—Original Article—

Long-lasting changes in motoneuron discharges following 50 Hz tetanization of afferent nerves in cats

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Summary

The effects of 50 Hz tetanization on motoneuron discharges were studied in non-immobilized, non-anesthetized, decerebrate cats. Motoneuron discharges were monitored by recording either muscle (hamstring muscles or foot extensors) action potentials or ventral root (L7 or S1) discharges. In the latter case both ventral and dorsal roots were cut and corresponding dorsal roots were stimulated. It was found that in 13 out of 32 cases the tetanization of the sciatic nerve at 4.0T for 5 s produced enhancement of monosynaptically evoked muscle action potentials (H-wave) for 20–25 min. Three categories of potentials were distinguished in ventral root discharge according to latencies and thresholds: monosynaptic, polysynaptic and late potentials. When the dorsal root was tetanized at 2.5–5.0T for 5 s, all of these 3 categories of potentials exhibited an enhancement of the potential lasting for more than 30 min. The late potential, which was the longest-latency polysynaptic potential (4.7–6.5 ms), was the most sensitive to the tetanization. Its enhancement could develop slowly, yet the degree of the enhancement was the greatest, as compared with other two categories of potentials. In contrast, the enhancement of these potentials were always immediate. In 15 out of 46 cases at least one of the 3 categories of potentials exhibited the enhancement. Since the long-lasting changes were induced only with the strength enough to activate polysynaptic pathways, interneurons were considered to be responsible for these plastic changes. The monosynaptic potential could show a long-lasting depression following the tetanization.

Key words: motoneuron discharges, interneuron, tetanization, long-term potentiation

Introduction

In the hippocampus a neural plasticity known as long-term potentiation (LTP) has been found to exist and extensively studied^{1–3}. LTP is an enhancement of transmission of synapses at dentate granule cell or hippocampal pyramidal cell which lasts for several hours or several days following repetitive afferent stimulation. In all of these studies LTP has been produced by tetanizing monosynaptic pathways. In the spinal cord long-lasting potentiations have been found to occur also in the monosynaptic pathway^{4,5}. On the other hand, there is a report that chronic stimulation of high threshold afferents leads to enhancement of dendritic activities of the motoneuron⁶.

The present experiments were designed to determine if long-lasting potentiation of motoneuron discharges could be induced by tetanizing polysynaptic pathways. It will be shown below

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that changes in polysynaptic pathways and/or those in the motoneuron itself were responsible for long-lasting monosynaptic and polysynaptic motoneuron discharges. In the course of the experiments it became apparent that muscle relaxants such as gallamine triethiodide hindered the development of plasticity in the spinal cord. Accordingly, non-anesthetized, non-immobilized, decerebrate cats were, as a rule, employed in the present experiments.

Materials and Methods

Eighty one cats (2.2–4.8 kg) were used. Under ether anesthesia the common carotid artery was ligated on both sides and the cat was decerebrated at the intercollicular level. Ether was then discontinued.

In 32 cats the spinal cord was not exposed. The electrodes were introduced into hamstring muscles (m. biceps-femoris & m. semitendinosus), and foot extensors (mm. gastrocnemius, soleus and plantaris). Electromyograms (EMGs) of these muscles were recorded with a pair of uninsulated needle electrodes by averaging these potentials. The sciatic nerve was stimulated near the portion where the biceps-semitendinosus nerve branches off. The stimulating electrodes were a pair of silver wires stuck on to a piece of insulating tape. After the nerve was placed on the electrodes, the tape was folded in two so as to insulate the nerve and the electrodes from the surrounding tissues. The wound made for introducing the electrodes was then sutured. In 49 cats that L7 and S1 roots were exposed by laminectomy. Both dorsal and ventral roots were cut. The dorsal root was mounted on two pairs of silver wire electrodes. A square pulse, 0.1 ms in duration, was delivered to the dorsal root via the distal pair. The action potentials produced by the pulse in the dorsal root was recorded with the proximal pair. The ventral root was placed on a pair of silver wire electrodes for monophasic or killed end recording. The roots were immersed in a pool of mineral oil whose temperature was maintained at 37–39°C. The rectal temperature was kept at 38–40°C.

Blood pressure was monitored in all cases in the common carotid artery with a mechanotransducer (Nihonkoden AP601G). Electrical activities of the roots and EMGs were displayed on a dual beam cathode ray oscilloscope (Nihonkoden VC11), whereas blood pressure was registered with a pen-writing oscillograph (Nihonkoden AJG124).

Results

1. Long-lasting changes of electromyograms (EMGs) following tetanization of the sciatic nerve

Fig. 1 illustrates the changes induced in hamstring muscles (HM) by 50 Hz tetanization of the sciatic nerve. In the control response 3 categories of potentials were produced (**Fig. 1, A: a, b, c**). Potential **b** was the largest and well synchronized. It was therefore the muscle action potential (EMG: M-wave) produced by the motor nerves contained in the sciatic nerve. Potential **c** was of the smallest amplitude and longest latency. It was therefore the EMG produced by afferent nerve fibers in the sciatic nerve by way of the spinal cord (probably the H-wave). Potential **a** was of the shortest latency and duration. It was the action potential produced in the sciatic nerve directly by the sciatic nerve stimulation. For tetanizing the sciatic nerve as a rule 50 Hz was employed because whereas 500 Hz tetanization could produce plastic changes in Glu terminals, 50 Hz

Fig. 1 In this Fig. and Figs. 2, 4, 6, 8, 10, each record consists of 25 averaged responses.

Each record in this Figure illustrates responses produced by stimulation of the sciatic nerve (0.1 ms, 0.5 Hz) recorded with the electrodes in hamstring muscles. The number of the left of each record shows time in minutes elapsed after the first 50 Hz tetanization which was given to the nerve immediately after the records in A were taken. A: controls. a: nerve action potential. b: M-wave. c: H-wave. Seven tetanizations were given between 1 and 31. Note that H-wave was enhanced following 7 tetanizations.

Fig. 2 This illustrates the data from the same experiments as shown in Fig. 1 with a magnification of 5 times.

Note that H-wave (c) was enhanced following the series of tetanizations (e.g., 31), as compared with the control (A). The 1st tetanization was given between A and 1; the 2nd between 2 and 6; the 3rd between 6 and 13; the 4th & 5th between 13 and 20; the 6th between 20 and 25; the 7th between 25 and 31 and the last two tetanizations between 31 and 54.

tetanization did not cause such changes^{7,8)} (see Discussion). Following the tetanization of the sciatic nerve 7 times, the M-wave exhibited a slight increase, whereas the H-wave showed a clear increase (Fig. 1, 31), as compared with the control responses (Fig. 1, A). The nerve action potential was slightly decreased. At 52 minutes following the 1st tetanization, the same tendency still persisted (Fig. 1, 52).

Fig. 2 illustrates these changes in detail. Since the M-wave showed only a little change (see Fig. 1), only the changes in the H-wave will be described here. Following 50 Hz tetanization at 4.0T for 5 s, the H-wave showed only a small change (Fig. 2, 1). However 2 min later it showed a definite increase (Fig. 2, 2). Another tetanization was given and the H-wave was depressed (Fig. 2, 6). In general, a little change or even a decrease occurred immediately following each tetanization, and slow development of the increase in amplitude were characteristic of the H-wave. Records shown in Fig. 2; 13, 20, 25, 31, 54 were all taken a few minutes after a tetanization. Accordingly, all of them show an increase in amplitude as compared with the control response.

The slow development of the enhancement of the H-wave following tetanizations can be fully

Fig. 3 The graphs were made from the data shown in Figs. 1 and 2. A: open circles indicate M-wave, while closed circles indicate H-wave. B shows nerve action potential. Note that H-wave is depressed immediately after the tetanization, yet it is subsequently enhanced. Other two potentials showed only a little change. Ordinate: peak to peak amplitude of the response divided by that of the control. Abscissa: time in minutes following the 1st tetanization.

Fig. 4 Potentials recorded with electrodes in foot extensors in response to tibial nerve stimulation (the portion of the sciatic nerve where the tibial and peroneal nerves merge). The number in each record shows the time in minutes elapsed after the 1st 200 Hz tetanization was given. The 1st potential is nerve action potential and the 2nd the H-wave. The 1st tetanization was given between A and 1, and the 2nd between 16 and 17. Note that H-wave was enhanced immediately after each tetanization, as compared with controls (A).

Fig. 5 Graphs were made from the data shown in Fig. 4. Note that H-wave was immediately enhanced following the tetanization.

appreciated in Fig. 3. Such changes occurred in 6 out of 32 cases and in 7 cases the enhancement was immediate. In the remaining cases the tetanization had a little effect. The enhancement following a series of tetanization lasted for 20–25 min. For example, in Fig. 3, 7 tetanizations (T1–T7) resulted in the slow enhancement of the H-wave. The enhancement lasted for about 20 min and then another tetanization (T8) was given.

It was thought interesting if such a slow enhancement could occur following tetanization of a nerve much smaller than the sciatic nerve. Therefore, the effects of tetanization of the tibial nerve were studied by recording EMGs from FE (foot extensors). Figs. 4 & 5 illustrate the changes induced in FE by 200 Hz tetanization, because 50 Hz tetanization was ineffective. In the control responses 2 categories of potentials could be distinguished. The 1st response was the nerve action potential and the 2nd was the H-wave, considered from their latencies. The tetanization (200 Hz, 4.0T for 10 s) enhanced the H-wave immediately (Fig. 4; 1, 17; Fig. 5; T1, T2). As a rule, however, 200 Hz tetanization was almost ineffective when 50 Hz tetanization was ineffective. Such cases as illustrated in Figs. 4 & 5 occurred only in 2 cases.

2. Long-term potentiation of dorsal root-elicited ventral root discharges

In Fig. 6A, the L7 dorsal root was stimulated at 2.0T. The stimulation produced two categories of potentials. One was the monosynaptic potential (a) and the other polysynaptic

Fig. 6 Figs. 6–9 illustrate the data from the same experiment.

Upper traces: L7 ventral root discharges. Lower traces: action potentials elicited in the L7 dorsal root (rootlet) by the same dorsal root stimulation (0.1 ms, 0.5 Hz). Upward deflections denote negativity. The number to the left of each record shows the time in minutes elapsed after the 1st tetanization (500 Hz, 2.0T, 5 s) was given to the dorsal root. A, B, 1–6: responses produced at 2.0T. 12: responses produced at 6.2T. 29–96: responses produced at 5.0T. Immediately after the records in 29, 34 and 95 were taken, the dorsal rootlet was tetanized (50 Hz, 5.0T, 5 s). 3 categories of potentials were produced as shown graphically at the bottom. a: monosynaptic potential. b: polysynaptic potential. c: late potential. Note that the late potential was slowly enhanced following the tetanization (e.g., 95).

potential (b), as distinguished by their latencies and thresholds. The monosynaptic potential tended to reduce the amplitude of the polysynaptic potential. Consequently, the dorsal root was divided into two and one of them was stimulated⁹. As a result, the amplitude of the polysynaptic potential was considerably increased (Fig. 6B). The rootlet was tetanized at 2.0T with 500 Hz for 5 s. An enormous enhancement of the monosynaptic potential occurred, known as post-tetanic potentiation (PTP)^{7,10}. The rootlet was tetanized at 2.0T with 50 Hz pulses for 5 s, which was ineffective (Fig. 6, 6; Fig. 7, arrow L). The rootlet was then stimulated at 6.2T and the polysynaptic potential was considerably increased (Fig. 6, 12). It is to be noted that a long latency (4.8 ms) polysynaptic potential was newly produced (Fig. 6, 12c). This potential will be referred as the late potential, because it was higher in threshold than all other polysynaptic potentials and conspicuously enhanced by tetanization of the dorsal rootlet, as will be subsequently described.

The rootlet was tetanized at 5.0T with 50 Hz pulses for 5 s. The tetanization enhanced the monosynaptic potential enormously (Fig. 6, 30; Fig. 7A, 1st arrow L). The shortest latency polysynaptic potential was also clearly enhanced (Fig. 6, 30), but the polysynaptic potential as a whole was only slightly enhanced (Fig. 7B, 1st arrow L). Essentially the same results were obtained when 50 Hz tetanization was repeated 5 min after the 1st 50 Hz tetanization (Fig. 6, 35; Fig. 7, 2nd arrow L). A remarkable fact was that the late potential, once depressed following the

Fig. 7 The graphs were made from the data shown in Fig. 6. A: monosynaptic potential. B: polysynaptic potential. C: late potential. Ordinate in A: the amplitude of the potential. Ordinates in B and C represent the area of the potentials as defined graphically in Fig. 7. Abscissa: time in minute. h: 500 Hz tetanization at 2.0T. 1: 50 Hz tetanization at 2.0T. L: 50 Hz tetanization at 5.0T. Arrows indicate the response immediately after the tetanizations. Note the slow enhancement of the late potential following 50 Hz tetanization at 5.0T.

2nd tetanization, began to be enhanced subsequently and reached the maximum value 30 min after the 2nd tetanization (**Fig. 7C**). The enhancement of the late potential was evident at 60 min after the 2nd tetanization (**Fig. 6, 95; Fig. 7C**). An enhancement lasting for more than 30 min will be referred to as the long term potentiation (LTP)^{1,2)}. The slow development of LTP was characteristic of the late potential. The polysynaptic potential also showed LTP, which however passed into a depression (**Fig. 7B**). The monosynaptic potential also showed LTP. Thus all 3 categories of potentials could exhibit LTP.

The 50 Hz tetanization at 5.0T for 5 s was carried out for a 3rd time. The effects of the tetanization was essentially the same as those of the preceding two 50 Hz tetanizations (**Fig. 6, 96; Fig. 7, 3rd arrow L**). In the meantime, the waveform of the action potential in the dorsal rootlet was changed although the stimulus strength was maintained at 5.0T (compare **Fig. 8, 121** with **Fig. 6, 96**). It was nevertheless assumed that the same number and kinds of nerve fibers as before were stimulated because the stimulus strength was the same 5.0T and changes in the waveform were due to those in the physical relationship between the rootlet and the electrodes. Then it becomes possible to compare **Fig. 6, 96** with **Fig. 8, 121**. It is obvious that the late potential is larger in the latter than in the former, whereas the relation in the magnitude is reversed concerning the other two categories of potentials. This shows that as with previous two tetanizations the late potential developed slowly following the 3rd tetanization.

All records in **Fig. 8**, except **Fig. 8, 121** were taken after the cat was paralyzed with panchronium bromide, a quick-acting muscle relaxant (0.4 mg/kg, i.m.) and the monosynaptic

Fig. 8 For the number in each record see the legend for **Fig. 6**.

Except 121, all the records were taken after the cat was paralyzed with panchronium bromide. Immediately after the records in 146 and 229 were taken, 50 Hz tetanization was given. Note the slow enhancement of the late potential following the tetanization.

potential was considerably enhanced, while the other two categories of potentials underwent a little change.

The rootlet was tetanized with 50 Hz pulses at 5.0T for 5 s. The monosynaptic and polysynaptic potentials were enhanced immediately (**Fig. 8, 147; Fig. 9A & 9B, arrow L**). In contrast, the late potential started to increase 1 min after the tetanization (**Fig. 9C**) and attained the maximum magnitude 4-5 min after the tetanization (**Fig. 8, 150; Fig. 9C**). Thus the slow development of the late potential was ascertained for a 3rd time. The monosynaptic and late potentials exhibited LTP after the administration of panchronium bromide. This differed from the effects of gallamine triethiodide as will be described below.

Fig. 8, 229 was taken 83 min after the tetanization shown in **Fig. 8, 147**. The pattern of the potentials was now similar to that of the original control response in that the peak amplitude of the polysynaptic potential was much larger than that of the late potential (c.f., **Fig. 6, 29**). Accordingly, it was considered that LTP had disappeared. The dorsal rootlet was tetanized at 5.0T with 50 Hz for 5 s for a 5th time. The slow development of the late potential was observed for a 4th time (**Fig. 8, 229-240; Fig. 9A'-C'**).

As described above, in the experiments illustrated **Figs. 6-9**, the L7 dorsal root was divided

Fig. 9 Graphs A-C were made from the data shown in **Fig. 8, 146-171**, whereas graphs A'-C' from those in **Fig. 8, 229-240**. A, A'; B, B'; and C, C' illustrate monosynaptic, polysynaptic and late potentials respectively. Note the slow increase of the late potential following tetanizations.

into two and only one of them was stimulated. In a final test, the test shock was given to the same rootlet with the same stimulus strength, but the other rootlet was tetanized at 5.0T with 50 Hz pulses for 5 s. In this test only small changes occurred and LTP was not produced (Fig. 8; 274, 276). This was confirmed in 7 additional cases⁹.

In 15 out of 46 cases (different ventral root discharges) studied at least one of 3 categories of potentials exhibited LTP. In 8 out of the 15 cases, the slow development of the late potential was observed, whereas in 4 cases the late potential was enhanced immediately after the tetanization. The LTP of the monosynaptic potential was observed in 7 cases. It should be stressed that the LTP of the monosynaptic potential could be produced by 50 Hz tetanization and that in all cases the tetanization was strong enough to activate polysynaptic pathways.

3. Long-term depression of the monosynaptic potential

In Fig. 7B, the polysynaptic potential exhibited LTP which was then followed by a depression lasting for about 30 min. A depression lasting for more than 30 min will be referred to as long-term depression (LTD)^{11,12}. Only the monosynaptic potential exhibited LTD which was not preceded by LTP. The LTD of the monosynaptic potential was observed in 8 cases.

In Fig. 10A, the S1 dorsal rootlet was stimulated at 5.0T. All the 3 categories of the potentials were present (a, b, c). In Fig. 10B, the rootlet was stimulated at 2.5T. The late potential was not produced with this stimulus strength. The rootlet was then tetanized with 50 Hz pulses at 2.5T for 5 s. All the potentials were enhanced and the late potential was now

Fig. 10 In A, the S1 dorsal rootlet was stimulated at 5.0T and in B-123 at 2.5T.

The number to the left of each record shows the time in minutes elapsed after the 1st tetanization (50 Hz, 2.5T) was given to the rootlet. Monosynaptic (a), polysynaptic (b) and late (c) potentials were produced. Note the slow enhancement of the late potential following the tetanizations (e.g., 55). Also note that the monosynaptic potential was depressed as time elapsed (e.g., 55; c.f., B). Records in 114-123 were obtained after the cat was paralyzed with gallamine triethiodide.

produced (**Fig. 10, 1**), although not so clear as in **Fig. 10A**. At 3 min after the tetanization, the late potential became larger and conspicuous (**Fig. 10, 3; Fig. 11C**, after the 1st arrow L). Thus the slow development of the late potential was confirmed also in this case. The rootlet was then tetanized at 2.5T with 500 Hz pulses for 5 s. An enormous enhancement of the monosynaptic potential occurred immediately following the tetanization (**Fig. 10, 4; Fig. 11A**, arrow H). The polysynaptic potential was almost uninfluenced, whereas the late potential became a little smaller (**Fig. 10, 4; Fig. 11B & 11C**, arrow H). Two more 50 Hz tetanizations at 2.5T for 5 s were delivered. Essentially the same changes were produced by these tetanizations. That is to say, the monosynaptic potential was enhanced; The polysynaptic potential was almost uninfluenced and the late potential was reduced immediately after the tetanization (**Fig. 10; 13, 14; Fig. 11; 2nd &**

Fig. 11 Graphs A-C were made from the data illustrated in **Fig. 10, B-75**, whereas graphs A'-C' from those in **Fig. 10, 114-124**.

Ordinate in A: amplitude of the monosynaptic potential. Ordinates in B and C indicate the areas of polysynaptic and late potentials, as defined graphically at the bottom of **Fig. 10**. Arrows H: the responses immediately following 500 Hz tetanization (2.5T, 5 s). L: the responses immediately following 50 Hz tetanization (2.5T, 5 s). Note the depression of the monosynaptic potential following the tetanizations. In contrast, the late potential exhibited a slow enhancement.

3rd arrow L). It is noted that the late potential became larger as time elapsed following the tetanization (**Fig. 10, 55; Fig. 11C**). Thus the slow development of the enhancement of the late potential was repeatedly confirmed. It is further noted that although every tetanization resulted in an immediate enhancement of the monosynaptic potential, the amplitude of the monosynaptic potential became reduced as time elapsed (**Fig. 10; Fig. 11A**). The reduction in the amplitude was due to tetanization and not due to nonspecific causes such as deterioration of neural activities because the polysynaptic potential remained unchanged and the late potential exhibited LTP (**Figs. 10 & 11**). The reduction in the amplitude lasted for about 60 min, and this was referred to as LTD.

During the early stage of the LTP, the late potential had two peaks (**Fig. 10, 3**). This was similar in pattern to the late potential produced by increasing the strength of the test shock to 5.0T (**Fig. 10A**). But at the height of LTP, the late potential assumed a round-peaked waveform (e.g., **Fig. 10, 55**). A similar phenomenon occurred also in the polysynaptic potential. Namely, the polysynaptic potential had initially two peaks (**Fig. 10B**). But in **Fig. 10, 55** it became round-peaked. Thus the polysynaptic potential also exhibited a plastic change in the waveform following tetanization, although it did not show LTP. The polysynaptic potential recovered its original waveform about 50 min after the last tetanization (**Fig. 10, 75**). Such a long-lasting change in the waveform of the polysynaptic potential and/or the late potential was observed in 3 other cases with or without LTP. It should be stressed that the change in the waveform was produced not by increasing the strength of the test shock, but by tetanization.

Gallamine triethiodide (10 mg/kg, i.m.) was then administered. The drug depressed polysynaptic potentials considerably (**Fig. 10, 114, c.f., Fig. 10, 75**). A remarkable fact was that 50 Hz tetanization was no longer effective (**Fig. 10, 123**), whereas 500 Hz tetanization was still effective in enhancing both monosynaptic and late potentials (**Fig. 10, 115; Fig. 11A'-C'**). It should be also noted that even with 500 Hz tetanization LTP was no longer produced.

Discussion

The present investigation revealed that long-lasting potentiation of motoneuron discharges could be induced by sciatic nerve and dorsal root tetanization. First of all it should be stressed that such a long-lasting change was produced only with the strength enough to activate polysynaptic pathways. Even the H-wave, which presumably was a monosynaptic reflex, exhibited a long-lasting potentiation only when polysynaptic pathways were tetanized. In the case of the dorsal root-elicited ventral root discharges there were 3 categories of potentials distinguished; monosynaptic, polysynaptic and late potentials. The late potential had a latency of 4.7–6.5 ms. It was therefore a polysynaptic potential. But it was distinguished from all other polysynaptic potentials by its higher threshold and its sensitivity to dorsal root tetanization. There were 3 classes of long-lasting changes resulting from the tetanization: LTP (long-term potentiation), LTD (long-term depression) and changes in waveform. All 3 categories of potentials exhibited LTP. In addition, polysynaptic and late potentials could show plastic changes in waveform. Only the monosynaptic potential exhibited LTD which was not preceded by LTP. These changes were not non-specific changes, because these changes were peculiar to each category of potential. For example, while the monosynaptic potential showed LTD, the late potential recorded from the

same ventral root exhibited LTP (**Fig. 10 & 11**). This was further supported by the fact that tetanization of the dorsal rootlet adjacent to the one, to which the test shock was given could not produce long-lasting changes⁹). These arguments suggest that the immediate cause for the long-lasting changes existed in the tetanized spinal cord.

LTP of the monosynaptic potential could be produced with 50 Hz tetanization at 2.5T–5.0T. It was however not produced with 500 Hz tetanization at 2.0T. It is obvious that at 2.0T the majority of high threshold afferents were not stimulated. It is known that 500 Hz tetanization can produce PTP while 50 Hz tetanization can not produce PTP^{7,8}) (See **Fig. 6**). It is also known that the changes responsible for producing PTP occur in group Ia terminals^{7,8}). Then it may be concluded that 50 Hz tetanization does not induce plastic changes in group Ia fiber terminals. These arguments suggest that tetanization of high threshold afferents produced LTP, as well as the potentiation of the H-wave.

It is known that the monosynaptic potential (or reflex) is produced by way of group Ia fibers. Accordingly, LTP of the monosynaptic potential must have been caused by plastic changes induced in the motoneuron itself by way of polysynaptic pathways. The nature of plastic changes is unknown at present. On the other hand, there is another possibility which could have caused LTP by modulating the electrical activities of group Ia fiber terminals. Namely, if presynaptic inhibition-inducing interneurons were tonically active in the present experimental conditions, a long-lasting decrease in presynaptic inhibition could produce LTP of the monosynaptic potential.

LTD was already known to occur in the cerebellar Purkinje cell^{11,12}). LTD of the Purkinje cell may be different in mechanism from that of the monosynaptic potential described in the present paper because two different inputs (climbing and parallel fibers) to the same Purkinje cell must be stimulated in order to produce LTD. On the other hand, LTD of the monosynaptic potential could be induced by making inhibitory interneurons and/or presynaptic inhibition-inducing interneurons tonically active through tetanization of high threshold afferents. Long-lasting potentiation of inhibitory interneurons was reported to exist^{13,14}).

That 50 Hz tetanization could induce LTP might exclude high threshold afferent terminals as the major sites for the plastic changes because 50 Hz tetanization could not possibly have caused plastic changes in nerve terminals, as discussed above. Otherwise, the plastic changes could have occurred anywhere along the polysynaptic pathway including the motoneuron itself. LTP of the polysynaptic potentials could be followed by LTD. This could be explained by the interplay of LTP of excitatory interneurons and that of inhibitory interneurons.

The peak of the late potential was much longer in latency than the highest peak of the polysynaptic potential. Yet the former could be larger in amplitude than the latter (e.g., **Fig. 6, 95**). Larger amplitude indicates that motoneurons were more synchronized and/or motoneurons were more activated. On the other hand, if the longer latency is due to more synaptic delays, one would expect that the motoneurons to be less synchronized and less strongly activated. Thus the longer latency and the larger amplitude of the late potential, as compared with the polysynaptic potential, appear to be contradictory. The contradiction can be solved however if the longer latency is due to some other mechanism than synaptic delays. The following possibility may be considered. The latency of the late potential was 4.7–6.5 ms. This is similar to the latency of the spikes driven by a slow depolarization in the motoneuron that was suggested as originating in the

dendrites (D-wave)⁶⁾. The latency of these spikes could be easily changed according to the changes in the rising phase of the D-wave. In fact, there was a variation in the latency of the late potential up to 0.9 ms, whereas the latency of monosynaptic and polysynaptic potential remained stable (e.g., compare Fig. 6, 30 with Fig. 6, 95). The H-wave could develop plastic changes slowly. The same was true of the plastic changes in the waveform of polysynaptic and late potentials. The slow development could be explained as being due to gradual changes in the activities of relevant interneurons. Neither the tetanization of the tibial nerve alone, nor that of the biceps-semitendinosus nerve alone could produce LTP in the ventral root or peripheral nerves. This could mean that in order to produce the plastic changes, more than a certain amount of impulses have to be sent into the spinal cord³⁾.

Gallamine triethiodide could hinder the development of long-lasting plastic changes. The cause is totally in the dark at present. The long-lasting plastic changes described above were observed only in about one third of the cases studied. The same is true of the LTP of the dentate granule cell, which is now generally regarded as the neurophysiological basis for memory mechanism²⁾. The reasons for these unresponsive cases have been not yet clarified.

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