INTRODUCTION

Rigidity is one of the major signs of Parkinson’s disease (PD). However, its pathophysiology has rarely been studied. This appears a little surprising since data obtained from animal physiology, which offers a scheme of neuronal circuits that might be hyper- or hypoactive, could be useful in the study of muscle tone problems, a classical area in neurological semiology.

Experimental models of PD have not yet been analysed using neurophysiological techniques. Thus, the information currently available derives from clinical data and clinical neurophysiology.

RELEVANT CLINICAL DATA

The term “rigidity” designates a particular form of muscle hypertonia. Rigidity is characterized by increased stiffness experienced during a passive mobilisation of a limb segment, irrespective of the direction of the mobilisation. This stiffness is modified little by the speed of the imposed displacement; it can sometimes be more marked upon slow mobili-
ensation. Rigidity is accompanied by normal tendon jerks. The intensity remains the same whether extensors or flexor muscles are stretched and regardless of the angle of the joint that is moved. Once a muscle group is stretched, the limb remains in the position that has been imposed and shows no tendency to return to the previous position. It is for this reason that rigidity is termed “plastic”. Rigidity may be constant (“en tuyau de plomb”) or, on the contrary, interrupted at regular intervals during large mobilization (“en roue dentée”). The interruption occurs at the same frequency as postural rather than resting tremor. Rigidity may be accompanied by visible contraction of the shortened muscle. This is the inverted myotatic reflex. Rigidity may be generalized i.e. involve the limb as well as axial muscles, for example orofacial, respiratory, paravertebral muscles, and so on.

Differential diagnosis must be carried out with respect to spasticity, “gegenhalten”, muscle fibrosis, antalgic contractions and chiefly fixed dystonia. It has been reported many times that stress, anxiety and chiefly contralateral contractions reinforce muscle rigidity. In this respect, a gradient emerges between distal and proximal muscles, the activity of the latter being more powerful. Moreover, reinforcement of muscle rigidity is more marked when the subject is standing than seated (1). Little is known about possible modifications of muscle rigidity during voluntary contraction. This problem has been broached through EMG recordings. EMG recordings of rigid muscles indicate a continuous but moderate discharge of motor unit potentials during passive stretching, but the EMG activity outlasts the movement and persists as long as the stretching is maintained. This activity corresponds to the tonic stretch reflex whose amplitude correlates well with rigidity intensity (2).

How rigidity contributes to disability is difficult to assess because it is rarely isolated and most often associated with akinesia. It is generally thought that muscle stiffness interferes with voluntary movement, particularly its speed of execution. In fact, in the presence of rigidity, more strength is needed to move a joint.

Rigidity is not a pathognomonic feature of PD. It is also a sign of many diseases of the basal ganglia (BG) and of some diseases of the mesencephalon and of the spinal cord (intramedullary glioma, stiff man syndrome, anoxia, etc.).

MECHANISMS OF RIGIDITY

Increased muscle stiffness may depend on physical modifications of muscles themselves or on neural mechanisms. As regards the former, modifications of rheological properties of muscles, chiefly in cases of long-lasting PD, have been reported (3,4). These authors have speculated that this physical modification could be secondary to non usage. Of course, this factor may play a role but, when considering the sometimes rapid tone fluctuations in on-off situations, it is clear that it is not a major role. On the other hand, the role of neural factors is demonstrated by several facts: abolition after section or anaesthesia of posterior roots (5), tone modification following neurosurgical intervention; influence of remote contractions, etc. Every pathophysiological hypothesis should be able to explain these facts. The link between dopamine deficit and rigidity does not appear to be direct: cholinergic mechanisms may be interposed between dopaminergic receptors and abnormalities that are ultimately responsible for the rigidity. In fact, anticholinergics can reduce rigidity but have no influence on akinesia, which correlates directly with the dopamine deficit.

Currently, two hypotheses have been proposed to explain rigidity in neurophysiological terms. The first proposes hyperexcitability in long loop reflex pathways, reflex pathways.
that relay in the brain, while the second postulates that the effector mechanisms are located at metameric spinal level; according to this latter hypothesis, the functioning of short reflex pathways is modified secondary to an inappropriate command of interneurones by one or several descending spinal pathways.

*Hypothesis of hyperexcitability within long loop reflex pathways*

From the mid '70s to the mid '80s, there was much discussion among neurophysiologists of reflex mechanisms not limited to the spinal cord but involving relays in the encephalon. This discussion took, as its starting point, the existence of EMG responses in active muscles when a movement is abruptly stopped. In this condition, three successive EMG bursts occur systematically (Fig. 1). The first one, named M1, appears in a delay that corresponds to the myotatic reflex of the muscle being studied. The second response, M2, appears after a delay shorter than a reaction time. It may not be of voluntary origin and is clearly a reflex response. The amplitude of the M2 response may vary according to the instructions given to the patient: for example “hold” or “let go”. This M2 response is considered by many researchers to reflect the activity within long loop reflex pathways. According to this view, this activity would origi-

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**Fig. 1** - A. EMG tracing when a movement is abruptly stopped. A) time 0, the interruption is followed by a silent period. A first EMG burst (M1) follows after a delay of ±25 ms (upper limb muscles). This delay corresponds to the latency of a tendon jerk. The second burst (M2) is seen after a delay of 50 ms. This delay is not long enough to attribute M2 to a voluntary response because it is shorter than a reaction time. It has been proposed that M2 is due to a long loop spinal-cortico-spinal reflex. The third burst (M3) is more complex, partially voluntary.

B. Differences observed between a control subject and a parkinsonian patient. The upper line represents the movement imposed on the wrist and the lower line, the rectified and integrated EMG of forearm muscles. In the control, the M1 response is very feeble and the M2 response is almost absent. In the parkinsonian patient, the M2 response is clearly increased.
nate in the primary endings of the neuromuscular spindles: action potential would travel in the Ia fibres as far as the spinal cord where they activate the motoneurones. In addition, action potentials would also be transmitted to the encephalon via the posterior columns of the spinal cord and would then be able to influence the sensorimotor cortex. The sensorimotor cortex is regarded as a reflex centre which would be able to send a message back to the spinal motoneurones via the corticospinal tract.

Although attractive, this hypothesis is not recognized unanimously. Some researchers think that the M2 response could reflect the late arrival at the spinal cord of primary afferents travelling in slower conducting fibres than the Ia fibres. Another view is that the different EMG bursts correspond to the segmentation of the discharge of the primary endings, which are highly sensitive to very minor stretching.

The long loop reflex hypothesis has proved popular because various teams of researchers have shown M2 responses in rigid patients that are clearly greater than inagematched controls. It has been objected that this increased amplitude is due to a background of permanent muscle contraction; however, this objection has been ruled out (6). Correlation between amplitude of the M2 response and rigidity intensity has been sought but the results obtained have been variable. In the view of some authors, this correlation is not strong (7).

As a result of the studies showing an increased M2 response it was suggested that the long loop reflex pathways are more excitable in parkinsonian patients and that this loop is the anatomo-functional basis of rigidity. As afferent as well as efferent pathways behave normally, the conclusion was that the hyper-excitability of these long loop pathways is located at the level of the sensorimotor cortex, which is facilitated or disinhibited. In fact, the supplementary motor area (SMA) normally inhibits the motor cortex; hence the hypothetic hyperexcitable long loop reflex may be complemented by another loop starting in the motor cortex, relaying in the BG and returning to the SMA. This loop would be less inhibitory and would remove a permanent inhibition from the sensory motor cortex. There are, as is well known, many data, both physiological and metabolic, that involve the SMA in the pathogenesis of PD. This explanation fits in with the classical schema, proposed by de Long (8), in which the BG project essentially to the cerebral cortex.

Although popular, the hypothesis presented above may raise objections. For example, cortical lesions are well known in neurology to induce spasticity but never rigidity that is clinically clearly distinct. According to the schema in Fig. 2, excitability of the sensorimotor cortex is modified, although the threshold for the motor response obtained either by electrical or magnetic stimulation of the cortex does not argue in favour of this (9,10). If the efferent pathway of this loop is the corticospinal tract, the excitability of the spinal motoneurones, as well as that of various spinal interneurones, should be increased. This is not the case. Moreover, cortico spinal projections innervate differentially extensor and flexor motor nuclei and proximal and distal muscles whereas rigidity is equal in all these muscle groups. More important, all the long loop reflex pathway-based theories rest on the discharge in the Ia fibres, which are very sensitive to the speed of the muscle stretch. As rigidity does not increase with higher stretching speed, the role of Ia afferents has to be questioned. If the increased amplitude of the M2 response is a well-established fact, it may be suggested that it does not reflect the causal mechanism of rigidity but rather corresponds to a compensatory mechanism opposing or correcting problems that have another explanation.
Spinal hypothesis

Rigidity may be a symptom of purely spinal diseases, for example spinal glioma. This supports the idea that the necessary and sufficient mechanisms for rigidity are present at metamic spinal level.

Physiologists working on animals have listed a series of spinal mechanisms whose dysfunction could explain a muscle hypertonia. The list is given in Table 1.

Theoretically, one single dysfunction would be enough but several mechanisms may in fact be working together and be associated.

It is possible to study non-invasively many of these mechanisms in man. Clinical neurophysiology offers techniques that allow the functioning of several spinal interneurones with specific functions to be assessed: Ia and Ib interneurone excitability, Renshaw inhibition, presynaptic inhibition, etc. These techniques, which are directly derived from those used in animals, are non-traumatic and painless; they provide quantitative results that allow normal values with their relative confidence intervals to be established. If the results obtained in pathology differ significantly from normal values, it may be deduced that the spinal mechanism under investigation is modified. In PD, results of spinal studies indicate that:

1) excitability of the alpha motoneurones is not modified (this argues against a possible hyperactivity in the corticospinal tract);
2) recurrent Renshaw inhibition is normal;
3) presynaptic inhibition acting on terminals of Ia fibres is normal (11);
4) modifications of reflexes elicited by exteroceptive stimulation are slightly modified;

Table I - Spinal mechanisms able to explain hypertonia

- Hyperactivity of alpha motoneurones
- Hyperactivity of gamma motoneurones
- Hyperactivity of excitatory Ia interneurones
- Reduction of presynaptic inhibition
- Reduction of recurrent inhibition (Renshaw)
- Reduction of Ia reciprocal inhibition
- Reduction of non reciprocal inhibition (Ia and Ib)

Fig. 2 - Rigidity explained by the hypothesis of hyperexcitability in long loop reflex pathways. A shows the cerebral loop and B, the spinal-cortico-spinal loop. The neuromuscular spindles are the starting point of the latter. Ia afferents reach the contralateral sensory motor cortex. Ia afferents are believed to activate cortico-spinal neurones whose discharge is sent back to spinal motoneurones via the cortico-spinal tract. This is the scheme of a long loop reflex. This long loop would be hyperexcitable in PD due to a functional modification within a cerebral loop, responsible for a reduced activity in the supplementary motor area (SMA). As this latter normally exerts an inhibition on the motor cortex, the cortex becomes hyperexcitable.
5) activity of the Ia inhibitory interneurone, responsible for the first phase of reciprocal inhibition, is significantly increased. Moreover this increase is well correlated with the rigidity intensity;

6) activity of the Ib interneurone, responsible for non reciprocal inhibition, is significantly reduced. This reduction is well correlated with the increase in Ia interneurone activity on the one hand, and intensity of rigidity, on the other (12);

7) Ia and Ib interneurones are influenced by various peripheral afferents as well as by descending pathways (13). Normally, the Ib interneurone integrates all the influences it receives and, in turn, exerts a tonic inhibition on the motoneurones. If these interneurones are less active, motoneurone pools escape permanent inhibition and this fact may explain parkinsonian rigidity. Moreover, Ib interneurones are good candidates to explain a series of clinical aspects of rigidity; for example, they are influenced little by the speed of mobilization and there is no known difference between the activity they exert on proximal and on distal muscles. Ib interneurones receive afferents that are loco-regional rather than purely metameric. They may be influenced by afferents originating from both sides of a joint as well as by contralateral afferents;

8) the only two significant abnormalities so far identified concern Ia and Ib interneurones. As there is no known modification in the peripheral afferents – even in the Ia fibres – and as no biochemical dysfunction has been reported at spinal cord level in PD, the functional abnormalities of interneurones are likely to be due to dysfunction in the descending spinal pathways. As a close correlation exists between the excitability modification of Ia and of Ib interneurones, it is more than likely that both changes reflect abnormalities in one single descending pathway. The descending pathways, which have a similar effect on the two interneurones, are thus not to be taken into account. The only descending spinal tract that exerts opposite effects on the two interneurones is the reticulo-spinal tract. Hence, it is reasonable to deduce that the messages travelling in this tract are reduced and abnormal. Moreover, it is likely that the nucleus of origin, where these messages are elaborated, also functions abnormally in PD. This nucleus is familiar to anatomists: it is the giganto-cellularis nucleus or nucleus reticularis giganto cellularis (NRGC). Its physiology, on the other hand, is less well known and there are contradictory views in the literature concerning the role it exerts on the spinal interneurones. The first experiments, which date back to 1966 (14), used electrical stimulation of the descending tract and favoured an inhibitory role on the Ib interneurones. But these results can be reproduced by intrathecal administration of a monoaminergic precursor; hence, it may be considered that the results were due to the stimulation of mono-aminergic fibres, which run close to the dorsal reticulo-spinal tract but which originate in fact from other nuclei, namely the locus coerules, the subcoerules and the raphe nuclei. More recent studies (15) have focused on the results of direct stimulation of the NRGC. In this case, the Ib interneurones are facilitated and a muscle hypotonia appears which resolves immediately upon cessation of the stimulation. So, it is now considered that NRGC facilitates the Ib interneurones directly while it inhibits Ia interneurones via a polysynaptic pathway. In accordance with these data, it may be proposed that the NRGC is less active in PD leading to a reduced facilitation of the Ib interneurones as well as a Ia interneurone facilitation. Finally, reduction in Ib activity is proposed as the final mechanism at spinal level explaining parkinsonian rigidity. The key role played by Ib interneurone is illustrated in Fig. 3.
Parkinson's disease and the reticulospinal pathways

The experimental data summarised above have led logically to the suggestion that the NRGC plays a role in the pathophysiology of rigidity. Other studies, not discussed here, suggest that another reticular nucleus, the nucleus reticularis pontis caudalis (NRPC), is also less efficient in PD. These nuclei are believed to "release" motoneurones from the postural constraints imposed by segmentary spinal reflexes, for example, in favour of a voluntary or automatic movement. Their dysfunction fits in well with clinical observations such as difficulties in initiating a movement or gait.

However, in order to subscribe to a hypothesis of a deficient subcortical pathway, responsible for some parkinsonian signs, an anatomo-functional link between the BG and the reticular nuclei should be proposed. This link has not, at present, been established by experiments designed specifically to study the hypothesis, although the animal models of PD could answer the questions that are still open. Caution is thus necessary before reaching firm conclusions. Figure 4 shows the possible relationships between the BG and tegmentum and from there to the reticular nuclei.

Anatomical and physiological data concerning the tegmentum and the reticular formation are still limited even in animals. It is
important to be aware of the limitations of a hypothesis involving nuclei that are not well known. However, the rich reciprocal connectivity between the tegmentum and the BG strongly suggests that the mesencephalon plays a role in the control of the parameters of a movement. First of all, connections between the mesencephalon and the substantia nigra pars compacta (SNc), the substantia nigra pars reticulata (SNr), both segments of the globus pallidus (GP), the caudate nucleus and the putamen, have been demonstrated (16,17). These efferences to the BG originate from separate neuronal populations, a fact which argues in favour of a parallel processing of messages. In fact, histological data suggest that mesencephalon nuclei could influence the output of the SN and the STN. Moreover, efferent pathways from the BG project onto the mesencephalic nuclei from where the projections to the BG start. Projections toward the mesencephalon have been identified from the pallidum, the SNr and the STN (18,19). The pallido-thalamic tract gives off several collaterals which constitute a pallido-tegmental tract. It thus appears that the mesencephalon may be a target for the BG efferents and is involved in anatomo-functional loops that start in the BG and return to it after relaying within the tegmentum. It is generally accepted that the output from the pallidum is inhibitory and that this inhibition is increased in PD. It has long been shown that the pallido-tegmental axons project onto the pedunculo-pontin nucleus, which is rich in cholinergic cells. However, more recent studies have shown that the connections of the pallido-tegmental tract are chiefly with a non cholinergic cell population. This population has been named the "midbrain extrapyramidal area" (20) and has glutamatergic excitatory projections toward the NRGC. Hence, it is tempting to propose that a modification in the BG could influence indirectly the spinal Ib interneurones following relays in the tegmentum and the reticular formation. This could be the pathway responsible for rigidity. In fact, in PD, an increased inhibitory activity in the GP, mediated by GABA, would inhibit MEA. Hence, the glutamatergic facilitation normally exerted by this region on the NRGC would be less active. The net results would be a reduced activity of the NRGC, which, via the reticulospinal pathway, would be responsible for the reduced activity of the spinal Ib interneurone. In other words, it seems reasonable to propose that the influence of the BG on motoneurones could express itself through a subcortical multisynaptic pathway with relays in the mesencephalon and the reticular formation. The physiological role of such a pathway is not yet well defined in normal conditions.
However, at the level of the mesencephalon, physiologists have described a locomotor region whose stimulations initiate gait in the cat. It may be considered that one of the roles of the mesencephalon and the reticular formation is normally to prepare motoneurones to receive a cortical command by releasing motoneurones from the postural constraints that are chiefly exerted by the intraspinal reflex circuits. In normal motricity, both corticospinal and subcortical pathways function in synergy. In PD, the cortico-spinal tract is affected little, if at all. On the other hand, the subcortical pathway does not function adequately and the motoneurones are no longer correctly assisted by the interneuronal machinery. Such a view should make it possible to explain the modification in long loop reflexes, namely the increased M2 wave, by a compensatory phenomenon: the voluntary command, no longer assisted by the spinal reflexes, requires an increased cortical activity.

REFERENCES