ELSEVIER

Electroencephalography and clinical Neurophysiology 97 (1995) 402–407

Soleus H reflex extinction in controls and spastic patients: ordered occlusion or diffuse inhibition?

A.A.J. Hilgevoord *, L.J. Bour, J.H.T.M. Koelman, B.W. Ongerboer de Visser

Graduate School Neurosciences Amsterdam, Clinical Neurophysiology (D2) and Department of Neurology, Academic Medical Center, AZUA, Meibergdreef 9, 1105 AZ Amsterdam, The Netherlands

Accepted for publication: 20 July 1995

Abstract

Extinction of the soleus H reflex at higher stimulus intensities is commonly attributed to retrograde conduction of action potentials in motor axons. This study was designed to gain further insight into the mechanisms underlying the extinction. The decrease of the H reflex was quantified in a group of controls and spastic patients, with and without depression of the H response by continuous tendon vibration. Response amplitudes were normalized as a percentage of the maximal M wave amplitude. Stimuli were normalized as a multiple of the M wave threshold. After normalization, the mean M recruitment curves, and similarly the fractions of motor axons activated, were equal in each group. In contrast, the mean H reflex amplitudes at the M threshold were different. The mean H reflex decrease, between 1.0 and 1.5 times the M threshold, was found to be the same fraction of the maximal H reflex amplitude in each group. The largest motor fibres, belonging to the largest motoneurones, are traditionally thought to have the lowest threshold for electrical excitation. Collision or retrograde inactivation should therefore preferentially affect the largest motoneurones, employed in only the largest H reflexes, at the lowest stimulus intensities. Our results are contrary to this hypothesis. Renshaw and/or Ib inhibition is likely to play a role in the initial decrease of the H reflex at higher stimulus intensities.

Keywords: Soleus H reflex recruitment; H reflex extinction; Vibratory inhibition; Spasticity; Normalization

1. Introduction

The soleus H reflex indicates the excitation of spinal motoneurones after electrical activation of Ia afferent fibres in the tibial nerve (Hoffmann, 1918; Magladery and McDougal, 1950; Pierrot-Deseilligny, 1966). With increasing stimulus currents the H reflex magnitude initially increases. At higher stimulus intensities, however, motor axons are also activated, resulting in an M wave in the EMG. Increasing the stimulus intensity further gives an increase of the M wave amplitude while the H reflex decreases. The extinction of the H reflex is commonly attributed to the antidromic volley evoked in the motor axons. This antidromic volley could lead to H reflex extinction through 2 basically different mechanisms.

(1) *Ordered occlusion:* motoneurones whose axons are electrically activated are excluded from contributing to the H reflex response. Axons with the largest diameter, belonging to the largest motoneurones, are traditionally thought to be activated at the lowest stimulus intensity (Hugon, 1973). According to the size principle, the recruitment of motoneurones proceeds in the opposite direction (Henneman et al., 1965). The largest motoneurones are therefore the last to be recruited, and the first to be affected by occlusion. Ordered occlusion could result, first, from collision of reflexly generated descending, and antidromic impulses in the motor axons. Second, ordered occlusion could be due to retrograde inactivation, where the arrival of the antidromic impulse at the axon hillock causes a refractory period in which the motoneurone is inexcitable (Gottlieb and Agarwal, 1976).

(2) *Diffuse inhibition:* the extinction process does not preferentially affect the largest cells of the pool but has an inhibitory effect which is distributed diffusely over the motoneurone pool. Diffuse inhibition could result from 2 processes. First, activation of inhibitory Renshaw cells by the retrograde volleys through motor axon collaterals. Renshaw cells project to multiple motoneurones, so their exci-

* Corresponding author. Tel.: +31 20 5662915; Fax: +31 20 5664440.

SSDI 0013-4694(95)00174-3

EEM 95536

tation may affect the whole motoneurone pool (Kots, 1977; Hultborn et al., 1979). Second, occlusion could affect both large and small cells randomly if the activation thresholds of the motor axons do not correlate well with the axon diameter.

The retrograde volley in the motor axons is not the only possible pathway for H reflex extinction. Activation of inhibitory afferents (Ib) could contribute to a decrease of the H reflex amplitude.

In this study we quantified the decrease of the soleus H reflex amplitude at higher stimulus intensities in controls and spastic patients with and without continuous vibration of the Achilles tendon. After normalization of response amplitudes and stimulus currents, the mean M recruitment curves, and thus presumably the average retrograde volleys, were equal in these 4 groups. This allowed us first to assess the effect of a similar retrograde volley when the H reflex amplitude is reduced by vibration and second, to compare controls and spastic patients. The average maximal H reflex amplitude was higher in the patients. This larger maximum is usually attributed to an increase in central excitability. However, the maximum is described best as the point beyond which the inibitory effect of a stimulus increase is larger than the excitatory effect. Therefore, we felt it was important to establish whether H reflex extinction was similar in controls and spastic patients.

2. Subjects and methods

2.1. Subjects

The control group consisted of 30 subjects (10 females, 20 males). The mean age was 33 years (range 21–63). From this group 70 H recruitment curves, 33 from the left and 37 from the right leg, were recorded.

From 33 patients (13 females, 20 males), with a mean age of 44 years (range 18–68), 50 H reflex recruitment curves were obtained, 26 from the left leg, and 24 from the right leg. Patients were selected for the presence of spasticity in the lower limbs. Clinical signs included paresis, a velocity dependent increase in muscle tone, hyperreflexia and/or clonus. The clinical situation had to be stable for 1 month. The severity of spasticity ranged from mild to severe. None of the patients used any medication known to influence spasticity. Results from subjects with traumatic spinal cord lesions, slowly progressive spastic paraparesis and spondylotic myelopathy did not differ significantly and were pooled.

In most subjects both legs were examined in the same session. A few controls were examined twice in separate sessions. Either both legs or the most affected leg were examined in the patients. As a group, the results from the left and right side did not differ and were pooled. Means were calculated by considering all recruitment curves as separate samples. Standard errors are based on the number of subjects.

All subjects gave informed consent. The study was approved by the local ethical committee.

2.2. Methods

The techniques used to obtain a soleus H reflex recruitment curve have been described previously (Hugon, 1973; Ongerboer de Visser et al., 1989). The posterior tibial nerve was stimulated with a 1 msec pulse (Grass S88) through a surface electrode in the popliteal fossa. For recording, disc electrodes were placed 3 cm apart over the

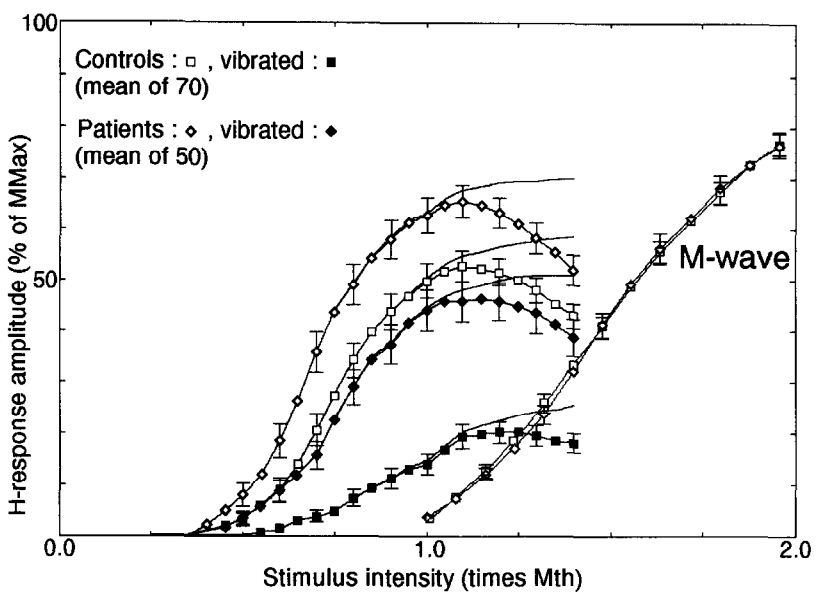

Fig. 1. Mean H response and M wave magnitude in each group as a function of the normalized stimulus intensity. The continuously rising maximized H curves enable an assessment of the effect of the H reflex decrease on the mean H reflex amplitude.

soleus muscle below the insertion of the gastrocnemius tendons. The EMG signals were amplified and filtered (3 Hz–10 kHz), digitized (10 kHz) and stored on computer for analysis.

A variable number of 15–35 EMG responses at different stimulus intensities were obtained to construct the H and M recruitment curves. The stimulus intensity was gradually increased from below the threshold for the H response to supramaximal for the M wave. Subsequently, recording was repeated during continuous vibration of the Achilles tendon with a Bruël & Kjær 4809 vibrator (1 mm/100 Hz). The M recruitment curves with and without vibration were compared to exclude trials associated with electrode displacements. The inter-stimulus interval was at least 30 sec.

Stimulus currents and response amplitudes were normalized to enable a comparison of recruitment curves from different individuals. Peak-to-peak amplitudes were expressed as percentage of the maximum M wave amplitude (M_{max}). Stimulus intensity was expressed as a multiple of the M wave threshold (Mth) (Hilgevoord et al., 1994a).

2.2.1. Assessment of H reflex extinction

In every subject, the difference between the maximum H response (H_{max}) and the measured H response amplitude was determined at the downgoing slope of the H recruitment curve. The H reflex decrease was expressed as a percentage of both M_{max} and H_{max} and the mean was calculated for controls and spastic patients, with and without Achilles tendon vibration.

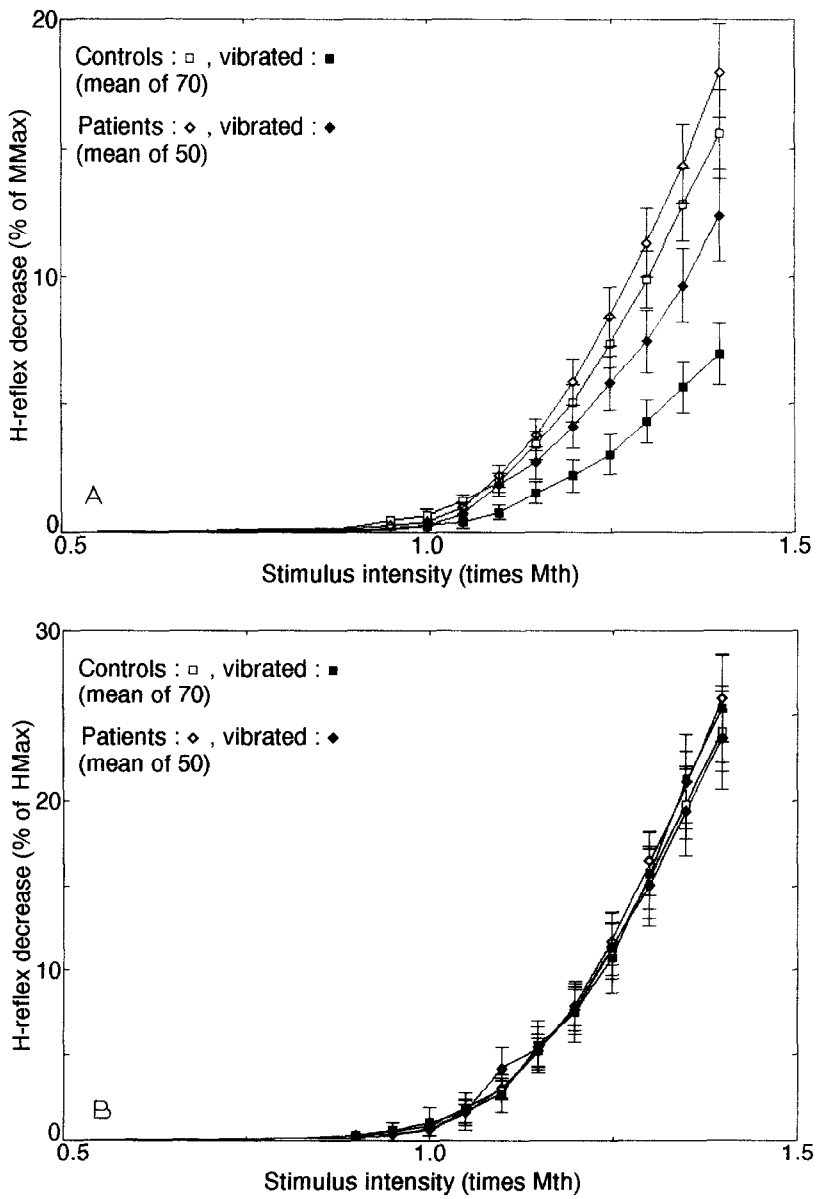

Fig. 2. H reflex extinction expressed as the mean in each group of the maximal minus the actual H reflex amplitude at every normalized stimulus intensity. The decrease of the H reflex amplitude is normalized as a percentage of M_{max} (A) and as a percentage of H_{max} (B).

3. Results

The mean H reflex amplitude (% of M_{max}) at every stimulus intensity (×Mth) in controls and patients, with and without vibration is shown in Fig. 1. After normalization, the M wave recruitment curves do not differ significantly; only the unvibrated means are displayed. In contrast, the mean H reflex amplitude curves are different in controls and patients and in the unvibrated and vibrated conditions. The effect of the decrease of the H reflex on the mean amplitude in each group is visualized through a "maximized" curve, which is constructed as follows. In the recruitment curve of each individual, every H reflex amplitude at the decreasing slope of the curve is replaced by H_{max}. From these constructed curves, a mean amplitude at every normalized stimulus intensity is calculated for each group. This procedure does not aim to remove every effect of extinction. The maximized curve simply displays the mean H response amplitude in each group after removing the decrease at higher stimulus intensities. The divergence between the maximized and the mean H response curve indicates the onset of an H reflex decrease at a stimulus intensity close to the Mth. The divergence starts as early as the rising slope of the mean H response curve. This is because the H reflex amplitude is initially depressed in a few subjects, whereas in the majority it has not yet reached the maximum.

As expected, extinction increases with stimulus intensities above the Mth. The onset of the decrease does not differ clearly between groups. The H reflex decrease as a percentage of M_{max} is largest in the group with the highest mean H response amplitude (Fig. 2A). However, as a percentage of the maximal H response, the mean decrease is similar for all groups (Fig. 2B). In addition, for both controls and patients, the H reflex decrease (% H_{max}) was similar for subjects with different levels of vibratory inhibition.

4. Discussion

The mean normalized M recruitment curves were equal in all groups. The H reflex amplitudes differed. However, the average H reflex decrease was an equal fraction of the maximal H reflex amplitude in each group. A distinction between the potential mechanisms responsible for H reflex extinction can probably be made based on the H reflex decrease in the different groups. Two basic neurophysiological principles were applied: (1) The largest motoneurones are the last to be recruited by an increasingly large excitatory input. This is the "size principle" of Henneman et al. (1965). (2) Motor axons with larger diameters are traditionally assumed to have lower thresholds for electrical excitation than smaller ones (Gottlieb and Agarwal, 1976; McNeal, 1976; Rattay, 1986; Panizza et al., 1992). Overall, the largest motor axons belong to the largest motoneurones (Cullheim, 1978). Even if some overlap between the thresholds of fibres of different sizes exists, larger motoneurones would tend to be affected earlier by occlusion.

These two principles have the following consequences for the manner in which ordered occlusion should affect the H reflex amplitude in each individual:

(1) The largest motoneurones are recruited only in the largest H reflexes. If occlusion is limited to the motoneurones whose axon is activated, then the largest H reflexes should be affected at the lowest stimulus intensities.

(2) Once affected by ordered occlusion, the H reflex amplitude decreases with higher stimulus intensities. This decrease cannot be compensated by an increase in synaptic excitation because excitation has to recruit increasingly larger motoneurones. However, the larger the motoneurone, the greater the chance that it is already affected by occlusion.

The H reflex decrease (% of H_{max}) quantifies the fraction of motoneurones that were recruited for the H response, which is lost due to extinction. Ordered occlusion will initially affect a number of the largest motoneurones. Smaller H reflexes employ smaller motoneurones. Consequently, the depression of the H response due to an ordered occlusion process should be less in a group with a smaller mean H reflex amplitude. In contrast, our results show that the decrease is the same fraction for all groups. Diffuse inhibition can probably result in an equal relative decrease of the H response in each group even when the excitatory drive differs, because the H reflex decrease was expressed relative to H_{max}. This maximal amplitude will also be affected by a diffuse inhibition.

Although the H reflex decrease was quantified in 4 diferent groups, this comparison seems justified. The normalized M recruitment curves, and therefore, probably, the average retrograde volleys in the motor axons were similar in each group. Vibration does not affect the motoneurone excitability, but reduces the H response by a premotoneuronal mechanism (Ashby and McCrea, 1987; Nielsen and Hultborn, 1993). The last motoneurone recruited is the first de-recruited by vibration (Desmedt and Godaux, 1978). The maximum H reflex amplitude may be influenced by peripheral stimulation conditions. For each group in which the H reflex is depressed by vibration, these conditions remain the same. Equal peripheral conditions could not be assumed in a comparison of subjects with large versus small H reflexes. The mean H reflex amplitude was higher in the spastic patients, but the initial slope of the H recruitment curve was similar to that in the controls (Hilgevoord et al., 1994a). Vibratory inhibition is decreased in spasticity (Delwaide, 1971; Ashby et al., 1980; Bour et al., 1991). However, the overall relation between H reflex amplitude and the level of vibratory inhibition has a similar shape in controls and patients (Hilgevoord et al., 1994b). This suggests that the relative

distribution of the motoneurone thresholds, and thus Henneman's size principle, is preserved in the patients.

4.1. How can an antidromic volley lead to diffuse H reflex inhibition?

(1) The motoneurone recruitment order, with an increasing Ia afferent volley, may be influenced by non-size related factors (Clamann et al., 1983).

(2) Peripheral motor axons may be activated in a purely random order.

(3) The antidromic volley may activate inhibitory Renshaw cells.

The first possibility would be contrary to the size principle. It cannot be excluded, however, that the axon diameter is not the primary factor determining the excitation threshold with surface stimulation. For example, the distance from the stimulating electrode may be important. However, the H response in a single motor unit may disappear at higher stimulus intensities without the occurrence of an M response in this unit (Trontelj, 1973). This is a strong argument against collision or retrograde inactivation. Thus even with a random order of excitation of motor axons, occlusion cannot be the explanation for the extinction of the H reflex.

Lastly, Renshaw cell activation could cause a diffusely distributed inhibition (Hultborn et al., 1988). The rise time of the motoneurone EPSP (Ashby and Zilm, 1982; Burke et al., 1984), due to Ia afferent stimulation, may be long enough to be affected by the activation of Renshaw cells through fast conducting motor axons (Miles et al., 1989). Recurrent inhibition does not affect the recruitment order (Clamann et al., 1974). The decrease of the H reflex found in this study was similar in controls and patients. In previous studies an increase in recurrent inhibition was found in some spastic patients (Katz and Pierrot-Deseilligny, 1982; Shefner et al., 1992). However, due to methodological differences, these findings cannot be used to exclude a role for Renshaw cell activation in H reflex extinction.

Activation of inhibitory (Ib) afferents at higher stimulus intensities could contribute to reflex extinction. Ib inhibition can affect the Ia composite EPSP in the motoneurones even though the conduction velocity of Ib afferents is somewhat slower than that of Ia afferents and their projection onto the motoneurones is disynaptic (Pierrot-Deseilligny et al., 1981). However, although Ib inhibition could depress the maximal H reflex amplitude (Crone et al., 1990), it may be of lesser importance for the decrease of the H reflex at higher stimulus intensities. The H reflex amplitude was usually maximal slightly above the M wave threshold (Hilgevoord et al., 1994a) and decreased as the M wave increased in size. Previous reports indicate that the maximum level of Ib inhibition can already be reached below M threshold (Pierrot-Deseilligny et al., 1979, 1981).

In conclusion, the mean decrease of the H reflex at higher stimulus intensities, relative to the maximum amplitude, remains unaltered when the H reflex is depressed by tendon vibration. In addition, the decrease is similar in controls and patients with spasticity of the lower limbs. This result is difficult to explain if H reflex extinction were based on an ordered occlusion process. The decreasing slope of the H reflex recruitment curve is often simply discarded in analyses. However, insight into the nature of H reflex extinction could increase our knowledge about the mechanisms underlying motoneurone excitation and inhibition in man.

Acknowledgements

A.A.J.H. was supported by a grant from the Netherlands Organization for Scientific Research (NWO), Project No. 900-550-080.

References

Ashby, P. and McCrea, D.A. Further observations on the depression of group Ia facilitation of motoneurons by vibration in man. Exp. Brain Res., 1987, 69: 1–6.

Ashby, P. and Zilm, D. Characteristics of postsynaptic potentials produced in single human motoneurons by homonymous group I volleys. Exp. Brain Res., 1982, 47: 41–48.

Ashby, P., Verrier, M. and Carleton, S. Vibratory inhibition of the monosynaptic reflex. In: J.E. Desmedt (Ed.), Progress in Clinical Neurophysiolgoy, Vol. 8. Karger, Basel, 1980: 254–262.

Bour, L.J., Ongerboer de Visser, B.W., Koelman, J.H.T.M., Van Bruggen, G.J. and Speelman, J.D. Soleus H-reflex tests in spasticity and dystonia: a computerized analysis. J. EMG Kinesiol., 1991, 1: 9–19.

Burke, D., Gandevia, S.C. and McKeon, B. Monosynaptic and oligosynaptic contributions to human ankle jerk and H-reflex. J. Neurophysiol., 1984, 52: 435–447.

Clamann, H.P., Gillies, J.D. and Henneman, E. Effects of inhibitory inputs on critical firing level and rank order of motoneurones. J. Neurophysiol., 1974, 37: 1350–1360.

Clamann, H.P., Ngai, A.C., Kukulka, C.G. and Goldberg, S.J. Motor pool organization in monosynaptic reflexes: responses in three different muscles. J. Neurophysiol., 1983, 50: 725–742.

Crone, C., Hultborn, H., Mazières, L., Morin, C., Nielsen, J. and Pierrot-Deseilligny, E. Sensitivity of monosynaptic test reflexes to facilitation and inhibition as a function of the test reflex size: a study in man and the cat. Exp. Brain Res., 1990, 81: 35–45.

Cullheim, S. Relations between cell body size, axon diameter and axon conduction velocity of cat sciatic alpha motoneurons stained with horseradish peroxidase. Neurosci. Lett., 1978, 8: 17–20.

Delwaide, P.J. Etude Expérimentale de l'Hyperréflexie Tendineuse en Clinique Neurologique. Editions Arscia, Brussels, 1971.

Desmedt, J.E. and Godaux, E. Mechanism of the vibration paradox: excitatory and inhibitory effects of vibration on single soleus muscle motor units in man. J. Physiol. (Lond.), 1978, 285: 197–207.

Gottlieb, G.L. and Agarwal, G.C. Extinction of the Hoffman reflex by antidromic conduction. Electroenceph. clin. Neurophysiol., 1976, 41: 19–24.

Henneman, E., Somjen, G. and Carpenter, D. Excitability and inhibitability of motoneurons of different sizes. J. Neurophysiol., 1965, 28: 599–620.

Hilgevoord, A.A.J., Koelman, J.H.T.M., Bour, L.J. and Ongerboer de Visser, B.W. Normalization of soleus H-reflex recruitment curves in controls and a population of spastic patients. Electroenceph. clin. Neurophysiol., 1994a, 93: 202–208.

Hilgevoord, A.A.J., Koelman, J.H.T.M., Bour, L.J. and Ongerboer de Visser, B.W. Stimulus-response relations of soleus H-reflex and vibratory inhibition in controls and spastic patients. Mov. Disord., 1994b, 9 (Suppl. 1): P552.

Hoffmann, P. Über die Beziehungen der Sehnenreflexe zur willkürlichen Bewegung und zum Tonus. Z. Biol., 1918, 68: 351.

Hugon, M. Methodology of the Hoffmann reflex in man. In: J.E. Desmedt (Ed.), New Developments in Electromyography and Clinical Neurophysiology, Vol. 3. Karger, Basel, 1973: 277–293.

Hultborn, H., Lindstrom, S. and Wigstrom, H. On the function of recurrent inhibition in the spinal cord. Exp. Brain Res., 1979, 37: 399–403.

Hultborn, H.J., Katz, R. and Mackel, R. Distribution of recurrent inhibition within a motor nucleus. II. Amount of recurrent inhibition in motoneurones to fast and slow units. Acta Physiol. Scand., 1988, 134: 363-374.

Katz, R. and Pierrot-Deseilligny, E. Recurrent inhibition of alpha-motoneurons in patients with upper motor neuron lesions. Brain, 1982, 105: 103–124.

Kots, Y.M. The Organization of Voluntary Movement. Neurophysiological Mechanisms. Plenum Press, New York, 1977: 27–60.

Magladery, J.W. and McDougal, D.B. Electrophysiological studies of nerve and reflex activity in normal man. I. Identification of certain reflexes in the electro-myogram and the conduction velocity of peripheral nerve fibres. Bull. Johns Hopk. Hosp., 1950, 86: 265–290.

McNeal, D.R. Analysis of a model for excitation of myelinated nerve. IEEE Trans. Biomed. Eng., 1976, 23: 329–337.

Miles, T.S., Le, T.H. and Türker, K.S. Biphasic inhibitory responses and their IPSPs evoked by tibial nerve stimulation in human soleus motor neurones. Exp. Brain Res., 1989, 77: 637–645.

Nielsen, J. and Hultborn, H. Regulated properties of motoneurons and primary afferents: new aspects on possible spinal mechanisms underlying spasticity. In: A.F. Thilmann, D.J. Burke and W.Z. Rymer (Eds.), Spasticity: Mechanisms and Management. Springer, Berlin, 1993: 177–192.

Ongerboer de Visser, B.W., Bour, L.J., Koelman, J.H.T.M. and Speelman, J.D. Cumulative vibratory indices and the H/M ratio of the soleus H-reflex: a quantitative study in control and spastic subjects. Electroenceph. clin. Neurophysiol., 1989, 73: 162–166.

Panizza, M.E., Nilsson, J., Roth, B.J., Basser, P.J. and Hallett, M. Relevance of stimulus duration for activation of motor and sensory fibres: implications for the study of H-reflexes and magnetic stimulation. Electroenceph. clin. Neurophysiol., 1992, 85: 22–29.

Pierrot-Deseilligny, E. Etude par le Réflexe Monosynaptique (Réflexe H) de Certains Méchanismes Impliqués dans la Régulation Tonique Posturale Normale et Pathologique. Thesis, Faculté de Médecine, Paris, 1966.

Pierrot-Deseilligny, E., Katz, R. and Morin, C. Evidence for Ib inhibition in human subjects. Brain Res., 1979, 166: 176–179.

Pierrot-Deseilligny, E., Morin, C., Bergego, C. and Tankov, N. Pattern of group I projections from ankle flexor and extensor muscles in man. Exp. Brain Res., 1981, 42: 337–350.

Rattay, F. Analysis of models for external stimulation of axons. IEEE Trans. Biomed. Eng., 1986, 33: 974–977.

Shefner, J.M., Berman, S.A., Sarkarati, M. and Young, R.R. Recurrent inhibition is increased in patients with spinal cord injury. Neurology, 1992, 42: 2162–2168.

Trontelj, J.V. A study of the H-reflex by single fibre EMG. J. Neurol. Neurosurg. Psyschiat., 1973, 36: 951–969.