

Recurrent collaterals of motoneurons

Anatomy

The recurrent collaterals of motoneurons were discovered in 1883 by Golgi (see his *Opera Omnia*, vol. ii, 1903) and described as very fine fibrils returning from the axon to the grey matter of the spinal cord within which they subdivide in a complex fashion and spread diffusely ('senza determinato confine'). There are brief references to the old anatomical literature in Eccles, Fatt and Koketsu (1954) and in Scheibel and Scheibel (1966). Some of the early attempts to study their function have been mentioned in Granit (1955, p. 212). Ramón y Cajal (1899, 1904) established recurrent collaterals as a common feature in nervous centres. This arrangement suggests that the firing rate at the output end of a centre has some kind of regulatory function within its pool of neurons.

The spinal cord of a large number of mammals of different species were studied by Scheibel and Scheibel (1966), mainly by the Golgi stain. In transverse sections they saw 3–4 collaterals per axon but 20–30 per cent of the motoneurons were without them. The collaterals were found to spread widely both medially and laterally in the cross-section, making contact with both motoneurons and 'proprio-neurons' (as they call them, refusing to admit the existence of Golgi II type of cells). The branching was limited to the ipsilateral side. In the sagittal sections they saw the majority of the collaterals project back within one half-segment of the parent soma.

The work of Scheibel and Scheibel refers to the motoneurons which will be discussed below. There are other motoneurons such as those of the phrenic which are lacking recurrent effects altogether (Gill and Kuno 1963).

The Renshaw cells

In the present connection we can neglect the early observations on suppression of excitability after an antidromic shock (see, e.g., Creed *et al.* 1932) because the introduction of sweep circuits for precise timing and

MECHANISMS REGULATING THE DISCHARGE OF MOTONEURONS

small electrodes for localization of events made all the difference to research in this field. The modern era may be said to have been introduced by Renshaw (1941) when he—once more—showed that a shock backfired into a motoneuron pool produced a depression of excitability lasting some 40–50 ms, sometimes also an enhancement. His next step was to push small electrodes into the spinal cord and repeat the experiment. In certain places he then found cells in the spinal cord which responded at very high initial rates of discharge, 1,000–1,500 impulses per second, to the antidromic shock. These were the ones nowadays

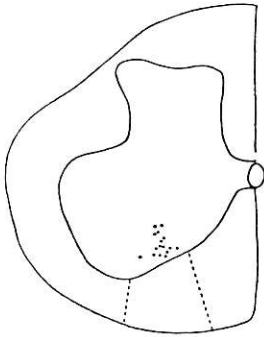


Fig. 35. Diagrammatic representation of the area studied in the lumbo-sacral region of four cats. The diagram was drawn so as to fit as closely as possible the outline of all sections. Positions of the marks are indicated by the black dots. Broken lines delineate the extent of the ventral root exit zone (Thomas and Wilson, *Nature*, 1965).

spoken of as Renshaw cells. Eccles *et al.* (1954) found such cells in the ventromedial region of the cord.

Marking techniques for microelectrodes (glass pipettes) have since been developed by Thomas and Wilson (1965) and Willis and Willis (1966) for the localization of isolated Renshaw cells. Figure 35 shows the position of markings obtained in the experiments of Thomas and Wilson. Both teams agree that the Renshaw cells are located in Rexed's (1954) lamina VII which is the region where they were found in the electrophysiological experiments of Eccles *et al.* (1954) and later by many other workers.

The most obvious effect of backfiring into a motoneuron pool is the familiar depression of excitability and Eccles *et al.* (1954) set out to investigate (i) whether this was a real postsynaptic inhibition and (ii) whether it could be correlated with the discharge of the Renshaw cell. This was done by simultaneously recording from a Renshaw cell and a near-by motoneuron, varying antidromic stimulus parameters and comparing pharmacological specificities. The discharge pattern of the Renshaw cell and the course of the postsynaptic inhibitory response varied in parallel, from which it was concluded that they were related as

RECURRENT COLLATERALS OF MOTONEURONS

cause and effect. This conclusion was supported by a set of close pharmacological parallels of behaviour. The thick lines in Figure 36A are inhibitory postsynaptic potentials from three different motor nerves (see caption). The uppermost is a large antidromic response whose ripples come from pulsations of neighbouring Renshaw cells, the lowermost is elicited from a motor nerve which was without a significant recurrent effect on that cell. The records B are samples of Renshaw cell discharges to different motor nerves. In the circuit diagram of Figure 36 the recurrent collaterals are shown to terminate on the Renshaw cells, the latter to send out branches making inhibitory contacts with motoneurons. The pharmacological evidence in favour of this general circuit diagram is extensive but cannot be reviewed in this context (see for development of Renshaw cell pharmacology, Brooks and Wilson 1959; Longo, Martini and Unna 1960; Curtis and Ryall 1966a, b).

The Renshaw cell is an interneuron and so its membrane potential is subject to 'biasing', by positive or negative influences, as the case may be. Renshaw (1946) saw some of his cells also discharging to stimulation from the afferent end, as did Eccles *et al.* (1954), who found that such

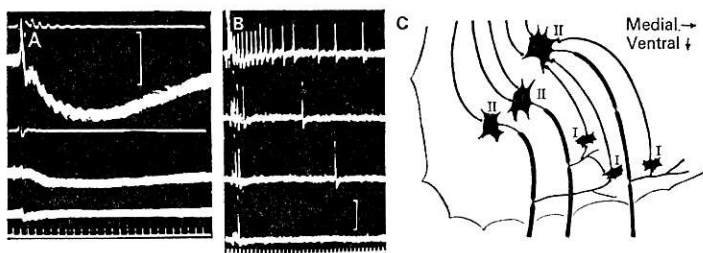


Fig. 36. A. Intracellular recording from a biceps-semi-tendinosus motoneuron. The potential simultaneously recorded by a surface lead on the dorso-lateral aspect of the spinal cord is shown above the first two intracellular records. The main curves show, reading from top to bottom, hyperpolarizations produced by antidromic volleys in the biceps-semi-tendinosus and in the semi-membranosus motor axons, while the lowest record shows zero effect of a plantaris antidromic volley. The motoneuron was not invaded antidromically by the impulse in its own motor axon, so in the uppermost record there is no complication by the positive afterpotential. All records are made by the superimposition of about 40 faint traces to eliminate random noise. Time in milliseconds: potential scale, 5 mV. B. The upper record shows the rhythmic response set up in an interneuron by an antidromic volley in the biceps-semi-tendinosus motor axons. Other records, going downward, are responses of the same interneuron elicited by antidromic volleys in the motor axons to gastrocnemius, flexor longus digitorum and the deep peroneal group of muscles respectively. Time in milliseconds: potential scale, 0.5 mV. C. Circuit diagram showing motoneurons (II) with their axons and recurrent collaterals which run to Renshaw cells (I). The latter have inhibitory synapses on the motoneurons (Eccles, Fatt and Koketsu, *Aust. J. Sci.*, 1953).

MECHANISMS REGULATING THE DISCHARGE OF MOTONEURONS

discharges were evoked by Gr III afferents. The effect was genuine, not consequent upon the firing of motoneurons. Afferent 'biasing' of the Renshaw cells has since been seen by several workers (e.g. Frank and Fuortes 1956; Curtis, Phillis and Watkins 1961; Wilson, Talbot and Kato 1964). The pinna reflex can fire the cells (Haase and Van Der Meulen 1961). More commonly the various reflexes from the skin produce an inhibition of the Renshaw cell, extensively studied by Wilson and Talbot (1963) and Wilson *et al.* (1964). The time relations, as explored in their work, necessitated the insertion of an interneuronal

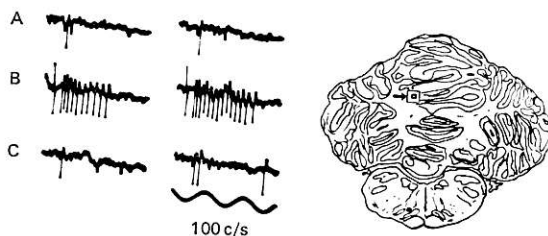


Fig. 37. Decerebrate cat. A. Antidromic test shocks to gastrocnemius nerves were adjusted so that only one or two discharges from Renshaw cell were elicited. B. Cerebellar conditioning by a single shock to the point in the arrowed inset results in strong facilitation. C. After cessation of cerebellar conditioning original rate of discharge reappeared (Haase and Van Der Meulen, *J. Neurophysiol.*, 1961).

link between the afferent source and the Renshaw cell (Wilson 1966, and Fig. 38 below). Supraspinal effects were demonstrated by Granit, Haase and Rutledge (1960) and Haase and Van Der Meulen (1961). These were both excitatory and inhibitory. Structures at various levels within the reticular formation and in the cerebellum were stimulated in those experiments. Figure 37 illustrates a cerebellar facilitation of the antidromically elicited response of a Renshaw cell.

A prototype of all recurrent circuits is found in the primitive lateral eye of the horseshoe crab *Limulus* (Hartline and Ratliff 1957) in which the large nerve fibres from each ommatidium are provided with branches with inhibitory terminals on one another. The output discharge to illumination of the eye thus operates a built-in suppressor mechanism that has become known as lateral inhibition. Some comparisons between the recurrent and lateral inhibitions will be made below. Here the work of Hartline and his colleagues is mentioned merely in order to emphasize the obligatory character of that inhibition compared with the recurrent variety which is facultative. By this term is meant that its mechanism, as we have seen, is available for the organism to use or not

RECURRENT COLLATERALS OF MOTONEURONS

to use or to apply in a graded fashion according to the requirements of the moment. Its interneuronal organization, as sketched by Wilson (1966) in Figure 38 is complex. It seems likely, however, that the recurrent fibres (RC in the diagram) furnish the most potent projections for the Renshaw cell.

It is a task for future workers to demonstrate when and how the recurrent circuit is used facultatively. Much of what has been done

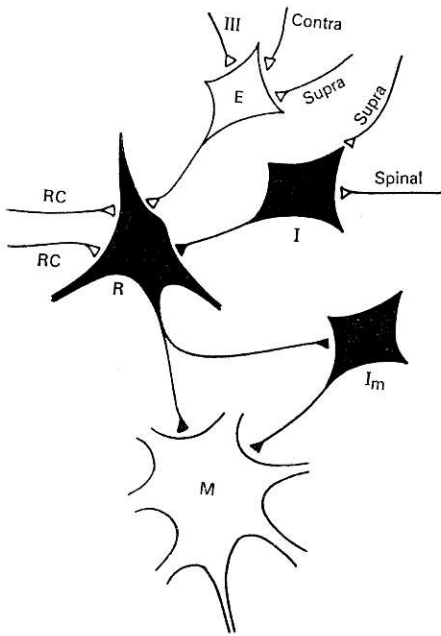


Fig. 38. Diagram of input to and output of a Renshaw cell (R), showing minimal number of synapses on the cell itself. Excitatory cells and terminals shown in white, inhibitory cells and terminals shown in black. Recurrent collaterals from several motor nuclei are indicated by fibres RC. Excitatory interneuron (E) is impinged upon by ipsilateral Group III fibres (III), high threshold contralateral fibres (Contra), and descending fibres (Supra). The inhibitory interneuron (I) may receive inputs from descending fibres (Supra) and spinal afferents (Spinal). Also shown is another inhibitory interneuron (I_m), which has inhibitory synapses on a motoneuron and is in turn inhibited by the Renshaw cell, which also has inhibitory endings directly on a motoneuron. References on which connections are based are given in text (Wilson, *Muscular Afferents and Motor Control*, Nobel Symp. I, Stockholm, 1966).

consists in attempts to understand its role in the organism as a governor when it is operated by antidromic stimulation in imitation of 'natural' firing.

Distribution of recurrent inhibition

A study of the convergence patterns of individual muscle nerves (Eccles *et al.* 1961a) on eighteen Renshaw cells is summarized in Table 1 over-leaf.

The table shows that one particular muscle nerve tends to be dominant and that effective stimulation is restricted to two or three muscle nerves. These are organized in the table in the approximate sequence of

MECHANISMS REGULATING THE DISCHARGE OF MOTONEURONS

Renshaw cell number	L6 and upper L7					Mid L7					Lower L7 and S1			
	Q	SM	SG	FDL	Per.	Pl.	Pop.	LG	AB	ST	IG	PB	MG	Sol.
1	6	5	13
2	.	.	13	.	2
3	.	.	10	.	5
4	.	.	7	2	7	.	.	.
5	.	3	7	3	8
6	.	.	10	3	3	.	.	3	8	3	3	.	.	.
7	.	17	4	.	8	.	5
8	.	16	.	.	8	3	.	.	.
9	14	9	9	.	.	.	1	.	.
10	6	.	18	8	6
11	32	2	.	28	.	.
12	20	9	.	13	.	.
13	10	.	12	1	.
14	5	22	.	.
15	3	.	6	.	5	7	12	9	.
16	26	26	17
17	5	2	.	5	4	13	.
18	2	.	8	7	.	7	10	21	4

Table 1. The convergence of antidromic volleys in muscle nerves on to 18 Renshaw cells. Each muscle nerve was tested separately and in the columns are the numbers of impulses discharged from the respective Renshaw cell in response to a maximal antidromic volley in the alpha motor fibres. Numbers in bold type show the contribution from the dominant muscle nerves. The symbols labelling the columns correspond to the following muscle nerves: Q, quadriceps; SM, semi-membranosus; SG, superior gluteal; FDL, flexor digitorum longus+flexor hallucis longus; Per., peroneal; Pl., plantaris; Pop., popliteus; LG, lateral gastrocnemius; AB, anterior biceps; ST, semitendinosus; IG, inferior gluteal; PB, posterior biceps; MG, medial gastrocnemius; Sol., soleus (Eccles, Eccles, Iggo and Lundberg, *J. Physiol.*, 1961).

their motoneuron nuclei which are elongated, parallel structures partly overlapping within adjacent segments (Romanes 1951). The most interesting feature of the table is seen to be that proximity in the spinal cord is an important factor determining the effect of the antidromic shock. When several nerves cause an effect, these very evidently obey the rule of proximity of their motoneurons.

Eccles, Eccles, Iggo and Ito (1961b) returned to this problem by measuring in 474 motoneurons the amount of IPSP that the recurrent mechanism produced. The largest amounts were as a rule generated by

the volley in the impaled motoneuron's own nerve. The antidromic spike of the cell had then been blocked by a short hyperpolarizing pulse through the intracellular electrode. This had been done in order to avoid the complication of an after-hyperpolarization. Again the conclusion of Renshaw (1941) and Eccles *et al.* (1954, 1961a) was confirmed, viz. that the detectable pattern, as reflected functionally, was one of nuclear proximity in the cord. The authors state: 'The segmental gradients of effectiveness of various muscle nerves in generating RIPSPs (=recurrent inhibitory postsynaptic potentials) are thus in good agreement with the segmental locations of their respective motor nuclei' (p. 489). Similar results were obtained by Wilson, Talbot and Diecke (1960). The proximity rule was found valid also in the cervical spinal cord (Thomas and Wilson 1967).

In the meantime another organizational factor had been discovered. Granit, Pascoe and Steg (1957) had found that the recurrent inhibition in the lumbo-sacral region of the cat's spinal cord tended to be highly potent on the motoneurons that responded tonically to repetitive stretching (in the manner illustrated in Fig. 5). Many motoneurons that in this test remained phasic were altogether without recurrent inhibition (see the section on *Anatomy*, p. 47). Kuno (1959) soon confirmed this conclusion in a study comparing the relative amounts of recurrent inhibition in gastrocnemius and soleus motoneurons. Eccles *et al.* (1961b) tested it by correlating the inhibitory postsynaptic potentials with conduction velocities of the efferent axons. Their conclusion was that 'motoneurons with long after-hyperpolarizations always received a larger total RIPSP than motoneurons with brief after-hyperpolarizations, though the receptive field may be just as extensive' (p. 485). While cell size may be a contributing factor determining the larger effects of recurrent inhibition on the small tonic motoneurons, it cannot provide a full explanation of this finding. It throws no light on the facts that many phasic motoneurons are lacking this mechanism (Granit *et al.* 1957) and that Holmgren and Merton (1954) had found antidromic volleys as weak as 25 per cent maximal to be capable of setting up a complete block of a tonic discharge. Recurrent inhibition is thus far more powerful in the direction phasic→tonic than the other way round.

Interpretation of distributive factors

The transverse distribution of recurrent inhibition in the cord between motor nuclei of different provenance regardless of function is likely to signify that the recurrent collaterals exercise a general restraining

MECHANISMS REGULATING THE DISCHARGE OF MOTONEURONS influence on the discharge rates of motoneurons (Eccles *et al.* 1961b), apparently directed chiefly towards the small tonic ones. Granit *et al.* (1957) regarded recurrent inhibition of the tonic motoneurons as a mechanism stabilizing their firing rate to suit the slow muscle fibres to which they send their axons. The strong proprioceptive control of these motoneurons is well known to depend on the gamma executive for the intrafusal musculature and so the recurrent circuit may also be regarded as a natural antagonist of the gamma loop. The advantage of a governor on the efferent side lies in its independence of irregularities in the synaptic response of the motoneuron due to excessive or highly variable depolarizing pressures. The firing rate, so to speak, regulates itself, as will be shown below.

Granit *et al.* (1957) also discussed the possibility that the phasic motoneurons generally suppress their tonic partners, silencing slow muscles during the activity of the fast musculature, but stated that they could find no definite support for this view. However, Eccles *et al.* (1961b) have taken it up again as one of the possible roles of recurrent inhibition in motor control. This proposition should be tested experimentally. It may well prove to be valid.

Quantitative aspects of recurrent inhibition

The illustrations of discharges of Renshaw cells to single antidromic shocks (Figs. 36 and 37) should not lead to the conclusion that this is the way they fire when excited by the recurrent spikes of normally active motoneurons. When, in imitation of normal motor activity, the antidromic shocks are delivered at frequencies from 5 to 50 per second, the bursts disappear at rates between 5 and 10 per second and the Renshaw cells start firing at slow rates (Haase 1963), as they do in natural motor activity.

Granit and Renkin (1961) used antidromic tetani at different frequencies to establish the quantitative relation between firing rate and the amount of recurrent inhibition. The indicator was a tonically firing motoneuron whose discharge rate was measured before, during and after a period of recurrent inhibition. The normal firing rate (F_n) of the motoneuron was given as the average of the values before and after the period of recurrent inhibition. The value obtained during inhibition (F_i) was subtracted from F_n and the difference plotted as ordinates in Figure 39 against the frequency of the antidromic tetanus on the abscissae. The relationship is linear and saturation takes place at a rate of around 40 volleys per second.

The result shows that the amount of recurrent inhibition, just as that of lateral inhibition in *Limulus* (Hartline and Ratliff 1957), is proportional to the firing rate. Thus rapidly firing motoneurons inhibit slowly firing partners in a motor act more effectively than the latter can inhibit in return, assuming the inhibition to be mutual. The dependence of recurrent inhibition on the discharge rate of the inhibiting motoneurons should make it an important complement to after-hyperpolarization as a frequency limiter (cf. also Margaria 1959). When afferent excitation of a motoneuron increases, it also antagonizes after-hyperpolarization with increasing efficiency and consequently the firing rate rises. In this situation a frequency limiter of tonic firing dependent on

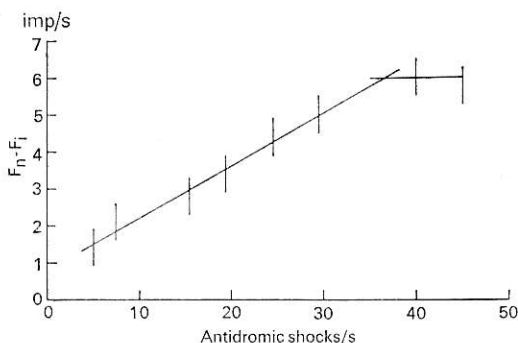


Fig. 39. Experiment showing effect of antidromic stimulus rate (abscissa) on $F_n - F_i$. The horizontal line shows final value of the latter (Granit and Renkin, *J. Physiol.*, 1961).

firing rate itself can apply the corrective required for holding down tonic activity to the constant rates of discharge actually observed in the stretch reflex (see p. 25). The mechanism would operate between tonically firing motoneurons such as, for instance, those of soleus. It was pointed out above that the motoneurons belonging to the nerve of their own muscle tended to produce good recurrent inhibitions between themselves. Figure 39 also shows that the effective range of recurrent inhibition agrees with the firing range of tonic motoneurons.

By stimulating the severed gastrocnemius-soleus nerve of a decerebrate cat it is possible, within limits, to push its motoneurons to higher frequencies of discharge than those obtainable in the stretch reflex which forces its way against autogenetic inhibition. In the experiments to be reported, single fibres were functionally isolated in root filaments and the effect of a constant antidromic tetanus at about 55–65 volleys per second from some other filament or from the rest of the root was

MECHANISMS REGULATING THE DISCHARGE OF MOTONEURONS superimposed on the firing cell. Sometimes a very thin filament was found as effective as the remaining portion of the root. The aim of the experiment was to find out whether recurrent inhibition was algebraically additive. The experiments differ from those reported above in being throughout extracellular and 'synaptic', instead of making use of synaptic additions in combination with firing induced by transmembrane stimulation.

In Figure 40 are plotted the results of an experiment with a motoneuron that could be forced to fire up to rates of 38 impulses per second.

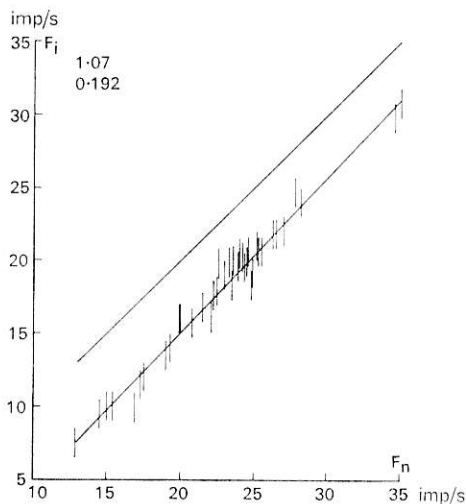


Fig. 40. Frequency of discharge (F_n) of motoneuron plotted against the reduced frequency (F_i) during a constant recurrent inhibition. The line above it is drawn for the case of $F_n = F_i$, for the recurrent inhibition having no effect on the firing rate of the motoneuron (Granit and Renkin, *J. Physiol.*, 1961).

The discharge frequencies without inhibition (F_n) are on the abscissae, on the ordinates those with recurrent inhibition superimposed (F_i). The upper line is at 45° and thus illustrates the case of no effect of the inhibitory stimulus ($F_n = F_i$). The line through the readings, whose slope with perfect algebraical summation should be 1.00, has a regression coefficient of 1.07, with a standard error of 0.192.

In these experiments eighteen motoneurons were studied. If all the experiments are treated as a single one of 470 observations and the regression coefficients are weighted with respect to the number N of the individual observations in each experiment, one should obtain the average value of the slope constant. This proved to be 0.996 which is

near enough to the theoretical 1.00 to show that recurrent inhibition is additive and hence removes the same number of impulses whatever the firing rate of the motoneuron investigated. The average standard error (s/\sqrt{N}) for measuring $F_n - F_i$ was 0.240, the mean difference $F_n - F_i$ being 5.5 impulses per second.

The two properties of recurrent inhibitions which now have been established by a quantitative analysis, are a replica of those characterizing the lateral inhibition of the *Limulus* eye (Hartline and Ratliff 1957). In the eye this mechanism establishes contrast (see p. 61). Recurrent inhibition probably fulfils similar tasks in motor control, as also postulated by Brooks and Wilson (1958), Brooks (1959) and Wilson *et al.* (1960) on general grounds. It follows from the algebraical additivity that a constant inhibition becomes relatively more effective on slowly firing motoneurons. These can easily be pushed below the firing threshold. Add to this that motoneurons firing at faster rates are powerful inhibitors of their slowly discharging partners from which they receive little inhibition in return, and there is one more decisive factor operating to concentrate the firing to the best-supported motoneurons within a 'pool' of co-contracting synergists. By this mechanism the so-called 'fringe' neurons and those belonging to weak synergists will effectively be held in check.

In the eye of *Limulus*, those ommatidia which are diffusely illuminated, and hence discharge slowly, are suppressed by the mechanism of lateral inhibition. By this mechanism of contrast the best-illuminated cells are thus made to deliver a sharp image. Something can be said for calling the recurrent inhibition of motoneurons an equivalent mechanism of motor contrast (Brooks 1959). Looking at recurrent fibres in these two cases from the teleological standpoint of bio-engineering, it makes sense to have a corrective of this type which acts in proportion to the firing rate at the output. Unless it had been valuable, this elegant mechanism, designed far back in the phylogenesis, would never have survived evolution up to the mammalian stage. Its only improvement on the way consists in the insertion of an interneuron—the Renshaw cell—to make it facultative and thus increase its usefulness.

Recurrent inhibition at work. Surplus excitation

With maintained tonic discharges it is possible to see something of the recurrent mechanism in operation, always granted that antidromic stimulation provides a fair imitation of it. The experiment illustrated in Figure 41 is an attempt to find out what a maximal and constant

MECHANISMS REGULATING THE DISCHARGE OF MOTONEURONS

recurrent inhibition can do to a maintained tonic discharge. The diagram shows that the tonically active spike in the filament (S) is amplified to elicit the antidromic stimulus (Stim) for the rest of the ventral root (VR). The indicator spike (in S) is produced by stretching the gastrocnemius-soleus muscle, and the control record 1 below the diagram (no recurrent inhibition) illustrates that this spike really is tonically active during the time required for the experiment. In the

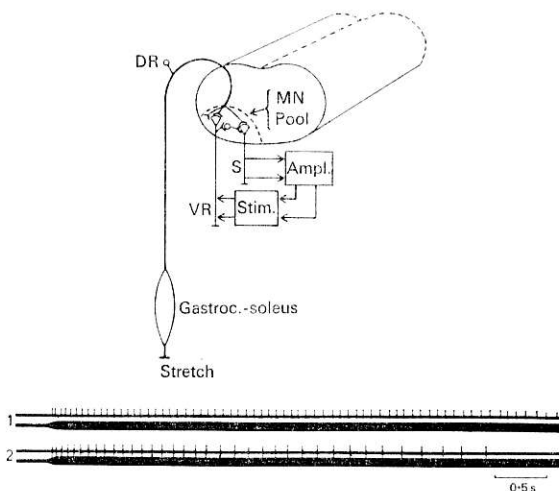


Fig. 41. Experimental arrangement in diagram and sample of experiment on functionally isolated single fibre below. Symbols, DR, dorsal root; VR, ventral root; S, single fibre from ventral root; MN, motoneuron. Spike from single ventral root fibre amplified and connected to start antidromic shock from stimulator to portion of VR of same segment. Recurrent loop shown. Spikes activated by stretch of knee extensors in the manner shown by record 1 below. Record 2 is same strength of pull but with antidromic shock locked to tonically discharging spike (note artifact). Rate and length of pull (15 mm) indicated by length-recorder below (Granit and Rutledge, *J. Physiol.*, 1960).

record 2 of Figure 41 the spike (in S) is connected up to evoke the full recurrent effect obtainable from the root (VR). What is shown is that the inhibition provides means of smoothly ending a tonic muscular contraction by the mere automatism of it being present. No special grading of inhibition is required. This may well be one of the roles it has to play in the normal life of an animal, i.e. smoothly stopping lingering excitations.

In view of the results of the previous section, which showed recurrent inhibition to be strictly additive, it is surprising now to find it apparently cumulative (in Fig. 41). Part of the explanation may lie in the locking of

the inhibition to the firing spike, because, as the frequency is suppressed by the recurrent volley, the latter has a chance of recovering its potency in the gradually lengthening intervals between the spikes. Another possibility that cannot be excluded is the occurrence of some post-tetanic potentiation at the synapses on the Renshaw cell. In natural discharges the inhibition would actually be locked to the firing spikes and so be cumulative in the manner shown. The result illustrated in Figure 41 can thus be regarded as a demonstration of the process of frequency limitation in operation.

In pursuing these problems (Granit, Haase and Rutledge 1960; Granit and Rutledge 1960) we were nevertheless compelled to emphasize a different and more fundamental explanation of the cumulative effect of recurrent inhibition. It turned out that it was by no means necessary to lock the spike to the recurrent mechanism in order to obtain a cumulative depression of its firing rate. In order to understand what takes place, it is necessary to realize at the outset that frequency limitation as a concept implies that a motoneuron (within limits) has become independent of the quantity of excitation to which it is subjected. A given constant firing rate can be supported by a greater or lesser surplus of excitation. When the margin of excitation barely suffices for maintaining a given rate of discharge, the recurrent hyperpolarization effectively stops the firing. With a greater surplus of excitation the level of depolarization in the motoneuron will be re-established from spike to spike more readily.

In Figure 42 an antidromic tetanus is inserted into a running tonic discharge at the constant intervals marked by the small oblongs on the abscissa. The moments 1, 2 and 3 of the plotted curve reappear in the records 1, 2 and 3 of the inset. The important point to note is that it takes increasingly longer time after the recurrent tetanus for the stretch reflex to return and re-establish its firing rate. The increase of this pause from 1 to 3 is out of proportion to the change in firing rate, which is not really observable until after the moment 2. Until then the frequency of discharge has been constant for some 20 s. It is better understood today than when the experiment was done, that the gain of this tonic motoneuron would have been very low and so one should not expect great changes in firing rate in spite of the long duration of the experiment (over 70 s). But from the increasing duration of the recovery of the maintained stretch reflex after each recurrent inhibition one is entitled to suggest that there was a gradually increasing loss of drive on the excitatory side. Where the diagram ends on the right, the reflex abruptly gave up at the last antidromic attack and never returned. From several

experiments of this general type it was concluded that the cumulative effect of recurrent inhibition is essentially a measure of the time course of a dwindling excitatory surplus and has less to do with the recurrent process as such.

If this explanation of the cumulative effect of recurrent inhibition is correct, it should be possible to prevent 'cumulation' by post-tetanic

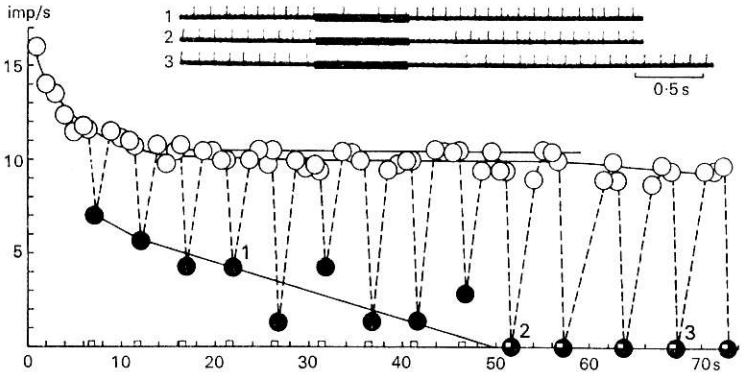


Fig. 42. Antidromic tetanus inserted into tonic stretch reflex of functionally isolated single fibre. Pull of 15 mm on knee extensors. Tetanic antidromic inhibition at 114 per second inserted for 0.7 s at regular intervals as marked by rectangles on abscissa (running time). Frequency of discharge constant between the two parallel horizontal lines. ●, number of impulses (imp/s) during the periods of recurrent inhibition. Inset: original records at moments marked 1, 2 and 3 in the diagram. Note that when delayed recovery after recurrent inhibition begins, then discharge frequency fails to reach its original level immediately (at this rate of repetition of antidromic stimulation periods). Discharge stopped for good with last period of stimulation, having been four times temporarily silenced (Granit and Rutledge, *J. Physiol.*, 1960).

potentiation of the stretch reflex. This proved to be the case (Granit *et al.* 1957). Also by electrical stimulation of the muscular afferents it is possible for some time to support firing well enough to prevent recurrent inhibition becoming cumulative.

The non-visible surplus of excitation in the stretch reflex may partly, at least, come from maintained depolarization at the distal portion of the dendrites. An analogy is provided by some cells in the lobster cardiac ganglion (Hagiwara and Bullock 1957) in which the firing zone is far enough from the soma never to produce more than small fluctuations, synchronous with the spikes, in the membrane potential of the latter. It is not necessary to assume that after-hyperpolarization restores the membrane potential over the whole dendritic network of a motoneuron. We simply do not know the answer. Do the dendrites of

motoneurons have a 'maintenance function' of the type suggested? Or should one assume that a maintained input frequency fully accounts for this function? At any rate, without it a tonic motoneuron easily falls a prey to recurrent inhibition.

Recurrent excitation

While it is possible to suggest a number of tasks for recurrent inhibition based on experimental results such as those mentioned above, it is not so easy to allot a role to recurrent excitation. The most important disclosure of research on recurrent excitation is the finding of Wilson and Burgess (1962a) that it is a disinhibition, i.e. a release from an inhibition which consequently leads to excitation. Interesting contrast phenomena are produced in the *Limulus* eye by disinhibitions alternating spatially with inhibitions (see summary by Ratliff 1965) and the recurrent excitations in the spinal cord may be analogous effects. In pharmacological tests, recurrent facilitation behaves like recurrent inhibition (Wilson 1959), suggesting a fundamental similarity. Wilson (1966) points out that in the spinal cat recurrent facilitation is more labile than recurrent inhibition, but seems to believe that at times the two systems are activated independently. Recurrent facilitation is best detected with firing flexor cells as indicators (Wilson and Burgess 1962b).

When discussing mechanisms regulating the firing rate of motoneurons, it is necessary to consider the roles to be allotted to the mechanisms described, even when such designations remain proposals. The aim, after all, is to carry teleological understanding to its limit in order to find out whether a logical structure of knowledge can be erected that way. Recurrent facilitation can at the moment be fitted into this programme by the general statement of Wilson *et al.* (1960) that recurrent excitation is more prominent when extensors act upon flexors and serves to maintain a 'proper balance of excitability between flexors and extensors' (Wilson 1966) by opposing the Ia reciprocal type of inhibition from extensors on flexors.

Concluding remarks

'Most mechanisms in the nervous system have various tasks to perform and we can but humbly admit our ignorance when trying to make sense out of the masterpieces of biological engineering involved in motor control. It is hard enough to unravel some major features of design' (Granit 1966, p. 158). I can think of a no more fitting end than this quotation to

state my attitude to the material presented in this lecture. In particular it holds for recurrent effects, as a look at the complex interneuronal system of Figure 38 should make obvious. The recurrent collaterals may themselves branch within this system and produce effects which have not yet been revealed or, if observed, seem difficult to interpret (Hultborn, Jankowska and Lindström 1968a). Recurrent inhibition may, on occasion, also reach the gamma executive (Brown, Lawrence and Matthews 1968; Ellaway 1968; Grillner 1969) though recurrent inhibitions were not found to do so (or only exceptionally) in the experience of several authors such as Granit *et al.* (1957), Hunt and Paintal (1958), Eccles *et al.* (1961b) and Voorhoeve and von Kanten (1962), all using antidromic stimulation. How are such discrepancies to be interpreted? We do not know, but they may be due to involvement of the interneuronal system that makes the circuit facultative. Interneurons can, of course, introduce numerous combinations of effects; it is indeed, their purpose to produce flexibility and adaptability of otherwise fixed control systems. As an example may be mentioned the work of Hultborn *et al.* (1968b) indicating a common interneuron affected by recurrent inhibition and monosynaptic Ia excitation, likely to be the one mediating Ia inhibition to motoneurons. With such complex interactions a question of prime importance always concerns the frequency of their employment in the organism. This is but rarely answered.