

POST-TETANIC POTENTIATION OF POLYSYNAPTIC REFLEXES OF THE SPINAL CORD

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INTRODUCTION

The residual effect of high frequency repetitive stimulation on the responses of many tissues to single stimuli has been widely demonstrated. Following tetani of various durations and frequencies striated muscles respond to single shocks with longer and more powerful twitches (11). Such potentiation of the muscle twitch has been obtained in both denervated and partially curarized muscle (1, 7). Post-tetanic decurarization is believed to be a prejunctional phenomenon due to the release of more acetylcholine following post-tetanic stimuli (7). Post-tetanic facilitation has also been shown in sympathetic ganglia (8) and in the spinal cord.

In the spinal cord Woolsey and Larrabee (14) have demonstrated that, following tetanization of a dorsal root, increased dorsal root potentials and reflexes were elicited by stimulation of the tetanized or of a neighboring root. Lloyd (9) has shown marked selective post-tetanic potentiation of the monosynaptic reflex pathway in the spinal cord. Following tetanization of an afferent nerve, test shocks applied to this nerve elicit reflexes larger than control size for several minutes (4, 9). This effect is restricted to the tetanized pathway, and has been correlated with a hyperpolarization of the primary afferent nerve endings (9). What seems to be a potentiation of polysynaptic reflexes has been observed by Sherrington and Sowton (12), and reference to post-tetanic potentiation of polysynaptic reflexes is made by Downman, Eccles, and McIntyre (2). Lloyd (9) found little, if any, such enhancement in polysynaptic pathways. Lack of clear polysynaptic potentiation has been ascribed to a property of initial internuncial relays (9) or to the lack of an internuncial subliminal fringe extensive enough to signal potentiation (3). The present experiments show that polysynaptic reflex potentiation is present in the cat spinal cord, and that internuncial relays are involved in the potentiating mechanism. Part of this work has been presented in a preliminary report (13).

Methods

Experiments were performed in spinal cats. Transection of the cord at the first cervical level was carried out under ether. The lower lumbar and upper sacral regions

of the cord were exposed and the roots, once prepared for stimulation, were immersed in a pool of mineral oil regulated between 36–38°C. In some experiments peripheral nerves were used for stimulation. Potentials were recorded by means of condenser-coupled amplifiers. Blood pressure was recorded as routine with a catheter inserted into the carotid artery and connected through a strain gauge to an amplifier and ink-writer.

Since the complexity of the polysynaptic response made it impossible to use peak height as a measure of reflex size, all measurements were made with a planimeter in terms of the area enclosed by the base line and the irregular potential peaks. This type of measurement of the voltage-time area of the polysynaptic response, repeatable within about 5 per cent, can be assumed to represent the sum of the individual action potentials making up the response (5). A similar analysis was recently used by Wright (15) to determine changes in polysynaptic reflexes.

It will be noted that the monosynaptic spike was lacking or inconspicuous in some of the experiments. While a monosynaptic reflex was usually evoked on stimulation of a whole dorsal root, it was frequently absent or quite small following stimulation of some of the dorsal rootlets employed. Supramaximal shocks were used at all times to minimize the effects on reflex size of variation in afferent fiber threshold.

RESULTS

1. Post-Tetanic Potentiation of the Polysynaptic Reflex.—On stimulation of a dorsal root a many peaked polysynaptic response is recorded from the ventral root of the same or of a neighboring segment. In the experiment shown in Fig. 1, stimuli were applied to the seventh lumbar dorsal root every 2 seconds, and the reflex whose area is plotted in the graph was recorded from the corresponding ventral root. As seen in Fig. 1 A, repetitive stimulation of the dorsal root for 10 seconds at a frequency of 50/second resulted in a post-tetanic increase in the response area, with a maximal increase of 90 per cent shown by the first response after the end of repetitive stimulation. The duration of the increase in the reflex is seen to have been approximately 15 seconds. Figs. 1 B and 1 C show that increases in the frequency of repetitive stimulation from 50 to 500/second had no significant effect either on the magnitude or on the duration of the post-tetanic increase. While the post-tetanic potentiation obtained with different frequencies varied somewhat, in most animals the maximal potentiation was evoked by frequencies of 25 to 100/second. Increases to higher frequencies in the order of 500/second often resulted in decreases in post-tetanic potentiation. The experiment shown in Fig. 2 demonstrates the difference in the effect of frequency changes on post-tetanic potentiation of the monosynaptic and polysynaptic pathways. In this experiment stimulating frequencies of 25, 50, 100, and 500/second were used. Following stimulation at 25/second no marked potentiation of the monosynaptic reflex was seen, while a definite potentiation of the polysynaptic reflex was obtained. As the frequency was increased relatively small changes took place in polysynaptic post-tetanic potentiation while, as shown previously (4, 9), there was a considerable increase in post-tetanic potentiation of the monosynaptic pathway.

Polysynaptic post-tetanic potentiation remains relatively stable following widely different frequencies of repetitive stimulation, while following a similar spectrum of tetanizing frequencies monosynaptic post-tetanic potentiation varies considerably. Furthermore, with the use of lower tetanizing frequencies pronounced polysynaptic post-tetanic potentiation has often been observed

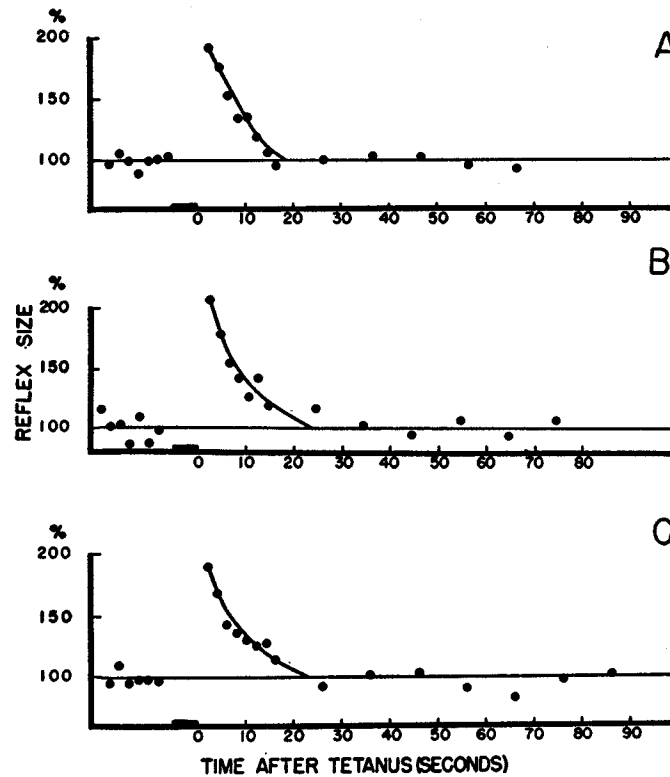


FIG. 1. Post-tetanic potentiation of polysynaptic reflexes following repetitive stimulation 10 seconds in duration at frequencies of A, 50/second; B, 100/second; C, 500/second. 0 time was fixed at the end of repetitive stimulation, shown as a black block on the time line.

while the monosynaptic reflex remained relatively unchanged. These facts suggest the presence in polysynaptic pathways of factors different from those involved in the potentiation of the monosynaptic reflex. This difference is further suggested by the observation that the peak of polysynaptic post-tetanic potentiation invariably occurs earlier than that of monosynaptic post-tetanic potentiation (see Fig. 2). It has been shown by Lloyd (9) that the development of monosynaptic potentiation is opposed by a state of depression which becomes more severe as the number of conditioning volleys increases. This interaction

between potentiation and depression is manifested in a different manner in the two pathways, as the more powerful monosynaptic potentiation increases markedly after high frequency stimulations which, as stated above, frequently decrease the potentiation of the polysynaptic response.

2. *Heterosynaptic Post-tetanic Potentiation.*—The experiment illustrated in Fig. 3 shows the effect of tetanization of one dorsal rootlet upon the ventral root response evoked by stimulation of that and of a neighboring rootlet. The supramaximal test shocks were alternated between the rootlets, which were thus stimulated at 4 second intervals. Dorsal root recording was from the tetanized rootlet only. It can be seen that tetanization of a rootlet resulted in an increase in the size of the reflex evoked by stimulation of this rootlet (Fig. 3 A). Fig. 3 B shows that tetanization of a particular rootlet produced an increased response also to stimulation of a neighboring rootlet. In this experiment the potentiation of the response to stimulation of a neighboring rootlet was manifested by a general increase in the area of the reflex. As seen in Fig. 4, the decay of the post-tetanic potentiation seen on stimulation of the tetanized or neighboring rootlet had the same time course and the response to stimulation of the two pathways was increased to the same extent. While this type of response was frequently seen, in other cases post-tetanic potentiation was longer lasting and more pronounced in the tetanized than in the neighboring root. In other experiments it was seen instead that greater post-tetanic potentiation could be obtained in a given rootlet by repetitive stimulation of a neighboring rootlet than by repetitive stimulation of the rootlet itself.

3. *Potentiation of the Early Polysynaptic Discharges.*—Increase of the ventral root response following repetitive stimulation of a dorsal root was commonly combined with another event, namely predominant potentiation of the first polysynaptic peak (see Fig. 3 A). This great increase in the size of early polysynaptic peaks was observed frequently whether the test stimulus was applied to the tetanized or to a neighboring rootlet, as can be seen in Fig. 5, where A represents post-tetanic potentiation in the tetanized, B in a neighboring rootlet. Such a change in the pattern of the polysynaptic discharge, sometimes unaccompanied by large area increases, was consistently seen in a number of experiments. The predominance of potentiation of the early part of the response varied, as in some cases the increase in the area was caused almost entirely by the increase of the first polysynaptic peak, while at other times the area increase was generalized (Fig. 3 B), but most often potentiation of the early peak accounted for 50 per cent or more of the total increase in the area of the response. Such a result is illustrated in Fig. 6, in which are plotted the changes in (1) the total area of the response, (2) the area of the 1st millisecond of the response, and (3) the area of that part of the response occurring after the 1st millisecond. In this case the increase in the early polysynaptic reflex was responsible for approximately 75 per cent of the area increase brought about by potentiation.

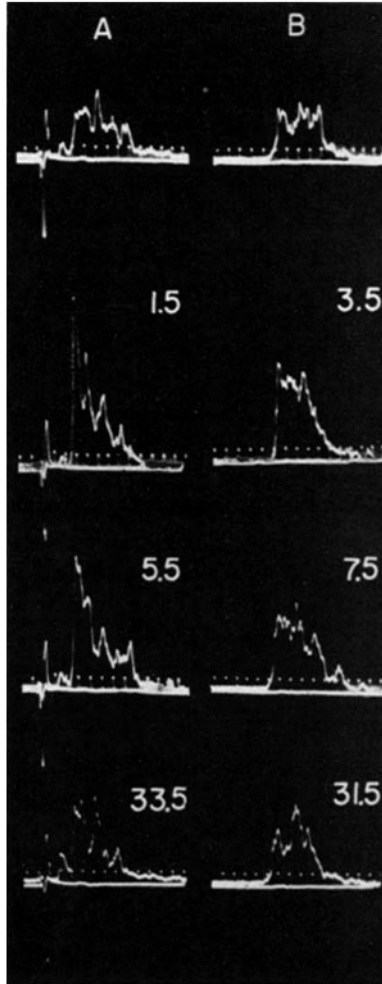


FIG. 3. Post-tetanic potentiation following 10 seconds of repetitive stimulation at 50/second of one rootlet of DRL7. Upper beam shows ventral root response, lower beam dorsal root recording from the "tetanized" root. A, tetanized rootlet. Top frame before tetanus, following ones at indicated time (in seconds) following repetitive stimulation. B, similar recording following test stimulation of a neighboring rootlet after repetitive stimulation of the rootlet shown in A. Time in milliseconds.

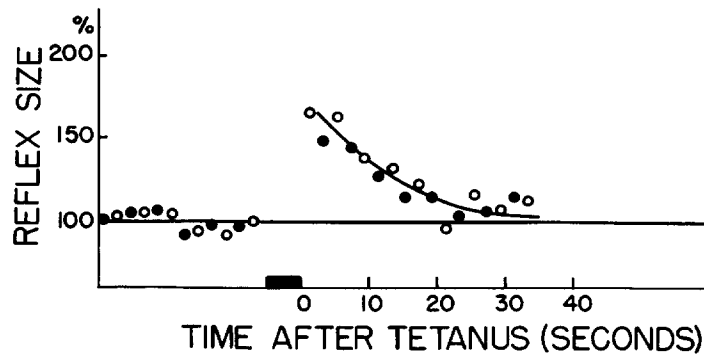


FIG. 4. Effect of 10 seconds of repetitive stimulation of one rootlet of DRL7 on test shocks applied to the tetanized rootlet (open circles) and a neighboring rootlet (filled circles).

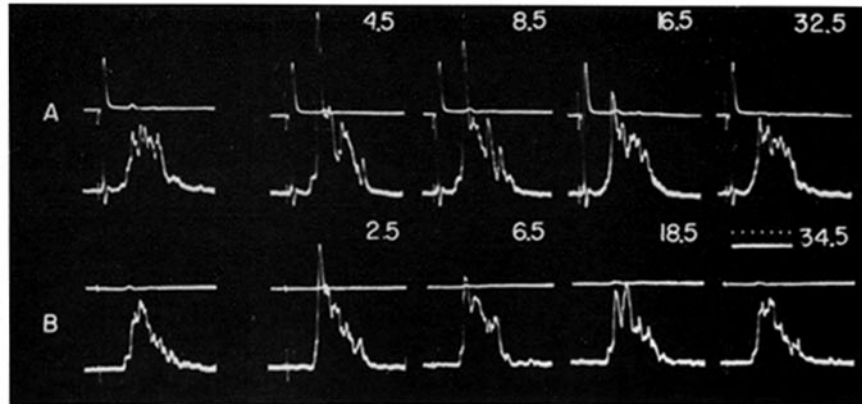


FIG. 5. Effect of a 5 second tetanus at 50/second applied to one rootlet of DRL7. Upper beam shows recording from the dorsal root of the tetanized rootlet, lower beam the reflex as recorded in VRL7. A, post-tetanic potentiation in the tetanized rootlet. First frame, control, following ones at the given number of seconds after tetanus. B, neighboring rootlet response, again with first frame as control. Time in milliseconds. The monosynaptic reflex is seen as a foot at the base of the first polysynaptic spike.

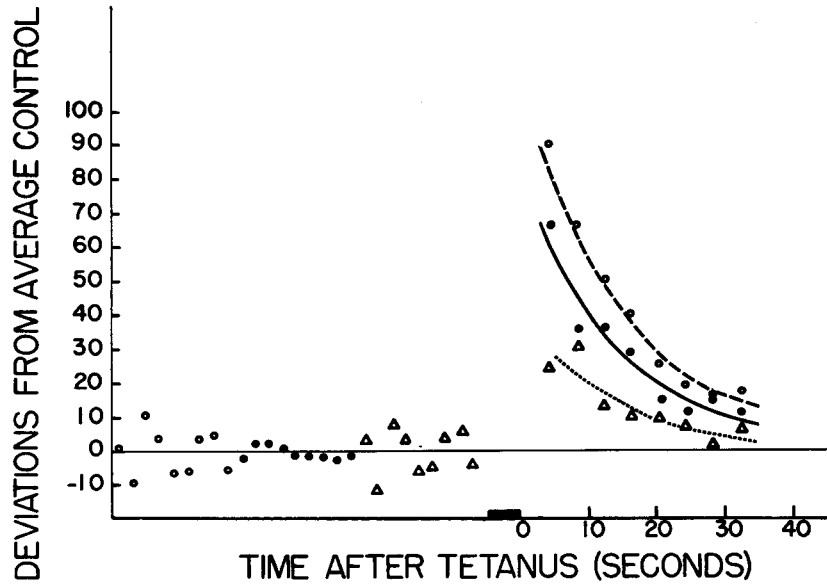


FIG. 6. Post-tetanic potentiation of the early part of the polysynaptic discharge on stimulation of a tetanized rootlet of DRL7, recorded from VRL7. Changes in the total area (open circles), the area of the first millisecond of the response (filled circles), and the area of the rest of the reflex discharge (triangles) following repetitive stimulation at 50/second for 5 seconds are plotted as deviations from average controls (in absolute area units). Controls shown at left are the simultaneously occurring controls for the three areas, and average values were total area 100, first millisecond area 16.5, remainder of area 83.5 area units.

DISCUSSION

These experiments demonstrate the presence of a post-tetanic effect, generally of 15 to 25 seconds' duration, which results in an increased efficiency of polysynaptic pathways in evoking reflex discharge. This effect can be explained, with a minimum of further assumptions, in terms of the mechanisms previously suggested for the potentiation in monosynaptic pathways (9, 10).

The existence of post-tetanic potentiation in polysynaptic pathways does not by itself necessitate the involvement of internuncial elements in the potentiation process. It could be suggested that polysynaptic post-tetanic potentiation, like post-tetanic potentiation of monosynaptic reflexes, is evoked by a change occurring at the primary afferent terminals. This change, by making the stimulated pathway a more effective one, may lead to an increased discharge of the internuncial neurons further downstream. While potentiation of the monosynaptic reflex, as described by Lloyd (9), is of considerably longer duration and reaches greater heights than the potentiation of the polysynaptic reflex described above, it could be assumed that the very nature of a polysynaptic pathway, consisting as it does of several neurons, prevents the change in the afferent terminals from acting as effectively as it does in the simpler monosynaptic arc.

While such an explanation would suffice to explain the potentiation of the polysynaptic discharge in many cases, it is inadequate in those instances in which potentiation was observed upon stimulation of one rootlet following tetanization of another rootlet, an event similar to the enhancement of reflex discharge originally observed by Sherrington and Sowton (12) and Woolsey and Larrabee (14). Nor does the explanation seem to suffice in those cases in which marked increase in the polysynaptic reflex has been seen without noticeable concurrent potentiation of the monosynaptic spike, as occurs following stimulating frequencies of 25 to 50/second. It has been shown that following tetanization of dorsal roots the motoneurons, as judged by their response to antidromic volleys, are in a state of depression (9). Since the same conditions can be assumed to prevail in the experiments described above, motoneurons themselves can be discarded as the site of origin of potentiation changes. Heterosynaptic potentiation, on the other hand, shows that the change evoking potentiation cannot occur exclusively at primary terminals. A considerable portion of the post-tetanic potentiation observed in polysynaptic pathways must therefore be ascribed to changes occurring in interneurons. These internuncial changes can essentially take place in two ways. One is that following repetitive stimulation there remains a hyperexcitability of internuncial cell bodies themselves, leading to a greater bombardment of motoneurons and, in turn, to an increased discharge of the latter. Alternately, it is possible that some interneurons can be made to fire at a high enough frequency during repetitive stimulation to result in a hyperpolarization of the endings of these secondary neurons. Stimulation of another afferent pathway impinging

on these same interneurons would then result in an increased reflex due to the post-tetanic effect in this second step in transmission. This possibility is suggested by the finding (6) that the discharge frequency of interneurons is often higher than the stimulating frequency: stimulation with 10 to 20 shocks per second can result in trains of firing at frequencies of 75 to 150/second. In this manner the action of internuncial terminals could be potentiated by frequencies of repetitive stimulation too low to affect primary afferent terminals significantly. It is possible that hyperpolarization of both primary and secondary terminals is involved in the observed increases in the polysynaptic reflex, but this cannot be decided on the basis of available evidence.

It appears that post-tetanic changes in reflexes are manifested in at least two ways: (1) In a large fraction of cases there is a sizeable increase in the voltage-time area of the ventral root response. (2) Combined with this, and observed in some cases in which the area of the reflex remains relatively unchanged, is a change in the pattern of the response. As shown in Figs. 5 and 6, the result of tetanization is to increase the earlier components of the discharge to a greater extent than the later ones. This change, revealed by the frequent potentiation of the first polysynaptic spike, demonstrates the predominance of post-tetanic potentiation in shorter internuncial pathways. The great increase in the early polysynaptic discharge may mask increases in the later part of the response due to the relative refractoriness of motoneurons that have already fired. It is clear that since the responses of early polysynaptic reflexes are greatly enhanced, the locus of polysynaptic post-tetanic potentiation must partly be placed at the lower order internuncial links.

It has been shown that the time course of polysynaptic potentiation is in the order of 15 to 25 seconds, of the same order of duration as the facilitation seen by Sherrington and Sowton (12), and considerably shorter than that of the similar phenomenon observed by Lloyd for the monosynaptic spike (9). It must be assumed that this difference, as well as the fact that the onset of polysynaptic potentiation precedes that of monosynaptic potentiation, is due to a difference in the properties of the pathways involved.

It can be concluded that potentiation of polysynaptic reflexes may be explained in terms of mechanisms in many ways similar to those involved in the post-tetanic potentiation of monosynaptic reflexes. This polysynaptic potentiation, which involves post-tetanic changes in certain internuncial pathways, can modify spinal reflex discharge by bringing about an absolute change in the amplitude of the discharge and a synchronization in the firing of spinal motoneurons.

SUMMARY

The phenomenon of post-tetanic potentiation has been studied in the cat spinal cord with particular reference to polysynaptic responses. Following tetanization of dorsal roots, these reflexes show an increased response, as meas-

ured in terms of their voltage-time area, with a predominant change in the earlier reflex pathways. Both of these changes in the reflex discharge have a time course of 15 to 25 seconds.

Post-tetanic potentiation is also observed in response to stimulation of a dorsal rootlet following tetanization of another rootlet in the same or in a neighboring segment. This effect can be explained by post-tetanic changes in the terminals of secondary, and possibly higher order, internuncial cells, essentially similar to those changes in the primary afferent terminals which give rise to potentiation of the monosynaptic reflex.

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