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Short-latency autogenic inhibition (IB inhibition) in human spasticity

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SUMMARY The inhibitory effect of IB interneurons on motoneurons was tested in both legs of six hemiplegic adults. On the normal side, an inhibition of 10 ms, (14·6%) was observed in all cases and was similar to that described previously. On the spastic side, the same technique results in a facilitation of same duration reaching a maximum of 15%. Hence the IB inhibitory effect is, at least functionally, absent in spasticity. Disappearance of IB inhibition is an additional mechanism to be considered in interpreting spasticity.

In cat, Golgi tendon organs, sensitive to muscle tension, project via large diameter fibres (IB fibres) on to the motoneurons of the muscle from which they originate, to inhibit them. Their activation results in a postsynaptic short lasting inhibition (IB inhibition). This latter appears after a short latency indicating that the interneuronal IB pathway is di- (eventually tri) synaptic. The IB inhibition, also named autogenic, is mediated through a special interneuron[1] which is thought to be glycinergic. The IB interneuron receives many segmentary afferents both cutaneous and proprioceptive. It is also influenced by supraspinal excitatory (from the cortico- and rubrospinal tracts) as well as inhibitory (from the dorsal reticulospinal tract) projections. A tonic inhibition of the IB interneuron has been described in the cat decerebrate rigidity preparation.[2]

For a long time, the IB inhibition has been considered as a protective mechanism against muscle extreme tension. However, the demonstration that active contraction of only few motor units is able to activate Golgi tendon organs suggests rather that IB inhibition plays a role in the ongoing control of the motor output.[3 4]

In the intact man, it is generally believed that the IB pathway is similar to that described in the cat.[5–7] It has been suggested that it could play a role in the clasp-knife phenomenon described in spastic patients. In fact, it is not known whether IB interneuron excitability is modified in human spasticity and, if so, in what direction. It might, however, be hypothesised that a reduction in IB inhibition could contribute, besides other mechanisms, to the hyperexcitability of the myotatic reflex which is the basis of spasticity.[8]

The present study has been undertaken to assess IB effects on the spastic side of hemiplegic patients and to compare the results with those obtained on the normal side. To do this, the technique proposed by Pierrot-Deseilligny *et al*[9] has been used. It is based on the assumption that very few IA fibres arising from the gastrocnemius medialis (GM) have excitatory projections on to soleus motoneurons. As a consequence, stimulation at threshold of the GM nerve used as conditioning manoeuvre activates only IB fibres and provokes an almost pure inhibition of soleus motoneurons which can be reflected in Hoffman reflex amplitude (fig 1).

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Patients and methods

Patients After agreement of the local Ethical Committee, six hemiplegic adults (age from 26 to 76 years) were studied, one on two occasions. They were free of myorelaxant drugs which were stopped for at least one week. Some characteristics of the patients are reported in the table. The degree of spasticity has been assessed using the Ashworth scale.[10] The patients were seated comfortably in a special armchair during the experiment whose duration did not exceed 1 ½ hour. Both legs were studied systematically; they were fixed rigidly with the knee flexed at 120° and the ankle at 100°.

The technique of testing IB inhibition has been described in full detail by Pierrot-Deseilligny *et al*.[7 9] Only a summary will be given here.

Conditioning stimulation A 1 ms electric shock was delivered through bipolar surface electrodes (DISA 13K60) fixed on the gastrocnemius medialis nerve (GM nerve) at the lower part of the popliteal fossa, 6 to 8 cm below the

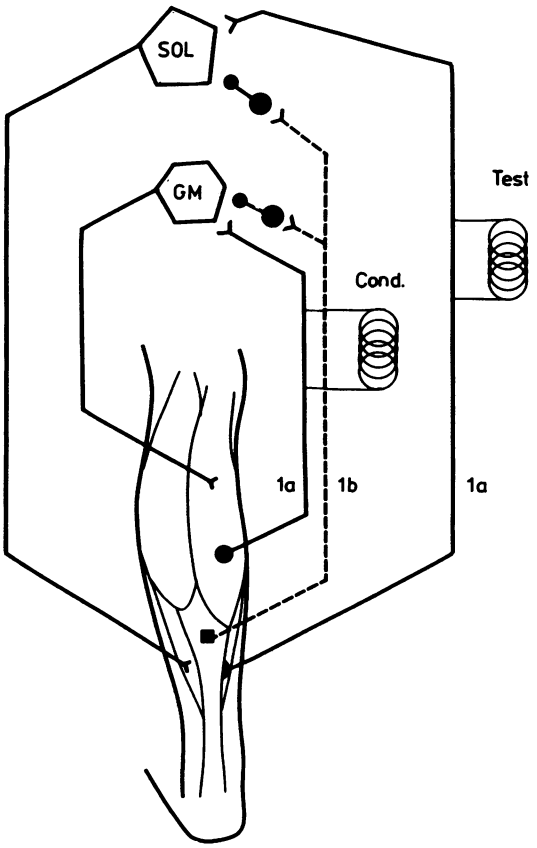

Fig 1 *Schematic diagram summarising the connections between gastrocnemius medialis (GM) nerve and soleus (soleus) motoneurons. The Ib inhibition technique is based on the assumption that very few Ia fibres from GM nerve have monosynaptic projections on soleus motoneurons. Conditioning stimulation of GM nerve (COND) can be expected to have an almost pure Ib effect on soleus motoneurons. Excitability of soleus motoneurons is tested by recording soleus H-Reflex (TEST).*

electrodes stimulating the posterior tibial nerve. The intensity was adjusted to 95% of the motor threshold for gastrocnemius medialis. It has been verified systematically that an intense GM nerve stimulation (4 × thresh.) was not able to elicit a H response in the soleus. This could have been possible by current diffusion to the posterior tibial nerve.

Test response The soleus H reflex, used as the test, has been evoked by posterior tibial nerve stimulation through bipolar electrodes (DISA 13K60) fixed at the upper part of the popliteal fossa. On both legs, a rectangular 1 ms shock was given at an intensity such that the amplitude of the reflex corresponded to 15% of the maximum motor response of the soleus (M response). In every case, the ratio between maximal

Table *Patients' characteristics*

Patient	*Age (yr)*	*Pathology*	*Side*	*Ashworth index*
M.R.	61	Stroke	R	3
R.A.	65	Stroke	L	2
P.J.	56	Stroke	L	3
H.J.	76	Stroke	L	1
V.J.	68	Stroke	R	2
P.G.	26	Stroke	R	4

amplitudes of the H reflex and the M response has been calculated. Reflex and motor responses were recorded from the soleus by surface electrodes fixed on the Achilles tendon and 3 cm above. The ground electrode was placed on the calves. After amplification (Tektronix 5223) the reflex responses were digitised (Apple II) and averaged (n = 16). The peak to peak amplitude with SEM has been measured.

After having obtained basal values, the H reflex has been conditioned at various delays after the conditioning stimulation: 2, 3, 4, 5, 6, 8 and 10 ms. Values without conditioning have been recorded at each interval too. The results have been expressed in percentage of control values in terms of delays separating the conditioning and the test. Significance of differences between both sides has been established using the paired *t* test.

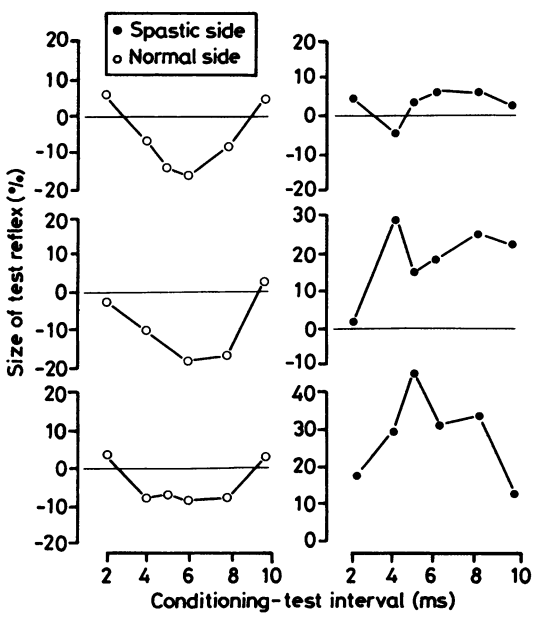

Fig 2 *Time course of the effect of GM nerve stimulation on soleus H-reflex observed on three hemiplegic subjects. Each symbol represents the mean amplitude of 20 soleus H-reflexes. Open circles represent results recorded on the normal side and filled circles indicate results from the spastic side. The size of test reflex (ordinate) represents the difference, expressed as a percentage, between control reflexes and test reflexes.*

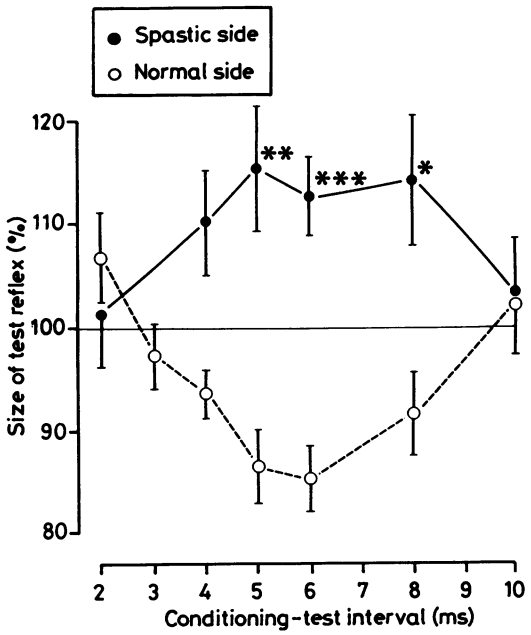

Fig 3 *Time course of the effect of GM nerve stimulation on soleus H-reflex. Each symbol represents the mean value of 20 averaged soleus H-Reflex. Each symbol represents the mean value of 20 averaged soleus H-reflex recorded on the 6 patients respectively results from the normal and the spastic side. The vertical bars represent standard errors of mean at each conditioning-test interval. (***: $p < 0.005$; **: $p < 0.025$; *: $p < 0.05$).*

Results

Normal side

The average H max/M max ratio measured on the normal side was 27%. Following a conditioning GM nerve stimulation, an inhibition of the soleus H reflex was systematically observed (fig 2). This inhibition showed a time course similar to the Ib inhibition reported by Pierrot-Deseilligny *et al*[9] in normal subjects: the inhibition began after an interval of 2 ms, reached a maximum after 6 ms and returned to the control level after an interval of 10 ms. On average, the maximum inhibition amounted 14·63% of the test reflex and has been seen for a conditioning-test interval of 6 ms (fig 3).

Spastic side

The average H max/M max ratio was 67% on the spastic side. Contrary to what has been observed on the normal side, the GM nerve stimulation led to a clear facilitation of the soleus H reflex (fig 2). This facilitatory effect presented the same time course as the inhibition observed in the normal side. In fact, the two curves are specular. The peak value of the facilitatory effect reached 15, 24% on average. The maximum has been seen for a conditioning-test interval of 5 ms (fig 3). The amount of maximal facilitation measured in each patient is moderately correlated with the degree of spasticity assessed by the Ashworth scale (r = 0·6) (fig 4).

Discussion

The results show a clear cut difference between the effects of GM nerve stimulation on soleus H reflexes recorded on the normal and on the spastic side of hemiplegic subjects. On the normal side our results confirm those previously reported by Pierrot-Deseilligny *et al*[9] in normal subjects. The low intensity of the conditioning stimulus (0·95 × MT, see *Method*) and the short latency of its inhibitory effect on soleus H reflex suggest that this inhibition is mediated by group I afferent fibres. As proposed by Pierrot-Deseilligny *et al*,[9] it is likely that this short-latency autogenic inhibition is mediated by the disynaptic Ib pathway, even if it has been shown, in the cat, that Ia afferent fibres also contribute to these autogenic inhibitory effects. However, an exact discrimination between Ib inhibition and autogenic Ia inhibition is not possible because of the very discrete difference between the activation threshold of these fibres.[7] Ib inhibition is thus preserved on the normal side of hemiplegic patients.

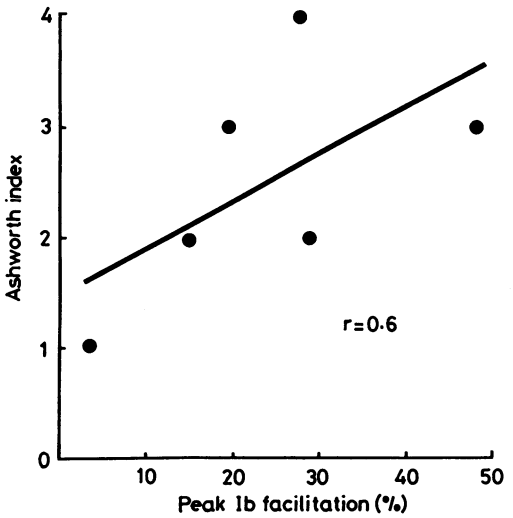

Fig 4 *Linear regression "peak Ib facilitation" (value of the maximum facilitation of the soleus H-reflex recorded on the spastic side, when conditioned by a GM nerve stimulation) and the intensity of spasticity (Ashworth index).*

On the contrary, GM nerve stimulation failed to inhibit soleus H-reflex on the spastic side and evoked a clear facilitation of the test reflex. Could this difference between both sides be attributed to methodology? Since the test stimulus was adjusted to obtain on both sides a soleus H reflex equal to 15% of M Max, response test reflexes were thus identical and not linked to the H Max amplitude which was in fact increased on the spastic side.[11 12] The test reflex used on both sides activates the same number of motor units and could not explain a change of sign in the results. On the other hand, intensity of the conditioning stimulus, expressed as a percentage of the threshold for the M response of the GM muscle (see *Method*), was not statistically different on the two sides. So it can be assumed that the conditioning stimuli activate the same group of afferent fibres. What is the nature of group I afferent fibres responsible for the H reflex facilitation? At first sight, the role of IA fibres is likely to account for a facilitation. In fact, even if the technique for testing IB inhibition is based on the assumption that very few IA afferent fibres from GM have excitatory projections on to soleus motoneurons, such connections cannot definitively be ruled out;[9] the so-called IB inhibition observed in normal subjects could simply reflect the algebraic sum of a moderate facilitation mediated through IA afferents and a more intense inhibition brought about by IB fibres. When applied on the spastic side, the technique could reveal a clearly more marked IA facilitation leading as a net result to a facilitation. The duration of the facilitation could be explained by the temporal dispersion within the IA volley. Assuming a conduction velocity between 60 m/s for the fastest and 40 m/s for the slowest IA afferent fibres[13] and a peripheral pathway of 83 cm, the IA message would arrive at the spinal cord after delays ranging from 13·83 to 20·75 ms and a dispersion of 7 ms would be compatible with facilitation duration. A problem arises, however, with the onset of the facilitation which occurs exactly at the same delay (2 ms) as the disynaptic IB inhibition. For that reason, it has to be hypothesised that the IA facilitation is mediated by a disynaptic pathway. This is not impossible. In the cat, oligo- and polysynaptic pathways for the IA group fibres have been demonstrated[14 15] and arguments in favour of an oligosynaptic contribution to soleus H reflex in man also exist.[16]

Although Ia effects are good candidates to explain it, another mechanism could, however, be responsible for the facilitation of soleus H reflex after GM nerve stimulation. An inversion of the sign of the force feedback (Ib pathway) has been described in the premamillary decerebrate cat.[17] On the basis of both experimental data and mathematical models of stretch reflex, it has been found that the disynaptic inhibitory pathways from Golgi tendon organs may give a positive value to the force feedback. In other words, in the premammillary decerebrate cat, the Ib pathway is possibly facilitatory. This hypothesis agrees with the spike-triggered averaging study of Watt *et al*[18] who found that Ib effects are facilitatory in 18% of synergistic motoneurons. In the light of these data, it could be suggested that a defacilitation or an active inhibition of Ib inhibitory pathway, due to supraspinal lesions, could make the Ib excitatory pathway dominate. However, such a pathway has never been described in man and this mechanism remains purely hypothetical.

Whatever the facilitatory mechanism actually involved, it appears that the Ib inhibitory effect is, at least functionally, absent in spasticity. Thus, this absence of Ib inhibition is to be considered as an additional spinal mechanism underlying human spasticity.[19]

This conclusion leads to a consideration of the IB role in muscle stiffness and the interpretation of clasp-knife phenomenon.

It has been suggested by Nichols and Houk[20] that the major function of both length (Ia afferent pathway) and force feedback (Ib afferent pathway) is to maintain linear relationship between length and tension in muscle. In other words, their muscle stiffness regulation hypothesis emphasises muscle stiffness as the property regulated by the stretch reflex. According to their view, if Ib inhibition is depressed or absent in spasticity, an increased muscle stiffness should appear, especially during active contraction, since Golgi tendon organs are known to become active during muscle contraction.[21]

The clasp-knife phenomenon was initially attributed to a Ib inhibitory effect acting on homonymous motoneurons[22 23] because it was found that Golgi tendon organs had a high threshold of activation.[24] This hypothesis has been widely criticised since the finding that the active contraction of only a few motor unit activates GTO and that GTO do not discharge in relation with the clasp knife phenomenon.[25] The discussion concerns chiefly the quadriceps muscle, as the clasp-knife phenomenon, if present, is always difficult to detect in the soleus. However, if our results can be extrapolated to quadriceps, they would constitute an additional argument against a role of IB inhibition in the explanation of that sign; if IB inhibition is functionally absent in spasticity, it is clear that it cannot be responsible for motoneuron inhibition underlying clasp-knife phenomenon.

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