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Mario Wiesendanger

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I. Some Mechanisms Regulating the Motor Output

Introduction

The aim of this review is to familiarize the neurologist with neural mechanisms important for the understanding of central motor disorders, to point to new and promising developments in clinical neurophysiology and, last but not least, to discuss reliable methods for assessing muscle tone in patients. In the first part, spinal and supraspinal effects on motor units as well as spinal interactions will be summarized as far as the results, mainly derived from animal experiments, are relevant to the general problem. Much weight is given to the stretch reflex because this segmental reflex arc, with its many avenues for modulation from peripheral and supraspinal sources, has a key position in motor control. For obvious reasons no attempt was made to cover all aspects nor to present a systematic account. Thus, some important reflex pathways, such as the tonic neck and labyrinthine reflexes, all contributing to the excitatory state of the final common path, had to be neglected. There is a wealth of new discoveries on the physiology of the motor control systems which, so far, has only been incorporated to a small extent even in newer textbooks of physiology. The neurophysiologically interested reader is referred to reviews by LUNDBERG (1964, 1967), MATTHEWS (1964), MARCHIAFAVA (1968), PHILLIPS (1969), BROOKS and STONEY (1971), and EVARTS et al. (1971). At the time of finishing his review, a monograph by GRANIT (1970), embracing many years of his and others' work, and devoted to motor control had just been published; it is particularly recommended. Also no attempt was made to relate the role of various brain areas to the control of muscle tone as shown by studies of well-defined brain lesions in monkeys. The results of such an approach have been reviewed by MAGOUN and RHINES (1947), by DENNY-BROWN (1966, 1967) and by METTLER (1967, 1968). A remark about the pyramidal tract, hardly mentioned in this review, may be appropriate. As has been discussed in more detail elsewhere (WIESENDANGER, 1969), "pure" lesions of the pyramidal tract at the medullary level (the only place where the corticospinal fibers are well delineated and uncontaminated by other fiber systems) have not been described in human pathology. Transection of a bulbar pyramid in monkeys resulted in an impairment of the fine motor control of the fingers but not in spasticitiy of the "pyramidal syndrome". Similarly, those lesions in humans coming nearest to the experimental lesions in monkeys did not produce a spastic syndrome (BUCY and SIQUEIRA, 1964). However, some states of increased muscle tone, produced by lesions or by pharmacological agents will be discussed with respect to their possible use as models for spasticity or rigiditiy in humans.

The second part gives an account of reflex studies in humans, especially with regard to their relevance for evaluating the excitability of a given motoneuron pool. It will be introduced by a presentation of methodological aspects in the study of the motor system in humans. Again, the purpose is not to review the various technological problems systematically but rather to discuss some selected principles and also some methods recently introduced in clinical neurophysiology. A special section is devoted to the possible role of the gamma-system (the efferent fiber system to muscle spindles including its reflex and supraspinal control) in the normal and abnormal motor control of humans. The final chapter will summarize the most important methods used to evaluate abnormal muscle tone in patients.

Several reviews on the same general subject of muscle tone, each centering on particular aspects, some of which were barely touched upon in this review, have been published recently (JANSEN, 1962; RUSHWORTH, 1960, 1962, 1964; LANDAU, 1969; PEDERSEN, 1969).

The survey of the literature was concluded at the end of 1970.

1. Spinal Mechanisms Regulating the Output of Alpha-Motoneurons

Recording from dorsal root filaments in an immobile, anesthetized animal discloses a steady traffic of afferent signals reaching the spinal cord; these are mainly from slowly adapting receptors of the integument and of deep structures. When animals move about freely one has to imagine that, in addition, a large number of fast adapting receptors will come into play informing the central nervous system about position changes, velocity of movement, transient changes of contacts, etc. All these incoming signals influence the interneuronal and propriospinal network which, in turn, exerts its influence on the final common path, the motor unit. Virtually nothing is known, however, about the interactions within the spinal cord in an awake, freely moving animal. Nevertheless, the introduction of microelectrophysiological methods in the last 20 years has considerably enlarged our knowledge about the microcircuitry in spinal segments. In fact, the spinal segment with its clearly defined and well accessible input was an ideal model to start the meticulous work of unravelling the neuronal connectivity of nervous tissue. Furthermore, this system can be studied in isolation from superposed brain mechanisms and without anesthesia.

There is no need to describe segmental reflex pathways systematically; the principles of organization of spinal reflexes are dealt with in every textbook of physiology. The purpose of this chapter is to concentrate on newer results concerning the stretch reflex pathway. In animal experiments, the motor output may be measured in terms of tension or length changes of a particular muscle or muscle group (SHERRINGTON, 1947). More subtle changes of excitability are usually measured by means of the *monosynaptic test reflex* (RENSHAW, 1940). Variations in amplitudes of the synchronized ventral root volley were taken to indicate changes in excitability of the motoneuron pool under investigation as produced by preceding conditioning stimuli. By virtue of their lowest threshold in the muscle nerve, the group I fibers involved in the monosynaptic reflex (vide infra) may be excited in isolation by weak electri-

cal stimulation. The most precise information with regard to subthreshold excitatory or inhibitory effects was, however, gained from intracellular recordings by means of glass micropipettes which impale spinal neurons (BROCK et al., 1952; ECCLES, 1964). Excitatory and inhibitory effects are recognized by transient membrane potential changes, the so-called *excitatory postsynaptic potentials* or *EPSP's and the inhibitory postsynaptic potentials* or *IPSP's.*

The stretch reflex: central connections of the group Ia-afferents. It is now well established that the primary spindle endings provide the largest and most rapidly conducting stem fibers of muscle nerves, the Ia-fibers, having monosynaptic connections with motoneurons of the muscle from which the spindle afferents originate *("homonymous facilitation")* and with motoneurons of neighbouring and synergistic muscles *("heteronymous facilitation").* In addition, the Ia-afferents have collaterals impinging on interneurons, some of which are inhibitory to motoneurons of antagonists. This *reciprocal organization* is the basis of the *myotatic reflex.* The now classic notion is derived from experiments on hindlimbs of cats. More relevant for reflex studies in humans are, however, experiments performed in subhuman primates. PHILLIPS and coworkers (1969) have recently performed a thorough study on the stretch reflex pathway of the baboon's hand and forearm. Two important results are noteworthy: 1. Maximal Ia-volleys resulted in monosynaptic EPSP's which were always below the threshold for a propagated action potential of the motoneuron. This is in line with experiments in humans; electrical stimulation of the low threshold muscle afferents elicited no or only small monosynaptic reflexes (H-reflexes, see second part of this review) in the absence of a background facilitation. 2. The central distribution of Ia-afferents from one particular muscle is not confined to alpha-motoneurons of the same muscle; in the hindlegs of cats, there was considerable spread to neighbouring muscles. These two points are relevant for the later discussion of the stretch reflex as a servomechanism.

Besides their segmental effects the Ia-afferents convey information to supraspinal structures. There are two main ascending projections, one to the cerebellum, the other to the somatosensory cortex. A fast conducting system projecting to the cortical area 3 a which is situated at the bottom of the Rolandic fissure has recently been established in the baboon (PHILLIPS et al., 1971).

The tonic stretch reflex and the receptors involved. To the clinician, the phasic tendon reflex is the best known stretch reflex. It was shown by LLOYD (1943) that a brisk stretch of the muscle monosynaptically activated the motoneurons *via* the Ia-afferents. Thus, this reflex is the counterpart of the electrically evoked monosynaptic reflex. The stretch reflex, as originally described by LIDDELL and SHERRINGTON (1924) was, however, clearly a tonic phenomenon, i. e., the tension was produced by passive elongation of the muscle and maintained as long as the muscle was held in this position. A prominent tonic stretch reflex was only observed in good decerebrate preparations. For the soleus muscle of decerebrate cats, there is a linear relationship between length and tension of the muscle (MATTHEWS, 1959). However, it is not possible to elicit a maintained reflex tension in a spinalized or intact preparation. This demonstrates that the tonic stretch reflex is under powerful supraspinal control. The situation is similar in humans: tonic stretch reflexes (evaluated qualitatively by slow passive movements in one joint) are not present in normal subjects, but may appear, as a release phenomenon, in patients with lesions in descending tracts.

The following receptors are candidates of the tonic stretch reflex (MATTHEWS, 1970): 1) the so-called primary spindle endings with the group Ia fibers; 2) the secondary endings with the group II fibers; 3) the Golgi tendon organs with the group Ib fibers.

The function of the 3 receptor types (especially of the muscle spindles) has been studied intensively in recent years, but there is still no definite answer as to their respective roles in the stretch reflex (MATTHEWS, 1970). The most important characteristics of the receptors shall be summarized briefly. The distinction between spindle afferents and Golgi afferents is made according to their different behavior during a muscle contraction: the muscle spindles, situated in parallel to the main muscle fibers, are silenced during muscle contraction; on the contrary, the Golgi receptors, situated in series with the muscle fibers are elongated during muscle contraction and therefore activated. The primary and secondary endings are distinguished by the different conduction velocity of the stem fibers (primaries[1]: > 80 m/sec, secondaries[1]: < 60 m/sec). In order to get more precise information about the relevant parameters of the muscle which are signalled back to the spinal cord, well-defined input functions were compared with the resulting spike trains recorded from the dorsal root filaments (MATTHEWS, 1964).

Fig. 1 from the review of MATTHEWS (1964) summarizes the characteristic pattern of spike trains resulting from a ramp stretch, a tendon tap, and sinusoidal stretching. The primary endings are very sensitive to small changes in length as evidenced by the

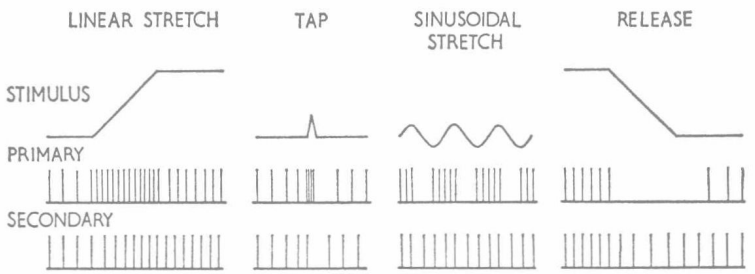

Fig. 1. Typical responses of a primary and a secondary spindle ending to various length changes of the muscle (from MATTHEWS, 1964)

"dynamic" responses, though the spike frequency is also related to the steady state length of the muscle ("static response"). Thus, the primaries inform the spinal cord about length *and* velocity. On the other hand, the secondaries are predominantly length detectors and very poor velocity detectors. CROWE and MATTHEWS (1964) introduced the term *dynamic index* of the muscle spindle which is a measure of the difference between the dynamic response and the static response. The values for a given spindle, not deprived of its central connections, were not fixed but changed considerably according to the efferent activity acting on muscle spindles (see p. 6). The Golgi tendon organs are sensitive to tension, chiefly to tension produced by

[1] Values from cat experiments (MATTHEWS, 1964), lower values were obtained in primates (CLOUGH et al., 1968).

active contraction of the muscle rather than to passive stretch (HOUK and HENNEMAN, 1967; ALNAES, 1967). From these receptor properties it follows that all three receptors may be involved in the tonic stretch reflex. By virtue of their central effects it was doubted, however, that the secondary endings (which are commonly believed to belong to the afferents producing a general flexion of the limb) and the Golgi afferents (which are inhibitory to the agonist and excitatory to the antagonist) play a role in the tonic stretch reflex. Recent investigations on the tonic stretch reflex made it clear that the question is still not settled and that the secondaries may well contribute to the tonic stretch reflex (MATTHEWS, 1970). The hypothesis was discussed by this author that central connections of polysynaptic pathways are not rigid and that, under certain conditions, afferent signals may be re-routed *via* other internuncial chains.

Tonic activation of motor units by vibration and related effects (MATTHEWS, 1967). It is well known that the vibration of tendons is a powerful stimulus to activate muscle spindles (ECHLIN and FESSARD, 1938). In recent years vibration has been an important procedure in studying the properties of various receptors. Also, it is a more "natural" stimulus than electrical stimulation of the afferent fibres for the study of reflex effects. It was shown that vibration at 100—500 cycles per second and with an amplitude of 25—50 μm provided a selective stimulus for the primary spindle endings; the sensitivity could be as low as 10 μm. By contrast, the secondary spindle endings and the Golgi endings have a much higher threshold (BROWN et al., 1967). Discharges of motor units occurred after a latency of about 10 msec (MATTHEWS, 1966). With higher amplitudes of vibration ($>$ 100 μm) phasic discharges were also observed at the onset of vibration (ANASTASIJEVIC et al., 1968). The tension rose slowly and reached a plateau whose magnitude depended on the frequency and amplitude of vibration. With increasing tension the primary spindle endings became less, the Golgi endings more sensitive to vibration (BROWN et al., 1967). The pathway for this so-called tonic vibration reflex (TVR) is not fully understood, but it is likely that polysynaptic pathways are involved. Moreover, supraspinal centers play an important role since a well developed TVR was only evoked in decerebrate preparations (MATTHEWS, 1966).

Vibration of a tendon also has secondary effects on the excitability of motoneurons which are more diffuse and occur even in absence of muscle contraction. This is indicated by a depression (sometimes preceded by a facilitation) of monosynaptic test reflexes (GILLIES et al., 1969, 1970; BARNES et al., 1970 a, b). A similar depression of monosynaptic test reflexes was observed in humans (DE GAIL et al., 1966; LANCE et al., 1966; RUSHWORTH and YOUNG, 1966; MARSDEN et al., 1969; DELWAIDE, 1970), and it was suggested that this mechanism plays an important role in the pathophysiology of spasticity (DELWAIDE, 1970). Therefore, the vibration-induced depression shall now be analyzed in more detail.

It was discovered some years ago that a burst of activity in primary afferent fibers (cutaneous or muscular) or descending fibers may reduce the synaptic efficacy of reflex afferents without affecting the *postsynaptic* membrane of the motoneurons. The phenomenon was therefore called presynaptic inhibition. The development of concepts and the (partly still unsolved) problems may be studied in the reviews of ECCLES (1964) and in the published articles of a recent symposium (v. EULER, SKOGLUND and SÖDERBERG, 1968). In this context it may be briefly noted that presynaptic

inhibition is paralleled by a depolarization of the primary afferent terminals in their intraspinal course. Several tests of presynaptic inhibition are based on this so-called primary afferent depolarization or PAD. It was shown that a sustained discharge of muscle spindles resulted in presynaptic inhibition as evidenced by PAD (COOK et al., 1967; BARNES et al., 1970 a, b; GILLIES et al., 1970) which could explain the inhibitory effect on monosynaptic reflexes when "injected" onto a background of vibration. It may be added parenthetically that in these experiments good evidence was presented that an occlusion in sensory or motor fibers or the participation of Golgi afferents was unlikely to account for the depression of the test reflex. As will be seen in the second part of this review, these results are important because it was found that a vibration-induced depression of monosynaptic test reflexes was much less prominent in spastic patients than in normals (HAGBARTH and EKLUND, 1968; DELWAIDE, 1970). It was therefore suggested by DELWAIDE (1970) that stretch reflexes in spasticity are, by virtue of defective presynaptic inhibitory control, relatively released.

Control of the stretch reflex by the gamma-system. The term "reflex", used in experimental and clinical studies requires comment. As defined by SHERRINGTON (1947) the reflex has the property to be set off by a range of specific ("adequate") external stimuli, its magnitude of output being related to the magnitude of its input. This definition reminds us that reflexology has developed from analytical work using more or less synchronized "natural" stimuli (tendon taps, cutaneous stimuli) or graded electrical stimuli to activate a defined set of afferent fibres. Today many terms used by engineers are also applied to biological systems (input, output, feedback, servo-control, gain, comparator, etc.) because it has proven useful to proceed as in systems analysis and to find a formal description of input and output functions. The mathematical expression of the processing within a system is called the transfer function. WAGNER (1925) was one of the first to call attention to the similarities of technical servo-mechanisms and proprioceptive reflexes (see WAGNER, 1954). The original concept of the stretch reflex as a servo-loop was derived from experimental findings on the tonic stretch reflex in the decerebrate cat. As mentioned previously an external load applied to the muscle is compensated by a proportional amount of active, i. e., reflex tension which tends to keep the muscle at constant length. In this situation the stretch reflex represents a negative feedback loop stabilizing muscle length. In addition it was recognized by WAGNER (1954) that the muscle spindle, due to its sensitivity to velocity, may compensate, to some extent, the delays inherent in the servo-loop. Since the discovery of an efferent control system acting on muscle spindles, the gamma or fusimotoneurons, the concept of the stretch reflex as a homeostatic principle had to be modified. Two types of gamma-fibers were distinguished according to their effect on muscle spindle responses to stretch. *Dynamic* gamma-fibers enhance the dynamic response of the primary spindle endings to a ramp stretch; on the other hand *static* gamma-motoneurons enhance the static response of primary as well as secondary muscle spindle endings and have a depressing effect on the dynamic response (MATTHEWS, 1964).

Knowledge about this additional input to the stretch reflex *via* the "gamma-route" led to the "follow-up servo" hypothesis of movements first proposed by MERTON (1953): command signals (from higher centers) could be transmitted *via* gamma-fibers to the muscle spindle having the function of a comparator. A "mis-

match" between the (gamma-induced) spindle length and the actual muscle length would produce an error signal transmitted *via* the spindle afferents back to the motoneurons. Depending whether the spindles accelerate or decelerate their discharge, the motor units increase or decrease their output. Thus, some types of movements could be initiated *via* the gamma-loop.

The transmission of command signals would have to be effected *via* the static gamma motoneurons since, according to results of LENNERSTRAND and THODEN (1968), the dynamic gamma motoneurons are not appropriate to compensate the unloading effect during movements, i. e., to maintain a spindle discharge despite shortening of the muscle. As mentioned previously, it is unlikely that a spindle discharge is powerful enough to discharge the alpha motoneurons without concomitant facilitation from other sources. The original conception of Merton had therefore to be altered and it was proposed that command signals are transmitted to both, gamma and alpha motoneurons. Such a "gamma-alpha linkage" (GRANIT, 1955 a) has indeed been observed on many occasions when stimulating various structures of the brain. In engineering terms, such an arrangement means that both, the comparator and the amplifier of the servo loop, are under parallel control from higher centers. The utility of this "servo-assistance" would be evident whenever a movement deviates from its "intended" course (MATTHEWS, 1964).

New evidence has been adduced for the validity of the servo theory of voluntary movements. It has been found that gamma motoneurons of the baboon's hand and forearm receive a fairly direct input from the motor cortex, and it was concluded that this system probably works in parallel but independently from the cortico-motoneuronal system (see below; PHILLIPS, 1969). Furthermore, HAGBARTH and VALLBO (1968) succeeded in recording from single muscle spindle afferents in humans by inserting metal microelectrodes in peripheral nerves. The majority of units were indeed activated at onset of volitional activity as seen in the electromyogram (VALLBO, 1970 a, b). This finding ist strongly in favor of an alpha-gamma co-activation during voluntary movements.

2. Supraspinal Control of the Motor Apparatus

The control of spinal reflexes by higher structures. The condition of decerebrate rigidity provides the most dramatic evidence that spinal reflexes are under powerful supraspinal control. Obviously there is a tonic, i. e., ongoing supraspinal influence. This influence is excitatory to extensor muscles from the lower brainstem and inhibitory from more rostral structures. Restricted lesions may produce small, but definite changes of excitability in spinal reflex pathways. Thus, pyramidal lesions at the bulbar level resulted in weak flexor reflexes in hindlimbs of cats (LAURSEN and WIESENDANGER, 1966 a). More subtle studies involving intracellular recordings from spinal interneurons and motoneurons revealed that descending tracts often are excitatory to interneurons of segmental reflex pathways (LUNDBERG, 1967). Thus it is quite possible that a large part of the control exerted on motor units by higher structures involves the spinal reflex paths, the "unit reactions" of SHERRINGTON (1947) or to use again an engineering term, the subroutines. Moreover, descending tracts may markedly influence the accessibility of interneuronal paths for a given sensory

input (OSCARSSON, 1965). Stimulation of the sensorimotor cortex has a net excitatory action on flexor motoneurons and an inhibitory action on extensor motoneurons. These effects are partly mediated by the *pyramidal tract* which was shown to excite interneurons intercalated in the flexor reflex path. A further convergence was found on interneurons of the Ia inhibitory pathway and on the Ib pathway (reversed myotatic reflex). Similar detailed investigations were made with respect to the *rubrospinal tract*, the *vestibulospinal tract* and different components of the *reticulospinal tract* (LUNDBERG, 1967). These microelectrophysiological observations have enormously complicated our knowledge of the spinal cord organization. A conclusion of great significance for the understanding of "normal" operations of the spinal mechanisms is that they are not fixed: descending tracts may change the efficacy of spinal pathways from moment to moment by altering the excitatory state of interneurons. Some circuits may be "switched on" for one type of motor task and "switched off" for another type of movement (LUNDBERG, 1970). It has also been demonstrated in humans that changes in synaptic efficacy in the stretch reflex arc do indeed occur just prior to or during voluntary movements (REQUIN, 1967; GOTTLIEB et al., 1970).

Direct actions of the motor cortex on alpha motoneurons. It seems that in nonprimates the motor control by the brain is essentially exerted by mobilization or suppression of spinal reflexes, the lowest order building bricks.

Already in cats, there is, however, a tendency for establishing direct or "private" lines from the cortex to the motoneurons. Thus, it was found by VASILENKO and KOSTYUK (1966) that the pyramidal tract may exert its influence on motoneurons *via* interneurons not involved in the reflex pathway. In primates, direct cortico-motoneuronal connections are now well established morphologically and electrophysiologically (KUYPERS, 1964; BERNHARD and BOHM, 1954; PHILLIPS, 1969) and it seems that this system is of growing importance phylogenetically (PHILLIPS, 1971) as well as ontogenetically (KUYPERS, 1964). It must be assumed that a large part of the lowest order building bricks are then incorporated in the brain (the "colonies" of Betz cells). This "encephalization" was linked with the enormous development of digital motor skill. A review on this aspect of motor control has recently been published by PHILLIPS (1969).

Supraspinal effects on gamma-motoneurons. Many sites were described which, upon electrical stimulation, had facilitatory or inhibitory effects on gamma-motoneurons (GRANIT, 1955 a, 1970). Of particular interest with respect to the servo control theory of movements (p. 6) is the influence from the motor cortex (GRANIT, 1955 b; AKERT and MORTIMER, 1961) which is, at least partly, mediated by the pyramidal tract (KATO et al., 1964; LAURSEN and WIESENDANGER, 1966 b; FIDONE and PRESTON, 1969). The gamma-motoneurons of the baboon's forelimb receive a fast, possibly monosynaptic projection from the motor cortex (CLOUGH et al., 1971). Recently it was shown that the pyramidal tract may facilitate both the dynamic and static response of muscle spindles (YOKOTA and VOORHOEVE, 1969) with a preponderance for a dynamic facilitation (VEDEL and MOUILLAC-BAUDEVIN, 1970). Exploration of the brainstem with stimulating electrodes disclosed separate descending fiber systems to dynamic and static gamma motoneurons. Regions in the pontine reticular formation and in the medial bulbar reticular formation produced static effects whereas regions in the lateral bulbar reticular formation had ipsilateral dynamic

effects (VEDEL and MOUILLAC-BAUDEVIN, 1969 a, b). Stimulation of the red nucleus (APPELBERG and KOSARY, 1963) and neighbouring structures (APPELBERG and JENESKOG, 1969) enhanced the dynamic response of muscle spindles. GRILLNER et al., (1969) reported descending monosynaptic connections from Deiter's nucleus to gamma-motoneurons (probably static gamma-motoneurons). All these results were not always clearcut and there are conflicting reports which add to some confusion about the organization of the supraspinal gamma-control systems. This is, however, not surprising in view of the strong sensitivity of these systems to anesthesia and of the pitfalls of electrical brain stimulation. It can be concluded, however, that the gamma-system is under powerful supraspinal control and that the control of dynamic and of static properties of muscle spindles is mediated by separate descending control systems.

3. Experimental Models of Disorders of Muscle Tone with Particular Reference to the Role of the Gamma-System

We wish to concentrate on a few models and to discuss the relevance of these models to states of disturbed muscle tone in humans.

Decerebration. The intensive studies of GRANIT and collaborators (GRANIT, 1955 a, 1970) on the gamma-system had a particular influence on the concept that the gamma-system may be the key for the understanding of muscle tone. In fact, it was consistently observed that gamma-motoneurons have a tonic activity. This "gamma-bias" may be altered by segmental and supraspinal influences. De-efferentation of muscle spindles reduced the activity and reactivity of muscle spindles and is thus a clear demonstration of the tonic gamma-bias on muscle spindles (ELDRED et al., 1953). Two varieties of decerebration (GRANIT, 1955 a) shall be briefly characterized: 1) Intercollicular decerebration (the classic procedure used by SHERRINGTON) *increases the gamma-bias.* The increased stretch reflex observed in this condition is therefore, at least partly, due to greater sensitivity of the muscle spindles. 2) Anemic decerebration is achieved by an occlusion of the basilar artery and both carotid arteries (POLLOCK and DAVIS, 1929). This procedure results, in the chronic stage, in a hyperactivity of alpha-motoneurons associated with a *depressed gamma-bias.* In these "alpha-cats", deafferentation failed to abolish the rigiditiy, a finding which is quite in contrast to the experiment of SHERRINGTON (1947) on classically decerebrated cats ("gamma-cats"). Various maneuvers typically co-activated gamma- and alpha-motoneurons ("Alpha-gamma-link") in anesthetized or classically decerebrated cats, but only alpha-motoneurons in "alpha-cats". It was demonstrated by POLLOCK and DAVIS (1929) that anemic decerebration also destroyed the anterior lobe of the cerebellum, and it was therefore concluded that this part of the cerebellum plays an important role in the linkage of alpha- and gamma-motoneuron activation (GRANIT, 1955 a). Decerebrate rigidity has often been compared with spasticity or rigidity in humans. The discovery of two different mechanisms responsible for increased muscle tone was of course a challenge to neurologists and pharmacologists and has led to speculations about the role of the gamma-system in spasticity and rigidity (see second part of this review). GRANIT (1955 a) himself was inclined to compare both forms of decerebrate rigidity rather with spasticity than with the Parkinsonian type

of rigidity. The similarity between classical decerebrate rigidity and spasticity in humans lies in the release of stretch reflexes of the antigravity muscles. In both conditions, deafferentation abolished the increased muscle tone (SHERRINGTON, 1947; FOERSTER, 1927). In both, a rapid stretch produces a pronounced reflex contraction which, on further stretch "melts" away, a symptom called the clasp-knife phenomenon. The stretch reflex in spastic patients tends to oscillate and to exhibit a clonus. Decerebrate rigidity is, however, also characterized by its *exaggerated static properties,* i. e., by its linear length-tension relationship in the steady state. These static properties are lacking in spasticity; the stretch reflex is largely velocity-dependent (BURKE et al., 1970) and a reflex contraction may fail to appear if the muscle is stretched slowly. On the other hand, the dynamic properties are much less marked in Parkinsonian rigidity. The tendon reflexes are weak and a reflex contraction is also produced by relatively slow stretching of both flexors and extensors giving the condition a plastic quality. To be sure, it is not known whether there is a linear relationship between length and reflex tension in Parkinsonian rigidity.

Moreover, decerebrate rigidity lacks the characteristics of the cogwheel phenomenon of Parkinson patients. Thus, both spasticity and rigidity share different aspects of the decerebrate rigidity of cats and monkeys; it is not, therefore, an adequate model for either spasticity or rigidity.

Reserpine rigidity (STEG, 1962, 1964). In rats, injections of reserpine induced muscle "tremor", "rigidity" and "akinesia", a symptomatology, which according to the author, resembled Parkinsonism. The rationale of this drug effect is that reserpine blocks the uptake of monoamines and lowers the monoamine content in the brain (as was found in Parkinson patients). L-DOPA had a reversible effect (STEG, 1966). Gamma- and alpha-motoneurons were recorded in unanesthetized nerves of the rat tail. The most interesting point of this drug-induced rigidity was that alpha-motoneurons were overactive, gamma-motoneurons depressed. The rigidity was abolished by striatal lesions (ARVIDSSON et al., 1967), but not by deafferentation. It is possible that more subtle changes in the gamma-fiber control system occur which could no have been detected by STEG. Thus, HENATSCH (1965) reported in a preliminary note that, in cats, reserpine had variable effects on muscle spindles but that there was a trend to a reduction of the *dynamic* sensitivity of muscle spindles. In summary, the pharmacological model needs some more investigation, preferrably extended on primates, in order to assess the changes in both, the static and dynamic gamma-bias. The conclusion that Parkinsonian rigidity is of the "alpha type", as observed in the model of STEG, seems therefore premature.

Interneuronal or spinal rigidity. Temporary ischemia of the lumbosacral cord results in an intensive rigidity, the histological basis of this condition being a massive loss of interneurons with relative preservation of motoneurons (KOSMAN et al., 1951; GELFAN and TARLOV, 1959; BIERSTEKER and v. HARREVELD, 1963; MURAYAMA and SMITH, 1965; GELFAN, 1966). The rigidity developed within 1 to 3 weeks and was assumed to be due to hypersensitivity of partially denervated motoneurons (GELFAN and TARLOV, 1959). In fact it was shown that the motoneuronal membrane has lost a large number of boutons (GELFAN and RAPISWARDA, 1964). We shall only deal with this late effect of asphyxia although it is well known that it also produces acute effects on muscle tone (BIERSTEKER and v. HARREVELD, 1963). There are conflicting reports with regard to the immediate cause of alpha-motoneuron discharges.

GELFAN and TARLOV (1959) suggested that motoneurons start to fire "spontaneously" without afferent drive since, in their experiments, dorsal rhizotomy did not abolish the rigidity. On the other hand OKA and v. HARREVELD (1968) maintained that the rigidity represents a "gamma-tonus" although it was reported from the same laboratory (TRUBATCH and v. HARREVELD, 1970) that most gamma-motoneurons were probably destroyed during ischemia. The reviewer is rather in favor of Gelfan and

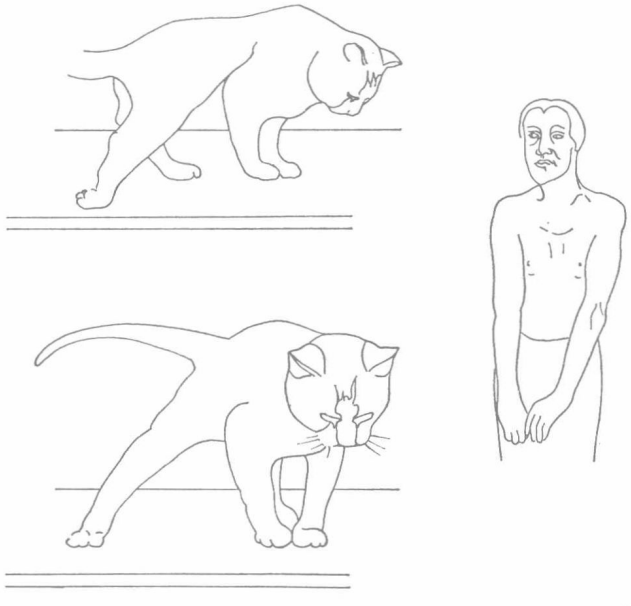

Fig. 2. Rigidity in a cat produced by intradural deafferentation of the right hindlimb. Histological analysis of the lumbosacral spinal cord revealed a pronounced loss of interneurons on the deafferented side (from experiments described in WIESENDANGER, 1964). On the right, intense "interneuron rigidity" of the arms, particularly of the extensor and adductor muscles, in a patient suffering from a glioma of the cervical cord. The tumor progressively infiltrated and destroyed the intramedullary tissue leaving motoneurons essentially intact (redrawn from RUSHWORTH, 1962)

Tarlov's interpretation, because there is no doubt that a true alpha-rigidity may develop as a consequence of interneuron destruction. It was shown by WIESENDANGER (1964, 1967), that complete intradural section of the dorsal rootlets of one hindlimb also resulted, after a similar delay of 1—3 weeks, in a pronounced rigidity (Fig. 2). Histological analysis of spinal cord segments again disclosed a reduction of interneurons on the side of the section, probably due to interference with the vascular blood supply during the intradural operation. Thus, the cause of "deafferentation rigidity" which had long ago been observed in dogs (BICKEL, 1897) and in cats (RANSON, 1928) with deafferented hind limbs, is probably the same as the cause for the late asphyxial rigidity. Prolonged electromyographic recordings of extensor muscles of the rigid limb revealed a profuse steady discharge even if the unanesthetized animal, suspended in a sling with freely hanging legs, was perfectly still (WIESENDANGER, 1964). This rigidity is based on a purely spinal mechanism since spinali-

zation did not abolish deafferentation rigidity (CARDIN, 1952). A similar observation was made in rats made rigid by asphyxiation (MATSUSHITA and SMITH, 1970). Of course it cannot be excluded that some afferent inputs may add to the rigid state such as lack of presynaptic inhibition (MATSUSHITA and SMITH, 1970), increased stretch reflexes (OKA and v. HARREVELD, 1968; MATSUSHITA and SMITH, 1970), and increased tonic neck and labyrinthine reflexes (STAVRAKY, 1961). Intracellular recordings from rigid preparations revealed abnormal repetitive discharges of motoneurons to single afferent volleys and also "spontaneous" spike discharges, although the membrane potentials were found to be in the normal range (COLLEWIJN and v. HARREVELD, 1966; NIECHAJ and v. HARREVELD, 1967).

Intensive "muscle spasms" have been described in patients suffering from subacute necrotizing myelopathy, a vascular disorder of the spinal cord. In some postmortem examinations of such and other patients with invading lesions of the spinal grey matter (Fig. 2), pronounced loss of interneurons was a consistent finding (KIFFIN et al., 1960; RUSHWORTH et al., 1961; TARLOV, 1967). It may be noted in this context that dorsal rhizotomy in 2 patients with "intractable spasms and rigidity" of spinal origin were not or only little improved by dorsal root section (TARLOV, 1966).

The first part of this review shall be summarized by drawing the following *conclusions:*

1. There is general consensus that the rigidity, produced in animal experiments, regardless of origin, is characterized by *enhanced stretch reflexes.* It must be made clear, however, that the stretch reflex is just a means of *testing* the reactivity of the motoneurons, the final common path.

2. There are four possible *mechanisms* all of which may contribute to increased stretch reflexes. a) Autochthonous increase of excitability of spinal motoneurons due to *denervation hypersensitivity.* Rigidity due to interneuron destruction following asphyxia of the spinal cord may most probably be ascribed to such a mechanism. b) Increase of excitability of alpha-motoneurons due to a *preponderance of facilitatory descending activity on alpha-motoneurons.* Rigidity produced by anemic decerebration was given as an example. c) *Removal of tonic presynaptic inhibition* acting on muscle spindle afferents. So far no experimental model has been described fulfilling the criterion of a release from supraspinal control by means of decreased presynaptic inhibition; but it was anticipated that such a mechanism could indeed be important in explaining exaggerated stretch reflexes. The findings supporting this view will be discussed in detail in the next part of the review. d) Increase of muscle spindle sensitivity due to an *enhanced gamma-bias* (which in turn has an indirect effect on the alpha motoneurons *via* the "gamma-loop"). Rigidity of classical decerebration was discussed as an example. It should be noted that the rigidity described under a) and b) is of the "alpha type", i. e., it persists after dorsal rhizotomy. In contrast, the rigidity described under c) and d) depends on an intact stretch reflex arc; consequently the increased muscle tone disappears after dorsal root section. However, an increased gamma-bias is only necessary to explain the condition described under d), and it must be stressed that disappearance of exaggerated stretch reflexes by blocking the Ia-afferents or the gamma-efferents does not necessarily mean that an increased gamma-bias was the cause of the increased muscle tone, as has often been concluded in the past.

3. With the possible exception of interneuron rigidity, none of the models described fits in all details the disorders of muscle tone known in neurology. To take an example, several features of rigidity produced by classical decerebration resemble spasticity, but some other important features (such as the tonic component of the stretch reflex) are clearly different in the two conditions.

4. Despite these dissimilarities between the results of animal experiments and the findings in human spasticity and rigidity, it is hoped that the neurologist, familiar with neurophysiological concepts, will be rewarded in his attempts to overcome the many confusions inherent in those diseases resulting in altered muscle tone. We will consider these problems in the second part of this review and attempt to deal with the difficulties of applying various neurophysiological methods to patients.