

The History of Reflexes Part 2

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PART 2: FROM SHERRINGTON TO 2004

During the twentieth century the neurophysiological mechanisms of the reflex has been intensely described in relation to other neuronal functions. We shall analyse these reflex mechanisms in comparison to the development of the neurosciences. Studies on spinal cat reflex physiology were being carried out by Sherrington's school at the same time as the revolution in nervous system histology was taking place. After the discovery of 'la reazione nera' (the black reaction) by Golgi (1843-1926) in 1873, the structure of the CNS gave rise to much debate. There were those who claimed that the nerve cells were all connected together by central networks. Golgi, following J. von Gerlach (1820-96), explained that the relations between two cells are continuous, whereas Waldeyer (1836-1921), in his 1889 review of the 'neuron theory', reported that the cell body has short extensions called dendrites, as suggested by His (1831-1904), and one much longer one, called the axon, as suggested by Kolliker (1817-1905). C. Sherrington (1857-1952) named the contacts between contiguous neurons for the first time in 1897 in a textbook edited by M. Foster, where he called them 'synapses'. Most histologists agreed with this theory, and the greatest of them all was in fact S. Ramon y Cajal (1852-1934), who arrived on the scene from his native Aragon in 1889 at the international anatomical meeting in Berlin. Within about 20 years had described most of the main centres involved, especially those in the spinal cord: his figures are still perfectly valid to day.

This was the context in which Sherrington began to make his mark. Few people have ever been as influential: Ramon y Cajal was the anatomist and Sherrington the physiologist of the nervous system. This was the beginning of an extraordinary period when most of the reflexes of the cat spinal cord were described in great detail. In 1895, Sherrington was appointed as a professor at the University of Liverpool, where he worked for about 18 years. In 1913, he moved to Oxford. He began to focus on the spinal cord, to which he devoted most of his research. To determine the cutaneous fields, he used a nerve degeneration technique consisting of cutting three roots above and three roots below the one he wanted to characterize. He studied the patterns of muscle innervation and the various motor nuclei located in the spinal cord. The spinal reflexes were studied in cats with 'decerebration rigidity'. CNS transection at the level of the mesencephalon induces extension rigidity in the head, the four legs and the tail in response to hyperactivity of the gamma loop (see Paillard, 1969). Sherrington studied in detail the knee-jerk reflex in the cat.

Sherrington soon became convinced of the importance of muscle sensory information (Swazey, 1969). From 1894 onwards, he established that one-third to one-half of all the myelinated fibres in the motor nerves do not degenerate after section of the ventral roots. In 1889, Ruffini eventually identified the muscle spindles observed for the first time in 1860 by Wiersmann and mentioned by Khun in 1863. In 1906, Sherrington, in a paper given in honour of J. H. Jackson, defined proprioception as opposed to extero- and interoception. Another fundamental concept developed by Sherrington was that of the motoneuron, which was at first assimilated to a final common pathway. These cells receive excitatory as well as inhibitory information from very diverse sources, from both descending and segmental pathways, and each motoneuron integrates all these influences and commands the set of muscle fibres projecting from it (Figure 1). At this level, the cell body works out a sort of algebraic sum of opposite effects. At this period, in comparison with the present-day picture, the soma was thought to play a much more important role and there was no awareness of the importance of the spatial organization of the membrane receptors in the dendrites.

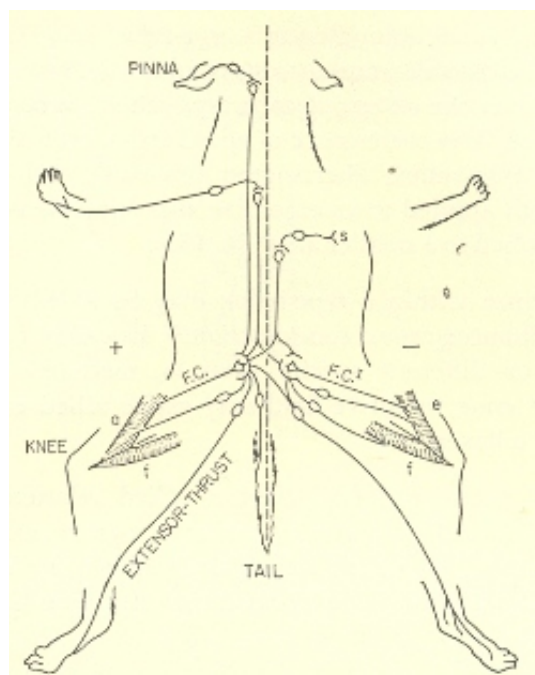


Figure 1: The principle of the 'common path'. This diagram from C. Sherrington illustrates the common path (FC). Motoneurons from the vastus crureus muscle of a dog or a cat, an extensor muscle of the knee, receive convergent informations from different types of reflexes. Reflexes with excitatory effects (+) are on the left, those with inhibitory effects (-) on the right.

In 1904, Sherrington was invited to the USA, where he gave a series of 10 lectures at Yale University (the Silliman Lectures). This was the starting-point of his famous book, *The Integrative Action of the Nervous System*, published in 1906 (Figure 2).

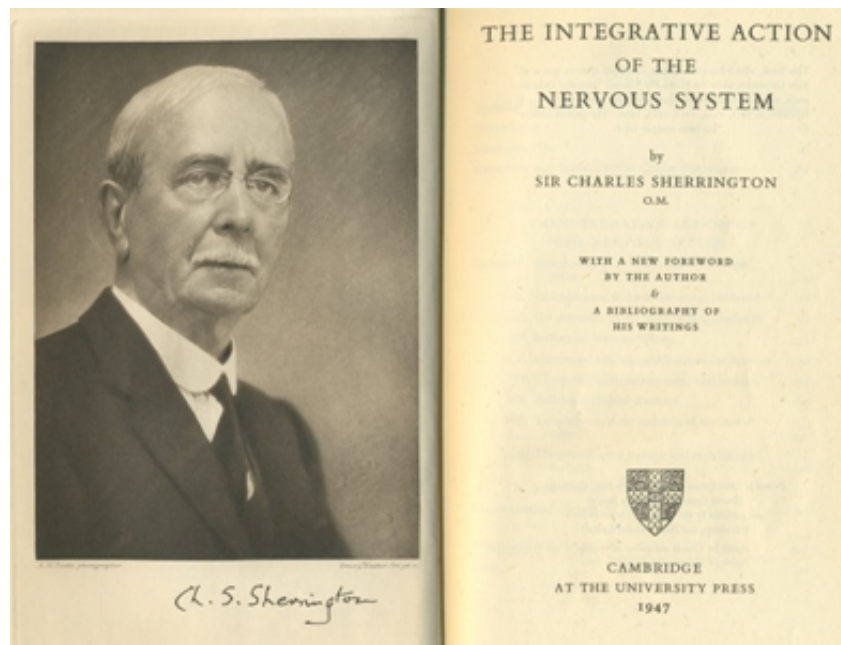


Figure 2: First page of Sherrington's famous book, *The Integrative Action of the Nervous System* (1906); this is the 5th edition of 1947.

The main theme here was the idea that the integrative power of the CNS is due to a set of reflexes coordinating the separate activities of the different organs. This book was an essential contribution, since it gave an overall functional description of the whole CNS. In the Introduction, the author began by describing the simple reflex, which he took to be the most basic functional unit of integrative action visible in the spinal animal, before dealing with the complex patterns of reflex muscle integration controlled by the brain in intact animals:

"There is the coordination which a reflex action introduces when it makes an effector organ responsive to excitement of a receptor, all other parts of the organism being supposed indifferent to and indifferent for that reaction. In this grade of coordination the reflex is taken apart, as if separable from other reflex actions. This is the 'simple reflex'. A simple reflex is probably a purely abstract conception, because all parts of the nervous system are connected together and no parts of it is probably ever capable of reaction without affecting and being affected by various other parts, and it is a system certainly never absolutely at rest. But the simple reflex is a convenient, if not a probable fiction" (p. 7).

With this approach, Sherrington obtained major findings about the physiology of the spinal cord. Working on the decerebrate cat, he and Liddell described the myotatic reflex in 1924 and 1925. When the quadriceps, a knee extensor muscle, was lengthened, they observed that after a very short latency there was a great increase in the muscle force; this force disappeared when the muscle was relaxed. When the nerve of the muscle was cut, a similar stretching movement induced only a residual force due to elastic deformation of the muscle. The difference between the two tensions corresponds to the reflex response (Figure 3A). Two components can be distinguished in this myotatic reaction: a fast, phasic component due to the brief lengthening, and a tonic one corresponding to the maintained stretch. The second part of the reflex mainly occurred in the slow extensor leg muscles providing the forces required to resist the pull of gravity. In the same study, Liddell and Sherrington also established that if a flexor muscle, the posterior biceps, is also stretched during an extension reflex, this reflex is sharply abolished (Figure 3B). This provided evidence that the activity of flexor and extensor muscles is coordinated. It was only in 1943 that Lloyd, upon recording the latency of the electrical activity occurring in the dorsal and ventral roots, established that this mechanism involves only a single synapse (Figure 3C).

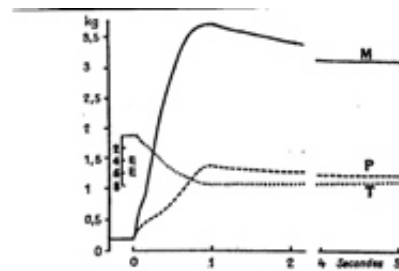


FIG. III a, 5. — Réflexe myotatique d'un muscle quadriceps chez le Chat décerébré.

(D'après Liddell et Sherrington, Proc. Roy. Soc., 1924, B 96, 212-242).

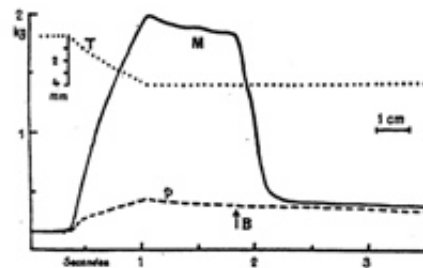
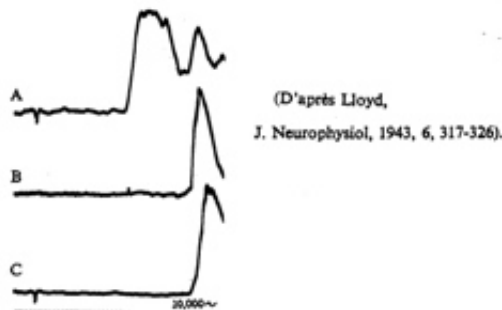


FIG. III a, 11. — Inhibition du réflexe myotatique d'un muscle quadriceps provoquée par l'étirement d'un muscle antagoniste, le muscle biceps postérieur.



(D'après Lloyd,
J. Neurophysiol, 1943, 6, 317-326).

Figure 3: Myotatic reflex of the quadriceps muscle in a decerebrate cat (from Laporte Y. 1976, *Activité réflexe de la moelle épinière*. In Kayser C., *Physiologie*, 3rd ed. Flammarion, Paris, III, Chapter 3.

Upper traces (A): The muscle tendon is attached to an isometric myograph. T: The muscle is stretched from 8mm. for one second. M is the delivered tension and P the developed tension when the muscular nerve is cut.

Middle traces (B): Inhibition of the myotatic reflex of the quadriceps muscle by stretching of the antagonist muscle, the posterior biceps (Liddell and Sherrington, 1924 and 1925).

Lower traces (C): Monosynaptic transmission in a myotatic reflex: A: afferent volley in the first sacral dorsal root after a short stretch of the triceps sural muscle. B: monosynaptic response of the first ventral sacral root after stimulation of the corresponding dorsal root. C: reflex discharge recorded in the same ventral root after a stretch of the muscle (Lloyd, 1943).

In 1932, Sherrington obtained the Nobel Prize for discovering the 'motor unit'. He shared this prize with Adrian, who described how isolated sensory units function. We can mention and endorse Ragnar Granit's judgement that:

"[Sherrington's] greatest contribution to the physiology of the nervous system was to supply the functional equivalents of the anatomical (bases of neural organization). His experiments led up to the functional unit, his concepts centered around unitary behaviour of cells activated or inhibited at synapses, and his 'integrative action' . . . is the knitting together of cells activated across synapses for a common goal . . . in the present era unitary analysis of nerve cells and their axons, pushed a second time to frontier of research by Lord Adrian's work in the twenties and thirties, has given a richer harvest than any other approach to the physiology of the central

nervous system" (cited in J. P. Swazey (1969), p. 175).

However, Sherrington's work focused so strongly on the reflexes that he missed some important discoveries. One of his contemporaries working on very similar lines, T. Graham-Brown (who, in response to an article published in 1910 by Sherrington on 'reflex stepping', wrote two major articles, one in 1911 and the other in 1914), reported that the processes underlying cat locomotion are due to spinal 'half centres': if the dorsal roots of an acute cat are cut, the ventral roots are still able to induce a rhythmically patterned activity. It seemed that these data were forgotten for 60 years, for it was only in 1971 that Viala and Buser (1971) presented on a spinal paralysed rabbit a central rhythm (Figure 4).

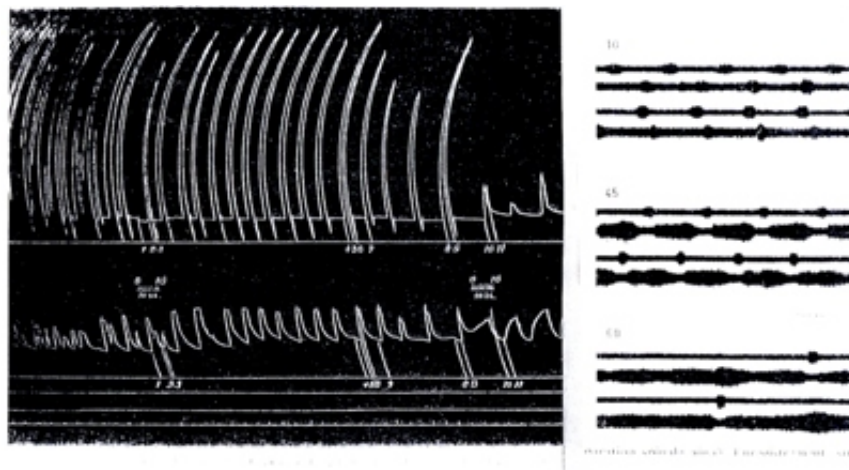


Figure 4: Central rhythmic activities recorded at the level of the spinal cord. Sixty years separate these two recordings. Left: In a decerebrate cat the rhythmic contraction of the tibialis anticus (upper) and of the gastrocnemius (lower) muscles is recorded, after a complete de-afferentation with section of all the dorsal thoracic roots (Graham Brown, 1911, Fig. 1). Right: Fictive locomotion in a spinal rabbit is induced by bath application of 5HTP, L-Dopa and Amphetamin; here the activities of the anterior tibialis and of the gastrocnemius right and left motor nerves are recorded 15, 45 and 60 min. after the amphetamin injection (Viala and Buser, 1971).

A sort of compromise between the two hypotheses was presented in a study by Engberg and Lundberg (1969), showing that in the chronic cat, the extensor hind limb muscles are activated before the leg touches the ground. It confirmed a central origin of the alternative command (Figure 5) and meant that although the reflexes described by Sherrington are useful for coordination purposes, they do not explain the rhythmic alternating pattern typical of locomotion (see Wetzel and Stuart, 1976).

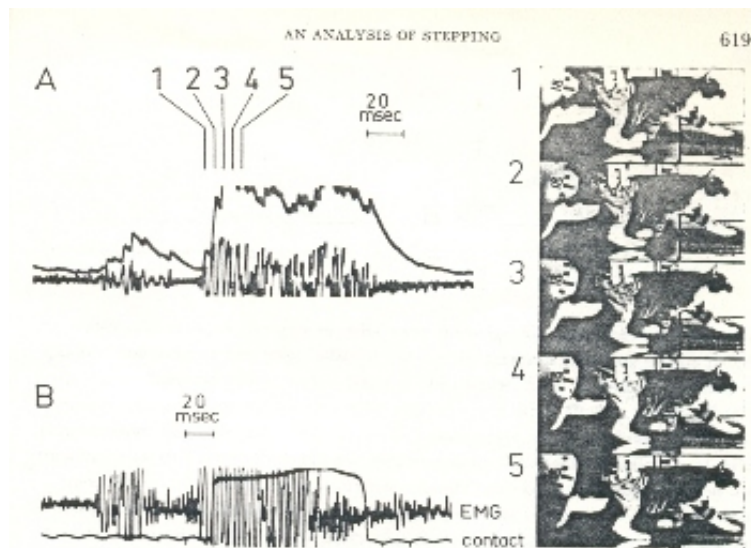


Figure 5: Analysis of the onset of main extensor activity during walking.

A: direct and integrated activity from the vastus lateralis related to five pictures of the hindlimb movements (200 pictures/sec). The foot does not touch the ground before the number 3. The extensor EMG recorded with the ground contact demonstrates that it arrives earlier. (Engberg and Lundberg, 1969).

B: Without the integrated EMG the spare beam is used to indicate foot contact with the ground. The upward deflexion when the foot touches the ground is before the EMG activity.

With his 'dualistic approach' to the CNS, Sherrington's picture of the brain involved completely separating the physiological and psychological functions. In his studies on the primate cortex, he accurately described the limits of the motor cortical area in the chimpanzee (Grünbaum and Sherrington, 1903), and concluded:

"We thus see from the biological standpoint, cerebrum, and especially the cerebral cortex, as the latest and highest expression of a nervous mechanism which may be described as the organ of, and for, the adaptation of nervous reactions" (Sherrington, 1947, p. 390).

In his opinion, the cortex communicated with the external medium through 'receptors, which may react to the objects at a distance' and were sensitive to odour, light and sound; these receptors play an essential role in controlling the various spinal cord reflexes. Sherrington insisted on the fact that the spinal activities are modulated by the cerebral cortex. He always maintained that the activity of the CNS has a sensory but never a central origin.

The next few episodes in the story of the spinal cord and the various types of reflexes focus on the disciples of Sherrington, the most famous of whom was surely J. Eccles (1903-91), who published an enormous amount of data on this structure. Eccles was working in Oxford in 1927 with R. Granit before joining Sherrington. He learned the antidromic motoneuron stimulation technique with D. Denny-Brown. In collaboration with Sherrington, he discovered the existence in the motor nerves of two populations of motor fibres, a large-sized one and one with a much smaller diameter. These scientists underestimated the importance of the second population, which they took to be merely motoneuron collateral branchings. It was only in 1945 that L. Leksell established that the small-diameter population corresponded to another group of motoneurons, the gamma population, or fusimotor command, as it has been called in contrast to the skeletomotor command. In 1946, Lloyd clearly described the 'myotatic unit': each muscle is commanded by motor units which elicit the contractions, while a parallel structure controls the muscle spindles via the gamma motoneurons. The large-diameter (20- μ) Ia afferents facilitate the activity of the motoneurons of the stretched muscle and the 'homonymous' muscles (synergistic muscles) monosynaptically, whereas they inhibit the motoneurons of the antagonist muscles disynaptically. The Golgi tendon organs, which reflect the muscle tension when it contracts, send afferent

messages to the spinal cord via other large fibres, the Ib afferents, which inhibit the homonymous muscles disynaptically and facilitate the antagonist muscles (Laporte and Lloyd, 1952).

It was Eccles who gave the first complete description of the myotatic reflex, when he started using intracellular techniques on the cat spinal cord. In 1950, this new method had already been presented in two papers: a study by Nastuk and Hodgkin on the use of intracellular recording methods on muscle fibres (1950) and a preliminary report by Fatt and Katz on a similar neuromuscular transmission process (1950). Eccles was lucky to be working in Dunedin (New Zealand) with an electronic engineer, J. S. Coombs, who was able to build a suitable amplifier for recordings of this kind, and an expert, Brock, capable of finely stretching the glass micropipettes. These experiments were carried out around Christmas 1950 and the results were first published at a meeting of the local Medical Society on 31 July 1951 (see Brock et al., 1951). The first results obtained confirmed that the synaptic facilitation was attributable to a relatively long depolarization. The authors called these excitatory and inhibitory responses, the excitatory post-synaptic potentials or PPSEs and Inhibitory post-synaptic potentials or IPSPs. When Eccles discovered that the inhibitory effects corresponded to hyperpolarizations, this staunch defender of electrical conduction at the synaptic level immediately changed his mind and recognized that the sole possible explanation for the synaptic exchanges observed was a process of chemical secretion (see Eccles, 1992). When Dale (1954) heard about Eccles's remarkable conversion, he said it reminded him of "Saul on his way to Damascus when the sudden light shone and the scales fell from his eyes!" In a book published in 1957, Eccles summarized the various circuits in the spinal cord, including the classical stretch reflex pathway, the antagonist connections and the recurrent inhibitory pathway described in 1940 by Renshaw. Eccles then stopped working on the spinal cord, but several other groups continued to investigate various aspects of these spinal reflexes. Here we will describe the research carried out along four different lines.

Lundberg's group, in collaboration with E. Jankovska in particular, described in great detail the pattern of organization of the various types of interneurons, which were classified as Ia, Ib and group II: their names correspond to the types of sensory fibres they receive (Baldissera et al., 1981, Jankowska, 1992 and Hultborn, 2001). These authors observed great convergence between the descending pathways and the sensory afferent (Figure 6).

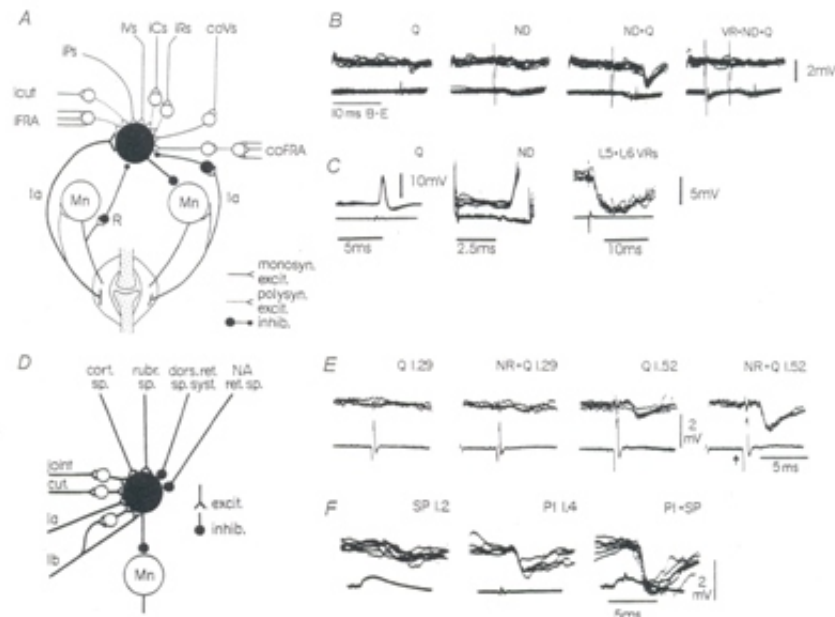


Figure 6: Convergence on interneurons in the pathway of reciprocal Ia inhibition (A-C) and on the interneurons in the Ib inhibitory pathway (D-F).

On the right (A and D) are represented the circuit diagrams (both interneurons being in black), that which summarize both, the peripheral as the supraspinal connections of these two types of

interneurons. On the left is represented the motoneuronal intracellular response after different types of stimulation (Hultborn, 2001).

Various muscular and cutaneous afferents and others originating from joint receptors and various descending tracts such as the cortico-spinal, rubro-spinal, reticulo-spinal pathways were all found to converge onto interneurons of the same kind. In humans, Crone et al. (1990) found a parallel with what occurs in the cat and described several spinal reflex circuits in patients, which they suggested might be involved in various activities. P. Rudomin and R. F. Schmidt (1999) reported that before reaching the motoneurons, afferent sensory messages may be filtered by Gabaergic interneurons, some of which are activated centrally and others via peripheral afferents. These new data on presynaptic inhibition greatly complicated the picture of spinal activity and meant that reflexes definitely are reorganized in the central networks.

The neuro-muscular command has been studied by R. Burke et al. (1973), who performed some remarkable research on the cat Gastrocnemius muscle (Figure 7). Using an intracellular method to study motoneuronal activity, this group obtained a complete picture of the various kinds of motor units, depending on the type of muscle fibre contraction they induce. Three types of units were defined in this way: the first group (S) induces slow contractions with only weak tetanic effects, but they are continuously active and are mainly involved in maintaining muscle tone. The second group (FR) are of the fast resistant type and are involved in most common movements. Their histochemical profiles are intermediate ones. The last group (FF), which are of the purely phasic type, are the most powerful, but they are highly fatigable because of their anaerobic metabolism.

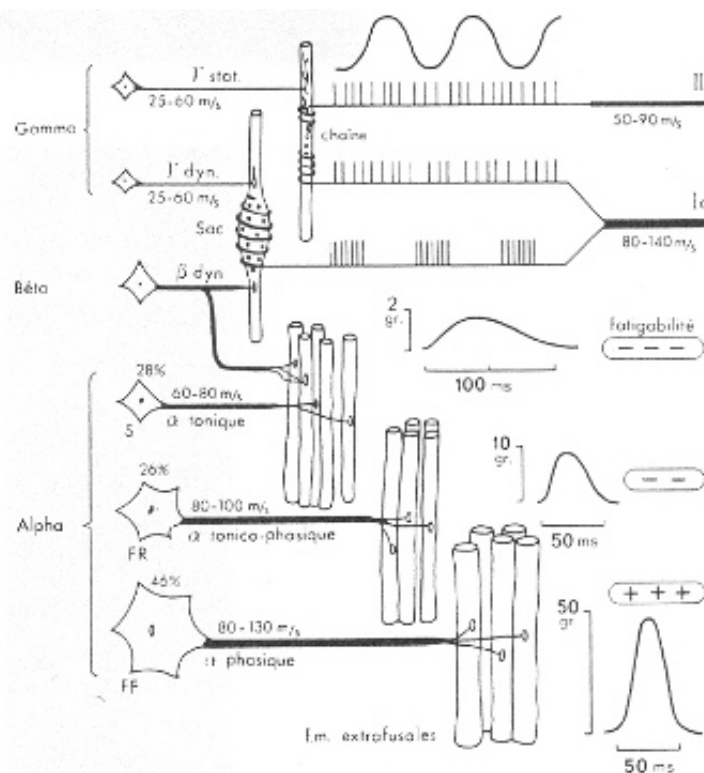


Figure 7: Different types of alpha and gamma motoneurons and their respective role. The alpha motoneurons constitute different types of motor units with slow fibres (s), fast-resistant fibres (fr) and fast fibres (ff). In the muscle spindles, the static gamma motoneurons stimulate the chain fibres and the dynamic gamma motoneurons stimulate the bag fibres (Paillard, 1976).

Once Baker (1967) had described the anatomical distribution of the muscle spindles, P .B. C. Matthews (1972) gave a complete picture of their microphysiological behaviour. The fusimotor command is in fact a twofold mechanism based on two types of gamma motoneurons, the one phasic and the other tonic. If a sinusoidal stretch is imposed on an isolated muscle spindle, stimulation of the phasic gamma motoneurons increases the sinusoidal response, while static

conditions give rise to a slow, continuous muscle spindle activity (Figure 7). The phasic gamma motoneurons preferentially innervate the nuclear bag fibres, while the static gamma motoneurons innervate the nuclear chain and the group II receptors. Paillard (1955) compared the responses of the soleus muscle to a mechanical stimulation applied to the Achilles tendon with the Hoffmann reflex occurring when electrical stimulation is applied to the popliteal nerve (Figure 8).

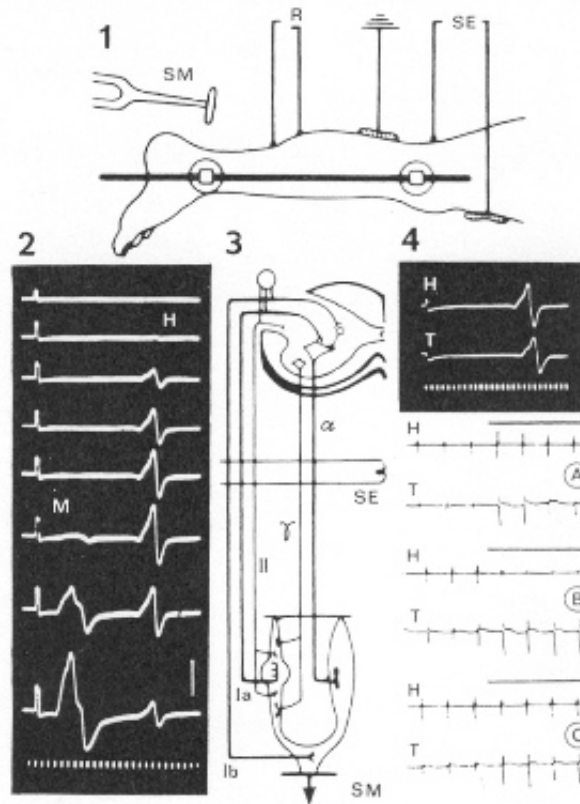


Figure 8: Comparative study of Hoffmann (H) and of jerk tendon reflexes in Human.

- 1) Dispositive of the experiment: SM: mechanical stimulation, R: recording of the EMG soleus. SE: electrical stimulation of the external popliteus nerve. 2) Response of electrical stimulation with the H reflex and the M response. 3) General schema of the sensory and the motor pathways. 4) Comparative responses of the two reflexes: H is induced in the right limb and T is induced in the left limb (from Paillard, 1955).

These comparisons were most fruitful, since the first response was found to involve the entire gamma loop, the muscle spindle, the Ia afferent and the spinal centre, whereas the second response involved only the Ia receptor group and the spinal centre (Paillard, 1969). Some centrally controlled behavioural activities differentially affecting one reflex or the other then yielded new insights into the central spinal regulations occurring in humans. Several authors, and in particular P. B. C. Matthews (1991), established that the stretch reflex gives rise to several responses involving other loops running through the cortex and the cerebellum. A large number of physiologists and psychologists used this reflex to investigate the role of the central structures and understand how they function. The great variability shown by these motor responses seemed likely to reflect the variability of some central structures (Figure 9).

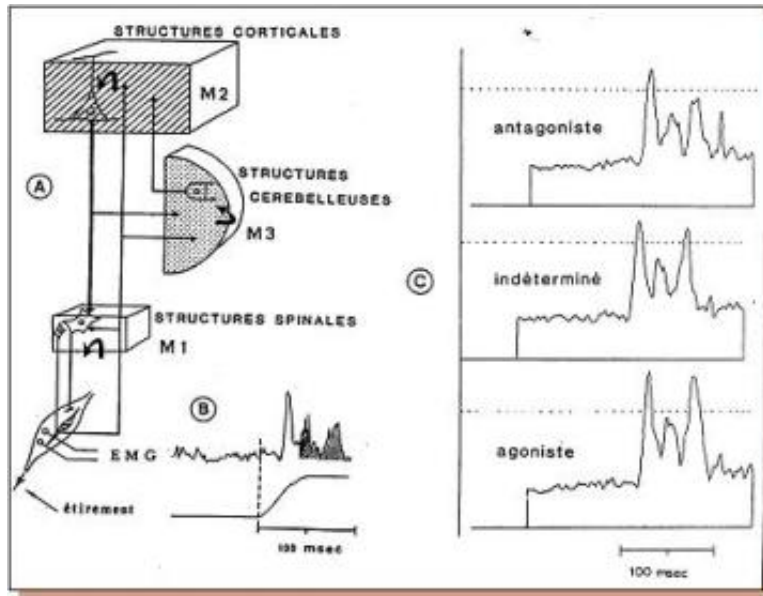


Figure 9: The complex segmented response seen on stretching a human muscle. Left: A stretch reflex induces 3 EMG bursts in the peripheral muscle. The first correspond to the monosynaptic response (M1); the second involves a cortical loop (M2) and the third goes through the cerebellum (M3). Right: Three types of EMG responses recorded in different muscles (Antagonist, Undetermined and Agonist).

The role of the multifunctional peripheral sensory loops was found to be twofold: first, they play a crucial role in the adaptation of flexors and extensors during posture and movements; and secondly, they contribute to anticipatory mechanisms occurring prior to the performance of actions. Merton (1953) put forward a hypothesis based on the 'follow up servo' assumption that the gamma loop plays a preparatory role for a forthcoming activity. According to this hypothesis, the fusimotor neurons are activated before the alpha motoneurons, so that the circuit activated prepares a given muscle by putting it in the most suitable position before the start of a movement (see Figure 10 and Paillard, 1976).

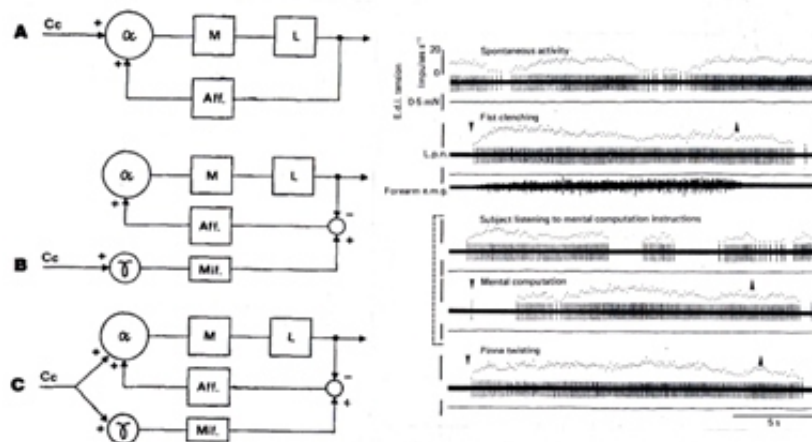


Figure 10: The alpha and gamma motor commands. Right: The different conceptions on the control of the extrafusal muscles (M) with the group I afferences (Aff.). A: Direct alpha command with proprioceptive afferenes. B: Indirect alpha command through gamma loop. (Merton theory) C: Motor coactivation of alpha and gamma motoneurons (from Paillard, 1976). Left: Modulation of the discharge of a fusimotor fibre of the Extensor digitorum longus in different situations. Instantaneous frequency discharge demonstrates the great variation of its activity depending upon some cognitive situations (for details see Ribot et al., 1986).

However, when both motoneuronal discharges were recorded together, no such early fusimotor response was actually observed. It therefore emerged that both commands are activated simultaneously. Very few studies have been carried out on fusimotor activation in humans. However, Ribot et al. (1986) recorded the activity of six gamma fibres. Although this is very small number, the results obtained in this study were extremely interesting, since they showed that gamma motoneurons are extremely sensitive and able to respond to stimuli of highly specific kinds (noise, emotion, cognitive tasks, etc.). If a subject is able to watch his own gamma discharge pattern, he can control it voluntarily. The gamma control seems to be mainly a central contribution to adapting peripheral activity to the ongoing task requirements (Figure 10).

Reflexes, not only in mammals but also in all animal species (Gray 1950), attracted considerable attention in the field of physiology during at least the first part of the twentieth century. A completely different picture of motor control gradually emerged from these studies from that described above. Wachholder (1928) was one of the first authors to suggest that movements are centrally initiated, but his work unfortunately remained completely in the shade. One important discovery was made by Berger (1929), who, fifty years after Caton (1875), described electrical activities in the human scalp. He found 'the alpha rhythm', which seemed most intriguing, being present only when the subject's eyes were closed, i.e. when no external visual afferent messages were being processed. The opening of the eyes abolished the response. Other rhythms were soon described and the cortex was found definitely to have its own separate pattern of activity. The idea that there existed a well-organized central activity was in fact generally recognized only when intracellular recording techniques became available. Studies on a large number of invertebrate preparations showed that a basic rhythmic pattern is present even when the central nervous ganglia are completely isolated and devoid of sensory inputs. B. Alving (1968), upon recording the rhythmical activity of one of the large neurons of an *Aplysia* using intracellular methods, established that this rhythm was of internal origin. She was able to maintain this neuronal activity even after attaching dendritic extensions with a hair to separate them from diverse afferents. In another invertebrate, the lobster, the isolated 'stomatogastric' ganglion showed several complex rhythmically patterned activities: the pyloric rhythm occurring in 14 neurons was recorded, for instance, after studying and identifying all the synapses involved (Selverston and Moulins, 1987). The Central Pattern Generator (CPG) has by now been definitely recognized as the structure responsible in both Invertebrates and Vertebrates for a whole range of very different motor behaviours (Delcomyn, 1980), especially locomotion (Grillner, 1981). During the same period, it was clearly established that neurons possess membranous currents of many more kinds than was previously thought to be the case, and that most of them are voltage-dependent. R. Llinas, who described a large number of new currents in the cerebellum (1988), summarized this particularity by saying that 'neurons are not platonic!' In addition, other studies showed that a whole range of neurotransmitters and neuromodulators, such as amines and peptides, controls their activation.

In conclusion, reflexes have been the first neuronal mechanisms in the history of research on the CNS to be properly and scientifically described. For a long time, they were the sole neural mechanisms to have been investigated at the anatomical, physiological and psychological levels. Research in this field focused at first on the sensory integration aspects and the CNS was taken to be a 'responding' system rather than a 'constructive' one. Since scientists at that time lacked the technological tools enabling them to explore the centre of nervous operations in greater depth, some of them, such as the behaviourists, opted for studying the CNS from the outside. However, as the French philosopher Merleau-Ponty (1908-61) pointed out (1942), a reflex can provide experimenters with a tool but it is not a behaviour:

"The reflex exists: it is a very special case of behaviour, which can be observed under given conditions. But it is not the main topic on which physiology focuses: it is not by studying reflexes that we will be able to understand the rest. Reactions obtained at the laboratory on a sick organism or under artificial conditions cannot be called biological reality. The aim of biology is to grasp what makes a living organism alive: the answer is neither a set of superimposed elementary reflexes nor the intervention of a vital force, as the mechanists and the vitalists with their realist

approach would have it – but its undecomposable patterns of behaviour” (ed. 1990, p. 48).

Nowadays, thanks to the revolutionary advances made in Neuroscience, we have a much more comprehensive and centralized functional picture of the CNS; studies are being carried out routinely on the brain in relation to various kinds of ongoing behaviour. What can be said about reflexes these days? The CNS is composed of several networks at each level: in the spinal cord, CPGs governing motor activity and the motility of the viscera have been described, and in the cortex neuronal assemblies are known to constitute the substrate for the most complex activities such as sensory integration, associative activities, preparation for action, etc. The circuitries underlying reflexes of various kinds are by now well known. Monosynaptic reflexes do of course exist, but an increasing amount of data are now available suggesting that these reflexes may in fact involve populations of central interneurons that are somehow linked to given neuronal networks. Monosynaptic reflexes may therefore involve neuronal networks by which they are closely controlled. This assumption is supported by at least three examples showing that reflex variability is closely correlated with central network activity: Clarac et al. (2000) have established, at least in invertebrates, that a stretch reflex which plays a postural role can be switched to an assistance reflex when a locomotor command is triggered. The activation of various types of interneurons results in this case in the formation of a new network that completely transforms the neural reflex circuit (Figure 11).

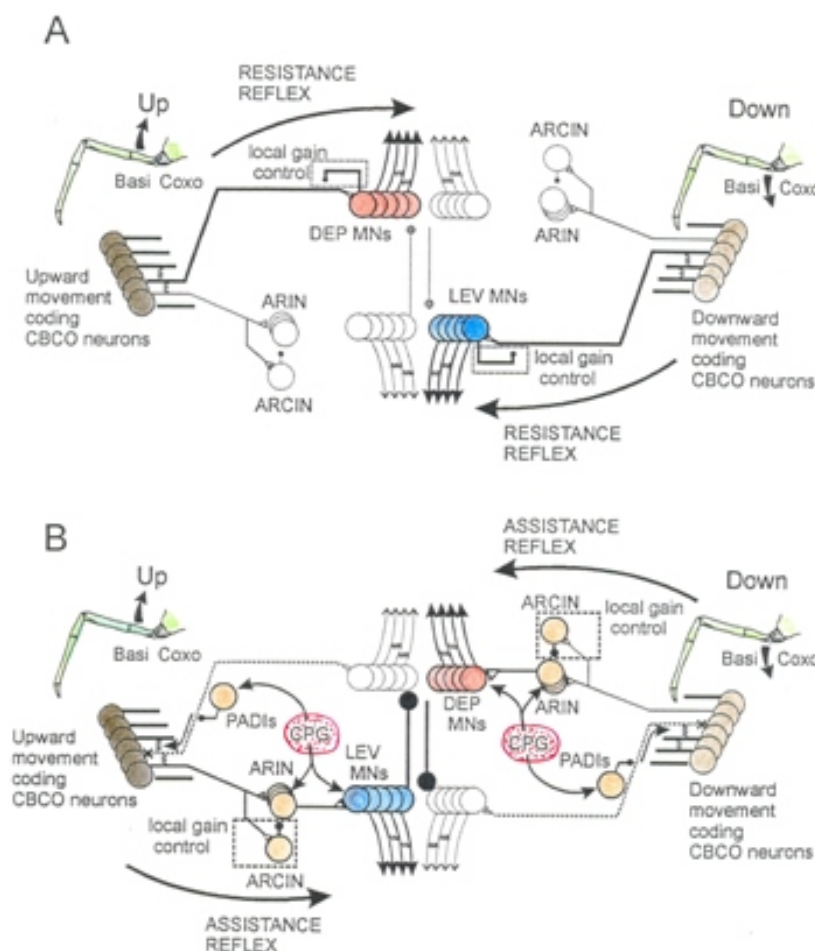


Figure 11: The modulation of the stretch reflex in the crayfish. In an 'in vitro preparation' the sensori-motor regulation is studied when a mechanoreceptor (CBCO) is stimulated. A: The levation (up) or the depression (down) of the CBCO strand induces a resistance reflex (analogous to a stretch reflex), which facilitates the motoneurons controlling an opposite movement. B: When the CPG is present, it induces a fictive locomotion; the reflex circuits are changed due to a presynaptic filter and to the activity of a group of interneurons (assistance reflex interneuron: ARIN). In that case, the mechanoreceptor (CBCO) facilitates the ongoing fictive movement.

Volpaw (1997), in his operant conditioning studies on the rat, monkey and humans, showed that reflexes are extremely variable and depend greatly on adaptive learning processes. This author established that the changes occurring in the neuronal circuitry are not only physiological but also anatomical, and suggested several points in the circuit where these modulations might occur (Figure 12).

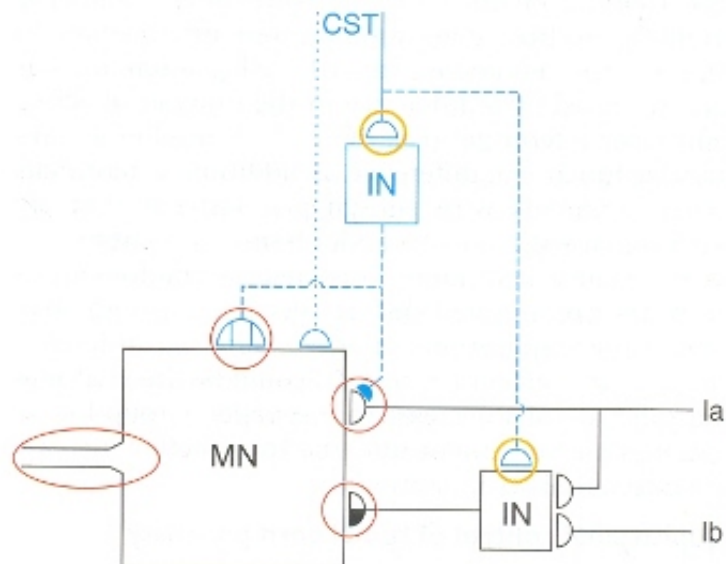


Figure 12: Reflex modulation due to spinal cord plasticity. MN indicates the motoneuron population of the triceps surae, Ia and Ib indicate Group I afferent neuron population and each IN indicates the spinal interneuron populations (open terminals are excitatory and solid terminals are inhibitory). Both, the peripheral and the descending pathways (in particular the cortico-spinal tract: CST) can deeply modulate the strength of the reflex (from Volpaw, 1997).

The last example is provided by the findings of Petersson et al. (2003) on the nociceptive skin reflex, which was first described long ago by Descartes. A painful stimulus applied to the skin is known to lead to a reflex muscle contraction serving to remove the skin from the harmful stimulus. The withdrawal is due to various skin modules acting via interneurons in spinal circuits. At birth, this reflex response is not yet set up, since it takes two weeks to become functional. This highly original learned mechanism is associated with sleep (Grillner, 2004; Figure 13). All these examples therefore show that even very short circuits such as the reflex ones have similar properties to those of the other central circuits.

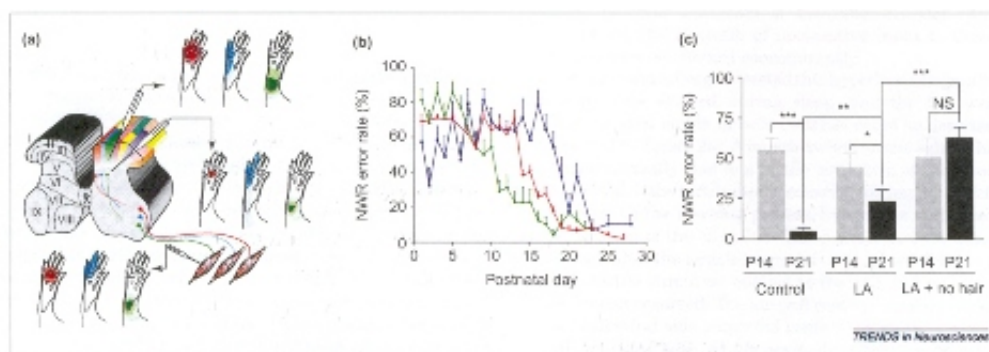


Figure 13: The nociceptive withdrawal reflex (NWR) is not efficient at birth in the rat; it needs three postnatal weeks to develop. (a): Afferent axons from different defined cutaneous areas project to columns of nerve cells in the dorsal horn; they connect the motoneurons via reflex encoder neurones. (b): reflex adaptation curves. (c): effects on sensory deprivation on NWR adaptation. Local anaesthesia (LA) or depilation delayed the adaptation (from Grillner, 2004).

The 'Reflex' has been presented here from Descartes to the present day as a sort of fundamental

component of the CNS. It has provided an ideal tool for investigating the complex pathways running between the nervous structures composing the CNS, and has made it possible to challenge previous ideas about these structures. Although it still provides clinicians with a useful tool, the CNS is now known to have its own functional principles, which need to be investigated using much more complex strategies. This means that a given reflex, with its wiring, is simply one of the many pathways involved in various combinations in the many networks of various kinds with which the CNS is endowed.

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