitive activity is not transmitted to the muscle and does not result in repetitive muscle action potentials. In further contrast to the soleus, gastrocnemius PTR is not a reproducible

phenomenon. Even in a single axon its occurrence is erratic and its intensity and duration are variable.

The dependence of soleus PTP on PTR was substantiated by applying tetanic stimuli directly to curarized muscles. PTR does not occur in these preparations because in addition to preventing transmission of neural events to the muscle, tubocurarine abolishes PTR generation in the motor nerve terminal (Standaert, 1964). The results of these experiments are presented in Fig. 5 *a*. A comparison of these data and those of Fig. 3 *a* indicates that conditions which abolish PTR in soleus nerve also virtually abolish PTP of soleus muscle. It is noteworthy, however, that a small degree of potentiation does occur in these preparations, and that in the lower frequency range it closely approximates the PTP produced by the indirectly stimulated, non-curarized muscle. It is also of interest that the PTP produced by the curarized soleus muscle, although considerably less extensive than the PTP of the non-curarized gastrocnemius, has a frequency and duration dependency remarkably similar to the latter. Furthermore, although not shown in Figs. 3 *a* and 5 *a*, prolonged periods of low frequency stimulation lead to appreciable soleus PTP. For example, contractions approximately 150 per cent of control strength were developed by indirectly stimulated, non-curarized muscles and directly stimulated, curarized muscles after 5 minutes of 5 CPS stimulation.

PTR was confirmed as a cause of PTP in soleus muscle by simultaneously recording the electrical and mechanical activities of single motor units. The results are illustrated in Fig. 6. The upper part of the figure presents a record of the muscular activity of a single soleus motor unit. It can be seen that in the post-tetanic period the contractile tension in response to a single stimulus is either the same as in the control period, or is several times greater. The lower part of the figure contains the records of the electrical activity of the axon of this motor unit in the post-tetanic period. A comparison of the electrical and mechanical records reveals a perfect correlation between the occurrence of PTR in the axon and PTP in the muscle. Those stimuli which elicit repetitive activity in the motor axon lead to a potentiated muscle twitch; those which are not followed by repetitive activity produce a twitch of pretetanic strength. These results were duplicated in this and other experiments. At no time was there a dissociation between PTR and PTP. Repetitive activity in the nerve always occasioned an increase in twitch strength and, conversely, an increase in twitch strength was never seen in the absence of neural repetitive activity.

It is noteworthy that the potentiated twitches in Fig. 6 are not all of the same strength. The explanation for this most probably lies in the time of the occurrence of the repetitive potentials. As pointed out earlier (Standaert, 1963) not all repetitive nerve potentials are equally effective in provoking

repetitive muscle action potentials. Those which are generated too soon after the stimulus-evoked potential, or after a preceding repetitive potential, may fall within the refractory period and, therefore, be ineffective. Those occurring after a somewhat longer interval evoke abnormal muscle potentials which apparently are not fully effective in initiating a maximal muscle con-

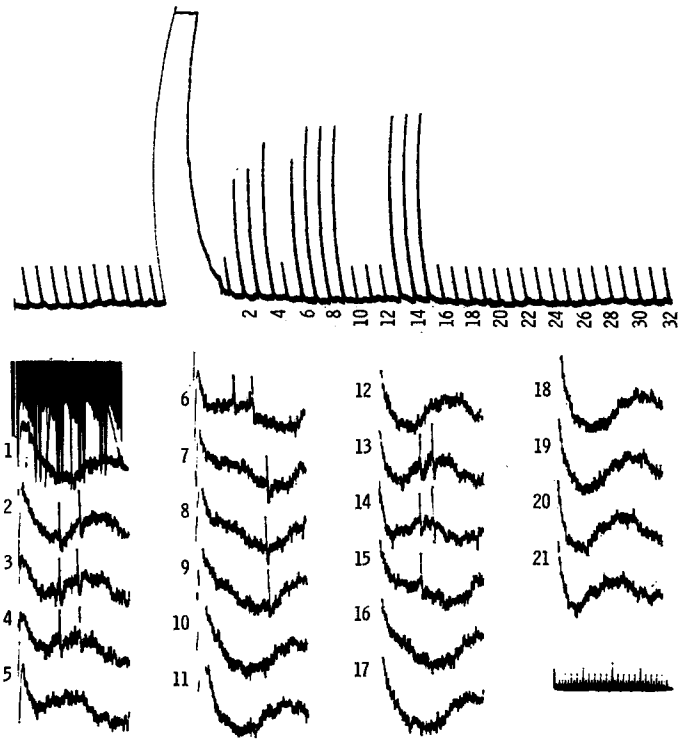

FIGURE 6. PTP and PTR in a soleus motor unit. Upper record, isometric contraction tension evoked by a single neural stimulus once every 2.5 sec. before and after a 10 sec., 250 CPS indirect stimulus. Lower records, simultaneously recorded post-tetanic electrical activity in the axon of this motor unit. Stimulus-evoked action potential arrives at the nerve terminal approximately 2.5 msec. after the stimulus artifact at the left of each trace. Other potentials are post-tetanic repetitive activity. Time marks, 0.5, 1, 5, 10 msec.

traction. Only those nerve potentials which occur 4 or more msec. after a preceding potential are capable of eliciting relatively normal repetitive muscle potentials and maximal contractions. In the experiment illustrated in Fig. 6, the repetitive potentials in traces 2, 3, 4, and 6 occurred 2.5 to 3.5 msec. after the stimulus-evoked or preceding repetitive potential. Muscle potentials were not recorded in this experiment but, from the considerations outlined above, it can be surmised that, if they were recorded, they would have been abnormal. The repetition in traces 2, 3, 4, and 6 was less effective in enhanc-

ing muscle contraction than the single, but delayed repetitive potentials seen in traces 7, 8, and 9. In traces 13 and 14, the second repetitive potential occurred about 2 msec. after the first. Since this is less than the refractory period of the muscle they were ineffective and the contraction is no greater than that produced by the fifteenth stimulus and its single repetitive potential.

Gastrocnemius PTP proved to be quite different in origin. The preliminary studies described above indicated that in this muscle PTR occurs too rarely to account for PTP and that a different mechanism must be involved. Experiments with directly stimulated, curarized muscle and single motor units confirmed this impression. Fig. 5 *b* presents the results of the curarized muscle studies. It is apparent that in this muscle PTP occurs even in the presence of tubocurarine. Furthermore, a comparison of Fig. 5 *b* with the corresponding results in non-curarized muscle presented in Fig. 3 *b* reveals that the drug has little effect on gastrocnemius PTP, particularly in the lower frequency range. With stimulus frequencies of 200 CPS and greater, however, less PTP occurred in the directly stimulated, curarized muscle than in the neurally stimulated muscle. There are two probable reasons for reduced PTP at these frequencies. Most important is a technical difficulty which was particularly apparent with the 500 CPS stimulus; the gastrocnemius muscle apparently is not capable of responding to repetitive stimuli delivered at 2 msec. intervals. The directly stimulated muscles did not develop a tetanic contraction in response to this stimulus but merely contracted briefly and then became quiescent for the remainder of the stimulation period. Subsequently they uniformly failed to develop PTP. Because these responses did not seem truly comparable with the other results, the data for the 500 CPS stimulation were omitted from Fig. 5 *b*. A similar but less pronounced effect appeared during prolonged stimulation at 200 CPS and may account, in part, for the lack of correspondence between the graphs of Figs. 3 *b* and 5 *b*. In addition, it should be noted that although PTR is rare in gastrocnemius, it is most likely to occur after prolonged, high frequency stimulation and, although occurring in only a small portion of the motor units, can make a significant contribution to the PTP.

The results of experiments in which the mechanical and electrical activities of single gastrocnemius motor units were recorded simultaneously are illustrated in Fig. 7. The upper portion of the figure depicts the record of the twitch tension produced by the motor unit. It can be seen that PTP in this muscle is graded; the potentiation is greatest immediately after the tetanic stimulus and successive twitches are progressively weaker. The lower portion of the figure shows the electrical activities of nerve and muscles of this motor unit. The first pair of traces was obtained in the control period, all others in the immediate post-tetanic period. Minor alterations occur in the form of the muscle action potential, but repetitive activity does not occur in either the

nerve or the muscle. It is apparent that PTR is not a necessary concomitant of gastrocnemius PTP.

Since PTR does occur occasionally in gastrocnemius, an attempt was made to determine the effect of repetitive activity on the contractile tension of gastrocnemius motor units. Unfortunately, PTR did not occur in any of

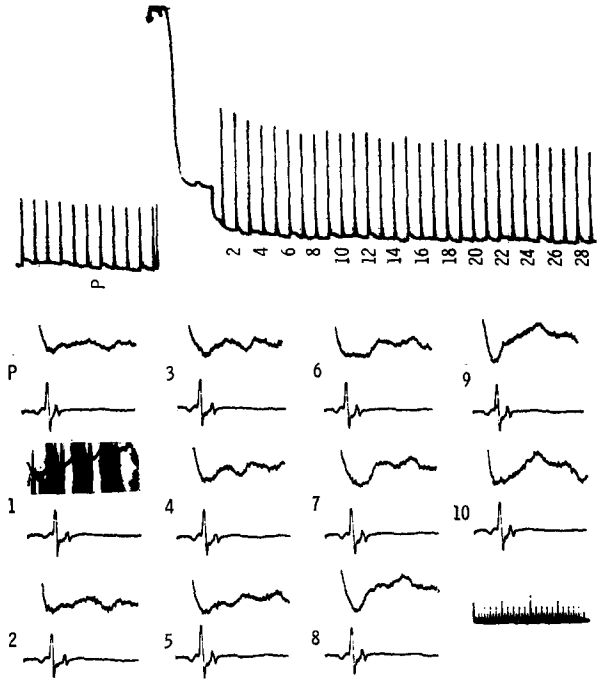

FIGURE 7. PTP in a gastrocnemius motor unit. Upper record, isometric contraction tension evoked by a single neural stimulus once every 2.5 sec. before and after a 10 sec., 200 CPS indirect stimulus. Lower records, simultaneously recorded electrical activity in axon (upper trace of each pair) and muscles (lower trace of each pair) of this motor unit. Stimulus-evoked nerve action potential is obscured by the stimulus artifact at the left of each trace. Stimulus-evoked muscle action potential is polyphasic because the electrode is not in the end-plate region. First pair (*P*) is a pretetanic recording. First post-tetanic nerve trace is partially obscured by the tetanic stimulus artifacts. Time marks, 0.5, 1, 5, 10 msec.

these single motor unit experiments. Therefore, the effect of repetitive activity was simulated by applying appropriately spaced paired stimuli to the motor axon. At intervals of less than 0.7 msec., the second stimulus had no effect, but two stimuli 0.8 to 12 msec. apart produced contractions approximately 500 per cent of control strength. Longer intervals produced progressively weaker contractions until at an interval of 50 msec., the contraction was only 140 per cent of control strength. These intervals are similar

to, but shorter than those for corresponding effects in soleus (Eccles and O'Connor, 1939). These results are noteworthy in several respects. The increase in contractile tension is similar to that produced by PTR in soleus (*cf.* Fig. 6) and is much greater than that produced by PTP in the absence of PTR in the gastrocnemius (*cf.* Fig. 7). Furthermore, since PTR, when present, always occurs within 15 msec. after the stimulus-evoked action potential, it is apparent that the occurrence of PTR must result in a considerable increase in gastrocnemius contractile tension. Even though PTR occurs in only a small fraction of the gastrocnemius motor units, the relatively great increase in the contractile tension developed by these motor units must contribute significantly to the PTP of the whole muscle.

DISCUSSION

These results were anticipated, in part, by others. Rosenblueth and Morison (1937) were the first to describe muscle PTR and to indicate the importance of repetitive activity in potentiating contractile tension. Surprisingly, their observations were made despite the handicaps of using the gastrocnemius muscle and also barbiturate anesthesia; barbiturates usually suppress PTR. Perhaps because of these factors, later workers were not able to confirm the Rosenblueth and Morison results and discounted the important relationship between PTR and PTP. In addition, the demonstration of PTP in the absence of PTR by Brown and von Euler (1938) provided an alternative explanation of the phenomenon. The discovery and investigation of PTR in cat soleus nerve by Feng *et al.* (1939) was the first recognition of a neural basis for PTP. These workers also recognized a fundamental difference between soleus and gastrocnemius PTP and questioned the necessity of postulating a single mechanism for both (Feng *et al.*, 1938). However, they did not pursue their investigations of the phenomenon.

The results herein demonstrate that there are at least two mechanisms for PTP. In cat soleus muscle the increase in contractile tension is caused predominantly by the occurrence of repetitive action potentials in the post-tetanic period. Medial gastrocnemius muscle potentiation, on the other hand, occurs largely in the absence of repetitive activity. However, both muscles are capable of both types of post-tetanic response; a small amount of soleus PTP occurs in the absence of PTR and, conversely, PTR occurs occasionally in gastrocnemius and contributes to its PTP.

Soleus PTR has been investigated and found to originate in the motor nerve terminal (Standaert, 1963). Gastrocnemius PTR has not been studied as intensively but it resembles soleus PTR in all essential aspects and probably is generated by a process similar to that occurring in soleus nerve. The origin of the potentiation that occurs in the absence of PTR is not as well established. The fact that it occurs in curarized, directly stimulated muscle to the same

extent as in the indirectly stimulated, non-curarized muscle effectively rules out the motor nerve and the motor end-plate as possible factors in its generation and points to events occurring within the muscle itself. Whether the process is related to the contractile elements, to the muscle membrane, or to the coupling process between the electrical and mechanical events is not known.

Many authors have tried, without notable success, to correlate PTP with the size of the post-tetanic muscle action potential (for references, see Hughes, 1958). Their results, however, cannot be accepted as conclusive evidence of a lack of correlation because they are based almost entirely on recordings made with gross electrodes on the whole muscle and changes in the muscle potential may have been obscured by temporal dispersion or movement of the muscle in relation to the electrode. Furthermore, there is reason to believe that reinvestigation of the problem with modern technique might be fruitful. A primary consideration is the fact that both the action potential and the contraction are responses whose magnitudes are determined in large part by the resting membrane potential. Their usual apparent constancy merely reflects the constancy of the membrane potential under most experimental conditions. Under other conditions their graded nature becomes apparent. Thus, several workers have shown that muscle contraction is graded and controlled by membrane depolarization; the greater the depolarization, the greater the strength of the resulting contraction (Gelfan, 1934; Brown and Sichel, 1936; Kuffler, 1946; Sten-Knudsen, 1954; Huxley, 1959; Hodgkin and Horowicz, 1960; Orkand, 1962). Similarly the magnitude of the muscle action potential depends on the preexisting membrane potential (Shanes, 1958).

The latter is significantly modified by repetitive activity. The records of MacFarlane (1953) and Shamarina (1961) show clearly that muscle membrane undergoes a post-tetanic hyperpolarization analogous to that which occurs in nerve. Although this hyperpolarization does not seem to have been investigated specifically, the experiments of Fatt and Katz (1951) on muscle hyperpolarized by anodal current suggest that single, post-tetanic action potentials are larger and longer than those in the pretetanic period. Since such augmented potentials produce a greater and more prolonged depolarization of the muscle membrane, they may be more effective in activating muscle contraction and/or in prolonging the active state (Ritchie and Wilkie, 1955).

In recent years the role of acetylcholine in PTP has been emphasized almost to the exclusion of all other possible mechanisms. In large part this is due to the semantic error of not distinguishing between PTP of muscle contractile tension and PTP of muscle end-plate potentials. The latter has been investigated by several workers (Hutter, 1952; Liley and North, 1953; Brooks, 1956; Hubbard, 1959; Hubbard and Schmidt, 1963) who have

concluded that the post-tetanic increase in end-plate and miniature end-plate potentials is due to an increased acetylcholine liberation by the motor nerve terminals. In general, these authors have been careful to point out that their results apply only to these electrical events, but their work frequently is cited as the basis for all post-tetanic neuromuscular phenomena. These generalizations seem to be ill-founded since neither of the two types of PTP of contractile tension described above seems to be related to an increase in acetylcholine liberation or end-plate potential.

The role of PTP in muscle function is conjectural but perhaps the most significant aspect of soleus PTP is a negative one. The results presented in Fig. 3 *a* show that post-tetanic contractile tension is relatively unaffected by the stimulation frequencies encountered in the soleus nerve *in vivo*. This is in keeping with the "slow" muscle function of providing stable, well regulated muscle tension for postural control. On the other hand, it is noteworthy that a small percentage of soleus axons generate repetitive potentials after, or in some instances, during prolonged 5 to 20 CPS stimulation (Standaert, 1963). The possibility that repetitive potentials occur in muscles responding to voluntary or reflex drive is suggested by the observations of Hoff and Grant (1944) and Denslow (1948) who noted that electromyograms from cat and human postural muscles frequently contain pairs of potentials interspersed among rhythmic 10 to 20 CPS activity. These double potentials resemble PTR muscle potentials in timing and appearance and in the fact that they rarely occur in the gastrocnemius muscle. Their occurrence probably leads to an increase in muscle tension, but it seems unlikely that such activity plays a major role in postural muscle function. More likely, the repetitive activity is an incidental phenomenon reflecting the prolonged after-potentials produced in these motor nerve terminals.

In contrast to the soleus, gastrocnemius contraction tension is strongly influenced by short, preceding, periods of low frequency activity. Indeed, this effect is so great that the muscle develops a different twitch tension for each frequency of stimulation below its fusion frequency. Furthermore, the effects are prolonged and the tension changes only gradually as the stimulus is changed from, for instance, 0.1 to 0.4 CPS, to 1.0 CPS and back again. The functional significance of this dependence on prior activity is probably reflected in the familiar "warm-up period" in sports, where it is widely recognized that a period of preliminary activity greatly enchances muscular strength. The importance of this phenomenon is pointed up by the fact that the nerves to "fast" muscles rarely discharge at frequencies high enough to cause complete fusion of the muscle contractions (for gastrocnemius, 50 to 100 CPS). Therefore, these muscles almost always operate under conditions where contraction strength is graded by stimulus frequency and where PTP is a prominent phenomenon. Interestingly, another aspect of PTP is also

recognizable in sports where it is frequently observed that a contestant is unable to resume normal muscle function immediately after his maximum exertion, but requires a "cooling-off" period before he is able to function smoothly under the lesser demands of the post-trial period. It seems likely that, having taken advantage of PTP to increase his strength for the contest, the athlete then suffers from the even greater PTP consequent to high frequency stimulation of his muscles during the contest.

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