MOTONEURONE AND MONOSYNAPTIC REFLEX EXCITABILITY STUDIED IN MAN

by

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A thesis presented for the degree of

Doctor of Philosophy

of the University of Southampton

Department of Physiology & Biochemistry
The University
Southampton

November 1976

ACKNOWLEDGEMENTS

I would like to express my sincere gratitude to the following persons; Dr. E.M. Sedgwick for his enthusiastic supervision throughout this work and in particular for his constructive criticism and encouragement during the preparation of this thesis; Professor G. A. Kerkut for the provision of laboratory facilities and helpful suggestions for writing this manuscript; the head of the department, Professor K.A. Munday for the opportunity of working at Southampton.

In addition I am indebted to Dr. L. Illis for his continuous interest in the work and in particular for the opportunity of working on patients with multiple sclerosis, treated by spinal cord stimulation. I wish to thank Dr. A. Oygar for provision of MS patients with spinal cord stimulation. Dr. A. D. Thornton of the ISVR has been most helpful with provision of computer programmes. I want to thank him most sincerely.

I am grateful to my colleagues, Jan Roberts and Brian Smith for reading and making comments on this thesis and to the many volunteer subjects without whom this work would not have been possible.

Financial support of the Egyptian Government is gratefully acknowledged.

In conclusion I would like to thank my parents for their inculcation in me of a desire to pursue advanced academic studies and their continuous encouragement at all times.

Overall thanks are to my God for giving me health and continuous inspiration to establish this work.

ABBREVIATIONS

@-MN	Alpha motoneurone
A-Ch	Acetyl choline
AP, APs	Action potential or potentials
ATP'ase	A denosine triphosphatase
ATR	Achilles tendon reflex
CNS	Central nervous system
CV	Conduction velocity
EEG	Electroencephalography
EMG	Electromyography
EPSP, IPSP	Excitatory or inhibitory postsynaptic potential
FF	Fast contracting fast fatigue muscle fibre
FR	Fast contracting, fatigue resistance
Group II	Secondary afferent fibres
HT	High threshold type of muscle fibre
HZ	Hertz or (C/sec cycle per second)
JPs	Joint position sense
K^+	Potassium contents
L	left
Lx	xth lumbar level
LL, UL	Lower limb or upper limb
LLR	Long loop reflex
LT	Low threshold type of muscle fibre
Ma	Milliampere
Min	Minute
M-response	Muscle response
mm, cm	millimeter, centimeter

M	Mega-Ohm
MN	Motoneurone
MND	Motoneurone disease
MNP	Motoneurone pool
MRC	Medical Research Council
MS	Multiple sclerosis
msec, μsec., sec.	Millisecond, microsecond and second
msec/cm	millisecond per centimeter
MT	Medium threshold type of muscle fibre
MSR	Monosynaptic reflex
mV	Millivolt
P	Probability of error
PPS	Pulse per second
R	Right
Sx	Xth sacral level
SC	Spinal cord
SCS	Spinal cord stimulation
SFAP	Single fibre action potential
SmFAP	Single muscle fibre action potential
SFEMG	Single fibre electromyography
Tx	Xth thoracic level
TVR	Tendon vibration reflex
μ	Micron
UMNL	Upper motor neurone lesion
V	Volt or volts
WNC	Wessex Neurological Centre
$X^{o}C$	X degree centigrade

Y or	Gamma motoneurones
Ia, Ib	Spindle primaries, the afferent of tendon organs
<	Less than
>	More than
+ve, -ve	Positive or negative

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ABSTRACT

FACULTY OF MEDICINE

PHYSIOLOGY AND BIOCHEMISTRY

Doctor of Philosophy

MOTONEURONE AND MONOSYNAPTIC REFLEX EXCITABILITY STUDIED IN MAN

by Mohammed Ahmed El-Sabbahi Awadalla

Natural stimulation of the skin and muscle was found to modulate the monosynaptic reflex and motoneurone excitability as judged by the H-reflex. Skin cold and mechanoreceptors inhibit the reflex as does muscle vibration while cooling of the muscle resulted in facilitation. The effective skin areas were of the same spinal segments as the muscle investigated.

The motoneurone pool was inhibited for 50 msec. after a conditioning electrical stimulus. The postulated mechanism for this is transmitter depletion and the evidence obtained supports this. Moreover the evidence excluded the involvement of Golgi tendon organs.

The motoneurone excitability measured by the recovery curves was tested in young and old subjects and significant differences were found. Degeneration in the large diameter afferent fibres and motoneurones could account for the findings.

Electrostimulation of the spinal cord in MS improves the abnormal recovery curves towards normal. Other electrophysiological studies using the implanted electrodes were made and demonstrated changes in monosynaptic reflex excitability.

Monosynaptic and motoneurone excitability were studied at the unitary level using single fibre EMG techniques and early physiological conclusions were confirmed. Motoneurones recovered from inhibition

in a definite pattern. Different properties were noticed for units of the soleus which suggested a division into two groups according to their order of recruitment during incremental stimuli; blockage and inhibition. One group was recruited and blocked early followed by the other group with increasing stimuli. An opposite order was demonstrated during mechanoreceptor stimulation. A new hypothesis was explored, controversial to Henneman's size principle and implies that the external requirements of the movements determine the order of recruitment of the different motoneurones.

Clinically in myotonic dystrophy significant changes were found in monosynaptic and motoneurone excitability. Neurological defects were shown which confirm the involvement of the nervous system in this disease.

I. INTRODUCTORY SECTION

INTRODUCTION

1. Preliminary remarks

In clinical neurology one is faced with diseases manifested by hypertonia, hypotonia or uncontrolled movements. The main output of the central nervous system consists of integrated movements, the method of organization of which is a continuing challenge to experimental workers. These automatic and volitional commands emanating from central nervous system express themselves through the highly controlled function of the motoneurones. These are the final common path to the muscle which faithfully obeys impulses descending from the nerve cell. However, these cells are subject to sophisticated mechanisms making it an efficient integrating system. The internuncial network, the suprasegmental and the supraspinal computing mechanisms, handle the data coming to it through the vast numbers of nerve fibers from the afferent receptors, process it and execute the response through the motoneurone cells. One can imagine the motoneurone as a cell body with thousands of terminals on it. Hence Sherrington's concept of a motoneurone pool for expressing these relations. The shortage of methods of investigation of motoneurone defects forms a problem in the pathophysiology of diseases.

At the outset it should be emphasized that, as far as motoneurones are concerned, the essential problems no longer center around reflexes, though reflexes are still the helpful tools they have always been in this field. The essential problems concern the biasing or setting of the various mechanisms by which motoneurones operate reflexively or otherwise.

A number of reflexes have been described which are claimed to utilize monosynaptic as well as polysynaptic paths. The stretch reflex is the best representative of these and has been studied by myography, electromyography, monosynaptic testing and ultimately by intracellular recordings in animals.

The study of motoneurone excitability using monosynaptic induced reflexes is worthwhile as it represents these complex mechanisms as simple reproducible potentials. It is hoped that much information can be gained by this method.

We must not forget O'Leary's comments in (1956) "We fear that this area of investigation is becoming one where the achilles of speculation has been running too far ahead of the turtle fact".

PREVIOUS WORK

The classical approach to the study of reflexes stems from Sherrington's work and consists of the accurate observation of the reflex response of an innervated limb to various stimuli. By the beginning of this century these simple observations were supplemented by myographic recording of the contraction of the individual muscles and then later by electromyographic observations of their activity. This was mainly supported by the development of the isometric myograph as well as improvements in the high speed recording which led to a peak of activity based on these methods in the mid to late 1920's. In the early 1940's the recording of efferent activity shifted to the ventral root and effects on the motoneurone (MN) became detectable by activating them monosynaptically and seeing whether the number driven to discharge changed.

The fundamental observation of the flexor reflex was made by Stephen Hales in about 1730 but the word "reflex" was not used until about forty years later. The concept of reflex was elaborated by Robert Whytt in 1755 and later by Marshall Hall in 1833. Serious investigation was delayed till the end of last century when Sherrington took up the subject (Sherrington 1906).

The knee jerk had been introduced to the notice of scientists by Erbs & Westphal, working independently in 1875. It was shown to be a monosynaptic reflex by Jolly (1911), Snyder (1910) and finally after the extensive work by Hoffmann (1922). The estimation of the delay through one synapse was studied by Lorente De No' (1933) and other workers (Eccles et al 1937, Renshaw 1940) who found it ranged

from 0.7 - 1 msec. Lloyd, (1941, 1943), using more modern techniques, proved that the tendon reflex passes through one synapse.

The electrical equivalent of the tendon jerk was first demonstrated by Hoffmann (1918). Further study by Hoffmann, (1919, 1920, 1924) of the newly evoked reflex showed that agonistic muscle contraction facilitated the reflex while the antagonistic one inhibited it. He found also that this reflex is not affected by fatigue of the muscle.

The importance of this reflex did not come to light until Magladery et al (1950 a,b,c, 1951 a,b), Teasdall et al (1951), Park et al (1951), tested the physiological characteristics of Hoffmann reflex in normal man and called it H-reflex after its discoverer. They proved reasonably that it is transmitted through one synapse in a two neurone arc and studied the effect of ischaemic and post ischaemic limb states on the H-reflex. Since then a large number of workers have used the H-reflex in the study of the nervous system in man.

Recently it was evoked from the quadriceps muscle (Mongia 1972 a,b, Guiheneuc et al 1974) and the masseter muscle (Godaux et al 1975) a finding which made it possible to test a number of spinal segments by this reflex. Granit & Burke, (1973), supported, in the conference report of the control of movement and posture, Bethesda (1972), the validity of the H-reflex for answering questions about the integrative activity of the nervous system and more specifically the executive MNs provided that the experimenter was aware of its limitations. Furthermore Desmedt and others, (1973) and

Hugon(1973), put forward a practical guideline for better methodology in H-reflex studies.

The H-reflex proves to be useful in the physiological studies as well as the clinical investigations. In the physiological studies the H-reflex has been used to demonstrate the activation of reciprocal Ia inhibitory pathway during motor performance (Tanaka et al 1972, Mizuno et al 1971), the function of the fusimotor system in the reflex activation of MN (Landau & Clare 1964a, b) changes in the MN excitability during the preparation for movements (Gerilowsky 1975, Pierrot-Deseilligny et al 1971) as well as during motor acts (Gottlieb et al 1970, 1971, 1973a, b, Delwaide et al 1969, 1970, Delwaide 1971, Krassoievitch 1972). The ability to record the reflex in cats (Ekholm et al 1964, Mayer et al 1965, McLeod et al 1967), rabbits (Messina et al 1975) and rats (Murakami 1971) has helped to confirm the validity of studies in man.

On the clinical side the H-reflex has been used as a diagnostic measure for root lesions (Guiheneuc et al 1971, Braddom et al 1973, Deschuytere et al 1973), polyneuropathy (Diamontopoulos et al 1965, Mayet et al 1965, Wager et al 1974) and even for measuring maturation of the CNS (Mayer et al 1973, Hodes et al 1962, Thomas et al 1960, Stimson et al 1969). During surgery it was used to determine the lateral boundary of the ventrolateral thalamic nucleus (Vasin et al 1970, Laitinen 1970a) and for the assessment of the effect of stereotaxic operations for parkinsonism (Stefanis et al 1965, Tzavellas et al 1972, Olsen et al 1967, Laitinen et al 1970b).

The tested reflex showed significant difference in spasticity (Magladery et al 1952, Teasdall et al 1952, Languth et al 1952, Angel

et al 1963, Takamori 1967, Abdel Hamid 1967, Novikova 1970, Ioko et al 1971, Pierrot-Deseilligny et al 1973a, b, Wirski 1971, 1973, Ashby et al 1974, Spira 1974) rigidity (Yap 1967, Matsuoka et al 1966, Fiyita et al 1971, Olsen et al 1967) and cerebellar hypotonia (Olsen et al 1967a, Mayer et al 1965a, b, McLeod 1969) from that of normal subjects.

Since the H-reflex was applied in clinical practice in 1950, it is currently used as an index for monosynaptic reflex excitability (Takamori 1967, Mark et al 1968, Coquery 1963, Matthews 1970, Teasdall et al 1951, Miglietta 1971, Manikal et al 1973, Magladery 1955, Magladery et al 1952, Veale et al 1973b and c), Dietrichson 1973, Taborikova 1973, Mayer et al 1973, Gassel 1969, Lance et al 1975). On the other hand stimulation of the Ia fibres by vibration (Echlin et al 1938, Bianchoni et al 1964, 1963; Matthews 1966, Hagbarth et al 1968) exerts a prominent inhibitory effect on the H-reflex (Hagbarth et al 1966). Rushworth et al 1966, Lance et al 1973) probably by presynaptic inhibition (Delwaide 1971, 1973, Ashby et al 1974, Lance et al 1968, Gillies et al 1969, Yamanaka 1964). This is difficult to interpret with the classical hypothesis of Y-loop organization which holds the facilitatory role for the Ia afferents (Granit 1970). On the other hand it seems probable that an afferent "busy line" phenomenon also contributes to the suppression of the H-reflex during vibration (Hagbarth 1973).

I <u>H-reflex and natural and peripheral stimuli</u>

The receptor system was found to modulate the MN excitability

(Matthews 1933). The muscle spindle is a good example of these receptor systems and its complex function in this modulation presents the puzzle of the motor control. This was elegantly reviewed in two recent monographs (Granit 1970, Matthews 1972). A receptor like structure is excited in the muscle tendons (Golgi organs) and has a damping effect on MNs excitation of the synergistic muscles has been studied extensively (Laport et al 1952, Bradley et al 1953, Eccles 1957, Eccles et al 1957a, b, Hongo et al 1969, Houk et al 1970).

Skin receptors have not had much attention in their effect on the MN excitability. This was the case in spite of the presence of several different receptor organs in the skin (Mountcastle 1974). One group of these receptors are the mechanoreceptors which convey touch and pressure sensations (Adrain 1928, Vallbo et al 1968) which is transmitted by large afferent fibres (either gp IB or gp II) (Gasser 1943, Mountcastle et al 1966, Talbot et al 1968). To my knowledge no literature has been found which assesses the skin receptors effect on the executive discharge of the extensor MNs as studied by the H-reflex. This assessment will be one of the aims we will be looking for in this thesis.

The mechanoreceptors' threshold are influenced by temperature (Moutcastle 1974, pg. 377) a finding which encouraged the study of the thermoreceptors as well. On the other hand the thermoreceptors of the skin play an uncertain role in motor control. Their sensory modalities are conducted by the thinly myelinated delta group of fibres (Moutcastle 1974, pg. 377). The functional

properties of these receptors have been extensively studied by Darian-Smith et al (1972a, b), Johnson et al (1973). However, Douglas and Ritchie (1959) found evidence that both cold and touch are represented in the same fibres of the C afferent group, a finding which is not in accord with the law of specific nerve energies. This was further clarified by Darian Smith et al (1972) who found changes in the firing rate and threshold of each receptor to its specific sensory modality.

Cold spots are far more numerous than warm spots in ratios of 4:1 to 10:1 and cold receptors do not coincide with the warm receptors (Moutcastle 1974, pg. 375). For all modalities the skin surface is a mosaic of sensitive points (Rothman 1954).

In cat tongues the cold receptors were found to discharge continuously while their temperature held steady, but the actual rate of discharge depends on the temperature (Zotterman et al, 1968). Seventy per cent of the preparation of the superficial branch of the radial nerve in human subjects were found to react with increase in total frequency of discharge with cooling stimuli (Hensel & Bowman 1960). Large fibres in root filaments were found to be fired selectively by local cooling (Granit & Lundberg 1947).

So far the skin cold receptors have been studied for their effect on MN excitability by cooling the skin and muscles for 10 minutes. Cooling of the muscle will subject the MNs to the firing changes in the muscle spindles (Matthews 1933) which will cloud the effect of thermoreceptors skin firing. It will be one of our aims to study these effects separated from the bias of other receptors.

When the cooling procedure was applied for a long time, i.e. more than 10 min., the subcutaneous structures were affected as well. Knuttson et al (1969) found that the subcutaneous and intramuscular temperature fell slowly and linearly about 5°C in 20 min. For 5 min. cooling of the gastrocnemius muscle the temperature of the deep structure of the muscle reduced 1.2°C for a reduction of skin temperature to 10°C. (Wolf et al 1973). These muscle temperature reductions may affect the muscle spindle firing or the intramuscular nerve terminals which could be of therapeutic use. (Hedenberg 1970, Grant 1964, Hayden 1964, Showman et al 1964, Knuttson 1971). It was found by Lahouda (1972) that intra-muscular temperature decreased under voluntary contraction of the muscle. On the other hand ice application caused facilitation of the activity of isolated motor units (Clendenin et al 1971) and the increase of the antagonistic motoneurone pool excitability began 30 msec. before EMG instead of the normal 60 msec. (Ovsyanikov 1972).

The muscle spindle was found to be sensitive to temperature changes (Matthews 1933). A contradictory finding was reported on the muscle spindle behaviour during gradual cooling, in cats isolated tenuissimus muscle, by Lippold et al (1960) who demonstrated an increase in the afferent fibre discharges with lowering temperature up to 28°C below which gradual decline in frequency occurred until firing level reached zero level by 15°C; but Eldred et al (1960) reported that slowing occurred in the discharges of deafferented and intact annulospinal, flower spray and tendon organs afferents on gradual cooling of the same muscle of the cat.

The effect of cooling on spinal reflexes was studied for the first time by Knutsson & Mattson (1969) who found reduction of the ankle jerk to 66% of the control after 20 min. cooling. This reduction in ATR amplitude was not noticed by Urbscheit et al, (1970), but they reported an increase in the H-reflex amplitude and the extent of the hand-grip facilitation with cooling. However, Knutsson et al (1969) found that the H-reflex amplitude increased for the first few minutes of cooling after which it was insignificantly changed.

The assessment of the physiological effect of cooling on the MSR excitability in one case showed both contradictory results and moreover was not complete. The whole range of the Ia fibres has not been tested nor has the central excitability state of the spinal MSR. Furthermore cooling of the antagonistic muscle group as well as other groups of muscles of the same limb is important in terms of finding mechanism by which such stimuli act. H-reflex was used by a number of workers to study the effect of skin dermatomes stimulation on MSR excitability (Castaigne et al 1972, Pierrot-Deseilligney 1966, Pierrot-Deseilligney et al 1973). Painful stimuli of the skin were without effect on the H-reflex in experiments conducted by Magladery et al (1951), but causes marked inhibition as reported by Castaigne et al (1972). Hagbarth (1952, 1960), Hagbarth et al (1963) demonstrated facilitation of the spinal nociceptive skin reflexes and the EMG of the extensor muscles by stimulation of the overlying skin dermatomes. Inhibition in these muscles was reported by stimulation of other skin dermatomes. The opposite was the case for the flexor muscles.

However, Gassel (1970), Gassel et al (1970) reported that he could not find Hagbarth's pattern of effect while using the H-reflex. They demonstrated facilitation in the reflex by stimulation of the anteromedial, anterolateral, posterior mid leg and dorsal surface of the foot. Reflex inhibition was seen by stimulation of the foot planter surface.

Reviewing the previous literature one can find an important general defect in the work. Nociceptive or electrical stimuli for skin stimulation were used in all cases, a condition which, on one hand, lacks specificity for certain receptor endings and on the other is unnatural and may excite mixed reflex effects, e.g. flexor reflex, on the tested mechanism. This clouds the effect of the skin receptors of the dermatome stimulated. In this work the conditioning stimuli used will be natural and more importantly will be specific for particular groups of receptors.

From the standpoint of receptor function it is pertinent to ask if the muscle receptors i.e. muscle spindle, modulate the MN excitability in a way different from those of the skin. The Ia afferents are easier to manipulate in the human being as it has been shown to specifically fired by vibration (Granit et al 1956, Crowe and Matthews 1964). The effect of vibration on the H-reflex has been studied consistently since 1964 and shows inhibition (Yamenaka 1964, Lance 1965, Lance et al 1966, Hagbarth et al 1966, Rushworth et al 1966, Hagbarth 1973, Lance et al 1973, 1975). Recently Godaux et al (1975) reported facilitation of the H-reflex by vibration of the masseter muscle. The after effect of the

vibration showed contradictory results, either an inhibition (Hagbarth 1973, Arcangel et al 1971), or facilitation (Delwaide 1973). Quantitative analysis of the effect of the vibration was lacking in these works.

II H-reflex and the excitability cycle

The MN escitability was measured using H-reflex recovery curve (Magladery et al 1951, Magladery 1955, Olsen et al 1967, Gassel 1970, Ioko 1971, Masland et al 1972, Mayer et al 1973, Illis et al 1976). However the recovery of the MNP after a previous conditioning volley is still difficult to interpret. This is due to the involvement of different mechanisms which play an important role during the time course of the MN recovery (Haase et al 1975). The primary inhibition period of the MN after a conditioning volley has been the subject of debate since Hoffmann (1919), who reported 0.1 sec of MN inhibition after primary excitation. This period shortened with muscle contraction (Hoffmann 1924). It was shorter than normal in spastic patients with hyperactive recovery (Magladery et al 1952, Teasdall et al 1952, Languth et al 1952, Miglietta 1971, Takamori 1967, Olsen et al 1967, Yap 1967, Ioko et al 1971) and in parkinsonian's disease (Stefanis et al 1965, Fujita et al 1971, Krassoievitch et al, 1971, Matsuka 1966, Takamori 1971, Laitnen 1970) and longer than normal in spinal shock (Garcia Mullin et al 1972, Vernik et al 1972, Diamantopoules et al 1967) cerebellar diseases (Olsen et al 1967, Mayer et al 1965) as well as Holmes-Adie syndrome (McComas et al 1967, Krott et al 1972). This stresses the importance of analysing the factors participating in this inhibition period in order to illuminate the pathophysiology of

these diseases. One of those mechanisms which may play a role in the inhibition period is the group II volley for when the volley increases it causes greater internuncial activity (Magladery et al 1951). The recurrent inhibition by Renshaw cells may play an important role (Haase et al 1975, Eccles et al 1954) especially in the first part of this inhibition period as may the impulses in Ib afferents. (Hufschmidt 1960, 1961, 1962, 1966). Moreover the supraspinal inhibitory mechanism may influence the establishment of this period as well (Taborikova 1973, McLeod 1967).

Depletion of the transmitter at the Ia - @MN synapses by the conditioning shock was one of the favourite hypotheses put forward by Taborikova & Sax (1969), Curtis & Eccles (1960). We found that this hypothesis has not been tested properly in man.

III H-reflex and age related changes

It is usual to compare H-reflex recovery curve in healthy man with that in diseased states. In a number of studies the healthy volunteers have been young men whereas the diseased subjects were past middle age. Defects in the control of this type of study have been partly obscured by ignorance of age related changes in the H-reflex recovery curve. We have found no literature on this aspect of the H-reflex.

It is well known that the CNS undergoes age changes. Cottrell (1940) showed histologically, degeneration of the afferent as well as efferent large diameter nerve fibres with shifting in the spectrum towards smaller size in people of old age. This was confirmed in man by different authors (Magladery et al 1959, Wagman et al 1952) as well as in animals (Birren et al 1956, Rexed 1944).

Synaptic delay in MSRs and PSRs was confirmed in man (Magladery Magladery et al 1958, 1959, Saint Ambrogio et al 1961) and in laboratory animals (Wayner et al 1958).

Peripheral changes in the innervation pattern of the muscle has been shown by Gutmann et al (1965) and Carlsson et al (1964).

Centrally Wright et al (1959) found a decrease in number of nerve cells in the spinal cord but Gutmann et al (1966), Mayer et al (1958) found no changes in the rat spinal cord MNs with age while a decrease in the excitability of the muscle was found by Frubel et al (1969).

Differential decrements in cell numbers in various areas in the CNS were reported by many authors a long time ago (Critchely 1942, Hodge 1894, Ellis 1920 and Harms 1924). Gutmann (1972) stated "Still some cell death in the nervous system may be characteristic of the ageing process in man and animals (Gardner 1940, Brody 1955, Rockstein 1967) but clear interpretation of this data is missing".

MSR and MN accessability studies in man will shed some light on the mechanistic changes able to occur in the CNS due to ageing process.

IV H-reflex studied by SFEMG

Since the turn of the century development of reflex physiology due to Sherrington's and others' work, the integrative action observed at the final common path lacks the precise information available at an individual soma. The interference from adjacent cells was a continuous challenge to experimental skills. This caused Lloyd (1956) to state "questions arise from time to time concerning the behaviour of MNs in some circumstances of reflex acti-

vation that cannot be answered by observation of a population of MNs. It is then appropriate to resort to the study of individual members of the population. Even without the pressure of necessity it sometimes happens that the observation of individuals increases one's grasp of the population's workings".

The recording from a single MN by intracellular recordings (Fatt et al 1951, Eccles 1973) made it possible to gather a wealth of knowledge upon which most of our working hypotheses have been established. The recent development of single fibre EMG studies (Ekstedt & Stalberg 1963, 1969, 1973, Ekstedt 1964, Stalberg 1966, Stalberg & Ekstedt 1973) was a breakthrough in recording from the unitary part of the muscle. Trontelj (1968), (1973) moved the concept forward by recording the AP of a single MN using SFEMG techniques. Surprisingly, in spite of the ingenuity of this technique, it has not been used often. There are a large number of questions which can be answered by such techniques. It is difficult to rely on cross species assumptions to interpret the integrative activity in man. In animal muscles, different functions are reflected in the muscle fibre structure (Hess 1961); however such differences have not been found precisely in human muscle fibres (Coers and Woolf 1957). Granit & Burk (1973) crystallised the problem in their statement "It is impossible at the present time to identify the motor units recorded electromyographically in humans in terms of their probable physiological and histochemical characteristics. The relation of such data to the recent results from animal experiments remains speculative".

There is a prominent discrepency in the information gathered by recording from one unit of the nervous system, i.e. motoneurone, and the whole population of the MNP. These discrepencies stem from the fact that the CNS integration of movement implies the collaboration of different inputs in modulating the final motor act according to the moment's demand. Recording from a single MN can yield more accurate information regarding the problem. Synchronization of firing of MNs (Adrian & Bronk 1929, Buchthal et al 1950, Bigland et al 1954, Lippold et al 1957) forms one of these discrepencies in recording from a single MN due to the interference from the others. However, Taylor (1962) found no tendency of synchronization of MNs activity.

Moreover, the small diameter of the muscle fibre (from 10 - 100 μ) (Buchthal et al 1955) makes it difficult to record from single units. This led Buchthal et al (1957b) to claim that the motor unit is subdivided into small groups of 10 to 30 muscle fibres putting forward the concept of the "sub-unit" which was later showed to be invalid and abandoned at the Brussel EMG Congress (1972). Because the electrodes designed by Buchthal et al (1957a) were not fully practical, Ekstedt & Stalberg (1963) redesigned their needle multi-electrode to record from a single muscle fibre. It was not until 1968 that Trontelj recorded from a single muscle fibre activity, through the reflex arc. This was a new approach to study analytically the @-MN by looking at the mechanistic properties of these cells and their control by the motor apparatus. The correlation of activity of a single unit from the pool to the whole discharge from this pool during

reflex action is an important question needing answers.

Indeed SFEMG studies unmasked abnormalities in muscles shown to be normal by routine clinical and electromyographic investigations. This applies to diseases affecting either anterior horn cells (Stalberg et al 1975) or in the muscle itself (Schwartz et al 1975). In occular forms of myasthenia gravis SFEMG studies revealed pathological changes in muscles which did not show surface decrement of the whole muscle AP (Schwartz et al 1975).

The unique property of the SFEMG needle multielectrode of Ekstedt & Stalberg stems from its difference from other intramuscular electrodes. This can be identified from the following brief review of electrodes used for intramuscular recording of muscle potentials.

Since the development of the first concentric needle electrode by Adrian & Bronk (1929) different types of electrodes have been designed for intramuscular recordings. In spite of the long period of time since Adrian & Bronk's discovery, the concentric needle electrode is still the most practical electrode fulfilling its job and no more than slight improvements have been incorporated in new types of electrodes. One of the main disadvantages of the concentric needle electrode is that the leading off surface is presented at the bevel end of the cannula. This produces the possibility of recording from the muscle fibre injured by the bevel, which then give inappropriate results. In this electrode the diameter of the central wire is often about 100 μ. Two wires are sometimes flushed inside the cannula for bipolar recording (Landau 1951). Jasper & Ballem (1949), Bjork & Kugelberg (1953a, b), extensively used the sewing needle or entomological needle electrode which consists of a sewing needle insulated except for

the electrode tip which has a diameter of 25 - 50 μ. Any break in its insulated area during recording causes a false leading off surface with false recordings.

A thin tungsten wire insulated except at the extreme end was introduced into the muscle by an injection needle and left there for recording. It has proved helpful in the study of kinesiology. This electrode was consistently used by Basmajian (1962), Bigland & Lippold (1954), Lippold et al (1957). Very recently Van der Meulen (1973) in collaboration with several biomedical engineers developed an extremely small wire electrode that can be inserted into muscles and left in place for a long time, sometimes over six months and used for either stimulation or recording. The needle multielectrode has been introduced by Buchthal (1957) in which up to 14 wires were flush fitted inside an injection cannula and presented at the side of the needle. Different types of needle multielectrode were designed each for a specific function i.e. measuring motor unit territory or volume conduction of the spike (Buchthal et al 1957a, b). This was further improved by Ekstedt & Stalberg (1963) to get a reliable recording from a single muscle fibre. Fleck (1962) designed a needle electrode with one or several leading off surfaces presented at the side of the needle in one or two openings at opposite sides. The electromyographic myotome was designed by Bonsett et al (1961) to record intramuscular AP as well as to biopsy the muscle from the recording site. Beranek (1961) was the first to describe the use of glass capillary electrodes for intracellular recording in man.

One of the early phenomena studied early in animals but not in man was that of summation (Sherrington 1906, pg. 36). This phenomena was noticed in the early period of neurophysiological studies (Setschenow J. 1863, Sterling 1874) in conduction through the reflex arc. Sherrington (1906) described the two types of summation i.e. temporal and spatial summation.

It has been shown by Curtis & Eccles (1960) that the time course of temporal summation declined gradually over 15 to 20 msec. Collins et al (1966) demonstrated temporal summation in the C fibres evoked by electrical stimulation in conscious human subjects. Single pulse was without effect but when stimulation applied with c frequencies of 3/sec. the subject experienced pain which increased with increasing stimulation frequency.

Spatial summation has been studied by Coombs et al (1955), Eccles et al (1957) and they found it to result from the reciprocal overlap of the subliminal fringes for the effects produced in these fringe cells by the two sets of synaptic endings summated to bring them to threshold. This type of summation is found to be significantly important in the integrative function of the CNS (Mountcastle 1974, pg. 36).

Montcastle (1974) stated "spatial summation is a functional property of the segmental reflex mechanisms of the spinal cord". (Pg. 353). It has been shown that spatial summation occurs to a limited extent for some cutaneous senses e.g. pricking, burning or aching pain and was noted for other senses e.g. warmth and cold (Hardy et al 1940, Hazouri et al 1950).

Temporal and spatial summation has not been studied through the MSR arc in humans so far. Single fibre EMG studies for this

phenomena are unique and can shed light on the important aspect of the MN.

The soleus muscle was used as the recording site in all the work been done in this thesis. This was because the branch of the medial popliteal nerve to the soleus muscle contains a large number of sensory fibres arising from the muscle which evokes the largest H-reflex in the body. (Hugon 1973). Moreover most workers demonstrated histochemically (Henneman et al 1965, Burke et al 1971, 1973) and electrophysiologically (Burke et al 1971, 1973, Burke 1967, McPhedran et al 1975, Schmalbruch 1970, Buchthal et al 1973) that the soleus is a homogeneous muscle consisting of tonic slow type of fibres. However Warmolts et al (1973) pointed out that it was difficult to match the histochemical and EMG fibre AP of the human muscle because of the close interdigitation of muscle fibres of opposite type. Moreover most of the studies which confirm the homogenity of the soleus muscle were done on cats whereas in rat soleus the case was different as Stein et al (1962) showed that it composed entirely of type B andC fibres according to their histochemical studies of the fibre constituents for succinic dehydrogenase and glycogen. This was further supported by Edstrom et al (1968). However it was found that motor units may undergo transition between different categories according to the exercise history of the animal (Barnard et al 1970). This was emphasized by Engel in Bethesda Congress of EMG (1972).

In man Johnson et al (1973) reported that the superficial layer of the soleus muscle contains up to 14% of fast motor units and the deep layer up to 11% of the sampled motor units, in their autopsy study, was classified as fast units.

Electrophysiological studies confirm the above findings by demonstrating a long contraction time (Cooper et al 1930, McPhedran et al 1965, Buchthal et al 1970a, b) and small maximum tetanic tension (McPhedran et al 1965) of the soleus muscle unit.

The type of units in the muscle relate to the size of its efferent nerve as well as the MNs themselves. McPhedran et al (1965), Wuerker et al (1965), reported a smaller nerve diameter with a slower conduction velocity in the soleus muscle more than the gastrocnemius. It has long been held that the anatomical size of a MN should directly relate to the diameter and therefore to the C/V of the axon arising from it (Granit et al 1956, Henneman et al 1965). This correlation has now been directly demonstrated by Barrett & Crill (1971) in dye marked MNs.

Henneman et al (1965a, b) reported that MNs recruited in a well identified reproducible order during either isometric contraction or reflex activity. The tonic MNs were often recruited first followed by the phasic ones (Henneman 1957, Olson et al 1968). The tonic or small MNs are more readily discharged during activity than the large MN. This increases the functional usage of the small MN cells. Henneman (1974) stated "The usage of any motor unit, in fact, is probably in inverse ratio to its size" (Montcastle 1974, pg. 622). This order of recruitment was confirmed

by Ashworth et al (1967), Freund et al (1972, 1973, 1975), Milner Brown et al (1973). The order was found to be the same even during stimulation of the supraspinal centres (Somjen et al 1965). On the other hand this order was found to be reversed under various conditions in normal subjects (Grimby & Hannerz 1968, 1973, Wyman et al 1974) and on proprioceptive blocking (Grimby & Hannerz, 1976) as well as in diseased states (Grimby & Hannerz 1970, 1972).

This picture of orderly recruitment is oversimplified and implies a stereotyped response by a muscle to varied external circumstances or demands. Granit et al (1973) questioned the ability of this recruitment order to perform quick tasks to which the tonic MN are ill-suited.

It is important to emphasize that the case in normal man is different from that in decerebrated cats and the latter may be different from normal cats (Creed et al 1932). Moreover, study of the order of recruitment with SFEMG techniques in normal man during H-reflex will give evidence of recruitment order during reflex activity but without the γ- system being involved. This is preceded by study of the properties of the different fibres in the soleus muscle. One of the important properties is the recovery of different MNs after a preceding identical pulse. This is explored by SFEMG in this thesis. To our knowledge no work has been published about MNP recovery study using SFEMG method.

Since the first discovery of the H-reflex by Hoffmann (1918) most workers ascribe the extinction of the H-reflex by supramaximal pulses to the collision in the same MN of the antidromic and orthodromic pulses (Hoffmann,1918,Magladery et al 1950, 1951,

Taborikova et al 1968 - see before). Magladery et al (1951) recorded ventral and dorsal root potential while provoking H-reflex with gradual incremental stimuli. They were able to record ventral root potentials only with subliminal stimuli to the M-response. This potential increased in amplitude gradually and then declined with reflex extinction; during that time the dorsal root potential could be recorded. They ascribed the reflex extinction to the collision of the antidromic and orthdromic pulses close to or within the cord. However there was some doubt about this phenomena as the only or even the important cause of reflex extinction (Gottlieb et al 1976). The second relevant cause of reflex extinction was that proposed by Paillard (1955) and confirmed by Taborikova & Sax 1969 that MN refractoriness by the antidromic pulse if it arrived at the cell soma before the orthodromic one. This could be the case if the C/V of the motor axons are higher or the same as the Ia fibres. On the other hand one could argue about the effect of Renshaw cell collaterals (Renshaw 1940) and its inhibitory effect on the MN as a relevant factor in reflex extinction. This will be either with discharge of the MNs or by antidromic stimulation as mentioned before. If that is the case it would have a different mechanism in reflex extinction from that of the collision blocking. Knowing the causes acting in reflex reduction is of importance for interpreting the H-reflex as a method and for studying integrative mechanism of the CNS. The order of reflex extinction, if there is any, will be studied using SFEMG method. To our knowledge this problem has not been

tackled before at least using SFEMG study. As we have seen before MNs are recruited in a certain order, a finding which suggests a certain order for the blocking of MN firing. A correlation between the two orders in terms of MN type will be discussed.

The different types of MNs are linked to a certain order at recruitment and blocking. On the other hand we will find in the first sections of the results that the skin mechanoreceptor stimulation will cause reflex inhibition. It was pertinent to ask which type of these MNs are inhibited first during scrubbing the skin. Henneman et al (1965) demonstrated the tendency of the large phasic MN to be inhibited first by stimulating the inhibitory pathways in the spinal centres. This order did not depend either on the excitory drive, the way of excitation or the way mediating the inhibition. However they were using electrical stimuli for stimulating the inhibitory pathways, a procedure which is too unnatural for the nervous system and non-specific. We have stimulated skin mechanoreceptors by natural stimuli in normal subjects. This was applied while recording the APs of a number of MNs sampled from the pool. In fact we were looking for a particular order of MNs in reflex inhibition in the same way as recruitment and blocking. Indeed this was an important question and needed to be answered after studying the MN order of recruitment in order to complete the study of this important aspect of the integrative activity of the spinal centres on the MNP. This completes the SFEMG study in this thesis and opens the way for another large set of questions to be asked in future work.

V. H-reflex and spinal cord stimulation

After using H-reflex for two years to answer questions about MSR excitability and to have studied some of its control mechanism we decided to use it clinically to investigate some important problems. It has long been held that the CNS undertakes structural reorganization after lesion (Von Monakow's 1902, Lashley 1938, Illis 1967, 1973 a,b) to restore the functional imbalance. It was important to know whether one can influence by treatment this plasticity of the CNS. We have had a unique chance of assessment of this plasticity during rehabilitation of MS patients by spinal cord stimulation (Illis et al 1976).

Spinal cord stimulation (SCS) for the amelioration of pain was introduced by Shealy et al (1970). The relief of pain was interpreted as due to the continuous stimulation of the substantia gelatinosa in the spinal cord which may function as a gate control to modify transmission to the thalamus (Melzack & Wall 1965). Since then SCS was used for the relief of pain (Nashold et al 1972, Shealy et al 1967, 1975, Canthen et al (1975), Clark (1975), Fox (1974), Grillo et al (1974), Nielson et al 1969, 1975), until Cook et al who were the first to notice significant improvement in voluntary motor control and sensory appreciation in patients suffering from MS who were treated for pain by SCS (Cook et al 1973). These findings directed attention towards the new concept of CNS reorganization put forward by Illis (1973) who showed anatomical reorganization of the CNS after a lesion of the cat's spinal cord (Illis 1964, Illis et al 1966, Liddell 1934). Repetitive stimulation of the SC may produce structural changes in

the synapses (Illis 1969). It may, however, increase the central excitatory state by increasing the feedback information (Illis et al 1976). Whatever will be the mechanism of action Cook et al (1973), Cook (1973, 1974a, b, 1976a, b) demonstrated a striking change in the motor control by SCS and it is important to explore the fundamental mechanism underlying these findings. This is the scientific burden of the nerophysiologists and is a step forward in the study of human neurophysiology.

VI H-reflex and dystrophia myotonica

The second clinical problem studied in this work was the exploration of the nature of the neurological deficiency in dystrophia myotonica, a topic subjected to long debate.

Dystrophia myotonica or myotonia atrophica was called Steinert disease, after Steinert (1909) and Batten & Gibbs (1909) described it. It has been reviewed by Thomasen (1948) and Caughey and Myrianthopolous (1963). It is a diffuse systemic disorder characterised by myotonia and muscle weakness and atrophy. This is associated with cataract, gonadal atrophy, heart disease, frontal baldness, endocrine malfunction, mental deficiency, pulmonary defect, bone changes as well as abnormalities of the serum immunoglobulin (Walton et al 1974, pg. 595). Caughey et al (1963) and Pruzanski (1966) reported that other congenital anomalies usually accompany dystrophia myotonica. It is a hereditary disease with a dominant autosomal gene although other modes of inheritance have been described.

There is a controversy in dystrophia myotonica as to the

primary affected site. It was first demonstrated to affect only the muscle fibres without the neurological apparatus. (Adie et al 1923, Wohlfart's 1951, Adams et al 1962, Adams 1969). This disturbance was mainly demonstrated after the histological (Harmans et al 1963, Coers & Woolf 1959, Coers 1955) histochemical (Golarz & Bourne 1963, Drachman et al 1976) and electrophysiological (Conrad et al 1961, papapetropoulos et al 1972, McIntyre et al 1959, Buchthal et al 1963) studies in this disease. Moreover, biochemical changes have been found particularly in the enzymatic activity (Weinstock et al 1958) muscle creatine (Kendutsch et al 1958) and muscle electrolytes (Baker et al 1958, Young et al 1959). The latter may be the cause of increased muscle fibre excitability seen in these cases (Conrad et al 1961, Kleeman et al 1961, Norris 1962, McComas et al 1965) as a decrease in the intracellular K ions and increases in Na concentration were found in dystrophic mice by Horvath et al (1960) as well as in humans by Ludin (1970). However, Lipicky et al (1973) reported a decrease in the resting chloride conductance in myotonic goats and human dystrophic muscles. On the other hand changes in the neural apparatus have been found to parallel the muscle fibre dysfunction. This was either in the terminal innervations (Coers & Woolf 1959, Woolf 1962 a, b, Woolf & Coers 1974), intramuscular nerve bundles (MacDermot 1961, Coers 1965, Harmans et al 1963) and the muscle spindle innervations (Daniel & Strich 1964, Swash 1972).

Exploring the dystrophic muscle by a needle electrode showed a background activity of two types. The first was an episode of

polyphasic muscle twitching and ascribed to be of motor unit activity (McComas et al 1965, Gatz 1960). The second type was high frequency diphasic bursts of pulses of 200 per second and attributed to single muscle fibre discharges (McIntyre et al 1959, Lennman 1963). The motor unit activity type depends upon intact nerve supply so that it was not noticed after nerve section or curarization (McComas et al 1965) while the second single fibre type was still commonly occurring (McIntyre et al 1959, Floyd et al 1955, Lanari 1946) even after end plate degeneration (Brown & Harvey 1939). Geschwind et al (1955) reported that these potentials were abolished by substances which stabilize the muscle fibre membrane such as quinine and procaine amide.

Curarization or local blocking of the motor nerve does not abolish the myotonia (Goodgold & Eberstein 1972). Lowering temperature provoked the myotonic response and increased the showers of the spontaneous potentials noticed in these cases (Buchthal et al 1963) a finding suggesting that these spontaneous activities are not a mere fibrillation potential from a denervated muscle.

On the electrophysiologic side not only the resting membrane potential was lower than normal in dystrophic muscles (McComas et al 1965, Conrad et al 1961) but also the miniature end plate potential was reduced (Conrad et al 1964, McComas et al 1965, Katz et al 1957) and had a prolonged time course (Conrad et al 1964).

Denny Brown et al (1941) were the first who turned attention towards the involvement of neural apparatus in dystrophia myotonica in man. The delayed renewal of contraction in the myotonic muscle following release of voluntary grasp (after spasm) was

attributed to a central reflex disorder. This was interpreted to be a physiological response of lengthening reaction in muscle stretched by sustained myotonic contraction in the antagonists (Landau 1952).

McComas et al (1965) demonstrated, in dystrophic mice of the Bar Harbor 129 strain, an involvement not only of the muscle fibres but also the motor end plate, peripheral nerve as well as the motoneurone itself, a finding which was confirmed later on by McComas et al (1971).

Recently Stalberg et al (1973) reported an increase in the neuromuscular jitter as well as increase in the fibre density by SFEMG. A lowered amplitude of the motor unit potential in the EMG examinations was noticed by Buchthal et al (1963), Salafsky (1971) and attributed to the reduced number of fibres contributing to the motor unit potentials and to the lowered fibre density. The same was found by Ludin (1973) in the intracellularly recorded AP of the intercostal muscle in dystrophic humans. The latter was attributed to the decrease in intracellular K+ content.

The involvement of motoneurones in dystrophia myotonica was drawn clearly by the elegant experiment of Salafski (1971). He found that minced muscle from normal mouse did not regenerate when transplanted to a dystrophic animal whereas the dystrophic muscle regenerated well when transplanted to a normal animal. In the latter case the muscle gave a normal amplitude of AP after regeneration, but in the former one it did not show normal AP amplitude. These results were interpreted as MN dysfunction with abnormality in the trophic effect of the MN on the muscle. A

little while afterward McComas et al (1971) forwarded the concept of sick MNs in myopathic muscles including dystrophia myotonica.

The electrophysiological findings of neural involvement in dystrophic muscles were supported by histological results as well. Daniel et al (1964) reported an increase in the intrafusal muscle fibres, which were unusually thin, with thickening of the spindle capsule in dystrophic muscles. Abnormal innervation of the muscle spindle was demonstrated. This was not supported in subsequent surveys of the pathology of the muscle spindle in various neuromuscular disorders (Lapresle et al 1964, Cazzato et al 1968, Patel et al 1968, Harmans et al 1963), but was confirmed by Swash (1972) in myotonic dystrophy in humans studied by autopsy. Moreover Woolf & Coers (1974) reported an increase in the terminal innervation ratio which is in strong support to the neural involvement in mytonic dystrophy. A striking axonal sprouting within the muscle was noticed (Woolf et al, 1974, MacDermot 1961, Coers 1965) with dual or multiple innervation of the muscle fibres (Harman et al 1963).

There was a pertinent question of whether the myotonic dystrophy affects primarily the muscle fibre with subsequent neural involvement or the opposite. Further studies are needed to explore the MN as well as the peripheral nerve involvement in this disease. The scanty data concerning these two sites forms an important part of the puzzle around dystrophia myotonica. So far no H-reflex studies have been reported in myotonic dystrophy which can help to cover this important gap.

Some results, based on specific firing of the Ia fibres by vibration (Bianconi 1963) suggest that the Ia polysynaptic pathways inhibit monosynaptic reflex by presynaptic inhibition (Delwaide 1973, Matthews 1966). Parts of these results were inspired by findings in the literature and in earlier work in this thesis that the recovery curve could be used potentially to interpret the MN excitability in diseased states (Matthews 1970).

Finally, whatever the primary site of the disease, further information is needed to explore the systemic derangements in an illness which continues to challenge clinical science.

ORGANIZATION, LIMITATIONS AND AIMS OF EXPERIMENTS

To begin with, measurement of the MSR and MN excitability in normal subjects was done. It is well known that the large fluctuations of the MNP (Granit et al 1973) forms a troublesome factor in using the H-reflex. These fluctuations were measured and the least changeable reflexes were used. We cannot presume that a stimulus excites a fixed percentage of the MN pool because of fluctuations and the number of mechanisms which operate at the spinal level, to alter the excitability of the @-MNs e.g. presynaptic inhibition. Visual, computerized and statistical measurements of reflex changes were used with all their limitations.

Reflex changes were measured by the excitability recovery curves at different sessions. Our aim was to establish the reproducibility of these curves as well as other parameters of the reflex. Strong support from the literature as well as the consistency of our findings gave confidence for further work.

Having established the limitations of our measurements, we went on to study the modulation of the MSR excitability by natural stimuli. Of great importance in this part of the work was the stimulus used. It was purely natural and the type of stimulus which could occur during normal activities. Most of the stimuli used before to excite skin nerves and receptors had been electrical (see above for references) which may recruit other structures than the tested ones. Electrical stimulation is an unnatural method of testing as it supplies the CNS with a synchronous volley which asks "a stupid question" (Matthews 1972, pg. 333).

The electrical stimuli, apart from being an unnatural way of testing, are not fully specific to a particular type of sensation. Stimulation of the posterior tibial nerve gives synchronous volleys in mixed fibre types which excite different pathways. However a finely graded stimulus will excite the mixed nerve in a certain order, according to fibre diameter, the large followed by the smaller diameter fibre (Matthews 1972, pg. 334). This helps one to select fibres of a limited range of size for testing, as introduced by Lloyd (1943, 1946). However electrical stimulation yields a wealth of information by virtue of its synchrony and precise control of its timing.

In this work we have tried to use natural stimuli in order to get "sensible answers" (Matthews 1972, pg. 333) expressing the normal activity of the CNS.

On the other hand and because these stimuli are natural some adaptation occurs (Vallbo et al 1967, 1968) a point which was considered by the experimenter. We were interested in the initial effect of these stimuli. The interpretation of these results is usually difficult when dealing with such a complex system. Animal studies of the effect of natural stimuli were helpful and the information provided from such experiments was used in interpreting our results. However one has to be careful about the interspecies differences which are known to exist in the organization of the nervous system (Jackson 1958. Vol II, pg. 74-75m 79m 399-400). Information extracted from human experiments was used when available.

It was important to study the factors which could modulate the MSR excitability during the recovery cycle. There are many peripheral and central events which could play a role in producing the different phases of inhibition and excitation during the recovery cycle but none has clearly established to stand in causal relation to the changes seen. One of the earliest proposed causes for the initial inhibition was depletion of transmitter substance from the syneptic ending. Moreover the testing and conditioning volleys are assumed to excite Ia fibres while they sometimes do, there has been no method of excluding or measuring the contribution made by the Ib and other afferent fibres.

In this work we have tried to accommodate these two problems by using different stimulus strengths and different lengths of train of stimuli.

There is a lack of normal data on the changes in the H-reflex with age. It was decided to test some of the old subjects to explore any possible changes. The aim was to look at the changes in the MN excitability with old age in subjects who were clinically well and active. The information derived provides a base for further investigations and not least it must be taken into account during clinical measurements and physiological experimentation. Again the interpretation of these results was potentially supported from the literatures with studies on man and animals side to side with our previous findings (see above for recovery studies).

The synchrony of the H-reflex discharge always obscures the behaviour of its single units (Lloyd 1956). This stimulated us to study MSR excitability at the unitary level using SFEMG. The reliability of such a technique was of prime importance to obtain meaningful information. However, the experimenter depends upon the findings of others for the method of identification of an AP from a single muscle fibre and subsequently from a single MN. After mastering this technique an extensive study of some of the previous findings was performed within the limitations of recording from one unit out of the whole MNP. We tried our best to apply our studies on unbiased samples of the system under study but the problems of sample bias are similar to the problems of bias with single unit recording in the CNS of animals. The clear cut information gained by this technique was encouraging and enabled us to test the order of recruitment, blocking and inhibition to be devised. This provides interesting physiological findings and it opens another field of study for those interested in factors controlling the order of recruitment of motor units.

The fact that the soleus, from which recording was made is a homogeneous muscle was appreciated. On the other hand the presence of a spectrum of differences between fibres was clear in our records.

With the experience gained and with "normal" data it was decided to investigate clinical problems.

The application of spinal cord stimulation, for the first time in the U.K., in rehabilitation of the MS patients with the dramatic improvement in the clinical condition gave us the opportunity of

making new studies on the control of excitability of the MSR. Moreover it opens a new era of study of human neuro-physiology and more specifically the integrative mechanism of the spinal cord. In this work the MSR excitability was studied in response to stimulation of supraspinal pathways using different parameters of stimulation. We don't know exactly which pathways we were stimulating other than that the posterior column tracts were included. This does not exclude the possibility of stimulating other pathways by spread of stimulus currents.

As this technique was new in clinical practice, animal experiments were the important pillar upon which interpretation of data was established. Of more importance was the uncertainty of the site of the lesion in these MS patients. This and the fact that abnormal cord was being studied were the prime limitations of this study.

In the following section patients with dystrophia myotonica were investigated. This section is intended as a contribution to the debate on the involvement of muscle fibres and central changes in the disease. The relation between both systems was measured in different ways e.g. $^{H}/_{M}$ ratio and recruitment curve. The discrepency noticed in $^{H}/_{M}$ ratio in the previous study of this work as a proper measurement for MNP fraction was appreciated. Moreover it was used as a way of examining relations between two different subsystems in a crude way. The variations in the clinical condition over different decades of life urged subdivisions of patients according to their disability. The small number of patients is a cogent limitation, but in the end it was tempting

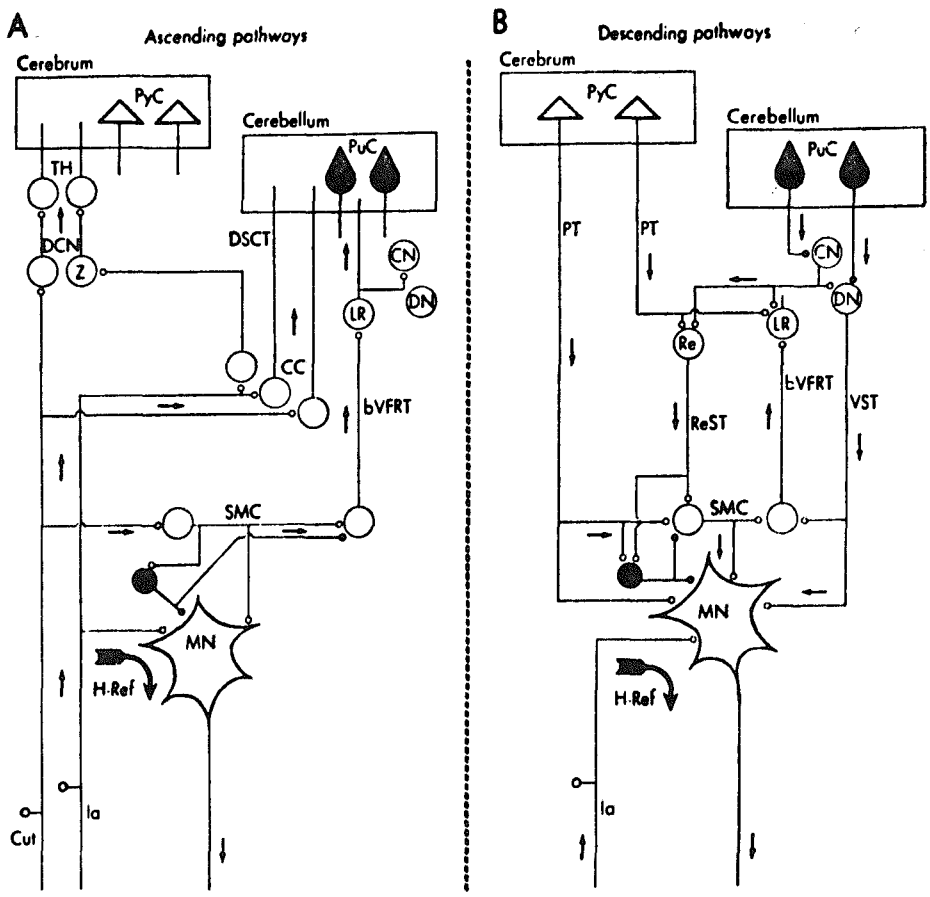


Fig. 1 Asending (A) and descending (B) pathways possibly involved in supraspinal influences on H-reflexes (H-Ref). PyC, pyramidal cells; PuC, Purkys cells; Cut, Cutaneous fibre; Ia afferent fibre; DCN is dorsal column nuclei with Z component; TH, ventrobasal thalamus. (From Taborikova 1973).

to think that this work provides useful information not hitherto available .

Finally it ought to be stressed that, because of the complexity of the human CNS, a degree of uncertainty is inherent in the interpretation of all experimental results. Information from animal experiments was of much help in spite of the interspecies limitations. These difficulties are admitted in order to avoid repetition in the text. When a mechanism of action is suggested, it will usually be the simplest one which is compatible with the results, neuroanatomy and strong supporting evidence from the literature.

Fig 1. shows the pathways involved in H-reflex elicitation with reference to some of the spinal and supraspinal mechanisms.

MATERIALS AND METHODS SECTION

METHODS

MATERIALS

Subjects

Normal males and females volunteered in numbers quoted in each part of the work. They had no past history of neurological disturbances. Subjects of certain age groups were chosen to suit the requirements of the project.

Chemicals

(a) 'Boots' PR spray (pain relieving skin spray) was used for superficial cooling of the skin. It contains 85% of trichlorono fluromethane and 15% of dichlorodifluoromethane in 200 g. cans.

(b) Absolute alcohol of Koch-light laboratories was used as skin cleanser.

(c) Cam creme ECG electrode cream of Kent Cambridge was used for good coupling between plate electrodes and skin.

Electrodes

(a) Stimulating electrode

Standard EEG scalp electrode, the stem of which passes through foam rubber padding, was used for unifocal stimulation. The assembly was held firmly by a broad rubber strip wrapped around the limb. The indifferent electrode was a rectangular metal sheet 5.5 x 4.5 cm.

(b) Recording electrodes

Two Copland-Davis (Palmer) recording electrodes were attached over the appropriate muscle and an earth electrode was placed to minimise the stimulus artifact.

Setting up the subject for recording

After scrubbing the site of fixation of the electrode using a scrubbing brush, absolute alcohol was used to wash the skin. The procedure was repeated until the skin became slightly red. This removed most of the degenerated cells as well as its superficial grease and the skin resistance fell significantly.

Position of the subject and electrodes

The subject lay prone on a comfortable examination couch, the left knee supported in a slightly flexed position by a foam rubber supporting pad, the feet hung over the edge of the pad and bed, so that the ankle took up its neutral position. The left posterior tibial nerve was stimulated unifocally through the standard EEG scalp electrode. The assembly of the electrode was held firmly over the popliteal fossa by a broad rubber strip wrapped around the leg. The indifferent electrode was fixed over the anterior surface of the lower third of the thigh 10 cm. above the patella.

The recording electrodes used in deep cooling were fixed over the medial head of the gastrocnemius and over the soleus muscle 2 cm. below the point of attachment of the two heads of the gastrocnemius. The earth was placed over the lateral head closer to the stimulation site.

In all the other work the two recording electrodes were placed over the soleus muscle alone. The active electrode was placed 2 cm. lower than the point of separation of the gastrocnemii, the other electrode 5 cm. distal to it and on a straight line between that and the tendoachilles. The earth electrode was placed over the lateral surface of the lower leg halfway between the two recording

electrodes. The electrodes were fixed to the overlying skin by their points to the site of recording again by an adhesive plaster to avoid any movement of the electrodes during muscle contraction. In appropriate experiments a small thermistor was attached to the skin overlying the area under investigation by adhesive plaster, and the temperature of the skin surface was noted. All the assembly and the lower leg were covered by cloth to ensure fixation and warmth.

Comment

Hugon, Delwaide, Pierrot-Desilligney, Desmedt and others (1973) reported that sitting position in a specially equipped chair with devices for holding the leg is convenient for long experimentation and minimises reflex changes. Such a chair was not available and the most comfortable position for the subject and for recording situation was chosen. This was a prone position using foam rubber pads to keep the subject in the most comfortable position. Electrode stability was monitored by recording M-response recruitment curves before and after the experiment. Any change in the curve would mean changes in the stimulating conditions and the results were discarded. Care was taken not to choose obese subjects or subjects with respiratory problems.

Advice was given to the subject not to move his neck or his other limbs during recording.

Stimulation

Ideal stimulation of the Ia afferent fibres has been shown to be 1 msec. duration stimuli (Veale et al. 1972). It causes

firing of the Ia fibres and evokes a comparatively stable H-reflex with minimal excitation of the M-response. We found that stimulation with shorter duration pulses did not produce such stable results and there was usually contamination with direct motor fibre excitation expressed as a small M-response. Stimulation was with a frequency of 0.2 pulse/sec in most of our experiments. A frequency of 0.33 PPS was used in those experiments which needed longer recording periods to make the total time of the experiment shorter. Using 0.2 PPS in these experiments would have made it very long. According to the standard recovery curve of H-reflex the test reflex returns to satisfactory stable amplitude for recording after 5 sec. Its stability after three seconds and its recovery from the inhibition imposed on it by the conditioning stimulus was quite sufficient for most experiments. This frequency of stimulation was used also in those experiments in which adaptation of the receptors occurred.

Recording

Recording from the soleus muscle has been done in most of our experiments. It has been shown that the motor fibres in the branch of the posterior tibial nerve to the gastrocnemius are more numerous than the sensory fibres emmerging from it. The converse was found for the soleus muscle. In spite of this, recording from gastrocnemius and soleus was done in those experiments in which general effect of the external stimuli on the MNP was examined. Both muscles were used in these situations. It was mainly used in showing the effect of deep and superficial cooling on MNP. Care was taken that H-reflex constituents and

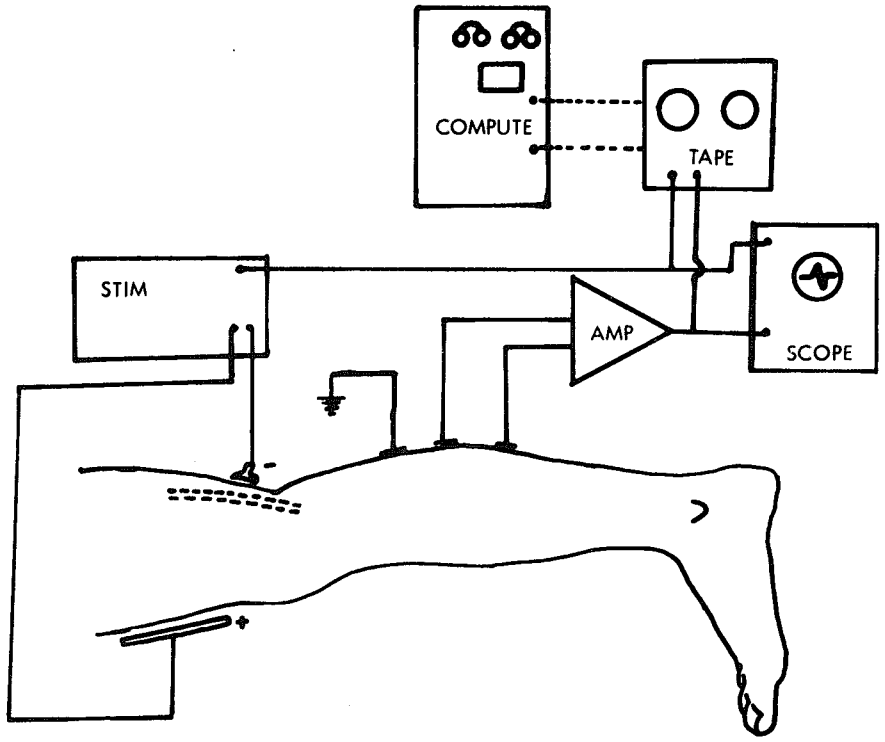


Fig. 2 Diagram of the recording set-up of the H-reflex

shape of the M-response (Hugon 1973) were similar. This means that those motor units fired in H-reflex corresponded to the Ia fibres stimulated electrically. Secondly the motor units fired in H-reflex were part of those fired in soleus and not other muscles. This can be done by setting up the stimulating and recording electrodes in appropriate positions. Care was taken not to move either the stimulating or the recording electrodes during experiments.

Instrumentation

A diagram of the recording set up is illustrated in Fig. 2.

'Devices' type digitimer triggers 'Devices' Ltd. stimulator to evoke a stimulus every three or five seconds, or even double equal stimuli with variable time interval as wanted. The digitimer triggers a 902 A Tektronix oscilloscope in conjunction with a PDP-12 computer. A Grass 902 stimulator was used sometimes for stimulation and triggering.

The EMG signal was amplified (x 1000) using a bandwidth of 0.8 - 1000 Hz. by a 'Devices' 3160 amplifier. It was recorded on magnetic tape by FM-system (Racal-1000 tape recorder) on one channel. A second channel of the tape carried a vocal commentary and a third the trigger pulse.

Analysis was done using PDP-12 computer. In part of our work the displayed EMG signals photographed by a 'NIHON KOHDEN' oscilloscope camera.

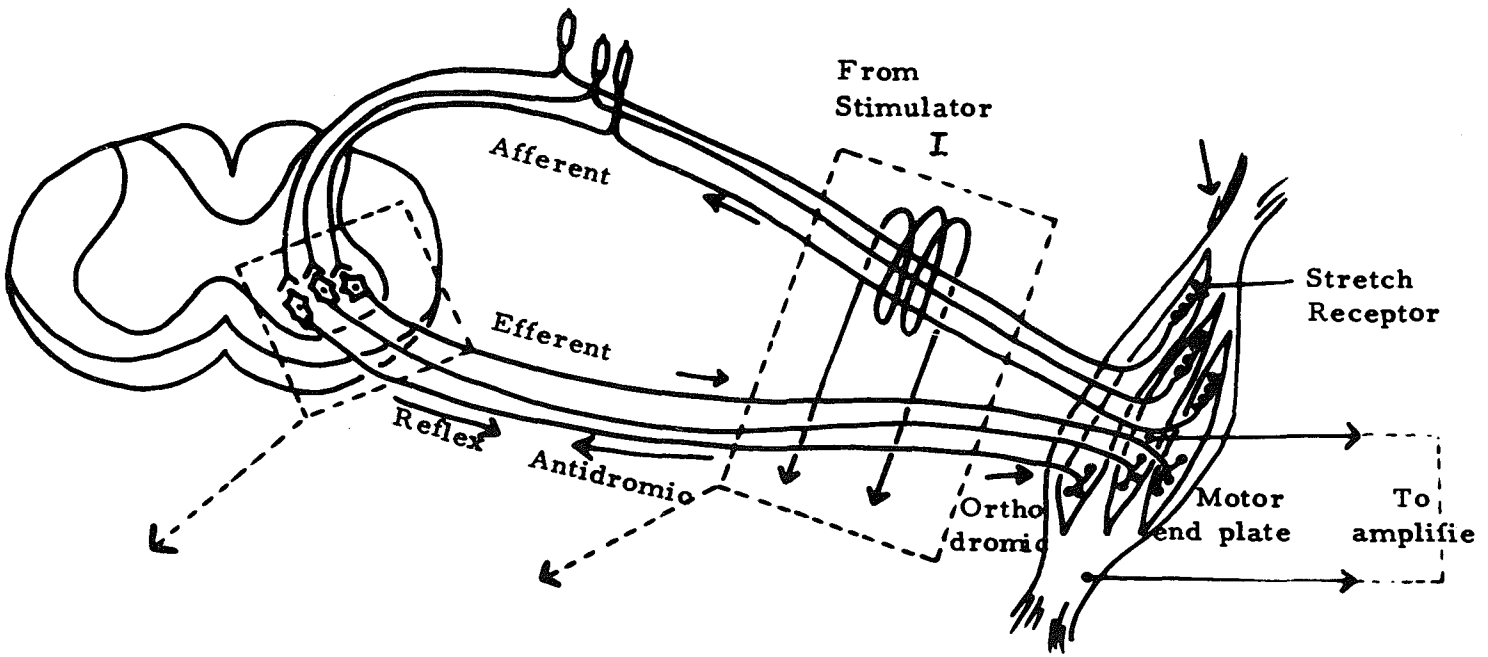


Fig. 3 The mechanism of the H-reflex.

STANDARD RECRUITMENT CURVE AND MECHANISM OF THE REFLEX

A schematic diagram of the mechanism of the reflex is shown in Fig. 3 .

With a stepwise incrementation of the stimulus intensity to the posterior tibial nerve at the point 'I' a stimulus pulse invades the peripheral nerve in either direction, centrally and peripherally, depending upon the threshold level of the nerve fibres to the stimulus. With stimulus above the threshold level of the Ia fibres, the pulse invade the Ia axons orthodromically toward the spinal cord. It passes through the posterior horn to s ynapse on @-MN cells in the anterior horn of the spinal cord. If sufficient Ia fibres are activated the @-MN cell is excited and its discharge goes through the motor axon orthodromically i.e. peripherally, towards the muscle, in which it evokes a contraction of a size determined by the numbers of the MNs excited.

With incrementive stimuli the number of the Ia fibres excited is increased, the number of the @-MN cell fired increases also and the muscle potential becomes higher in amplitude. Up to a certain level no muscle action potential is evoked directly from the site of stimulation, as motor axons are of higher threshold. The only deflection that can be seen in the EMG is a potential elicited after the time taken by the stimulus to travel through the whole two neurone arc and back to the muscle. This can be shown clearly in Fig.13 through pathway 'A'.

By gradually increasing the stimulus strength, most of the Ia fibres are excited as manifested by a maximal H-reflex. At that level the threshold of the largest fibres of the motor axons

is reached. This causes them to fire, sending an impulse orthodromically towards the muscle to elicit a potential in it of a size corresponsing to the number of the motor axons fired by the stimulus. Because of the short distance between the site of stimulation and the muscle compared to the whole reflex arc, the muscle deflection occurs within a short time coinciding with the time elapsed between stimulation and arrival at the muscle. That was a long time before the Ia-@-MN motor axon potential arrived at the muscle and elicited the reflex contraction. This can be shown in the schematic diagram through pathway 'B'.

With higher stimuli, the number of motor axons fired increases gradually with an increase in the direct muscle action potential until 100% of the motor axons were excited producing a maximal muscle potential or M-response. At the same time an antidromic invasion of the pulse centripetally through the motor axons toward the @-MN cells occurs. The latter may collide with the orthodromically invading pulse either in the somata or in the motor axons. The latter assumption is the most likely and is based on the difference in conduction velocity between the Ia and motor axons. The central collision weakens the orthodromically travelling potential and so a dwindling of the reflex response with higher stimulus intensity is seen. This collision increases in magnitude with increase of the antidromically invading pulse until it overcomes all the reflex discharge and causes the reflex to vanish. This can be seen clearly in Fig.13B .

STANDARD RECOVERY CURVE

With identical double stimuli to the posterior tibial nerve the first of these passes rapidly to the spinal cord and evokes the previously mentioned reflex. It is well known that the @-MN cells pass through a period of refractoriness after excitation by the primary signal (Lorente De No 1935). This happened for those MNs excited by the first stimulus. This period of refractoriness may depend on many factors which will be discussed later in the results. The recovery of the MN cells from this inhibition is gradual depending upon various factors. By incrementing the interval between the conditioning SI and test S2 stimuli recovery can be measured and its pattern can be displayed. The intervals were measured from the rising phase of the conditioning pulse to the rising phase of the test one. Generally 60% of the maximal H-reflex was used as a test reflex in most of our measurements. The reflex was found to be quite stable at that level with no great fluctuations.

PROCEDURES

Conditioning of the reflex by different natural stimuli was applied. The following were the various stimuli used:

A. Superficial cooling

Superficial cooling of the skin was achieved by spraying the area with 'Boots' PR spray. Cooling results from rapid evaporation of its compounds (trichloromonofluromethane and dichlorodifluromethane). The spray was applied for 10-15 seconds while recording H-reflexes. The skin was permitted to rewarm before

another application. The spray reduced skin temperature abruptly from 26-28°C. to 0-3°C. and the skin temperature returned to normal within 60-80 sec. Freezing of the skin was felt by the subjects so that three out of fourty suffered from mild frost-bite after the experiments.

B. Deep cooling

Deep cooling was achieved by placing ice bags over the area of the limb under investigation and leaving them in position for up to 45 minutes. Skin temperature fell down from 26-28°C. initially to 5-10°C. after 15 minutes and remained in this range with little further fall. The small thermistor probe was attached to the skin of the area under investigation underneath the center of the ice bags and fixed in position by an adhesive plaster. Deep cooling did not produce a fall in body temperature and subjects felt comfortably warm throughout the experiment in spite of the intense local cooling.

Rewarming of the skin was done by application of a rubber bag with water at 40°C. Temperature returned to normal with five minutes.

C. Touch and pressure

We have called these two types of stimuli touch and pressure although the difference between them is mainly one of degree. Touch was by passing a ball of cotton wool over the skin rather more firmly than the neurologists customarily uses to test touch sensibility.

Pressure was by drawing a dry scrubbing brush over the skin using light pressure. It is important to emphasize that these stimuli were moving and therefore rapidly adapting mechanoreceptors were

being continually excited.

D. Vibration

Vibration using 'Pifco' type vibrator model NO 1556 was used to elicit a continuous vibration for 30-60 sec on the achilles tendon. It was of 50 c/sec. Care was taken not to cause any change in the reflex before or after application of the pad of the vibrator on the achilles tendon and eliminate the factor that the tendon was stretched or unloaded. These may affect the accuracy of the results and was avoided by applying the vibrator head on the tendoachilles with mild support. The control reflex was recorded before vibration and this was followed by vibration of the tendon while recording the reflexes. After switching the vibration off the vibrator was kept in position while recording the post-vibratory reflexes until the point of full recovery. An intervibratory period of one to two minutes was left before applying another period of vibration.

PROCEDURE USED WITH DEEP COOLING

After preparing the subject for recording and putting the stimulation on for five minutes the following procedure was adopted.

1. Recording of H-reflexes with incrementing stimuli for the recruitment curve.
2. Recording of the recovery cycle of the MNP with gradual stepwise increase in interstimulus intervals.
3. Measuring skin temperature before cooling.
4. Cooling with ice bags for 15 min.
5. Recording skin temperature after 15 min.
6. H-reflex recording with incrementing stimuli for the recruitment curve.

This was repeated at 30 and 45 min. with recording of the recovery curve.

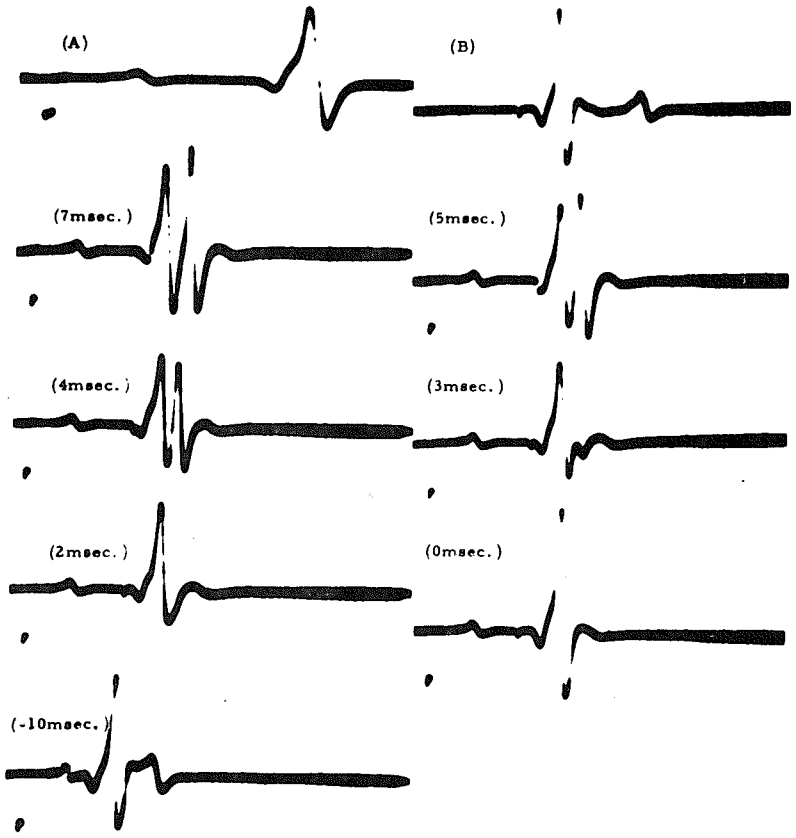


Fig. 4 Measurement of the fraction of the MNP participating in the H-reflex, by refractoriness technique. Maximum H-reflex (A), preceeding a maximum M-response (B), at 7, 5, 4, 3 and 2 msec., noticed gradual reduction of the M-response as it passes through the refractory period after the H-reflex. At 0 and -10 msec. the M-response had recovered again.

7. Removal of ice bags.
8. Placement of hot water rubber bag on the calf muscle and keeping it in position for a while until skin temperature returns back to pre-cooling level.
9. Recording of recruitment of the H-reflex with increasing stimuli for the recruitment curve.
10. Recording the recovery curve.

MEASUREMENT OF THE FRACTION OF MNP UNDER VARIOUS CONDITIONS

Measurement of the Fraction

This was measured using two techniques:

I. Refractoriness technique II. H max/M max ratio

I. In refractoriness technique (Taborikova 1966, Taborikova et al. 1968) We recorded the maximal H-reflex and the latency of the reflex was measured. With other maximal stimuli to the muscle giving muscle action potential (AP) with no H-reflex, the two potentials were separated by 7 msec. so that M-deflection leads the H-reflex. Fig. 4 showed maximum reflex and maximum muscle AP separately, then with the two stimuli superimposed on each other so that M-response leads the H-reflex. By stepwise decrease of the interstimulus interval the M-response will be evoked early until it passes through the refractory period of the muscle fibres following the H-reflex potential. At that time the M-response will be diminished in amplitude (Fig. 4) and the degree of inhibition depends upon the number of motor units fired during the H-reflex potential and therefore refractory to the M-response. This will indicate the fraction of the MNP participating in the H-reflex. The degree of reduction

of the M-response was expressed as the percentage of the control to give the fraction of the whole MNP fired.

II. In H max/M max ratio technique (Angel & Hoffmann 1963) maximal H-reflex was elicited. Averaging of not less than five stimulus response epochs was done and the same for maximal M-response after stimulation of all the motor fibres. Maximal H-reflex expressed as percentage of maximal M-response is considered an index of the fraction of the MNP excited in the H-reflex.

The two previously mentioned techniques were used for determining the MNP fraction under various conditions. The following conditions were applied:

(a) Contraction of the calf muscle

This was done by instructing the subject to contract his calf muscle. The foot was held to prevent any deviation during contraction. The subject was told to keep the foot in position during recording. Contraction was continued for 25 sec. followed by a relaxation period of 10 sec. The latter was followed by another set of contraction and recording. Only a fraction of maximal force was generated.

(b) Isotonic contraction of the tibialis anterior muscle

Isotonic contraction of T.A. is so called because contraction is associated with movements of the ankle joint to full dorsiflexion. The foot was moved by the experimenter toward dorsi-flexion. At the end of the movement, the subject was instructed to hold the foot in position during recording for 25 sec. after which a relaxation period of 10 sec. was allowed.

(c) Isometric contraction of tibialis anterior

This is so called because contraction of T.A. muscle was not associated with any noticable movement of the ankle joint. The subject was instructed to contract his T.A. muscle by pulling the experimenter's hand with sufficient power. Movement of the ankle joint was avoided by foot fixation against the experimenter's hand and the edge of the bed. That was done for 25 sec. while recording, with a relaxation time following it.

(d) Passive stretching of the calf muscle

This was called passive stretching because the foot of the subject was stretched to full dorsiflexion position by the experimenter during recording. The subject was instructed and encouraged to be completely relaxed during manoeuver and recording.

(e) The MNP fraction was measured with the application of the following manoeuvres:

1. Superficial cooling of the sole of the foot.
2. Deep cooling of the calf muscle for 15 min.
3. Vibration of the tendoachilles.
4. Mechanoreceptor stimulation by scrubbing sole of the foot.

H-REFLEX WITH REPETITIVE STIMULI

This is so called because H-reflex was recorded at first with one pulse that evoked the reflex. This was followed by increasing the frequency of stimuli within a 5 msec. gate to obtain two pulses in succession. Frequency was increased gradually so that 5 pulses were elicited in succession evoking one reflex. This was obtained by setting a 5 msec. stimulus gate with a frequency of 1000 PPS. The next step was to increase the gate

in one msec. steps while recording the reflex. The number of pulses was increased gradually up to 20 pulses at 20 msec. gate, the limit of our experiments.

The impulses were spread over the entire width of the gate duration so that with two pulses in 5 msec., one pulse was evoked at zero msec. i.e. at the start of the gate, and another one at 5 msec. i.e. end of the gate. All pulses were of the same intensity and of the same duration. The reflex amplitude used to investigate the effect of repetitive stimuli was 60% of the maximal H-reflex of the subject. This was chosen for many reasons.

1. The existence of a good range for facilitation and inhibition. This can be shown from the recruitment curve.
2. Relative stability of the reflex at this level as a large fraction of the MNP was excited by the Ia's and a small fraction of the motor axons were fired as shown by a small M-response.
3. Most of the MNS fired in H-reflex are acting as judged by the amplitude of the reflex. No significant obliteration or collision occurred from the antidromic pulses.

In old subjects in whom one cannot evoke 60% of the maximal H-reflex without an M-response the maximum H-reflex was used even if it was associated with an M-response.

STUDY OF THE RECOVERY OF THE MNP AFTER ACTIVATION IN THE H-REFLEX

This study can be classified into two main categories:

I Factors affecting recovery of MNP measured in young subjects.

II A comparative study of the recovery of the MNP in young and old subjects.

I Factors affecting recovery of MNP measured in young subjects

In this study different strength of stimulation for the conditioning pulse were used. These stimuli were supposed to fire different types of afferent fibres to show the effect of the various systems i.e. different afferents, on the recovery of the @-MN cells.

Experimental procedure

1. Stimulation with a stimulus subthreshold to the skin sensation. The subject was asked to determine the stimulus threshold for his sense. Stimulus lower than this threshold was used as a conditioning to the test reflex.
2. Stimulation with pulses at threshold level of skin sensation, but just below the threshold of any apparent potentials in the muscle. The subject was asked to check the sensation.
3. Stimulation with a stimulus that evokes an H-reflex equal to 50% of the test one. The two stimuli were compared to obtain an accurate measure of the conditioning pulse to the test one.
4. With an identical stimulus at S1 and S2 recording of the time course for the standard recovery curve.
5. With a supramaximal stimulus used as a conditioning pulse. This was called supramaximal because it evoked a maximal M-response with no H-reflex.

The previous steps were followed using single pulses. Ten young subjects were tested in this study. Their ages ranged from 19-29 years. All of them were healthy with no past history of neurological symptoms.

The same experiments were performed using a 5 msec. gate with five pulses of the same intensity as a conditioning stimulus. Changing the intensity of the conditioning stimuli as described above was performed. Nine healthy normal subjects were investigated in these experiments.

II Comparative study of the recovery of the MNP in young and old subjects

Twenty four subjects were tested in this study. All were fit and working. None had any history of central or peripheral nervous system diseases. There were 14 old subjects (60 - 72) including one female and 10 young subjects (19 - 31 years) which included five females. In this study the previously mentioned recovery curve was determined by identical stimuli to the posterior tibial nerve with variable inter-stimulus intervals to assess the latency and degree of recovery of the MNP in both groups. As well as the changes in the pattern of recovery.

SINGLE FIBRE ELECTROMYOGRAPHY (SFEMG)

Recording of single muscle fibre action potentials (SmfAP) requires the following materials:

1. Single fibre needle electrode

A "Medelec" SF 25 electrode was used. It consists of a 25μ diameter silver wire threaded inside a stainless steel cannula of 0.457 mm diameter. The wire electrode is insulated by epoxy resin and terminates flush with the side of the cannula. The active surface is presented at the side of the needle away from the cutting bevel, to minimize injury to the fibres from which

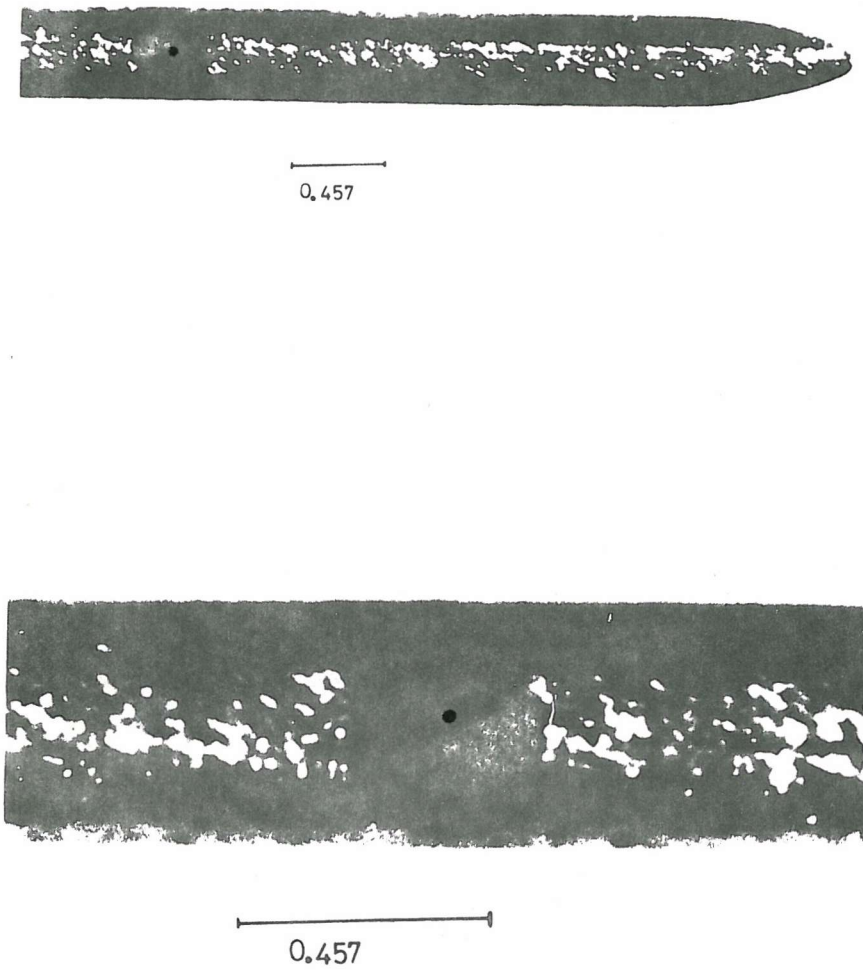


Fig. 5 Single fibre EMG electrode with the leading off surface presented at the side of the cannula at the centre of the epoxy-resin. Magnified 44X (upper) and 90X (lower).

recording takes place. The diameter of the leading off surface is 25 μ (Fig. 5) with an insulation resistance >100 MΩ in a dry electrode. The cannula of 25 mm. length was fixed in an axial NAH/A needle holder of "Medelec". The latter had an insulation resistance >100 MΩ and > 50 V. dielectric strength.

Recording is between the leading off surface and the cannula.

Displaying and photographing equipments

The SmfAP was displayed on a 902A Tektronix oscilloscope after amplification. Auditory display was by using an audioamplifier and loudspeaker. The consecutive APs were photographed by a "NIHON KOHDEN" oscilloscope camera.

Stimulation and triggering

Nerve stimulation was applied by a "Devices" Ltd. stimulator which elicited a stimulus every five seconds. Double pulses of identical intensity were used. In cases of conditioning the test H-reflex with a different pulse strength or by a train of pulses, a second stimulator of the same type was used connected to the same electrodes.

The pulse width ranged from 100-1000 μsec. depending upon the number and type of fibres to be excited.

The intervals between pulses as well as oscilloscope triggering were arranged by a "Devices" digitimer.

Stimulation of the posterior tibial nerve was performed using the electrode assembly described before, for the ordinary H-reflex recording.

Recording

Recording was from the soleus muscle in all experiments. There are two motor points from which the soleus muscle AP can be recorded easily (Walthead and Tchicaloff 1968). They are about two thirds of the way down from the knee. Each is at a point about 75 mm on either side of the midline. The lateral motor point and from which most of the recordings were performed, can be discerned by contracting the soleus muscle against resistance and it is halfway down the lateral bulk of the soleus muscle. The medial motor point was identified on the medial side of the belly of the soleus during contraction as it is near the medial subcutaneous surface of the tibia. In some cases the motor point was identified by looking for the site from which the soleus muscle contracts forcibly by the least stimulus intensity.

After sterilization of the recording site, by absolute alcohol, and the single fibre needle electrode, using 0.5% Savlon (ICI Ltd.) (for 10 minutes), the latter was introduced in the muscle during slight contraction and with the visual and auditory display. In a successful trial, high frequency as well as low frequency muscle APs were noticed.

The next step was to get closer to a fibre. This was by moving the electrode either vertically, in a cone shape, or around its longitudinal axis until it gets as close as possible to the fibre. That a single fibre recording was achieved was determined by the following criteria:

Criteria of single fibre action potential

The criteria shown by Ekstedt (1964), Ekstedt & Stalberg (1973)

Stablerg & Ekstedt (1973) was followed in order to identify SmfAP from compound AP. It is a smooth biphasic spike potential of a similar shape to those recorded from the isolated muscle fibres by Hakansson (1956, 1957). The APs were of identical shape at consecutive discharges. The time resolution in the system was of at least 10 msec. to display the shape faithfully. Because the AP is generated from one single muscle fibre it always followed the all-or-none principle (Trontelj 1968, 1973). The AP did not show any fractionation under any condition. The similarity in shape of the AP at consecutive discharges, as well as duration and amplitude was very helpful in single muscle fibre identification. Threshold level of a SmfAP and subsequently of a motorneurone threshold did not change during recording.

Latency of the muscle AP was the same at all consecutive discharges with a neuromuscular jitter of 30-40 μsec. (Stalberg, Ekstedt & Bromen 1971). With increasing stimulus intensity no similar fibre of the same shape and latency can be discerned in the same motor unit. The SmfAP can be identified from the auditory display as a clean sharp sound.

Single Fibre H-reflex recording and action potential display

Because of the wide difference in threshold level of the H-reflex and direct muscle AP, SfAP of a single motorneurone can be recorded easily without any interference from the latter. A proper adjustment of the stimulating and recording electrode in conjunction with the pulse width and threshold, a biphasic potential of short duration and large amplitude could be evoked after about 30 msec. from the stimulus artifact. These potentials fulfill

all the criteria mentioned before of the SfAP.

To study the potential shape at consecutive discharges, horizontal magnification of the potential was applied. Two, five, ten and twenty times magnification were used, with a sweep speed of 5 msec./cm. which was triggered by the stimulus artifact. This was used also to study MN recovery with paired pulses. Appropriate magnification was used to study MN recruitment. After assurance that recording was performed from single muscle fibre, slower sweeps were used to study other phenomena e.g. early recovery and summation, MN conditioning by subthreshold single and trains of pulses, and central collision of orthodromic and antidromic pulses.

Superficial recording and monitoring

Superficial recording of H-reflex using the technique described before was performed. Copland-Davis electrodes were used with the active electrode fixed to the motor point and the reference to the distal end of the fibrous part of the soleus muscle, two inches above the tendenous part. The active electrode was adjusted to the motor end plate zone by recording the optimum potentials. This procedure gives the largest H-reflex from either medial or lateral strip of the soleus muscle. The earth electrode was fixed in between the stimulating and recording sites.

The recruitment of MNs seen by single fibre recordings were judged in relation to the superficial recording (Freund et al 1974). The motor units which fire after a certain latency equal to the initial phase of the surface deflection (+ve deflection), were labelled as early or fast motor units. Those which parallel the second phase of the surface deflection (-ve deflection), were

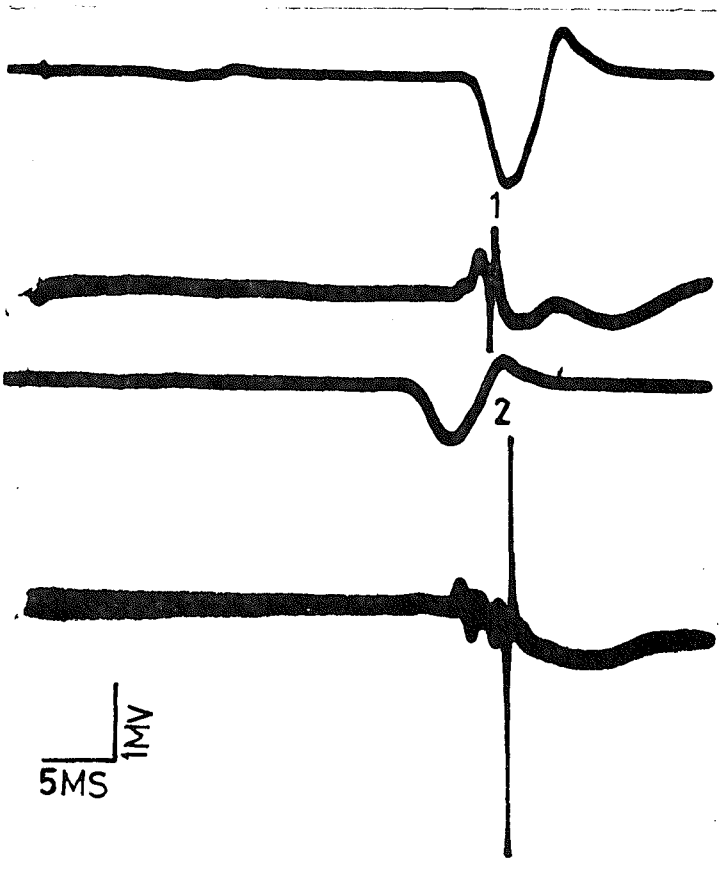


Fig. 6 SFEMG studies. Two muscle fibres from two different subjects. Unit 1 is an early and 2 is a late type of MN compared to the superficial records (upper traces).

notified as late or slow units. These were subdivided into very early, early, late, and very late depending upon the part of the surface potential during which they occur.

Fig. 6 shows an example of different types of motor units compared to the superficial recording.

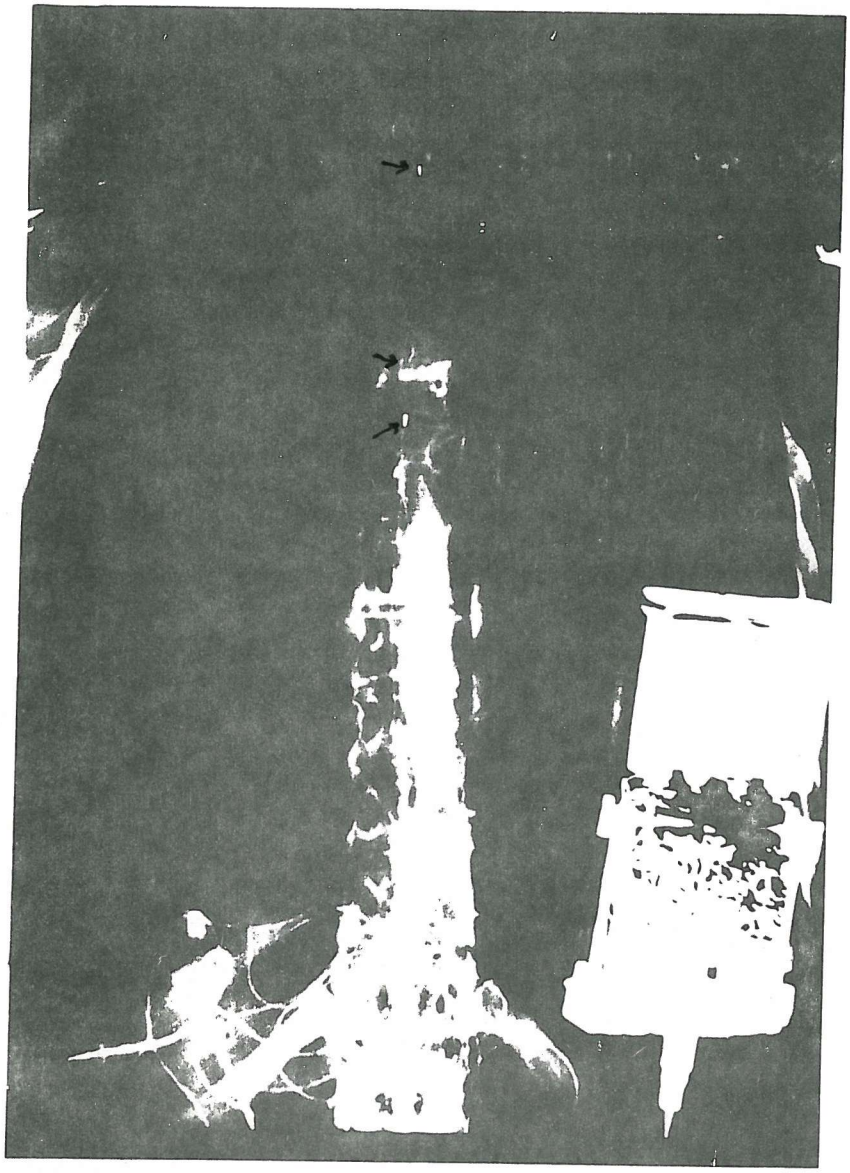
Subjects and single fibres isolated

There were 37 young unpaid volunteers available for this study. 23 males and 14 females with ages ranging from 18 to 36 years were tested. In every subject a number of single fibres were isolated and tested. More than 200 single fibres were isolated in total and 45 single fibres were from one subject in different sessions. The number of single fibres studied in each type of test will be quoted in the results. In all subjects there was no past history of neurological disturbances. Recording was performed while the subjects lay in the prone position. They were encouraged to adopt the most relaxed position and the degree of relaxation was also monitored by the absence of all motor unit activity before and in between stimulation. No subject suffered any untoward aftereffects from the proceedure.

Spinal cord stimulation

This work has been done in conjunction with Drs. Illis and Oygar in Wessex Neurological Centre, Southampton.

Patients: Six patients were tested. Five were suffering from multiple sclerosis and one had motorneurone disease. History of illness and complaints will be described in the case report of every patient. The multiple sclerosis (MS) patients were diagnosed



X-ray of the vertebral column in case 1, Mrs. SE, with the spinal cord electrodes (arrows), receiver, antenna and the stimulator transmitter used in SCS.

by the consultant neurologist and fulfilled Schumacher's criteria (see appendix). Of the five MS patients three were males and two females.

Electrode implantation and set up

Spinal cord electrode implantation was done by a neurosurgeon (Dr. Oygar) and was by the technique of Professor A. W. Cook (1976) and described in Illis, Oygar, Sedgwick & Sabbahi Awadalla 1976.

The percutaneous procedure is performed using normal sterile technique. With the patient in the prone position on an X-ray table the skin is punctured in the lower thoracic area using 1% xylocaine local anaesthesia. Under fluoroscopic control an 18 gauge Tw x 2½ Hustead point epidural needle is introduced in the interspinous space to reach the epidural space in the midline. The stylet of the needle is removed and it is ascertained that there is no cerebrospinal fluid leakage. A ⅛ inch platinum probe stainless steel teflon insulated sterile electrode (David & Geck USA) is passed through the needle pointing rostrally. The electrode is advanced under fluoroscopic control to midthoracic levels and positioned in the midline of the posterior epidural space. The needle is removed and a second electrode is introduced so that the two are positioned between T4 - T6 vertebral levels and about one vertebral level apart. Having fixed the electrode to the skin with nylon sutures, X-rays are obtained to document their position.

The electrodes are then connected to a receiver (Avery Co., Farmingdale, USA) with the positive electrode rostral. The loop antenna from the stimulator is placed over the receiver and a sterile dressing is applied to secure the electrodes and the

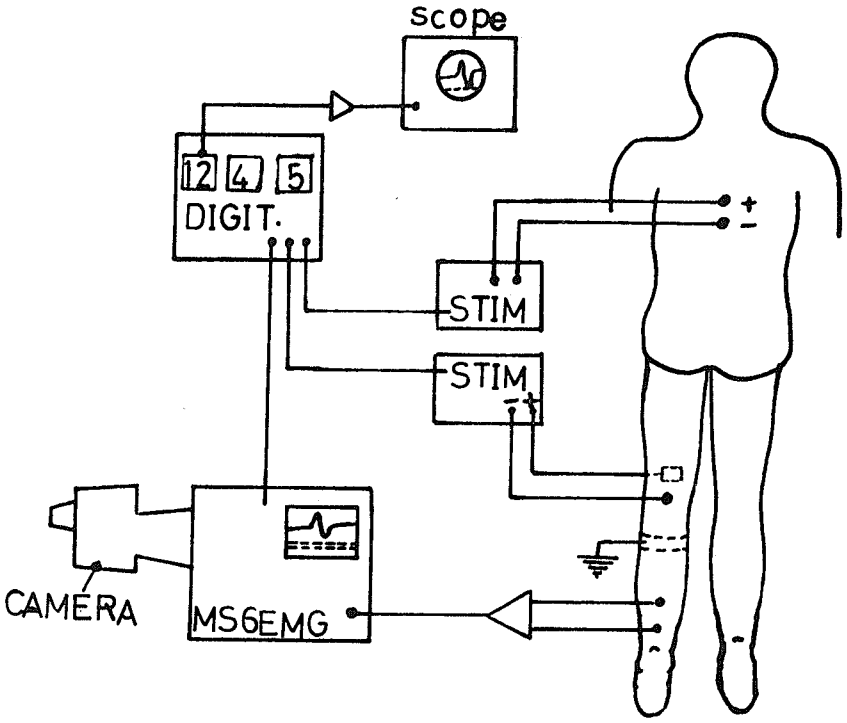


Fig. 7 Diagram of the recording set-up used for H-reflex studies in patients with MS and treated by spinal cord stimulation.

receiver.

The spinal cord is then stimulated with 200 μsec. width pulses at 33 HZ at a voltage adjusted between 0.5 - 11 volts (Avery Co. Spinal cord stimulator) according to the patient threshold of sensation.

This method was a temporary stimulation to the spinal cord to test its effectiveness in MS patients, and the electrodes were removed after 10 - 14 days. In the MN disease patient the receiver was implanted subcutaneously on the left side of the chest wall, so that the stimulating arrangements were permanent.

Instrumentation and procedure of H-reflex studies

A diagram of the recording set up used for H-reflex studies with spinal cord stimulation (SCS) is illustrated in Fig. 7.

Patients were tested before dorsal column electrode fixation routinely. H-reflex recruitment curve and recovery curves were determined. Reflex changes following mechanoreceptor stimulation of the sole of the foot using a scrubbing brush were performed. In some patients the H-reflex during vibration of the tendoachilles was tested.

After dorsal column electrode fixation and SCS for variable time, which will be noted in patients' reports, the same tests were reapplied. In a second investigation the following was tested in four out of the five MS patients.

1. The H-reflex recorded by the routine method was conditioned by a single shock to the spinal cord at variable time intervals. Spinal cord conditioning pulses were 0.2 msec. width and at

threshold level of spinal cord sensation. In one patient the changes in reflex amplitude were measured with gradually incrementing stimuli to the spinal cord. This was applied at a conditioning interval of 20 msec. prior to the test reflex pulse.

2. Changes in the H-reflex were measured, conditioned by a burst of stimuli to the spinal cord applied at variable time intervals. 200 msec. duration pulses were used at sensory threshhold level. The length of pulse train and number of pulses used were as quoted in the results.
3. The H-reflex was measured during a continuous stimulation to the spinal cord using 0.2 msec pulse width and variable stimulus intensity. In one patient pulse duration was changed gradually and the effect of pulse rate on H-reflex was measured.
4. In a third series of experiments, changes in H-reflex amplitude and recovery were measured while altering voltage, pulse width and rate of SCS using the Avery Co. Farmingdale stimulator.
5. After 10 days of SCS the electrodes were removed. Clinical as well as electrophysiological follow-up studies were performed.
6. In the elctrophysiological follow-up routine H-reflex recruitment and recovery curves were measured. Reflex changes to vibration of tendoachilles and mechanoreceptor stimulation of the sole of the foot were recorded. The periods of follow-up are quoted in the results.

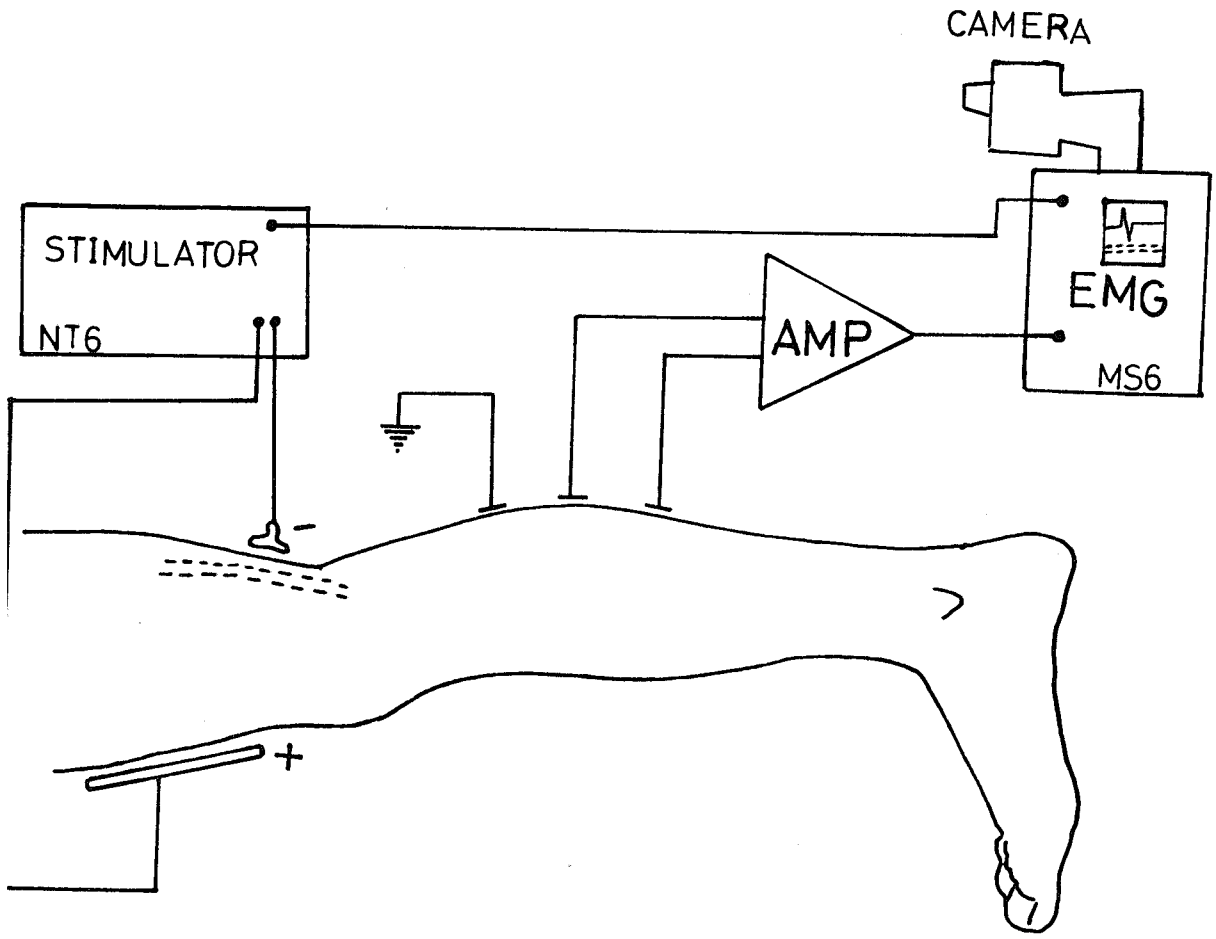


Fig. 8 Diagram of the recording set-up used for H-refex studies in patients with dystrophia myotonica.

H-reflex studies in dystrophia myotonica

The H-reflex was studied in patients suffering from dystrophia myotonica. Nine patients, five males and four females, were tested, their ages ranging from 9 - 51 years. The diagnostic feature will be discussed in the results.

Routinely H-reflex recruitment and recovery curves were measured in every patient. The H-reflex changes to vibration of the tendoachilles and scrubbing the sole of the foot were tested as well. In some cases changes were noticed with deep cooling of the calf muscles, using ice packs, for 5 - 10 mins.

Instrumentation

A diagram of the experimental set-up in Fig. 8 is illustrated. "Medelec" NT6 stimulator triggers "Medelec" MS6 EMG and evokes one pulse of one msec. width every five seconds. The assembly of the stimulating electrode as described before was used, as well as the large plate indifferent electrode placed on the front of the thigh.

The procedure described previously for setting up normal subjects was repeated before recording began.

Recording the soleus muscle EMG was by a pair of silver-silver cloride dup electrodes attached to the skin with Blenderm surgical tape No. 1525 (Minnesota mining and Mig. C. USA). An electrode jel was injected to fill the silver cup for good coupling. The earth electrode was a stainless steel strap electrode (Disa). The latter was sited in between the stimulation and recording assemblies.

Preamplification and further amplification of the signals was by AA6MK $^{1}/_{M}$ "Medelec" type amplifier. Signals were photographed on a UV sensitive recording paper using fiberoptic system of "Medelec" for further analysis.

"Pifco" type vibrator model 1556 was applied on the tendo-achilles to elicit continuous vibration of 50 HZ. Mechanoreceptors stimulation was by a dry scrubbing brush applied to the sole of the foot as described before.

STATISTICAL ANALYSIS AND COMPUTATION

In all of these experiments the mean ($\bar{x}$), standard deviation (Sx) and standard error of the mean ($S\bar{x}$) were calculated for each set of data. The following equation was used for determination of the mean:

$$\bar{X} = \frac{\sum X1}{n}$$

Where X1 = the individual values in a set of data.

n = the number of observations.

The following equation was used for determination of the standard deviation:

$$Sx = \sqrt{\frac{\sum (X1-\bar{X})^2}{n-1}}$$

Where X1 = the individual value in a set of data.

$\bar{X}$ = the mean.

n = number of observations.

The following equation was used for determination of the standard error of the mean

$$S\bar{X} = \frac{S\,X}{\sqrt{n}}$$

Where S X = standard deviation

n = number of observations

Individual values are reported as $\bar{X} \pm Sx$

Student unpaired T-test was used to calculate the significance of the difference between two sets of data during comparison. The values $\bar{X}$, $S\bar{X}$ and n for both sets of data were used for this calculation using the following equation.

$$T = \frac{\bar{X}1 - \bar{X}2}{S\bar{x}\ \text{diff.}}$$

Where $\bar{X}1$ = mean of the first group

$\bar{X}2$ = mean of the second group

$S\bar{x}$ diff = standard error of the difference between the mean of both groups.

The value of 'P', the probability that the observed differences between groups had arisen by chance due to the inherent variability in the parameters being measured was calculated from the value for t and (n-2) where N = (n1 + n2)

and n1 = number of observations in first set of data.

n2 = number of observations in second set of data.

The value of 'P' was obtained from the Documenta Geigy scientific tables (7th edition, 1970; Eds. Diem, K. & Lentner, C.).

A model 9810 A Hewlett-packard calculator was used as well as PDP-12 computer for all calculations.

Computation

A computer-based system for collecting, averaging and displaying H-reflex APs was devised. The EMG was amplified and the PDP-12 computer was triggered by the digitimer to sample the amplified signals after analogue to digital conversion. The raw data was monitored on an oscilloscope and simultaneously recorded on analogue tape. Peak to peak measurement and latency of the potentials were computed by a programme written in Focal-12 language. This was as follows:

```
Ø1.Ø1   C  PROGRAM $MSØ2VMH
Ø1.Ø2   C  RUNS FROM LSFC12
Ø1.Ø3   C  FOR CALCULATION OF V/M V/H CURVES
Ø1.Ø4   C  DATA SAMPLED AT 25Ø USEC INTERVALS
Ø1.1Ø   O  C;O T;E
Ø1.2Ø   L  O, F1, I,#O, 1
Ø1.3Ø   A  !,"START BLOCK NUMBER, OCTAL", NS
Ø1.4Ø   A  !, "NUMBER OF BLOCKS",R
Ø1.45   D  6
Ø1.5Ø   O  C; D 3
Ø1.7Ø   A  ! "START OF M",MS;A "END OF M", MF
Ø1.8Ø   A  ! "START OF H",HS;A "END OF H", HF
Ø1.85   T  !!," AMPM   LATM    AMPH    LATH    BLOCK NO"
Ø1.9Ø   C  THESE FIGURES SHOULD BE IN MSEC

Ø2.1Ø   F  I=(MS*4),1,(MF*4); D 7
Ø2.2Ø   S  AM=MX-MN; S LM=Q/4; D 3
Ø2.3Ø   F  I=(HS*4), 1, (HF*4); D 7
Ø2.4Ø   S  AH=MX-MN; S LH=Q/4
Ø2.45   D  8
Ø2.5Ø   T  !, %4.ØØ,AM,"   ",%4.Ø2,LM,"   ",%4.ØØ,AH,"  ",%4.Ø2,LH,"  ",BN
Ø.26Ø   S  KK=KK+1
Ø2.65   S  CN=CN+1
Ø2.7Ø   I  (R-CN)E,2.99;D  1.5; G 2.1
Ø2.99   T  !!;O  S;Q

Ø3.1Ø   S  MX=-2Ø46;  S  MN=2Ø46

Ø6.Ø1   C  OCTAL TO DECIMAL SUBROUTINE
Ø6.1Ø   S  C1=F1 TR(NS/1ØØ); S  C2=FITR((NS-C1*1ØØ)/1Ø)
Ø6.3Ø   S  C3=FI tr(NS-C1*1ØØ-C2*1Ø)
Ø6.4Ø   S  KK=C1*64+C2*8+C3

Ø7.1Ø   C  SUBROUTINE FOR MAX/MIN VALUES & LAT OF MAX
Ø7.2Ø   S  P=F1(KK*256+1)
Ø7.3Ø   I  (P-MX) 7.6, 7.6
Ø7.4Ø   S  MX = P
Ø7.5Ø   S  Q=1
Ø7.6Ø   I  (P-MN) 7.7;R
Ø7.7Ø   S  MN=P

Ø8.Ø1   C  DECIMAL TO OCTAL SUBROUTINE
Ø8.1Ø   S  B1=FITR(KK/64)
Ø8.2Ø   S  B2=FITR(KK-B1*64)/8)
Ø8.3Ø   S  B3=FITR(KK-B1*64-B2*8)
Ø8.4Ø   S  BN=B1*1ØØ+B2*1Ø+B3
```

Displaying of the stored averaged potentials was possible by a window screening programme (MAGSPY) written in core language (DIAL) and displayed on the PDP-12 computer screen. Results of the averaging and measurements were written out by teleprinter.

RESULTS AND DISCUSSIONS

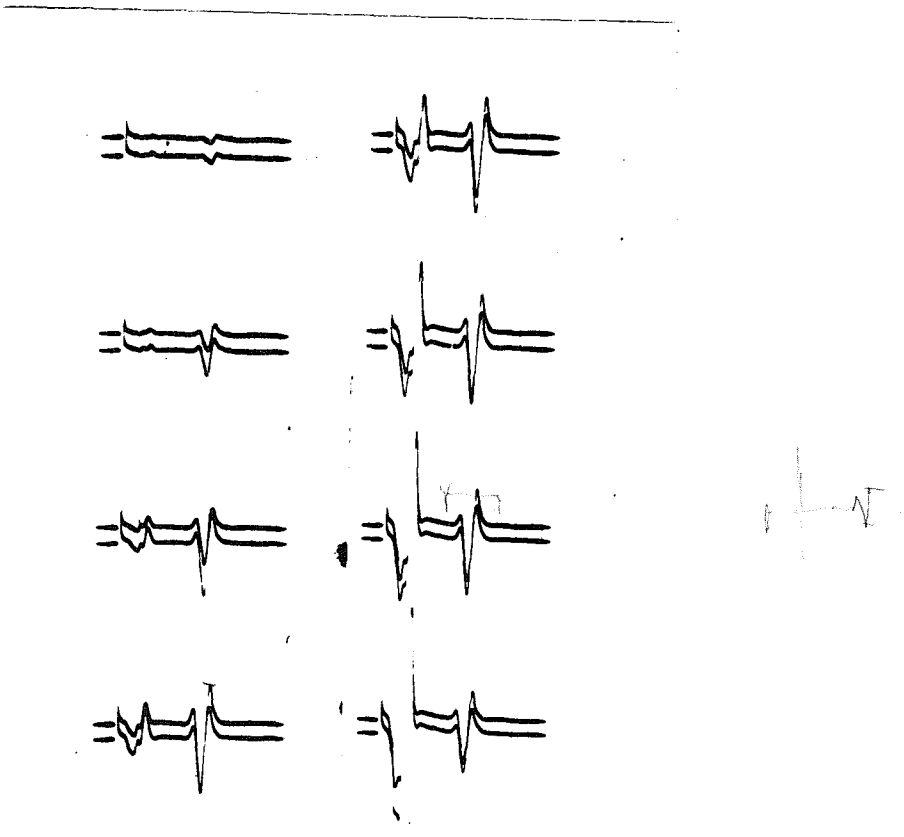


Fig. 9 Just threshold stimulus to the posterior tibial nerve elicits the H-reflex after 30 msec. from the stimulus artifact. The reflex increased gradually with incremental stimuli up to a maximum. When the stimulus intensity reached the threshold level of the motor axons they fired giving an M-response preceding the H-reflex. Further increase of the stimulus intensity reduced the H-reflex while the M-response grew to a maximum.

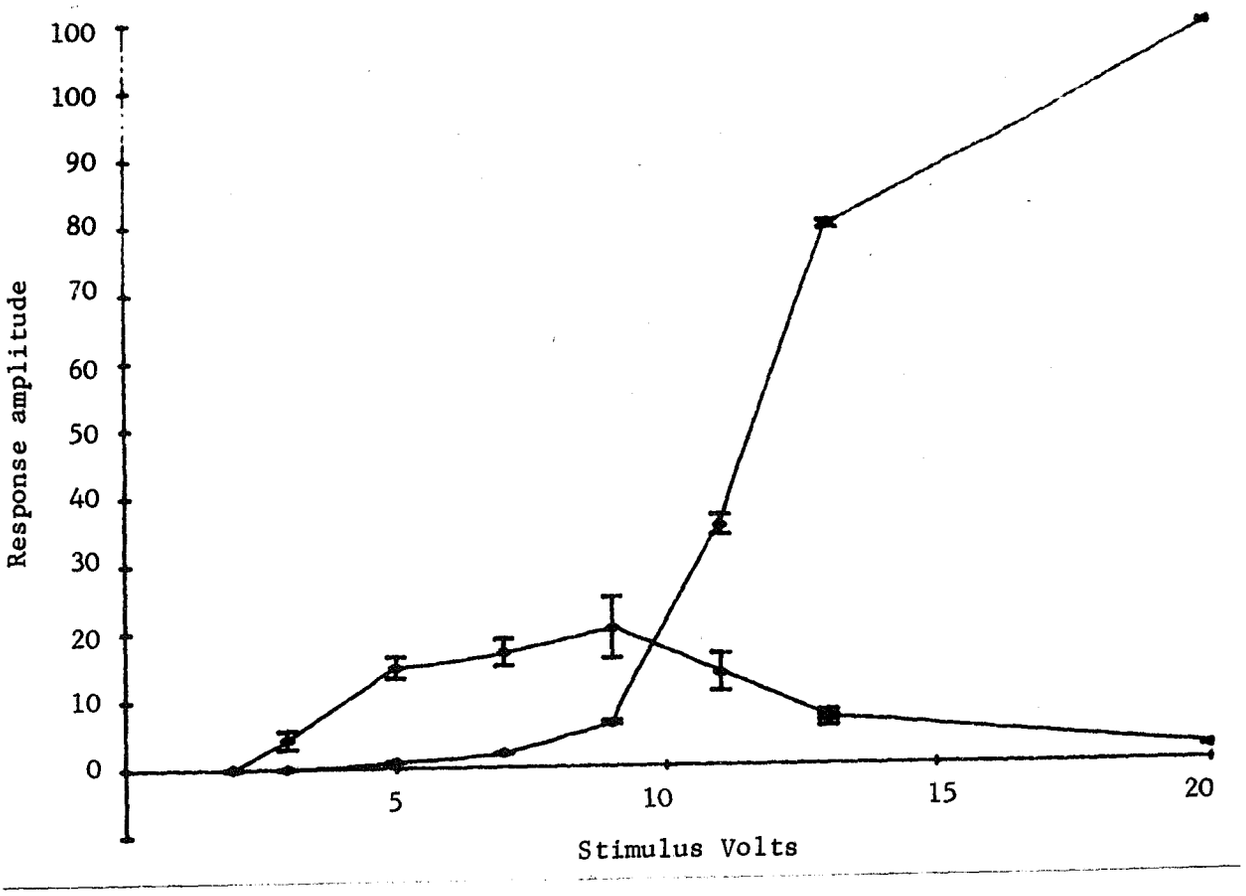
CHAPTER I

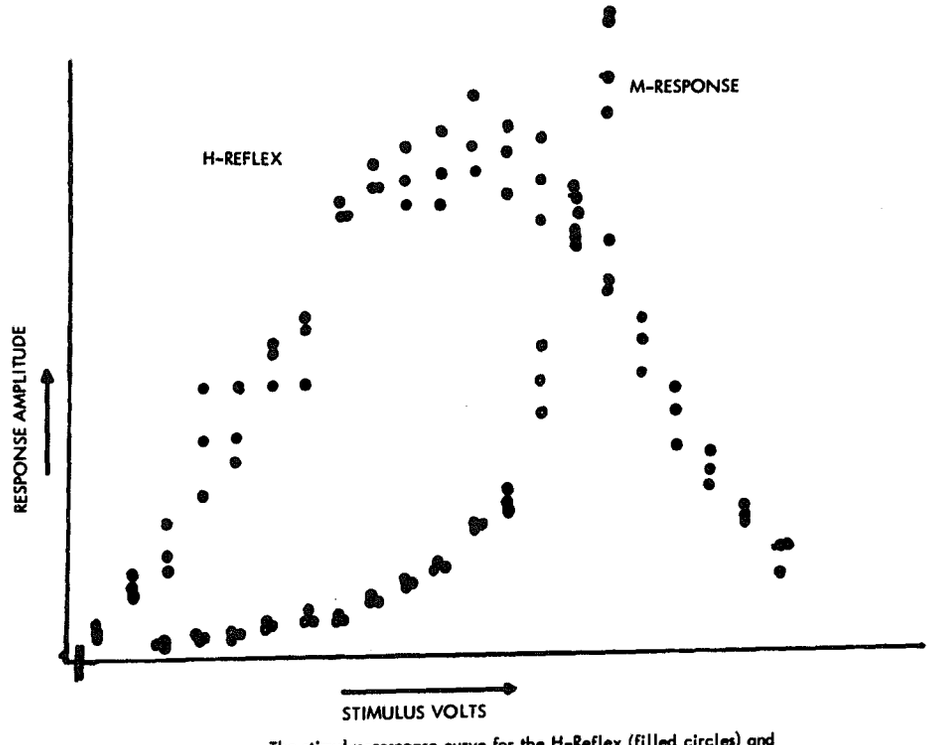
H-REFLEX BASIC STUDIES

I H-Reflex with incremental stimuli and recruitment curve

Incrementing stimulation of the posterior tibial nerve, after accurate placement of the electrodes, evokes an H-reflex which increases gradually in amplitude with increase in stimulus strength (Fig. 9). The reflex latency varied from 24 to 30 msec. in all normal subjects tested. With further increase in the stimulus strength, the M-response started to appear 6 to 8 msec. after the stimulus artifact (Fig. 9). The latter increased gradually with further increase of stimulus amplitude, while the H-reflex declined gradually until it disappeared. There was a useful interval in stimulus amplitude between H-reflex and M-response thresholds. Fig. 9 shows H and M responses with incrementing stimuli. Plotting of the potential amplitude against the stimulus strength gives the recruitment curve shown in Fig.10 In this curve 20 consecutive responses for each point were averaged and the mean response amplitude plotted with one standard deviation on either side of the mean.

Great fluctuation was seen in the reflex with fixed stimulus intensity. This fluctuation was found to be less with submaximal reflexes of 60 to 80% of the maximum (Fig.10). In all of our work this reflex value was used as the standard. Moreover it was used as a control value for plotting the recovery curves using identical pulses. This was applied to avoid, as much as possible, these fluctuations. Because this is a smaller H-response than the maximum it should be possible to see both increases and decreases





The stimulus-response curve for the H-Reflex (filled circles) and M-response (open circles)

Fig. 10 The recruitment curve is the plotting of response amplitude (ordinate) against the stimulus strength. Averaging 20 responses showed that the submaximal reflexes are the most stable of the curve (upper). Mean $\pm$ SD plotted. The scatter of the points in the lower curve showed the same findings.

in the H-reflex as a result of any procedure that is carried out.

The shape of the reflex is a good index of the synchronism of the @-MNs. It was similar to M-response shape, but longer in duration, in those cases where the same motor axons and Ia fibres connecting to its mother cells were excited by stimulation. This finding is similar to the report of Hugon (1973). In the ideal cases the H-reflex was always longer in duration than the M-response. This can be explained due mainly to the asynchrony in the @-MNs firing and due to the variations in the conduction velocity of the motor axons.

During recording from various subjects we noticed that in some individuals the voltage range for reflex excitation i.e. the range from the smallest sub-threshold to supramaximal stimuli was larger than in other individuals. This range was over 100 volts in some subjects while it was 20 volts in others. We noticed no relation between this range and other factors.

The threshold of reflex excitation varied considerabely from one subject to another and differences were seen between the H-reflex threshold level in young and old subjects. It was fairly easy to elicit a large H-reflex without M-deflection in most young subjects.

II <u>The fraction of the MNP participating in the H-reflex</u>

Measuring the fraction of the MNP by $^{H}/_{M}$ ratio can give a distorted result due to the MNs asynchrony. This was overcome in the work of Taborikova (1966), Tabrikova et al (1968) by using the refractoriness technique. We used the same method and obtained

similar results. On the other hand the fluctuation of the MNP was high with this method due to the application of two successive pulses.

The MNP was measured by the two techniques in a comparative study in order to note the discrepencies and to assess the validity of the techniques for measuring the fraction of the MNP.

In 10 young subjects, all were male, with ages ranging from 19 to 36 years the MNP fraction measured by refractoriness and ranged from 44 to 89% with a mean value of 69% (Table I). This was slightly higher than that found by Taborikova et al (1968) who demonstrated a mean value of 50% of the pool participating in the H-reflex.

Table 1 MNP fraction participating in H-reflex

Manoeuvre Technique	Standard	Cont. calf	Cont. T.A. Isometric	Isotonic
Refractoriness	69	79	44	25
$^{H}/_{M}$ ratio	69	81	41	28

On the other hand the MNP of the same subjects was measured by the $^{H}/_{M}$ ratio and ranged from 51 to 90% with a mean value of 69%. In spite of the relatively similar values of the means of the two techniques the individual results showed significant variation. In some subjects the $^{H}/_{M}$ ratio was considerably higher than the fraction measured by refractoriness e.g. 90% and 66% of the MNP respectively, while in others the refractoriness gave a higher value.

When the fraction was measured during contraction of the calf muscle, the mean fraction value increased to 79% and 81% of the MNP using refractoriness and $^{H}/_{M}$ ratio respectively. Again there was a large variation within subjects of the fraction value measured by the two techniques. Some subjects showed significant increase in the fraction value while others had a smaller one during contraction of

the calf. The latter was observed when using the refractoriness technique. The $^{H}/_{M}$ ratio showed more reasonable results as 6 out of 7 exhibited significant enlargement of the fraction value.

Contraction of the dorsiflexors of the foot, either isometric (without movement) or isotonic (with full dorsiflexion of the foot), caused significant inhibition of the test reflex. The latter ranged from 46 to 59 with a mean value of 54% of the control, with isometric contraction, while it ranged from 8 to 59% of the control with isometric contraction. These values were similar to those of other workers (Delwaide, 1971, 1973, Gottlieb et al, 1969, Burke et al 1971, 1973). Furthermore the fraction value showed significant reduction to a mean value of 44% and 25% of the MNP, when measured by refractoriness technique, respectively. $^{H}/_{M}$ ratio gave a mean value of 41% and 28% of the MNP for isometric and isotonic contraction respectively.

Concluding the above results one can say that there was a poor correlation of the value of the fraction measured by the two techniques. Although the means of all subjects gave similar figures for both techniques, some subjects showed considerable variation. This may be due to fluctuations of the MNP when measured by refractoriness produced by the relatively asynchronous discharge of the MNs which affects $^{H}/_{M}$ ratio measurement. These discrepencies in the results shown make these techniques less than reliable for measuring the MNP fraction. On the other hand the similarity of the means of all subjects, with each manoeuvre, and their tendency to be enlarged or reduced according to the type of the manoeuvre, needs some attention.

Apart from a few instances these measurements were not applied in this work and these techniques cannot be recommended without reservations.

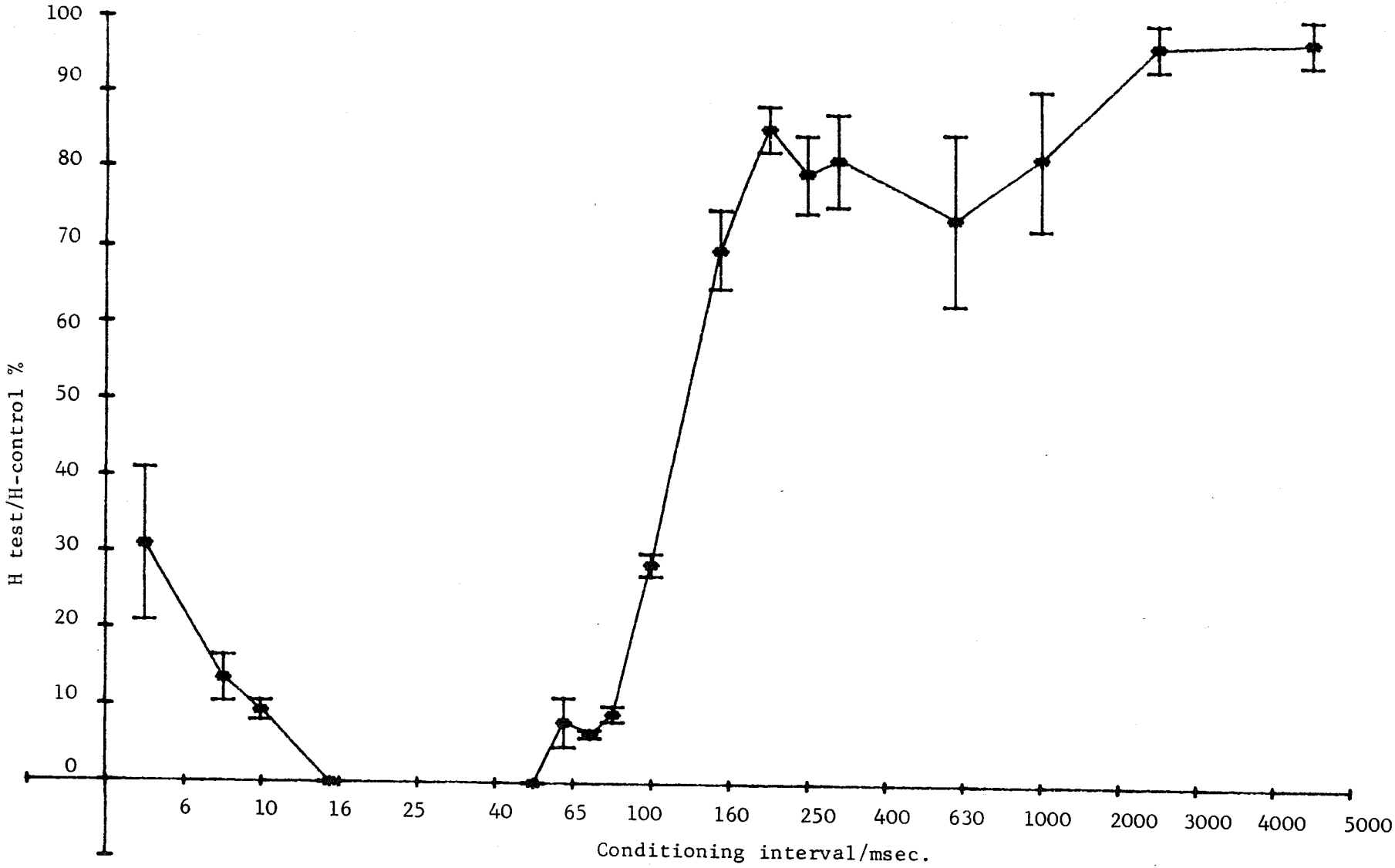


Fig. 11 Recovery curve of the H-reflex in one normal subject

III The Recovery Cycle

Using two identical stimuli giving maximal H-reflex with no M-response i.e. 60 to 80% of the full H-reflex possible to be recruited, the percentage of the second reflex was plotted against the interstimulus interval. This conditioning interval varied from 0 to 1000 msec. in most experiments. Along this time course the test reflex passed through various changes which were characteristic in each subject (Fig. 11). The following phases are described:

1. Primary or early facilitation period

In this part two successive reflexes were seen, H_1 and H_2 over an interstimulus interval of 5-15 msec. The test reflex declined gradually as the conditioning interval increased until it was completely abolished at 20 msec.

In our work we have not recorded or studied this period systematically.

2. Primary or early inhibition period

A further increase of the conditioning interval inhibited or almost totally depressed the test reflex for up to 45 msec. in young subjects (Fig. 11). This inhibition period varied from one subject to another. It was noticed that this period shortened dramatically during contraction of the calf muscle. The same was reported by Hoffmann (1922). Furthermore this period was always of the same length in the same subject in different recording sessions provided that the stimuli used, evoked equal H-reflex of submaximal size.

3. Early recovery and reflex turnover

The test reflex starts to recover gradually with further

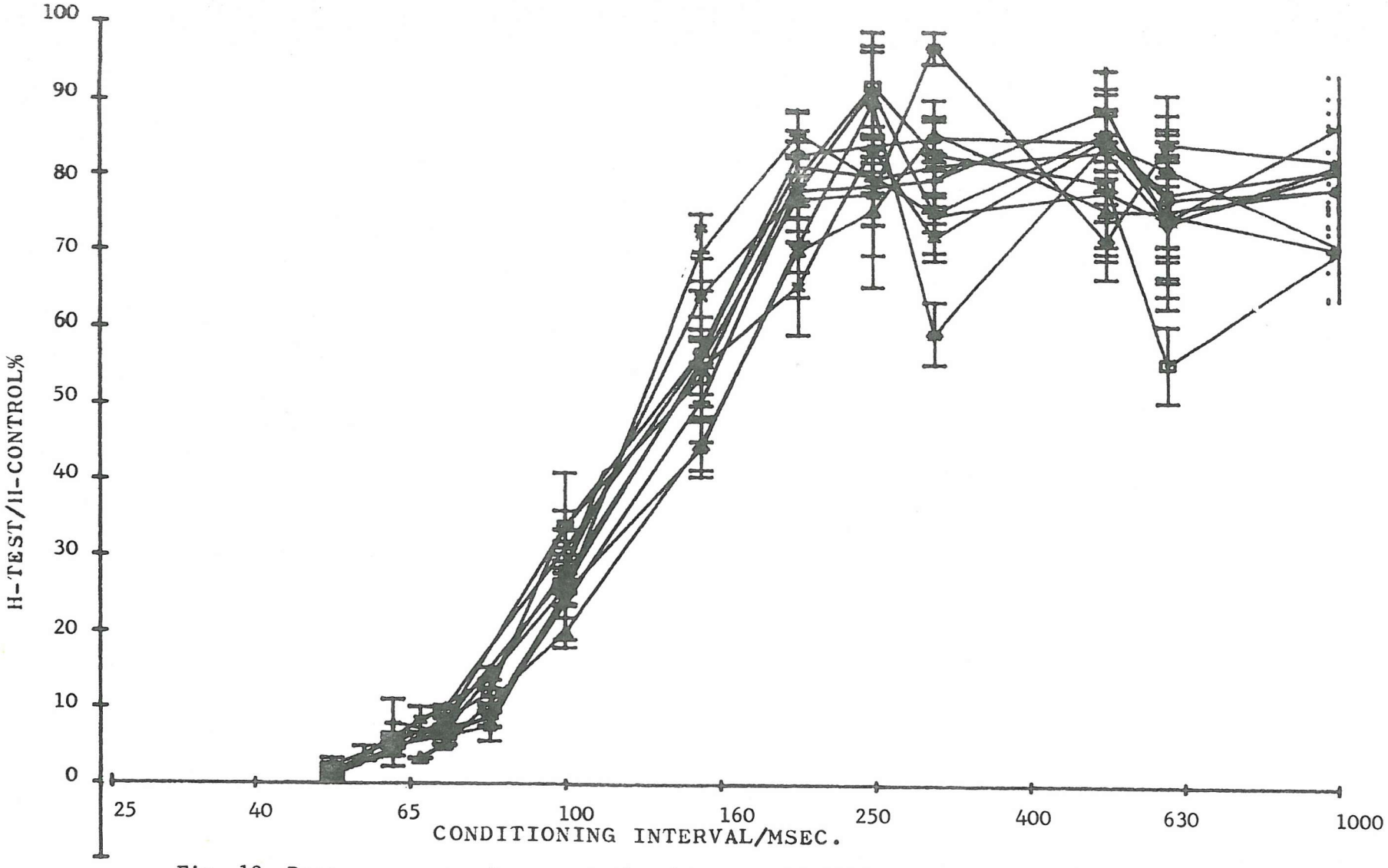


Fig. 12 Recovery curve of one normal subject on 10 different occasions .

increase of the conditioning interval. The recovery of the reflex varied from one subject to another and ranged from 35 to 60 msec. with a mean value of 45 msec.

When the test reflex recovered it increased in amplitude gradually with each incrementation in the conditioning interval until it reached a maximum at 200-300 msec. This was less than 100% of the control. This recovery turnover phase was noticed to be the most sensitive part of the curve in that it altered in different clinical disturbances. It is a good index of the monosynaptic reflex excitability. In normal subjects this phase did not show great changes at different recording sessions (Fig. 12).

4. Late or secondary inhibition period

With a further increase of the interstimulus interval, the test reflex shows a mild inhibition which lasts from 350 to 900 msec. The degree of the reflex inhibition was not as large as the primary inhibition period and varies from one subject to another. Under different recording conditions the inhibition was noticed not to fluctuate more than 20% of the control reflex amplitude. The test reflex reached 80% of the control during this period.

5. Final reflex recovery

The reflex recovered completely with further increase in the conditioning interval. It increased in amplitude gradually until it reached the control value when the conditioning interval was 3 sec. or more. (Fig. 11).

Recording of the recovery cycle of one subject in 10 different recording sessions gave interesting results. In Fig. 12 this study was expressed as the mean and the standard deviation of 10 different sets of recordings. Submaximal reflexes of the standard value were

used. The reflex recovery turnover phase did not show significant fluctuations. The test reflex recovers after 50 to 60 msec. in all recording sessions. Moreover the test reflex recovers smoothly up to the maximum. Greater fluctuations were seen in the test reflex after the turnover point. This shows the H-reflex recovery curve is accurately reproduced on different occasions in the same subject.

Discussion

Recruitment of the H-reflex with incrementing stimuli showed a progressive increase in the reflex amplitude until it reached a maximum. This was due to the increase in the number of the Ia fibres being stimulated. The motor axons were not subjected to the stimuli due to their higher threshold. With further increase in stimulus intensities a M-response starts to appear while H-reflex reached the maximum. All the Ia fibres were probably excited at this level giving maximal reflexes while the lower threshold motor axons fired to give a small muscle AP. Further increase in intensity of stimuli produced progressive diminution of the reflex while the M-response enlarged significantly. This is because with a higher stimulus more motor axons were excited which is expressed in the M-response. These excited motor axons carry the volley distally to the muscle to evoke the action potential, as well as centrally to collide with the orthodromically invading volley either in the axon or the somata. These results confirmed the findings of the previous authors (Hoffmann 1918, Magladery et al 1951, Delwaide 1971, and Hugon 1973).

The pathway for H-reflex and M-responses can be traced in the distance time plottings of Fig. 13A, B, from Taborikova & Sax 1968. The distance between the posterior tibial nerve at the site of stimulation and the MNP as well as to the soleus muscle (SM) distally, is

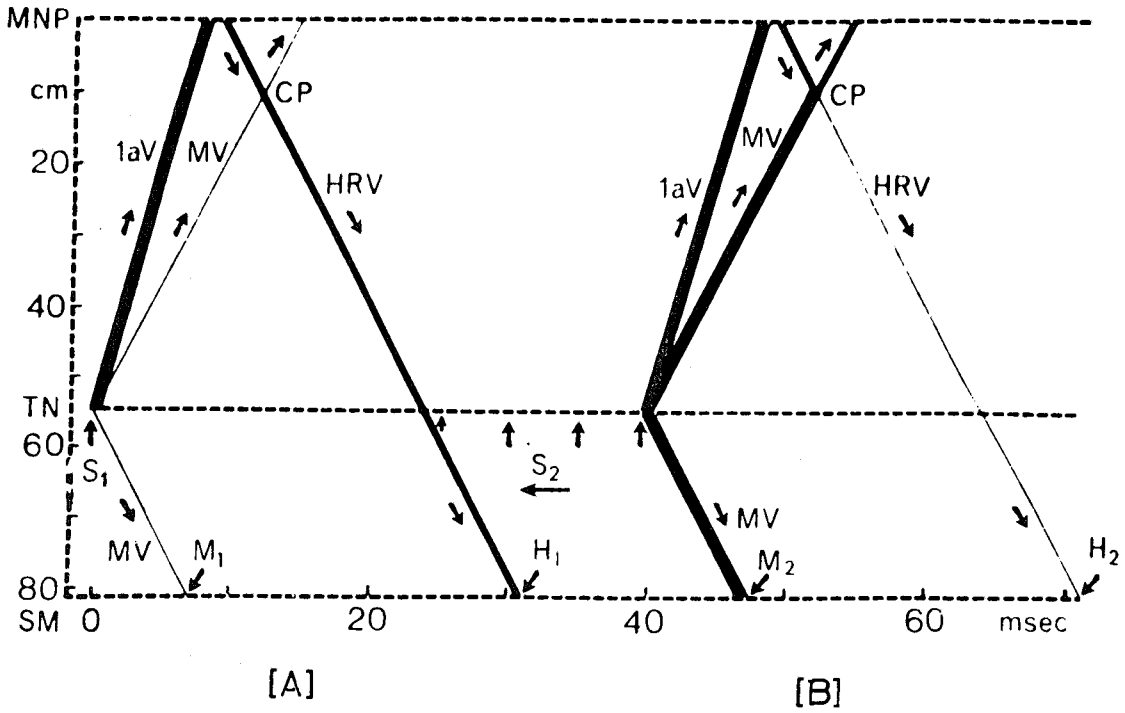

MNP
cm
20
40
TN
60
80
SM
0
20
40
60
msec
1aV
MV
CP
HRV
S1
S2
M1
H1
M2
H2
[A]
[B]

Fig. 13

Distance time plotting showing the pathways for H and M-responses evoked by weak S1 (A) and strong S2 (B) stimuli. The approximate distances are shown from the motoneurone pool (MNP) to the stimulating electrode of the posterior tibial nerve (TN) and the recording electrode on the soleus muscle (SM). Zero in the time co-ordinate (abscissae) gives the time of stimulus (SL and S2) to TN. In (A) the weak S1 sets up a large Ia volley (IaV) that evokes the H-reflex volley (HRV) and a small number of motor axons excited giving a small motor volley (MV) propagating in both directions, but more slowly than the IaV and colliding at CP with HRV. In (B) the strong S2 evokes both large IaV and MV, in both directions. The collision at CP point was enough to cause blocking of almost all HRV so that M2 will be large and H2 very small. As shown by the horizontal arrow, as S2 is moved earlier, there will be eventually a reduction of the M2 response in all those motor units responding to S1 by HRV. (From Taborikova & Sax 1968).

expressed in the ordinate. The abscissa expresses the time taken by the stimulus to propagate either to the MNP (orthodromically through the Ia as IaV, or antidromically in the motor axons as in MV) or to the muscle directly as in orthodromic (OMV).

Zero in the time co-ordinate is the time of the tibial nerve stimulation. With subliminal stimulus only the H-reflex discharge is expressed in the muscle SM after a freely propagating pathway through IaV-MNP-HRV. With threshold stimuli the direct muscle action potential is elicited through a short distance (OMV) and the antidromically propagating pulse AMV collides with (HRV) at (CP) point and reduces its further propagation to the periphery. This can be shown by the diminution of the thickness of HRV line after CP point peripherally. The thinning of the distal HRV pathway depends upon the thickness of the AMV to match the whole central HRV immerging from MNP.

The amplitude of the H-reflex is a measure for MSR excitability to a synchronous afferent volley. Moreover the accessibility of the MNs to peripheral stimulus could be easily estimated by the reflex amplitude. However, without the mechanism of presynaptic inhibition (see later discussion of Natural Stimuli), it was possible for the H-reflex amplitude to become a standard measurement for MN excitability.

The recovery of the MN after previous excitation i.e. the recovery cycle, confirmed the previous findings of Magladery et al (1951), Olsen et al (1967), Mayer et al (1973). It is suggested that the primary excitation period is due to firing of @-MN on the subliminal fringe, as the MN did not reach the firing level by the conditioning stimulus. The test shock causes them to become excited expressing themselves in the H2 reflex.

The primary inhibition period is subject to contradictory opinions. It will be one of our studies in the following sections.

CHAPTER II

EFFECT OF NATURAL PERIPHERAL STIMULI ON MSR EXCITABILITY

In this chapter the effects of natural stimuli and their effect on the H-reflex are described. The natural stimuli employed were scrubbing the sole of the foot for mechanoreceptors, superficial skin cooling using cold spray for thermoreceptors, and vibration of the tendoachilles for muscle receptors.

Further study of the cooling effect was done by application of ice packs on the skin for 30 minutes. In these studies H-reflex recruitment and recovery curves were used when appropriate.

The fraction of the MNP involved was measured during application of these stimuli and significant changes were found.

I Effects of mechanoreceptors

A. Touch: Superficial touch by drawing cotton wool over the skin caused no changes in the H-reflex. This was the case when touch stimulation was applied on various skin dermatomes of the lower limbs. The test reflex was of a mean value of 98% of the control when touch was applied over the calf area in seven subjects (two were female).

B. Pressure: Scrubbing of the ipsilateral skin dermatomes produced significant inhibition in the H-reflex. The degree of inhibition varies according to the dermatome stimulated. Twenty two young subjects were tested with this manoeuvre, five were females, and their ages ranged from 18 to 45 years. Scrubbing various dermatomes gave the following results:

1. Ipsilateral calf area:- "L_4, 5 S_2" dermatome

Seventeen subjects were studied of which five were females. H-reflexes were significantly inhibited in all subjects tested to a mean value of 65% of the control (65.3 $\pm$ 3.6) (Table 2). The degree of inhibition varied from one subject to another. It was greater in some of them so that the test reflex was reduced to 19% of the control, but in others it was mild and gave a reflex value of 87% of the control. The test reflex was variable during the procedure and returned abruptly to the normal value after cessation of scrubbing.

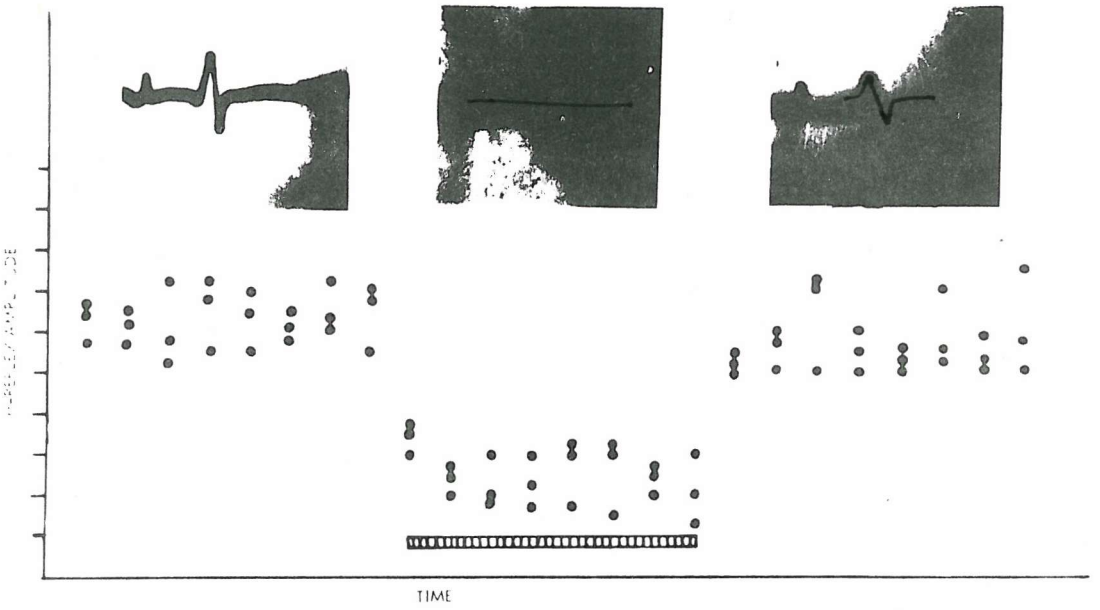
Table 2 Effect of stimulation of skin mechanoreceptors and cold receptors on H-reflex. The values expressed as the percent of the control. Mean $\pm$ S.D of all subjects tested

Site of stimulation / Type of stimulation	Sole of the foot	Calf area	Ant-thigh	Dorsal foot	Tibial Surface	Post thigh
Scrubbing	49$\pm$10	65$\pm$4	70$\pm$13	83	56$\pm$11	97$\pm$15
Cooling	61$\pm$8.5	80$\pm$6	78$\pm$11	85$\pm$10	89$\pm$11	85$\pm$10

2. Ipsilateral sole of the foot:- "L_5 S_1" dermatome

This was the area which resulted in greatest inhibition of the reflex by scrubbing. Twenty subjects were tested of which five were female. The test reflex was inhibited to a mean value of 49$\pm$10% of the control (Table 2). It ranged from 28-88% of the control.

Fig. [illegible]



The H-reflex was evoked 1 sec and its amplitude is plotted against time. The bar marks a period of scrubbing the sole of the foot.

The figure is compiled from 3 separate runs in the same subject.

Specimen traces are shown above the graph

Similarly to the calf, the reflex manifested higher variations during scrubbing, its amplitude fluctuating during the manoeuvre. Fig. 14 shows the effect of scrubbing the sole of the foot during continuous recording of the H-reflex and demonstrates the abrupt inhibition and recovery. Above the graph are three sample traces before, during and after scrubbing and we can see that the H-reflex does diminish in size whereas the minimal M-response which was present in this case stays exactly the same indicating that there has been no change in the stimulus volley or the position of the electrodes.

These results were supported by measuring the fraction of the MNP participating in the H-reflex during scrubbing. A mean standard fraction of the MNP measured by refractoriness was 69% and was lowered to 42% when scrubbing was applied to the sole of the foot (Table 3). Furthermore when the MNP fraction was measured by $^{H}/_{M}$ ratio it was of a mean value of 69% and reduced to 44% by scrubbing the sole of the foot (Table 3).

Table 3 Fraction of the MNP participating in the H-reflex during stimulation of the skin cold and mechanoreceptors

Subject	Refractoriness			$^{H}/_{M}$ ratio		
	Control	Scrubbing	Cooling	Control	Scrubbing	Cooling
LN	44	70	70	72	69	64
TB	88	40	-	71	45	-
AC	74	19	-	61	12	-
GB	50	-	47	80	-	54
CR	65	21	-	51	47	-
MK	90	-	92	85	-	70
CJ	74	63	75	61	47	50
Mean$\pm$SD	69 ± 7	42 ± 11	71 ± 9	69 ± 5	44 ± 9	59 ± 5

It is important to note that the degree of reflex inhibition depends upon whether the whole sole was stroked or just a small area and whether the stimulation was intense or mild. The degree of inhibition increased when stroking the whole sole with an increased intensity. In all subjects mild scrubbing of the whole sole was applied. Care was taken that the end of the stroke occurred at the heel and coincided with the foot movement in the reflex action. This was to avoid any artifact or obstruction of the foot movement. No changes were seen either in the reflex latency or in the M-response.

3. Dorsal surface of the foot:- "L_5 S_1" dermatome

Scrubbing dorsal surface of the foot of the ipsilateral limb produced mild reflex inhibition to a mean value of 83% of the control (Table 2). This was applied to five subjects out of which two were female and they all demonstrated variable results ranging from 54 to 103% of the control.

4. Tibial surface:- "$L_{4,5}$" dermatome

When the anterior aspect of the lower leg was stimulated by scrubbing the test reflex was inhibited to a mean value of 56% of the control (Table 2). This was applied to eight subjects of which five were male. The test reflex ranged from 31 to 115% of the control. It was inhibited in most records during application of the scrubbing with an abrupt return to normal value after cessation of the stimulation.

5. Anterior thigh surface (Quadriceps Area):- "$L_{2,3}$" dermatome

Scrubbing of the skin overlying the quadriceps muscle demonstrated a reflex inhibition to a mean value of 70% of the control (Table 2).

This was tested in ten subjects out of which four were female. The test reflex ranged from 32 to 117% of the control.

6. Posterior thigh surface (Hamstrings area): $L_{2,3}$ S_2" dermatome

When the skin overlying the hamstrings muscle was scrubbed the test reflex showed no significant changes. It ranged from 54 to 111% with a mean value of 97% of the control (Table 2).

It is worth noting that scrubbing various dermatomes of the contralateral limb caused no changes in the test reflex and no changes were seen in the M-responses. Table 4 shows the areas most affected by mechanoreceptors stimulation in all subjects tested.

Table 4 Significance of the difference between various skin areas of lower limb during mechanoreceptors stimulation in all subjects tested

	Sole of the foot	Calf area	Ant Thigh	Dorsal foot	Tibial Surface	Post Thigh
Mean $\pm$ S.E	49 ± 3	65 ± 4	70 ± 10	83 ± 145	56 ± 11	97 ± 15
P.	0.001	0.001	1.8(NS)	0.66(NS)	0.02	0.03(NS)

II Effects of vibration

Vibration was one of the most effective manoeuvres which affected the MNP and the H-reflex. Reflex inhibition was the result of application of the vibration to various sites of the ipsilateral limb.

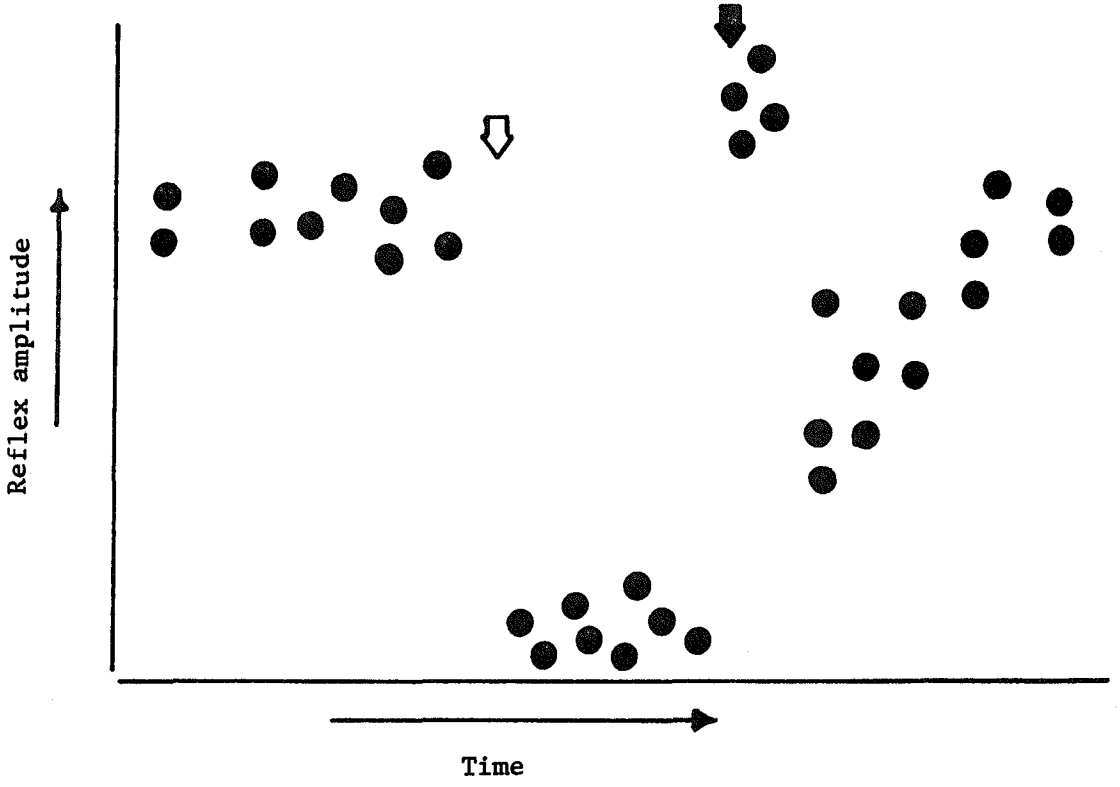


Fig. 15 Vibration of the tendoachilles at 50 C/sec. inhibits the H-reflex. After cessation of the vibration facilitation of the tested reflex for a short time was followed by a secondary inhibition with a gradual recovery. The reflex was evoked every second.

1. Tendoachilles

Vibration of the tendoachilles caused significant inhibition to a mean value of 28% of the control (Table 5). The degree of reflex inhibition varied from one subject to another and ranged from 9 to 85% of the control. This was tested in 18 subjects of which 6 were female. The reflex was inhibited abruptly after the vibration started and continued to be inhibited all the time of stimulation without any tendency to adaptation and recovery (Fig.15) In most subjects i.e. 15 out of 18, the degree of inhibition was enormous so that the reflex amplitude was less than 36% of the control. The reflex was frequently seen to be completely abolished.

Table 5 Effect of vibration on the H-reflex

Site of stimulation	Tendoachilles	Calf skin	Hamstring skin	T.A.* tendon	Ligamentum patellae
% of the control Mean $\pm$ SD	28 ± 6	55 ± 7	42 ± 0.6	30 ± 3.5	80 ± 3.7

* T.A. Tibialis anterior tendon

During recording it has been noticed that the degree of reflex inhibition depends upon the amplitude of the vibration. Large amplitudes produced more inhibition than small. In all the work large amplitudes of vibration were applied. On the other hand, the reflex amplitude and the fraction of the MNP fired plays an important role in the degree of inhibition by vibration. Submaximal to maximal reflexes were largely inhibited by vibration, but a supramaximal reflex was only slightly inhibited. After cessation of the

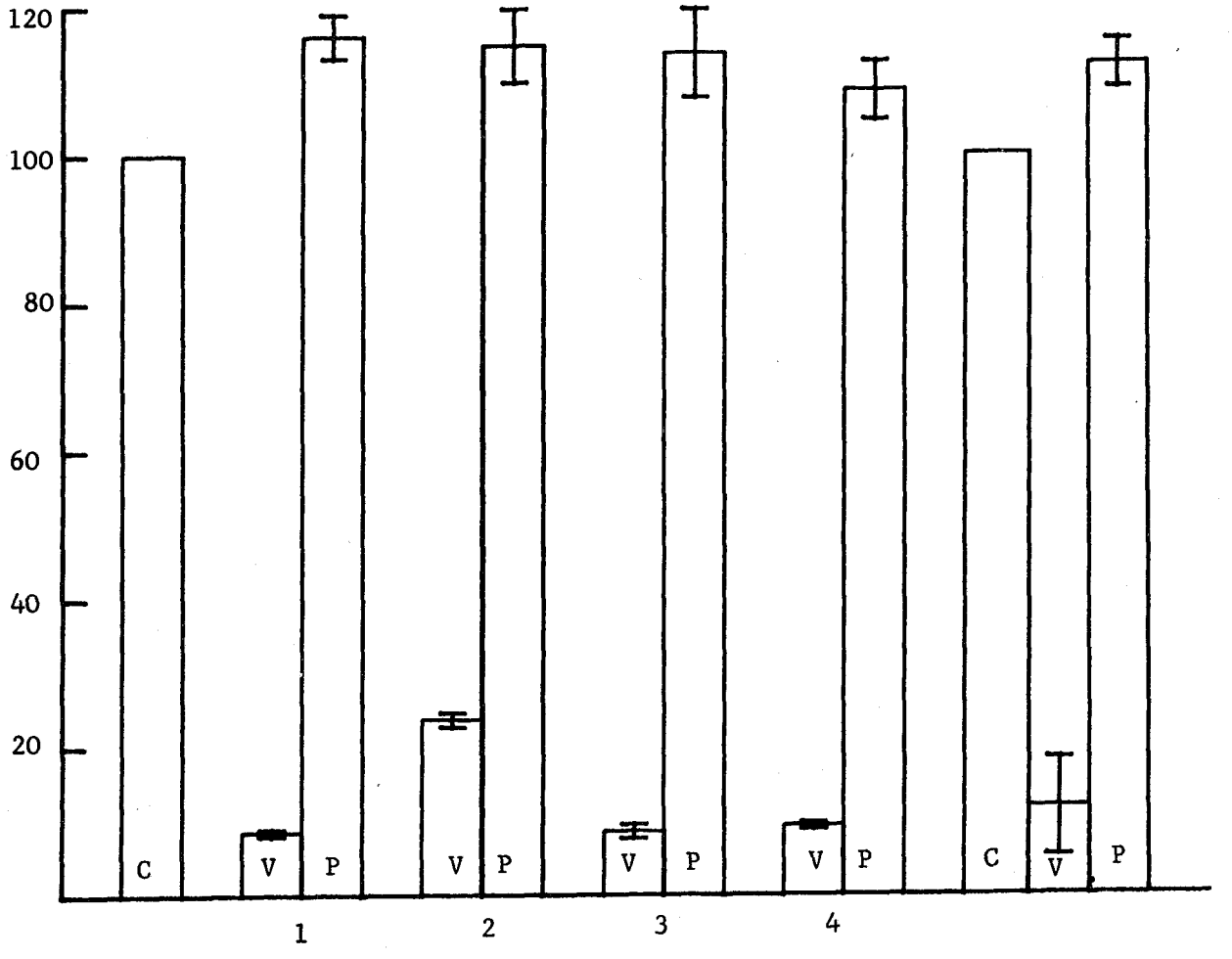


Fig. 16 Effect of vibration on the H-reflex in one normal subject. In four trials the test reflex was inhibited dramatically during vibration (V) and became larger than the control (C) after vibration (P). The mean of the four trials are presented at the end of the histogram. (Mean $\pm$ SD).

vibration the test reflex returned with mild facilitation in most subjects. The degree of facilitation varied from one subject to another from 102 to 152% of the control. This after-vibratory period lasted from 20 to 30 seconds, after which the reflex was mildly inhibited again. Gradual return to the normal value was seen afterwards. Sometimes the post-vibratory facilitation period could not be seen and the reflex passed directly to the secondary inhibition period with gradual recovery. No changes were noticed in the M-response or in the reflex latency. Fig. 16 shows a histogram demonstrating the effect of vibration on submaximal reflexes during the primary inhibition and post-vibratory facilitation period.

The fraction of the MNP participating in the H-reflex during vibration of the tendoachilles was measured and supports the previous findings. The fraction of the MNP ranged from 0-55 with a mean value of 15% of the whole pool, when measured by refractoriness (Table 6). $^{H}/_{M}$ ratio gave a fraction value ranging from 8 to 45 with a mean value of 28% of the whole pool (Table 6). These show a similar result to those using reflex amplitude as an index for measuring the degree of inhibition.

Table 6 Fraction of the MNP participating in the H-reflex during vibration of the tendoachilles

Subject	Refractoriness		$^{H}/_{M}$ ratio	
	Control	Test	Control	Test
TB	88	0.0	71	20
PY	66	0.0	90	45
SV	48	3	83	8
MK	90	55	85	39
Mean$^{+}_{-}$S	73 $\pm$ 2σ	14.5$^{+}_{-}$14	82 $\pm$ 8	28$^{+}_{-}$9

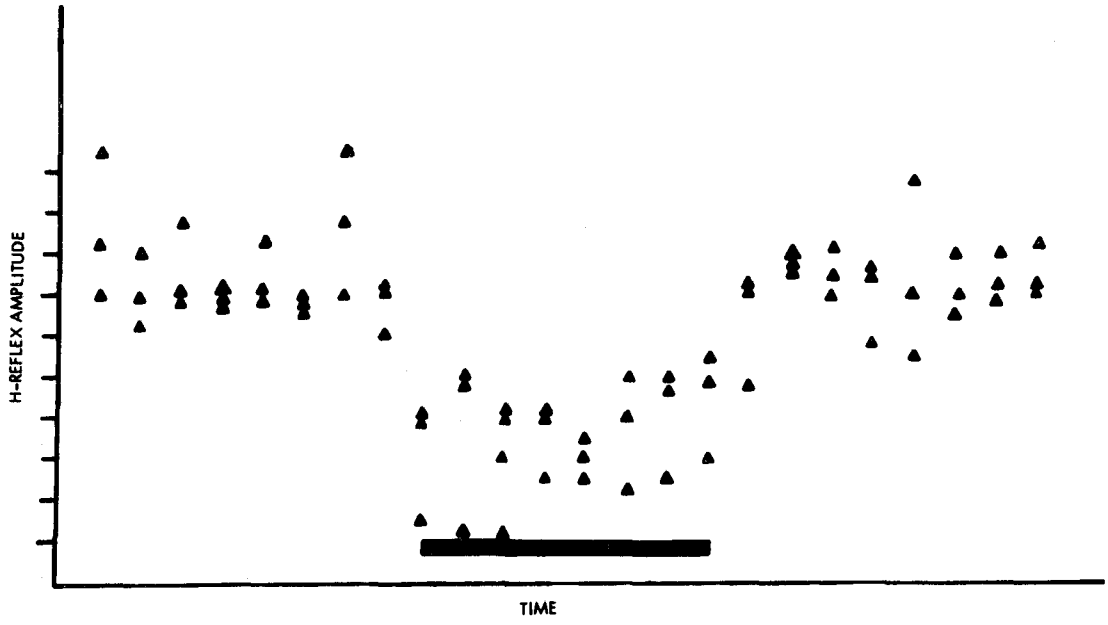
2. Other areas

The vibration was applied to the skin overlying the calf muscle, the hamstrings, as well as to the ligamentum patellae and tendon of the tibialis anterior muscle. At all sites the test reflex was inhibited (Table 5). This may be due to spreading of the vibration to the soleus muscle, a possibility which is supported by the findings that reflex inhibition decreased with vibration further away from the soleus muscle as in the case of the ligamentum patellae.

Vibration of the contralateral tendoachilles produced no change in the H-reflex amplitude.

III Effects of thermoreceptors

In this section the effect of temperature change has been determined on the MSR excitability in healthy young subjects. The skin cold receptors were stimulated by pain relieving skin spray. It is a halogenated hydrocarbon consisting of trichloromonofluoromethane and dichloradifluoromethane, the evaporation of which causes the feeling of intense cold. The skin temperature over the affected areas was monitored in most experiments and was about $30^{o}C$ or just below at the start of the experiment and fell rapidly to a very much lower temperature, sometimes as low as 3 degrees centigrade. After the spray the temperature returned to its normal value within one to one and a half minutes. Forty nine subjects in all were tested out of which 22 were female. Their ages ranged from 18 to 35 years. Various degrees of reflex inhibition were noticed when the coolant was applied to different dermatomes.



The H-reflex was evoked 1/sec and its amplitude plotted against time. The bar marks a period of cooling the sole of the foot.

Fig. 17 Cooling the skin of the sole of the foot resulted in reflex inhibition with a little habituation at the end of the period of cooling.

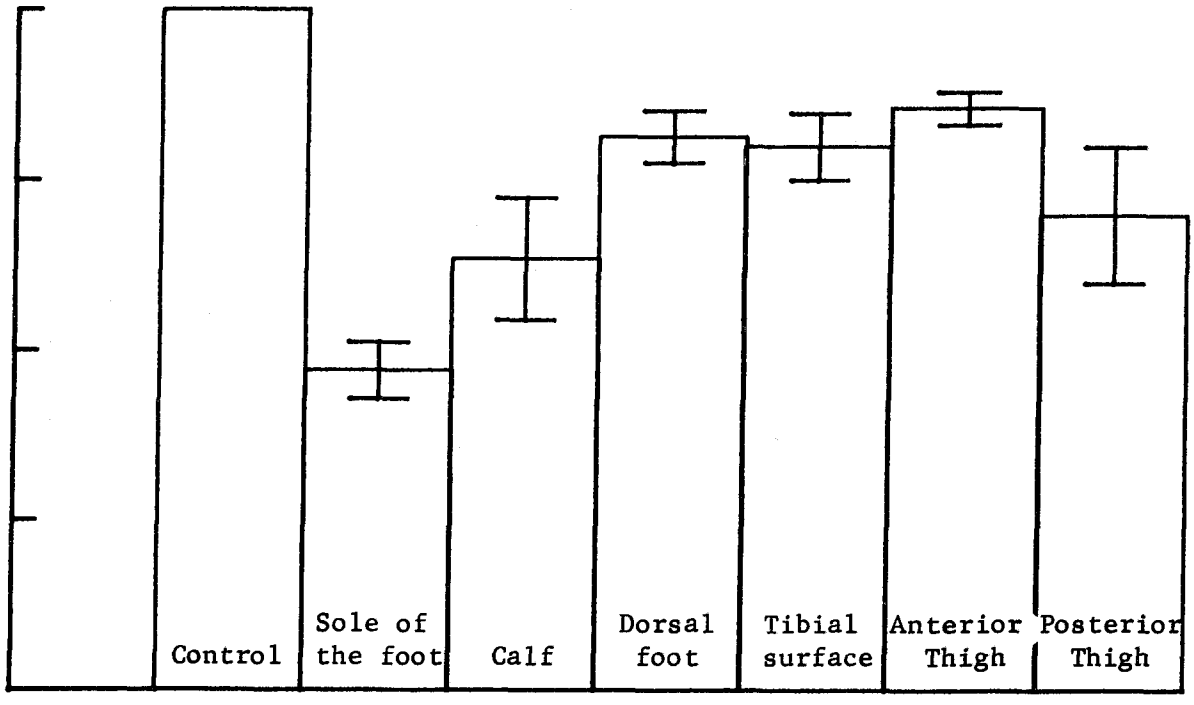


Fig. 18 (A) The sole of the foot and the calf skin are the areas effective when cooled (A). Suprimposed traces (B) showed clearly the reflex inhibition with no effect on the M-response.

A. Extensor skin dermatomes

1. Sole of the foot:- "L_5 S_1" dermatome

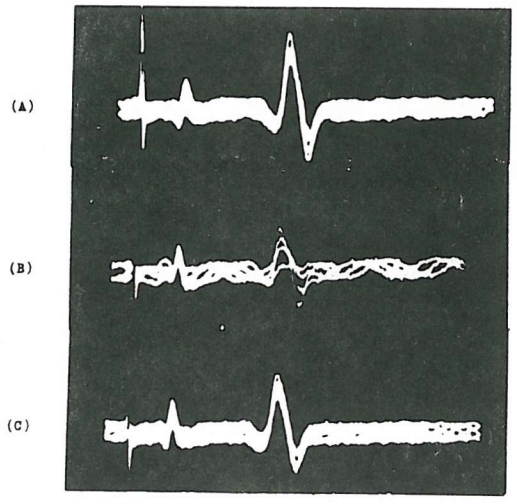
This was the area most affected by application of the coolant (Fig.19). A result of cooling the sole of the foot is shown in Fig.17 . In this curve the magnitude of the H-reflex is plotted against the time. The spread of the dots gives some idea of the variability of the H-reflex and it is clearly seen that during cooling there is a reduction in the H-reflex amplitude. The reflex habituates a little at the end of the period of cooling. This was followed by return of the reflex to former value when cooling ceased. Above the graph are three sample traces before, during and after cooling sole of the foot and it is clearly seen that the H-reflex does diminish in size whereas the minimal M-response which was present in this case stays exactly the same indicating that there has been no change in the stimulus volley.

The test reflex ranged from 24 to 87% of control in all subjects tested with a mean value of 61%.

2. Calf area:- "$L_{4,5}$ S_2" dermatome

When the cooling was applied to the skin overlying the calf muscle, the test reflex was inhibited in most subjects tested. Twenty two volunteers were studied of which four were female. The degree of inhibition was smaller than that from the sole of the foot and it can be seen from Fig.17 that the test reflex varied greatly during cooling but it was inhibited in individual sweeps. The reflex returned abruptly to the control value after cooling ceased. No changes were seen in the M-response amplitude or

Fig. 18 (B)



.Suprimposed H-reflexes(A)before(B)during (C)after superficial cooling of the calf skin.

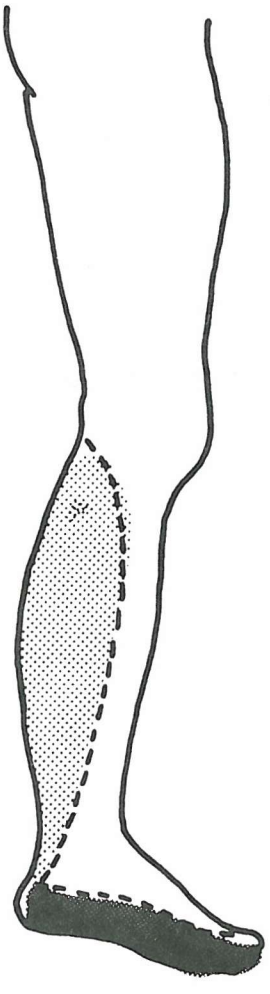


Fig. 19 Skin areas in which stimulation inhibits the soleus H-reflex

latency. Fig. 17 shows that the test reflex was inhibited abruptly when cooling was applied. However with continuous stimulation the reflex habituates towards the end and returns to normal value after cooling ceased. In all subjects the test reflex ranged from 19 to 120% with a mean value of 80% of the control (Table 2).

B. Flexor skin dermatomes

1. Skin overlying anterior tibial muscles "L_5" dermatome

The skin overlying the tibialis anterior is supplied by other roots (L_5) from that of the calf and sole of the foot. When this dermatome was cooled the test reflex did not show great changes. It was reduced to a mean value of 89% of the control (Table 2). In four subjects out of eleven tested the reflex was slightly facilitated above normal value and ranged from 107 to 121% of the control.

2. Dorsal surface of the foot:- "L_5 S_1" dermatome

Moderate inhibition of the reflex was seen which ranged from 30 to 102% with a mean value of 78% of the control (Table 2).

3. Posterior surface of the thigh:- "$L_{2,3}$ S_2" dermatome

Cooling the hamstrings dermatomes did not cause significant changes (Table 2). The test reflex was slightly inhibited but with large fluctuation in amplitude which clouded the effect of the cooling.

Fig. 18 showed the effect of superficial cooling of various dermatomes tested in one young normal subject.

Summing up the results Fig. 19 showed those areas of skin which when stimulated by scrubbing and cooling, produced an inhibition of the H-reflex. It is clearly shown that inhibition was

most pronounced by scrubbing $L_{4,5}$ $S_{1,2}$ dermatomes. The soleus muscle is known to be supplied by L_5 S_1 nerve roots. The inhibition therefore appears to be organised according to the spinal segmental innervation.

DEEP COOLING AND H-REFLEX

Further study of the effect of cooling on the MSR excitability was tested by cooling of the skin and the underlying structures. This was achieved by cooling the area under study for 30 to 45 minutes by application of ice bags. The parameters measured were that of reflex amplitude, shape, duration and latency. However MSR excitability was tested to see whether there is any change in the recovery of the MNP. To complete this study, recruitment and recovery curves were used whenever appropriate.

Cooling of the skin and underlying structure has been applied before by Knuttson et al 1969 who demonstrated a slow linear decrease in the subcutaneous and intramuscular temperature which fell about $5^{o}C$ in 20 minutes. This may change the firing behaviour of those deep neural structures e.g. muscle spindles and other receptors. On the other hand the inhibitory effect of the skin cold receptors will also operate and affect the results. The latter problem was partly overcome by quick rewarming of the skin, leaving the underlying structures cool.

These studies were applied to 48 subjects of which 16 were females. Their ages ranged from 18 to 36 years.

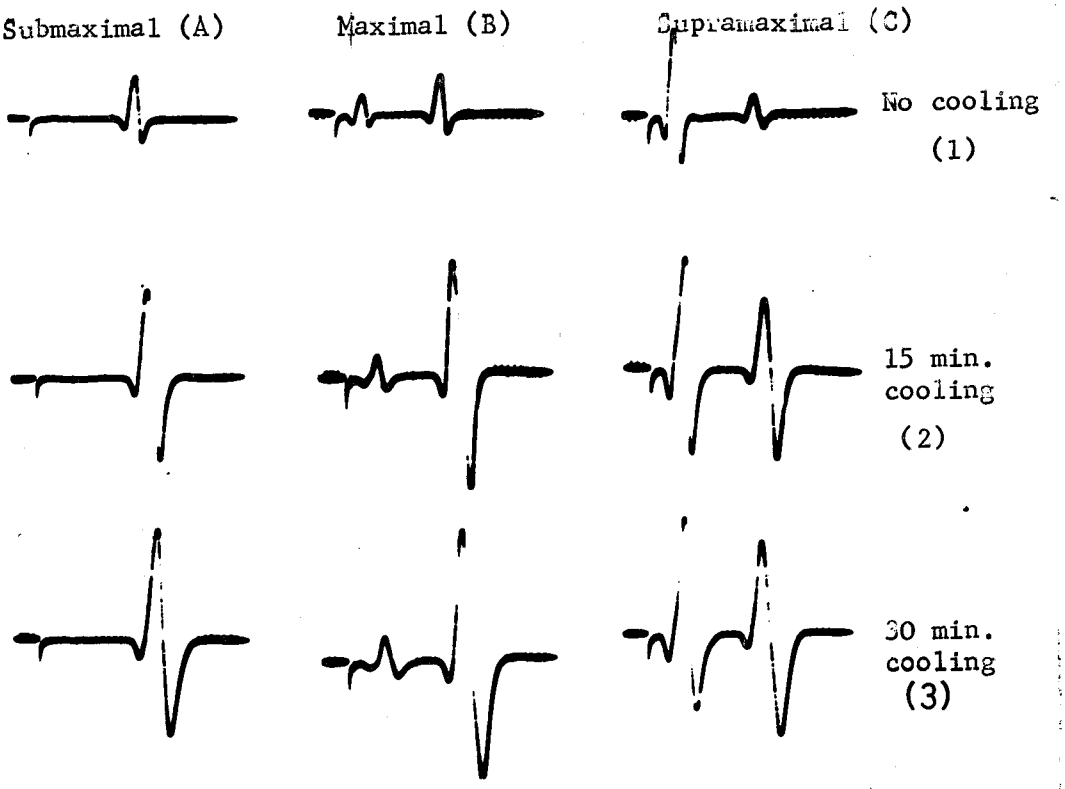
The effect of the deep cooling depends upon the site of the application and the muscle cooled. This will be explained below.

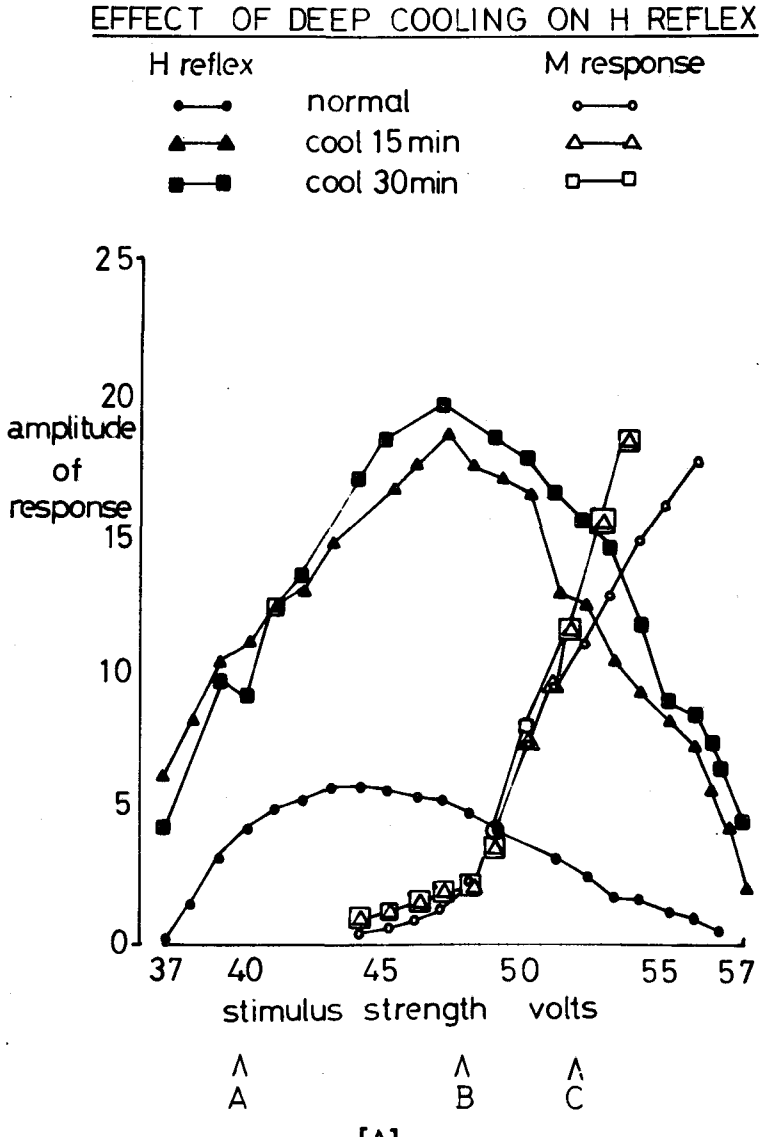
However cooling of the calf muscle, the group from which recording was made demonstrated characteristic features which need detailed explanation.

Calf muscle

A. Reflex characteristics

Amplitude: Cooling of the calf muscle for 15 mins. demonstrated significant facilitation of the reflex. Its amplitude ranged from 200 to 450% of the control (Fig.20). This was noticed to occur in response to various stimulus strengths (Fig.21). There was no change in the amplitude of the M-response which is shown in Fig.20 B and C. In this figure a sample of H-reflexes evoked with a stimulus strength subthreshold (A), threshold (B) and suprathreshold (C) to M-response were used as a control [1] before cooling was applied. When the calf muscle was cooled for 15 mins. the subthreshold H-reflex increased to 250% of the control, while the threshold one was 380% of the control [2]. With further cooling for 30 minutes, the test reflex was further facilitated to 310%, 415% and 550% of the control in the subthreshold, threshold and suprathreshold reflexes respectively. [3] There was no significant change in the M-response which indicates that there has been no changes in the stimulus volley. Mild facilitation was noticed in the supramaximal M-response. The reflex amplitude was stable and did not show large fluctuations. The facilitation increases with larger stimulus volleys. The findings were consistent in all subjects tested. However the degree of reflex facilitation varied considerably from one subject to another and no definite factors were seen to affect this.


Submaximal (A)
Maximal (B)
Supramaximal (C)
No cooling
(1)
15 min.
cooling
(2)
30 min.
cooling
(3)


EFFECT OF DEEP COOLING ON H REFLEX
H reflex
M response
normal
cool 15 min
cool 30min
25
20
amplitude
of
response
15
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5
0
37
40
45
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55
57
stimulus strength volts
A
A
B
C
[A]

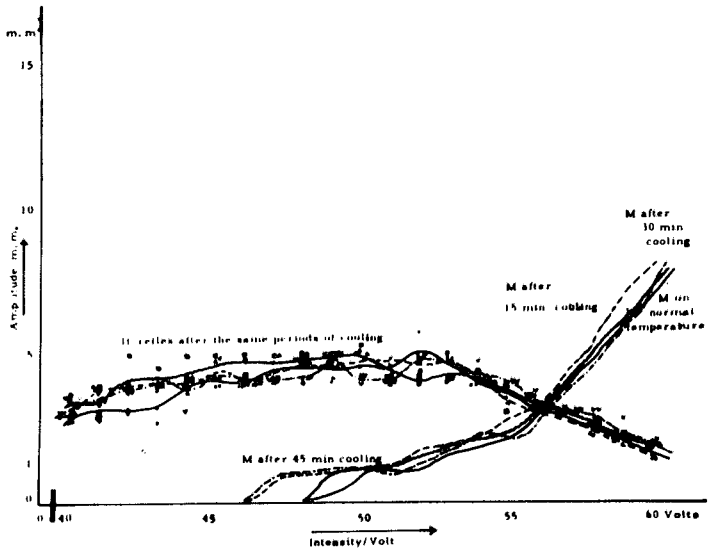

m. m
15
10
5
1
0
M after
10 min
cooling
M after
15 min cooling
M after 45 min cooling
40
45
50
55
60 Volts
Intensity/Volt

Fig. 21 (B)

Fig. 20 Cooling the calf muscle and its overylying skin for 30 minutes produces enormous facilitation of the test reflex to more than 300% of the control with no or little effect on the M-response.

Fig. 21 Recruitment curve before, 15 and 30 min. after cooling the calf muscle. (A), Contralateral cooling showed no effect (B).

Quick rewarming of the muscle produced fluctuation between further facilitation of the reflex and mild reduction in amplitude which lasted for about 5 to 7 minutes after which the test reflex returned to the normal value.

These findings were supported by measuring the fraction of the MNP fired by the H-reflex. Cooling of the calf muscle for 15 minutes enlarged the MNP fraction from 69 to 87% of the whole pool (a mean value of all subjects). Five subjects, all males, were tested in this study and all demonstrated larger fractions after cooling. The latter ranged from 81 to 93 with a mean value of 87% of the pool.

There was no change of the reflex when the contralateral calf muscle was cooled for 30 minutes.

Duration: The duration of the test reflex was larger after cooling of the calf (Fig. 20). The longer the cooling period the longer was the duration. The same goes for the M-response as well. It is important to note that duration change was noticed only with cooling of the calf muscle i.e. the muscle group from which recording was made. This increase in duration with cooling was consistent in all subjects tested and there was no significant difference between various subjects. However the responses duration returned to normal value after rewarming for 10 minutes. No other changes were noticed in the potential shape during cooling.

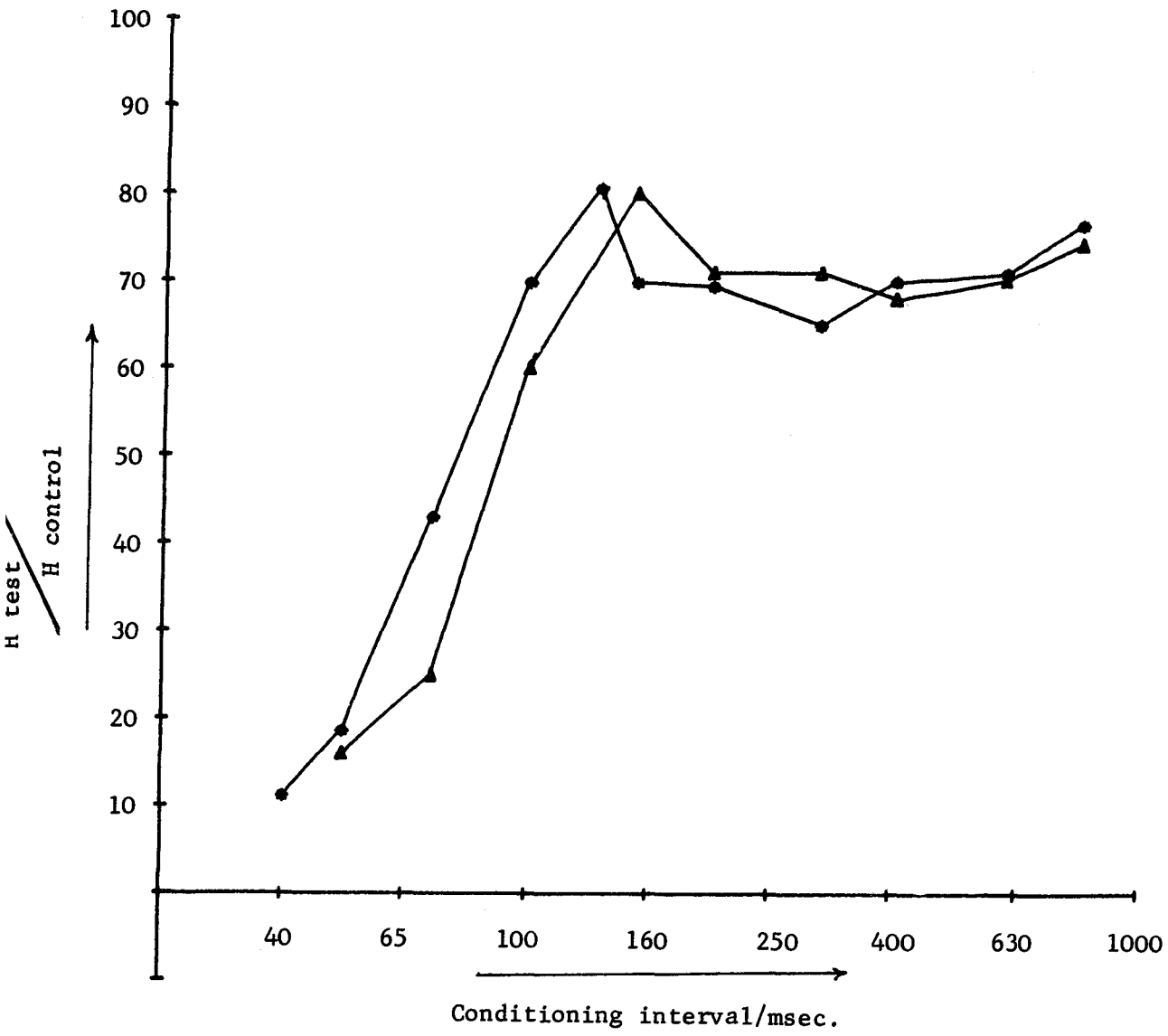


Fig. 22 Recovery curve showed mild changes after 30 min. cooling of the calf muscle. Recovery of the test reflex was 10 msec. later than the control (*) after 30 min. cooling (▲)

Latencies: The response latencies did not change. That may be because cooling was applied only to the muscle, and did not affect the conduction velocity of the peripheral nerves.

B. Recovery of the MNP

The only change noticed in the recovery curve was a slightly later recovery of the test reflex with a longer inhibition period. This is shown in Fig.22. The change in the recovery time varied from one subject to another and ranged from 5 to 20 msec. later than the pre-cooling recovery time.

OTHER AREAS

Cooling of the tibial, hamstrings or quadriceps groups of muscles produced similar results.

(a) Reflex shape

The most interesting was the change noticed in the reflex amplitude. Fig.23 shows the recruitment of the MNs with incremental stimuli after cooling of the tibial group (a), quadriceps group (b) and hamstrings muscle (c). In all cases, the H-reflexes evoked by a stimulus subthreshold to the M-response were facilitated. On the other hand supramaximal reflexes were either the same amplitude with cooling or even inhibited slightly. No changes were noticed in the reflex duration and the latency was the same even with intense cooling. The M-response stayed the same in amplitude and duration during cooling.

After rewarming, the test reflex continued to be facilitated for two to five minutes after which it started to return to normal value (Fig. 23).

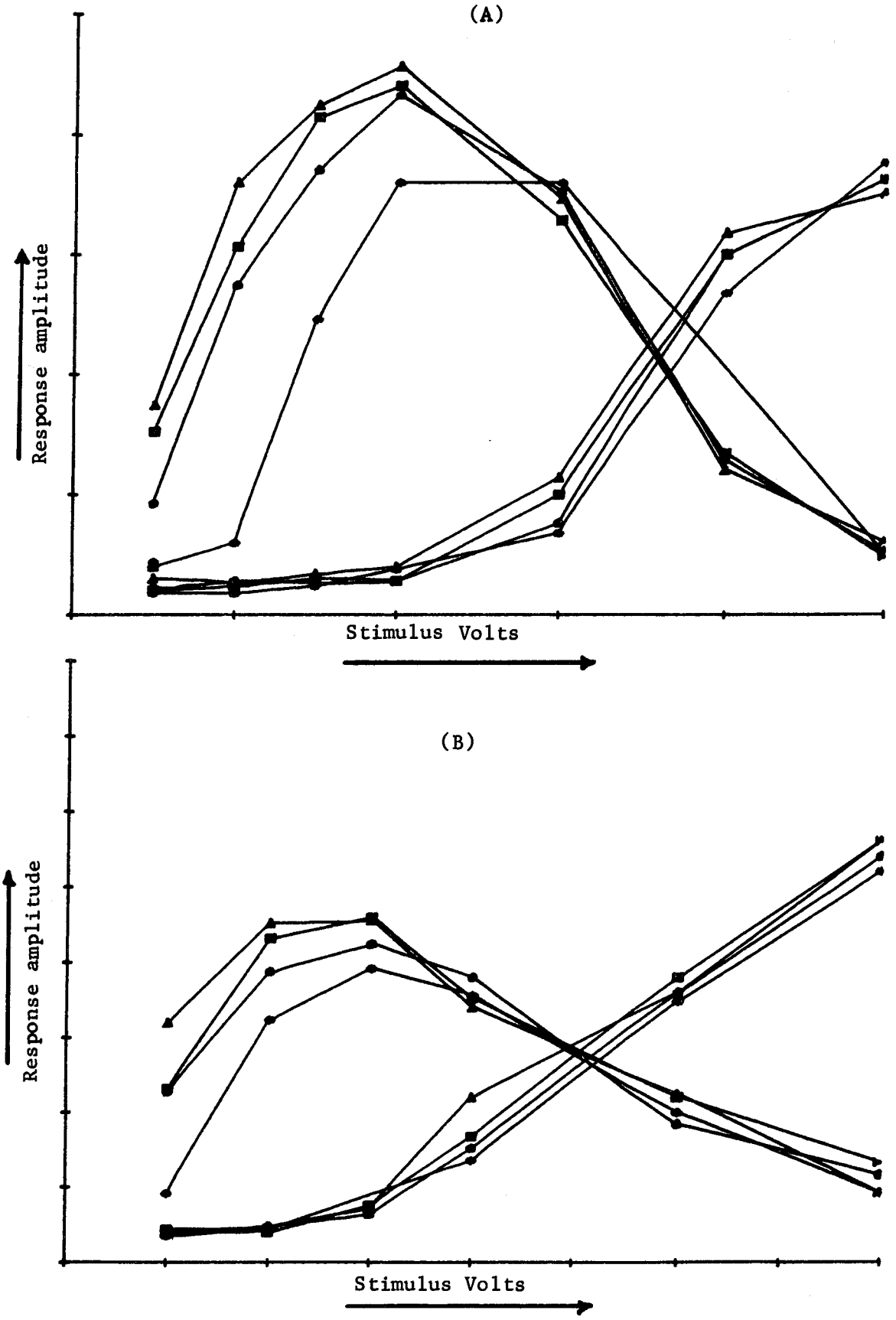
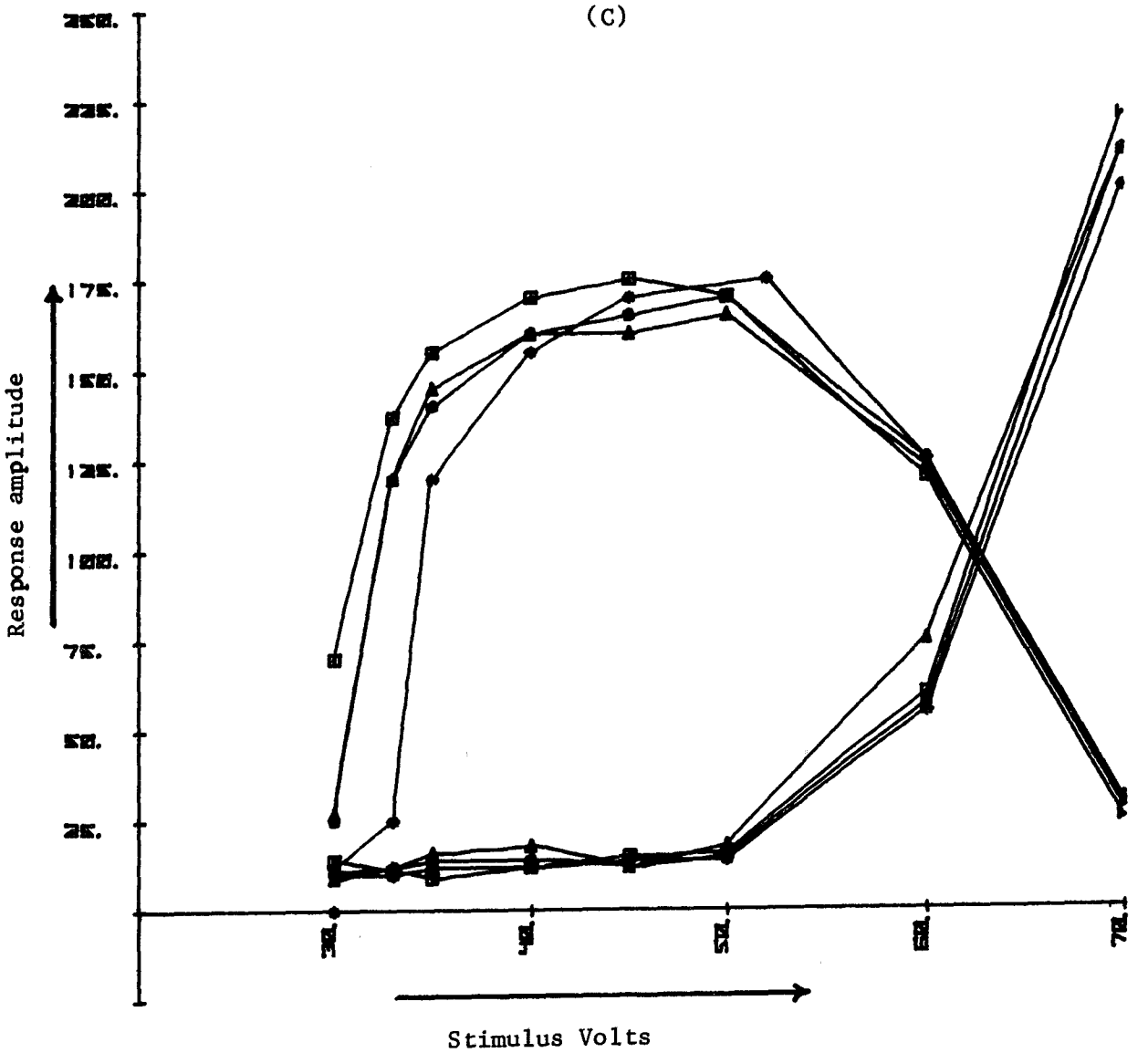


Fig. 23 Cooling the tibial group (A), quadriceps (B) and Hamstrings (C) produced mild facilitation of the rising limb of the recruitment curve with no effect on the M-response. The control reflex (*) showed after 15 min. (●), 30 min. (▲) cooling and continued for a while during rewarming of the skin (■).

(C)



(b) Recovery of the MNP

No changes were noticed in the recovery curve with cooling of muscle groups other than the calf muscle.

Discussion

The modulation of the MSR excitability by skin and muscle receptors and studied by natural stimuli signify the complexity of this modulation mechanism. The effect depends upon the receptor stimulated and subsequently the segmental or suprasegmental pathways involved. This modulation mechanism will be discussed in detail with each type of receptor stimulated.

I H-reflex inhibition by mechanoreceptor stimulation

On starting this work we expected to demonstrate a facilitation of the soleus MNs by stimulating the calf, in the same way as Hagbarth & co-workers (1963). Hagbarth (1952) in decerebrated cats and Hagbarth & Finer (1963) in man demonstrated a certain pattern of effect for the skin receptive field on MN excitability. They reported that each of the extensor muscle studied was inhibited from most parts of the limb but excited from a skin area localized over the muscle itself. Contrary to that, the flexor muscles were excited from all skin areas but inhibited from the skin overlying the muscle itself. These influences of skin on reflexes were explained by effects on either the @ - or ϒ -MNs (Eldred & Hagbarth 1954).

Our results were clearly contrary to Hagbarth's and some explanation is necessary. Hagbarth used noxious stimuli and showed excitation of the underlying soleus. The reflex response to any one stimulus was short lived and had a latency of 60-80 msec.

This response rapidly habituated to repetitive stimuli.

The experimental procedure applied here is very different and most important, these stimuli are not noxious. It is not possible to claim that the effects demonstrated here are segmental reflexes as the stimulus continued for up to 30 seconds and in that time any suprasegmental pathway could be recruited. However, the fact that the most effecive dermatomes are innervated by the same roots as the soleus muscle, that is $L_{4,5}$ $S_{1,2}$ the major effect possibly is segmental.

Many of Hagbarth's subjects were maintaining muscle contraction at the time of stimulation, ours were relaxed and remained relaxed. Maintained muscle activity involves a number of segmental mechanisms which would be quiescent in our subjects. Moreover Gassel (1970) reported that it was not possible to confirm Hagbarth's experimental conclusions in relaxed human subjects using electrical stimuli. However Gassel & Ott (1970, 1973) demonstrated two phases of mild facilitation of MSR's after a primary period of inhibition when the skin of the planter surface of the foot was stimulated electrically. They used the ankle jerk as a test reflex preceded by noxious stimuli. Stretch reflex of the quadriceps found to be facilitated by scratching the skin over the muscle but was without effect when other skin areas were stimulated (Clarke 1966). H-reflex inhibition by cutaneous stimulation of the small and great toe of the ipsilateral limb was demonstrated by Pierrot-Deseilligny's group (Castaigne et al 1972, Pierrot-Deseilligny et al 1973).

Some workers found that skin stimuli were without effect on the H-reflex (Magladery et al 1951, Isaacs et al 1968). However

Wirski (1973b) reported inhibition in the H-reflex by cutaneous stimulation of the skin.

It is interesting to note that the same effect i.e. H-reflex inhibition, was found either with stimulating mechanoreceptors or skin cold receptors (Sabbahi Awadalla & Sedgwick 1976). Rudomin et al (1972, 1975) demonstrated a control mechanism which affects information transmission from the Ia fibres to MNs and found a positive correlation between monosynaptic responses of a single MN and the information transmitted by stimulating skin nerves. The MSR variance reduced during cutaneous stimulation and they proposed that the control system works presynaptically.

The reflex inhibition is probably not only due to segmental mechanisms but also to supraspinal ones. The segmental reflex inhibition by cutaneous stimulation is probably mediated by large diameter as well as small diameter skin nerves exciting the inhibitory interneurones (Hultborn 1972, Hultborn et al (1972), Fedina et al 1972). Hultborn's group (1972) found in cats that Ia IPSP was increased by afferent volleys in low threshold cutaneous nerves. The convergence occurred on a common interneurone which exerted its effects on the MNs by pre-synaptic inhibition (Eccles 1963, see later). Eccles & Lundberg (1959) demonstrated the supraspinal control of these interneurones during the flexion reflex in decerebrate preparations.

The supraspinal mechanism which modulated the MN excitability by cutaneous stimulation was found to be similar to those of the LLR found in cats and monkey and probably in man (Shimamura et al 1964).

II H-reflex inhibition by cold-receptors stimulation

Skin cold receptors showed an inhibitory effect on H-reflex. This effect was more specific overlying the calf muscle and the sole of the foot. We found no literature which explains the effect of skin cold receptors on MSR's, but the fact that skin dermatomes, which inhibit the H-reflex significantly, were supplied by the same nerve roots to the muscle i.e. $L_{4,5}$ $S_{1,2}$ was of great interest. It has been reported by Douglas & Ritchie (1959) that the cold receptors and mechanoreceptors are represented in the same filament of nerve fibres, a finding which is not in accord with specific nerve energies. Some mechanoreceptors showed low frequency bursts of firing (5/sec) with cooling while with mild mechanical stimulation of the skin their discharge rates reached 50/sec. Sensation of touch and temperature could also be elicited from corneal stimulation by Lele & Weddell (1956) and confirmed later on by Bessou et al (1969). Their findings showed the similarities in coding mechanical and cold stimuli. This and other work shows that the law of specific nerve energies does not hold except for some fibres in particular circumstances.

Moreover Burton (1975) demonstrated in cats and monkeys that neurones responding to cutaneous cold receptors are distributed in laminae I, III, and VI of the spinal cord and that those types of neurones had a lower threshold for cooling than warming. He further confirmed the linked relationship between cooling and mechanoreceptors in terms of neurone discharge.

The effect of skin cold receptors on MSR excitability was

indirectly shown with rewarming of the skin after deep cooling of both skin and underlying structures. The H-reflex amplitude was larger which unmasked the inhibitory effect of the skin cold receptors on the MSR excitability.

It will be appropriate to postulate that the mechanism of reflex inhibition by skin cold receptors follows the same pathways and mechanism as that explained for mechanoreceptors stimulation.

III H-reflex facilitation by deep cooling

A further cooling of the skin and underlying structures showed an opposite result to that of skin cooling. Reflex facilitation was enormous and continued for a long time and it was inversely related to the degree of cooling (Sabbahi Awadalla & Sedgwick 1973). The relation between muscular and cutaneous temperature during skin cooling was the subject of number of studies by Wolf & Basmajian (1973), Lowdon et al (1975), Bugaj (1975). Lowdon & Moore (1975) reported a rapid decrease in intramuscular temperature of 15.9° C. in 5 mins. of skin cooling. However Wolf & Basmajian (1973) found that the deep muscles decreased in temperature 1.2 degrees for every 10°C of reduction of skin temperature. This was further supported by Mecomber & Herman (1971) on the soleus and gastrocnemius muscles. Moreover Knutsson & Mattsson (1969) demonstrated a slow and linear decrease in intramuscular temperature, usually by about 5°C in 20 mins.

This short review demonstrates that the intramuscular temperature in our experiments went down enough, after 30 mins. cooling, to a level which could affect the subcutaneous structures and their functions.

The results we demonstrated were different from those of Knutsson & Mattsson (1969), as the latter showed primary facilitation followed by fluctuation of the H-reflex amplitude. In our experiments the facilitation was enormous and reached to more than 300% of the control, and moreover it continued for 30 minutes or more. This was demonstrated at all reflex amplitudes using the recruitment curves. It is probable that the discrepencies Knutsson et al (1969) found in their results can be attributed to the method of reflex measurement, as they used one amplitude index which may be highly variable. This was the same with Urbscheit et al (1970, 1971), who used one amplitude index of the H-reflex for measuring the effect of deep cooling and reported increase in the H-reflex facilitation during handgrip after cooling.

By scanning the components of the stretch reflex and the other peripheral and central factors which can influence the MN excitability by cooling, one has to remember the following:

1. Skin cold receptors and their inhibitory effect on the MN discharge.
2. Muscle spindle firing changes (Eldred et al 1960, Lippold et al 1960).
3. Muscle fibres visco-elastic properties.
4. Peripheral nerve fibres, intramuscular nerve terminals, with large and small diameters and their sensitivity to cooling.
5. Segmental spinal effect of skin and/or muscle cooling on MN discharge.
6. Different sensitivity of MN types to cooling influenced by peripheral nerve activity.

7. Supraspinal effect of skin and/or muscle cooling on MN discharge.

The H-reflex facilitation by deep cooling in this work is not due to muscle spindle firing changes (Eldred et al 1960, Lippold et al 1960). The ankle jerk, which does depend on the excitability state of the muscle spindle (Herman 1969) either did not alter (Urbscheit et al 1970), was reduced (Knutsson et al 1969a, Knutsson 1970, Mecomber & Herman 1971), or even abolished (Hartviksen 1962, Miglietta 1964) by local cooling. This was attributed to a decrease in the excitability of the fusimotor system. Furthermore the H-reflex bypasses the muscle spindle. Additionally changes in the reflex behaviour occur while the intramuscular temperature was not changed much i.e. after a short period of cooling (Mecomber et al 1971, our experimental observations).

The H-reflex facilitation is not also due to visco-elastic properties changes of the muscle fibres as the facilitation was pronounced only in the reflex amplitude without the muscle AP i.e. M-response, which was even reduced as Knutsson demonstrated (1970). However the strength of phasic stretch reflex was lowered after 30 minutes cooling with cold water in normal subjects (Petajan & Watts 1962). This was even shown in spastic cases (Petajan et al 1962, Knutsson 1970, Miglietta 1962, Boes 1962).

It is probable that the intramuscular nerve terminals are affected by cooling. Herman & Byck (1964) and Douglas & Malcolm 1955 showed that cooling caused a differential block of nerve with inhibition of small γ-fibres when the @-fibres were conducting

impulses normally. This may be the main reason of ATR reduction by cooling as well as the differential response of spastic cases to cooling and cryotherapy (Urbscheit et al 1971, Knutsson et al 1969b).

It is more likely that the mechanism of H-reflex facilitation by skin and muscle cooling was mainly due to the increase in the MNs discharge after getting them free from the inhibitory effect of the skin cold receptors. As we have seen before not only the skin cold receptors inhibit the H-reflex but also the mechanoreceptors, both of which are represented in the same filament of nerve fibres (Douglas & Ritchie 1959). By cooling the skin and muscle for 15 to 30 minutes skin nerves are anaesthetized including the cutaneous cold receptors which leads to a reduction of inhibition of the MNP, thus permitting greater output. Indeed when the muscle temperature is decreased only a few degrees, a marked reduction of skin temperature has already occurred which is sufficient to suppress afferent discharges from cutaneous receptors. Supporting evidence for this has been reported by Hertviksen (1962) who have shown that a rapid reduction of reflex activity occurs at a time when no change can be noted in intramuscular temperature. This effect is probably mediated segmentally and/or supraspinally through the long loop reflex (Shimamura et al 1964).

The H-reflex facilitation was seen when cold was applied on the skin overlying the calf muscle, tibialis anterior, hamstrings and quadriceps muscles with the most prominent effect on calf cooling. This indicates the degree of convergence of skin nerves of different dermatomes on the soleus-gastrocnemius MNs at segmental

level. One could argue that supraspinal pathways could be the link of this convergence. This is a possible assumption; however the findings with mechanoreceptors stimulation and its inhibition for the H-reflex supports a segmental mechanism more than supraspinal one. Mild inhibition of the H-reflex was noticed with mechanoreceptors stimulation of skin areas other than the calf & sole of the foot. This further supports the cutaneous receptors effect as the cause of H-reflex facilitation by disinhibition during cooling.

The supramaximal H-reflexes did not show such facilitation as submaximal ones. Cooling other areas than the calf skin showed no significant changes such as would support a supraspinal mechanism. This could be attributed to the inhibitory effect of the secondary fibres which are probably recruited with supramaximal stimuli. (Magladery et al 1951) or the excitation of the smaller fibres which act polysynaptically (Mayer et al 1965). Inhibition of the H-reflex by these pathways is probably more powerful than the counteracting disinhibition of skin receptors.

When the skin was quickly rewarmed, the reflex fluctuated but still showed enormous facilitation for over 5 mins. This long term facilitation is interesting and denotes a continuous facilitation of the MN discharge. It is difficult to ascribe these findings to any segmental mechanism, as there is no known spinal mechanism which could have such a long term effect. However, one could argue about the irregular discharge of the cold receptors after rewarming; this may be an important factor in the long term facilitation.

These results further support the previous assumption in discounting Hagbarth's findings for the flexor and extensor skin areas

and their effect on MN discharges. Inhibition was demonstrated for the H-reflex by skin cooling of different skin areas. The same findings were demonstrated with mechanoreceptors stimulation and moreover H-reflex facilitation was found when cold receptors of different skin areas were anaesthetized by a deep long period of cooling. Local cooling showed suppression of the delta wave AP in the saphenous nerve completely at 8.6°C. (Herman & Byck 1964). It has been shown by Burton (1975) in cats and monkeys by single neurone recordings, that in many neurones the discharge rates declined at extremely cold temperatures.

The effect of deep cooling on MSR excitability is a complex mechanism which is difficult to interpret by one factor. However its effect of increasing MN discharge is unlikely to be a direct mechanism as Urbscheit et al (1970) thought. An intermediary pathway could be involved which could keep the MN excitability at a higher level for some time after rewarming.

IV Mechanisms of H-reflex inhibition by vibration

Vibration inhibits the H-reflex as shown by previous workers (Hagbarth & Eklund 1966, Hagbarth 1973). Vibration is a well-known selective stimulus to the Ia fibres as shown by Bianconi et al (1963). This inhibition could be explained by one of two mechanisms, that is

the "busy line" and presynaptic inhibition. Afferent "Busy line" (Hagbarth 1973) was suggested to be the cause of this inhibition especially when the tendon jerks and phasic stretch reflexes were suppressed during muscle vibration (De Grail et al 1966, Hagbarth et al 1966, Lance et al 1966, 1973, Rushworth et al 1966, Delwaide 1971, 1973). The main reason for this suppression may well be that the primary endings are so engaged by the vibratory stimulus that they are not able to respond efficiently to a transient superimposed muscle stretch or more impulses in the Ia's. In multiunit recordings from human muscle nerves, the afferent response to a tendon tap, which normally appears as a distinct shower of impulses, stands out vaguely against the barrage of impulses produced by vibration (Hagbarth 1973).

It seems probable that the afferent "busy line" phenomenon also contributes to the reflex suppression, but its main cause may be attributed to the central mechanism of presynaptic inhibition (Lance et al 1968, Gillies et al 1969, Yamanaka 1964, Delwaide 1971, 1973). The on-going depolarization of the large afferent fibres, first noticed by Matthews (1934) and Barron & Matthews (1935, 1938) and which cause the dorsal root potentials (Howland et al 1955, Koketsu 1956, Mendell & Wall 1964, Wall 1958, 1962, Eccles et al 1962a, b) and the augmentation of this depolarization by afferent volleys (Mendell & Wall 1964, Wall 1964) caused by vibration, may block the central nerve terminals and decrease the effectiveness of any incoming signals in the same fibres. Presynaptic control could mean controlling "the depth of penetration of impulses into the terminal arborization and therefore the distribution of the arriv-

ing impulses over the dendrites and cell bodies of the receiving cells" (Melzack & Wall 1962). The control of arriving impulses is considered to be necessary for organizing the input to the neurones that are the first step in onward transmission and this is controlled by T-cells - intrinsic neurones of the substantia gelatinosa and are connected to supraspinal centres. It is known that there are descending fibres from the brain that could induce presynaptic inhibition of primary afferent fibres, both at segmental level and at posterior column nuclei level and also descending fibres, running to interneurones with both facilitatory and inhibitory effects (Nathan 1976). Tendon vibration reflex in cats fires cells of reticular formation of the brain stem (Gillies et al 1971) which inhibit the α-MNs.

Nathan (1976) wrote critically about the function of the T-cells mentioning that "This neurone is supposed to be firing at most times at a slow rate and this rate of firing is associated with discriminatory sensations". Moreover the input to the spinal cord consists of two opposing kinds - an input in non-myelinated and small delta fibres that has the effect of inhibiting neurones of the substantia gelatinosa and an input in larger myelinated fibres that has the effect of exciting these neurones. According to the Gate-Control theory of pain (Melzack & Wall 1965, Melzack 1973), the neurones of the substantia gelatinosa are thought to induce presynaptic inhibition of posterior root fibres and so prevent or reduce onward transmission of impulses coming from the periphery. It is a fact now that the posterior root terminals can be subjected to presynaptic inhibition; this occurs at every segment and at the ending

of the large afferent fibres at the posterior column nuclei. That was shown by Andersen et al (1962, 1964, 1968) Schmidt (1965) and Jabbur & Banna (1968, 1970).

However, the histological findings have not always been found to support the presynaptic inhibition. In spite of the findings of axo-axonic contacts in the cuneate nucleus by Walberg (1965) and his final conclusion in support of the presynaptic inhibition, Szentagothai (1968) showed that all of these axo-axonic contacts were the wrong way round for presynaptic control of the afferent terminals.

It seems that there is strong supporting evidence for the presynaptic inhibition hypothesis from the physiological studies. However much work is needed to confirm this hypothesis histologically in order to be able to work out the deficiencies affecting the nervous system due to malfunction of this presynaptic inhibition.

It is appropriate to ascribe the inhibition in the H-reflex by vibration, to presynaptic inhibition (Gillies et al 1969). Moreover the fact that the H-reflex was inhibited by cutaneous stimulation fits well with this hypothesis. According to this hypothesis it is expected that stimulation of these cutaneous receptors would evoke the first positive wave of Mendell & Wall (1964), in the dorsal root, which indicates hyperpolarization of the membrane of the afferent fibres and produces facilitation and then it counteracts the effects of presynaptic inhibition. When the test volley of the H-reflex arrives in the Ia fibres, the increase in the membrane hyperpolarization and consequently the presynaptic

inhibition suppresses the volley from penetrating to the @-MNs.

The facilitation of the H-reflex after cessation of the vibrations is a peculiar finding. TVR continues for a while after cessation of vibration (Hagbarth 1973, Arcangel et al 1971). It seems probable that this reflex facilitation is mainly due to release of the monosynaptic pathways from the supraspinal inhibitory mechanism after cessation of the vibration. H-reflex inhibition by vibration was found to be less effective in patients with UMNL (Ashby et al 1974).

It is attractive that our results fit well with the current hypotheses. However these hypotheses have to await for histological support to locate all its different elements. This does not exclude the more confirmed findings of Renshaw cell inhibition (Haase et al 1975) or the post-synaptic inhibition (Coombs et al 1955, Mountcastle 1974, pg. 199, 200).

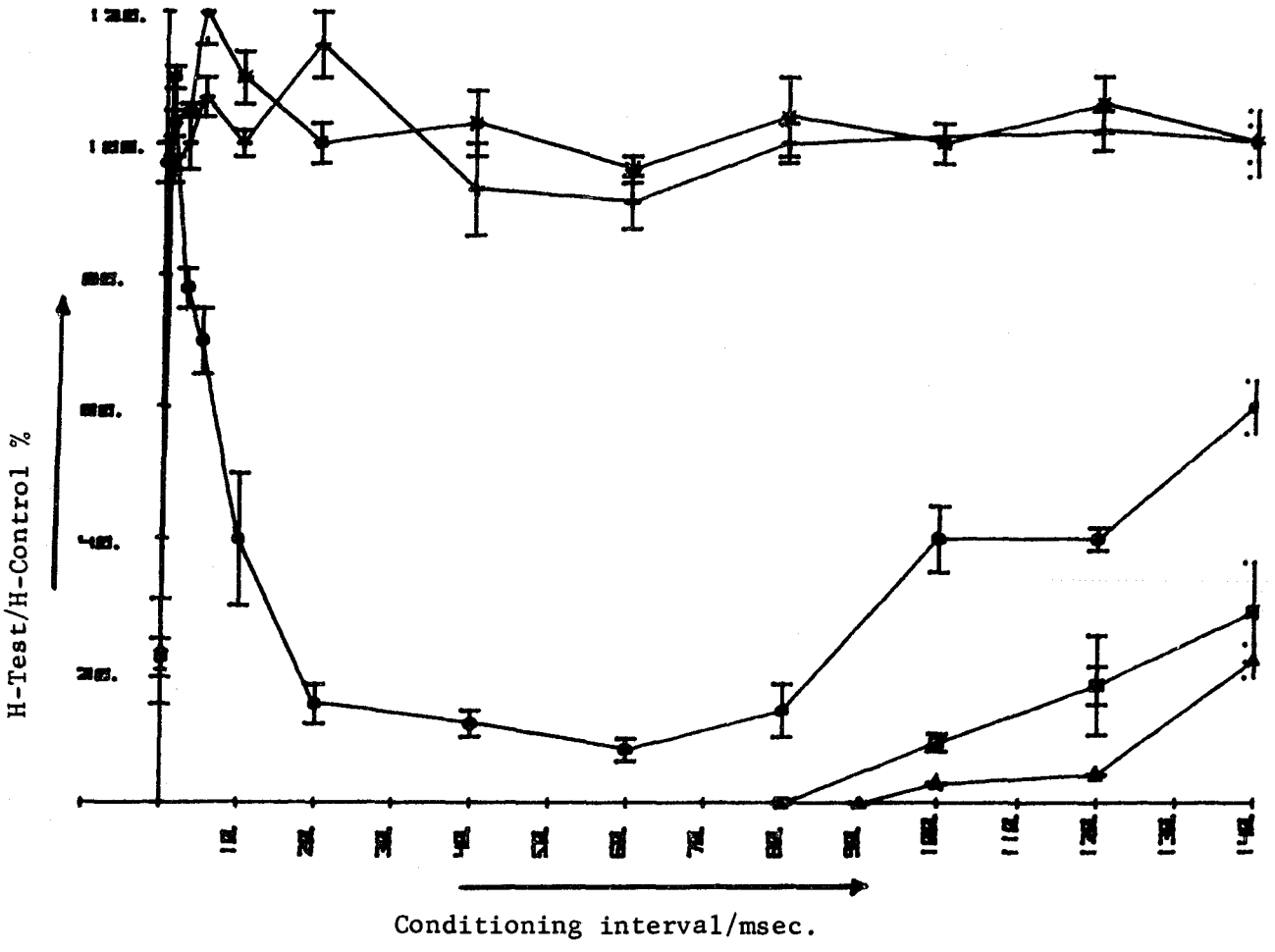


Fig. 24 Recovery curves with a conditional single shock, subliminal to skin sensation (*), subthreshold to H-reflex (+), evoking 50% of the control reflex (●), identical (■) and supramaximal to test shock (▲). The test reflex showed apparent inhibition with higher pulses

CHAPTER III

STUDY OF THE RECOVERY OF THE MNP

As we have seen in the previous chapter, there are a number of peripheral factors modulating the monosynaptic excitability. At the same time, there are a number of central factors which modulate this excitability. In addition the excitation of the spinobulbospinal mechanism may have have a significant effect (Gassel 1970). An effect of the recurrent discharge of the muscle spindle by the first pulse cannot be excluded. On the other hand refractoriness of the MNs due to transmitter depletion by the conditioning pulse was one of the assumptions forwarded by Taborikova et al (1969). This hypothesis was tested by changing the conditioning shock either in intensity, or in frequency. The test reflex showed the following changes:

I MNP recovery after a preceding variable single pulse

In this study 10 normal subjects with ages ranging from 19 to to 29 years were tested and the results are summarized in Table 7 . Fig. 24 showed the recovery curve of the H-reflex when conditioned by a variable single shock.

1. Conditioning with stimulus intensity which causes no sensation showed no effect on the test reflex. Conditioning pulses ranged from 5-15 volts and were subthreshold for an H-reflex and for skin sensory fibres beneath the electrodes.
2. Conditioning with a stimulus intensity which evokes no potentials but reached the threshold level for sensation showed significant changes in the test reflex.

These are shown in Table 7 and are explained in the following:

(a) Facilitation period

The test reflex showed a varying amplitude from one subject to another. It varied from 95 to 200% of the control with a mean value of 126%. In five subjects the test reflex was close to the control value. In the other five subjects it showed a higher value. This period lasts for the first 10 msec. in most subjects, while in others it extends up to 40 msec. after the conditioning shock.

Table 7 The recovery time of the H-reflex when conditioned by a single pulse of variable intensity

Subject	Age	$S_1 \ll S_2$ * MSEC.	$S_1 < S_2$ ǂ MSEC.	$S_1 = S_2$ MSEC.	$S_1 > S_2$ ǂǂ MSEC.
MS	29	100	80	80	100
IW	26	60	40	60	60
TL	22	80	80	80	80
MC	24	100	40	80	80
RW	24	-	80	60	80
GS	21	-	100	100	80
SA	23	60	60	80	60
EB	21	-	30	30	40
AB	22	100	100	100	100
CS	17	-	30	30	30

* $S_1 \ll S_2$ = H-reflex conditioned by a stimulus intensity of low strength to evoke no potentials but above the threshold of sensation.

ǂ $S_1 < S_2$ Conditioning by a stimulus strength which evoked 50% H-reflex of the control.

ǂǂ $S_1 > S_2$ Conditioning by supramaximal pulse.

(b) Inhibition period

No significant changes were noticed on the test reflex. In those cases where inhibition did occur the test reflex ranged from 40% to 90% of the control. This inhibition period lasts from 10 to 80 msec. after which the test reflex starts to recover again. In two subjects, the inhibition period lasts longer i.e. up to 100 msec. In four subjects the test reflex did not show any inhibition and was equal to the control value.

(c) Recovery

Following the mild inhibition, the test reflex started to recover gradually. This occurred 60 to 100 msec. after the conditioning pulse. Six subjects showed a consistent recovery at this period. By the end of this recovery time, the test reflex returns to its control value.

3. Conditioning with a stimulus intensity which evokes a reflex equal to 50% of the unconditioned test showed the following:

(a) Facilitation Period

The test reflex did not show an actual facilitation above the control value. It ranged from 85 to 100% of the control in nine subjects out of ten. In one subject it was facilitated and reached 140% of the control. This period lasts for the first 20 msec., after the conditioning pulse, at the end of which the test reflex starts to pass through the following inhibition period.

(b) Inhibition period

With further increase of the conditioning interval the test reflex showed significant inhibition in all subjects tested. The test reflex was largely inhibited and showed a very small deflection ranging from 5 to 15% of the control in most subjects. This inhibition lasted for 30 to 80 msec. in 8 out of 10 subjects. In the other two subjects it lasted longer i.e. up to 100 msec.

(c) Recovery

By the end of the inhibition period the test reflex starts to recover gradually. This was 30 to 100 msec. after the conditioning shock (Table 7). It recovered faster than those conditioned by identical pulses (Fig.24).

4. Conditioning with identical stimuli (standard recovery) showed the following changes in the test reflex:

(a) Facilitation period

The test reflex was apparent for the first 3 to 20 msec. of the time course with variable reflex amplitude from one subject to another. It ranged from 95 to 125% of the control. However it was not always possible to record the test reflex in this period, because of the interference from the conditioning reflex and from the M-response resulting from summation of the two pulses.

(b) Inhibition period

The test reflex decayed quickly from its maximum value, in the facilitation period, to start the primary inhibition period after 20 msec. from the conditioning stimulus. It continues to be inhibited for up to 60 or even 100 msec. after the first pulse.

The test reflex showed complete suppression in this period.

(c) Recovery

With further increase in the conditioning interval, the test reflex starts to recover gradually after the inhibition period. The recovery time varied considerably from one subject to another and ranged from 30 to 100 msec. (Table 7). Four out of ten showed a reflex recovery after 80 msec. In two subjects it recovered after 60 msec., while in the other two subjects the test reflex recovers earlier i.e. at 30 msec. In two subjects the test reflex recovers after a longer time of inhibition i.e. 100 msec.

The reflex recovery was slower than that conditioned by a smaller stimulus strength.

5. Conditioning with supramaximal pulses showed the following:

(a) Facilitation period

The test reflex was completely suppressed from the beginning of the time course so that this period no longer existed.

(b) Inhibition period

The test reflex inhibition continued for the first 30 to 60 msec. or even 100 msec. after the conditioning pulse.

(c) Recovery

The recovery time varied again, in this set of experiments and ranged between 30 and 100 msec. In four subjects out of 10 it recovered at 80 msec. In two subjects it recovered after 60 msec. while in the other two subjects the recovery time was earlier, i.e. 30 and 40 msec. In two other subjects the recovery time was later, after 100 msec.

It is important to note that the subjects who showed earlier recovery with identical pulse conditioning, exhibited early recovery when the test reflex was conditioned by low stimulus strength. The case was the same with subjects showing late recovery time. The test reflex recovered faster than that with identical conditioning, in 6 out of 10 subjects. In three subjects it was slower in recovery while in the last one it was equal (identical and supramaximal conditioning recovery).

II MNP recovery after a preceding pulse train of variable intensity

A preliminary study was carried out to choose the most reliable train of pulses which caused maximum facilitation. This study consisted of the evaluation of the reflex amplitude when evoked by repetitive stimuli of the posterior tibial nerve. The stimulus intensity and duration were uniform over the train. This study was done on 14 young subjects. The result showed that with repetitive stimulation the test reflex facilitated gradually up to a maximum with 3 to 7 successive pulses i.e. 1000 PPs for 3 to 7 msec. (Fig.25) giving a test reflex of 125 to 150% of the control. With further increase in the stimulation period it either continued to be facilitated up to 20 msec. of repetitive stimulation, or slightly diminished to return to the control value.

According to this study a conditioning train for 5 msec. of 1000 PPs frequency was applied (5 pulses) and the recovery of the MNP using variable intensity of this burst is shown in Fig. 26. The recovery cycle of the reflex using this method was investigated in 9 young subjects and the results are summarized in the following:

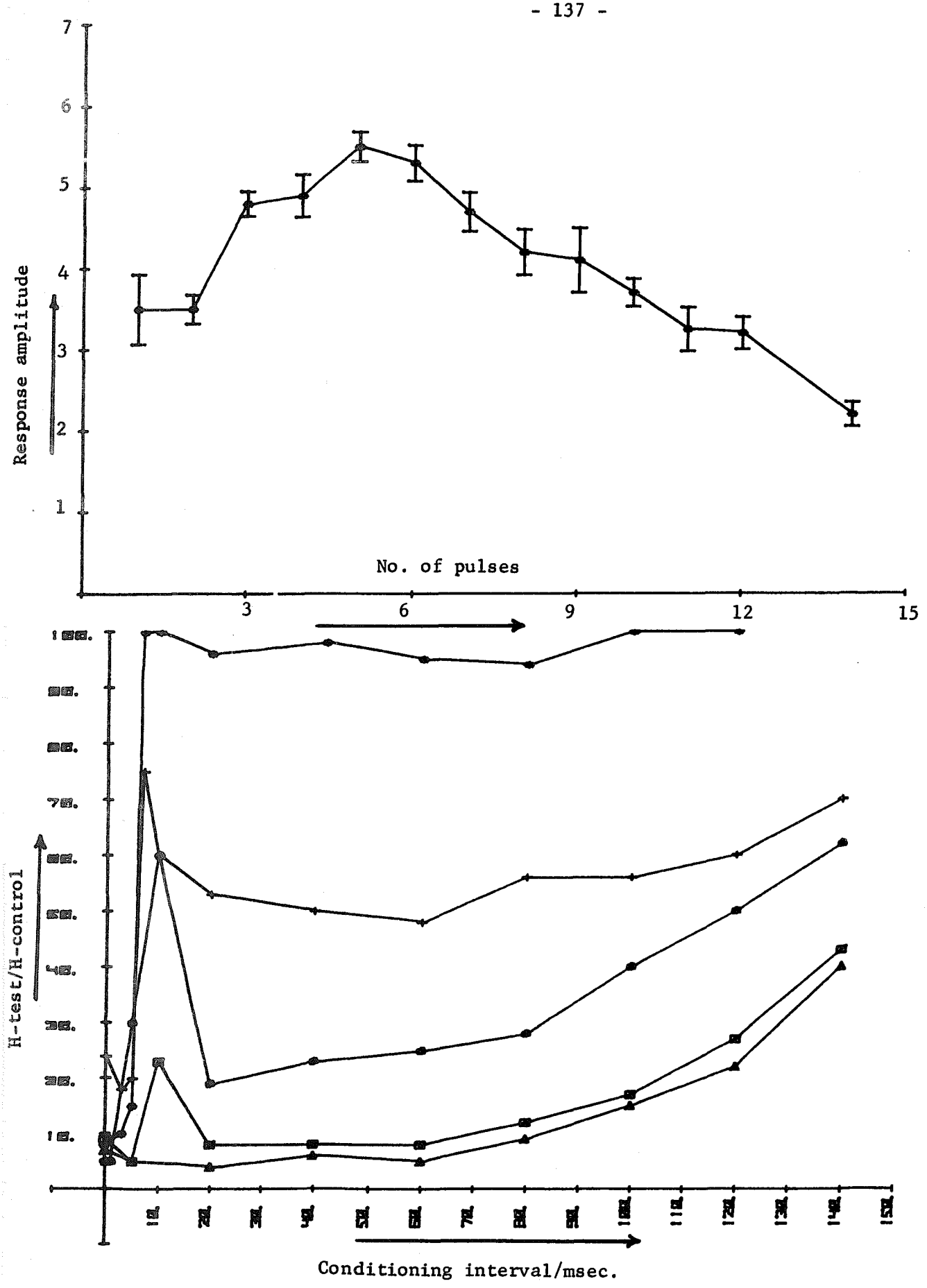

Response amplitude
7
6
5
4
3
2
1
No. of pulses
3
6
9
12
15
H-test/H-control
Conditioning interval/msec.

Fig. 25 Repetitive stimulation (1000 PPS for 5 msec.) resulted in facilitation of the reflex amplitude and was maximum with 5 or 6 pulses. With higher stimulation frequency the reflex amplitude dwindled to the control (Mean $\pm$ SD).

Fig. 26 Recovery curves with a conditioning train of pulses subthreshold to skin sensation (*), subthreshold to H-reflex (+), evoke 50% of the control reflex (●), identical (■) or supramaximal (▲) to the test shock. The inhibition period showed gradual increase with higher pulses

1. No changes were noticed in the test reflex when the train of pulses was lower than the threshold of sensation.
2. Conditioning with a stimulus intensity which evoked no potentials which are above the threshold level of sensation showed the following changes:

(a) Facilitation period

With incrementing interstimulus interval the test reflex showed facilitation above the control value. It ranged from 110 to 175% of the control. This was consistent in seven subjects out of nine and continued for the first 20 msec. In the other two subjects the test reflex showed no changes in the amplitude. By the end of this period the reflex returned to the control value.

(b) Inhibition period

No changes were noticed on the test reflex as it matched the 100% base line of the control, so that this period no longer existed.

3. Conditioning with a stimulus intensity which evoked an H-reflex 50% of the control showed the following:

(a) Facilitation period

The time course started with reflex facilitation which continued for the first 20 msec. The test reflex ranged from 25 to 120% of the control with a mean value of 62% of the control. It was lower than the control value in seven out of nine subjects. In one subject the test reflex was equal to the control while the ninth subject showed an anplitude of 120% of the control.

(b) Inhibition period

After the test reflex reached the maximum in the previous period, it dwindled gradually until it was completely suppressed. This inhibition lasted from 20 to 40 msec. and sometimes continued up to 100 msec.

The test reflex was largely inhibited in most subjects. It ranged from 5 to 30% of the control with a mean value of 16% of the control (7 subjects). In the other two subjects it was completely abolished.

(c) Recovery

A further increase of the conditioning interval caused a recovery of the test reflex after 40 msec. in two subjects. In the other three subjects it was after 80 msec. while other subjects showed either earlier i.e. 30 msec., or later recovery i.e. 100 msec. The mean recovery time was 69 msec. The test reflex recovers faster than when conditioned by identical pulses.

4. Conditioning with identical intensity of the pulse train showed the following:

(a) Facilitation period

The test reflex showed an amplitude smaller than that noticed in the previous stage i.e. conditioning with lower stimulus strength. This continued for the first 20 msec. of the time course.

(b) Inhibition period

This showed a complete suppression of the reflex in most subjects lasting from 20 to 30 msec. and sometimes extending to 100 msec. and was equal in duration to that of the previous stage.

(c) Recovery

Increase of the interstimulus interval showed a variable recovery time of the test reflex. It recovers after 80 msec. in three subjects. Two subjects showed reflex recovery at 100 msec. and other two at 40 msec. One subject exhibited recovery at 30 msec. and other one at 60 msec. The mean recovery time was 68 msec. The test reflex recovers slower than that conditioned with lower stimulus strength.

5. Conditioning with supramaximal pulses

(a) Facilitation period

The test reflex was completely suppressed from the beginning of the time course so that this period no longer existed.

(b) Inhibition period

It lasted from the beginning up to the recovery point. The test reflex was abolished in all subjects.

(c) Recovery

Increasing of the conditioning interval produced a gradual recovery of the test reflex. This recovery started after a mean time of 78 msec. and ranged from 50 to 120 msec. The test reflex recovered more slowly than with identical conditioning in 6 out of 9 subjects. It was faster in the other three.

From the previous study of the MNP recovery one can see that conditioning of the H-reflex with a preceding single pulse of various intensity did not cause significant changes in the recovery time of the MNP. The inhibition period lasted an equal time under various conditions in spite of the fact that the degree of inhibition might be slightly less when conditioning with lower intensity pulses. Supramaximal conditioning abolished the primary facilitation period. This was not due to increase of the inhibition mechanism, but may be due to another factor. It was associated with a greater degree of inhibition than that mentioned previously.

The case was the same when a burst of pulses was used. It was felt during recording that the degree of inhibition was greater in the latter cases but the test reflex was larger during recovery. A slight increase in the duration of the inhibition period was noticed with supramaximal conditioning.

It is pertinent to ask whether both parameters of inhibition, degree and duration, occur by a separate mechanism. If that is so it will be important to identify the factors affecting these mechanisms in order to be able to interpret the changes in this inhibition period seen in clinical conditions. It is worth noting that, the recovery pattern of the reflex depends greatly on the intensity of the conditioning pulse, which further supports a different mechanism for the degree of inhibition.

Discussion

This work has been designed to explore three important phenomena which may affect the primary inhibition period and the recovery of the MNP. These are the following:

(A) The effect of transmitter disorganization (depletion) at the Ia-@MN synapses by the conditioning volley and its effect on the inhibition period (Curtis & Eccles 1960), Taborikova & Sax(1969).

(B) The effect of recurrent discharge of the muscle spindle after contraction produced by the conditioning pulse (Bianconi et al 1964).

(C) The effect of autogenous inhibition of the @-MNs by impulses from the Golgi tendon organs (Matthews 1972, pg. 426, Houke et al 1970, Haase et al 1975).

Initially there are different factors which may affect the primary inhibition period and the following recovery and later facilitation period. These will be quoted as follows:

I Peripheral Factors

1. Recurrent discharge of the muscle spindle after contraction (Bianconi et al 1964).

2. Autogenous inhibition of the @-MNs by tension sensitive golgi tendon organs fired by the conditioning pulse (Laport et al 1952, Eccles et al 1957a, b).
3. Signals from cutaneous afferent nerve fibres (Gassel & Ott 1969).
4. Antidromic pulses invading MNs.

II Spinal Factors

1. Deficiency of the transmitter substance at synaptic junction (Curtis & Eccles 1960, Taborikova & Sax 1969).
2. Propriospinal inhibition of the @-MNs by interlimb reflexes (Gernandt & Shimamura 1961).
3. After hyperpolarization duration of the MNs excited by the first shock (Eccles et al 1958, Kernell 1965, Burke 1967).
4. Recurrent inhibition by Renshaw cells (Renshaw 1940, Haase et al 1975).
5. Types of MNs excited i.e. either tonic or phasic MNs.

III Supraspinal Factors

1. Excitatory supraspinal inputs.
2. Inhibitory supraspinal inputs.

Taborikova & Sax (1969) postulated that the primary inhibition period of the recovery curve depends, to some extent, upon the transmitter deficiency at the Ia synapses caused by the conditioning pulse. They used threshold conditioning stimuli for the H-reflex, to diminish this transmitter disorganization at the synaptic junction and found that the test reflex was inhibited to 50% in the first 50 msec. They relate the degree of reflex inhib-

ition to the degree of transmitter deficiency. Similar results have been obtained by Paillard 1955 but less inhibition was reported by Masland & Ariz (1972) using threshold conditioning stimuli for the H-reflex. The hypothesis forwarded by Taborikova & Sax 1969 assumed that with liminal conditioning pulse a small number of Ia's were excited and their synaptic transmitter became less available for a number of milliseconds. When a test volley followed the conditioning one, it excited only those Ia synapses which are not depleted by the conditioning pulse so that the test reflex amplitude depends upon the intensity of the conditioning volley. These results were in concordence with those of Curtis & Eccles (1960) who found, by intracellular recording, that the transmitter available at the synaptic junction does not return to control value after stimulation for several seconds.

Similar results to those of Taborikova et al (1969) have been found by Paillard (1955). However in our work this hypothesis has been studied using different conditioning intensities. It was clear from these results that the degree of reflex inhibition and subsequently the number of the Ia synapses disorganized was directly related to the conditioning intensity.

Moreover using a train of pulses of 1000 PPS for the same number of the Ia's i.e. governed by the stimulus intensities, does not produce greater reflex inhibition. Again the reflex inhibition depends only upon the conditioning intensity and not on the stimulation frequency.

One could argue about the desensitization of the post synaptic membrane to the transmitter substance as a factor in this inhibition

period. However Curtis & Eccles (1960) did not find such sensitization, even when they used a train of pulses. Moreover hyperpolarization of the MN membrane does not account for its recovery. It is demonstrated later in this thesis (Refer to SFEMG section) that small tonic MNs which have a longer after hyperpolarization (Eccles et al 1958, Kuno 1959, Burke 1967) recover earlier than those of large phasic MNs.

It is tempting to think that the synaptic efficacy after the conditioning stimulus can account for a great part of the primary inhibition period during the recovery curve. Of course this does not exclude the well-known inhibitory mechanism of Renshaw cells (Renshaw 1940, Haase et al 1975) taking part in this inhibition period. Renshaw cell activity and its effect on the time course of the MSR excitability were studied based on differential stimulation of the Ia and motor axons, as reported by Veal et al (1971, 1973). An early and late inhibition and facilitation period were demonstrated consistently in 11 young subjects. However, it is difficult to rely on such indirect methods for studying Renshaw cells in man, as the electrical stimulation is not considered to be a good method of differentially exciting axons. This work has not been pursued.

Surprizingly enough, this work reveals that the recurrent discharge of the muscle spindle, after muscle contraction, does not have a significant effect on the inhibition period and recovery. Hunt (1952) Granit (1950), and Granit, Kellerth & Szumski (1966) demonstrated a profound effect of the muscle contraction on the excitability of the MNs. However McLeod et al (1967) demonstrated

mild reduction in the duration of primary inhibition of the recovery curve of the MSR in cats after cutting the muscle nerve distal to the stimulation site. The recurrent discharge of the muscle, after contraction, will be either from the Ia spindle discharges during muscle relaxation and subsequently stretching of the muscle spindles (Bianconi et al 1964), or due to the firing of the Golgi tendon organs during contraction (Laporte et al 1952, Eccles et al 1957 a, b, Hagbarth et al 1950). In our work the conditioning volley was subthreshold to reflex contraction of the muscle and subsequently no recurrent discharges from the muscle, yet mild reflex inhibition was noticed. This was similar to McLeod's procedure when they severed the muscle nerve distal to the stimulation site in cats. Both methods gave similar results which discounts the effect of the muscle spindle and Golgi tendon organs in the primary inhibition period. In the work of Hunt (1952), Granit (1950), Granit et al (1966) anaesthesized decerebrated or intact cats with cut ventral roots were used. These works were different from ours and with different species.

Of more importance was the recovery time of the test reflex as it started to recover after a definite time regardless of whether the conditioning shock was liminal, identical or supramaximal, whether it was a single or a train of pulses.

Perhaps the most important point this study reveals is that the degree of reflex inhibition in the primary inhibition period is directly related to the conditioning stimulus intensity regardless of the frequency of this conditioning i.e. whether it is single or train of pulses, and regardless of whether it is

electrical or tendon tap (Magladery et al 1952, Languth et al 1952). Another finding is that the reflex recovery did not depend upon transmitter changes or peripheral factors. It depends mainly upon the integrity of the supraspinal centres with the spinobulbospinal pathway conducting the long loop reflex. Because it depends upon the time elapsed for the impulse transmission through the fast ascending and descending pathways, the test reflex recovers after a certain time regardless of whether the conditioning volley was subthreshold or suprathreshold to the M-responses or regardless of whether this conditioning was single or train of pulses. Complete transection of the spinal cord was associated with absence of the intercurrent facilitation period (Eccles 1966). This late facilitation is expected to be mediated by small skin nerves i.e. group III cutaneous fibres (Gassel 1970a) as electrical stimulation of the skin of the lower limbs caused reflex facilitation with a peak at 100 to 250 msec. However Gassel (1970b) demonstrated such facilitation when the H-reflex was conditioned by ankle or biceps jerk to the contralateral limb. He put forward evidence for long loop spinobulbospinal influence which is not mediated only by skin nerves. Moreover he noticed a period of mild reflex inhibition following the facilitation and lasting up to five seconds. Indeed the spinobulbospinal effect is not only facilitatory, but also inhibitory for the MN discharges. Vestibular caloric stimulation, or electric stimulation by an external electrode placed on the mastoid bone, produced facilitation in the ankle jerk but not the H-reflex (Delwaide & Delberg 1973). However Pierrot-Deseilligny et al (1973) demonstrated H-reflex inhibition at 50-100 msec. after

conditioning cutaneous stimulation to the small toe. Similar inhibition was noticed by Bathien & Hugon (1964).

It seems that the test reflex is subjected to a number of superimposed facilitatory (LLR) and inhibitory /¯LLR, transmitter disorganization, direct proprio-spinal influence (Gernandt et al 1961, Shimamura et al 1963)_/ influences interacting at 40 - 5000 msec. in the excitability cycle. Shimamura and colleagues (Shimamura 1963, Shimamura et al 1963, 1964, 1965) studied the long loop reflexes in cats, monkeys and man and defined its intricate organization. During our studies we were able to record this LLR from the tibialis anterior muscle by stimulation of the posterior tibial nerve in the same way as Shimamura et al (1964) but this work has not been extended.

Another piece of evidence for the LLR causing late H-reflex facilitation, stems from the work of Paillard (1955) and Taborikova et al (1966a, b) who conditioned the H-reflex or the ankle jerk by quick passive stretching of the muscle either by ankle jerk or by a catapult arrangement. The late faciliation period was noticed after a long primary inhibition. Eccles (1966) and Yap (1967) reported that there is no known mechanism which could produce such facilitation at the spinal level.

Finally it is possible to postulate, according to this work, that the change in the synaptic efficacy produced by the conditioning pulse plays an important role in the primary inhibition period. Additional factors especially Renshaw cell inhibition may have a significant effect as well. Yet, this factor needs detailed studies with a more direct method in man. Reflex recovery after

inhibition depends upon the spinobulbospinal pathways of the LLR and the integrity of the bulbar centres. These integral central mechanisms exert excitatory and inhibitory influences on the final executive discharge of the MN, causing the highly excitable small tonic MNs to recover first before the large phasic MNs. These LLRs are triggered by the Ia fibres and possibly the group III cutaneous fibres as well.

SP: In this work recovery was noticed to be after 60-100 msec. while in later work it occurred after 40-60 msec. with a mean value of 45 msec. in young subjects. It is important to emphasize that techniques were different, as in this work two stimulators with common electrodes were used, each to deliver a stimulus volley with a particular intensity. In these experiments some of the stimulus shunted through the output impedance of the inactive stimulator. In later work (age related changes) one stimulator was used in the control and experimental groups which gave two pulses of identical intensity with a particular interstimulus interval.

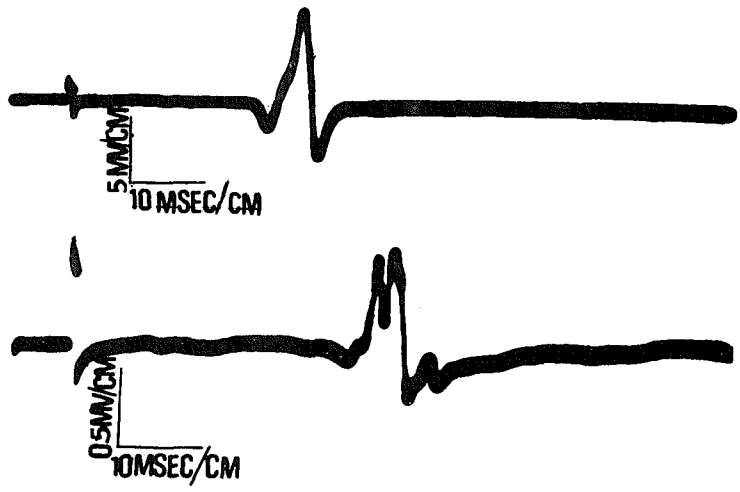


Fig. 27 H-reflex from one young (upper) and one old (lower) subject. In old subject the reflex was very small polyphasic and had a longer latency.

CHAPTER IV

AGE RELATED CHANGES AND MOTONEURON EXCITABILITY

H-reflex studies in elderly subjects showed significant differences in the monosynaptic reflex excitability from those seen in young subjects. The following were characteristic differences observed.

I Reflex amplitude and potential shape

Fig. 27 shows the H-reflex recorded from one young and one old subject. The most obvious difference was the threshold at which the reflex was evoked. It was not always possible to obtain an H-reflex without an M-response in old subjects and when the H-reflex was evoked it was of low amplitude, of long duration and polyphasic. The maximal reflex amplitude was smaller than that of the young subjects. The lower amplitude responses in old people suggest that the stimulus was able to recruit only a small proportion of the MNP. This possibility was investigated and discussed in MNP fraction studies in old aged people.

The changes in reflex duration and shape was marked in old subjects when compared to young ones. The latter showed a triphasic reflex of duration (8-12 msec.). In most elderly subjects the reflex was polyphasic. Six out of fourteen showed a polyphasic reflex in all records, so that one subject had a reflex duration of 20 msec. In three subjects the reflex was polyphasic in most records but in some it had a shorter duration with a triphasic shape. In five subjects the reflex was triphasic with a normal duration. During recording it was noticed that the older the subject, the longer in duration was the reflex potential.

II Latency changes

Table 8 shows the latency measurements of both the M-response and the H-reflex. Both were significantly longer in old subjects. The M-response was 20% later while the H-reflex was 27% later in old subjects. In young subjects the reflex latency ranged from 24 to 28 msec. with a mean value of 26 msec., while in the elderly ones it ranged from 28 to 40 msec. with a mean value of 33 m/sec. Nine out of fourteen old subjects showed a reflex latency ranging from 30 to 35 msec. while in the other three subjects it was of 35 to 40 msec. The reflex fired after 28 msec. in the last two old subjects.

TABLE 8 Latency measurement of the H-reflex and loop time (M-H latency) in young and old subjects

Young Subjects				Old Subjects			
Subject	Age	H-Latency	M-H Latency	Subject	Age	H-Latency	M-H Latency
RA	22	25	11	JG	70	32	20
LH	23	26	14	SP	70	28	14
SB	22	24	12	LB	61	28	12
CE	23	24	12	AM	60	30	12
PM	3	28	13	JM	64	34	19
MS	31	26	10	IC	71	31	13
JK	22	28	14	GL	63	36	18
LS	25	27	15	CC	64	36	-
JT	19	24	11	SS	68	34	18
MA	29	26	12	AL	72	34	18
VK	22	24	12	FT	65	34	20
				AS	66	32	16
				PL	66	31	15
				FR	63	40	22
Mean $\pm$ SD		26 $\pm$	12.4 $\pm$	Mean $\pm$ SD		33 $\pm$	17 $\pm$

There was about 7.25 msec. difference in the mean value between both groups (old and young) which was statistically significant at the 5% level.

A number of factors could be involved in the increased latency. The M-response gives the time taken by the stimulus to pass down the motor axon and across the neuromuscular junction. Subtraction of the M-latency from the whole H-reflex latency gives the time taken by the pulse to go through the reflex arc from the site of stimulation and back to the same site. I have called this the loop time. In the young subjects it was 48% of the total reflex time while it was 52% in old subjects. In the young subjects the loop time ranged from 10 - 15 msec. with a mean value of 12 msec., while in elderly ones it ranged from 12-22 msec. with a mean value of 17 msec. (Table 8). The changes were statistically significant at the 1% level (P = 0.001). (Table 9).

TABLE 9 Significance of the difference in latency measurement between young and old subjects.

	Latency of M response	Latency of H reflex	Loop time H - M	Loop time %
Young subjects 19 - 30 yrs	13.3 ± 0.4 N = 11	25.6 ± 0.5 N = 11	12.4 ± 0.4 N = 11	48.4% of total time
Old 60 - 72 yrs	15.9 ± 0.5 N = 13	32.6 ± 0.9 N = 13	16.7 ± 0.9 N = 13	51.8% of total time
Significancy	p = 0.001	p = 0.001	p = 0.001	

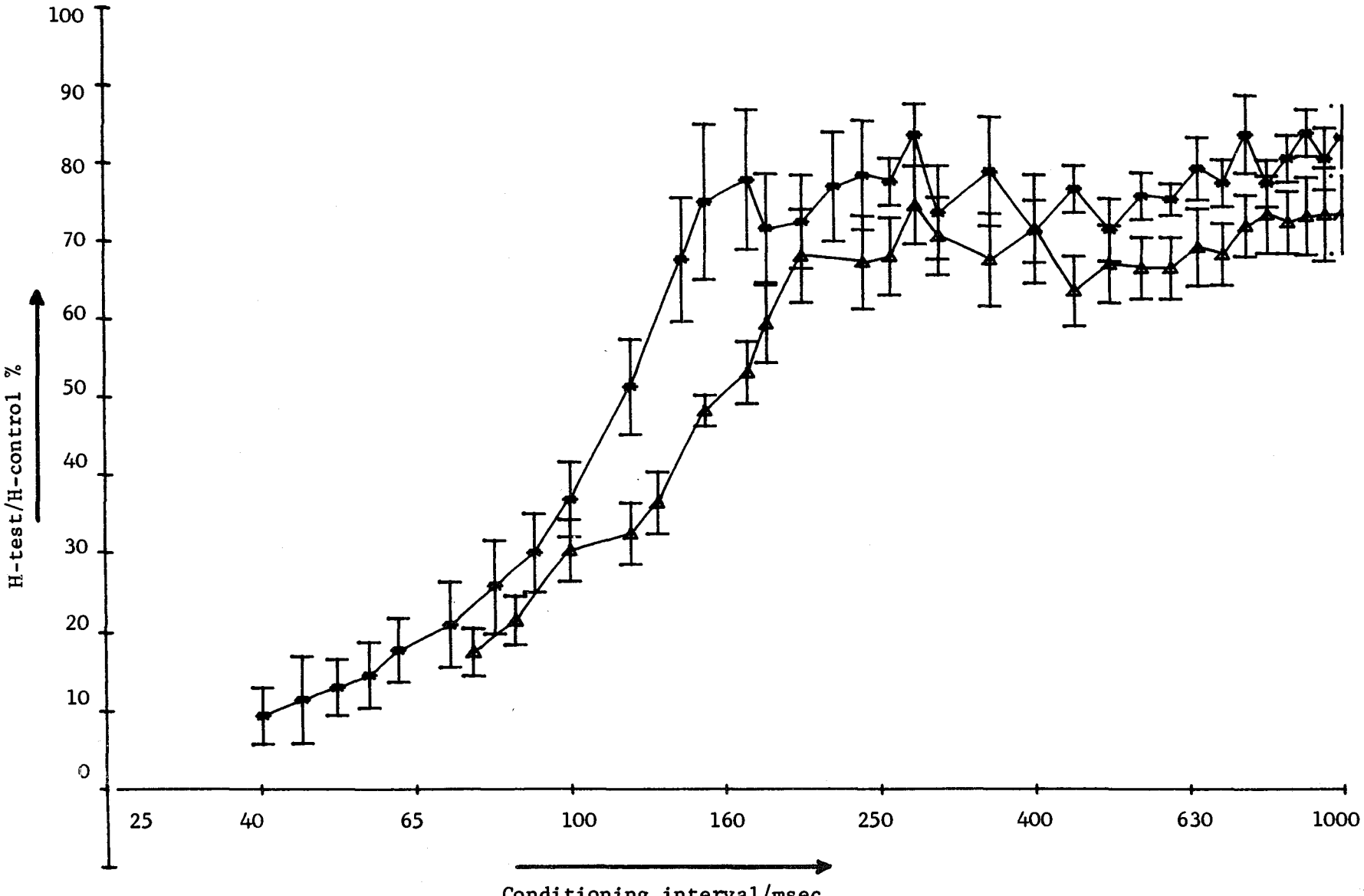


Fig. 28 Averaged recovery curve of 10 young (*) and 10 old subjects (△). In old subjects the test reflex recovered 40 msec. later and it was inhibited more than that of young subjects. (Mean ± SD).

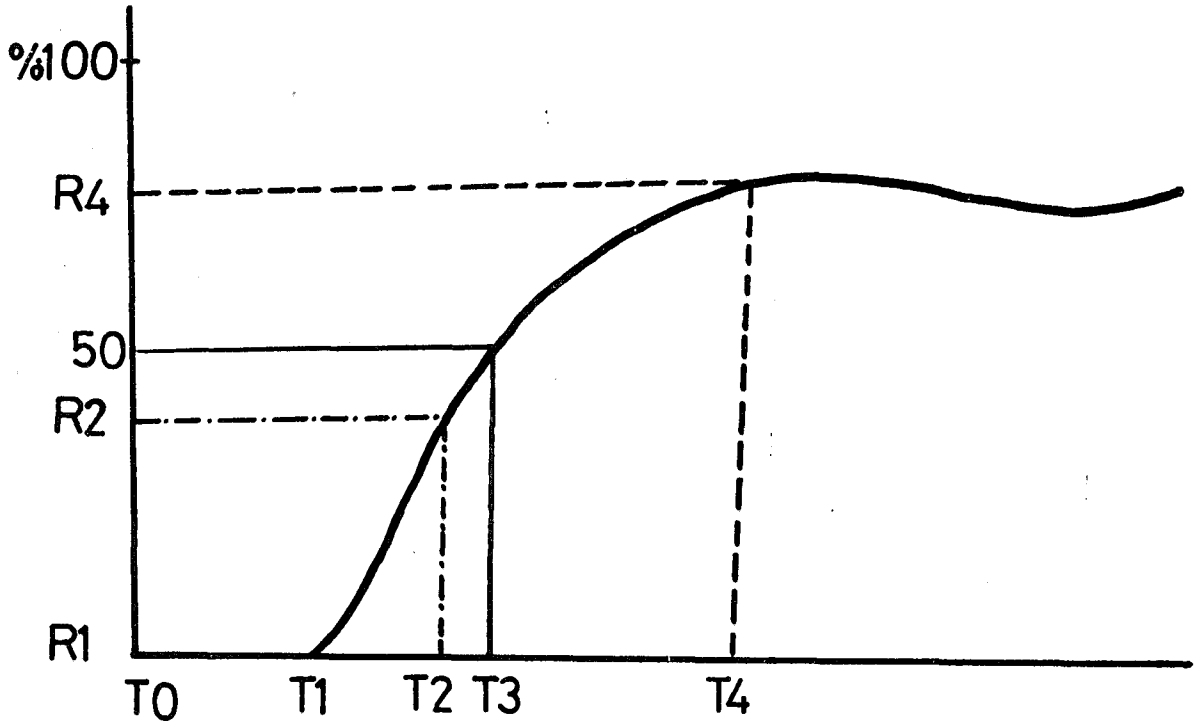


Fig. 29 Standard curve with the various parameters measured in young and old subjects' recovery curves (R = Recovery, T = Time).

This data indicates that factors central as well as peripheral, to the stimulating electrodes were involved in the latency difference between both groups of subjects.

III Recovery of the MNP in old aged subjects

The recovery of the second reflex after a preceding identical stimulus showed significant differences in old people. The averaged recovery curves for the 10 young and 10 old subjects tested are plotted in Fig.28 . For convenience the time axis is logarithmic. To make statistical comparison of these curves easier a number of points were defined for analysis and the results are given in Fig. 29

T0 is the time at which the conditioning stimulus was given.

T1 is the time by which the test stimulus must be delayed before a second H-reflex appears.

T2 is the time at which the second H-reflex recovered to 50% of its maximal recovery.

T3 is the time delay before the test reflex reaches 50% of the control value.

T4 is the delay time to maximal recovery of the second reflex.

T4-T1 is the recovery time after total inhibition.

R1 is the percentage of recovery of the second reflex at T1 time.

R2 is the recovery percentage at T2.

R4 is the plateau of recovery of the reflex.

Measurement of these parameters in old and young subjects showed the following:

TABLE 10 Measurements of the parameters studied in the recovery curves of 10 young subjects.

Subject	Age	Recovery	50% Max. Recovery		50% control	Max. Recovery		Recovery time
		T1	T2	R2	T3	T4	R4	T4 - T1
PM	22	55	100	39	126	280	78	225
CE	23	40	245	52	240	370	104	330
LS	25	45	115	44	115	280	88	235
RA	22	40	90	46	95	110	92	70
LH	23	60	135	35	160	280	69	220
JK	22	40	122	35	200	260	70	220
SB	22	40	115	60	110	150	120	110
JT	19	40	82	42	92	200	84	160
BJ	28	35	45	39	68	180	78	145
MS	31	40	125	63	132	170	125	130
Mean $\pm$ SD		44 $\pm$ 8	117 $\pm$ 52	45 $\pm$ 10	134 $\pm$ 53	228 $\pm$ 79	91 $\pm$ 20	185 $\pm$ 76

TABLE 11 Measurements of the parameters studied in the recovery curves of 13 old subjects.

Subject	Age	Recovery	50% Max. Recovery		50% Control	Max. Recovery		Recovery
		T1	T2	R2	T3	T4	R4	T4 - T1
PM	64	120	152	50	150	300	100	280
LB	61	75	125	36	150	260	71	185
AM	60	75	125	31	185	220	62	145
SS	68	160	-	56	-	410	113	350
AL	72	100	200	44	205	240	88	140
SP	70	65	130	43	150	280	85	215
IC	71	65	110	41	140	280	83	215
PL	66	60	130	33	160	280	65	220
FR	63	90	115	47	105	320	94	230
GL	63	140	155	30	143	450	60	310
CC	64	100	-	-	-	-	-	-
JG	70	85	-	-	-	-	-	-
WR	60	90	-	-	-	-	-	-
Mean $\pm$ SD		94 ± 30	138 ± 28	41 ± 9	154 ± 9	304 ± 73	82 ± 6	229 ± 68

1. T1 The second reflex recovered after a mean value of 44 msec. In young subjects (Table 10). This recovery ranged from 35 to 60 msec. Seven out of ten subjects showed recovery before 40 msec. while in one other subject H2 recovered after 45 msec. In the remaining two subjects the reflex recovered after 55 and 60 msec. inhibition time. These were significantly earlier than that showed in old subjects. In the latter the recovery time ranged from 60 to 160 msec. with a mean value of 94 msec./ (Table 11) In three subjects recovery time was longer and ranged from 100 - 160 msec. In the other seven subjects it ranged from 75 to 100 msec. while the shortest recovery time seen in old subjects was from 60 to 65 in three subjects only. The difference, in the recovery time, between both groups was significant to the 1% level (p 0.001) (Table 12).

The recovery in young subjects was smoothly increased in regular pattern (Fig. 28), while that in old subjects irregularly fluctuated as seen in the graph, and did not show smooth reflex recovery. This fluctuation continued up to maximum recovery.

2. T4 Once the second H-reflex appears (H2) it recovers in amplitude quickly at first, but after about 250 msec. further recovery is slow and variable. From Fig.28one can see a well marked turning point where the rapid recovery flattens out. This turning point was less easily seen in the older subjects. This turning points occurs at T4. Older subjects took longer time to reach this point and the difference was just significant to the 5% level. The mean delay time up to this turning point was 228 msec. in young and 304 msec. in old subjects. There was a great variability of the recovered reflex which clouds the issue, yet the figure shows clearly that the young

subjects make a quicker and more complete recovery from inhibition.

3. After the turning point (T4) has been reached the fluctuations obscure the difference between both groups. But the mean of the value of the different points between 200 and 1000 msec. in both groups was statistically significant to the 1% level ($p_{=}0.001$). This shows that the reflex in the older people, during its recovery, was more inhibited than those of young subjects. The degree of inhibition in the elderly subjects was up to 20% more than young subjects. This inhibition difference was prominent in the recovery turnover phase of the recovery curve (Fig. 28).

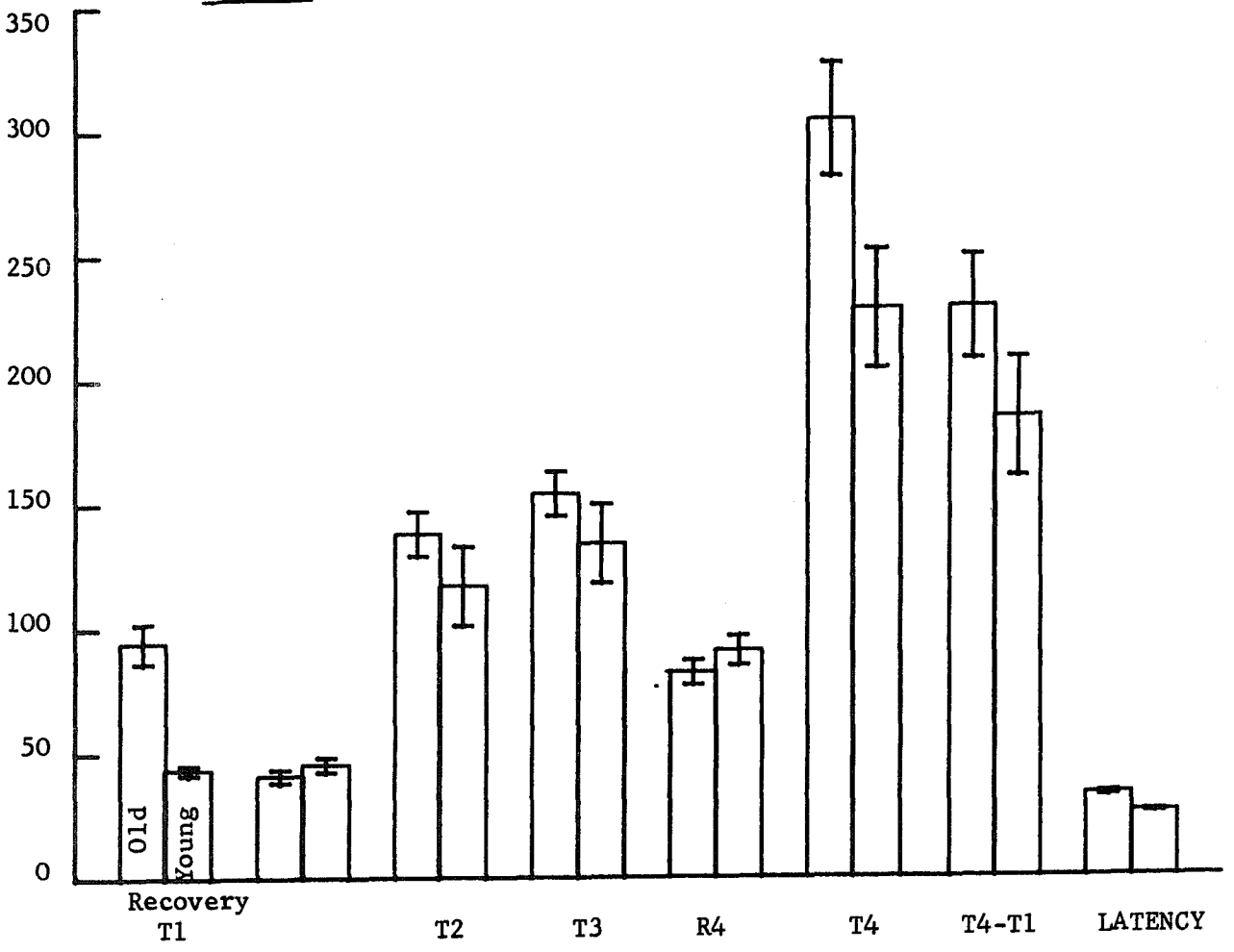
4. There was a slight difference between young and old subjects in other parameters but these were not statistically significant.

TABLE 12 Significance of the difference in the parameters studied in the recovery curves of young and old subjects.

Subjects and significance	Latency	T1	Maximum Recovery 50%		Maximum Recovery 100%		50% Full Recovery T3	Recovery time T4-T1
			50% R2	T2	100%	T4		
Young subjects	25.6±0.48 N (11)	43.5 ±2.48 N (10)	45.45 ±3.09 N (10)	117.4 ±16.4 N (10)	90.75 ±6.24 N (10)	228 ±24.89 N (10)	133.8 ±16.64 N (10)	184.5 ±23.96 N (10)
Old subjects	32.85±0.88 N (14)	94.23 ±8.37 N (13)	40.95 ±2.74 N (10)	138.00 ±9.23 N (10)	81.90 ±5.48 N (10)	304 ±23.0 N (10)	154.17 ±9.41 N (10)	229 ±21.4 N (10)
Significance "p"	0.001 "S"	0.001 "S"	1.896 N.S	1.094 N.S	1.066 N.S	0.05 "S"	1.066 N.S	1.385 N.S

Fig.30 is a histogram which shows the parameters tested in the comparative study of the recovery between young and old subjects.

Fig. 30



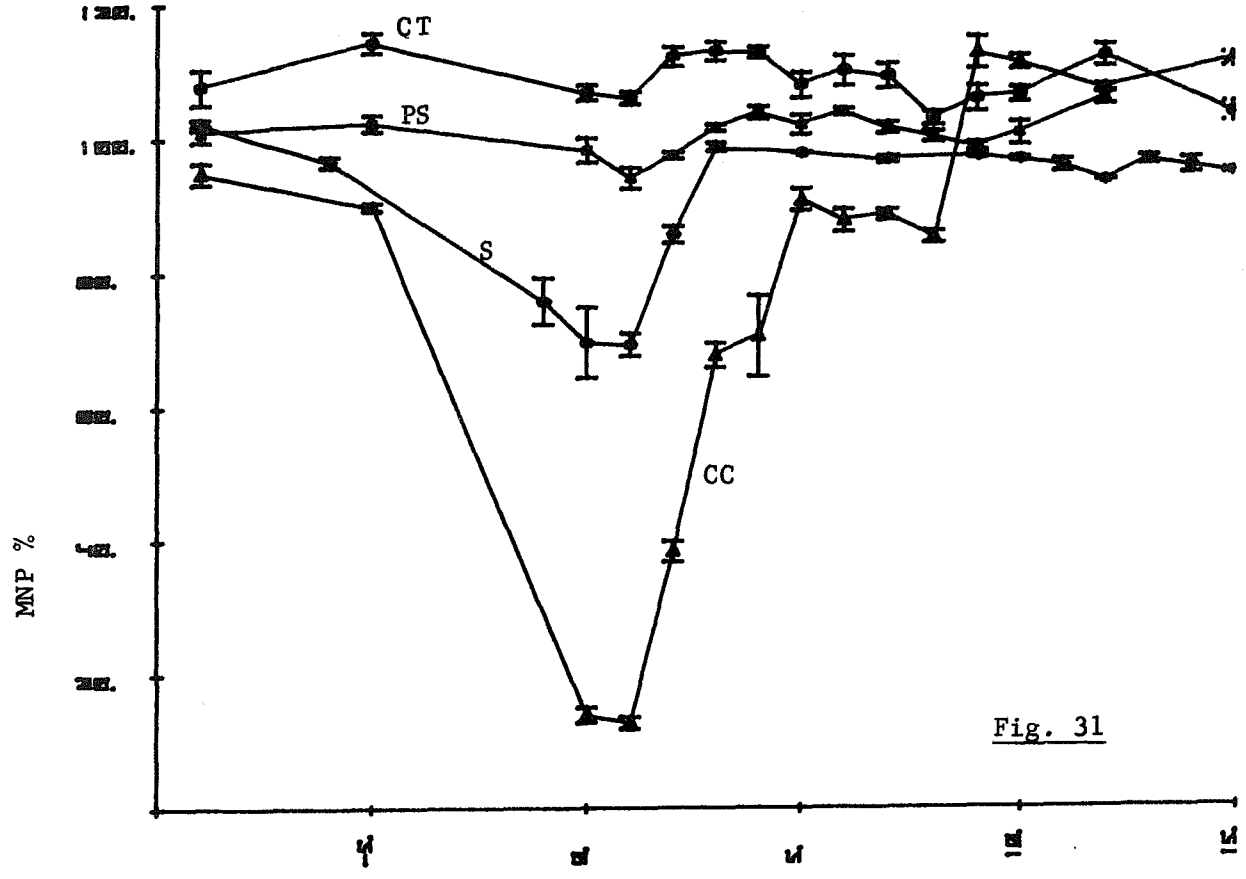


Fig. 31

Time interval between S2 and S1/msec.

Fig. 30 Histogram of the parameters tested in the recovery curves of young and old subjects. (Mean $\pm$ SD).

Fig. 31 MNP fraction measured by refractoriness in one old subject. The control fraction during rest (*) enlarged with contraction of the calf muscle (▲) and became smaller with passive stretching calf (X) and during contraction tibialis anterior (●). (Mean $\pm$ SD).

IV Fraction of the MNP

Further studies of the MSR and MN excitability in old aged subjects were performed. These were by measuring the fraction of the MNP participating in the H-reflex, in the resting state as well as during various manoeuvres. Four old subjects with ages from 61 to 68 were available, of which one was female. The results obtained emphasized the previous findings and are listed below.

1. Standard fraction of the MNP

Three subjects were tested for the MNP fraction. In all of them it was small and had a mean value of 21% of the MNP (Table 13). This was the case when measured by either techniques.

Table 13 Fraction of the MNP in the resting state in 3 old subjects

Subject	Refractoriness	$H/_M$ ratio
JM	30	40
SS	14	7
AM	20	17
Mean $\pm$ SE	21 $\pm$ 5	21 $\pm$ 10

In comparison to a mean value of 69% in young subjects the MNP fraction was significantly smaller in old subjects. This is supported by the small reflex amplitude recorded in old subjects. Fig. 31 showed the MNP fraction measured in one old subject.

2. MNP Fraction during contraction of calf

Isometric contraction of the calf muscle produced facilitation

of the reflex in four subjects to a mean value of 205% of the control (Table 14). This coincided with a large fraction value measured in three subjects.

Table 14 Effect of isometric contraction of the calf, tibialis anterior, vibration and scrubbing sole on the H-reflex in old aged subjects. Values are expressed as the percent of the control

Subject	Age	Contraction calf	Isom. Cont. T.A.	Vib-ration	Scrubbing sole
JM	64	78	45	-	-
SS	68	325	33	5	77
CB	61	178	5	13	44
AM	61	239	21	35	38
Mean $\pm$ SE		205 $\pm$ 10	26 $\pm$ 9	17 $\pm$ 9	53 $\pm$ 12

The mean fraction value was 46% of the MNP when measured by refractoriness. However the fraction did not show great changes when measured by $^{H}/_{M}$ ratio as it had a mean of 24% of the pool (Table 15).

3. Isometric contraction of the foot dorsiflexors

This manoeuvre inhibited the test reflex dramatically in old subjects to 26% of the control (Table 14), a finding that was supported by a small fraction of the MNP. The latter had a mean value of 0.0, when measured by refractoriness so that the test reflex was completely abolished and of 9% of the pool when measured by $^{H}/_{M}$ ratio (Table 15).

Three subjects were tested for the effect of vibration and scrubbing the sole of the foot and they demonstrated reflex inhibition to a mean value of 17% and 53% of the control respectively (Table 14). In two of them the fraction and the MNP was measured during these manoeuvres and both exhibited smaller fraction, measured by either technique, during vibration and mechanoreceptor stimulation (Table 15).

Table 15 Fraction of the MNP during various manoeuvres measured in old subjects

Subject	Refractoriness					H/M ratio				
	Control	Contraction calf	Contraction T.A.	Vibration	Scrubbing	Control	Contraction calf	Contraction T.A.	Vibration	Scrubbing
JM	30	87	0	-	-	40	34	19		-
SS	14	15	0	2.4	17	7	17	3.2	0.4	5
AM	20	36	0	6	9	17	22	4.3	12	6
Mean$\pm$SE	21$\pm$5	46$\pm$22	0	4$\pm$2	13$\pm$4	21$\pm$10	24$\pm$10	9$\pm$5	6$\pm$6	6$\pm$0.6

Summing up the above results one can say that the MSR excitability was significantly changed to a lower value in elderly people. This was either measured by direct or indirect method of the MN excitability.

Discussion

H-reflex studies in elderly subjects showed a set of results which indicate changes in the nervous system at the peripheral and spinal level. The interpretation of changes was extracted from similar findings in man using a different approach (Magladery et al 1958), or in animals (Gutmann et al 1972). Results explained in later sections i.e. H-reflex recovery studies, were very helpful in the interpretation of old ages results. The evidence for peripheral and central dysfunction will be quoted separately in some detail with the interrelation between both deficiencies.

I Evidence for peripheral dysfunction

Measurement of the H-reflex latency showed significant delay in the old more than the young subjects. As the reflex passes through peripheral and spinal paths, both sections could contribute to the recorded latency difference in elderly subjects. However, the conduction velocity in the peripheral nerve is of prime importance in reflex latency and any changes in it could prolong dramatically the reflex latency (Mayer & Mawdesly 1965). In fact the changes in the conduction velocity in old subjects were expected, as polysynaptic reflex delay was found to be increased from 192 in young to 226 msec. in 70 year-old people (Magladery et al 1958). Moreover Saint A'mbrogio et al 1961 demonstrated 60% increase in latency of rat polysynaptic reflexes. Although these findings were

explained by central latency changes, there was a tendency to believe in the contribution of peripheral nerve degeneration in causing such significant delay as well. Cottrell (1940) reported by histological techniques that degeneration occurs in the large diameter afferent as well as efferent fibres in old people shifting the spectrum to the smallest size. Moreover Magladery et al (1959) demonstrated from clinical observations that simple reflex phenomena which depend upon intact afferent paths are decreased or absent, and accompany changes in recognition of slight degrees of movement in the joints and vibration. These were explained by alterations in the peripheral nerve as well as dorsal roots or within the CNS itself at spinal and supraspinal level. On the other hand Timiras et al (1972) reported that nerve conduction velocities of afferent fibres neither in human nor in laboratory animals have shown any differences among different age subjects. This was contradictory to the findings of Wagman et al (1952), Norris and others (1955) in old people, and Birren et al (1956) in old rats, as both groups demonstrated reduction in conduction velocity. Rexed (1944) confirmed these findings histologically when he reported a decrease in the number of motor nerve fibres in old aged people. Wagman & Lesse (1952) reported 10% decrease in the conduction

velocity in old people and Norris and others (1955) relate the reduction in conduction velocity to increasing vascular changes, changes in membrane permeability, selective degeneration of the largest and fastest conducting fibres and temperature changes in the tissue of elderly people.

In our study the MSR demonstrated a 25% increase in latency in elderly subjects. This could be attributed mainly to the possible degeneration of the large diameter afferent fibres and firing of the smallest fibres with lower conduction velocity. This is probably more confirmed by the increase in the reflex threshold level and the difficulty in evoking submotor threshold of H-reflex and the very small reflex amplitude which could be elicited in most elderly subjects. All these findings may account for the contribution of the degeneration in the peripheral nerves, in the H-reflex prolongation in latency. However it may account for central spinal defects as well and this will be discussed later.

Mayer et al (1965) reported that the H-reflex latency could be used to detect polyneuropathy in its primary stages before muscle weakness. If old aged subjects suffered from polyneuropathy of such mild degree, accurate investigation will not be possible unless the normal latency change with age was determined. A number of similar examples could be drawn from the clinic which diminish the reliability of measurements if the age related changes were not taken into account.

Degeneration of the large diameter afferent fibres could possibly lead to excitation of the H-reflex polysnaptically.

Mayer & Mawdesly (1965) suggested that the H-reflex may fire polysynaptic pathways as well as mono synaptic ones. Magladery et al 1951 mentioned similar suggestion only superficially. One should be very careful in mentioning such assumptions especially after the accurate measurement of Magladery et al (1951) that the spinal delay of the Ia volleys was 1.5 msec. which coincides with dorsal and ventral root conduction in addition to a single synapse.

Moreover the reflex shape in old subjects was polyphasic and of long duration while that of the young was triphasic. In some old subjects the reflex duration was more than 20 msec. This could be due either to peripheral or central factors. Peripheral factors are the degeneration of muscle fibres and the loss of functioning motor units as reported before in old people. Carlson et al (1964) and Frubel-Osipova (1969) noticed that the EMG of the old people showed more polyphasic potentials. Moreover Campbell et al (1973) demonstrated that the surviving motor units were often hypertrophied and showed relatively slow twitches. This was confirmed by a number of workers (Peterson et al 1949, Hodes 1953, Frubel-Osipova 1969). A twofold prolongation in old age was found by Hodes 1953. Moreover Frubel-Osipova (1969) reported a decrease of the excitability of muscles in old people with an increase of absolute and relative refractory periods. Gutmann et al (1968) demonstrated 33% decrease in the motor units in old rats and a significant decrease in the muscle fibres of the motor units themselves (Gutmann & Hanzlikova 1972, pg. 23, 63). Not only were muscle fibres decreased in numbers (Guttmann et al 1966, Rowe 1969) but also in diameter as

well (Frubel-Osipova 1969, Rowe 1969). Moreover change of innervation pattern in muscles during old age was reported by Gutmann & Hanzlikova (1965). Increases in thickness in the muscle spindle capsule with a slight decrease in the mean number of intrafusal muscle fibres in the muscle spindles of old aged people were demonstrated by Swash et al (1972). These could account for the polyphasic H-reflex in old age. However desynchronization of the MNs (Taborikova et al 1968) in old people may cause long duration reflexes, but it is unlikely to be a factor in such polyphasic potentials.

II Evidence for central spinal dysfunction

There are a number of findings of our results which indicate changes in the spinal centres in old people. First of all was the significant increase in the loop time in old people which indicates a central defect in addition to the peripheral changes. Longer time elapsed for the passage through more than one single synapse. Progressive slowness of motor reactions is a well known observation accompanied with ageing (Gutmann & Hanzlikova 1972, pg. 97). However the longer loop time found in our results could be attributed to increasing synaptic delay such as those found in rats by Wyner & Emmers (1958) using monosynaptic reflex discharge. This was suggested to be due to decreased excitability at single synapse rather than conversion to polysynaptic response. Gutmann et al (1972) stated "It is difficult to know whether this increase in central delay is a direct result of age changes in the spinal MNs or whether alterations of other neuronal

pathways convering on MNs are more important". Another possible factor is the change in the transmitter release at the synaptic knobs in old people. Gutmann (1970) reported that dramatic changes in transmitter release apparently represented a significant event in development of old age changes in neuromuscular system and he suggested a decrease in Ach synthesis, liberation and hydrolysis in old people (Gutmann et al 1972, pg. 101).

The second important finding and probably the most characteristic one, was the delay and slowness in reflex recovery to normal value. In old people the primary inhibition period was longer and followed by a smaller test reflex than young subjects. It is difficult to explain accurately now changes which occur in the primary inhibition period, other than that old people exhibited lower excitability of the MNP. Taborikova et al noted that the primary inhibition period may be due to lowering of transmitter release after depletion of the transmitter by the conditioning pulse (Curtis & Eccles 1960). However Magladery et al (1951) reported that this period may be attributed to inhibition of the @-MNs by the internuncial neurones fired by the secondaries. Muscle spindle discharge (McLeod et al 1967) and recurrent inhibition of the Renshaw cell (Haase et al 1975) are important factors affecting the inhibition period.

To explain the results found in old subjects accurately, comparison with newborns is important to cover the whole developmental side of the problem. In newborns and infancy Mayer & Mosser (1969, 1973) demonstrated changes in H-reflex recovery curve from that of the adult

one. In the newborns the early inhibition period was relatively small (30 msec.) and in some was incomplete and followed by a period of rapid recovery. They suggested that this may be due to increase in the excitability of the @-MNs presynaptically due to development of the excitatory synapses on the dendrites before the inhibitory ones, as was found in Monkey by Bodian (1966). Another possibility was forwarded as lack of inhibition of spindle discharge on MNs as well as active ɣ-MNs.

The most likely interpretation of our results was the degeneration of some -MNs in the spinal cord with a decrease in the excitability of the other surviving neurones. Decreased total neuronal populations were noticed in the CNS with cell loss of the pyramidal cells in the 3rd cortical lamina (Critchley 1942) cells in post-central gyrus (Brody 1955), Purkinje cells in the cerebellum (Hodge 1894, Ellis 1920, Harmis 1924). Gutmann et al (1966) found no loss of motor nerve cells in the spinal cord of old rats. However Gutmann and Hanzlikova (1972) stated "Still some cell death in the nervous system may be characteristic of the ageing process in man and animals (Gardner 1940, Brody 1955, Rockstein 1967) but clear interpretation of these data is missing".

If degeneration of the MNs occurred in old aged people, the small and more tonic MNs are the most likely to degenerate first. These MNs recovered early in the recovery curve (Refer to SFEMG section) and are the more excitable ones. Moreover these types of MN are the most likely to be affected in dystrophia myotonica (Refer to dystrophia myotonica section). Decrease in the excitability of the surviving neurones should accompany MN degeneration in old age and such changes in the excitability were found at

single synapses by Wayner and Emmers (1958).

If degeneration of the MNs does not occur in old age, it will be more likely that the generalized decrease in the MN excitability would account for reflex recovery changes. The increase in threshold level of H-reflex firing and its small amplitude may provide another piece of evidence for @-tonic MN degeneration in these cases. The tonic MNs were found to have lower threshold level of firing when studied by SFEMG and it forms most of the population of neurones in the soleus muscle (Refer to SFEMG, Messina et al 1976). Messina et al (1976) attributed the large amplitude of the H-reflex recorded from the soleus muscle to the large number of tonic MNs. It is more likely that degeneration of these types of neurones could cause an increase in the threshold level of the H-reflex in addition to a smaller amplitude similar to our findings.

Other factors should be taken into consideration in the explanation of the previous results of the recovery curve. These lack strong evidence but similar findings have been traced before in animals. Lack of transmitter release at the synaptic junction in old people (Gutmann et al 1972) may affect to some extent the reflex recovery. However this is a constant factor in both conditioning and test shocks- but the delay in transmitter synthesis and release could account for certain delay. Degeneration of excitatory synapses with sprouting of others from the inhibitory interneurones to replace them, could account for the significant reflex inhibition during recovery. It has been shown before that sprouting of the synaptic endings of nerve cells in the brain and spinal cord, after degeneration of other cells, occurs in the old animals (Raisman 1969)

and may be so in man as well. However if the excitatory synaptic knobs on the α-MNs which develop first in newborns and monkeys (Bodian 1966) degenerate first, this could explain the prevailing of the inhibitory mechanism in old people.

A third suggestion is worth mentioning that changes in the conduction velocity in the long neuraxis spinobulbar tracts, similar to those found in the periphery, may cause some delay in the supraspinal excitatory mechanism (long loop-reflex) on the MNs contributing not only to the significant inhibition but also to the delay found in the reflex recovery.

The previous three suggestions could contribute to the inhibition found in the recovery of old people. However it is unwise to attribute any change in old people to solely one factor. Multiple systemic changes are often found with ageing and each change must affect the surroundings especially in such a hierarchy as the nervous system. However primary change was the main aim of this study and this has been explored with regard to other subsidiary ones.

CHAPTER V

SINGLE FIBRE EMG STUDY IN H-REFLEX

1. Observations on single fibre action potentials in soleus muscle

The MNs of the soleus muscle have characteristic properties. It was possible to record a large AP of single muscle fibre at the time when the superficial recording was without deflection. This was the case whether the H-reflex or the M-response was being recorded and indicates activity of the motorneurones of lowest threshold.

Consecutive discharges of the same MN during repeated H-reflexes shows variation of latency ranging from 550 to 3000 μsec. in 18 muscle fibres tested and has been called H-reflex jitter (Trontelj 1973), who found jitter values up to 2,500 μsec. It was observed that this latency variation depended upon whether the MN was fired by a threshold or suprathreshold stimulus. The variation was smaller with suprathreshold stimuli. The jitter also depended upon whether the MN was being fired during H_1 or H_2 as well as upon the conditioning interval between H_1 and H_2 (Fig.32). In high threshold MNs i.e. MNs fired with a stimulus strength sufficient to produce a M-response, the variation was smaller than low threshold MNs. MNs follow the all-or-none fashion in firing (see the methods for criteria of SFAP). The failure to fire was dependent upon the stimulus strength. Failures increased when the stimulus was slightly reduced to around the threshold level. Suprathreshold pulses showed a reliable MN firing with rare failures. This goes for the high and low threshold MNs. At near threshold levels an important factor was the background activity of

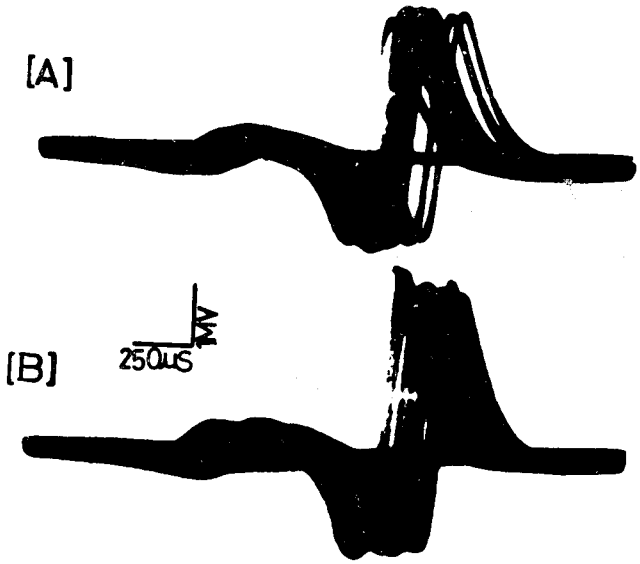


Fig. 32 Consecutive discharge of a single motoneurone during H-reflex, either H1 or H2 after recovery (B). This is the so called jitter of H-reflex. Failure of firing occurred sometimes and was more frequent in H2 than H1.

the muscle. Increasing muscle tension decreased the failure to the minimum. Failure was frequently seen in H_2 especially with short conditioning intervals. During recording it was observed that the latency was slightly increased before failure. This latency variation in the H-reflex was considerably longer than neuromuscular transmission jitter which is less than 40 μsec. (Stalberg et al 1971).

2. Identification of a single MN

A single fibre and therefore a single MN was identified on the basis of (a) An all or none response. (b) The action potential was of the same size and shape on each occurrence even with different stimulus strengths.

Each MN has a unique stimulus strength at which it is excited (threshold stimulus). For any MN this is constant during repeated determinations, so long as the degree of relaxation of the subject and other factors remain unchanged!

At threshold stimulation MN fired at some presentations but not at others, but a slight increase in stimulation resulted in reliable responses.

There was no similar potential, either im amplitude, duration, or shape which fired at the same threshold level.

3. Summation at the motorneurone

Stimulation of the Ia afferent fibres fires the MN producing the H-reflex. Sometimes a MN fails to be excited especially if the threshold of the MN has just been reached. If successive pulses of low intensity were applied they summate at the MN and cause it to fire. This is temporal summation and has been extensively studied

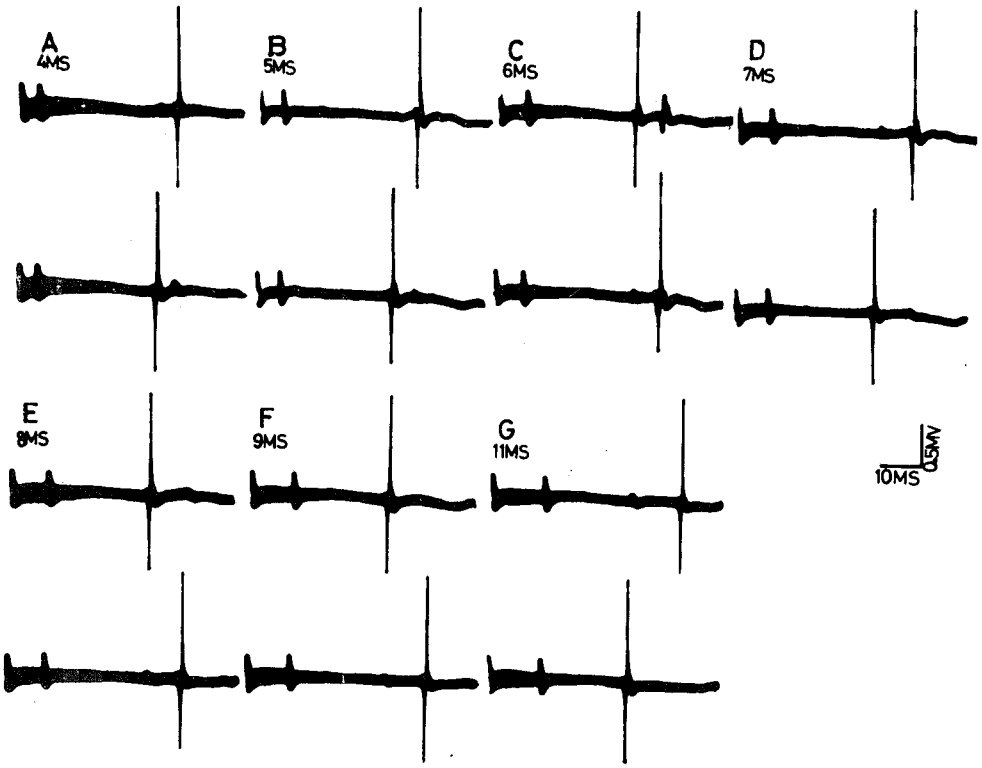


Fig. 33 Temporal summation at the motoneurone of the afferent volleys. The motoneurone fired either during H1 or H2, but never in both. It is all-or-none and in this figure summation occurs when the conditioning interval was from 4-11 msec. Traces are in pairs.

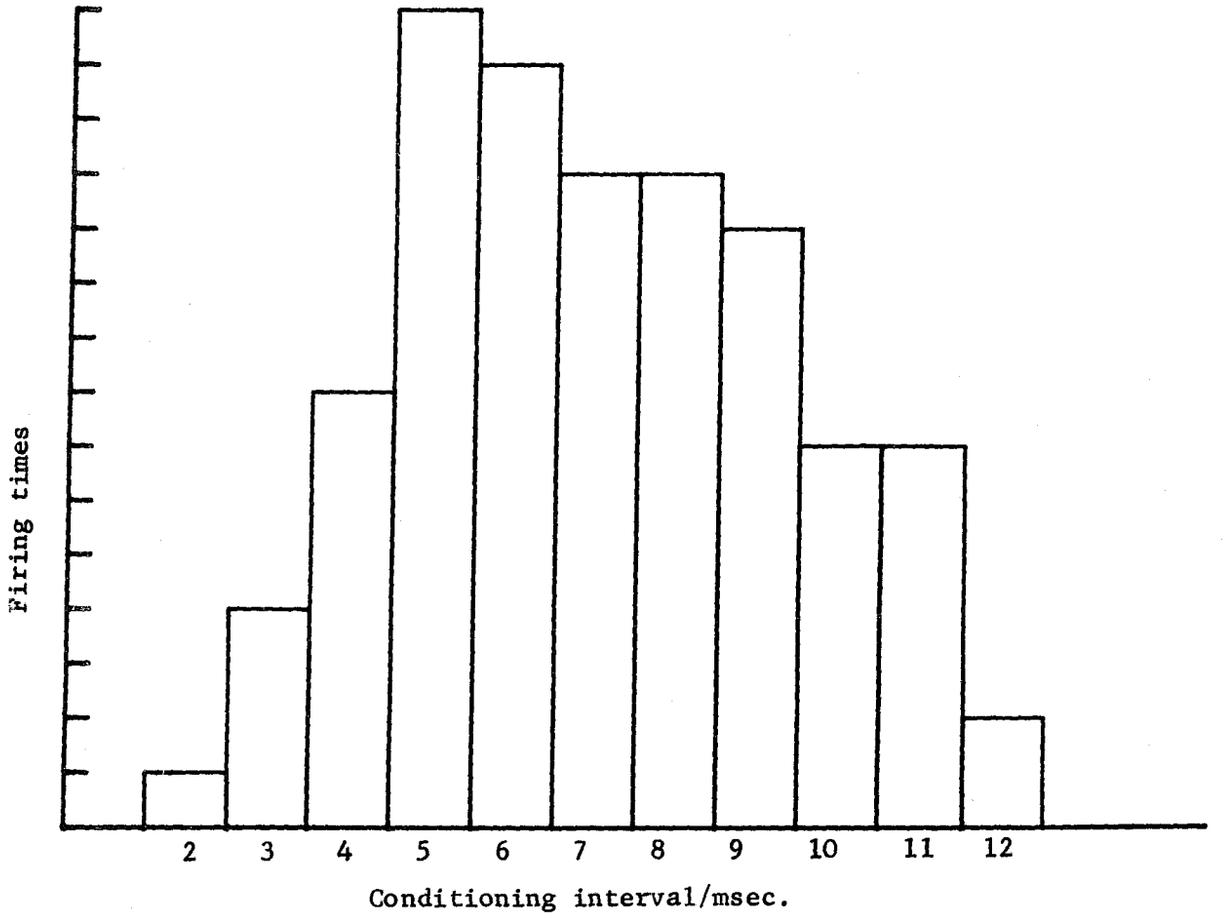


Fig. 34 Temporal summation was more frequent with conditioning intervals from 3 - 11 msec. (17 units) and it was maximum at 5 and 6 msec.

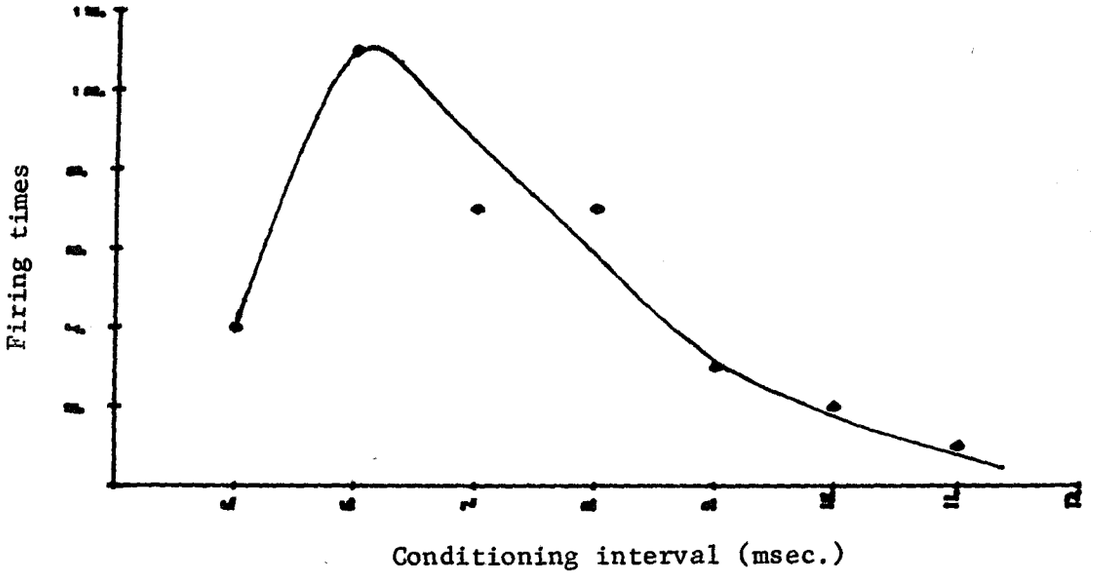


Fig. 35 In one unit tested for temporal summation showed maximum value at 6 msec. with increasing of the summation failure as the conditioning interval increased.

in animals. Here the phenomenon is studied in man.

3.1 Summation by paired sub-threshold stimuli

With two pulses of equal intensity and a conditioning interval in between, the stimulus amplitude could be adjusted so that the MN fired sometimes in response to S1 and sometimes to S2 giving H_1 or H_2. The firing of an MN in response to such stimuli followed a pattern which was reproducible and characteristic in each MN studied. 30 MNs were studied in all and 19 showed evidence of temporal summation. 11 MNs out of 30 fired only as part of H_1 and showed no evidence of excitation during H_2 with the short conditioning interval used. In the MNs which showed summation the following patterns were seen:-

1. With stimulus strength just suprathreshold to fire the MN, the latter fired during H_1 but never in response to the second pulse i.e. H_2 absent.
2. When the stimulus strength was reduced to just below threshold, the MN failed to fire during H_1 but the two pulses would summate to produce a H_2. This was identified by the latency.
3. When the stimulus strength was further lowered, neither of the two pulses separately nor both together caused the MN to fire.

This summation of sub-threshold stimuli was seen over a period of conditioning from 3-12 msec. (Fig.33). Most of the MNs were made to fire by summation over the period from 4 - 11 msec. At 3 and 12 msec. summation was rarely noticed. It was never seen at 1 or 2 msec. nor at more than 12 msec. intervals (Fig 34). It is felt that early summation was absent because of the relative refractory period in the afferent nerves. In Fig. 35 a sample of MN firing was plotted

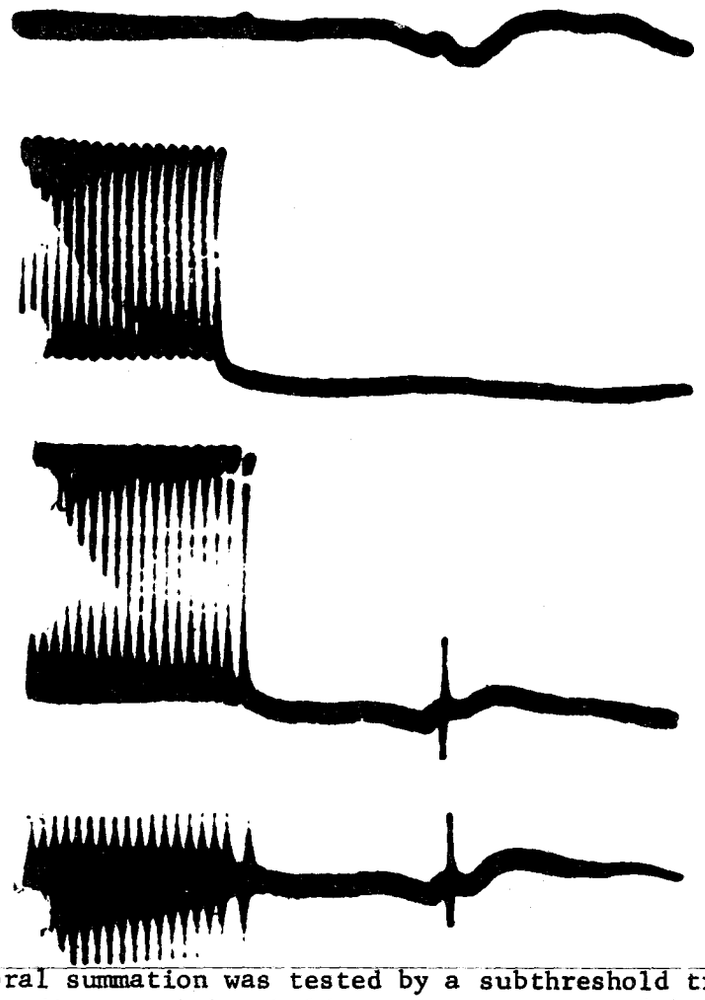


Fig. 36 Temporal summation was tested by a subthreshold train of pulses (A) preceding a subthreshold single test shock (B). When A & B are added to each other the MN fires giving an H-reflex with 1 (C) and 2 (D) msec. conditioning intervals.

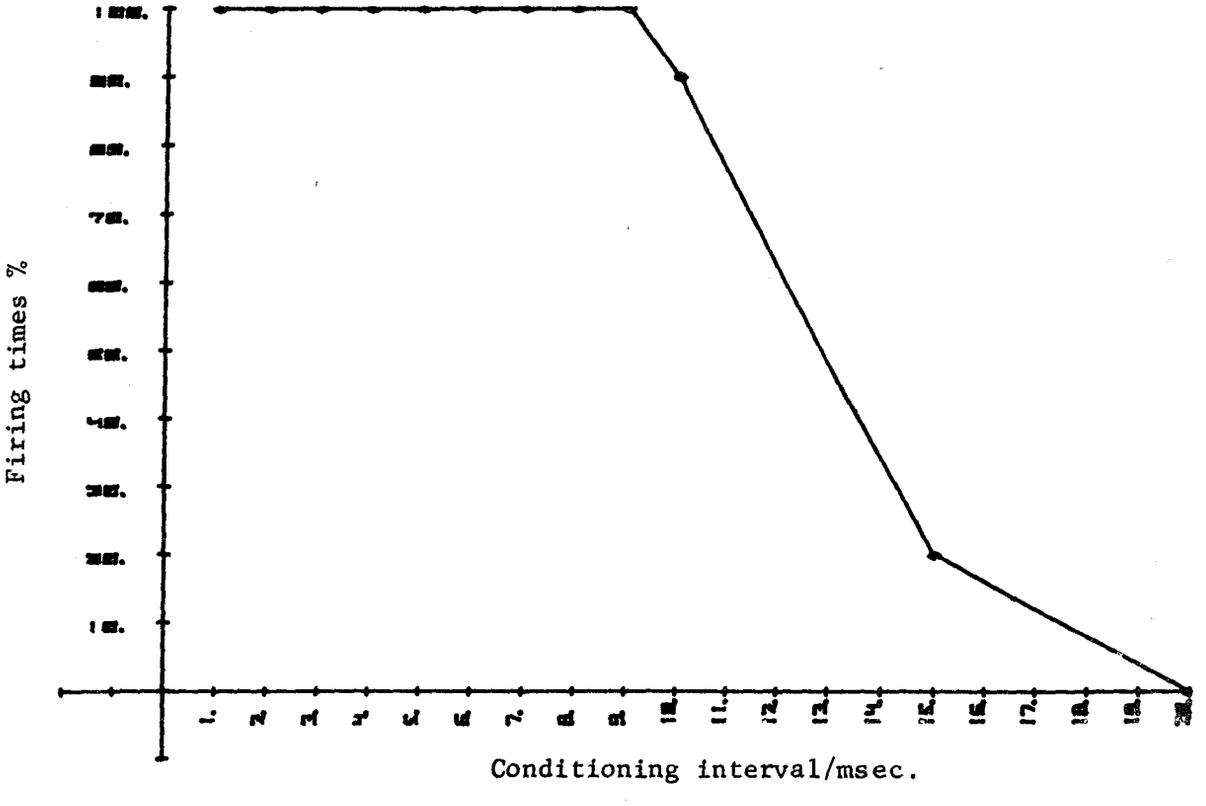


Fig. 37 The time course of temporal summation tested by train of pulses ranged from 1 to 15 msec. and was maximum up to 9 msec.

in terms of firing probability against the conditioning interval. The summation was most apparent at 5 - 9 msec.

Another type of summation was noticed during recording and involves a different mechanism. This was seen when using paired pulses of sub-threshold strength insufficient to produce temporal summation. The failure of the MN to fire was due to inadequate afferent excitation. Mild isometric or isotonic contraction of the soleus muscle now caused the MN to fire during H_2. The excitation from the supraspinal mechanism was added to the temporal summation of the paired pulses and made the MN fire during H_2. Furthermore, increasing contraction tension excited the MN sufficiently to cause it to fire during H_1. In these cases H_2 was never seen, together with H_1, the same as with temporal summation.

It is interesting to note that after muscle relaxation there was a short period during which the MN fired either during H_1 or H_2 and lasted for seconds depending upon the duration of the contraction. This period (after excitability period) ended with silence of the MN because of the inadequacy of afferent excitation.

3.2 Summation at the MN by a pulse train of sub-threshold strength

This set of experiments were designed to investigate the temporal summation using a burst of pulses. The test pulse was sub-threshold to MN firing. When this test stimulus was preceded by a train of pulses which was also sub-threshold, the two would summate giving an H-reflex (Fig.36). The pulse train lasted 30 msec. and had 1000 PPs. This summation observed lasted for 10 - 15 msec. after the train (Fig. 37) The reliability of the MN firing was maximum in the first 9 msec. after the conditioning train. This

stability decreased gradually and resulted in the failure of MN firing in some records at 10 - 15 msec. intervals. The failure rate increased with longer conditioning intervals. The MN firing stability was minimum at a 15 msec. and failed to fire in most records.

In this study 9 MNs (from 6 different subjects) were tested. One MN out of the 9 showed no summation at all. In one other MN summation was observed for 50 msec. In between those two extremes, 7 MNs had summation over periods from 5 to 20 msec. Summation was seen at 1 msec. conditioning interval in 5 out of 8 MNs. In two out of eight it started at 2 msec. while in one MN summation was not seen before 3 msec. of conditioning intervals.

It was noticed during recording that the summation time depended upon the stimulus strength of both the test and the conditioning pulses. The duration of summation increased slightly if the test stimulus strength increased closer to threshold. It was noticed that the stimulus strength used for the conditioning pulse train was very much lower than that used for a single conditioning pulse.

4. Time course of MN excitation, conditioned by a pulse train of low stimulus strength

From the previous section the MN was found to be free of temporal summation after 15-20 msec. This was usually followed by a period of inhibition or silence. This set of experiments was designed to scan the length of summation time in relation to the silent period, when the test MN was at firing level. The conditioning train was sub-threshold to MN firing. This was followed by a conditioning interval which lasted from 1 - 150 msec.

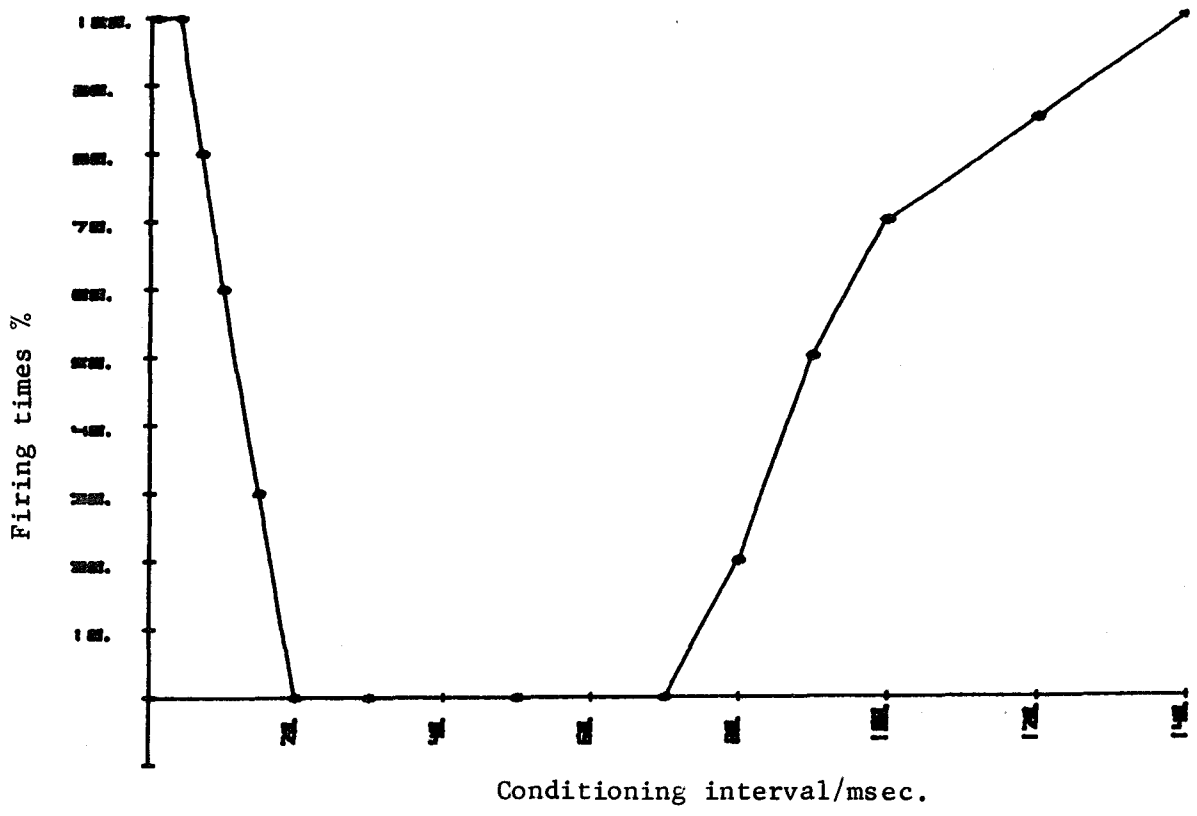


Fig. 38 Time course of a motoneurone excitation preceded by a conditioning train of subthreshold intensity. Primary inhibition with a following recovery can be traced in the time course.

Table16 presents the data of each MN subjected to this study.

Table 16 Time course of MN excitation, conditioned by a pulse train of low stimulus threshold

Motor unit	1 ry facilitation	Inhibition Period	Recovery
1	2 - 20	20 - 50	50 - 100
2	1 - 20	20 - 70	70 - 150
3	1 - 20	20 - 50	50 - 150
4	1 - 20	20 - 70	70 - 100
5	3 - 20	20 - 30	30 - 50
6	1 - 40	40 - 50	50 - 70
7	10 - 20	20 - 50	50 - 100
8	1 - 30	30 - 50	50 - 150
9	2 - 15	15 - 50	50 - 100

Nine MNs were tested. When the MN was excited, the conditioning train fired additional MNs. and an AP complex was seen instead of SFAP. This was seen consistently in all subjects during period called the primary facilitation period. Table (16). This period varied from one MN to another, but generally lasted for the first 20 msec. (Fig. 38). The newly recruited MNs failed to fire with the gradual increase of the conditioning interval. It was clearly seen that the MN under study was one of the components of the AP complex. Inhibition of the additional MNs occurred as well as in the MN under study after 20 msec. conditioning interval. This interval was

longer in some MNs and reached up to 40 msec. and shorter in others, 15 msec. only. The inhibition period lasted from 20 - 50 msec. in six out of nine MNs. In two MNs it was longer, 70 msec., but in the other MN it was shorter, 30 msec.

The inhibition period was prominent and was followed by a gradual recovery of the MN. Firing of the MN returns in some of the records but it remains silent in the others. This was the initial stage of the recovery period and noted in Table 16 by the earlier time interval. No AP complex was seen but only the AP of the MN under study. Gradual recovery was noticed. The probability of MN firing increased with increasing conditioning interval until it fired consistently without failure. Complete recovery is quoted for every MN in Table 16 as the end of the recovery time. In four out of nine complete recovery was reached after 100 msec. In three MNs complete recovery did not occur before 150 msec. Two MNs recovered after 50 and 70 msec of inhibition.

5. H-reflex blocking by supramaximal pulses studied by SFEMG

It is well known that increase of the H-reflex amplitude with increasing stimuli is due to the recruitment of more Ia fibres and therefore firing more MNs. (Hoffmann 1918, Magladery et al 1950). The supramaximal reflex dwindles in amplitude with further increase of stimulus intensity. This was interpreted as being due to central collision of the antidromic and orthodromic pulses either in the motor axon (Hoffmann 1922, Magladery et al 1951, Paillard 1955) or the somata (Taborikova et al 1968). However the recurrent inhibition of the Renshaw cells cannot be excluded (Renshaw 1941).

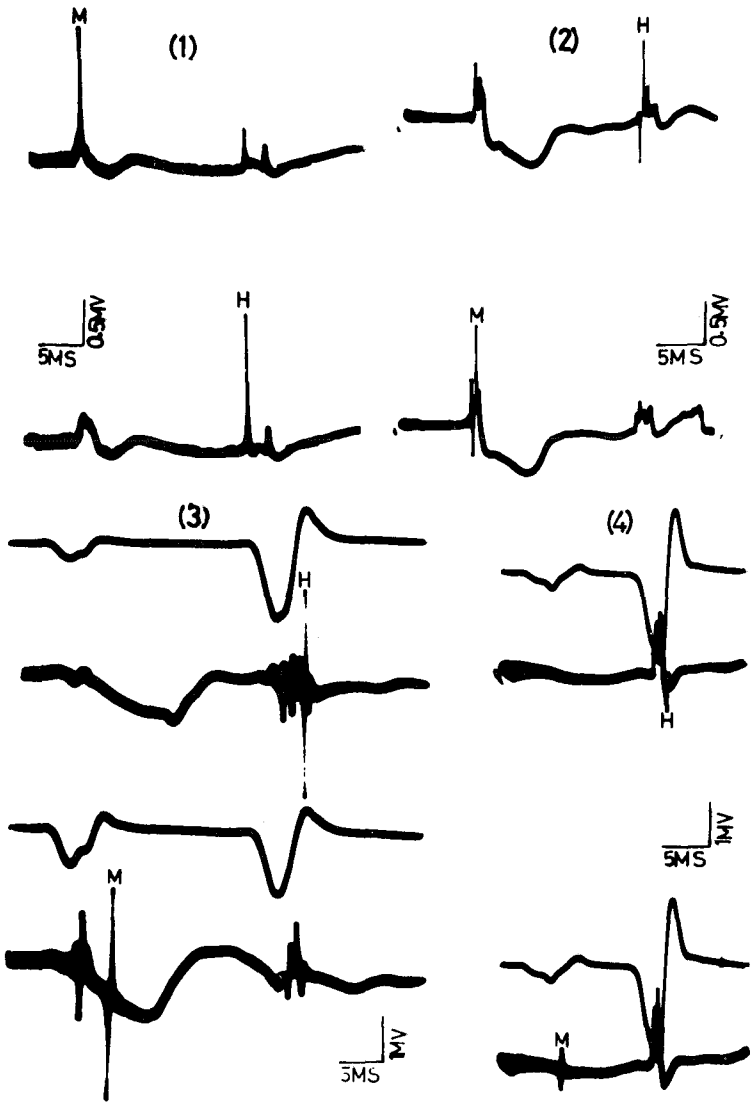


Fig. 39 The motoneurone fired during either the H-reflex or the M-response but not in both, at the same stimulus intensity. In this figure, four different motoneurones were excited during the H-reflex at a lower stimulus strength and during the M-response with higher stimulation. This was monitored by the superficial recording in units (3) and (4).

Gottilieb et al (1976) did not disprove the collision of the antidromic M-wave and the orthodromic H-reflex, in the motor axon, as the cause of extinction of the reflex, but they showed it to be unnecessary, claiming that collision elsewhere or recurrent inhibition may produce the effect. All studies have used surface recordings and none have examined individual motor units yet the results are interpreted as events occurring in individual units. For this reason SEFEMG could shed light on the cause of this phenomena.

The threshold difference between H-reflex and M-response played an important role in appreciating this phenomena. In 123 single MNs studied there was no one fibre which fired during both the H-reflex and M-response. Fibres fired during the H-reflex differed in amplitude, shape and duration from those excited during the M-response to same stimulus. It was possible to see the same fibre fired during H-reflex and M-response but always on different trials and often with different stimulus strengths. Fig.39 shows four different MNs excited during the H-reflex by low stimulus intensity; with slightly higher stimulus strength the same fibres can be recognised firing during the M-response while the H-reflex was blocked.

These MNs from different subjects give supporting evidence for the collision in the MN of the orthodromic and antidromic impulses. It was difficult to record precisely such clear fibre potentials during H and M-responses in more than a few instances. This was because at higher stimulus strength, recruitment of other nearby fibres clouded the clear representation of a single one. The fibres shown in this figure had nearly the same stimulus threshold for the H & M responses which made recording of this phenomenon

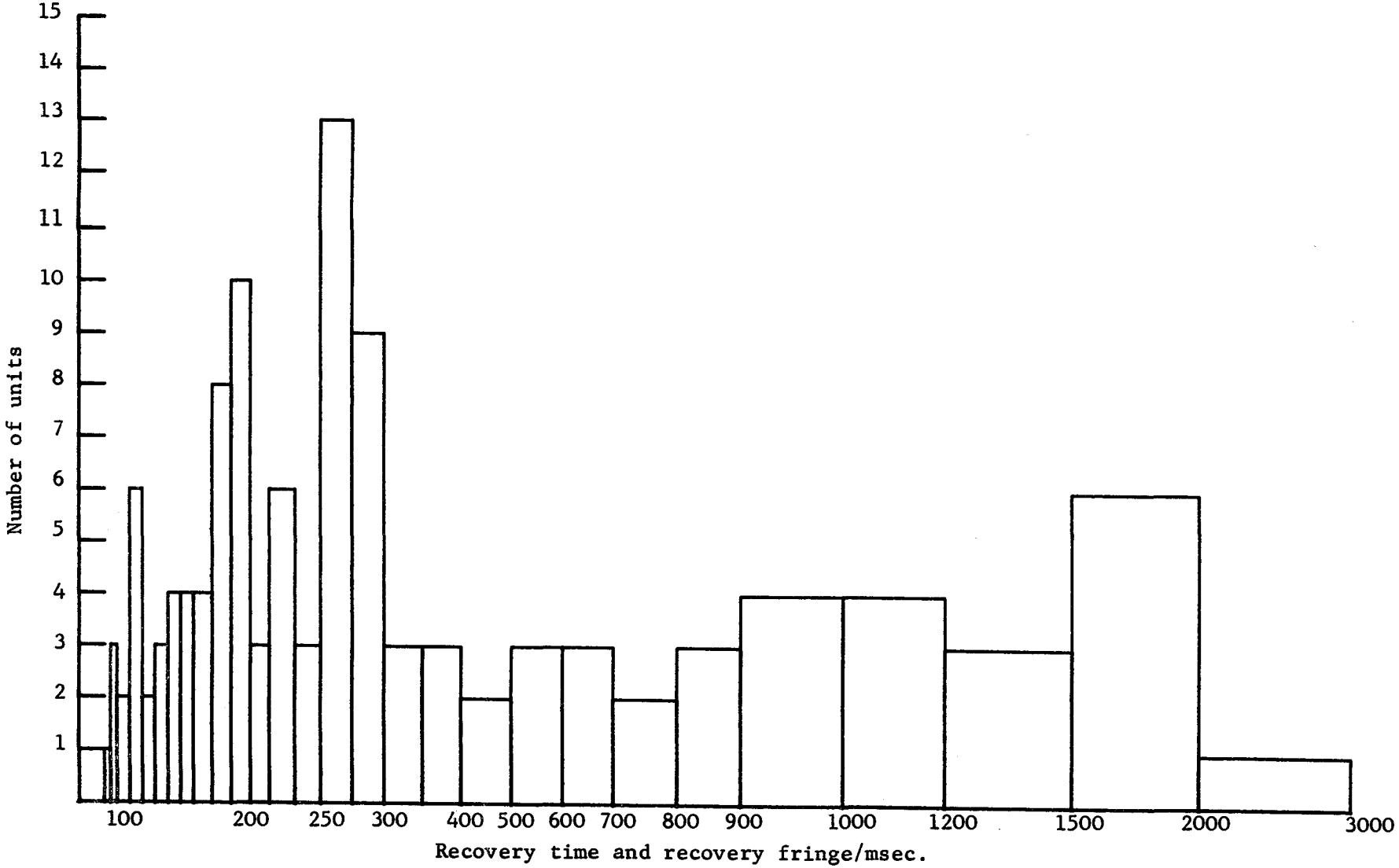


Fig. 40 Recovery times and recovery fringe of 117 motoneurones tested and showing that most of the MNs of the soleus muscle recover early and have a short recovery fringe. A smaller number of MNs recovered late and had a long recovery fringe.

possible. All our observations indicate that a MN fired antidromically never contributes to the following H-reflex.

6. Single motoneurone recovery with identical conditioning stimulus

The individual MNs in the MNP may recover in an orderly way, that is each MN has its own recovery time. Alternatively any one MN may show haphazard recovery while the proportion of MNs in the pool recovered at any one interstimulus time remains constant.

Recovery of the MNP after identical conditioning pulses was seen to be gradual and follow a pattern to be described below. This set of experiments was developed to test MN behaviour using SFEMG. Paired identical stimuli were used at threshold level for MN firing. 120 MNs were studied from 28 normal young subjects. These MNs had recovery times scattered over a long period (Fig. 40). Every MN had a definite time of inhibition after which it always recovered. Recovery of the potential was all-or-none, further supporting the identification of a single fibre. No one MN from the population studied recovered before 80 msec. Most of the MNs recovered in the first 250 msec. Other MNs had a late recovery time which sometimes reached 2200 msec. Most MNs with a relatively high threshold tended to recover early i.e. between 80 and 150 msec. (Fig. 40).

The period over which the recovery of the high threshold MNs varied was 2-15 msec. or up to 20 msec. This period has been called the recovery fringe. By the end of that period the MN was totally recovered without failure.

A number of MNs had late recoveries, after 150 msec. and up to 2500 msec. (Fig. 40). These MNs had a longer recovery fringe

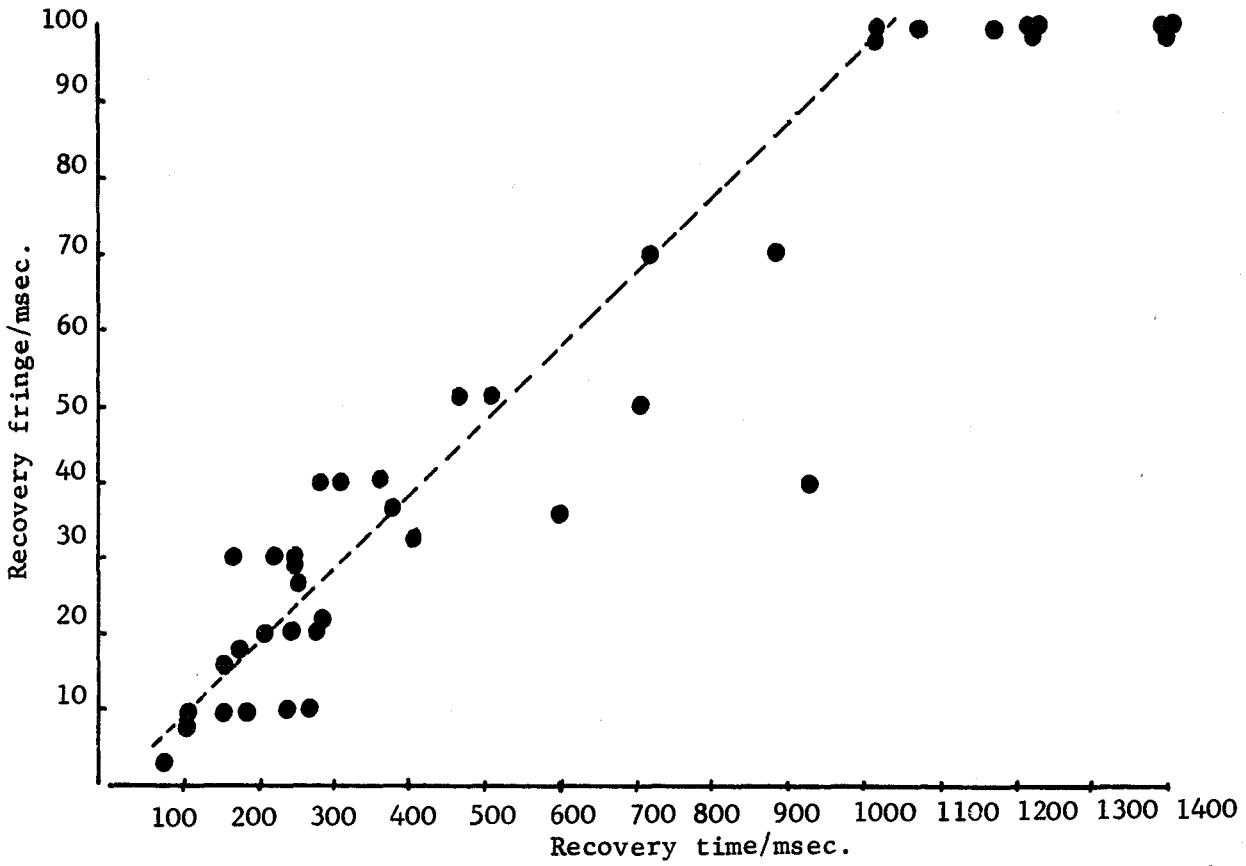


Fig. 41 Recovery time has an approximately linear relationship with the recovery fringe of various motoneurones. (40 units)

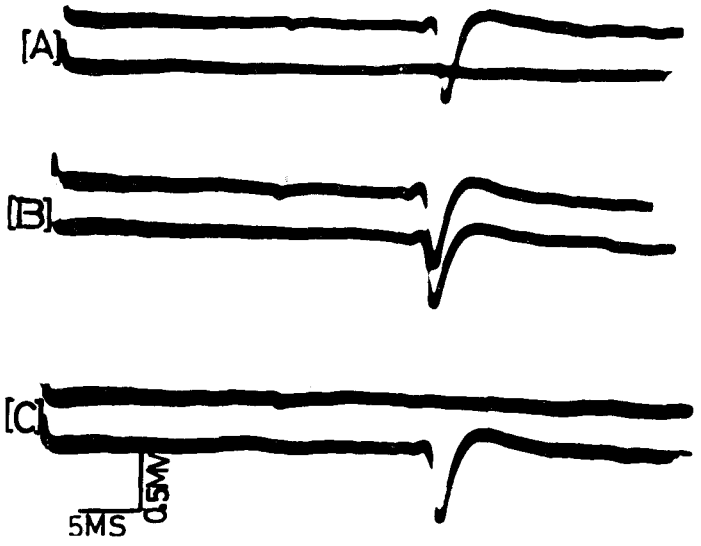


Fig. 42 At the recovery time the motoneurone either failed to recover (A) or showed full recovery (B). Sometimes the test reflex fired following failure of the conditioning reflex (C).

(30 - 100 msec.) during which their firing was unpredictable. These MNs were fired by low stimulus strengths i.e. low threshold MNs. The duration of the recovery fringe bore an approximately linear relationship to the recovery time (Fig. 41)

The recovery time of any MN was consistent throughout several testings so long as conditions were not changed. This means that a partially recovered H-reflex is always produced by the same MNs and not simply the same proportion of MNs.

An indication of factors determining the recovery time were sought. A clear tendency was observed that the MNs recruited in the H-reflex with weak stimuli giving a small surface potential recovered late, after 300 msec. Stronger stimuli recruited MNs which recovered earlier.

6.1 Factors affecting recovery of a single MN

The reproducibility of the recovery of each MN was quite consistent. The MN recovers after a certain inhibition time and this time may be shortened by factors such as the background activity of the muscle. As there is a linear relationship between the recovery fringe and recovery time, any change in the latter was always associated with parallel change in the former. It is worth noting that slight increase of stimulus strength to the MN did not cause it to recover earlier. On the other hand it shortened the recovery fringe considerably.

Mild tension of the body, head, or arm movements shortened the recovery fringe significantly and some MNs recovered earlier with these manoeuvres. During recording it was found that as the conditioning interval got nearer to the end of the recovery fringe, the

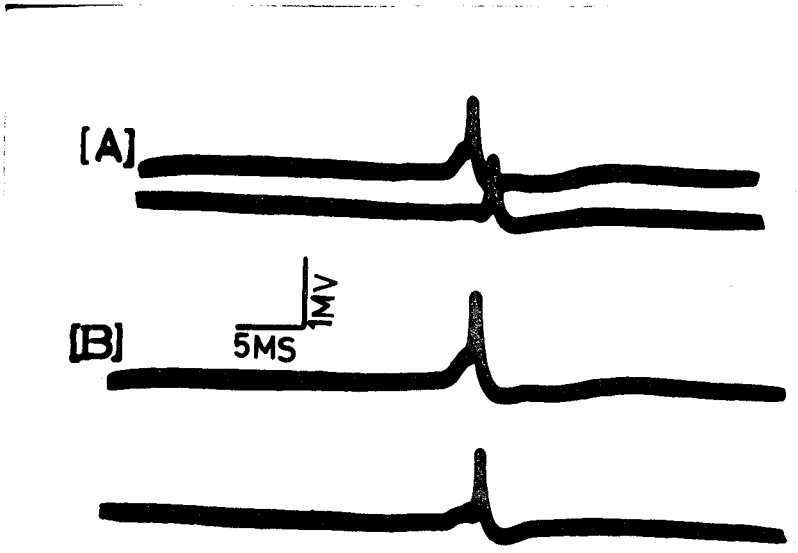


Fig. 43 At the recovery time (180 msec.) the test reflex had a longer latency than at the conditioning. When the conditioning interval increased to 500 msec. the latency difference decreased (B). (The beam was triggered by the stimulus artifact).

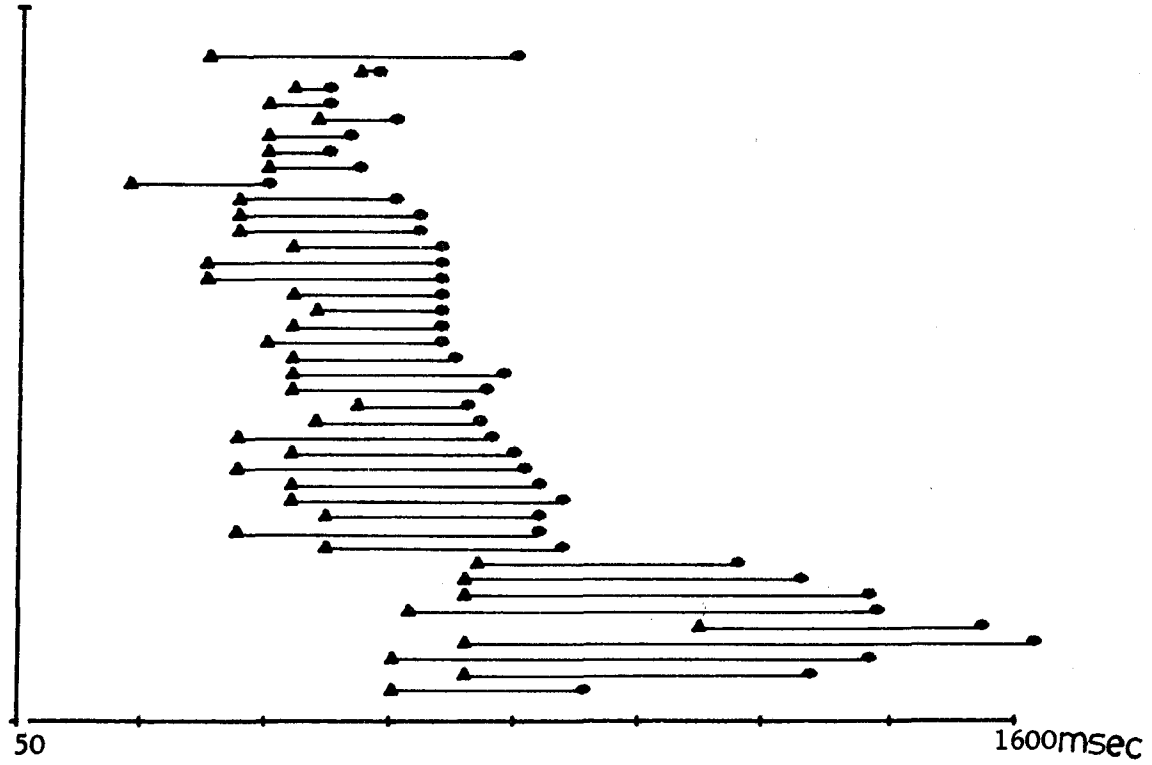


Fig. 44 The recovery time (*) shifted significantly earlier during mild contraction (▲). The longer the recovery time the greater the shift during contraction (41 units).

rate of recovery failure decreased to the minimum.

It is interesting to note that failure of the MN to fire following the conditioning stimulus does not prevent it from firing following the test pulse giving a H2. Some MNs failed to fire during H_1 but recovered normally during H_2 (Fig.42). This was frequently noticed and no additional factors were shown to affect it.

6.2 Recovery time and reflex latency

At the recovery time of each MN a slight increase in the latency was seen in the AP of H_2. It had a longer latency than H_1 (Fig.43). When the conditioning interval increased and the MN recovery became stable, the latency change decreased to the minimum (Fig.43) becoming the same as H_1. A gradual decrement in the latency change with increase of the conditioning interval could be recorded with more refinement of the method.

6.3 Recovery during muscle contraction

During contraction of the soleus muscle earlier recovery of the MNP was seen (Hoffman 1922). The change in the recovery interval depends upon the muscle tension (Hoffmann 1922). A set of experiments was constructed to evaluate the behaviour of the unitary parts of the MNP during contraction.

With mild isometric contraction of the soleus muscle, recovery of the single MN was earlier (Fig.44). The degree of the change was dependent on the type of MN fired. MNs which recover late and have a long recovery fringe, recovered earlier and with great reduction in the inhibition period, during mild contraction. Their recovery fringe becomes smaller with increased stability of recovery. The change in the recovery time was more than 100 msec. and sometimes shortened by 1000 msec.

MNs which recover early did not show much change in recovery time during contraction. In these MNs recovery changes ranged from 10 to 30 msec., but MNs with intermediate recovery time showed greater change in the inhibition period during contraction. It was quite clear that, the longer the recovery of the MN the greater the change, with earlier recovery, during contraction.

During recording, it was noticed that the greater change in recovery interval was dependent upon the muscle tension as well. This was difficult to record because of the recruitment of other MNs at higher tensions and electrode movements occurred and thus the unit studied was lost.

After muscle contraction stopped, the recovery time continued to be early for a short time after which it returns to its resting level. This after-excitability period continued for a number of milliseconds or even seconds and depends upon the period of contraction. The longer duration of contraction, the longer was the after-excitability period.

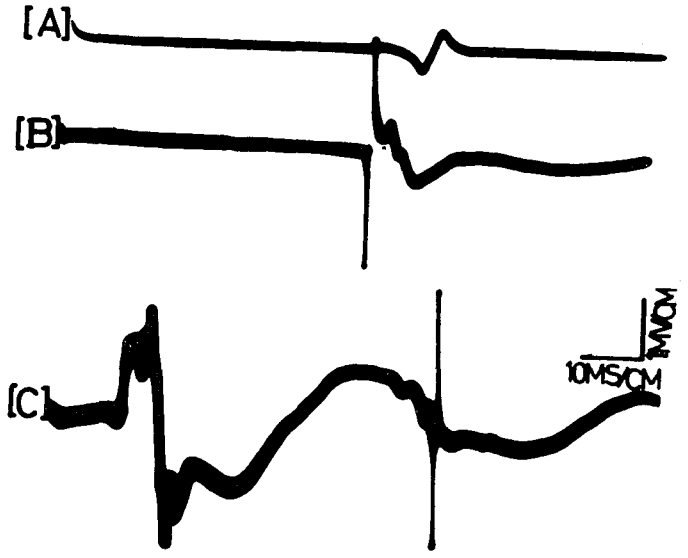
7. Recruitment order of motorneurones in single fibre H-reflex studies

The recruitment order of the MNs using H-reflex was studied by a stepwise incrementation of stimulus intensity with observation of the single MNs recruited. There were 32 sets of recordings available in this study. Fifteen normal young subjects with ages ranged from 18 - 30 years were tested.

7.1 Threshold of motorneurones

Motorneurone threshold was identified as low, medium, or high, according to its relative threshold to the muscle surface potential and the recruitment curve of the H-reflex.

Fig. 46 H-reflex study by SFEMG. The action potential of the whole MNP recorded by superficial skin electrodes (A) and consists of low threshold MNs fired first with just threshold stimuli and served by fast conducting nerve fibres (B), noticed no fibres were fired during M-response. With supramaximal pulses some of the MNs served by slowly conducting fibres were fired (C). M-response was fired at the beginning of the sweep.



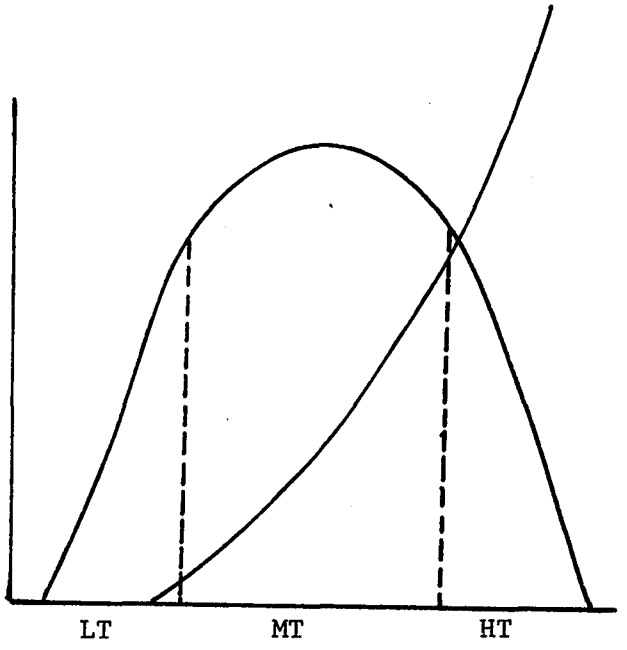


Fig. 45 Low threshold types of motoneurones were those which parallel the rising limb of the recruitment curve. High threshold types were those which parallel the decaying phase of the recruitment curve.

Low threshold MN were those which fired with small stimulus voltage so that no other muscle AP was elicited either at the single fibre electrode or on superficial recording.

High threshold MNs fire at high stimulus intensity at the time of the decaying phase of the superficial H-reflex. This situation was usually associated with a large M-response in the superficial record, as well as a large number of fibres recorded by the single fibre electrode at M-response latency. In this case the number of fibres recruited during M-response was larger than those recruited during H-reflex. This was due to blocking of the orthodromic pulses by the antidromic ones. A slight decrease of stimulus intensity allows more fibres to fire during the H-reflex, with obliteration of some M-response fibres. Fig. 45 shows the range from which different MN is sampled according to stimulus strength.

It was possible to record an AP from a single MN with a minimal stimulus strength which did not cause deflection with superficial recording. These MNs with such low thresholds could be recorded repeatedly with accurate placement of the stimulating and recording electrodes. It was easier to record from low threshold MNs because of the absent or slight interference from other excited MNs. Out of 123 single MNs isolated, 105 were classified as low threshold type. An example of low threshold MN can be seen in Fig. 46 .

High and medium threshold MNs were more difficult to record because of the interference from other excited cells, as well as from the M-response. The rejection of the electrode by the powerful contraction of the muscle, by high stimulus intensity, was a continuous restriction on stable recording conditions.

Out of 123 single MNs, there were 13 high threshold type and five with medium threshold. Fig.46 showed a high threshold MN fired with supramaximal stimulus strength.

7.2 Relationship between single fibre and surface potentials

Single fibre potentials were seen when no surface potentials were recorded at the gain used, therefore absence of surface potentials does not necessarily mean that muscle is entirely inactive. At these low stimulus strengths the MN with lowest threshholds are excited.

The single fibre potentials have a duration of $<$1 msec. whereas the surface potential has a duration up to 12 msec. (Hugon 1973). Therefore as the surface potential is a compound of individuals the individuals must have different latencies. Hence fibres can be referred to as early or late according to whether they fire early during the surface potential or later (Freund et al 1975).

It has been estimated by Stalberg et al (1970) that the conduction velocity in the efferent fibres inside the muscle was 13 m/sec. Such a low conduction velocity spreads the potentials in time and makes the interference from nearby fibres very small and unusual. It helps, as well, in the differentiation between the fast and slow MNs. However the potential field of the nearby fibres exists but accurate placement of the small leading off surface enables one to maintain a high ratio between the amplitude of the muscle fibre AP under study and the potentials from the surrounding motor units and other fibres overcame this problem. Again the small diameter of the leading off surface picks up the APs evoked at a very small distance from the electrode.

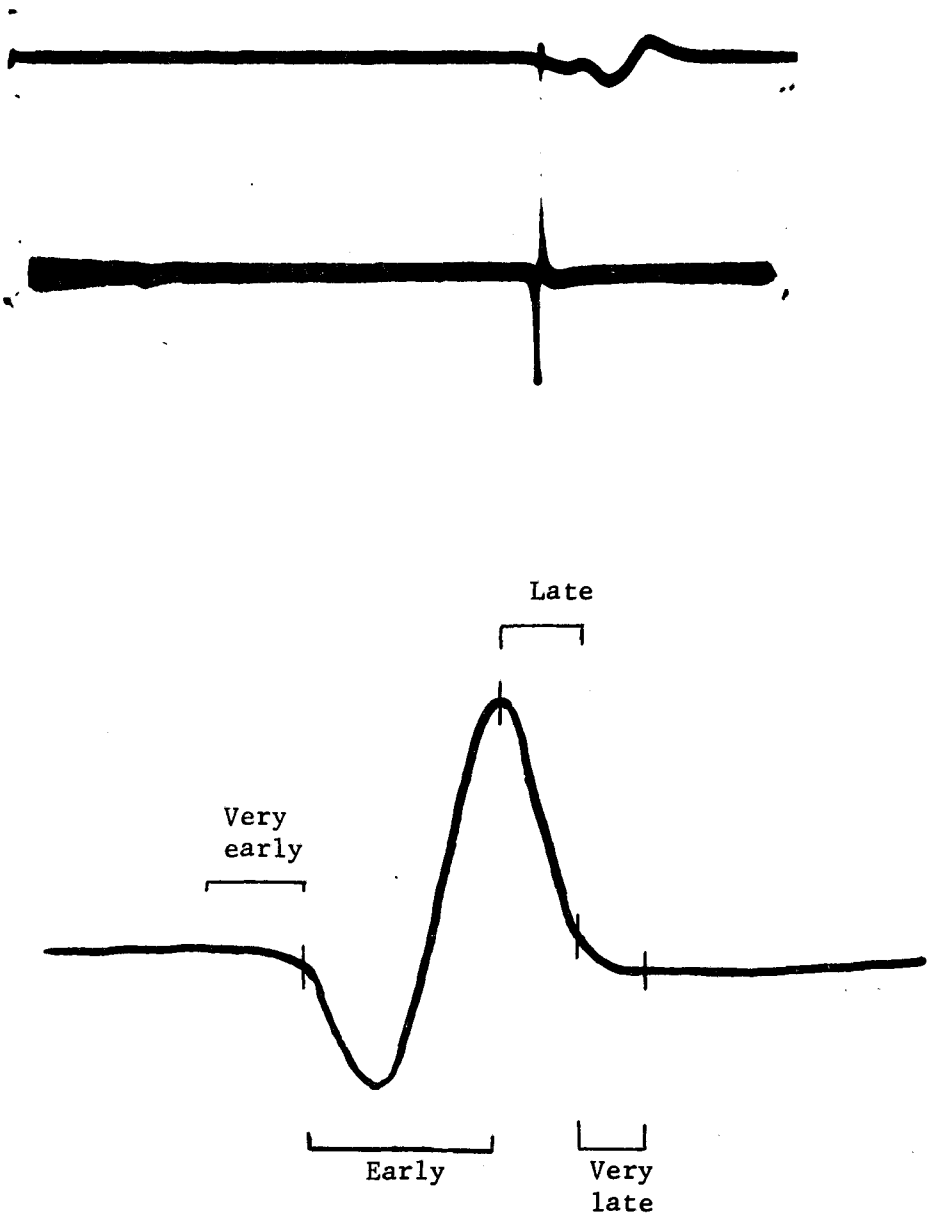


Fig. 47 The individuals of the MNP were compared to the superficially recorded action potential. Identification of the MN as very early, early late or very late indicates the relative conduction velocity of their axons and subsequently the type of the MN. An example of very early MN is shown above the schematic diagram.

Examiner's comment

While the conduction velocity of the motor axon contributes to the single unit H-reflex's latency one cannot argue that an early unit has a fast axon. Early responses would tend to result from highly excitable cells where the synaptic delay would be small. This could overcome any relative slowness in conduction velocity of the axon.

The evidence presented here against Henneman's size principle cannot be regarded too strongly in absence of any direct measurements of axon conduction velocity. Such measurements were attempted but failed.

Regarding the large distribution time of the superficially recorded potential (12 msec.) along which various individuals are fired, a clear identification of the extremes of the fibres spectrum can indicate different types of fibres.

7.3 Motorneurone threshold

Low threshold MNs excited with small stimulus intensity always had a latency ranging from very early to early (mentioned previously). Very early deflection of the single fibre in relation to the monitoring superficial record was often seen (Fig.47).

In 45 MNs tested for this study with low thresholds, 10 showed very short latencies with a deflection before the beginning of the superficial record. In 30 MNs the latency was short and synchronous with the rising phase (+ve going) of the superficial record. In 5 MNs out of 45 the SF reflex latency was relatively long and parallel to the later -ve going phase of the superficial recording. The SF latency was thus expressed relative to the total muscle activity. This set of experiments established that there is an orderly recruitment of MNs during H-reflex activity as measured by SFEMG. Further experiments to confirm this recruitment pattern were performed.

7.4 Recruitment of motorneurones excited in H-reflex

A stepwise incrementation of stimulus intensity fires low threshold MNs first with short latency. Sometimes two fibres of low threshold type were recruited with each other. The fibre with longer latency was always less stable and characterized by frequent failure of firing. This was because it was on the sub-

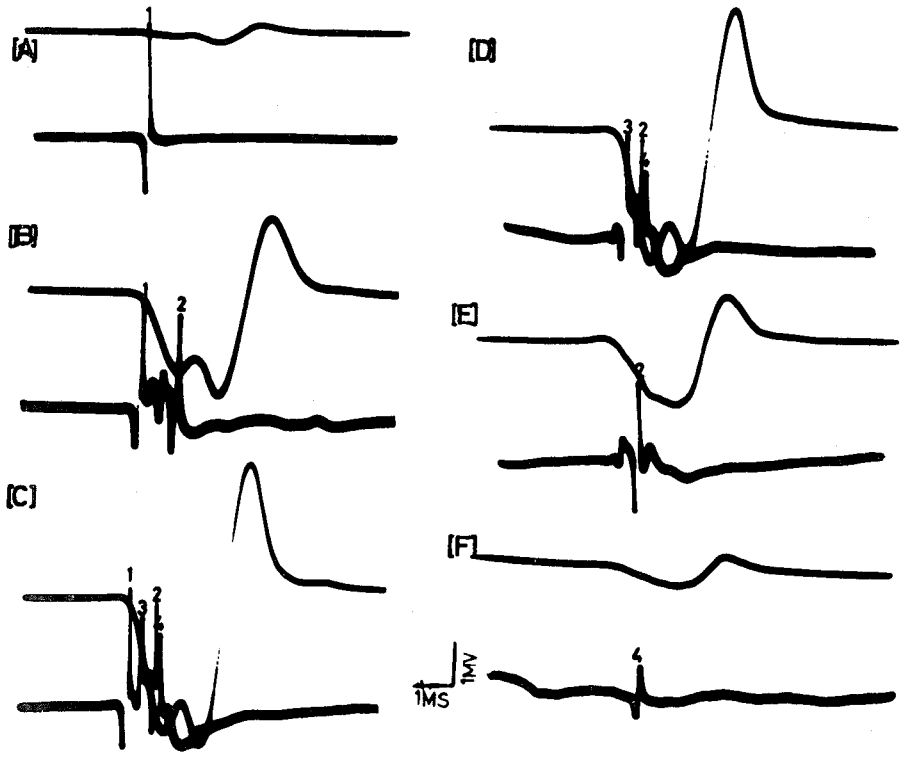


Fig. 48 Recruitment and blocking order of the motoneurones during H-reflex activity. Full explanations of the figure are presented in the text.

liminal fringe of firing. Mild increase in stimulus intensity fires more fibres which usually had longer latencies than those fired before. The newly excited MN did not affect the previously fired one, so that with high stimuli many muscle fibres adjacent to the leading off surface were excited, the latency of each depending upon the conduction velocity of its reflex arc and the threshold level of its MN cell. Failure of individual fibres within the population sometimes occurred. This failure frequently occurred in the newly recruited fibres. However, it was noticed to occur sometimes in fibres recruited at the beginning of the firing spectrum.

This recruitment order of the MNs with incremental stimuli is shown in Fig.48 and sampled from the soleus muscle of a normal young subject. Traces are in pairs, the upper trace for the AP recorded by the superficial electrodes, and the lower one for the single fibre recording. In this figure fibre 1 is recruited first with a very minimal stimuli. The superficial recording showed a mild deflection (A). Fibre 1 had a very short latency compared to the superficial deflection. It parallels the very beginning of the superficial record and showed no interference from other fibres. Slight increase in stimulus strength fired more fibres in the pool which increased the superficial deflection (B). The single fibre recording showed recruitment of a new fibre 2 with longer latency than fibre 1. However, the fibre first recruited does not show any change. It was clear that there were a number of other fibres recruited which did not appear in the single fibre record, maybe because they are a long distance from the leading off surface. With further increase in stimulation most of the MNP fired giving

a maximum H-reflex in superficial recording (C). Some of these fibres are presented in the single fibre recording as fibre 3 and 4. Fibre 4 had a longer latency than 1 and 2 previously recruited and followed the general order of recruitment. On the other hand fibre 3 fired with a shorter latency than fibre 2 and did not follow the general recruitment order. In this instance there was a general impression that this fibre (3) was recruited at the same time as fibre 2 in (B) and had a shorter latency, but failed to fire. This is justified by the small deflection seen in between fibre 1 and 2 which may have been fibre 3.

It was clearly seen from this figure that fibres fired in a certain order in relation to each other (single fibre) and to the whole population of the pool (superficial recording). Again this sample of fibres was seen to be some of the fastest fibres of the pool as it is presented in parallel to the beginning of the superficial record. All the other fibres in the pool were expected to fire with longer latency and distributed along the expansion of the superficial record i.e. should be recruited to the right of the sampled fibres. In some experiments latency difference of 9 msec. was seen between fast and first recruited fibre and slow and last recruited ones.

In some cases MNs with low thresholds fire with a very short latency followed by a high threshold fibre with long latency. Subsequent incremental stimuli cause newly recruited fibres to fire in between the previously fired ones.

In a few instances the fibres fired first had a long latency. This was followed by other fibres recruited with shorter latency.

Further incrementation of the stimuli recruited a third set of fibres in between the first two groups. This order was not frequently seen.

In summary therefore if the motor units were recorded in pairs or as a large group from the MNP, the order observed was (a) Low threshold MNs were recruited first (b) They were followed by the higher threshold ones with a longer latency.

7.5 Blocking order of motorneurones in H-reflex

Further increase of the stimulus strength caused the superficially recorded H-reflex to dwindle gradually. This was associated with gradual increase in M-response amplitude. In single fibre recordings the MN which fires first, in the recruitment order, is blocked first by increasing stimuli. This phenomenon followed precisely one fibre after the other up to complete blocking of all fibres at H-reflex latency. With supramaximal stimulation high threshold fibres were recruited with longer latency. These fibres were the last to be blocked and the first to be recruited with decrementing stimulus intensity. This is shown in the right column of Fig.48 . In (D) when the stimulation started to be supramaximal for the H-reflex, the superficial record showed slight decrease in amplitude (upper trace). This was represented in the single fibre (lower trace) record by blocking of some fibres. At this time fibre 1, which was recruited first in A, was blocked, leaving other fibres without change. Further incrementation of stimuli decreased the reflex in the superficial record (E). There was parallel blocking of fibre 3 but not other fibres. At this stage fibres 2 and 4 which fired later were still unblocked. In record E fibre 2 was fired, but 4 showed failure

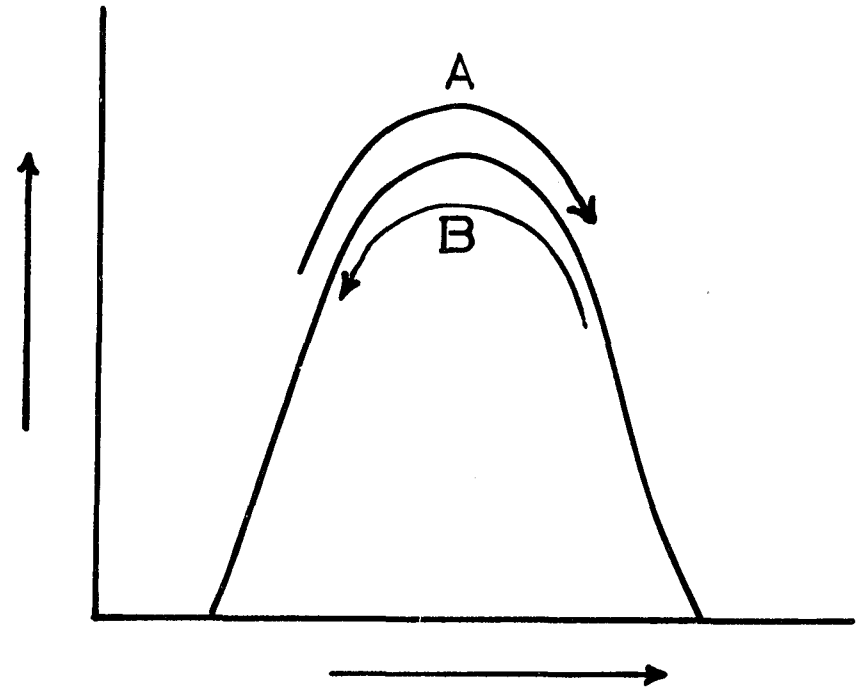


Fig. 49 Schematic diagram of the recruitment and blocking order either by incremental (A) or decremental (B) stimuli.

and not blocking. This is further supported by record (F) in which fibre 2 was blocked, leaving the highest threshold fibre 4 in the spectrum unchanged. This was associated with a smaller deflection in the superficial record.

Gradual decrease of the stimulus strength starting from a supramaximal pulses produces the opposite response. Recruitment of the high followed by the medium threshold fibres was the pattern noticed. This was followed by silence of the high threshold with firing of the low threshold MNs. The same pattern followed up to complete silence of all MNs in the muscle with subthreshold pulses. This reversed course is shown in Fig. 49.

These orders of recruitment and blocking of MNs in H-reflex were consistent in 28 sets of recordings out of 32. In three sets of recording the order was opposite to that explained before. In these few instances the low threshold fibres recruited first with long latencies followed by higher threshold ones with short latencies. There were some fibres recruited later with longer latencies so the usual pattern was not entirely reversed. In one set of recording the order was random and no pattern emerged. This was associated with firing of some fibres at short latencies followed by others at longer latencies. With further increase of stimulation newly recruited fibres were excited with short latency, so that there was no fixed behaviour in the recruitment pattern.

7.6 Inhibition order of motorneurones

Stimulation of the mechanoreceptors of the sole of the foot produces inhibition of the ipsilateral H-reflex (Sabbahi Awadalla & Sedgwick 1976). The order of this inhibition was further studied

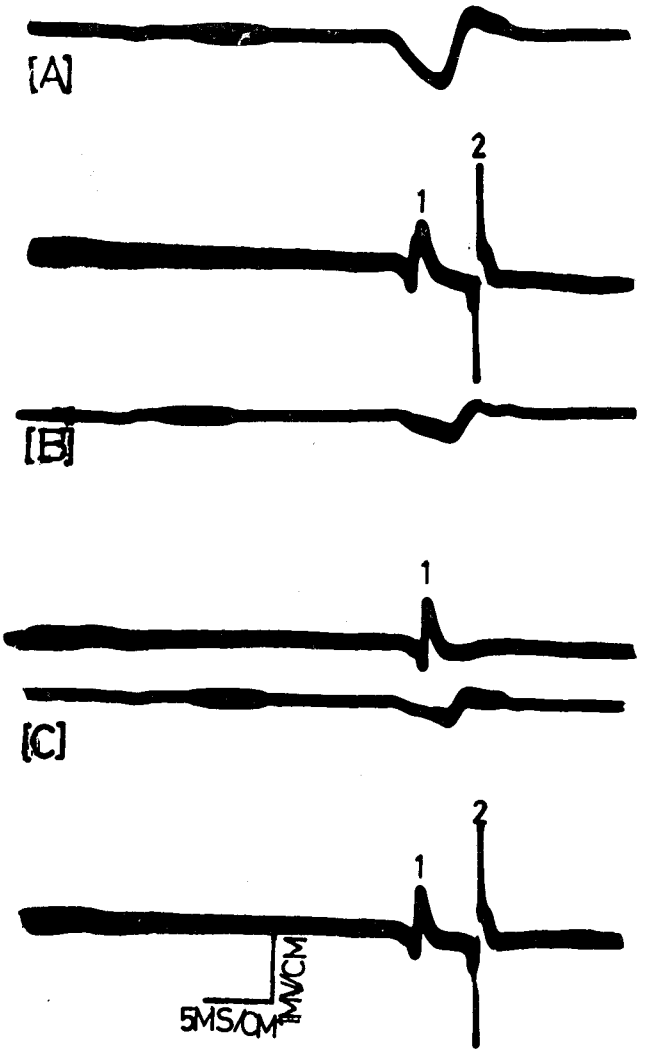


Fig. 50 Inhibition order of MNs by scrubbing sole of the foot. Two MNs were fired by stimulation (A). Scrubbing the sole of the foot produced inhibition of the superficially recorded reflex (B) (upper deflection of the pairs) with abolition of the last recruited unit (No. 2) while the other unit (No. 1) remains unaffected. After scrubbing the inhibited unit recovers (C).

by SFEMG to see which cells were inhibited first and whether there is any relationship between MN threshold level and its order of inhibition. Different fibres of various threshold levels were used for this study in which 17 units were available. Scrubbing the sole of the foot abolishes the last recruited fibre of a pair. This was the case in every manoeuvre whatever the threshold of the fibre. Consistent results were seen in 17 out of 17 sets of units studied. These were studied either in pairs or in a population of MN excited. More than 50 motor units, in all, were tested. This was associated with inhibition of the monitored superficial muscle record. The degree of inhibition in the superficial recording approximated the number of fibres abolished in the single fibre record. It depends on whether the whole sole was stroked or only a small area, whether the stimulation was mild or intense. Significant inhibition with abolition of a large number of fibres was seen with mild stroking over the whole area of the sole of the foot. Mild scrubbing of a small area inhibited only a few fibres sometimes one fibre only. That was usually the last recruited fibre in the potential. The order of inhibition was precisely opposite to the order of recruitment mentioned before. Fig.50 illustrates the inhibition order of MNs by scrubbing the sole of the foot in a normal young adult.

Inhibition of MNs by vibration of the tendoachilles was tried. Unfortunately movement of the SF electrode by vibration was a disturbing problem for this manoeuvre. In the few cases where the electrode did not move, the inhibition was complete and single units could not be compared.

8. Evidence for two types of motorneurones

From the previously mentioned data the MNs can be seen to behave in one of two ways. The borderline in between is not a clear cut one. But because the soleus muscle is considered to be a homogenous muscle (McPhedran et al 1965) it was difficult to call them slow and fast muscle fibres. It is perhaps safer to consider them as type B and C according to Henneman & Olson (1965). It has been shown by Johnson et al (1972) that the human soleus muscle contains only 13% of fast muscle fibres in its superficial layers and from which we recorded our samples. There was a possibility of recording from both these types of fibres. The characteristics of the two types of MNs from which we recorded our potentials were different and are listed below:

Character	High threshold units	Low threshold units
Threshold	High to Ia volley	Low to Ia volley
Latency	Long "late on surface record"	Short "appear early on surface record"
Collision blocking	Lost last on collision	Lost first on collision
Recruitment order	Recruit last	Recruit first
Recovery "at rest"	Early recovery with short recovery fringe	Late recovery with long recovery fringe
"contraction"	Shortened recovery only slightly	Shortened recovery, very markedly
Inhibition by mechanoreceptors	Inhibited first	Inhibited last

This is a tentative classification but the extent to which it can be sustained is considered in the discussion.

Discussion

The lack of information about the behaviour of single MNs in man makes it obligatory to depend upon information derived from animal experiments. The emancipation of the upper extremities from their role in progression in the quadripeds to manipulation in man as well as the intellectual development and corticalization of movement (Tokizane & Shimazu 1964) makes it potentially misleading to interpret human movements on the basis of animal experiments.

The development of recording techniques allows much more freedom in recording from single units in man e.g. single muscle fibre, by Ekstedt & Stalberg (1963), single nerve fibre by Vallbo & Hagbarth (1967), single MN by Trontelj (1968). This improves the understanding of the function of the MNP and some previous hypotheses have been abandoned e.g. muscle fibres subunit (Buchthal et al 1957), others need reorganization e.g. muscle spindle servo (Merton 1953, Marsden et al 1972) while other hypotheses were confirmed e.g. @ -γ linkage (Granit 1955) but need further elaboration.

In recording the AP from a single MN variations were seen in the reflex latencies. This was consonant with the previous findings of Trontelj (1969). It was attributed to the large fluctuations of MN excitability superimposed on the variations in the synaptic delay described by Eccles (1957) using intracellular recording of MSR in cat. Added to that is the latency variations due to the motor end plate, terminal nerve tree as well as any variation in the propagation velocity of the muscle fibre. The neuromuscular transmission variation was calculated from the jitter phenomenon and found to be 20 μsec. (Ekstedt et al 1973, 1974). Moreover the changes in the

propagation velocity of the muscle fibres did change significantly (Stalberg 1966, Stalberg et al 1971) with stimulation and exercises. Moreover the latency variation in the efferent segment of the reflex arc did not exceed 10% of the total variation (Trontelj 1969, 1970). Most of the H-reflex latency variation can be interpreted by events occurring at the MN especially the Ia - @ MN synapse. An obvious inference from the above results is that the H-reflex jitter could be used to indicate changes in the membrane excitability of the MN in some neurological diseases e.g. MND (Stalberg et al 1975).

It is probable that one of the important findings which indicates the level of the membrane excitability of the MN was the phenomena of occasional firing of a MN following threshold stimuli. At the threshold level, the H-reflex shows frequent failure. With stimulation slightly above threshold the number of failures was minimal. That is due to the spatial summation of newly activated Ia fibres and subsequently of more EPSP's (Coombs et al 1955, Eccles 1973, pg. 71). One could argue about the presence of active inhibition of the final discharge. This would be the case if the degree of inhibition predominates at higher stimulus intensities.

Evidence for summation

The previously mentioned results are perhaps more confirmed by the following findings in which two stimuli, both subthreshold to the firing level of the MN, resulted in its excitation giving an H_2 but not H_1 reflex. Temporal summation of the two EPSPs formed by the two pulses takes the MN to the critical firing level and this would occur if the time interval between the two stimuli

allows for addition of those EPSPs (Aidley 1975, pg. 133, 183). In fact this was the case in this work as the MN fires due to temporal summation over an interval of up to 12 msec. after which it fails. Such a long interval of time in which temporal summation is found to occur was interesting as the MN membrane must continue to be depolarized until the arrival of the 2nd pulse. One could argue that the first EPSP decayed quickly and that summation occurred between the EPSPs of the Ia polysynaptic potential evoked by the first pulse and the monosynaptic one by the second shock. The old idea that MNs are excited by Ia's only monosynaptically seems to be no longer tenable. Eccles & Lundberg (1959) noted some Ia monosynaptic post-excitatory potentials in interneurones. Later, MSRs especially of tonic MNs were found to be succeded by a number of polysynaptic wavelets in decerebrated cats by Tsukahara & Ohye (1964). In man (Lance 1965) as well as in decerebrated cats (Matthews 1966a, b, Anastasijevic et al 1968) the muscle spindle primaries were found to excite the MNs polysnaptically in the TVR.

Failure of summation in the first three msec. intervals is due mainly to the refractoriness of the Ia afferent nerve fibres by the first pulse (Pierrott-deseilleigny et al 1976).

Temporal summation was confirmed by using a subthreshold train of pulses preceding the test shock. The latter was subthreshold to the MN firing level, but when the conditioning train was added, the MN fired giving an H-reflex. This occurred at a long time interval, up to 15 msec. which is in accord with the previous findings. These results may indicate that the conditioning stimuli

either single or train, may excite the @-MNs through polysynaptic pathways.

When the stimulation intensities of the double pulses was low, temporal summation failed to fire the MN. Mild contraction or even a preparation for contraction of the calf muscle put the MN into action during H_2 and not H_1. This is due to spatial summation (Aidley 1975, pg. 184) of the corticomotoneuronal signals with the temporally summated Ia afferent pulses on the MN to make it fire. This shows the many-to-one nature of convergence onto the MN which is an important aspect of integration of the CNS and was discussed by Sherrington. The after excitability period in which this spatial summation occurred after cessation of contraction was presumably due to the after discharge in pathways involved.

Inhibition period of MN studied by SFEMG

When the MN, fired by a threshold stimulus preceded by a sub-threshold train of pulses, the previously mentioned temporal summation occurred which mobilized other MNs for up to 15 or 20 msec. after which this excitability ended. The MN under test was found to be inhibited for up to 50 or 70 msec. after which it recovered gradually. Here there is a period of reflex inhibition of the MN in which the tested MN was completely silent. It is probably due to reduction of transmitter availability at the synaptic junctions (Taborikova et al 1969, Curtis & Eccles 1960) as was proved before. It is not due to building up of the secondaries effects of inhibition on the MN as was reported by Magladery et al (1951). This would be the case only if the inhibition started earlier during using the

pulse train used for conditioning. It is unlikely to be due to autogenetic inhibition (Haase et al 1975) as the conditioning train was subthreshold to the reflex activity which excludes the intervension of the golgi tendon organs. However Laport & Lloyd (1952) found that feeble electrical conditioning curtailed the MSR facilitation and resulted in complete inhibition with even higher pulses. McLeod et al (1967) clarified the reflex effect of the muscle contraction (recurrent discharge) on the recovery curve in deafferentated cats and found it to affect the late part of the inhibition period. This confirms the earlier findings of Denny-Brown (1928), Holmgren et al (1954) in deafferentated cats. However the findings that in UMNL patients, this period was shorter than normal (Magladery 1955) demonstrated the supraspinal effect on the late section of the inhibition period as well. This does not exclude the effect of the Renshaw cell inhibition which may continue for up to 40 or 50 msec. (Renshaw 1941, Lloyd 1946, 1951). The early part of the inhibition period could be strongly affected by Renshaw cell activity (Eccles et al 1954). Moreover one could argue about the MN membrane hyperpolarization and refractoriness (Eccles & Sherrington 1931, Eccles 1931) being one of the causes of the inhibition period. However the fact that the pulse train was subthreshold for the MN firing; this in conjunction with the MN firing for the first 20 msec. after the train excluded this assumption. Moreover later in this section we will find no relation between the after hyperpolarization and the MN type during recovery which is evidence against the inclusion of the after hyperpolarization in the inhibition period.

In conclusion it is very unlikely that only one factor either from the peripheral or central NS can account for the period of primary inhibition.

H-reflex blocking with supramaximal pulses

One of the important phenomena studied by SFEMG was the blocking of the H-reflex by supramaximal pulses. The assumption of Hoffmann (1918) about reflex extinction by collision was held for a long time. This was confirmed by Magladery et al (1951) by recording of the anterior root potential with subliminal stimuli. The latter reduced in amplitude gradually with higher stimuli and it was possible to record dorsal root potential with these supramaximal pulses. However this does not exclude the Renshaw cell inhibition (Renshaw 1941).

. On the other hand Eccles et al 1954, Holmgren et al (1954) could find no recurrent inhibition in some 20% or more of the @-MNs. Moreover Kuno (1959) noted that stimulation of the medial gastrocnemius nerve inhibited about 25% of the soleus MNs. This means that a considerable number of MNs lack the recurrent inhibition, but still the H-reflex was blocked in all MNs with supramaximal pulses.

In this work the finding that the single muscle fibre fired during H-reflex and M-response at different stimulus intensities

provides evidence for the collision in the MN axon to account for the reflex extinction. With recurrent inhibition it was expected that the same MN would fire sometimes during the H-reflex and the M-response at the same stimulus strength. This was never found in any of the MNs tested. The accurate matching of the H-reflex and M-response firing of the same MN clearly indicates collison as the main factor for this block of the reflex. It is difficult to identify exactly the collision site whether in the axon (Magladery et al 1951) or the somata (Paillard 1955, Taborikova et al 1968, Mayer et al 1965). However if we relied on the threshold level of the afferent and efferent fibres to determine the conduction velocity it would be safe to note that the conduction velocity in the fast afferent fibres was conducting the H-reflex volley faster than the motor axons. The threshold level of the motor axon was much higher than that of the Ia afferent. It has long been held that the large diameter fibres have a lower threshold of electrical stimulation (Matthews 1972, pg. 334, Lloyd 1943, 1946) and conduct impulses more rapidly than small ones (Erlanger & Gasser 1937). This makes it more likely that the collision of the antidromic and orthodromic pulses occurs in the anterior root more than the somata. However this assumption needs more direct experimentation to measure the conduction velocity in the motor axon and the Ia of the reflex arc.

With increasing supramaximal stimuli the H-reflex of different fibres blocked in a certain order which was intimately related to the order of MNs recruitment. This will be discussed later.

Recovery order of MNs forming the pool

The recovery of different MNs after the inhibition period was characteristic for each MN. Some of the MNs recovered after an inhibition period of 80 msec. while others recovered after 1000 msec. It was found that the MN which was recruited first with increasing stimuli, , recovered late after a longer inhibition period. The opposite was the case with the more tonic MNs. This indicates a higher excitability in the tonic* MNs to a Ia volley than the phasic ones, a finding which is in accord with those reported in cats (Henneman et al 1965, Somjen et al 1965, Burke 1968). Moreover Kernell 1966 & Burke (1967) found that the total membrane resistence was greater in the small (tonic) more than in the large (phasic) MNs which implies that to the same currents the small cells would be more excitable than the large ones. Takahashi (1965) reported similar results for the cortical pyramidal cells. These are the tonic MNs which form most of the MNs recovered along the recovery turnover point in the excitability cycle. This part of the cycle exhibited significant changes in the UMNL (Magladery et al 1951, Illis et al 1976), cerebellar diseases (McLeod et al 1969) and dystrophia myotonica (see dystrophia myotonica section). It showed significant changes in

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* Neurones are considered "more tonic" or "more phasic" as a relative rather than an absolute division of their properties.

elderly subjects as well (see above results of old age). This reveals the higher sensitivity of these tonic MNs which are heavily used when compared to phasic MNs (Henneman 1974). In dystrophia myotonica Brooks et al (1969) reported degeneration in the small motor units of the affected muscles which indicates a selective disturbance to the tonic MNs. We have noticed similar findings in old aged subjected; a suggestion has been put forward that degeneration is most likely to occur in the tonic MN and this is based on changes in the recovery curves.

Eccles et al (1958) and Kuno (1959) reported a longer duration after potential or post-spike hyperpolarization for the tonic MN than the phasic ones. This was confirmed later by Kernell (1965) and Burke (1967). Furthermore Kernell (1965) emphasized the relation between the after-hyperpolarization duration and the rate at which MNs respond to steady transmembrane stimulation and concluded that cells with longer after hyperpolarization exhibit lower maximal firing rates and less variations in firing intervals than cells with shorter after-hyperpolarization. It seems probable from these findings that the after-hyperpolarization duration does not account for the inhibitory phase of the MN during recovery, as the tonic MNs were more highly excitable and recovered first after a shorter inhibition period than the more phasic ones. It is perhaps more difficult to relate the firing rate of a MN to its recovery after electrical shock. The electric shock is an unnatural code to the spinal centres and as stated by Sherrington (1906), pg. 12, "Electricity is always an artificial form of stimulus" and the output discharge may account for the "sensible answers" of the spinal

centres to the "stupid question" (Matthews 1973, pg. 333).

The recovery fringe may indicate fluctuations in excitation or inhibition (Mayer et al 1965) which normally control MN discharge. Our findings on the recovery fringe could be a reflection of variable firing rates found by Burke (1973) in phasic as apposed to tonic MNs. Related changes were also observed by Kernell (1965). The recovery fringe time for tonic MNs ranged from 2 to 20 msec. while that for the phasic MNs reached 100 msec. or even more, which may cause higher variation in the firing intervals of the latter type. The recovery fringe was intimately related to the MN type so that the whole MN population forms by conjunction of its different types a continuously linked and homogeneous entity. This recovery fringe was similar to the critical firing level described by Henneman's group (Henneman et al 1974) in decerebrated cats using different methods for measuring the rank order of MNs in the MNP. They noted that the MNs with lower critical firing levels were more excitable which supports our results in terms of smaller recovery fringe being linked to more highly excitable MNs.

Mild increase in the stimulus strength shortened the recovery fringe but not the recovery time, a finding which provides evidence for the recovery time depending upon the membrane resistance of the MN (Kernell 1966, Burke 1967). If this is the case, the recovery time and the recovery fringe could mean variations in the membrane resistance of different MN in the soleus muscle and supports Kernell's finding (1965) that tonic MNs have a higher membrane resistance than the phasic MNs.

The recovery study of the MNs of the soleus muscle in this work showed that most of the MNs were of tonic type which is in accord with the findings of other workers (McPhedran et al 1965, Burke 1967, Burke et al 1973) but still the spectrum shows phasic types of MN. The few MNs of the spectrum end have more phasic properties and are considered as phasic MNs. The finding that some MNs do not recover before 1000 or even 2000 msec. stresses the importance of elicitating the reflex every five seconds in the H-reflex methodology to ensure recovery of all MNs. Most of the MNs recover in the first 250 msec. which coincides with the recovery measured by superficial recordings. At such time the MNP showed recovery of the majority of its population.

The test reflex had a longer latency than the conditioning especially when the MN was still in the recovery fringe time i.e. the MN just recovered. As the interstimulus interval increased, the reflex latency decreased toward normal value gradually. This may indicate invariability in the transmitter substance, by the conditioning shock, at the synaptic knob (Refer to section of the recovery of the MNP). During recording we noticed that there is an inverse linear relationship between the interstimulus interval and the prolongation in the reflex latency. This could be measured accurately with more refinement of the technique but this was not pursued.

Recovery during mild contraction showed great changes in the recovery time of the MNs which became earlier. This indicates a spatial summation at the MN of the afferent and supraspinal signals.

The increase of the excitatory inputs on the MN overwhelms the inhibitory ones which causes the MN to recover earlier than during the resting state. The excitatory supraspinal inputs compensate the decrease in the transmitter organization in the Ia-@ MN synapses, thus causing an earlier recovery by firing the more excitable MNs i.e. the more tonic.

The earlier recovery of the MN during contraction could be explained in the light of MN firing by summation of subthreshold afferent pulses and subliminal contraction which was mentioned previously. In the former case (MN recovery) the lack of MN excitation in the recovery was mainly due to the disorganization of transmitter substance release whilst in the latter case i.e. MN firing by summation, the MN silence was attributed to the lack of the excitatory inputs. Moreover it is important not to forget the contribution of the γ-loop in the earlier recovery, shown during contraction. The sensitization of the muscle spindle and the increase in its discharge by the γ-bias (Matthews 1972, pg. 251), in addition to the spindle's increased recurrent discharge following the conditioning pulse (McLeod et al 1967) would shorten significantly the recovery time of the MN when the muscle was minimally contracted.

The finding that phasic MNs recovery time changed dramatically during contraction compared to those of the tonic MNs was of much interest. This indicates the powerful driving of the phasic MNs by the cortical influence more than the afferent influence (Denny-Brown 1929, Burke 1973). It has long been held that MNs innervating

slowly contracting muscle are more powerfully excited by muscle spindle afferents than are the cells of rapidly contracting muscle and extends this conclusion to the population of fast and slow motor units residing within a single mixed muscle. This may be attributed to the quantitative (Burke 1968a, b, Burke 1967, Rall et al 1967, Jack et al 1970, 1971, Porter et al 1969, Kuno et al 1969, Mendell et al 1971, Burke 1973) and qualitative (Creed, Denny-Brown, Eccles, Liddle & Sherrington (1932), pg. 73-77, Preston et al 1963, Bosemark 1966, Hongo et al 1969, Rosenberg 1970) difference of the synaptic inputs on the MN from the spindle afferents and supraspinal centres. This was applicable to our work as the tonic MNs recovered earlier because of their higher excitability and their powerful excitation by spindle afferents. Their recovery does not change significantly with cortical influence during muscle contraction. The case was opposite with phasic MNs which recovered later during resting state and very much earlier with contraction.

It is interesting to note that the recovery fringe was intimately related to the recovery time regardless of whether the MN recovered during resting state or during contraction. This indicates that the recovery fringe is a property of the excitatory level of the MN more than a property for the MN itself. With low excitability level of the MN there was a high variation in the firing while during high excitability level there was much lower variation. As the tonic MNs are highly excitable, by their inherent properties, the changes in the variation of the firing condition were not significant as the phasic MNs.

Relative difference of muscle fibre in the pool

During superficial recording of the reflex AP of the whole MNP, the AP duration was up to 12 msec. (Hugon 1973) while the AP duration of a single muscle fibre was less than a millisecond (Ekstedt & Stalberg 1973). Presumably the temporal relationship of the single muscle fibre AP to the whole muscle AP is fixed and considered theoretically a minute fraction of the whole (Fruend et al 1975). The muscle fibre which fires early in relation to the superficial recording indicates that it is supplied by a fast conducting motor axon which is connected to a more phasic MN (Henneman et al 1965). The muscle fibres which fire later indicate a slowly conducting motor axon and a more tonic MN. Of course this is a more relative classification and not an absolute one. One could argue about the relative contribution of the temporal fibre distribution around the leading-off surface to yield some discrepencies in the data measured by conduction velocity. However the finding that the different motor units interdigitate with each other (Warmolts et al 1973, Stalberg et al 1976), the exponential reduction of the AP amplitude with greater distance of the leading-off surface from the generator potential (Lornte de no 1947), the small latency difference recorded between single fibres relative to the very slow terminal conduction velocity (13 meter/sec., Stalberg et al 1970), all are in support to our data.

In recording the AP from a single MN, each single MN had a constant threshold level provided that the subject was completely relaxed. This was similar to the finding of Henneman et al (1974) as each MN was shown to have a rank order of firing within the pool.

They mentioned an uncertain range, during which the MN firing was unpredictable, with a critical firing level at its centre. This uncertain range was noticed during gradual incremental stimuli to the Ias, and just before firing level of the MN. In our results such an uncertain range has not been found during routine recording of different MNs, but similar findings were noticed during the more detailed studies of MN recovery and there uncertainties made up the recovery fringe.

The clear threshold difference between the H-reflex and the M-response and the possibility of recruiting a large fraction of the MNP (Taborikova et al 1968) was of prime importance in testing the behaviour of these MNs without interference from other muscle APs. The nerve fibre diameter and the variation in the conduction velocity of the fibres which give varying thresholds was of use in selecting different MNs (Rexed 1948, Granit et al 1956, Wuerker et al 1965). The more phasic MNs sending their AP through a fast large diameter motor axon while the more tonic MNs' AP are served by slow and small diameter motor axons (see above for references). It becomes certain now that each type of MN receives synaptic inputs from all afferents so that each MN receives a share of the afferent inputs (Burke 1973).

Evidence for recruitment, blocking and inhibition order

The existence of different types of motor unit with intimately related physiological properties raises the important question of how the CNS exercises control over the muscle apparatus. The order of recruitment of motor units and hence MNs in willed movement was of special interest and contributes to the debate on Henneman's

principle. Henneman and his group (1965), studied recruitment order extensively in decerebrated cats, recording from a dissected ventral root, either in response to intracellular stimulation (Henneman et al 1965a), reflexly due to stretch of the triceps surae muscle (Henneman et al 1965b) or in response to stimulation of the supraspinal centres (Somjen et al 1965). It was found that the small tonic MNs were recruited first followed by the larger phasic ones regardless of the type of synaptic drive. This was confirmed by many authors (Ashworth et al 1967, Burke 1967, Burke et al 1971, 1973, Fruend et al 1972, 1975, Milner-Brown et al 1973, Gydikov et al 1972). However this stereotype of recruitment order cannot match the variability in the afferent discharge. Changing proprioceptive afferent pulses in normal man is always followed by changes in the recruitment order of the MNs (Grimby & Hannerz 1968, 1973). Significant effect was found of the pre-movement state of the subject on the recruitment order (Hannerz et al 1973). The stability of the recruitment order depends upon whether the subject expects the stimulus or not, facilitating or inhibiting the MNP, blocking of the proprioceptive afferents or incrase their discharge, so that it was concluded that the normal man selects the recruitment order which is suitable for the motor act.

In willed gradual isometric or slow isotonic contractions recruitment of tonic followed by phasic MNs was seen. First because the high excitability of the tonic MNs, its long duration of contraction and its fatigue resistance (Burke 1967, 1973). The tonic was followed by the more phasic MNs at a higher level of

activity because the latter has a higher twitch tension (Wuerker et al 1965, Buller et al 1965). With fast movement this recruitment order does not fulfil the functional requirements. If the phasic MNs were recruited first followed by the tonic ones the organism would be able to cope with other external demands. Providing a suitable order to match external requirements seems to be a function of the CNS as it has a different type of mechanical apparatus "muscle fibres" at its disposal. This matching mechanism could be one of the higher functions of the nervous systems.

In this work we noticed that during reflex activity the more phasic MNs (B fibres) were recruited first followed by the more tonic ones (C fibres). The results were highly significant and a clear identification of various APs was one of the strengths of this technique. This recruitment order of phasic followed by tonic MNs was continued with recruitment of the more tonic MNs on higher stimuli until all the muscle units around the leading off surface were recruited. Our results confirm those of Grimby & Hannerz (1968), (1973), as the H-reflex, being a monosynaptic reflex, traces the fastest pathway at the spinal level and makes the stereotyped tonic-phasic MN recruitment order does not cope with the functional requirement of a fast response. In man Ashworth, Grimby & Kugelberg (1967) compared voluntary polysynaptic reflex activation with monosynaptic activiation of MNs and found that "in most instances identical units responded and in the same order independently of the mode of excitation" (pg. 96). However these structural hierarchies did not hold for some 20% of their motor units and the order of recruitment could be overruled by voluntary action and by

combining reflexes. Continuing their work by taking 200 recordings from tibialis arterior motor units Grimby & Hannerz (1968) could distinguish "A" units, which discharged only once or twice at the onset of contraction, from "B" and "C" units which took over with maintained contraction. The "B" units fired at rates of about 10/sec., the "C" units at about 6/sec. Stretch of an active muscle excited the "B" and "C" units. A long lasting vibratory reflex was carried by "C" units. An injection of lidocaine around the distal part of the muscle nerve made this discharge irregular (Tokizane & Schimazu 1964). "A" units were found responsive to the velocity of initiation of a contraction. In a more recent paper Grimby & Hannerz (1970) found the order of recruitment variable in phasic reflexes.

Granit et al (1973) stated "If very fast action were required in a particular movement, the force velocity properties of muscle fibres innervated by Small MNs might be ill-suited to the demands of the movement". Such a switching on mechanism, mentioned previously, was observed in the early decades of this century in Sherrington's laboratory (Creed, Denny-Brown, Eccles, Liddell & Sherrington 1932) in decerebrated cats as they noticed activation of fast muscle units and silence of slow one when the animal exhibited sudden jumping movement. Recently Marsden described similar observations in human's hand muscles (see conference report of "The control of movement and posture" by Granit & Burke 1973). Moreover Wyman et al (1974) did not find a fixed order of recruitment for the MNs in cats.

An obvious inference from the above results, one can postulate that in isometric and slow isotonic contraction, the order of tonic-phasic MNs recruitment fulfils the functional requirements of the movement. This is because of the higher excitability of the tonic MNs, graded increase in the force needed and the requirement for a fatigue resistance and slow contracting muscle units to cope with the movement. In the stretch reflex and possibly in the fast isotonic contraction, on the other hand, this order does not fulfil the functional requirements of the movement. A fast, short in duration and relatively more forcible contraction is needed to correct the disturbances in a movement. This would explain teleologically the phasic-tonic order of MN recruitment. "The functional requirement determines the order of recruitment of the MNs". This was confirmed by the statement of Granit et al (1973) "It seems possible that the fast twitch MNs capable of producing considerable force might initiate acts characterized by such requirements, while other sorts of movements would begin with mobilization of the small MNs, innervating slow twitch muscles and capable of long lasting tonic activity of low discharge rates."

According to this assumption the different MNs with their specific behaviour will be a tool of the switching on mechanism. If this is the case the assumption of Henneman and his co-workers (1965) that the phasic and tonic properties are not a fixed property of different MNs, is no longer tenable. We assumed that these properties are rather fixed ones and switching on different MNs is a mechanism sensitive to external demands. They stated "A cell

may respond in either mode according to the prevalent level of excitation". This is unlikely because in a quick forcible movement neither the velocity nor the tension of the muscle units of the tonic MNs will be suitable for the movement, even if they work phasically. The switching on mechanism which has been reported before emphasizes that human subjects can silence some early firing MNs in a preference of a late one (Kato & Tanji 1972, Basmajian 1963).

Somjen (1972) commented on the recruitment order of MNs put forward by his colleagues Henneman and by himself saying "It expresses a correlation not a law". He noted that there must be a physical factor which determines the firing of the MNs. If very powerful inputs are channelled to large neurones they may well excite a cell so singled out in preference to another. In fact there have been reports of the existence of "giant" synaptic endings, the action of which could enslave one neurone to another. The synaptic organization may play an important role in preference of MN firing on another (Burke 1973).

However Henneman et al (1965) found that the tonic-phasic recruitment order was the one observed during stretch reflex in decerebrated cats. They used the amplitude of the AP as an index of the MN size. In spite of the fact that the potential amplitude was found to be a good index of MN size in dissected anterior root (Granit 1970, pg. 12), it has been shown that it gets smaller as the recording electrode moves away from the potential generator (Lorente de No 1947). This calls into question the amplitude as

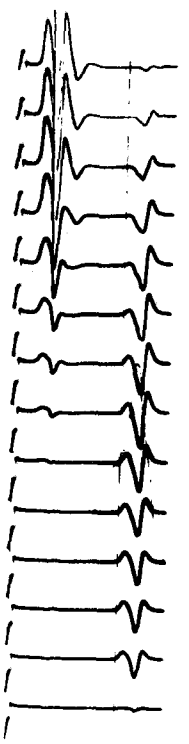


Fig. 51 Increasing stimuli while recording of the H-reflex showed no significant change in the latency of the rising phase. The continuous line showed that the rising phases are always of the same latency until blocking occurs.

a true index of the MN size. In our work the AP latency, compared to the whole MNP and to the other APs of the nearby muscle units to the leading off surface was used as an index of the relative MN size. The fact that large MNs are connected with large fast conducting motor axons validates the latency measurement as an index of the MN size. One could argue about the validity of the superficially recorded reflex potential as a control measure upon which different single fibres could be estimated for latency. If the superficially recorded reflex latency changed significantly with incremental stimuli it will not be suitable as a control for such measurement. For checking this phenomenon the following experiments were performed.

A superficially recorded H-reflex was photographed with gradual incrementation of stimuli looking for any change in the latency of the rising phase. The result of this experiment is displayed in Fig. 51 No significant change has been noticed in the reflex latency which is in support of our findings.

Moreover APs of single muscle fibres were compared not only to the superficial record, but also to each other so that the more tonic MN had a longer latency compared to the others. This validates our measurement regardless of whether any changes occur in the superficial record. Of more importance was the latency difference between the first MN fired and the last one. In some records the difference was of 9 msec. or even more which indicates recording from a very large and very small MNs in the pool. Grillner & Udo (1970) found that the recruitment order is highly non-linear so that most of the MNs are recruited at the beginning of the contraction.

In fact this was observed during recording and made it possible to compare a large fraction of the MNs from the pool before any possible change in superficial reflex latency on supramaximal pulses.

Moreover Henneman et al (1965) were studying MNs in pairs, one large and one small, which does not give an insight into the behaviour of the whole population of the MNP. In our work scanning of a large fraction of the MNP made possible a more valid comparison.

Henneman's group used decerebrated cats which were deprived of the cortical integrative mechanism. The organization of the suitable recruitment order in response to functional requirement was assumed to be lost in decerebrated cats. The disturbances in the recruitment order in spastic and parkinsonian patients (Grimby et al 1973) is also attributed to pathology of supraspinal centres. In our studies normal human beings were investigated using the fastest spinal monosynaptic reflexes. It is difficult to rely on cross species assumption to interpret results from humans. Granit et al (1973) stated "It is impossible at the present time to identify the motor units recorded electromyographically in humans in terms of their probable physiological and histochemical characteristics. The relation of such data to the recent results from animal experiments remains speculative." On the other hand Buchthal et al (1970) reported an order in which the tonic MNs were recruited followed by phasic MNs in soleus muscles while they were recording H-reflex. In their study the duration of

the mechanical tension was used as an index of the motor units recruited. It was not possible to identify individual motor units from the whole muscle torque by such an indirect technique, which makes their results more speculative. Moreover the increase in the reflex duration upon which Buchthal and his co-worker relied to interpret for the slowness of the soleus muscle units, is mainly due to the assynchrony of the MNs firing (Taborikova & Sax 1968) and the difference in motor axons conduction velocities. These important points should be taken into consideration when using the reflex duration as an index for MNs and muscle fibres characteristics measured in this way.

The fact that our record was taken from the soleus muscle recalls the question of the validity of this muscle for such study. It has long been held that the soleus is a homogeneous muscle. However Padykula and co-workers (Nachmias & Padykula 1958, Stein & Padykula 1962) distinguished three types of fibres A, B and C in mammalian striated muscle on the basis of staining for glycogen, succinic dehydrogenase, adenosine triphosphatase and non-specific esterase. Romanul (1964) separated eight types from A to H but later collected them in three groups. Of Stein & Padykula's three types A, B and C were found in the gastrocnemius, B and C in the soleus of the rat and cat. This was confirmed by Ogata and Mori (1964) in rats and by Henneman & Olson (1965) in cats. The three fibre types of Padykula's group were confirmed by another histochemical approach based on the appearance of differential enzymatic changes after induced muscular activity (Edstrom & Kugelberg 1968, Kugelberg & Edstrom 1968). The histochemical properties indicate

that white fibres (type A or I) have high glycolytic, low oxidative and high myofibrillar ATPase activities, that the intermediate fibres (type B or II) have low glycolytic, intermediate oxidative and low myofibrillar ATPase and that the red fibres (type C or III) have intermediate glycolytic, high oxidative and high myofibrillar ATPase activities (Close 1972). Furthermore Johnson et al (1973) reported that the superficial layer of the soleus muscle, from which recording was performed, contains 14% of fast muscle fibres similar to type A fibres of Padykula's classification. Buller (1965) stated "Indeed at the present time it would seem unwise to consider any mammalian muscle as composed of a homogenous group of motor units, at least as regard speed of contraction". Buller et al (1959) did not find a clear cut differentiation of gastrocnemius and soleus into fast and slow contracting muscle respectively in humans. If the soleus is considered to be a purely homogeneous muscle the fibre spectrum which is responsible for different functions will yield data about parallel spectrum of MNs in the spinal cord. However in this context Padykula's classification will be used as the soleus contains type B and C muscle fibres.

MNs blocking order in the H-reflex

The MNs blocked in a certain order with supramaximal stimuli. That is, MNs recruited first blocked first due to collision in the same neurone. When the threshold stimuli reached the level of the motor axons it excited them in a certain order, according to threshold and therefore fibre size, the large diameter first followed by the smallest. Thus blocking is likely to occur in the more phasic MNs followed by the more tonic ones. This is shown by a new piece

of evidence, the recruitment order, mentioned previously. As the order of MNs blocking and recruitment was similar and with the support of the previously mentioned facts one is tempted to think that the recruitment order is a mechanism of choice of the spinal cord while that blocking order is attributed to peripheral factors. The inhibition order, on the other hand, was opposite to the recruitment order as the MN fired last was inhibited first by scrubbing the sole of the foot. This is due to active inhibiting factors (see above results of natural stimuli), on the MNP, by the effect of the mechanoreceptors. It seems probable that the inhibitory mechanism manipulates the MNP in a sequence depending upon the axcitatory state of its individuals so that the last recruited MN, which is more likely the less excited cell of the pool, is inhibited with mild scrubbing while other MNs are inhibited only with intense scrubbing. This was in accordance with the findings of Clamann et al (1974) as they reported that every increase in the excitatory stimuli applied to a discharging MN required a proportionate increase in the inhibitory stimuli required to silence that unit. Furthermore this order was similar to what has been found before by Henneman et al (1965) in terms of MNs firing and inhibition sequence as in both works the last recruited MNs were inhibited first, but in Henneman's results it was the more phasic MNs while in ours it was considered the more tonic ones.

Perhaps of stronger support to these findings are the results of Burk, Jankowska & Bruggencate (1970), Burke (1973) who found that electrical stimulation of low threshold afferents in some skin nerves produces, in some types of phasic MNs, predominantly excit-

atory polysnaptic postsynaptic potentials while in some types of tonic MN in the same animal, predominantly IPSP are recorded. This was the case with either stimulation of the sural skin nerves or by repetitive stimulation of the contralateral red nucleus. It was assumed to be due to some qualitative differences in the distribution of the last order interneurones mediating polysynaptic activity from skin afferents and rubrospinal axons to the MNs which are related to the twitch type of the target motor units. There is evidence that the organization of synaptic input from some sources, which are mediated by segmental interneurones, may be qualitatively different to the phasic and tonic MNs within the same motor nucleus (Burke 1973).

However we have not found any disturbances in the recruitment order with the application of inhibitory stimuli. Grimby & Hannerz (1976) reported such disturbances when they reduced the afferent inflow by nerve blocking using either partial ischaemia or lidocaine They showed reversal of recruitment order of the phasic and tonic MNs. This has not been found in our work, maybe because of the difference of the methods used. In their work Grimby et al reduced the afferent inflow while in ours this was expected to be increased.

Are there two types of muscle fibres in the soleus muscle?

An obvious inference from the above discussion one is tempted to think of a tentative classification of MNs found in the soleus muscle into two different types. This is teleologically comparable to type B and C fibres of Padykula's group or even as an

opposite end of a spectrum the behaviour of which is generally homogeneous while its individual units vary smoothly. The properties of these MN types were extracted from the above results and listed in the previous table. In spite of the fact that these results could be applicable to other muscles, the final decision has to wait for more work on a good heterogeneous muscle like the gastrocnemius (Wuerker et al 1965).

CHAPTER VI

SPINAL CORD STIMULATION

CASE 1 Mrs. S.E.

A woman aged 43, whose illness began in 1974 with progressive L.hemiparesis and L.hemianthesia with subsequent improvement, suffered periods of deterioration in December 1974, February 1975 and September 1975 with weakness of the R leg, both legs and complete quadriplegia respectively. Improvement occurred very soon after each event. In December 1974 she developed burning pain in both legs up to the groin and this remained unchanged. In February 1975, she was unable to pass urine and was catheterised and has remained without any bladder sensation. Her condition had been static for the past 10 months. She could feed herself and wash her face. She could walk with great difficulty and pain for a few yards using a Zimmer walking aid. She could sit up in bed only with assistance.

On examination The only abnormality in the cranial nerve territory was of nystagmus on L and R lateral gaze. Both legs were spastic with extensor spasms. All limbs showed a pyramidal distribution of weakness of MRC grade 3-4 in the legs and 4 in the arms. Reflexes were increased and symmetrical with absent abdominal reflexes and bilateral extensor plantar responses. There was incoordination on finger/nose and heel/shin tests. Joint position sense was absent at the toes, vibration sense was impaired to the hips and there was a sensory level to touch and pain to T6 on the R and T7 on the L.

H-Reflex The R lower limb showed the recruitment of MNs with incremental stimuli seen in Fig. 52. The maximum reflex amplitude

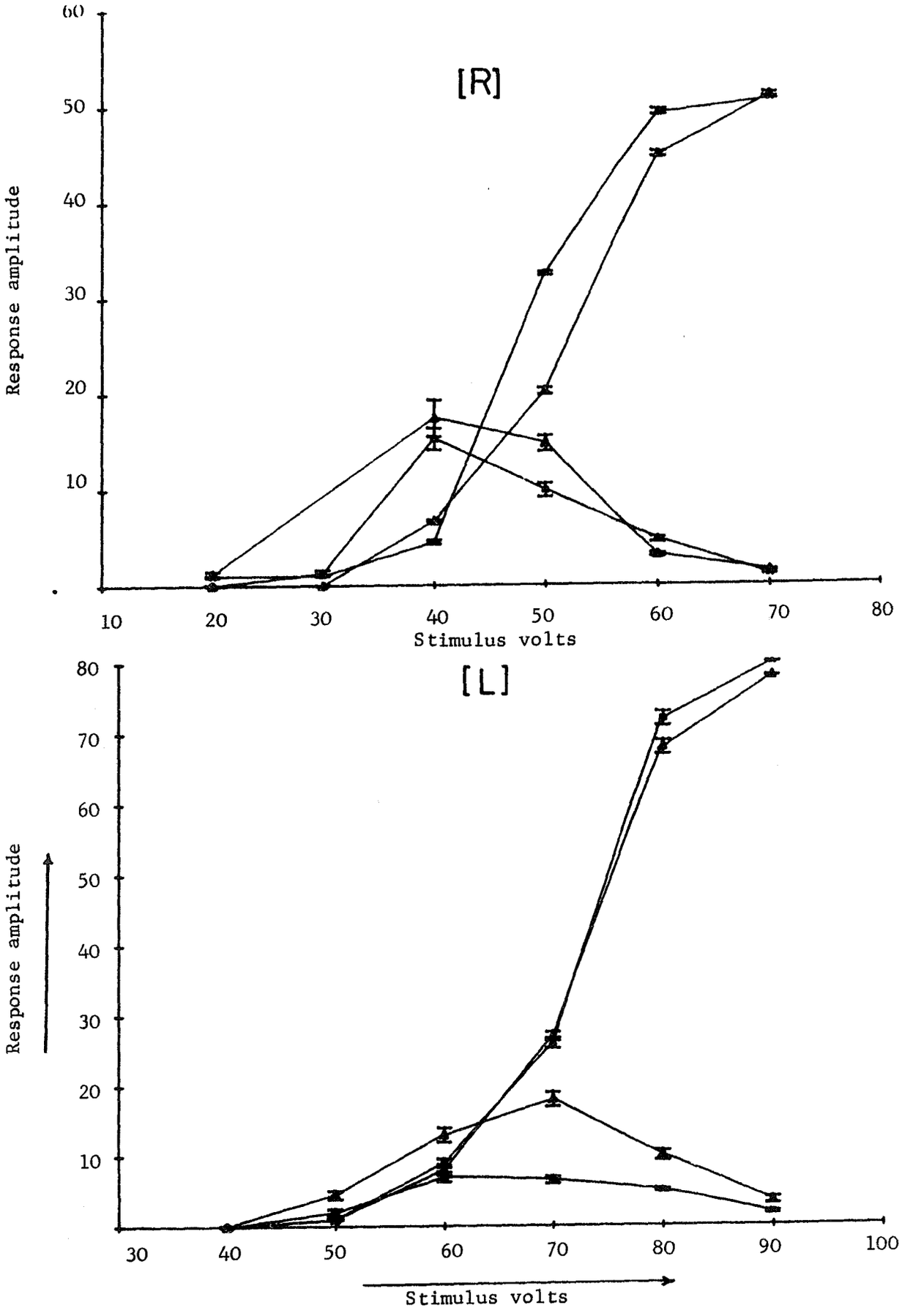


Fig. 52 Recruitment curve of right (R) and left (O) lower limb of case no. 1 (Mrs. SE) before (X) and during SCS (▲). H-reflex facilitation is clearly noticed.

was of 1 mV. In normal subjects it ranged from 3 to 8 mV.

$\frac{H\ max}{M\ max}$ was 33% (Table 17).

The recovery curve of the R leg (Fig.53) was of a spastic type with a hyperactive recovery time between 150-500 msec. after the conditioning stimulus and abolition of the 2^{ry} inhibition period. The test reflex sometimes became more than 200% of the control. Scrubbing the sole of the foot showed mild inhibition to 85% of the control (Table 17).

The L leg showed smaller reflexes with incremental stimuli (Fig.52) The maximum reflex amplitude was 0.25 mV. $\frac{H\ max}{M\ max}$ was 12% (Table 17). The recovery curve (Fig. 53) was of spastic type as well. It showed a facilitation period between 100-600 msec. with a test reflex reached sometimes to 188% of the control. Abolition of the 2^{ry} inhibition period was seen.

Procedure: The percutaneous procedure was carried out on 9th February 1976 and electrodes were introduced to T3 and T4/5 levels. The patient felt warm tingling sensations in the R arm and R leg and electrodes were adjusted until the sensation was across the chest and down both legs.

Electrodes were further adjusted on 11th February and were lying at T4/5 and T6 levels with recording electrode at C5.

During stimulation

24 hours after: The pain disappeared. She was able to use muscles innervated by C7-8 T1 segments fully for the first time for months. It was easier to dress herself. She could sit up from a supine position with arms folded across her chest. She would walk unaided.

48 hours after: Sensory level had lowered from T6 to T10 on the right and from T7 to L1 on the left.

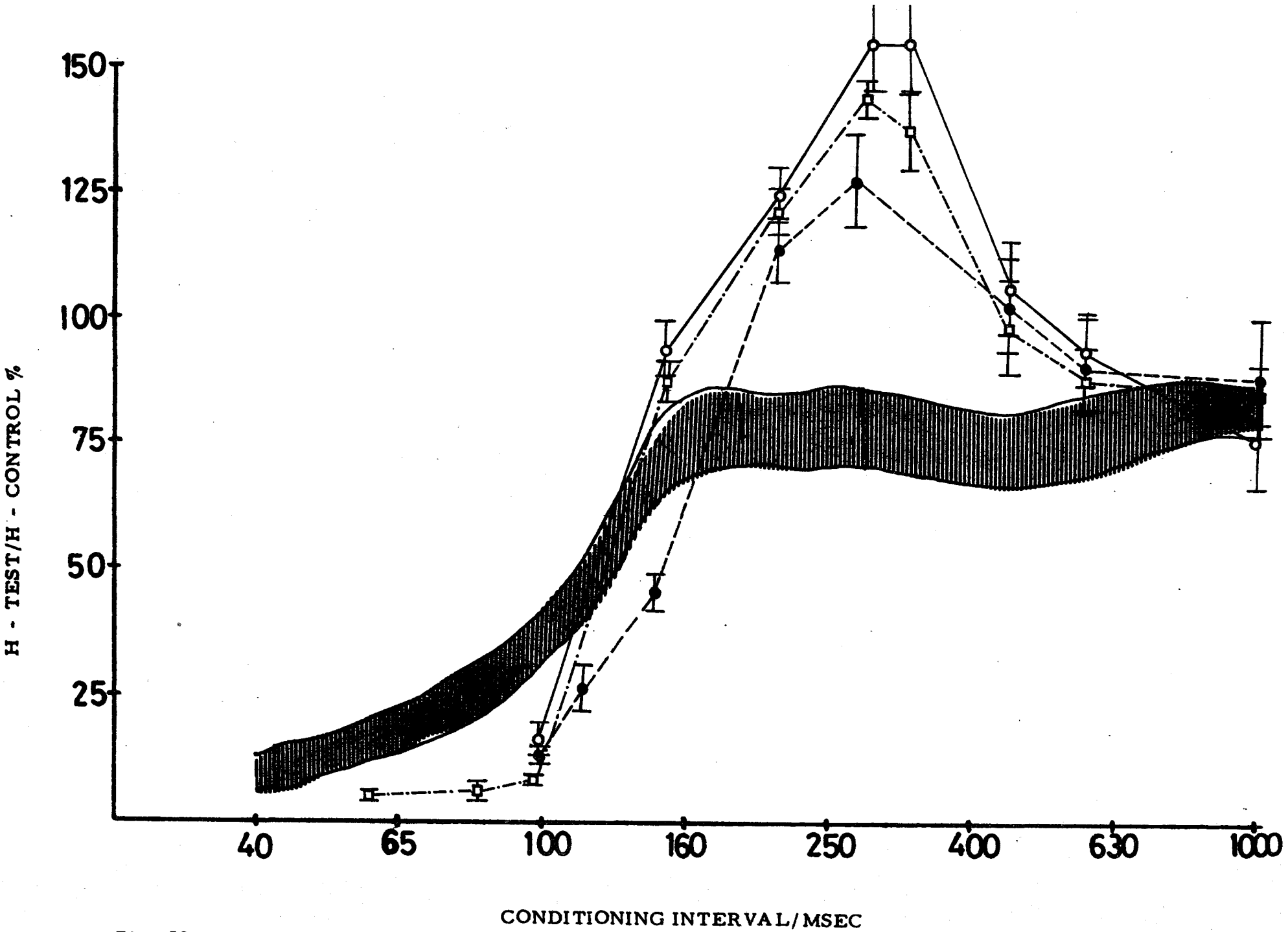


Fig. 53 Recovery curve of case no. 1 (Mrs. S.E.) of the right lower limb before (o), 3 days during (●), and 40 days after (◘) spinal cord stimulation (Mean ± SD).

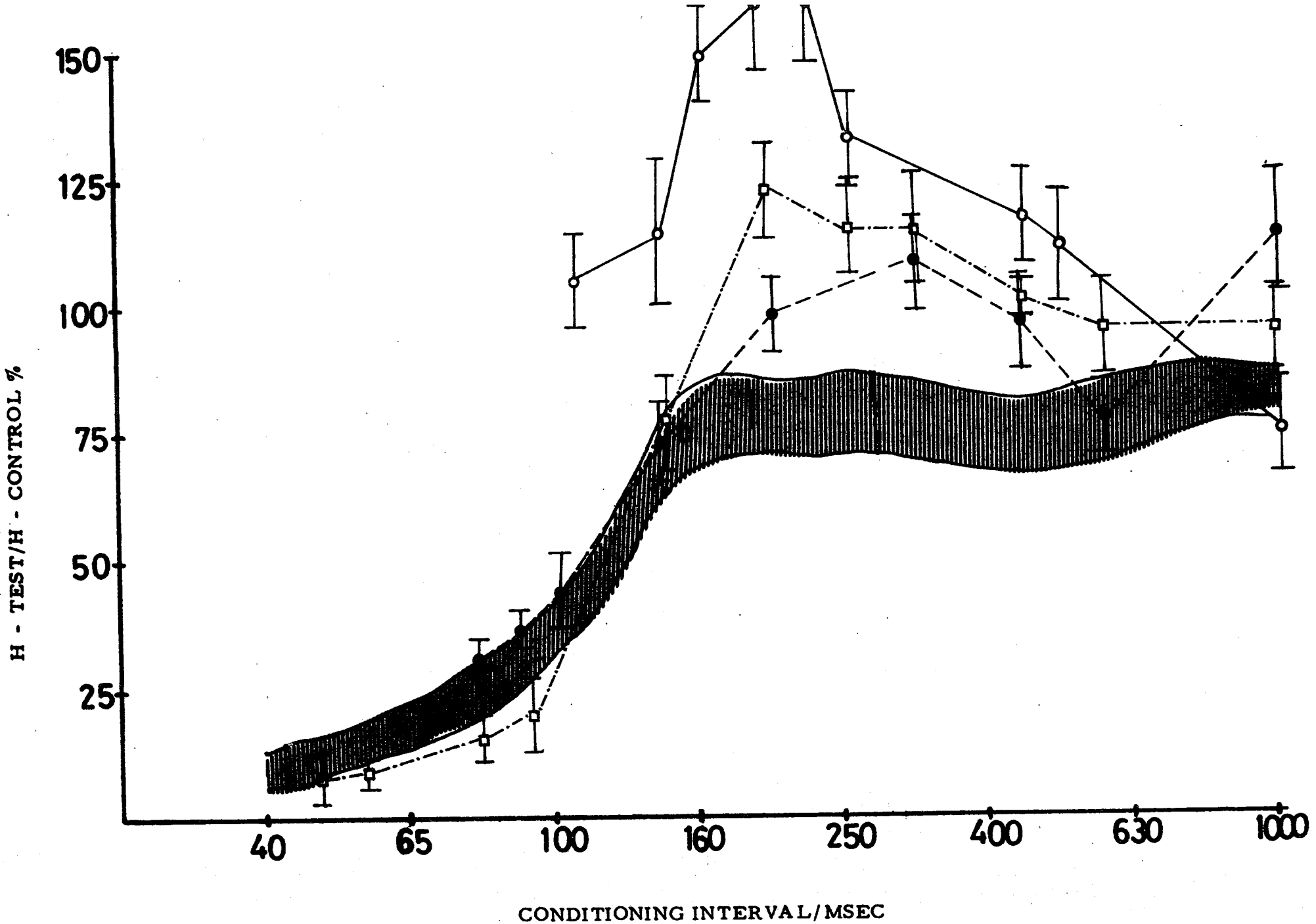


Fig. 54 Recovery curve of case no. 1 (Mrs. SE) of the left lower limb before (o), 3 days with (●), and 40 days after (□) spinal cord stimulation. (Mean ± SD).

72 hours after: Bladder sensation present.

H. reflex After continuous stimulation for 3 days with 2.5 V., 0.2 msec. for 33 PPs., the patient was tested for H-reflex changes. In the R leg the reflex recruitment with incremental stimuli is illustrated in Fig 52. The maximum reflex amplitude was 1 mV and $\frac{H\ max}{M\ max}$ was 33% again. (Table17).

Table 17 Effect of SCS on reflex amplitude and $H/_M$ ratio

Patient name	Leg	BEFORE		DURING		AFTER	
		H-amplitude mV.	$H/_M$ ratio	H-amplitude mV.	$H/_M$ ratio	H-amplitude mV.	$H/_M$ ratio
SE	R	1	33	1	33	1*	-
	L	0.25	12	0.1	10	0.3*	-
CP	R	3.5	75	3.5	81	-	-
	L	5.75	68	4	-	-	-
NE	R	3.1	58	-	-	-	-
	L	4	58	5.3	63	-	-
JM	R	0.94	9	2.94	32	-	-
	L	3.6	47	2.4	25	-	-
ES	R	4	74	5.3	76	2.8 ǂ 6 ǂǂ	51 88
	L	2.6	55	3.2	47	3.2 ǂ 5.43 ǂǂ	78 ǂ 84 ǂǂ
RE	L	0.1	-	0.01	54	-	-

* 40 days after removal of SC electrodes.

ǂ 24 days after removal of SC electrodes.

ǂǂ 49 days after removal of SC electrodes.

She showed dramatic change in the recovery curve towards a normal pattern (Fig 53). It was slightly hyperactive in the period between 200 and 500 msec., and the test reflex reached 125% in its utmost facilitation. The curve showed an apparent 2^{ry} inhibition period.

The test reflex was inhibited to 80% of the control by scrubbing the sole of the foot (Table 19).

In the L leg the reflex was 0.1 mV. with an $\frac{H\ max}{M\ max}$ of 10% (Table 17). The recovery curve showed significant changes towards the normal pattern (Fig.53). The test reflexes were slightly facilitated in the period between 200 and 500 msec., with a maximum amplitude of 112% of the control. The 2^{ry} inhibition period can be noticed to develop during spinal cord stimulation (SCS).

Scrubbing the L sole of the foot inhibited the test reflex to 85% of the control (Table 19).

It is worth noting that SCS showed no effect on the recovery time of H_2 in spite of the mean reflex amplitude increasing to 171% of the control by 2.5 volts pulses . The test reflex was 197% of the control when SCS increased to 3 volts (Table 18).

Table 18 Effect of SCS intensity on H-reflex amplitude

Patient name	Leg	SCS Intensity/Volt	H/Reflex facilitation H-test/H-control %
SE	L	2.5 3	171 197
CP	R	1	120*, 150 ǂ
	L	1.5	115
NE	L	2	104
JM	R	8	114
	L	6-8 11	182 141
ES	R	3	113
	L	3 4	228 298
RW	L	3	130

* Using DCS transmitter ǂ Using "Devices" Stimulator

After stimulation

Electrodes were removed after 10 days of continuous stimulation. There were no side effects.

48 hours later: Pain started in legs.

18 days later: Bladder sensation still present. Movements remain improved and can still walk unaided. She is able to take a bath on her own. Hands remain improved. She can still sit up from a supine position with hands folded across chest.

48 days later: Bladder sensation still present. She cannot stand up from sitting position without using her arms. She is still able to sit up from supine position. She is able to raise her legs together up to 60^{o}. Heel-knee test ataxic bilaterally. Briskly tendon jerks and Hyperthesia below T7 T8 for pin prick.

H-reflex: The patient was tested 40 days after removal of the electrodes. The R leg showed a reflex amplitude of 1 mV. (Table 17). The recovery curve showed mild declination toward normal pattern with a slightly hyperactive period between 200 - 300 msec. only. The test reflex was 136% of the control at its utmost value (Fig.54).

The L leg showed a smaller reflex amplitude of 0.3 mV. (Table 17). The recovery curve showed a higher curve than that during stimulation with a hyperactive period between 200 - 1000 msec. (Fig.54) It did not reach the pre-stimulation value. The test reflex was 121% at its utmost value.

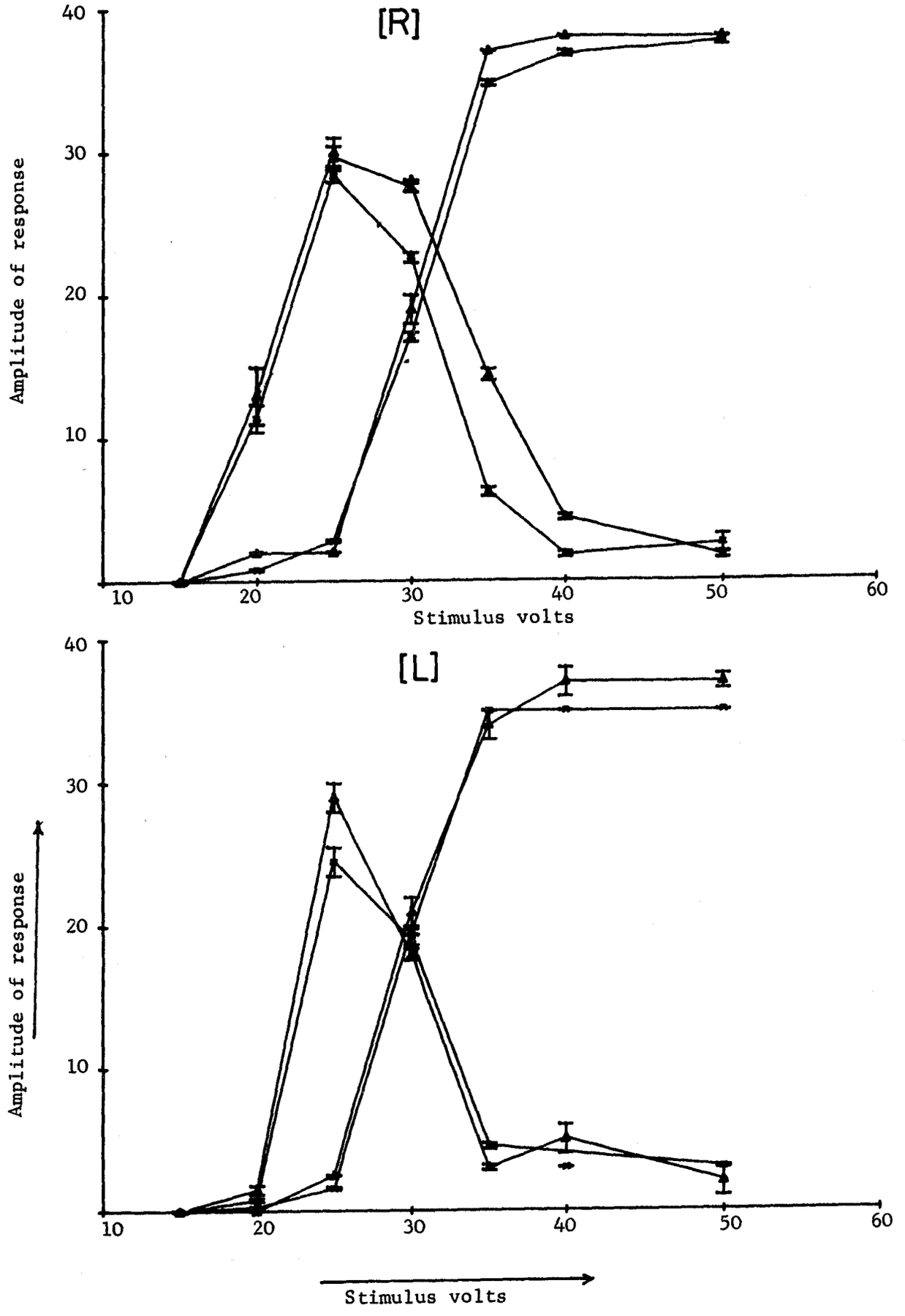


Fig. 55 Recruitment curve of case no. 2 (Mr. CP) of the right (R), and left (L) before (X) and during (▲) SCS.

CASE 2 Mr. C.P.

A man of 36 whose illness started in June 1971 with a R hemiparesis which was intermittent and gradually improved. In May 1972 he developed impotence (normal sexual urge but unable to develop an erection) and this remained unchanged. Further episodes occurred in 1973, 1974, and June 1975, consisting of numbness of feet, development of L'Hermittes sign and numbness of both legs respectively. From June 1975 he lost bladder sensation and sensation of passing faeces. He would go to the lavatory every 1-2 hours, day and night, to prevent incontinence.

On examination There was no abnormality in the cranial nerve territory. Tone and power was within normal limits. Reflexes were brisk with right ankle clonus and a right extensor planter response. Abdominal reflexes absent. There was heel/shin ataxia. Vibration sense was impaired to the sternum, joint position sense was absent at the toes and ankles and impaired at the knees. Touch was lost to T7 and pin prick was lost to T10. There was no cremasteric reflex.

H-reflex : The reflex recruitment of the R leg with incremental stimuli is shown in Fig.55. The maximum reflex amplitude was of 3.5 mV with an $\frac{H\ max}{M\ max}$ of 75% (Table 17).

The recovery curve of the R leg was lower than the normal value (Fig.56). The test reflex showed a slower recovery with a slightly smaller amplitude than normal.

The test reflex was not inhibited by scrubbing sole of the foot. It fell to a mean value of 97% of the control (Table 19). In normal subjects the test reflex was 50% of the control.

In the L leg the reflex was of maximum value of 5.75 mV. with an

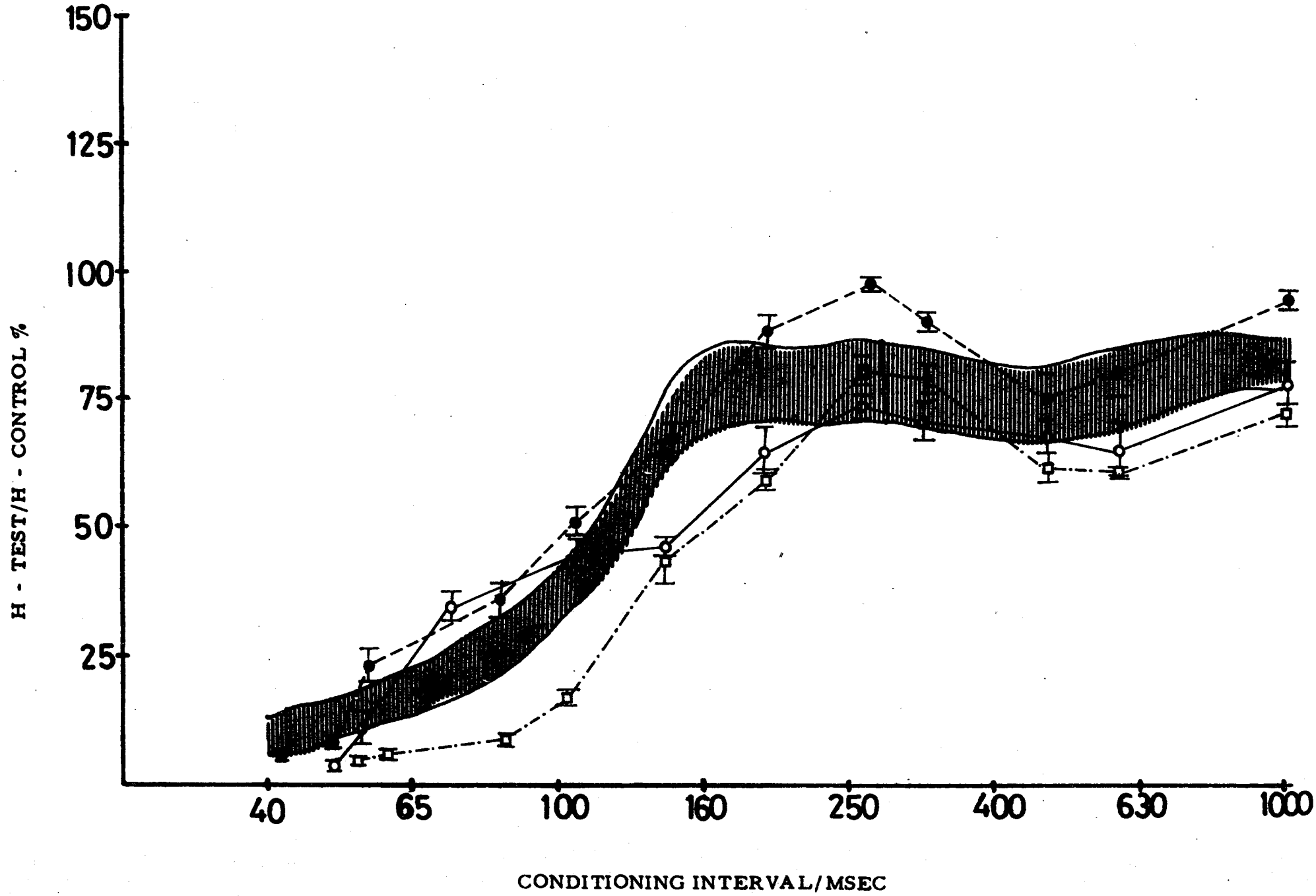


Fig. 56 (A) Recovery curve of case no. 2 of the right leg before (o), 3 days with (●) and 30 days after (□) spinal cord stimulation. (Mean ± SD).

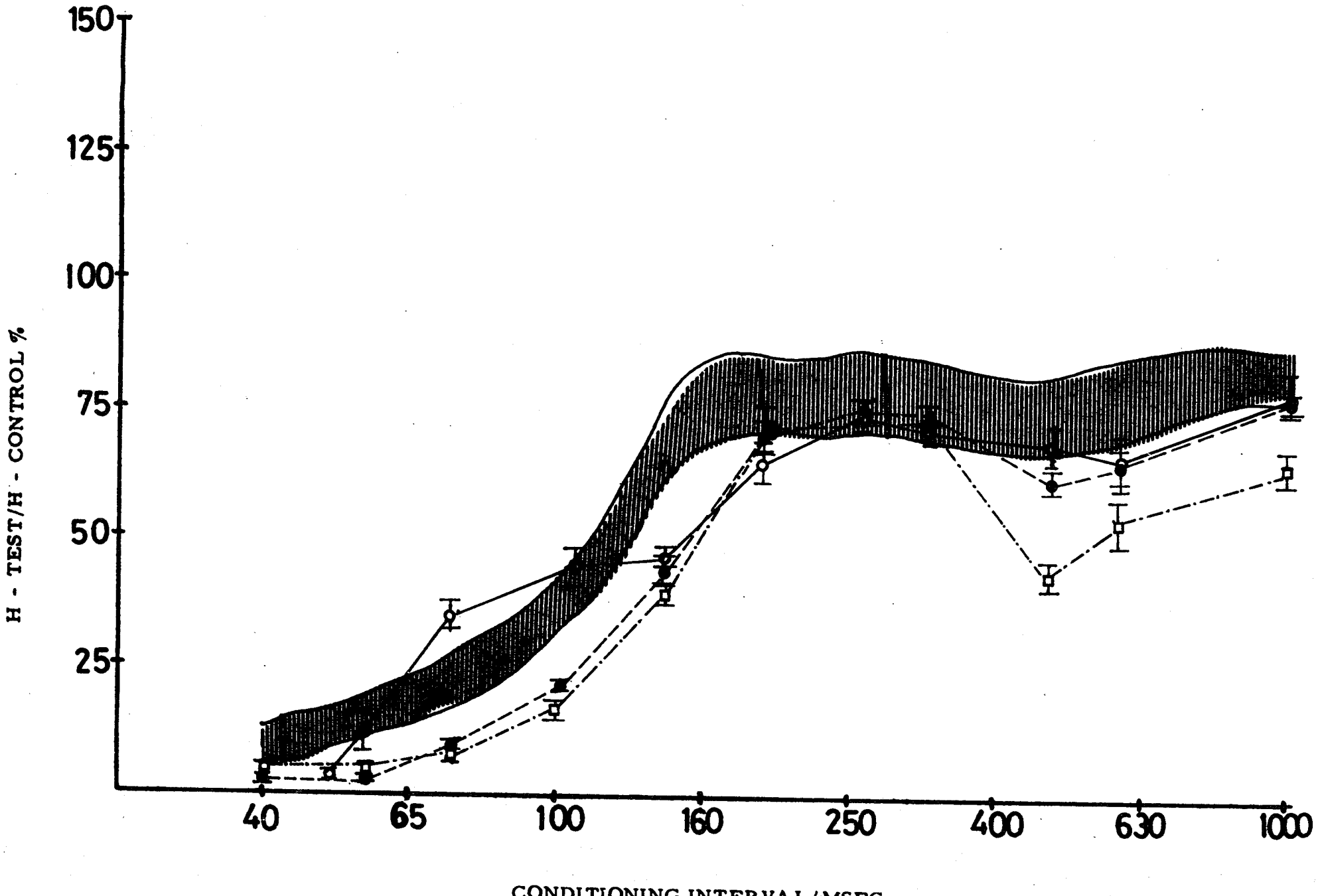


Fig. 56 (B) Recovery curve of case no. 2 of the right left before (o), 10 days during (●) and 6 days after (□) spinal cord stimulation. (Mean ± SD).

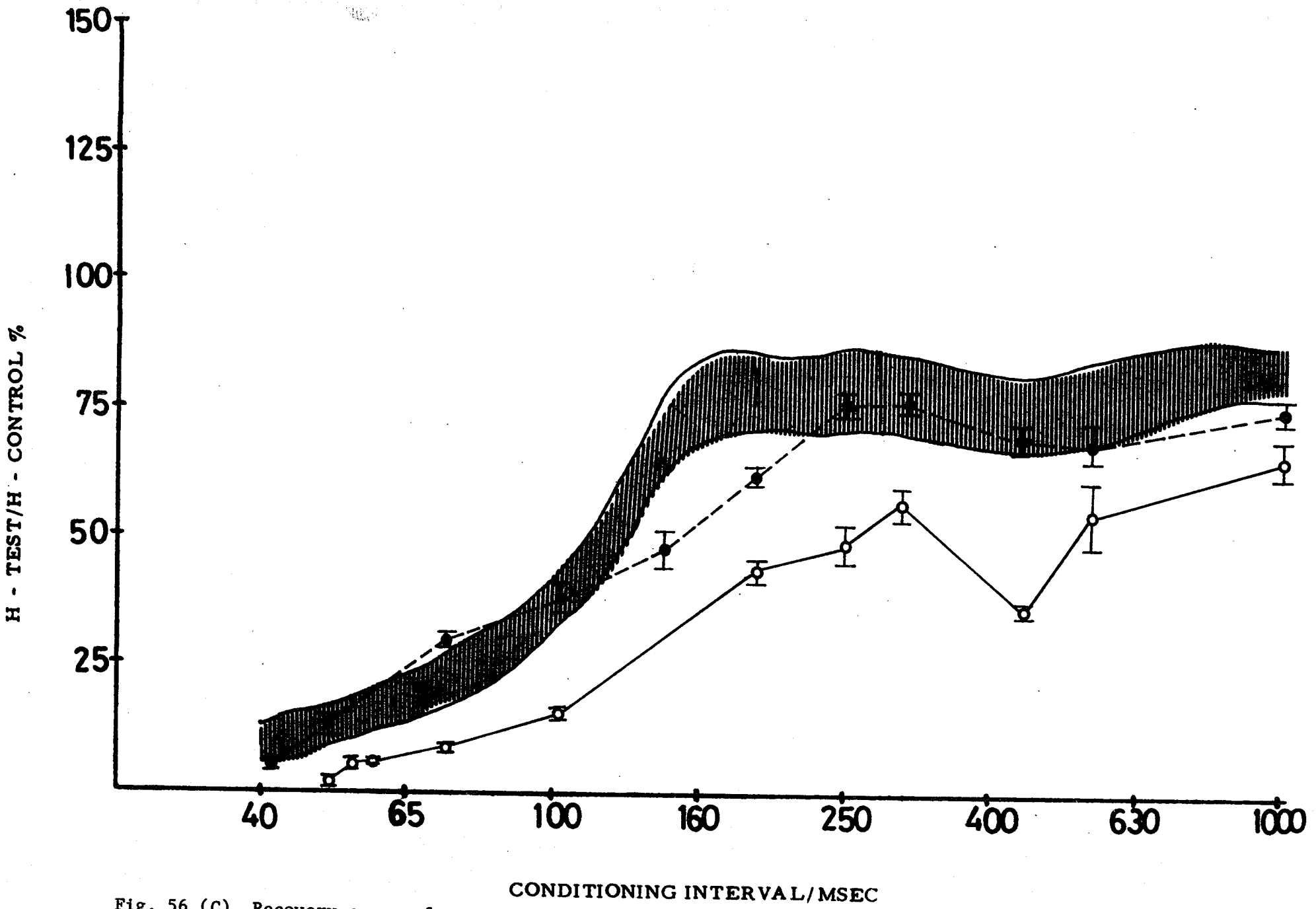


Fig. 56 (C) Recovery curve of case no. 2 (Mr. CP) of the left lower limb before (o) and 3 days with (●) spinal cord stimulation. (Mean ± SD).

$\frac{H\ max}{M\ max}$ of 68% (Table 17). The recruitment curve is illustrated in Fig.55 . The excitability curve (Fig.56) was lower than normal value. It was similar to curves seen in patients with cerebellar lesions. The Test reflex was slower in recovery and smaller in amplitude than normal, but it passed through various changes as seen in normal curves. The test reflex was 55% at its maximum recovery amplitude.

Mechanoreceptor stimulation of the foot showed a mean reflex value of 93% of the control (Fig. 57). The decrease in the inhibition of the reflex by scrubbing was consistent in all records.

Procedure: The percutaneous procedure was carried out on 1st March 1976 and electrodes were placed at T4 and T5 and a recording electrode at T2. Warm tingling sensations were felt from the chest downwards.

During stimulation

24 hours after: Bladder sensation returned. Touch level decreased to T10. Pin prick level decreased to T12. Cremasteric reflex present.

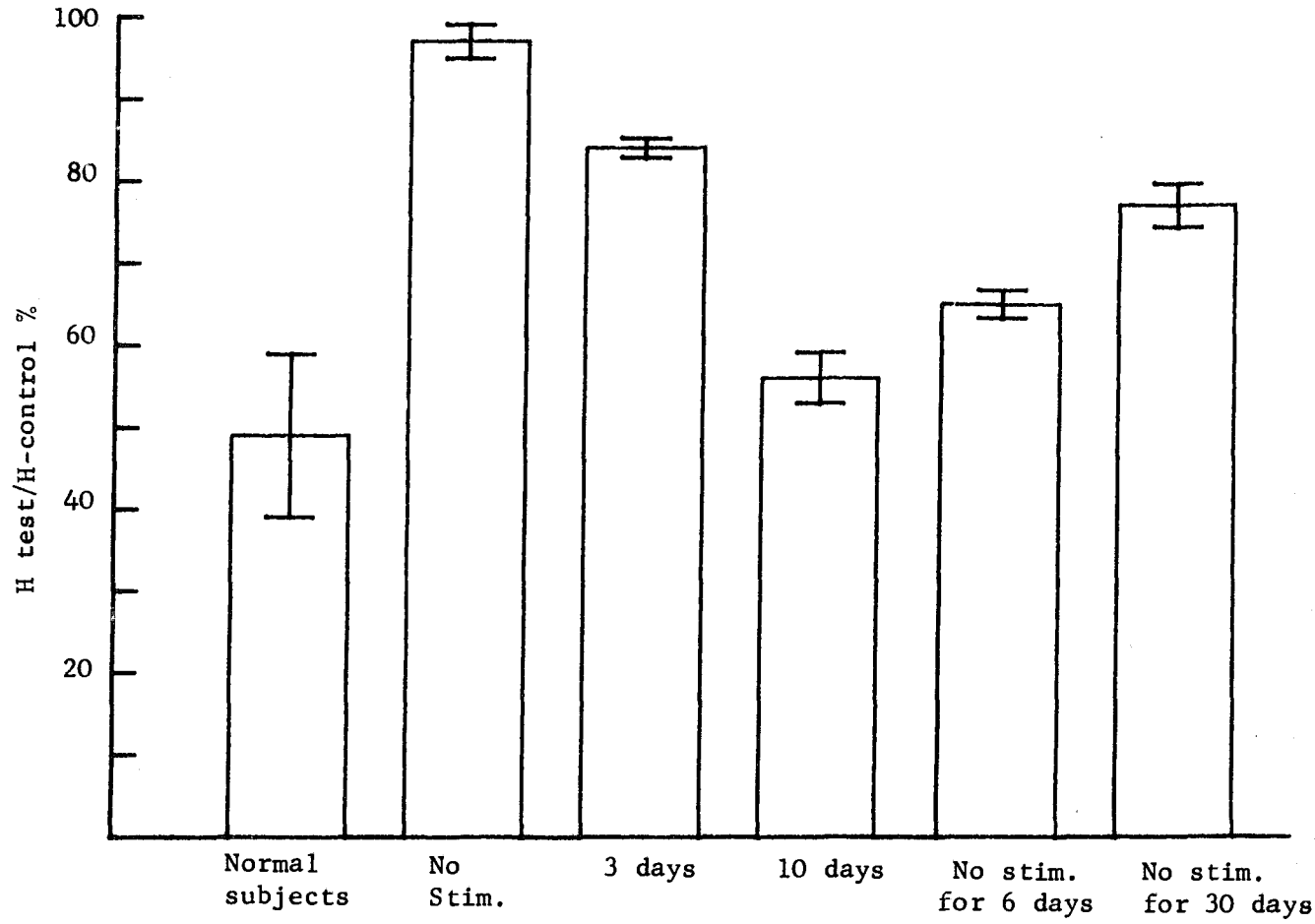
2 days: Says he goes to lavatory "when I feel my bladder full". Touch level -L1. Pin prick -L2.

3 days: Sensory level down to both knees.

9 days: Developed an erection for the first time since May 1972. Joint position sense present without impairment. Vibration sense impaired to hips. Touch and pin prick impaired over soles of feet only.

H-reflex: The patient was studied 3 days after electrode implantation and continuous stimulation with 1.5 volts, 200 msec. of 33 PPs.

R Leg Reflex amplitude 3.5 mV. $\frac{H\ max}{M\ max}$ = 80.6% (Table 17). The recruit-



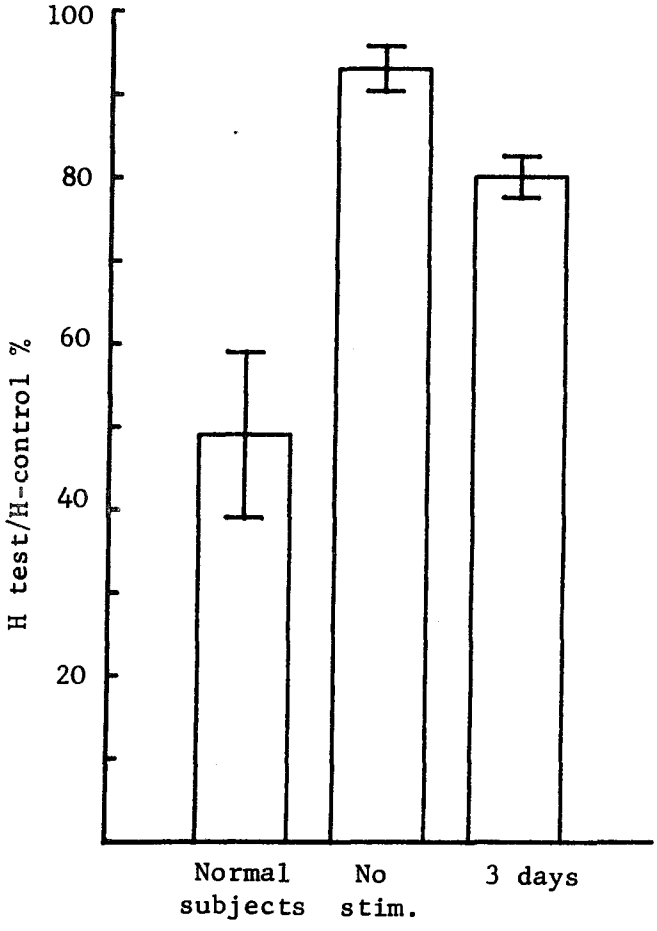


Fig. 57 Mechanoreceptor stimulation of the sole of the foot by scrubbing in case 2 (Mr. CP) of the right (upper, left (lower), before, during and after spinal cord stimulation.

ment pattern as seen in Fig.55with incremental stimuli.

The recovery curve (Fig.56) showed mildly improved reflex with a curve of an upper normal value. Mechanoreceptor stimulation of the sole of the foot showed a reflex ranging from 71 to 96% with a mean value of 84% of the control (Fig.57).

L leg Reflex amplitude was 4 mV. (Table 17). The recovery curve (Fig.56) clearly showed a dramatic return towards normal with a slightly earlier recovery time. Scrubbing the sole of the foot showed a reflex inhibition to a mean value of 80% (Table 19). SCS with the standard voltage produces facilitation of the mean reflex amplitude to 120% in the R leg and to 115% in the L leg. (Table 18)

Table 19 Effect of SCS on reflex inhibition by mechanoreceptors stimulation

Patient name	Leg	Before (SCS) H test/ H control%	During (SCS) % control	After (SCS) % control
SE	R	84	80	-
	L	-	85	-
CP	R	96.5	84, 56*	65, 77‡
	L	92.5	80	-
NE	R	97	-	-
	L	80	79 (99)‡‡	-
JM	R	139	7	-
	L	38	26	-
ES	R	92	63	-
	L	85	88	48

* 3 and 10 days during SCS ‡ 6 and 30 days after removal of SC electrodes

‡‡ SCS temporarily switched off

The patient was retested after 10 days with continuous SCS. The sensation to pin prick and touch extended to the toes. H-reflex studies showed the following findings in the R leg:

The recovery curve was slightly lower than that with 3 days SCS (Fig.56) but it was within the normal value. It seems that the CNS reacted with an increase in its excitability in the beginning of stimulation but this was not sustained. Spinal cord stimulation for a long time produced adaptation of the MN excitability.

The mean reflex value was inhibited to 56% by scrubbing sole of the foot (Fig.57). This was near normal standard seen in normal subjects (Sabbahi Awadalla & Sedgwick 1976).

After stimulation: Electrodes were removed after 11 days of continuous stimulation. There were no untoward side effects.

10 days after: Bladder sensation present. Sensory levels remain unchanged. The only deterioration is that legs feel stiff but with no objective change.

30 days after: Bladder sensation still present. Sensory paresthesia started.

H-reflex: The patient was tested 6 and 30 days after electrodes were removed and showed the following results in the R leg:

Recovery curve: The test reflex was lower than normal and returned to a cerebellar type. This was the case at 6 days and 30 days after removal of the electrodes (Fig.56). It recovers later than during SCS, with 10 msec. difference.

Scrubbing the sole of the foot inhibited the reflex to a mean value of 65% after 6 days from electrodes removal. 30 days after, the mean reflex value was 77% of the control.

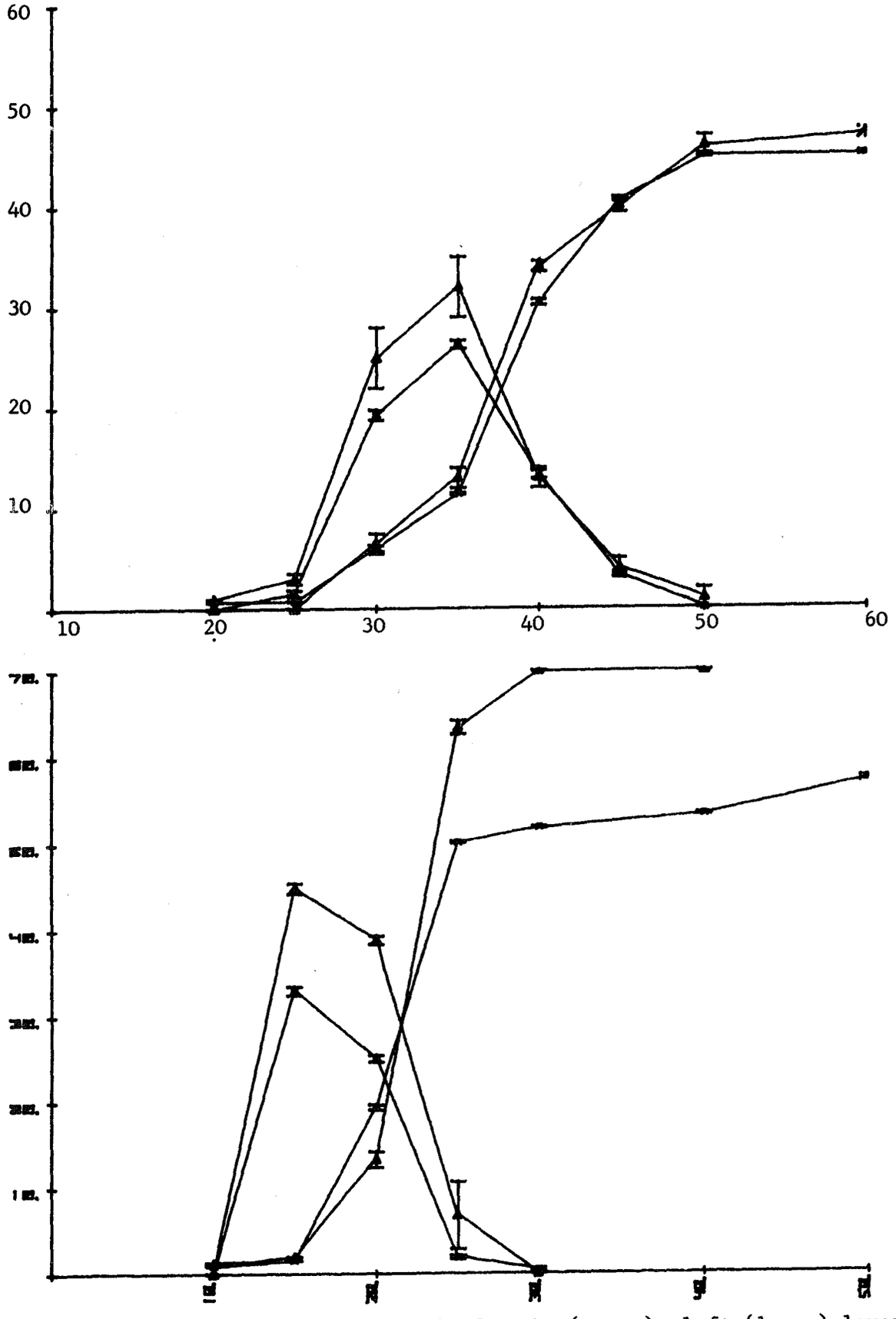


Fig. 58 Recruitment curve of case 3 of right (upper), left (lower) lower limb, before (X) and during spinal cord stimulation (▲).(Mean ± SD).

CASE 3 Mr. N.E.

A man aged 37 whose illness started in 1971 with loss of erection followed by a decrease of visual acuity in the L eye. After a flu-like state in 1973 he noticed weakness in R foot followed by improvement. Remission period in March 1973, October 1973 with progressive weakness in both LL, with inability to stand up or walk unaided. In 1974 he continued to get worse and a paraplegic state with extensor and adductor spasticity occurred. He had been wheel-chair bound since November 1973.

On examination: In the cranial nerve territory nystagmus was seen on horizontal conjugate gaze. Both legs were spastic with extensor and adductor spasm, with minimal voluntary movement. Increase ATR in LLs. with bilateral Babinski signs and sustained clonus.

Touch and pin prick sensations were impaired, the former to the level of T4-T5, the latter to T10 on the L and to T12-L_1 on the R side. Intension tremors were present in UL and vibration is impaired to the level of sternum. JPS was also impaired in the LL.

H-reflex: R leg The H-reflex was of a mean value of 3.1 mV. with an $\frac{H\ max}{M\ max}$ = 58%. The reflex recruitment with incremental stimuli is illustrated in Figure 58 .

The recovery curve was of spastic type (Fig 59) with a hyperactive test reflex. The test reflex was more than 100% of the control during the conditioning intervals after 150 msec.

Mechanoreceptor stimulation of the sole of the foot showed a mean reflex value of 96% of the control.

L leg: H-reflex was larger in amplitude than the R leg. Its maximum value was 4 mV. with $\frac{H\ max}{M\ max}$ = 58%. Fig.58 shows the recruitment

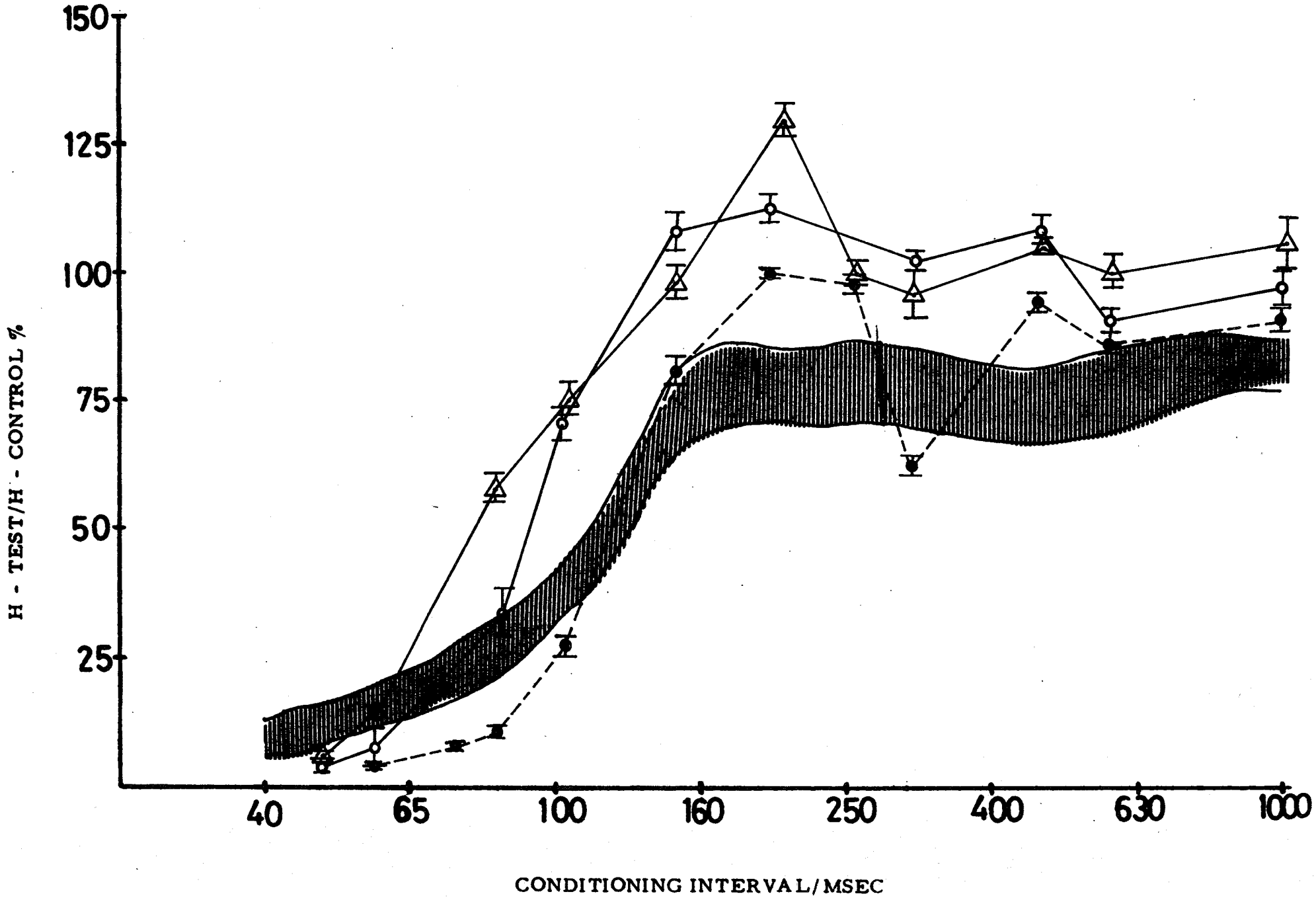


Fig. 59 Recovery curve of case 3 (Mr. E) of right lower limb before (Δ), left lower limb before (o), and 3 days during spinal cord stimulation (•). (Mean ± SD).

curve 5 days before SCS.

In the recovery curve (Fig.59) the test reflex was facilitated giving a spastic type of curve. It recovers fast and reached to more than 100% of the control in the conditioning intervals from 150 to 1000 msec. It showed abolition of the 2^{ry} inhibition period.

The test reflex was inhibited to a mean value of 80% of the control by scrubbing sole of the foot (Table 19).

Procedure: Percutaneous stimulation was done on the 1st of March 1976. Stimulating electrodes placed at T1 and $T3_{+}$ T4 and repositioned to T6 T7. Parasthesia were felt only in the R shoulder area. The electrodes were repositioned to the anterior column on 3.3.76. Patient felt pain sensation with the stimulation. X-ray showed the electrodes were mislocated and were over the anterior column. On 5.3.76 we noticed mild infection around the puncture site and the electrodes were removed.

During stimulation

No change in the clinical condition was seen.

H-reflex: The patient was tested 3 days after electrode implantation with continuous stimulation. He showed the following results.

L leg: It showed an increase in the mean reflex amplitude to 5.3 mV. with an $\frac{H\ max}{M\ max} = 62.5\%$. Fig.58 shows the recruitment curve during SCS. An increase in the reflex amplitude can be seen.

The recovery curve showed a slight decrease of the test reflex with a prominent change of the curve toward normal pattern (Fig.59). The 2^{ry} inhibition period developed during SCS. The test reflex recovers 10 msec. later than that before stimulation.

It is worth noting that the recovery curve returned to its pre-stimulation level when the SCS stopped for 15 minutes (Fig. 59).

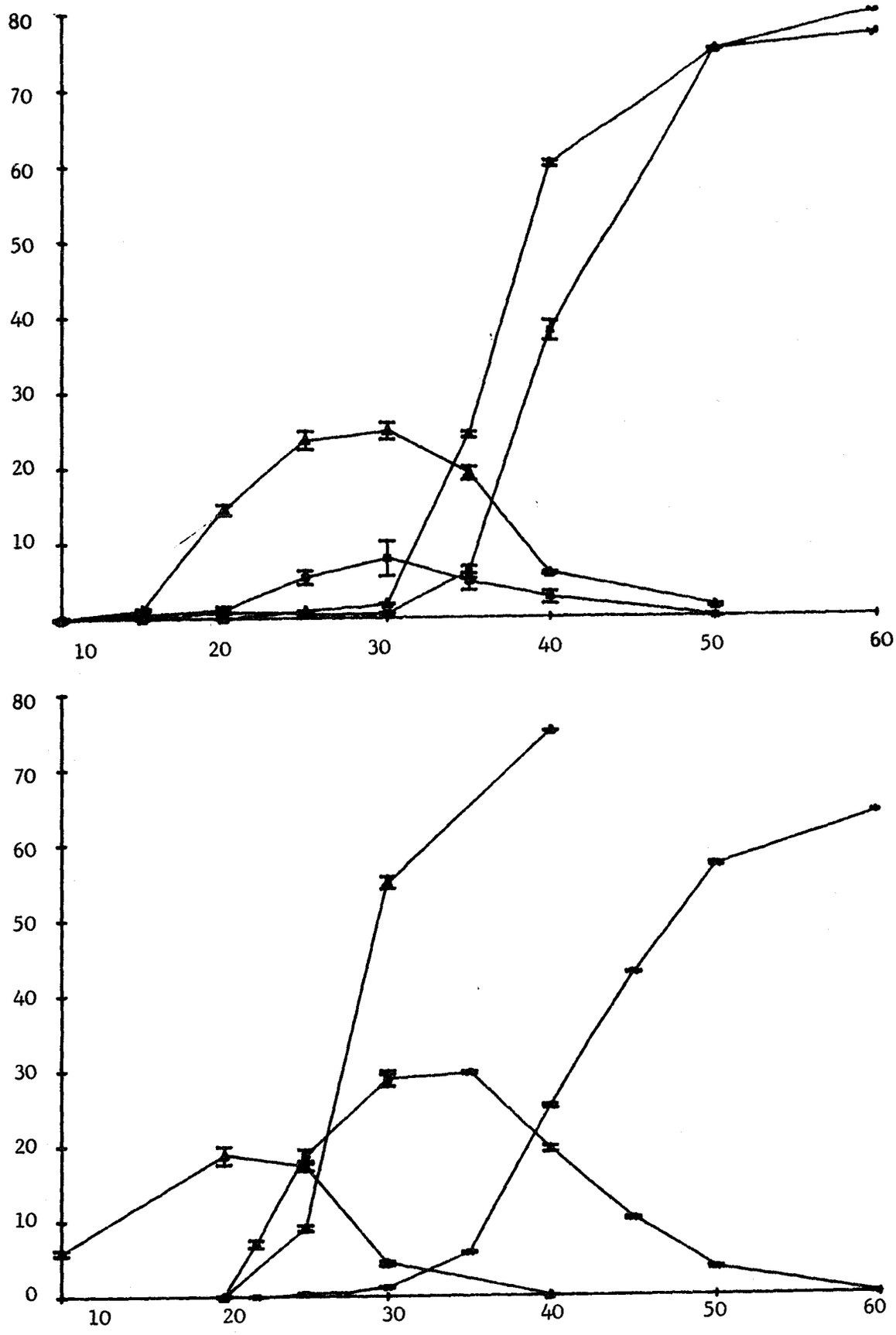


Fig. 60 Recruitment curve of case 4 (Miss JM) of right (upper), left (lower) limb, before (x) and during (▲) spinal cord stimulation (Mean ± SD).

Stimulation of the mechanoreceptors of the sole of the foot showed a mean reflex value of 79%. When the SCS stopped for 25 minutes and scrubbing applied again the reflex was inhibited to 99% of the control.

SCS did not show significant increase in the mean value of the H-reflex. It was 104% of the control with SCS. The patient exhibited mild superficial infection which urged removal of the electrodes and stopping SCS.

CASE 4 Miss J.M.

A girl aged 22 years was admitted with complaints of cerebellar ataxia involving the limbs and the trunk.

In her case history she had one epileptic fit without any neurological deficit in 1972. However, she later developed cerebellar ataxia in both arms and legs which got worse about August 1972. Her condition clinically remissed and later relapsed again. Stereotactic operations and a lesion to the L thalamus was performed in May and August 1974, following which, minimal improvement of the L arm ataxia was obtained.

On examination: Ataxia in heel-shin, finger nose test. Marked intention tremor. Gross inco-ordination of both arms and legs. Fine horizontal nystagmus to the L. Plantar extensor reflex. Cerebellar dysarthia. She is able to walk with help or by holding on to surrounding objects.

H-reflex R. Leg: The right leg showed a small reflex amplitude of a mean value 0.94 mV. The $^{H}/_{M}$ ratio was 9%. The reflex recruitment with incremental stimuli is illustrated in Fig.60. It is important to note that the R leg was clinically worse.

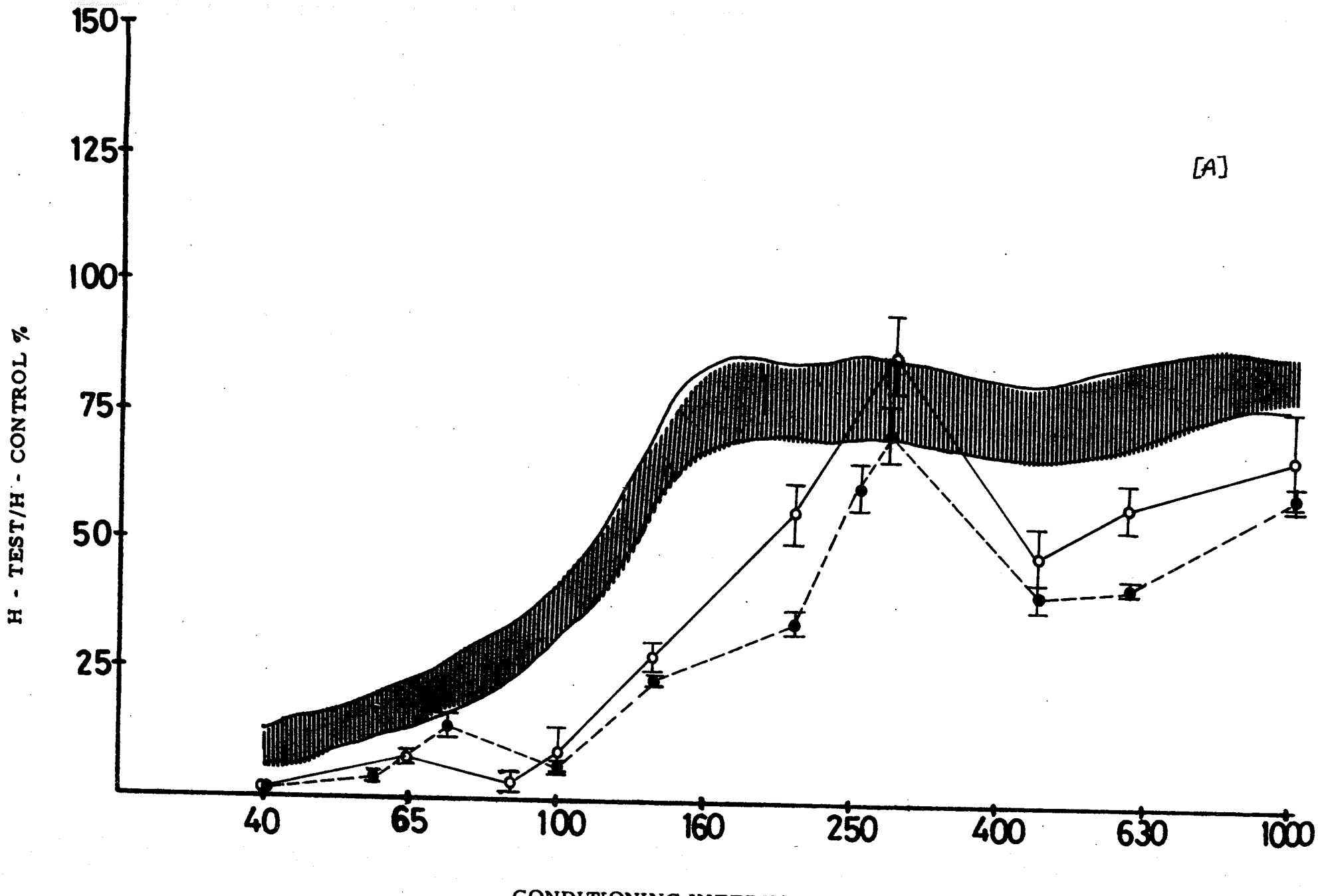
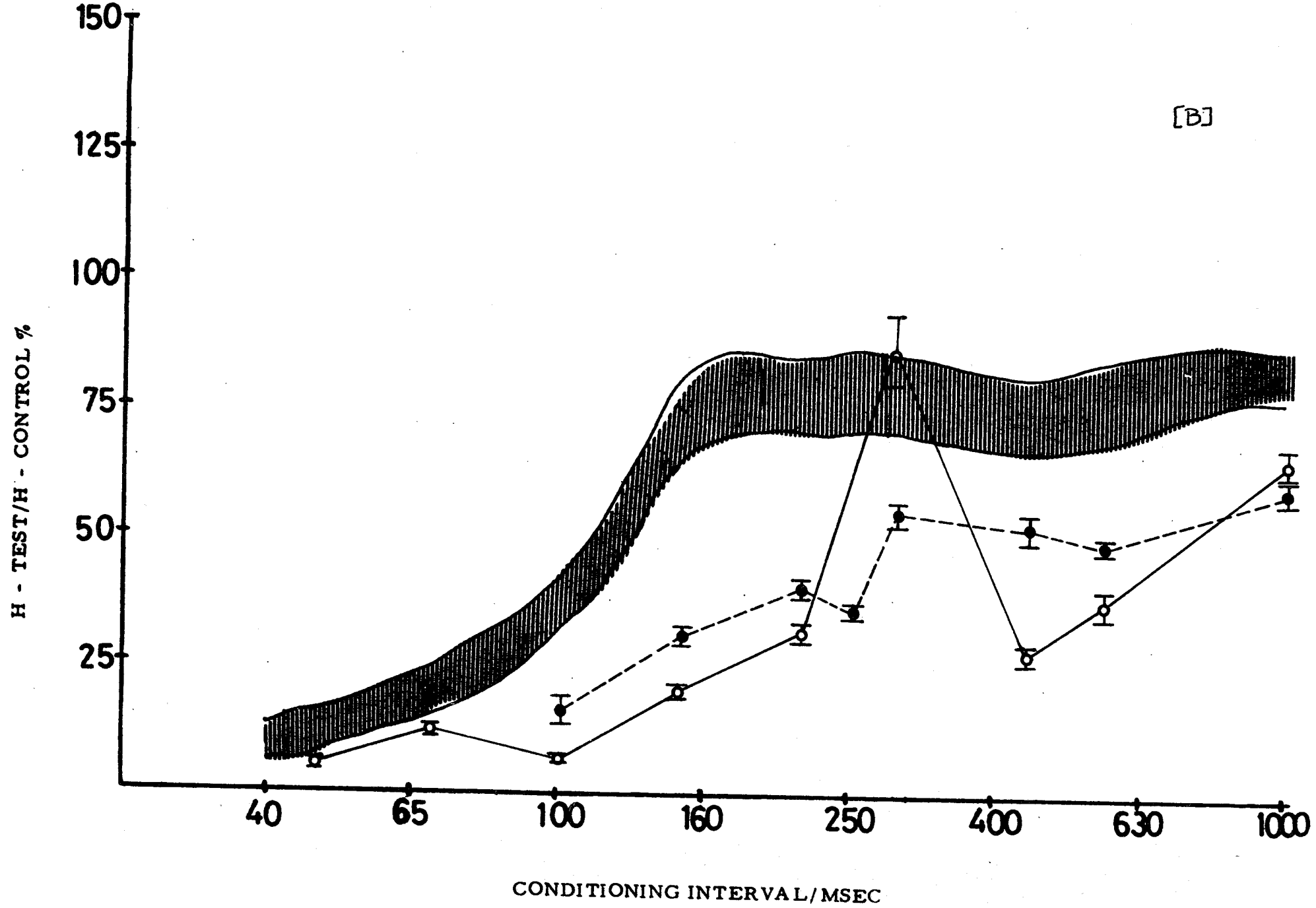


Fig. 61 Recovery curve of case 4 (Miss JM) of right (A), left (B) lower limb before (o) and 5 days during (●) spinal cord stimulation. Hatched curve are the mean ± SE of 10 normal young subjects (Mean ± SD)


[B]
150
125
100
75
50
25
H - TEST/H - CONTROL %
40
65
100
160
250
400
630
1000
CONDITIONING INTERVAL/MSEC

The recovery curve was of cerebellar type (McLeod et al 1967). It showed a normal recovery time. The test reflex was significantly smaller than the control value (Fig.61). A slow recovery was seen but the test reflex passed through the different changes encountered in the normal curve. The intercurrent facilitation period was between 200 - 300 msec. It showed a test reflex ranging from 53-85% of the control. This was followed by a prominent 2 ^{ry} inhibition period from 400-600 msec.

The test reflex did not show significant inhibition by scrubbing the sole of the foot. It was facilitated and had a mean value of 139% of the control (Fig.62). Vibration of the tendoachilles showed an inhibition of the reflex to 11% of the control (mean value) (Fig.63).

L leg: The L leg showed a larger reflex amplitude of 3.6 mV. as a mean value. The MNP fraction ($^{H}/_{M}$ ratio) was higher than the R leg. It was 47%. This can be shown in the recruitment curve in Fig.60 .

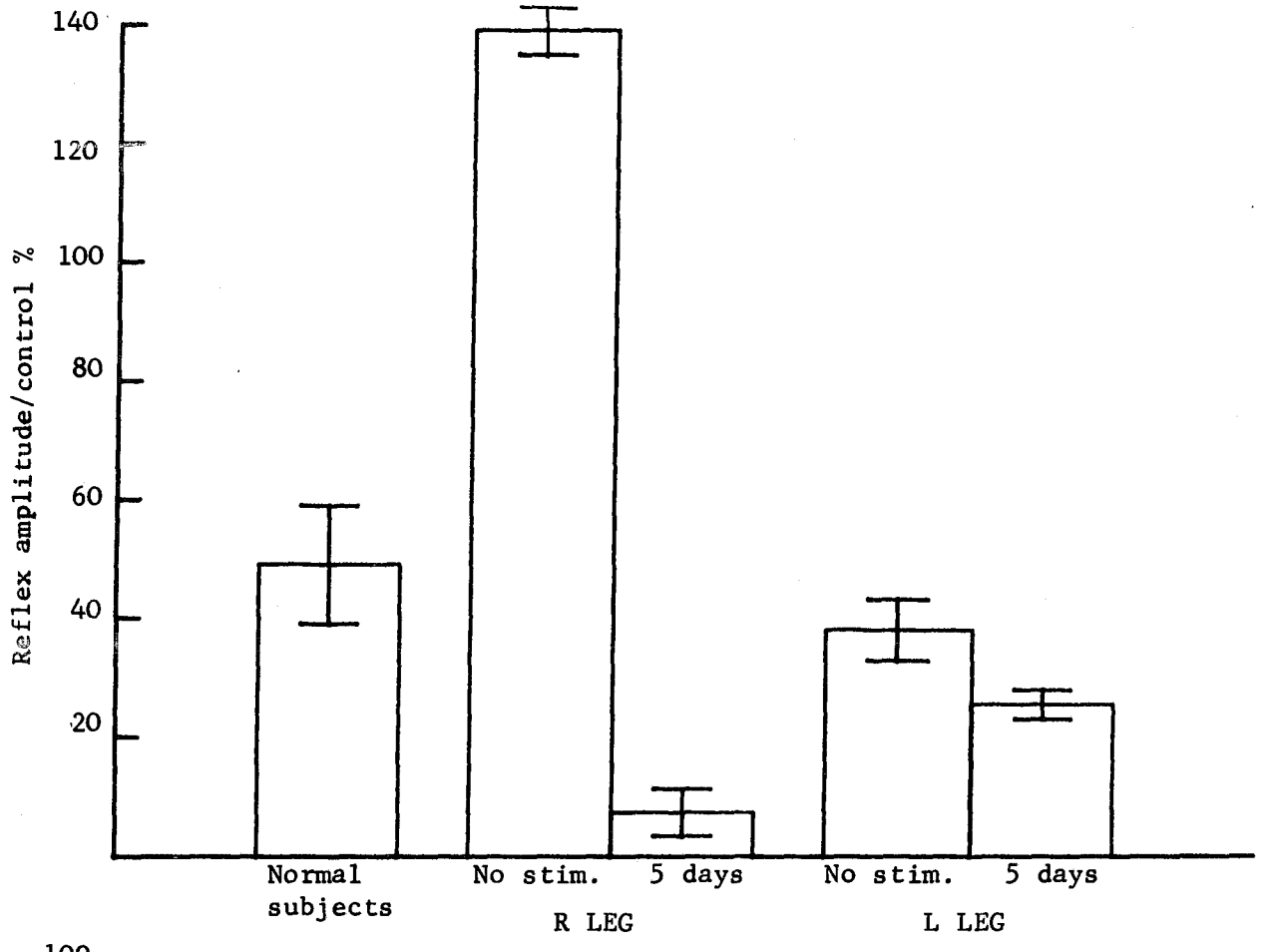
The recovery curve was significantly lower than the normal curves (Fig.61). It had a similar recovery pattern to that of the R side. Segmental stimulation of the mechanoreceptors showed inhibition reflex to a mean value of 38% of the control (Fig. 62). During recording it was noticed that segmental stimulation increased tremors in the ULs.

Vibration of the tendoachilles showed a mean reflex of 26% of the control (Fig.63).

Procedure: Percutaneous stimulation was applied on 22.3.76. The stimulation electrodes were placed at $T5_{+}$ T6 and the recording electrode at T4. The patient felt parasthesias in both LLs.

During stimulation: No changes were noticed in the clinical condition of the patient.

Fig. 62 Mechanoreceptor stimulation of the sole of the foot by scrubbing of the right and left leg before and 5 days during SCS.



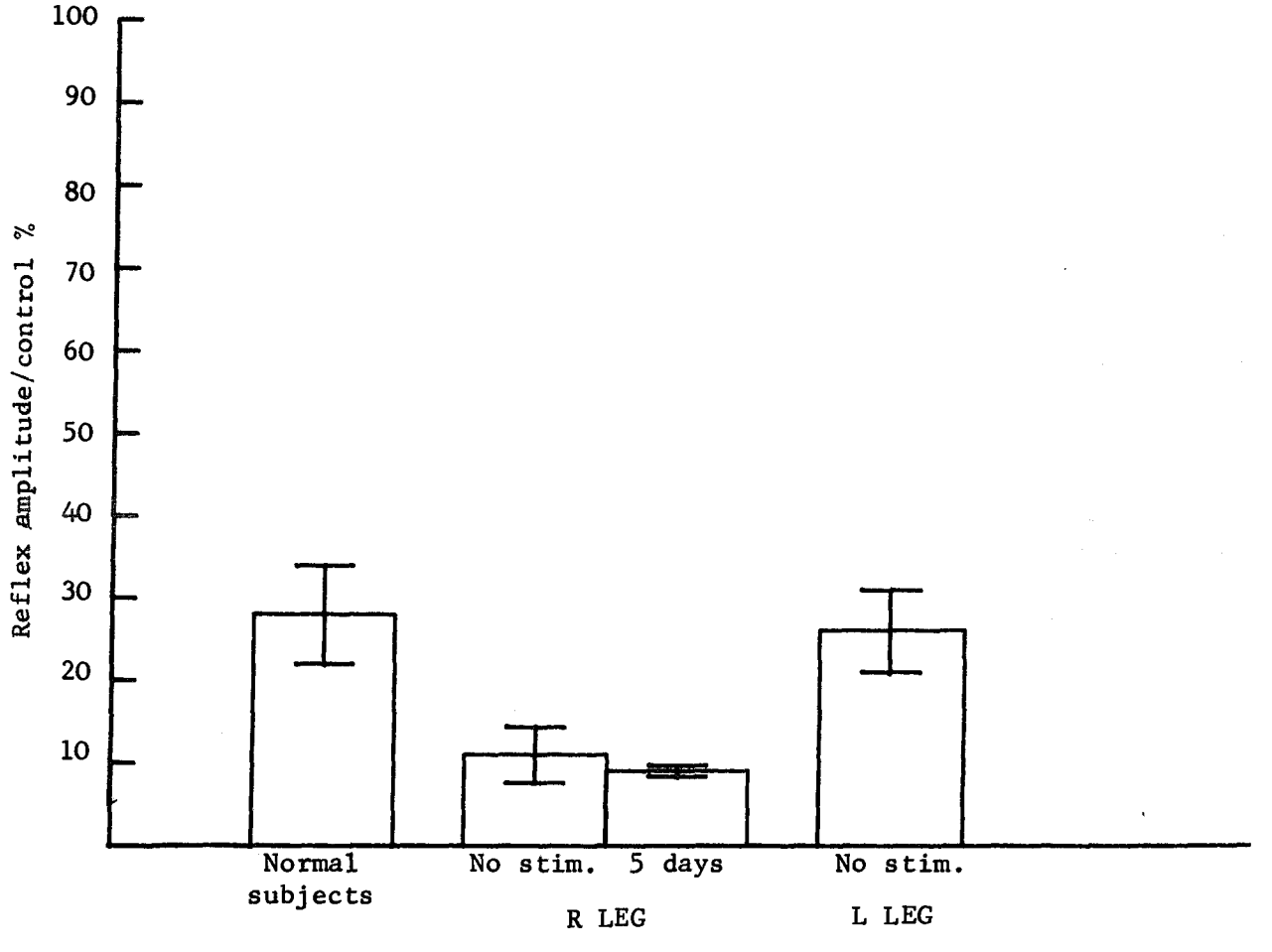


Fig. 63 Effect of vibration of the tendoachilles in case 4 (Miss JM) of the right and left before and during SCS.

H-reflex The patient was tested after continuous SCS for 5 days. The following results were noticed:

R leg: The R leg showed a larger reflex amplitude with a mean value of 2.9 mV. $^{H}/_{M}$ ratio was larger as well and was 32% of the MNP. This can be shown in the recruitment of the MNs with incremental stimuli in Fig.60.

The recovery curve showed a lower value than before SCS (Fig.61) No significant difference was noticed in the recovery time or amplitude prior to and during spinal cord stimulation.

Scrubbing the sole of the foot demonstrated a prominent inhibition of the reflex giving a mean value of 7.35% of the control (Fig.62).

Vibration of the tendonachilles showed a similar inhibition of the reflex giving a mean value of 9% of the control (Fig.63).

When the SCS was switched on with 8V. (which was the standard voltage for the patient), the test reflex increased to 114% of the value prior to stimulation.

L leg: Reflex amplitude was 2.4 mV. $^{H}/_{M}$ ratio was 25% . Fig. 60 showed the recruitment curve of the L leg during SCS.

The recovery curve (Fig.61) showed no significant change from that prior to SCS. It showed a later recovery of the test reflex, at 100 msec. Scrubbing the sole of the foot showed an inhibition of the reflex to 25.5% of the control (mean value) (Fig.62).

The test reflex amplitude increased to 182% when the SC was stimulated with either 6 or 8 volts (Fig.64). Using the highest tolerable pulse intensity of 11 volts the reflex showed a decrease in this facilitation. Its amplitude reached a mean value of 141% of the control (Fig.64).

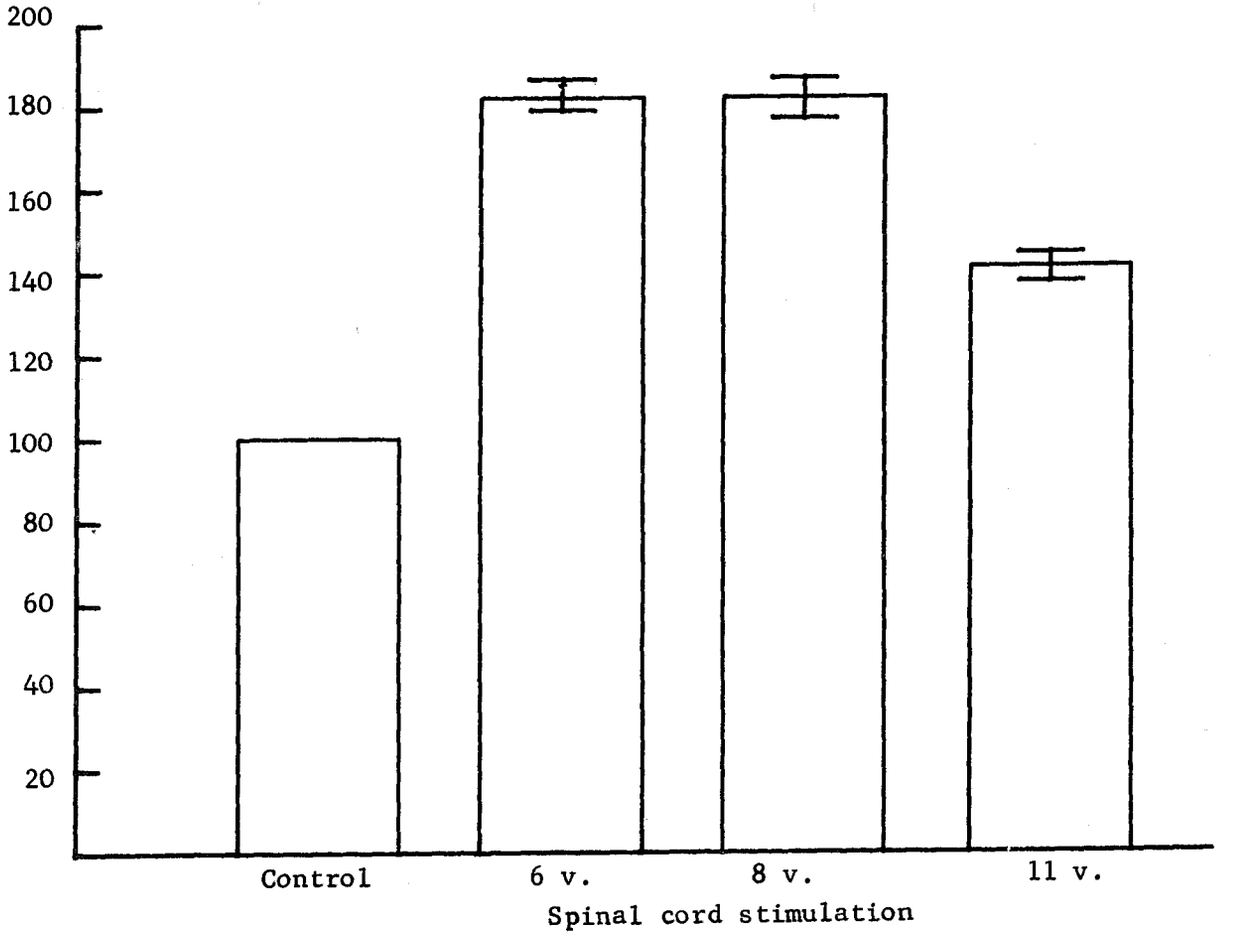


Fig. 64 Spinal cord stimulation using 6, 8 and 11 volts in case 4,Miss JM.

After 10 days of continuous spinal cord stimulation without improvement in the clinical condition the electrodes were removed and stimulation discontinued.

CASE 5 Mr. E.S.

This is a 41 years of age man admitted with complaints of unsteady gait and inability to keep his balance.

He was admitted in March 1975 with seven months history of progressive aches, tiredness and weakness of legs. His neurological examination disclosed a bruit over the R femoral area, absent L dorsalis pedis pulse, mystagmus in the lateral gaze, with ataxia in finger/nose and heel/shin tests.

He had an ataxic gait with pyramidal weakness in the lower extremities with increased ATR and bilateral plantar extensor responses. His JPS was impaired at the toes and VS was impaired to the iliac crest.

Recently he has developed difficulty with his gait and has used a cane since last October 1975. Also he complains of intermittent claudication. He gets pain in the LLs, in his calf, if he walks about 100 yards. Stepping up the stairs he has pain in both calf after 5 steps. During the last six months he has more difficulties with his bladder with urgency. Since last Christmas (1975) he has lost erection. During the last 6 months he has spasm and cramps in his legs during the night. His complaints were diagnosed to be due to M.S.

On Examination: There were extensor spasticities of the lower limbs. Brisk tendon jerks with absent superficial reflexes. Extensor plantar response. Bilateral sustained clonus. Finger/nose and heel/

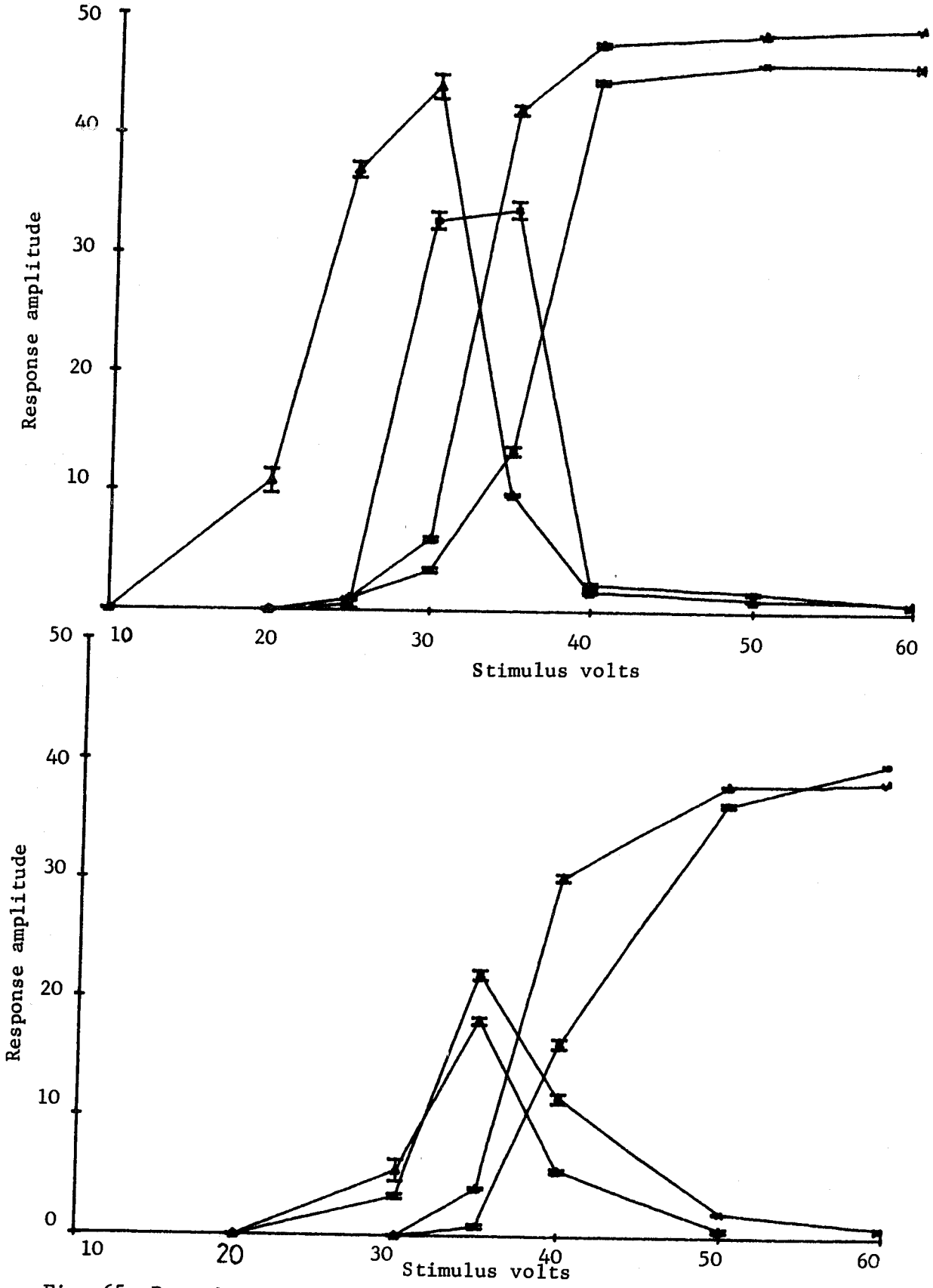


Fig. 65 Recruitment curve of case 5 (Mr. ES) of the right (upper), left (lower) lower limb, before (x) and during (▲) spinal cord stimulation (Mean ± SE)

shin ataxia. +ve Romberg sign. Absent joint position sense in the toes. Loss of pin prick and touch sensation up to ankle level.

H-reflex: R leg: The maximum reflex amplitude showed a mean value of 4 mV with $^{H}/_{M}$ ratio = 74% (Table 17). The recruitment with incremental stimuli is shown in Fig.65 .

In the recovery curve the test reflex was slightly facilitated giving a spastic type curve (Fig.66). There was no dramatic facilitation of the test reflex. It showed 2 ^{ry} inhibition between 300 - 600 msec. Generally speaking the recovery curve can be considered to be an upper normal value.

Scrubbing the sole of the foot did not show inhibition of the reflex. It has been noticed that in spastic cases the test reflex did not show significant inhibition as in normal subjects. It may be due to the hyperexcitability of the MNP in these cases. In this patient the mean value of the test reflex was 92% of the control with mechanoreceptor stimulation (Table 19).

Vibration of the tendoachilles demonstrates an inhibition of the reflex to a mean value of 63% of the control (Fig.67). This was larger than value seen in normal subjects (28%).

L leg The L leg showed a maximum reflex amplitude of 2.6 mV. as a mean value. $^{H}/_{M}$ ratio was 33% (Table 17).The recruitment curve of the L leg is seen in Fig.65 .

In the recovery curve the test reflex recovers faster than normal, with a hyperactive period between 40-300 msec. (Fig.66). The 2 ^{ry} inhibition period was clearly noticed. This was similar to spastic curves showed in UMNL. Mechanoreceptor stimulation of the sole of the foot demonstrated inhibition of the mean reflex value to 86% of the control (Table 19).

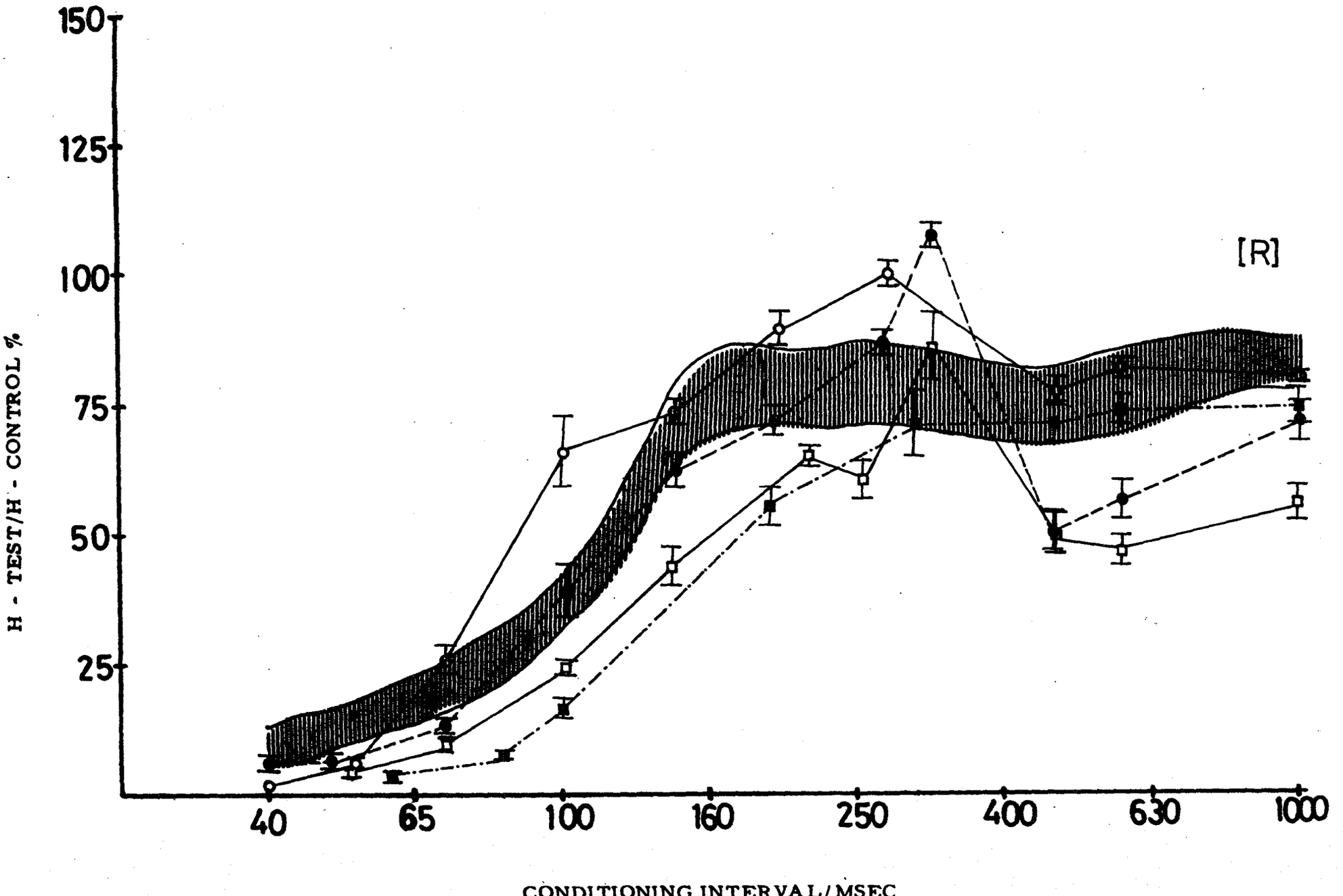
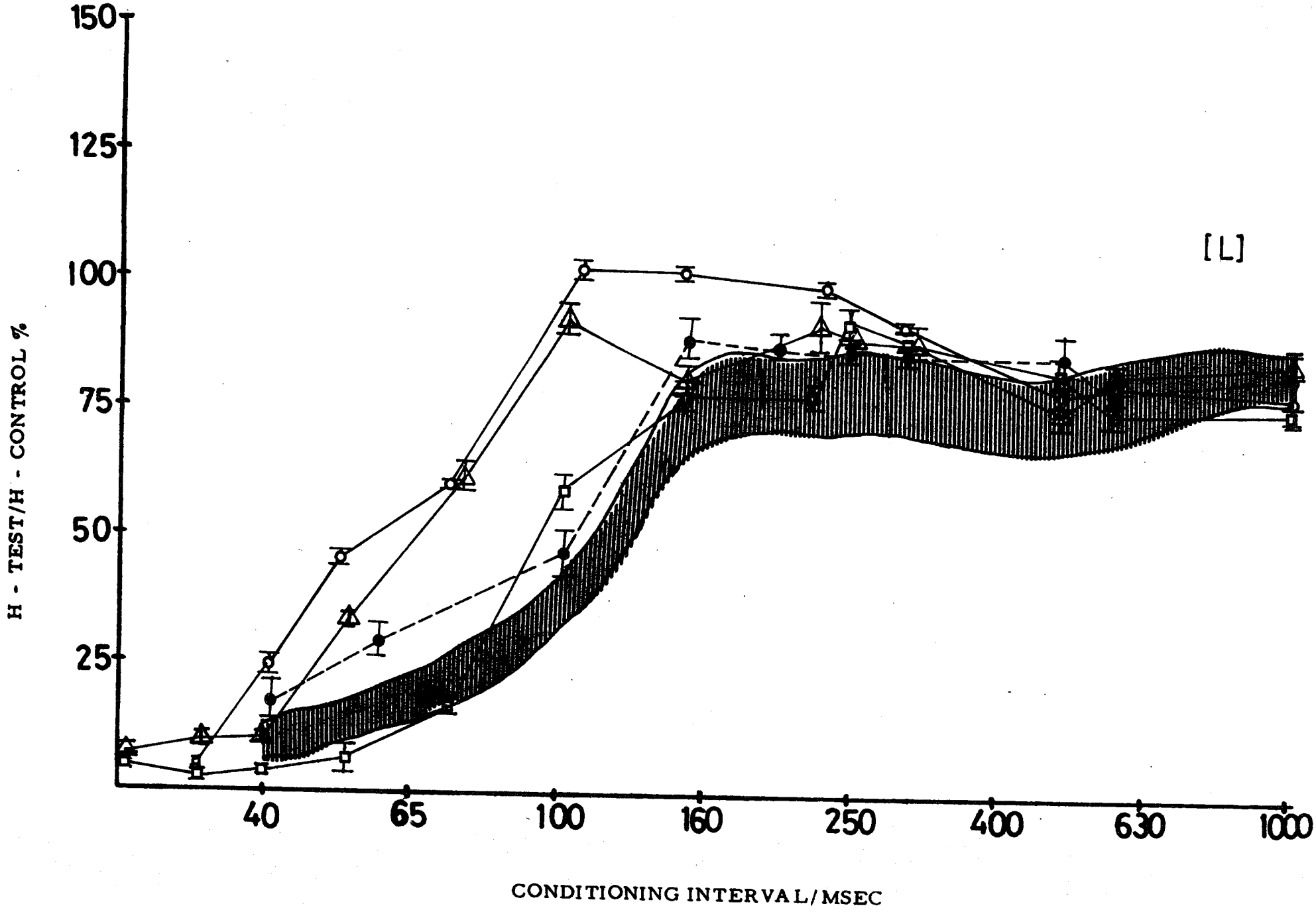


Fig 66 Recovery curve of case 5, Mr. ES, of the right (R), left (L), lower limb before (o), 6 days during (●), 24 days after (□) spinal cord stimulation. Mean ± SD).


150
125
100
75
50
25
H - TEST/H - CONTROL %
[L]
40
65
100
160
250
400
630
1000
CONDITIONING INTERVAL/MSEC

Vibration of the tendoachilles produces inhibition of the reflex to 60% (mean value) of the control (Fig.67).

Procedure: The percutaneous stimulation was carried out on 25 March 1976 and the electrodes were introduced to $T5_{+}$ T6 levels. The recording electrode was positioned at T1. Parasthesia was felt in both extremities.

During stimulation

24 hours: The pains were relieved and the patient did not experience nocturia.

4 days: Improved intermittent claudication and he was able to go upstairs without pain or tiredness. The bladder function returned to normal function. There was mild improvement in the ataxia.

10 days: Improvement in gait.

H-reflex: The patient was tested at 6 and 9 days after electrode fixation and continuous stimulation. He showed the following responses in the R leg:

The mean of the maximum reflex amplitude was 5.3 mV. with a fraction of 76% in $^{H}/_{M}$ measurement (Table17). The recruitment curve of the R leg with incremental stimuli is shown in Fig.65.

The recovery curve showed an inhibition towards the normal pattern (Fig.66). The change in the test reflex and the curve was not too dramatic. Generally speaking the excitability curve was of a lower normal value.

The R leg was tested again after 9 days with continuous stimulation for changes in the recovery curve. It showed a dramatic decrease than normal value (Fig.66). The slower recovery shown

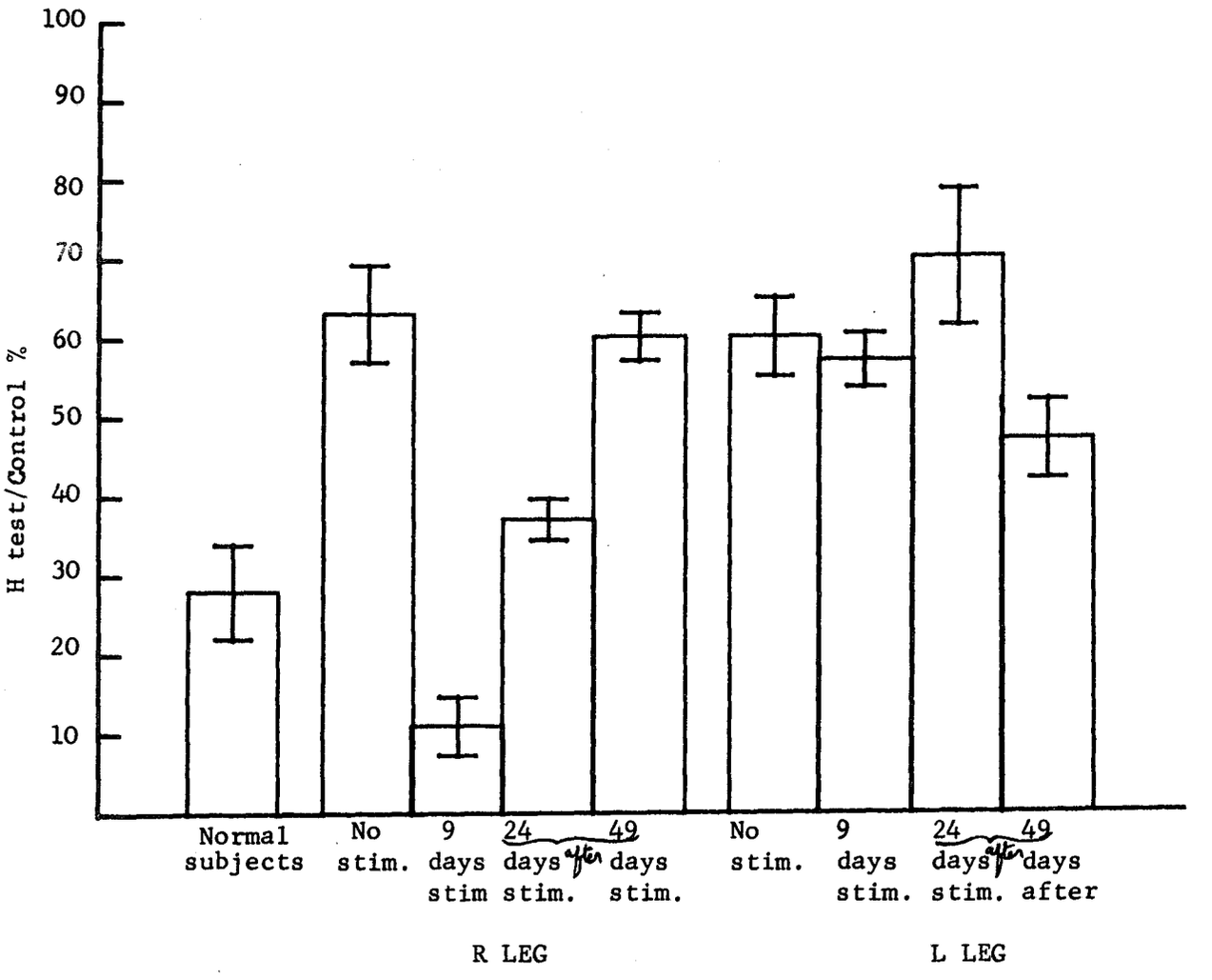


Fig. 67 Effect of vibration on the H-reflex amplitude in case 5 (Mr. ES) of the right and left lower limb, before, during and after spinal cord stimulation. (Mean ± SD) .

in this curve coincides with the decrease in tightness noticed by the patient. The recovery time comes later than that prior to SCS with 20 msec. difference.

By scrubbing the sole of the foot the reflex was inhibited to 63% of the control (Table 19). It showed a significant inhibition to a mean value of 11% by vibration (Table 20). It is worth noting that the patient noticed greater improvement in the R leg with SCS.

Table 20 Effect of SCS on reflex inhibition by vibration

Patient name	Leg	Before H test/ H control %	During % control	After % control
JM	R	11	8.6	-
	L	26	-	-
ES	R	63	11	37, 60*
	L	60	57	70, 47*
RW	L	79	-	-

* 24 and 49 days after removal of SC electrodes.

SCS with 3 volts (the standard voltage of that patient) produces an increase in the reflex amplitude to 113% of the control. The change was significant to the 1% level.

L leg: The L leg showed a larger maximum reflex with a mean amplitude of 3.2 mV. The MNP fraction fired by H-reflex was of a mean value of 47% measured by $^{H}/_{M}$ ratio (Table 17). The MNs recruitment with incremental stimuli is shown in Fig.65.

The recovery curve (Fig.66) showed a dramatic change towards the normal pattern. No change was seen in the recovery time.

Scrubbing the sole of the foot did not show any significant change. The mean reflex value was 88% of the control (Table 19). This was the case with vibration which gave a reflex inhibition of 57% of the control (Table 20).

The test reflex showed significant facilitation to 288% of the control by SCS with 3V. for 33 PPs. Increasing the stimulus intensity to 4 volts enlarged the reflex facilitation to 298% (Table 20).

After stimulation: There was a progressive weakness of the L leg with gradual return to the pre-stimulation condition within 24 days after removal of the electrodes. The bladder sensation remained.

H-reflex: The patient was tested 24 days and 49 days after removal of the electrodes. 24 days after stimulation had been discontinued, the patient showed the following results in the L leg:

The mean reflex amplitude was 3.2 mV., the same as that during SCS. It showed a larger fraction value of 78% (Table 17). The recruitment curve with incremental stimuli is shown in Fig.65 .

The recovery curve showed a gradual return to the prestimulation value (Fig.66). The faster recovery of the test reflex with an earlier recovery time is noticed in the excitability curve. The test reflex was not dramatically facilitated compared with the normal value.

Scrubbing the sole of the foot showed significant inhibition of the reflex giving a mean value of 48% of the control (Table 19).

Vibration of the tendoachilles showed a progressive return to the pre-stimulation value. The mean reflex amplitude was 70% during

vibration (Fig.67).

R leg: The R leg showed a dramatically smaller reflex amplitude than that during SCS. It had a mean value of 2.8 mV. with a fraction value of 51% (Table 17).

In the recovery curve the test reflex was smaller than normal with a slower recovery (Fig. 66). There was no significant change in the excitability curve of the R leg from that during SCS. This coincided with the observation of the patient, that his left leg was deteriorating more quickly than the R leg after removal of the electrodes.

The effects of vibration of the tendoachilles supports these findings as it showed a mean reflex amplitude of 37% of the control (Table 20).

Retesting the patient 49 days after removing the electrodes showed the following:

R leg: The maximum reflex amplitude had a large mean value of 6 mV. with an $^{H}/_{M}$ ratio of 88% (Table 17). The recruitment curve of this leg is shown in Fig.65 .

The recovery curve (Fig.66) showed a gradual return to pre-stimulation level. Although the curve was not as high as found in severely spastic cases, it showed a prominent decrease in the primary inhibition period. This inhibition period was shorter than normal with a slightly inhibited test reflex. The reflex recovery was faster than normal but did not show higher value unless after 250 msec to 1000 msec.

Vibration of the tendoachilles showed inhibition of the mean reflex value to 60% of the control (Fig.67).

L leg: The L leg showed a large reflex amplitude. Its mean value was 5.43 mV. These coincide with the increase of the MN discharge in spastic conditions. The MN fraction was larger than normal and was of a mean value of 84% (Table 17). This can be shown in the recruitment curve of this leg in Fig.65 .

The recovery curve showed a nearly normal value. The test reflex did not show complete inhibition in the primary inhibition period (Fig. 66). No prominent changes were seen from the curve plotted 24 days after electrodes removal.

Vibration gave a mean reflex inhibition to 47% of the control (Fig. 67).

CASE 6 Mr. R.W.

A man of 39 years of age with a history of illness started in 1973 when he developed cramps in the L leg at night. Soon after this he noted fasciculation in the L thigh muscles. Since then there has been a gradual and progressive weakening of the L leg, followed by the R leg and more recently both arms. He has experienced cramps and fasciculation in both legs, the lower abdomen and both arms. A diagnosis of motor neurone disease was made after intensive investigation.

On examination July 1975 BP $\frac{130}{80}$. General examination was negative. There was slight slurring of speech but no difficulty in swallowing. There were poor movements of the tongue and marked fasciculation. There was diffuse fasciculation in virtually all muscles of the arms and legs. There was wasting of the small muscles of both hands which was more marked on the L. There was wasting of both quadriceps, rather more marked on the R. There was weakness of neck reflexes as well as muscles of U and LLs. Reflexes were symmetrical. The R plantar was

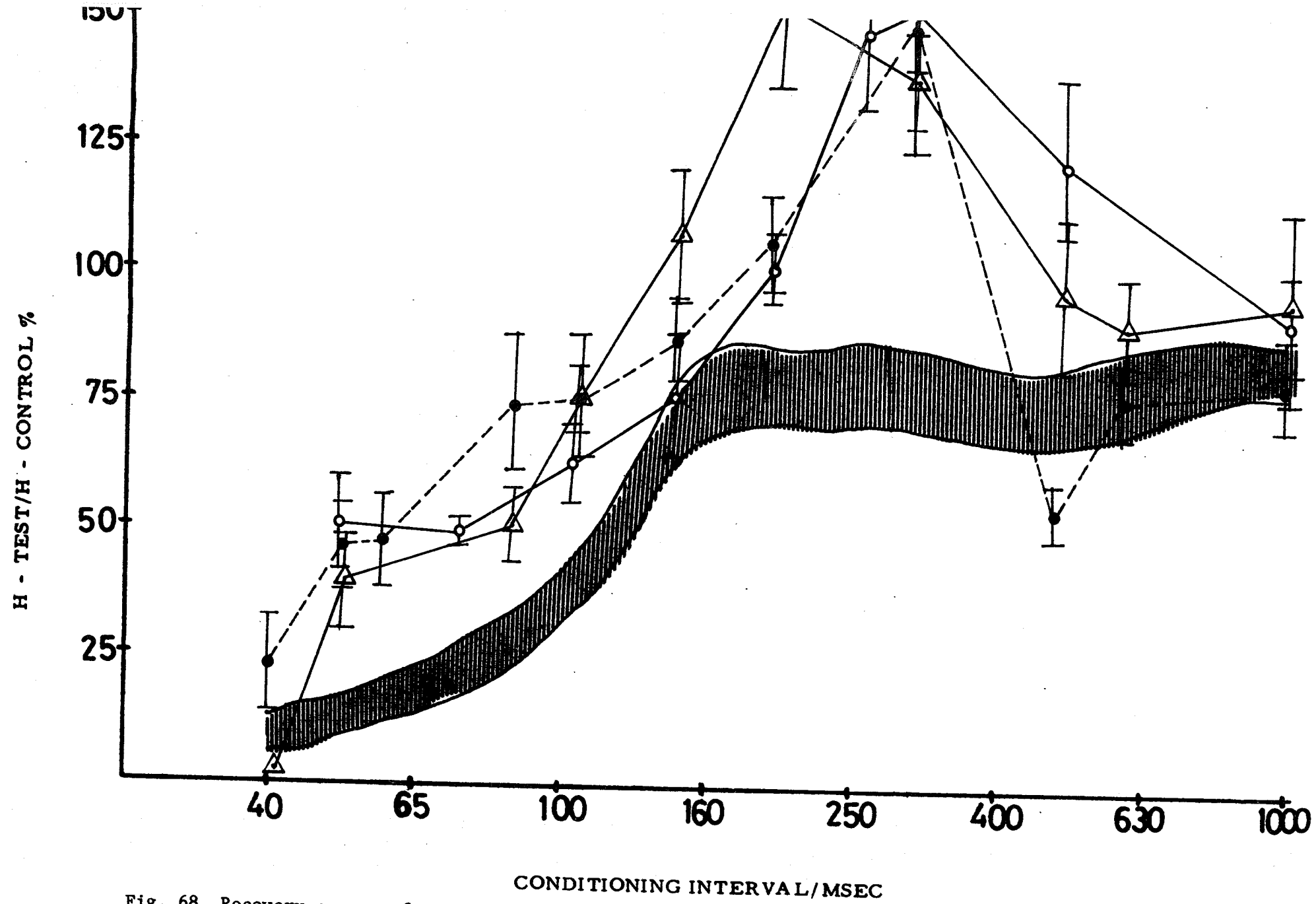


Fig. 68 Recovery curves of case 6 (Mr. RW) of the right lower limb before (o), during (●) and 14 hours (△) after spinal cord stimulation. (Mean ± SD)

equivocal and the L plantar flexor. There was no sensory loss.

H-reflex: The L leg was only tested. It showed a maximum reflex amplitude with a mean value of 0.01 mV. (10 μV.) (Table 17).

The recovery curve was of spastic type (Fig.68). It showed a hyperactive early facilitation period from 3 to 15 msec. The test reflex was 340% of the control. This was followed by a short inhibition period with a significant recovery at 50 msec. A fast recovery with a hyperactive period from 200 to 1000 msec. followed. No secondary inhibition period was seen.

It is interesting to note that the mean value of the H-reflex was inhibited to 79% of the control by vibration of the tendoachilles (Table 20). This inhibition was significantly smaller than the normal standard seen before. Tendon jerk (ATR) showed contradictory results. A significant facilitation of the reflex by vibration was seen. It was of a mean value of 134% of the control.

Stimulation of the median nerve at the wrist level showed an H-reflex in the abductor pollicas brevis, which cannot be evoked in normal subjects (Magladery et al 1950). Post-tetanic potentiation studies were applied in this patient. The H-reflex control value was 13.5, value after potentiation was 12.7, a very slight decrease was seen. Potentiation was a 30 msec. gate of 1000 pulses per second given for 500 msec. before the H-reflex was measured. Potentiation produces slight decrease of the reflex in this patient while in normal subjects it was facilitated. (Hagbarth 1962).

Procedure: Permanent implantation of the spinal cord electrodes and the receiver were performed in the USA by Professor A. Cook. Four electrodes were implanted, two of them at C7 for stimulation of the

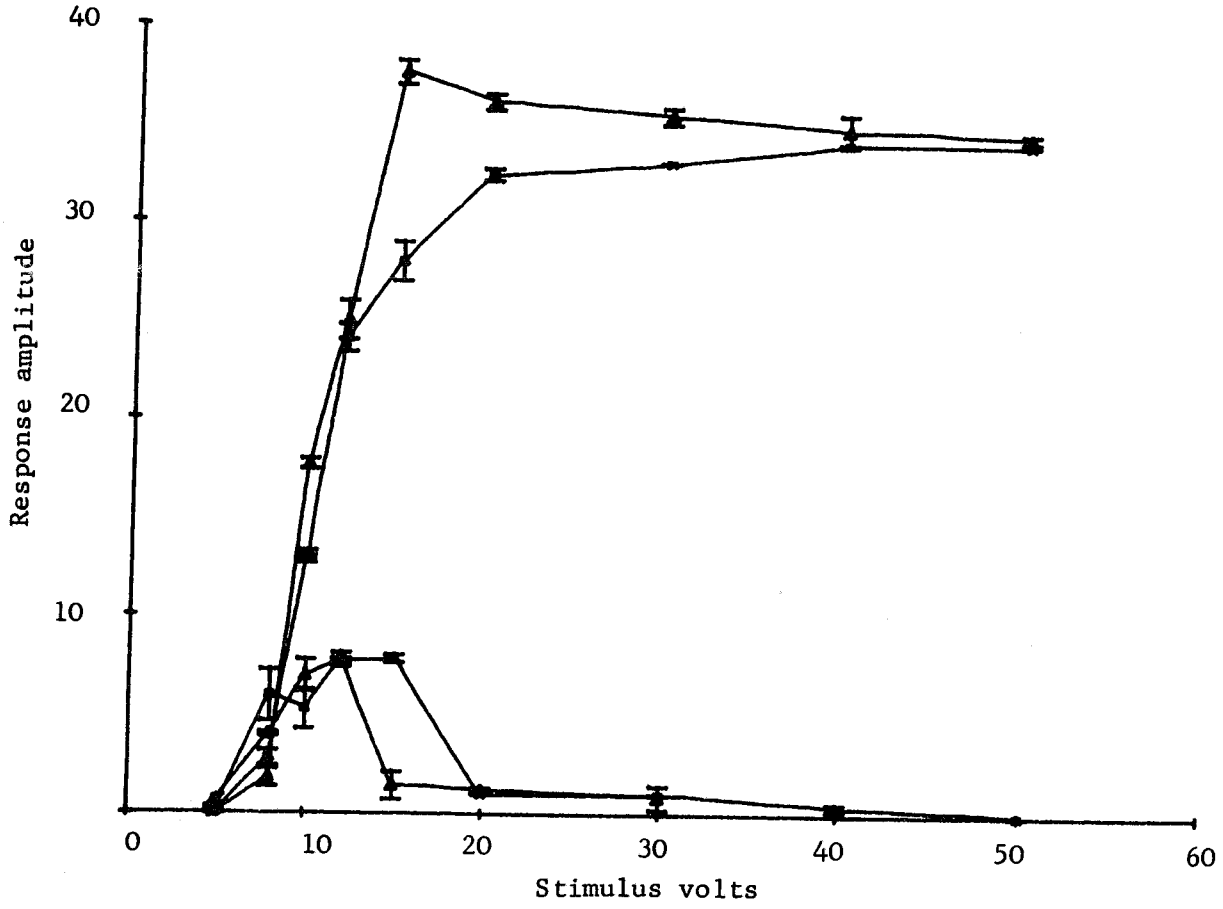


Fig. 69 Recruitment curve of case 5 (Mr. RW) before (x) and during (▲) spinal cord stimulation (Mean ± SE)

ULs. The other two electrodes for stimulation of the LLs were implanted at T4.

During stimulation: No changes were observed in the clinical condition of the patient.

H-reflex: The mean of the maximum reflex amplitude was 0.01 mV. $^{H}/_{M}$ ratio was 54% (Table 17). This can be seen in the recruitment curve (Fig.69). No significant changes were seen between switching the SCS on and off (Fig.69) but there was some change in the threshold level of stimulation. There was a significant decrease of the MN discharge from that of normal value.

The recovery curve showed no change during SCS (Fig.68). This was the case either during continuous SCS or when it was switched off for 14 hours.

A mean reflex value was 13 and showed slight facilitation to a value of 17 when the SCS was switched on. The reflex was increased by 130% and was significant to the 1% level ($P = 0.001$).

PHYSIOLOGICAL STUDIES OF SPINAL CORD STIMULATION AND ITS EFFECTS ON MN DISCHARGE IN MS PATIENTS

Stimulation of the spinal cord, particularly the dorsal column, was applied using a "Devices" type stimulator, through the implanted electrodes.

Experiments were constructed to study the effect of the following stimulus parameters on the MN discharge in H-reflex:

1. A single conditioning pulse to the spinal cord at variable intervals from the test. This pulse was at sensory threshold level applied to the spinal cord.
2. A single pulse to the spinal cord at fixed conditioning interval, with incremental voltage. This was further prolonged in order to study the relationship between the SCS voltage and the reflex amplitude with reference to the functional response of the patient to certain stimulus strengths.
3. Changes of MN discharge with different pulse duration of the conditioning.
4. Changes of MN discharge with different pulse rate conditioning to the SC.
5. Train of pulses to the SC at variable conditioning intervals from the test pulse.
6. Continuous stimulation to the spinal cord.

I H-reflex conditioned by single pulse to the spinal cord

This test was studied in four MS patients. The conditioning pulse was of sensory threshold to the spinal cord. This threshold was tested beforehand for different stimulus duration. A stimulus

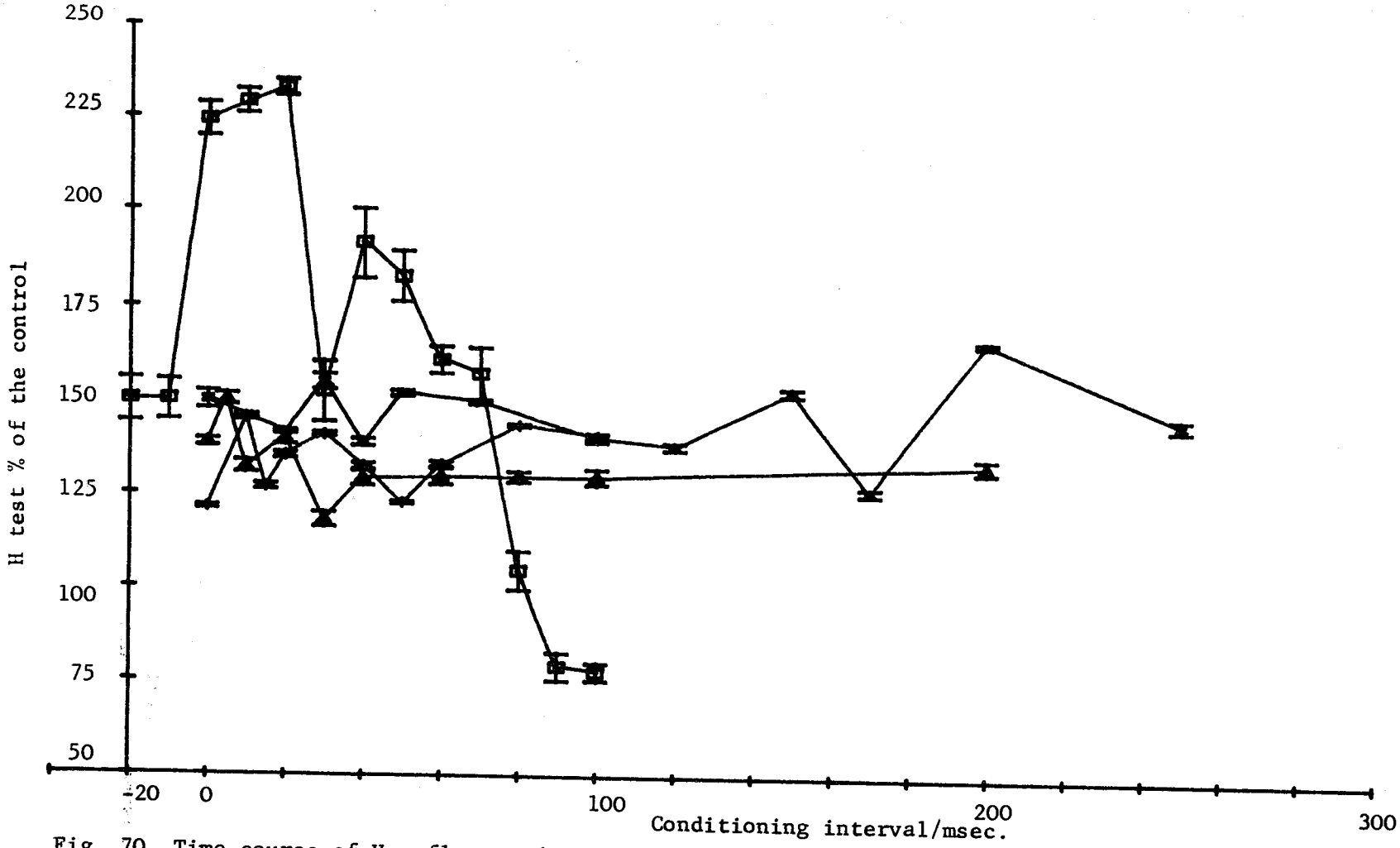


Fig. 70 Time course of H-reflex conditioned by a single shock, of threshold level, to the spinal cord in four patients. (Ordinate = test reflex % of the control). (Mean $\pm$ SD).

duration of 200 μsec. was used. The conditioning interval ranged from 0 - 100 msec.

Table 21 Effect of SCS (single, train & continuous pulses) on reflex amplitude

Patient name	Single shock* H test/ H control %	Pulse train % control	Continuous % control
SE	135	143	106
CP	150	120	117
JM	224	146	142
ES	139	125	120

* Single shock delivered at the same time with the test pulse.

The H-reflex showed significant facilitation over the 100% baseline in all four cases (Fig.70). The reflex facilitation ranged from 105 to 233% of the control. In Table 21 the effects of SCS with single shock of sensory threshold level, delivered at the same time with the test pulse, can be seen. In three out of four the reflex facilitation showed at all conditioning intervals. In the 4th patient the reflex showed mild inhibition to 78% with a long conditioning interval i.e. 90 and 100 msec. This was preceded by a gradual facilitation of the reflex to the maximum at 20 msec.interval. In the same patient the conditioning pulse was elicited 10 and 20 msec. after the test pulse. Both pulses summate on the MN and cause facilitation to 150% of the control. There was an enormous reflex facilitation between 0 and 20 msec. conditioning interval, after which the facilitation decreased gradually to a minimum at 80 msec. The two phases of

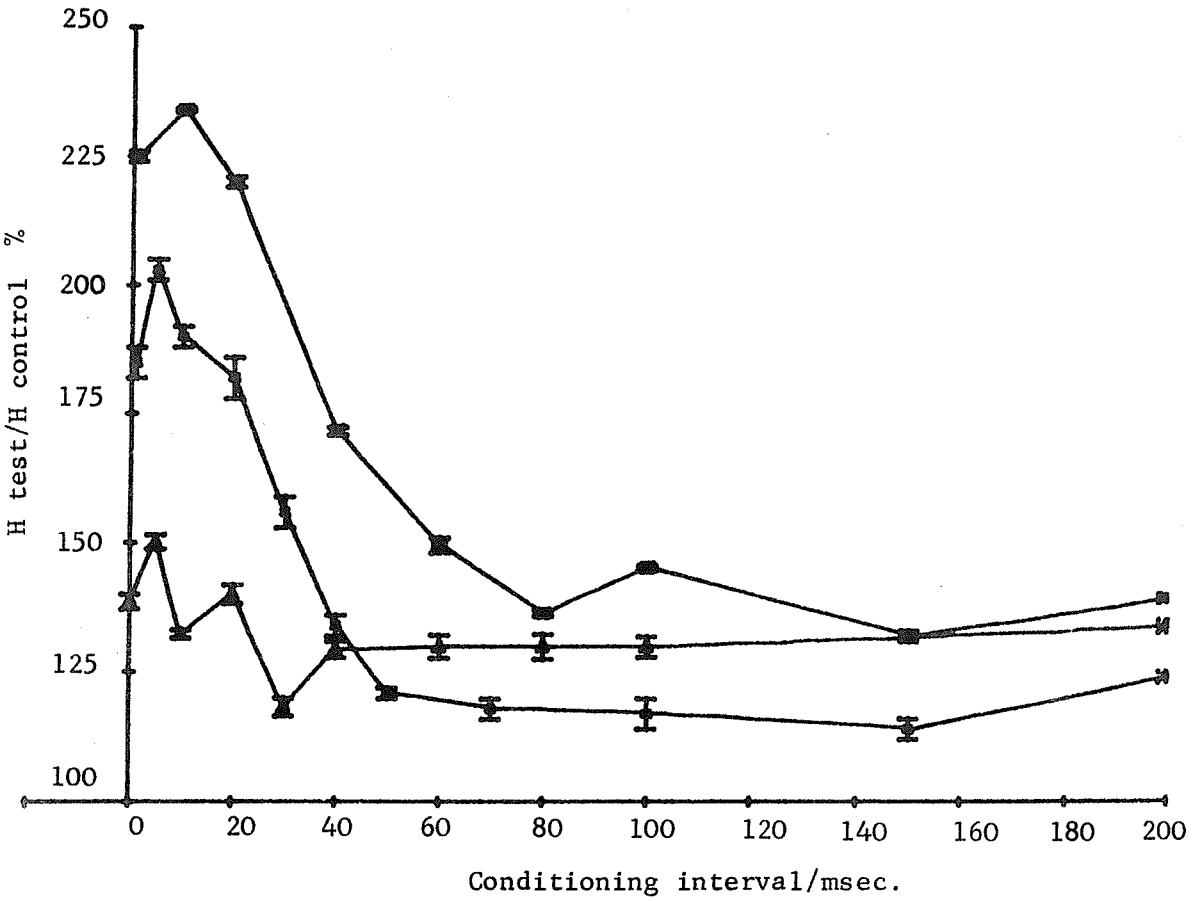


Fig. 71 H-reflex time course conditioned by a single pulse of 10 (▲) 25 (x) and 40 (●) volts, to the spinal cord in case 5, Mr. ES. (Mean ± SD)

facilitation are shown in the second patient (Fig 70).

In the other two patients the reflex facilitation was nearly of equal value at different conditioning intervals.

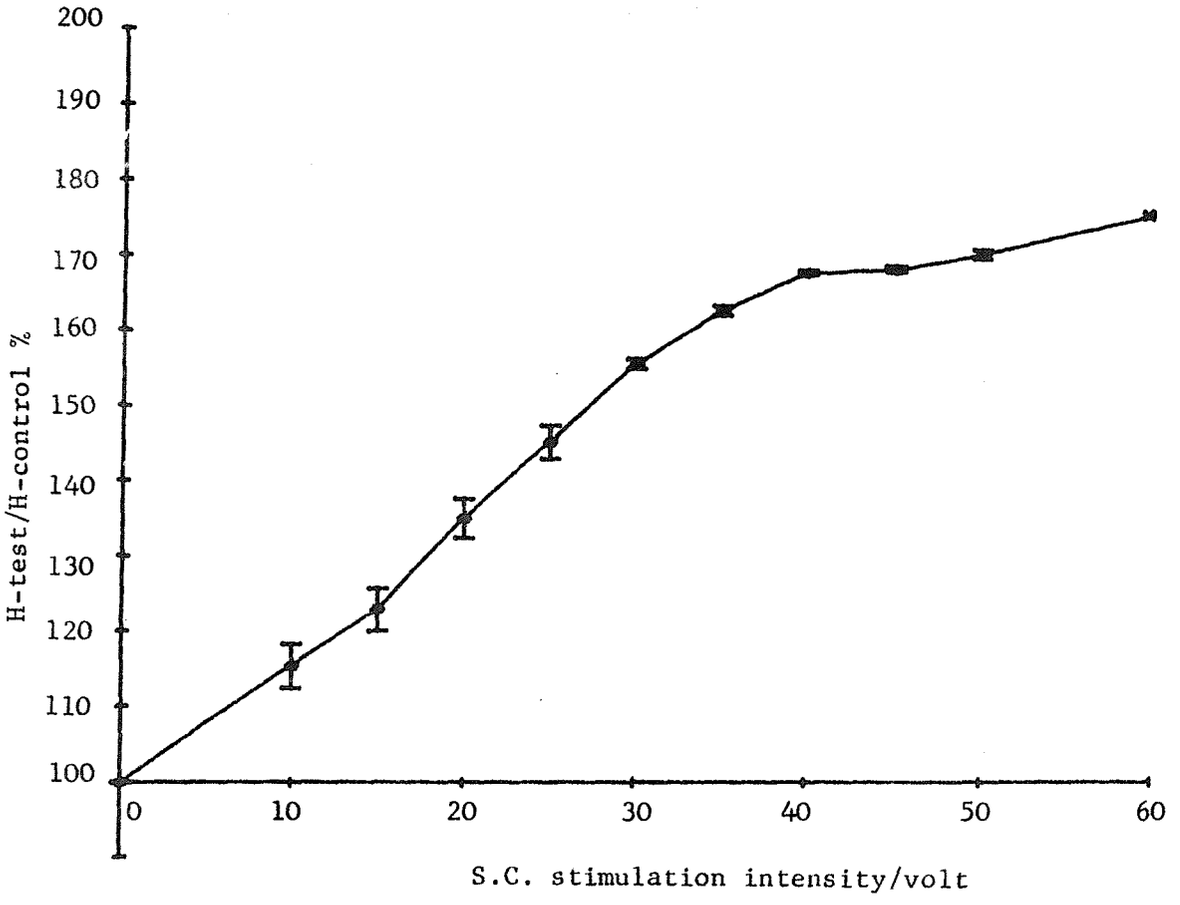
In one patient increasing the conditioning intensity at variable time intervals showed the two phases of reflex facilitation clearly (Fig. 71). The initial phase with a peak at 10 msec. and with a long decaying phase ended at 50 msec. The reflex reached to 230% of the control at its maximum, when the spinal cord was stimulated with 90 volts, and reached to more than 200% when stimulated with 25 volts. With 10 volts stimulation the reflex facilitation reached 150% of the control.

This initial facilitation period was followed by a second one in which the test reflex was slightly longer than the control. It ranged from 110-140% of the control according to the conditioning pulse strength. In this period the curve flattened with no reflex fluctuation.

II Effect of incremental stimuli to the spinal cord on the MN discharge

It can be seen from the last section that an increase in the voltage intensity in the SCS enlarged the reflex facilitation. This was further studied in the same patient with gradual incremental stimuli.

Stimulation of the spinal cord with single shocks (0.2 msec. duration) of incremental intensity and 20 msec prior to the test pulse is shown in Fig.72 . It showed a steep reflex facilitation with incremental stimuli up to 40 volts conditioning strength. The test reflex showed mild facilitation afterwards and up to 60 volts stimuli, which was the highest tolerable strength for the patient. The test reflex reached 168% of the control with 40 volts stimulation to


200
190
180
170
160
150
140
130
120
110
100
H-test/H-control %
0
10
20
30
40
50
60
S.C. stimulation intensity/volt

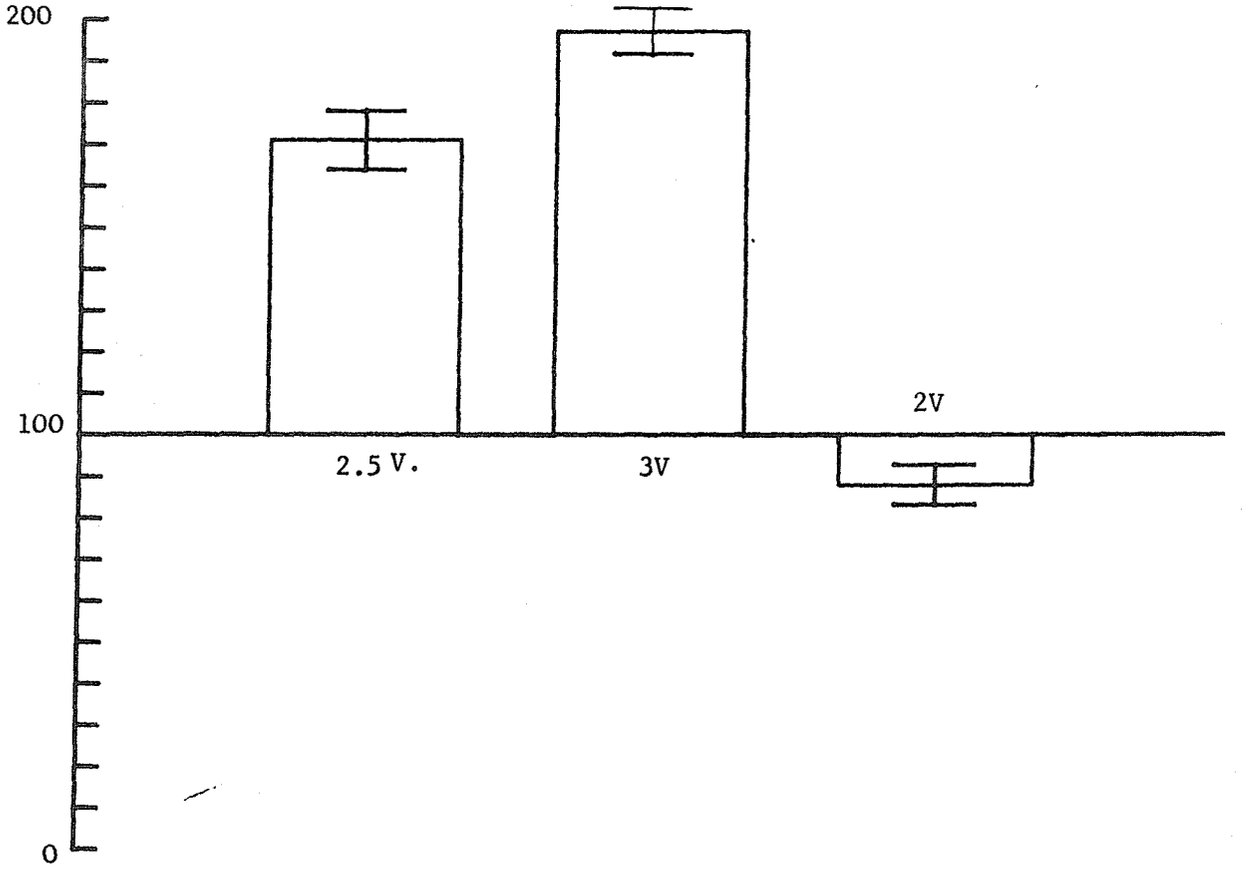

200
100
0
2.5 V.
3V
2V

Fig. 72 The H-reflex was facilitated with every increase in intensity of spinal cord stimulation, using single shocks, so that there was a linear relationship between spinal cord stimulation intensity and reflex amplitude.

Fig. 73 Using the transmitter stimulator with 33PPS of 0.2 msec. showed a functional stimulus intensity at which each patient responded. In case 1, Mrs. S.E., 2.5 and 3 mV. were used daily and showed maximum effect.

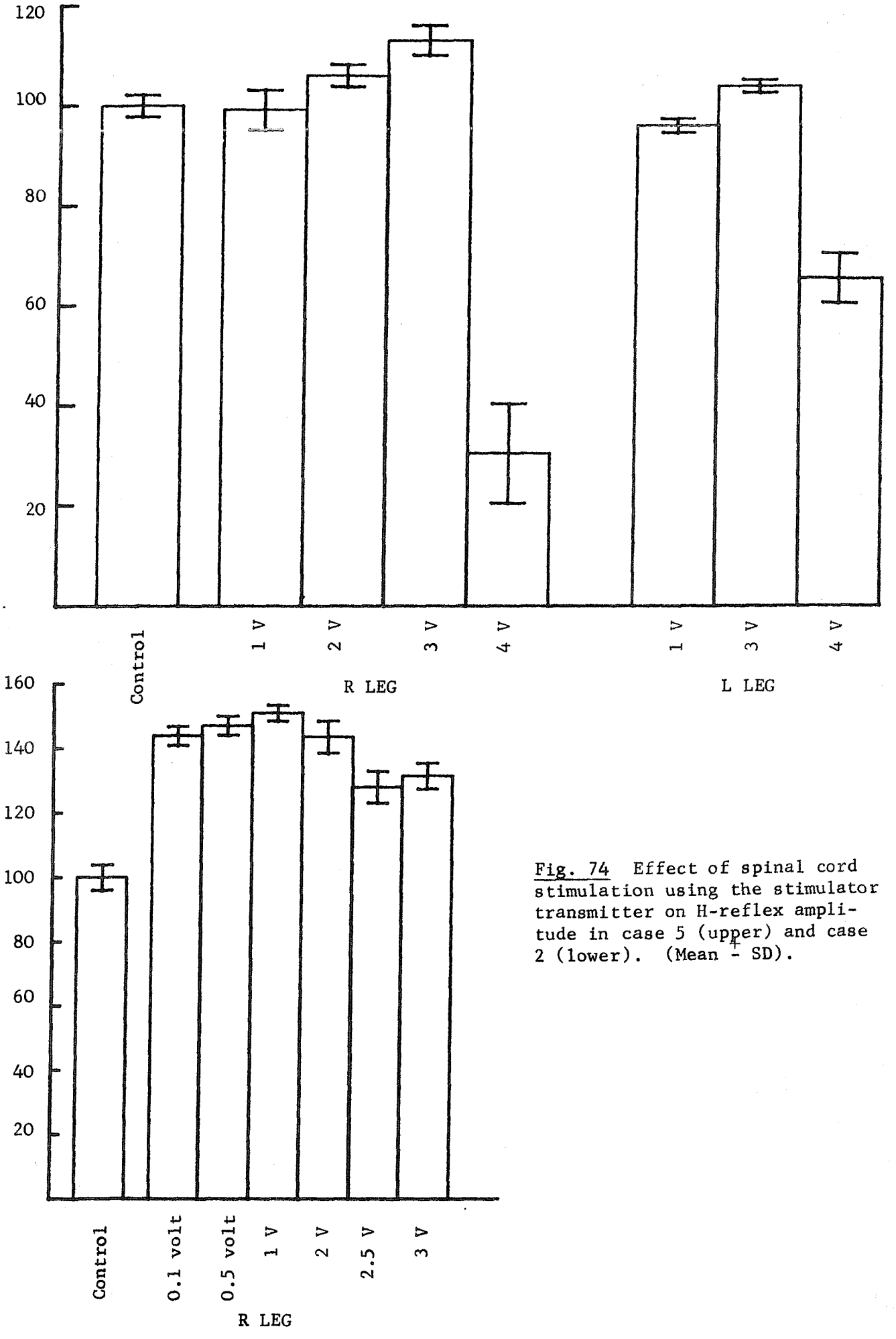


Fig. 74 Effect of spinal cord stimulation using the stimulator transmitter on H-reflex amplitude in case 5 (upper) and case 2 (lower). (Mean ± SD).

the spinal cord. This value increased to 175% with 60 volt pulses.

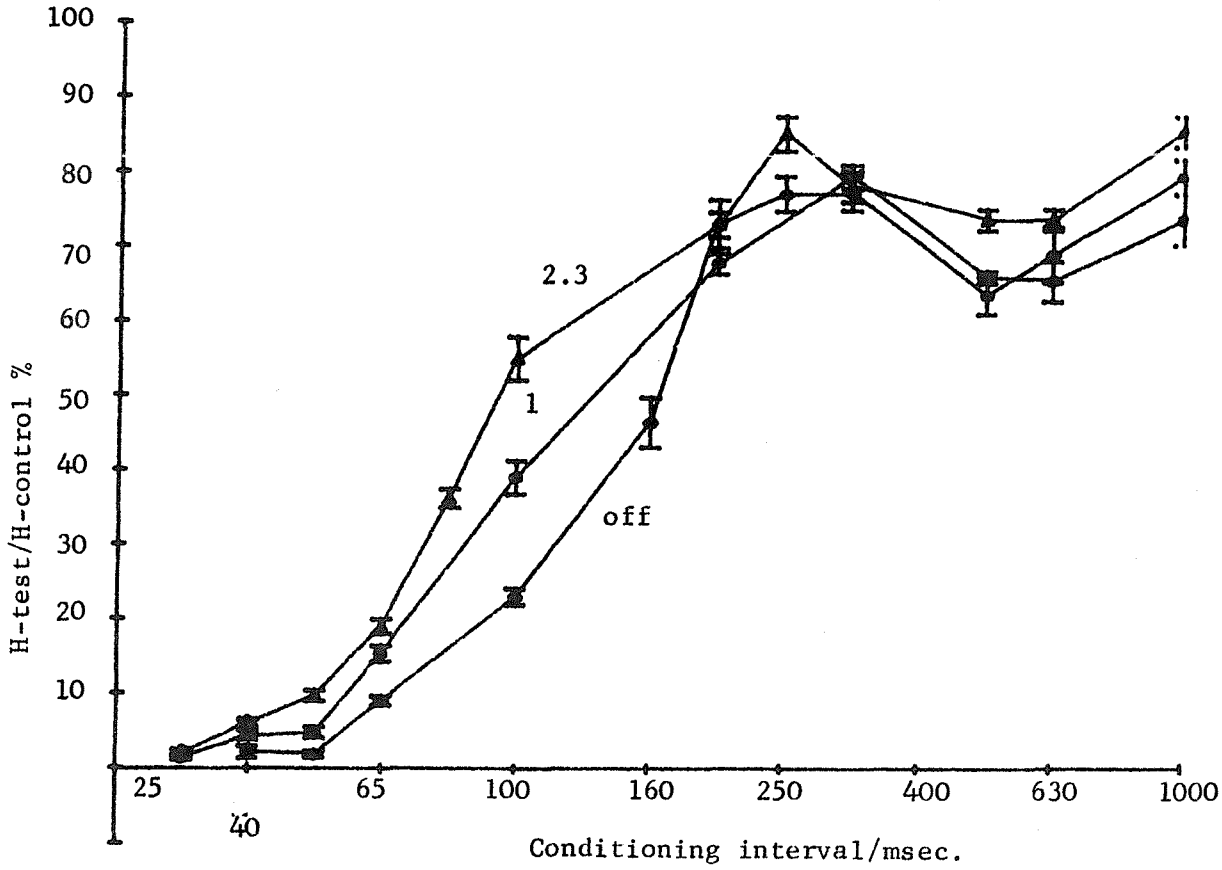
Incremental stimuli with SCS transmitter produced reflex facilitation as well (Fig.73). The test reflex showed facilitation to 171% with 2-5 volts stimulation of the SC. It increased to 197% with 3 volts pulses. Lowering the stimulus strength to 2 volts produced a mild inhibition of the reflex to 88% This supports the idea that the voltage intensity should be fixed at a certain level appropriate for the functional disturbances.

It is interesting to note that the functional response of every patient was optimal at a completely different stimulus strength e.g. patient (C.P.) responsed well to SCS with 1.5 volts, but Miss J.M. did not respond to less than 8 V., i.e. she did not feel the paresthesia in her legs with less than 8 V. stimuli.

The test reflex showed a parabolic type of curve with incremental stimuli in one patient. Stimulation of the spinal cord was applied using a stimulator transmitter with a voltage strength ranging from 0.1 to 3 volts. The test reflex increased to the maximum (151% of the control) with 1 volt stimuli. This was followed by a slight decrease in the reflex facilitation with a higher stimulus strength (Fig. 74).

In one other patient (E.S.) the reflex showed gradual decrease in amplitude with increasing stimulus strength to the SC by the transmitter (Fig.74). The test reflex showed a maximum value with 3 V. intensity. With a higher stimulus strength it inhibited to 30% of the control. It is important to note that this stimulus strength was the highest sensory threshold tolerated by the patient. This reflex inhibition with higher stimulation intensity and repetitive stimulation was noticed in all patients tested.

Fig. 75 Recovery curve in case 2, Mr. C.P., with SCS off (*) and on using 1 V. (●) and 2.3 V (▲) stimuli to the spinal cord. (Mean ± SE)



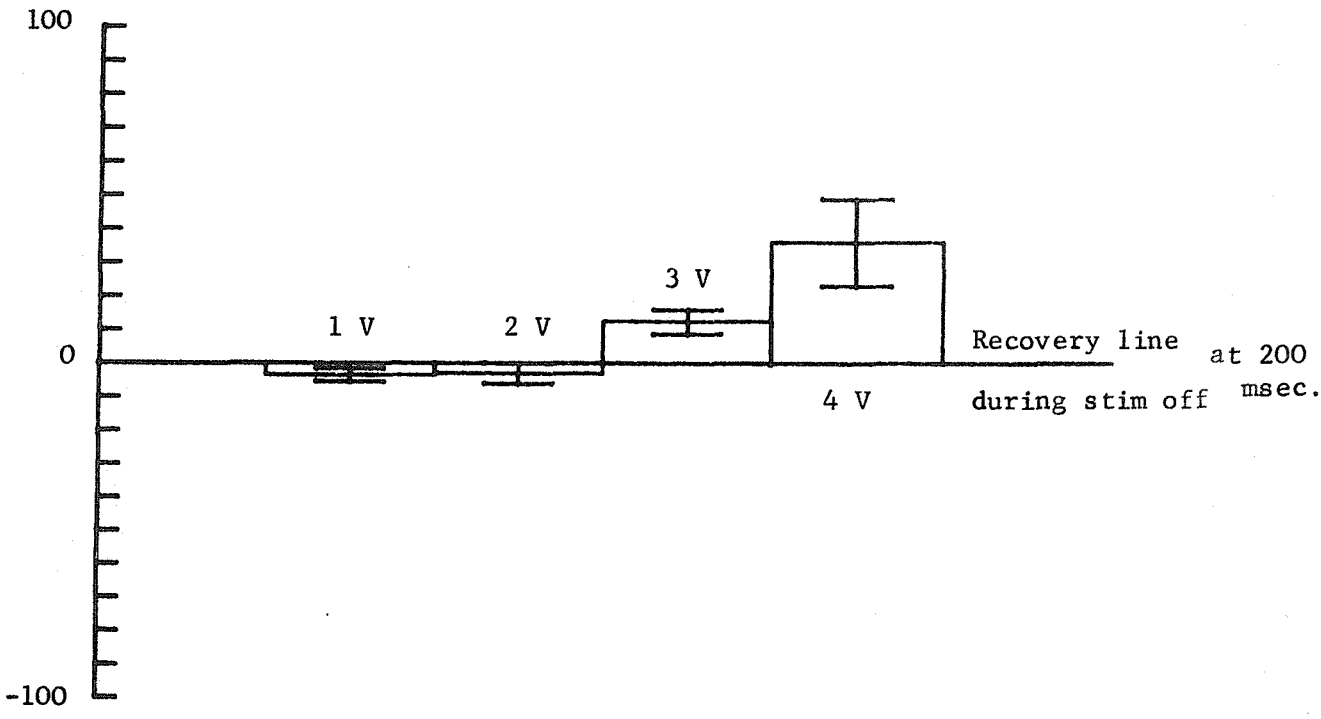


Fig. 76 Recovery of the MNP during SCS using different voltage intensity in case 5, Mr. ES. The zero line is the recovery during SCS off. Facilitation of the recovery was seen with 3 and 4 volts stimulation while it was slightly decreased on using 1 and 2 volts. (Mean ± SD).

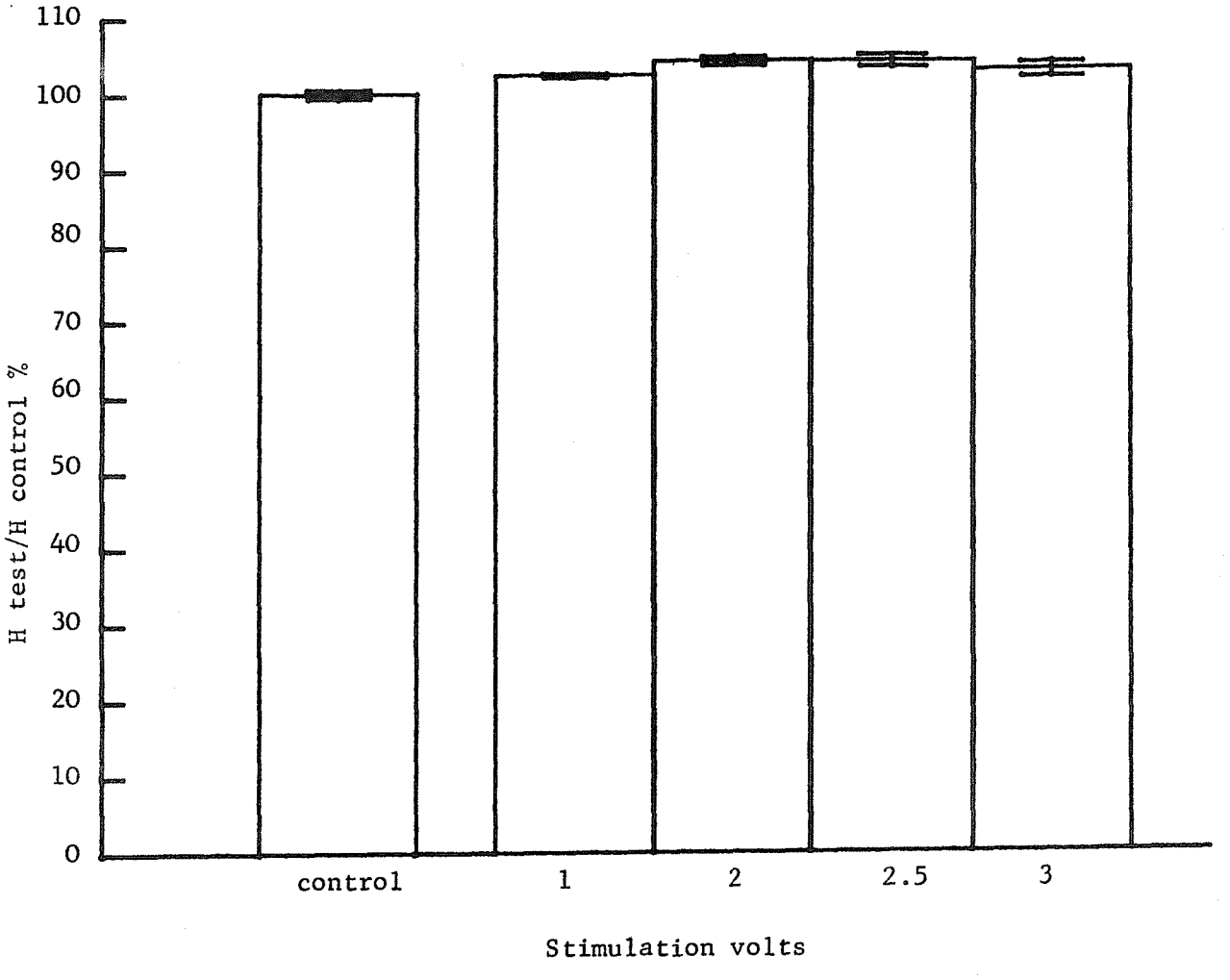


Fig. 77 Effect of incremental stimuli to the spinal cord, using transmitter stimulator, on the H-reflex amplitude in case 3, Mr. NE. (Mean ± SD)

In one other patient (J.M.) the reflex facilitation did not show the linear relationship with the voltage intensity. She showed an equal reflex enlargement with incremental stimuli followed by inhibition of the test reflex with supramaximal SCS.

It is worth noting that the reflex facilitation continued for a long time after switching the stimulation off, which shows the after effect of this procedure. It has been noticed in two patients (E.S. and C.P.) that the effect of increasing voltage intensity to the spinal cord manifested itself by increasing the recovery of the test reflex (Fig.75). This was further studied using paired pulses at 200 msec. intervals with different stimulus strength. Stimulation of the S.C. using 4 volts pulses showed a test reflex of 136% of the control. One volt stimuli showed a test reflex 96.5% of the control (Fig.76).

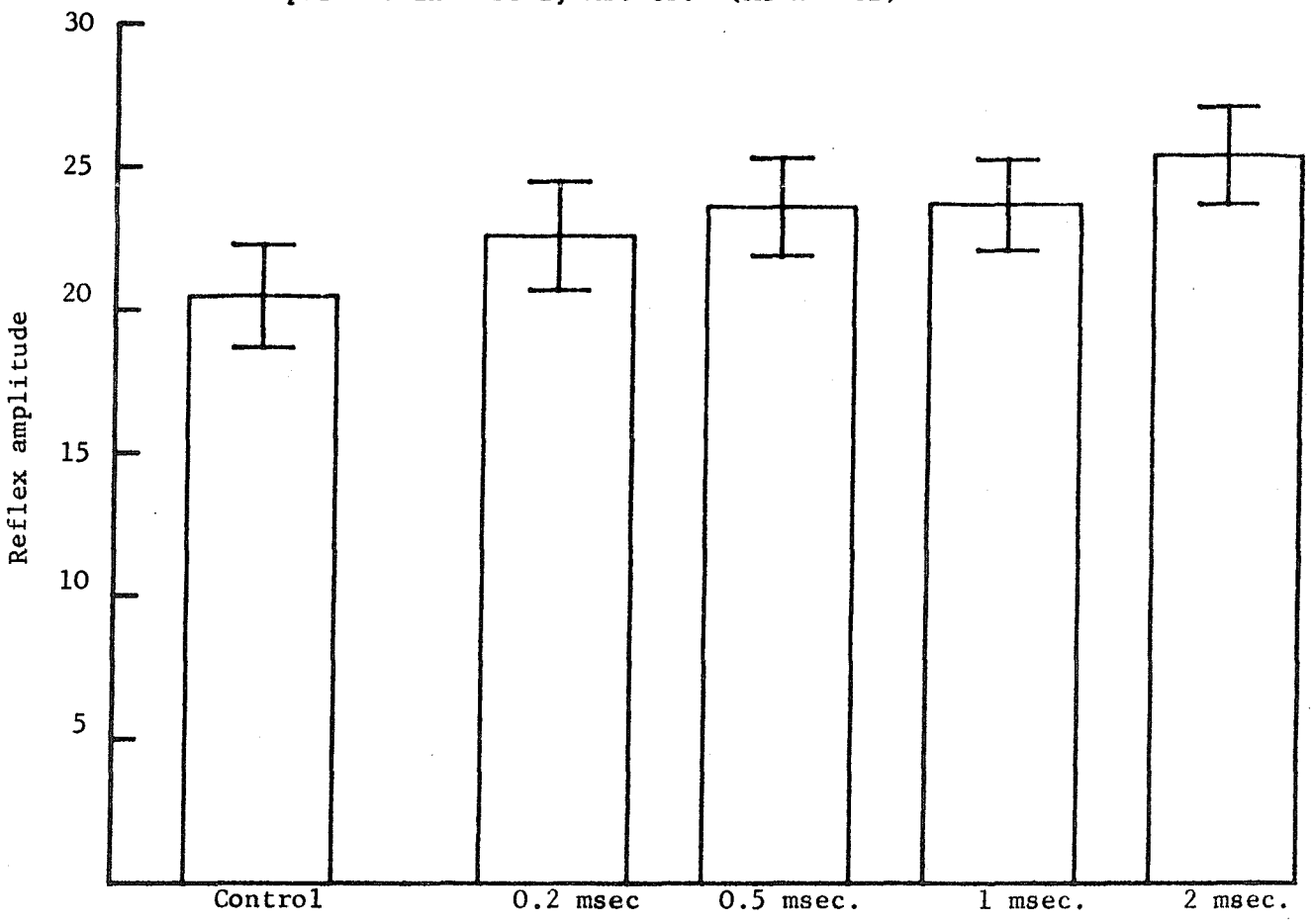
In one patient (N.E.) the reflex did not show significant facilitation (Fig.77) with SCS. This may be because of the different positioning of the SC electrodes in this patient as they were installed in the anterior column. With incremental stimuli ranging from 1 to 3 volts (in 0.5 V steps) the test reflex did not show significant changes.

III Effect of pulse duration to the spinal cord on the MN discharge

The pulse duration did not have a significant effect on the H-reflex amplitude. Using either the transmitter stimulator or an external stimulator of a "Devices" type showed the same results.

In one patient out of four the test reflex showed more facilitation with longer stimulus duration. Fig.78 showed reflex amplitude with SCS using different stimulus duration and equal strength. The

Fig. 78 Effect of pulse duration to the spinal cord on H-reflex amplitude in case 2, Mr. CP. (Mean ± SD)



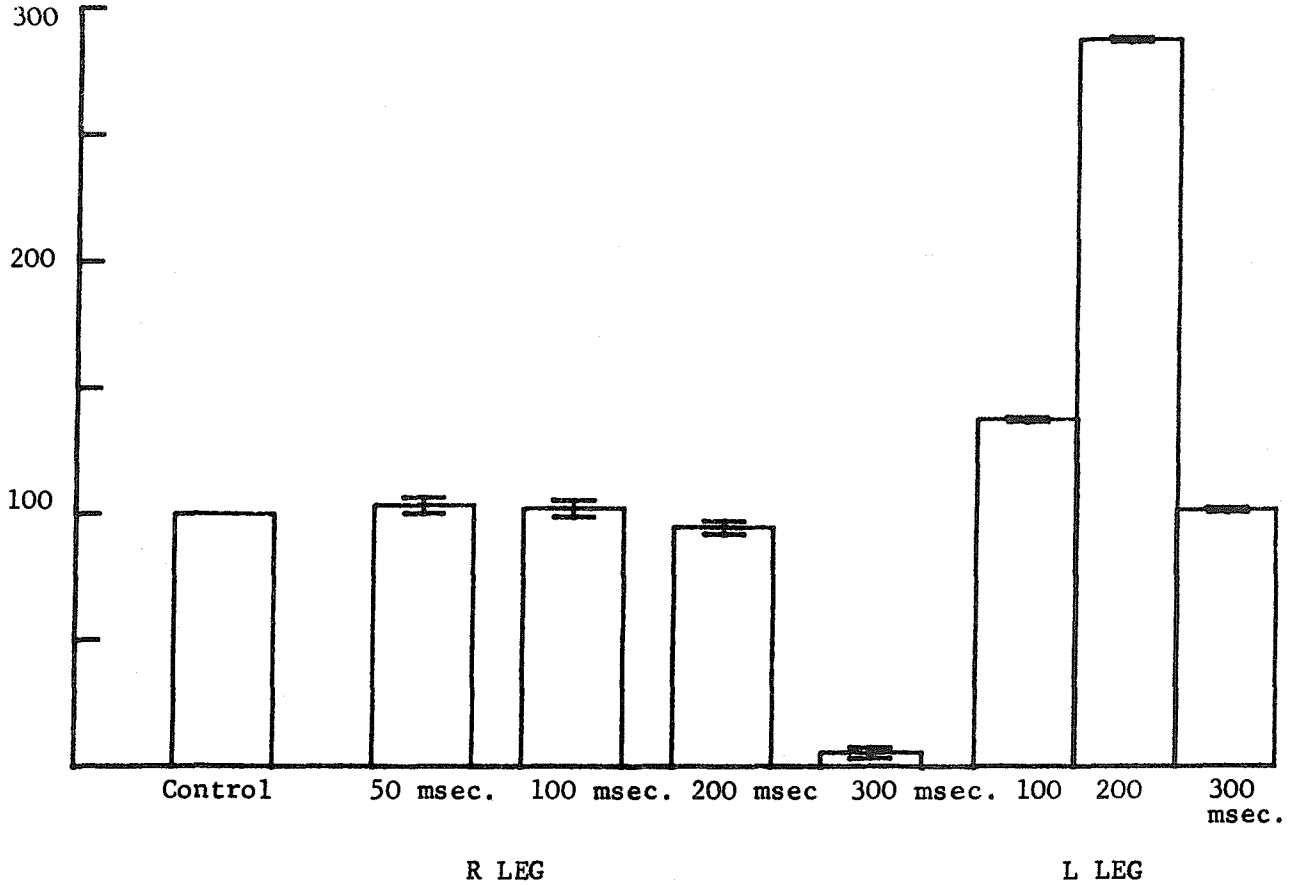


Fig. 79 Effect of pulse duration to the spinal cord on H-reflex amplitude in both legs of case 5, Mr. ES. (Mean ± SD).

test reflex increased gradually in amplitude with every increase in stimulus duration.

In the second patient (E.S.) the reflex showed mild facilitation (103%) in the R leg but was significant in the L leg and reached 287.5% when using a stimulus duration of 200 μsec. Further increase of stimulus duration produces significant inhibition of the reflex in both LLs. (Fig.79). The test reflex reached 5% of the control in the R leg with 300 μsec. pulses.

In a third patient, the reflex showed a maximum value with 200 μsec. pulses. It showed gradual inhibition with further increases of stimulus duration to 300 and 400 μsec. The test reflex reached 78% of the control with 400 μsec. pulses.

In the last (4th) patient no changes were noticed in the reflex with different pulse duration.

It is interesting to note that the long duration pulses (300 μsec or more) decrease the reflex inhibition, during recovery, in the excitability curve. In one patient (E.S.), who showed a good functional improvement, the reflex recovery with paired stimuli at 200 μsec. interval was tested using different pulse duration. Using 300 usec. pulses showed a test reflex 200% of the control.

In two patients, pulse duration did not have a significant effect on the reflex recovery (Fig.80). The test reflex was the same in amplitude with pulse durations ranging from 50 to 400 μsec.

IV Frequency change in SCS and the MN discharge

It has been pointed out by Cook 1976 that the stimulation frequency must be set to a certain level, mostly 33 PPs, for every

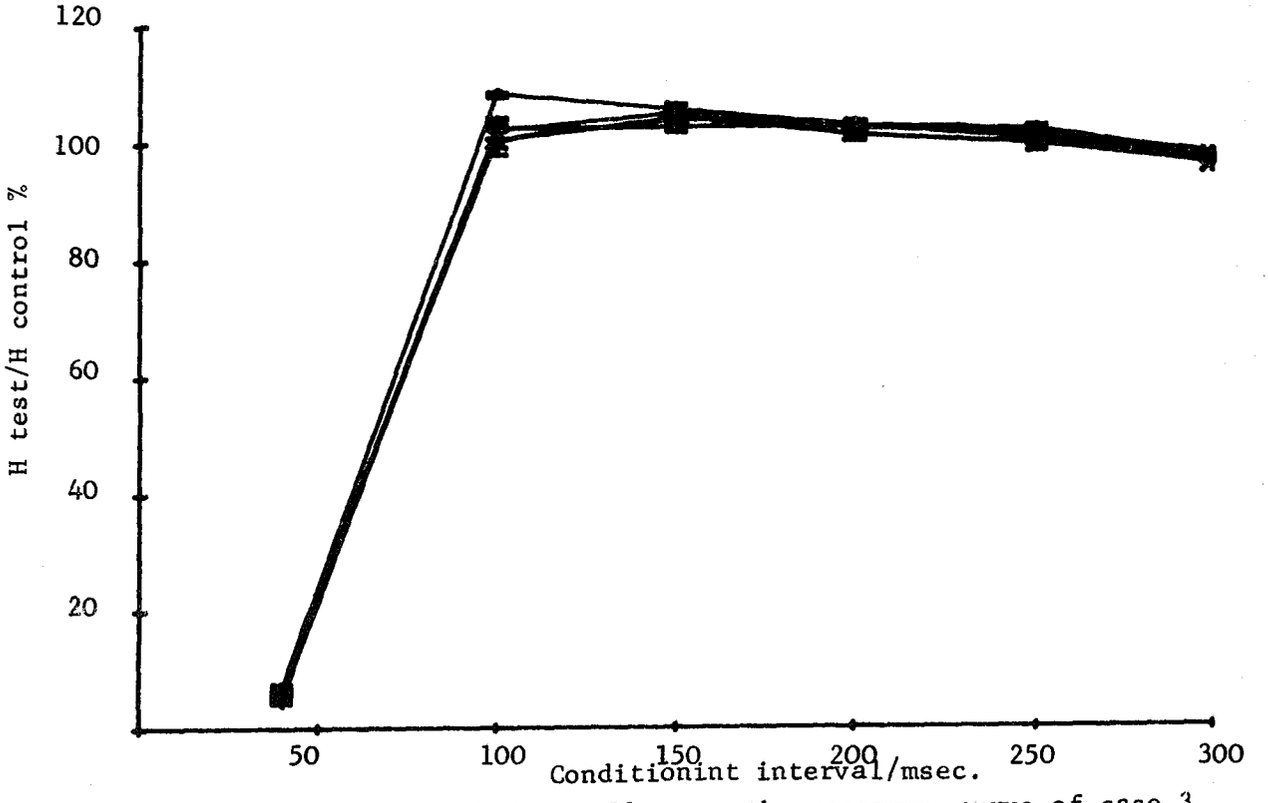


Fig. 80 Pulse duration had no effect on the recovery curve of case 3 (Mr. NE). In this graph pulse duration of 50, 300 & 400 msec. were used in stimulation to the spinal cord. All curves were nearly suprimposed on each other. (Mean ± SE).

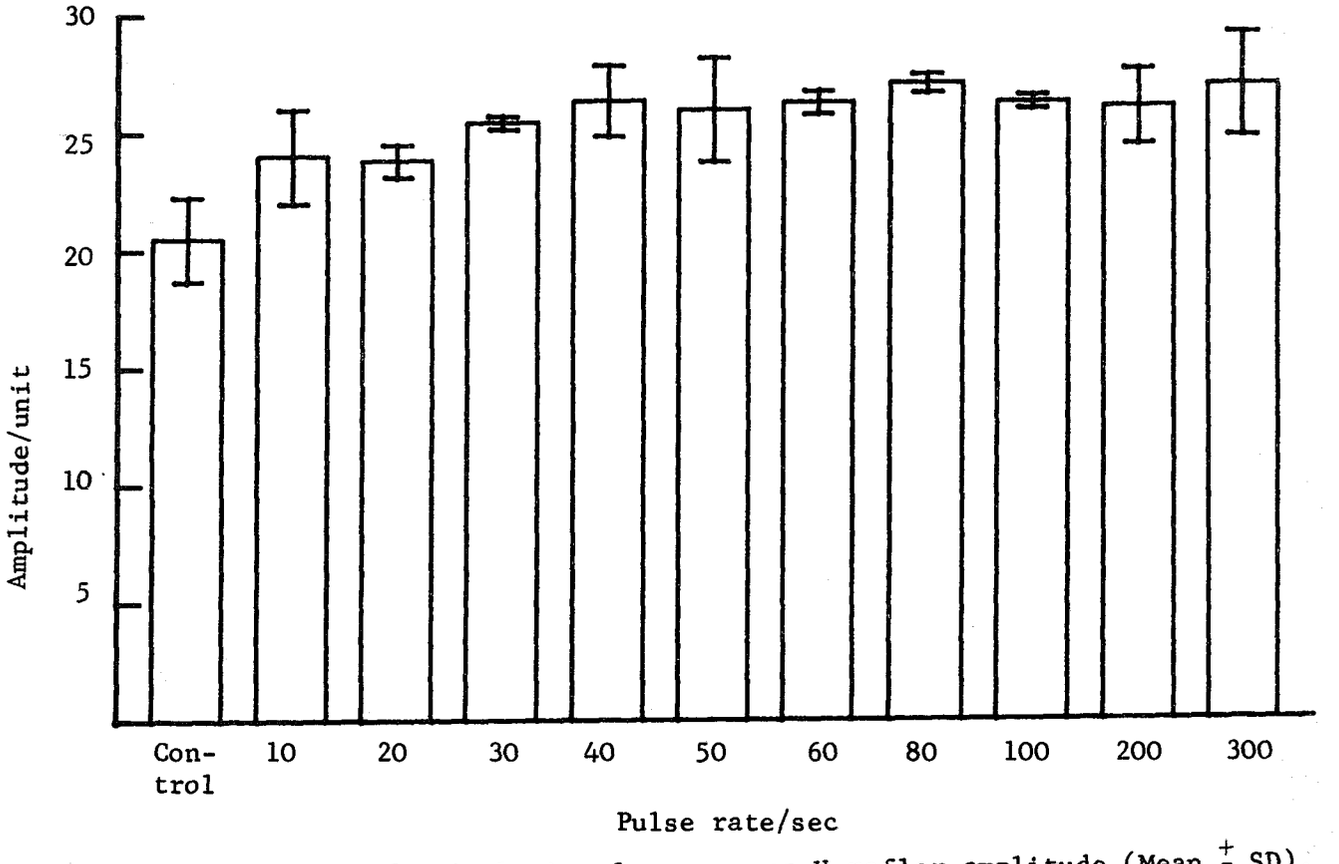


Fig. 81 Effect of stimulation frequency on H-reflex amplitude (Mean ± SD).

patient. This set of experiments was constructed to study the frequency change and the MN discharge in H-reflex.

Frequency changes had a different effect in all patients, according to their pathological condition. Generally speaking the test reflex showed mild facilitation with high frequency stimulation (Fig.81). With higher frequency of stimulation the reflex facilitation decreased to the minimum and sometimes showed inhibition to 74% of the control. This significant inhibition occurred in one patient (J.M.) and was associated with tremors in her limbs. Reversed polarity stimulation was applied in one patient and showed reflex inhibition to 86% of the control.

Most of the patients respond well to a stimulation frequency of 33PPs. In only one patient (N.E.) a frequency of 75 PPs was used, as it was the frequency at which he started to feel the paresthesia, described for stimulation, in his lower limbs.

In one patient (E.S.) the frequency changes were studied for their effect on the H-reflex recovery at 200 msec. and there was no significant effect. The test reflex was of nearly equal size at each of the different stimulation frequencies.

V MN discharge conditioned by a preceding pulse train at variable time intervals

After the significant facilitation had been observed in the H-reflex brought about by a single shock to the spinal cord, it was important to estimate the effect of the pulse train. This is because the train of pulses has an intermediate effect between that of the single shock and continuous stimulation.

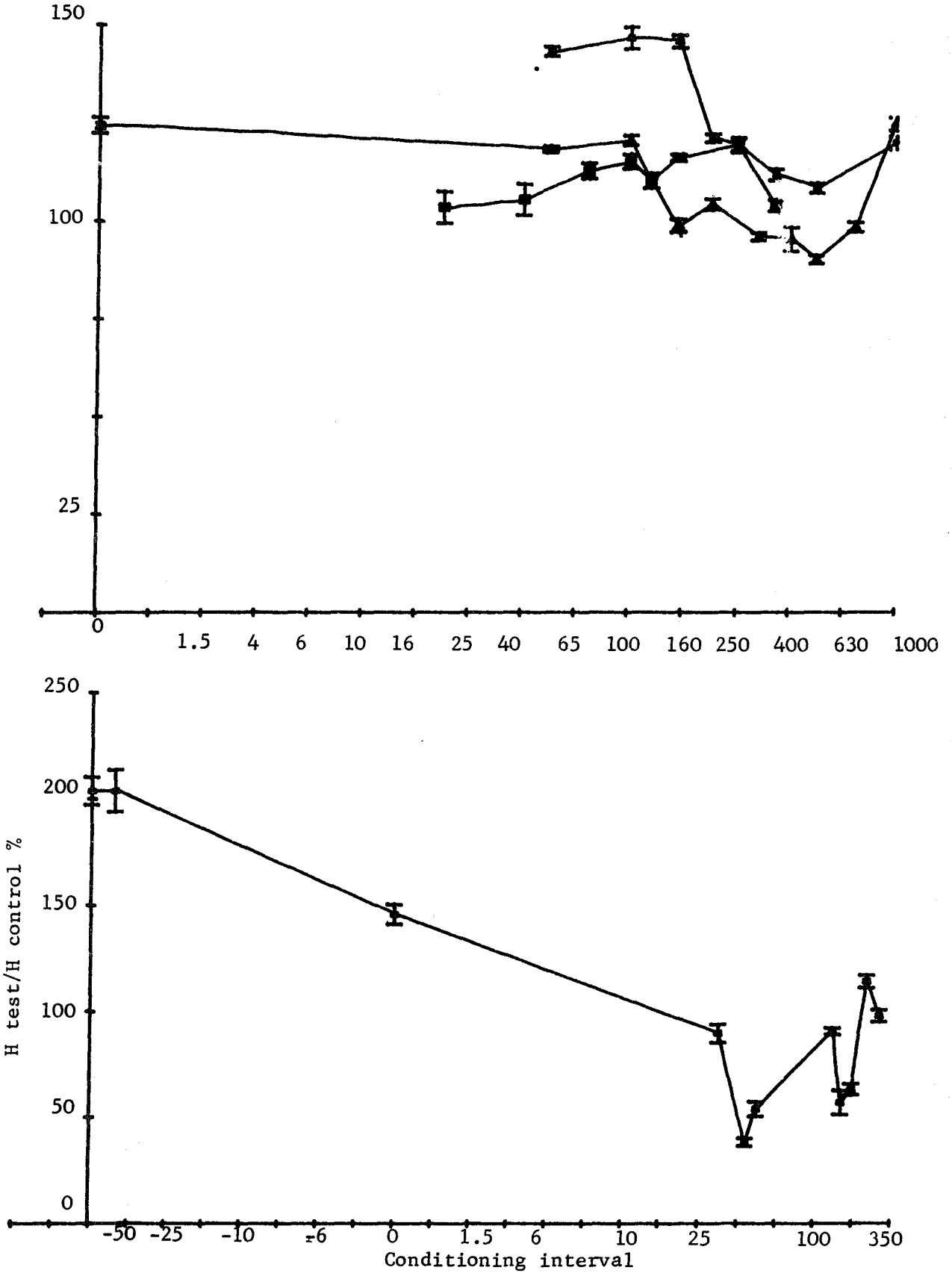


Fig. 82 Time course of H-reflex conditioned by a train of pulses to the spinal cord in four patients. In the lower graph, the test stimulus was delivered 50 and 80 msec. after the beginning of the pulse train which lasted for 100 msec. (Mean ± SE).

A burst of pulses for 100 - 150 msec. long of 0.2 msec. duration were used. The stimulation frequency ranged from 30 - 300 PPs. This was applied with sensory threshold voltage pulses to the SC. The conditioning intervals ranged from 350 - 1000 msec. Four patients were tested in this study. The test reflex showed a significant facilitation in all patients tested.

In one patient (C.P.) the test reflex showed mild facilitation for the first 50 msec. The test reflex was of 105% of the control. This was followed by a gradual rise in the facilitation up to the maximum at 250 msec. interval. The test reflex reached 120% of the control. At the conditioning intervals of 250 - 350 msec., the reflex showed a return to the control value in which the test reflex was 104% of the control (Fig.82)

In the second patient (S.E.) the time course showed a two phase curve of reflex facilitation (Fig.82). There was an initial facilitation phase which ranged from 0 - 150 msec. In this phase the test reflex reached 146% of the control. This was followed by a second phase, in which the reflex facilitation decreased. It was 119% of the control at its maximum. This continued for a period between 150 - 1000 msec. The test reflex was quite stable without significant variability.

In the other two patients the test reflex showed a three phase curve (Fig.82). The initial phase ranged from 0 - 100 msec. and showed significant reflex facilitation. It was 146% of the control at its maximum. This was the period in which the spinal cord experienced the after effect of the pulse train. It was followed by a second, relatively longer period of reflex inhibition. The

test reflex ranged from 38 - 99% of the control for a conditioning interval up to 250 msec. The inhibition period was longer in the second patient and continued up to 500 msec. In this patient the test reflex did not show significant inhibition and values ranging from 90 - 99% of the control. The inhibition period ended in a gradual recovery of the test reflex and further facilitation. This was the case in the last two patients and the reflex reached 144% of the control at its maximum.

In one patient (J.M.) the test stimulus was evoked 50 and 70 msec. after the onset of the 100 msec. pulse train. This was to permit study of the instantaneous effect of the burst of pulses on the MN discharge. There was significant facilitation of the test reflex to 204% of the control at both intervals (Fig.[82]). This was followed by a decrease of the reflex amplitude equal to that described in the initial facilitation period mentioned before.

It was clear that in all patients tested the initial facilitation period which lasted for the first 100 msec. was followed by a secondary stage in which the test reflex was either slightly facilitated or mildly inhibited.

VI Continuous stimulation to the spinal cord

Continuous stimulation of the spinal cord was applied using either the transmitter stimulator of the implant or by an external stimulator of a "Devices" type. Different stimulus frequencies, durations and voltages were used.

During recording it has been observed that the effect of SCS does not show an instantaneous effect on the MN discharge. The effect started gradually and continued for a long time, when the

transmitter was switched off.

Stimulation with single shocks to the spinal cord produces a significant facilitation. This was the case when the test reflex was conditioned by a burst of pulses. Continuous stimulation decreased the degree of facilitation (Table 21).

When the stimulation intensity was increased to supramaximal level, the patient always experiences difficulty in breathing with increased tightness around the chest and the abdomen. The patient who was suffering from tremors showed increased arm movements with higher stimulus voltage. It is interesting to note that, a slightly higher stimulus intensity which is initially felt by the patient, eventually becomes tolerable when used for a while. This was not the case with subsensory threshold stimuli. In the latter the patient did not feel the parasthesia in his limbs.

The pins and needles and parasthesia felt by the patient, when the transmitter was switched on , for the first time, or after a long time of switching it off, continues for some time, after which the patient shows adaptation to the sensation, until it disappears completely.

It was noticed by the patients that tightness in the LLs was one of the most characteristic features observed during SCS. It wears off and the sensation of pins, needles and parasthesia disappears after a period of one month after removal of the electrodes.

Discussion

It is very important to stress that this work is a preliminary study of a procedure which seems to be a complex one in the sense of its physiological effect. More work is needed to reveal an understanding of the mechanism of action of SCS.

In all cases studied H-reflex was facilitated by spinal cord stimulation. This facilitation was enormous in some cases while it was slight in others and it was assumed to be dependent on the site of the lesion as well as to its extent. In case 4, Miss JM, the reflex amplitude did increase in the R leg but did not change or even decrease in the L leg. The site of the lesion in this patient was assumed to be in the cerebellum. Furthermore case 6, Mr. RW, the reflex amplitude did not show any significant change during SCS and he was suffering from MND.

The increase in the reflex amplitude may be attributed to spatial summation of the Ia afferent signals and pulses traversing the descending pathways in the doral column tracts (Wall 1970). This may be showed more clearly when the spinal cord was stimulated by single shock just before or at the time of arrival of the Ia afferent signals. The reflex was significantly facilitated and this facilitation was directly related to the stimulus intensity to the spinal cord. In case 5 Mr. ES, a linear relationship was found between the reflex facilitation and stimulus amplitude to the spinal cord provided that the Ia and dorsal column signals arrive to the MN at an appropriate time. Recruitment of more inhibitory pathways is more likely especially with higher pulse

strength which recruits small fibres. Presumably their conduction velocities were lower than that of the large diameter descending as well as the ascending primary afferent fibres (Wall 1970). This may account for the facilitation of the reflex with single shocks to the spinal cord without any tendency toward inhibition similar to that seen with pulse train or continuous stimulation. Moreover the spatial summation and its facilitatory effect was even more powerful than the counteracting inhibitory action. There may be an alternative explanation for the reflex facilitation by SCS which depends mainly on the decrease in the presynaptic inhibition (Schmidt 1971), or propriospinal inhibition (Magladery et al 1951) due to blocking of impulses above the segmental recording site by the SCS. Larson et al (1974) reported that the somatosensory evoked potentials were abolished when the stimulating electrodes to the spinal cord were located in between the stimulating and recording electrodes (sites).

However when a train of pulses was delivered to the spinal cord the test reflex was facilitated by summation, but not the same as that with single pulses. Another factor was introduced which reduced the degree of facilitation. It is probable that with single pulses to the spinal cord, the large diameter descending fibres were excited while with pulse train recruitment of smaller diameter fibres commenced and caused reflex inhibition. This probably becomes more apparent when using continuous stimulation to the spinal cord, as the reflex facilitation decreased, in most cases, more than that with single or train of pulses. It is known that the dorsal columns are the only spinal tracts which carry

primary afferent fibres from all segments to the medulla (Wall 1970) With continuous stimulation it is assumed that there are two mechanisms which interact at the MN; spatial summation and supraspinal inhibition. The first was the more powerful one. The latter inhibition mechanism cannot only be attributed to stimulation of the smaller diameter fibres in the dorsal column tracts. Dispersion of the currents has been found in SCS (Larson et al 1974) which may stimulate other pathways than the dorsal columns tracts.

Stimulus duration of the spinal cord had no significant effect on the reflex amplitude while the stimulation frequency had minimal effect. The test reflex showed a maximum facilitation value with the daily used frequency of stimulation i.e. 33 PPs. This may be because of the normal frequency discharge of the MNs (Adrian & Bronk 1929, Granit 1970 pg. 141). Using higher frequency, the test reflex showed either a stable maximum amplitude or exhibited reduction in the facilitation. This may be due either to refractoriness of the tracts' axons (Pierrott-Deseilligny et al 1976) or to the recruitment of more inhibitory pathways. The latter is the most likely explanation with reference to the previous discussion.

Changes in the excitability cycle

The changes noticed in the excitability cycle were most interesting. In all cases, except case 4, Miss JM, the recovery cycle showed dramatic changes towards normal value during SCS. This was the case either in abnormally lower or higher recovery curves and it occurred gradually with time after SCS started. An abrupt change has not been seen which means that reorganization of the CNS was occurring (Illis et al 1976). These changes in the recovery

curves and CNS were in parallel with the improvement in the clinical condition of the patients. The clinical results confirm those of Cook et al (1973). There is no other study in human neurology with which to compare these results and there is no technique in neurological rehabilitation which produces such a fast and profound change.

Any hypothesis of how spinal cord stimulation works must seek to explain both the mechanism of the immediate changes and the continuing improvement after stimulation. After a lesion the intact nervous system reacts with considerable reorganization at the synaptic zone with the possibility of previously little used pathways becoming more effective (Illis 1967, 1973a, b). Cells of the rat thalamus deprived of their major input start to respond to new stimuli within a few days (Wall et al 1971) and previously "silent" synapses in the spinal cord of the cat become effective after partial denervation (Merrill et al 1972, Goldberger et al 1974). Repetitive stimulation may produce a structural change in synapses (Illis 1969). Furthermore, tetanus toxin produces a structural change in synapses (Illis et al 1970) and is also associated with long-term neurological sequelae (Illis et al 1971). It is possible to produce a structural change by altering the environment and such changes have been studied in the visual system (Guillery 1974).

The new sensory informations generated by activiation of the dorsal columns tract could increase the central excitatory state which may overcome the disturbances in the MN excitability by setting activity in some pathways which stopped working due to

decreased sensory input and feedback.

In case 4, Miss JM, the recovery curve did not show any improvement towards normal value, on the contrary it was lower and showed hypoactivity than that before SCS. This may be because the site of the lesion was higher than the level of stimulation. Larson et al (1974) reported pain relief in their patients, only up to the segmental level of stimulation. When pain developed at higher level the SCS was not effective.

The changes in the recovery cycle continued for a long time after SCS discontinued. It parallels the long lasting improvement felt by the patients. This long lasting after-effect was one of the most surprising findings in SCS. Most authors described an after effect for the SCS in relieving pains, which may last for hours (Larson et al 1974, Shealey et al 1967, 1970, Nashold et al, 1972, Long 1973, Nielson et al 1975). However in this work as well as in Cook's the after-effect continued for days or even months (Cook & Weinstein 1973, Cook 1976). It is surprising that most patients who suffered from loss of bladder sensation exhibited improvement in bladder function with SCS, and up to the time of writing this thesis they still had their bladder function improvement. Such a long lasting after-effect in functional ability may suggest strongly a structural change (Illis et al 1976). Enlargement of the boutons terminaux in the spinal cord of the cat has been demonstrated by Illis (1969) after repetitive stimulation of the posterior root for 65 minutes. This was suggested to be one of the causes of post-tetanic-potentiation. Similar changes have been found with tetanus toxins (Illis et al 1970) and illustrate the ability of the CNS in

structural reorganization. More interesting was that repetitive stimulation does not cause any degenerative or glial changes (Illis 1969), a finding which confirms the safety of SCS procedure. This will be the case as long as the final common discharging units i.e. the MNs, are in normal condition. If the latter exhibited changes e.g. MND, the functional reorganization will not be useful. This can be seen in case 6, Mr. RW who suffers from MND and did not show much change with SCS.

In case 2, Mr. CP, improvement was seen in the sensory parasthesia with regaining sense of superficial and deep touch down to the toes. The improvement was gradual and complete within 9 days and withdrawal of improvement after SCS discontinued was gradual as well and occurred over a month. This may be due to the increase in the sensory input through the dorsal column tracts which are mainly responsible for the tactile exploration of movement (Wall 1970). Structural changes have to follow to account for the long lasting after-effect.

It seems that a number of spinal cord functions were regained after SCS. Presynaptic inhibition, which seemed to be decreased in spastic cases (Ashby et al 1974) and was noticed in one of our cases (case 5, Mr. ES) was increased during SCS. This was tested by the H-reflex inhibition by vibration. If this was the case, so the SCS has local as well as remote effects.

When the H-reflex, conditioned by a single or a train of pulses to the spinal cord at variable time intervals, a consistent change was seen. In either case the test reflex was facilitated for the

first 100 msec. after the conditioning volley. This indicates a spatial summation of the afferent and supraspinal volleys on the MNs (refer to SFEMG section for references). All patients felt an increase in muscle tension or power during SCS. However it was interesting that Foreman et al (1976) noted inhibition in the discharge of the spinothalamic tract cells during dorsal column stimulation in monkey's spinal cord. This inhibition lasted for 100 msec. or more which was of similar time course to those seen in this work. Section of the dorsal column tracts abolishes this inhibition and facilitation of the cells was observed. On the other hand sections of the lateral column including the spinothalamic tracts had no effect on the cell discharge. These findings support the idea that SCS inhibits pain transmission at the spinal cord level.

However one could argue that SCS may facilitate the H-reflex by decreasing presynaptic inhibition. This is very unlikely, as it has been shown in one of our results that SCS actually increased the presynaptic inhibition mechanism and by which the H-reflex inhibited by vibration. Moreover the finding that the reflex showed more facilitation when the test and conditioning volley reached the spinal cord was in support to spatial summation mechanism. In addition to the previous assumption evidence can be put which stems from the reflex gradual facilitation with incremental increase in the conditioning intensity. In case 5, Mr. ES, when the test reflex was measured at variable time intervals, after three different levels of conditioning intensities,

it exhibited significant changes. The facilitation period was divided into two phases of a primary enormous phase which continued up to 50 msec. and a secondary mild facilitation phase, which continued up to 100 msec. The degree of reflex facilitation was directly related to the conditioning intensity and subsequently to the degree of spatial summation.

Conditioning of the test reflex with a preceding burst of pulses showed lower facilitation than that with single pulses. However the facilitation was larger in the first 100 msec. than afterward i.e. up to 100 msec. The existence of the facilitation for up to 1000 msec. was an interesting finding. It is unlikely to be due to spatial summation for such a long time. It may indicate a post tetanic potentiation of the MN by supraspinal burst of pulses. Hagbarth (1962) & Corrie et al (1964) reported facilitation of the H-reflex by tetanic stimulation of the peripheral nerves. The post-tetanic potentiation of the H-reflex lasts for 30 to 40 sec. Such potentiation was explained in terms of increased presynaptic action due to changes in afferent terminal fibres (Lloyd 1949, 1959) or in synaptic boutons (Eccles 1953, Eccles & Rall 1951, Illis 1969).

SCS may act on three different aspects of CNS function (Fig.§3).

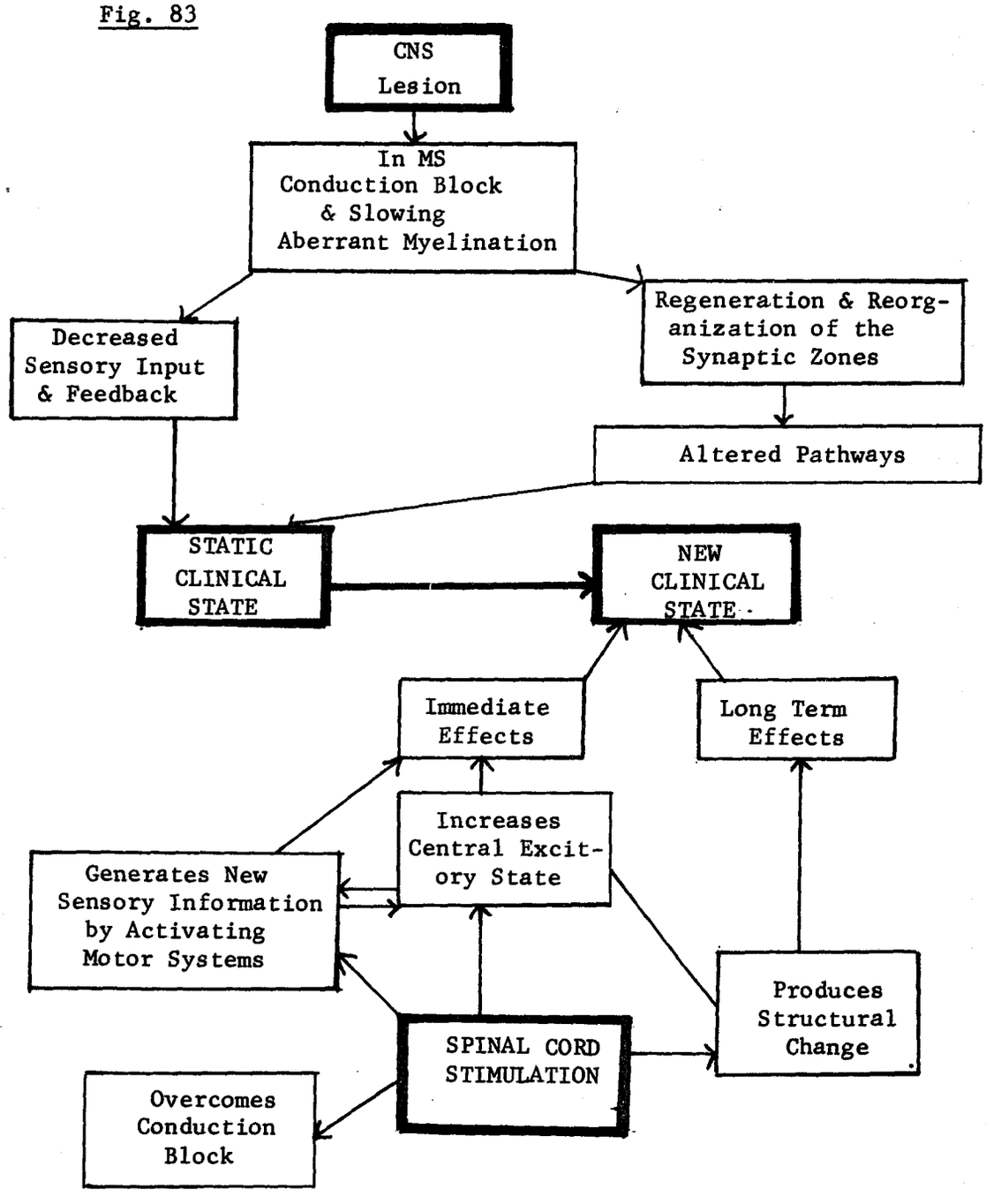
1. An effect on the lesion itself: environmental changes can alter conduction in demyelinated fibres (McDonald 1974) but our knowledge at present does not suggest that SCS can significantly affect this aspect of function. However repetitive stimulation may modify the molecular environment suffic-

iently to alter conduction through the lesion or part of the lesion.

2. Stimulation may modify the functional and anatomical reorganization which has been referred to.

3. Stimulation can be seen as increasing the central excitability state which by producing movement, further increases afferent inflow. Neurons are then more likely to reach their firing thresholds and inhibitory mechanisms have some activity upon which to operate. Wall (1970) has written thoughtfully on the importance of the dorsal columns for tactile exploratory movements.

Fig. 83



These factors are acting on an altered CNS, i.e. a nervous system which has already reacted to a partial lesion as described above. Without sensory feedback (with a decreased central excitatory state) no further improvement in function can occur and the clinical picture is static. SCS provides the increase in feedback and produces a new clinical picture. Whatever the mechanism of the stimulation, this experience so far is that it is beneficial and confirms the work of Cook. The changes seen in these patients have been dramatic, and clearly it is important to discover the fundamental mechanisms involved in rehabilitation by SCS. Further work is needed to discover these fundamental mechanisms which are considered to be a step forward in the field of neurological rehabilitation and human neurophysiology.

CHAPTER VII

DYSTROPHIA MYOTONICA

Patients suffering from dystrophia myotonica were tested for neurological dysfunctions using the H-reflex. Nine patients were thoroughly studied and classified into three groups according to the degree of their functional disorder. Out of nine patients five were male and four were female. Their ages ranged from 9-51 years. One patient was 9 years of age and the others between 25-51 years old. All but one patient were diagnosed as having dystrophia myotonica in Wessex Neurological Centre, Southampton. All showed typical symptoms of dystrophia myotonica, such as myotonia in the hand grip, characteristic weakness and wasting of sternomastoid and facial muscles. Frontal baldness was seen in most patients as well as relevant family history of the disease. Cataract in slit lamp examination was a common symptom in these patients. Electromyographic studies showed a typical dive-bomber myotonic discharge with a chain of high frequency motor unit discharge. The general findings on examination which characterized the different groups are listed below:-

I Subclinical group

There was only one patient (aged 9 years) in this category. He was the son of a clinically diagnosed patient. History of illness for two years.

On examination

Mild weakness in neck muscles and orbicularis occuli. Myotonia in the masseter muscles, as well as U and LL muscles especially seen in hand grip. No weakness was noticed in U or LL muscles. Reduced ankle jerks.

II Clinical Group

Four patients were tested in this group with ages ranged from 29-47 years. Three out of four were male. Two of them have a relevant family history and their history of illness ranged from 2-15 years.

On examination

In all patients there was weakness and wasting of sterno-mastoid muscles and orbicularis occuli. Bilateral facial weakness was noticed. There was mild weakness in the limb muscles especially small hand and foot muscles. In men no testicular atrophy was noticed, but all showed frontal baldness. The ankle jerk was reduced, but there was a normal knee jerk. Electromyographic studies showed that motor unit potentials size and duration were within normal limits. All showed myotonic discharge in their EMG.

III Incapacitated group

Four patients were studied in this group with ages ranging from 25-51 years. Out of four three were female and one was male. Two of them have a relevant family history and in the others family histories were unknown. History of illness ranged from 13-25 years or more.

On examination

Apart from the general symptoms mentioned previously, general weakness and wasting of limb muscles was noticed. Its distribution was mainly in the facial, sternomastoid, trapezei, forearm muscles, leg muscles as well as muscles of the trunk. The degree of weakness ranged from mild to severe or complete paralysis leading to deformities Foot drop, kyphoscoliosis and dysarthria were some of the findings

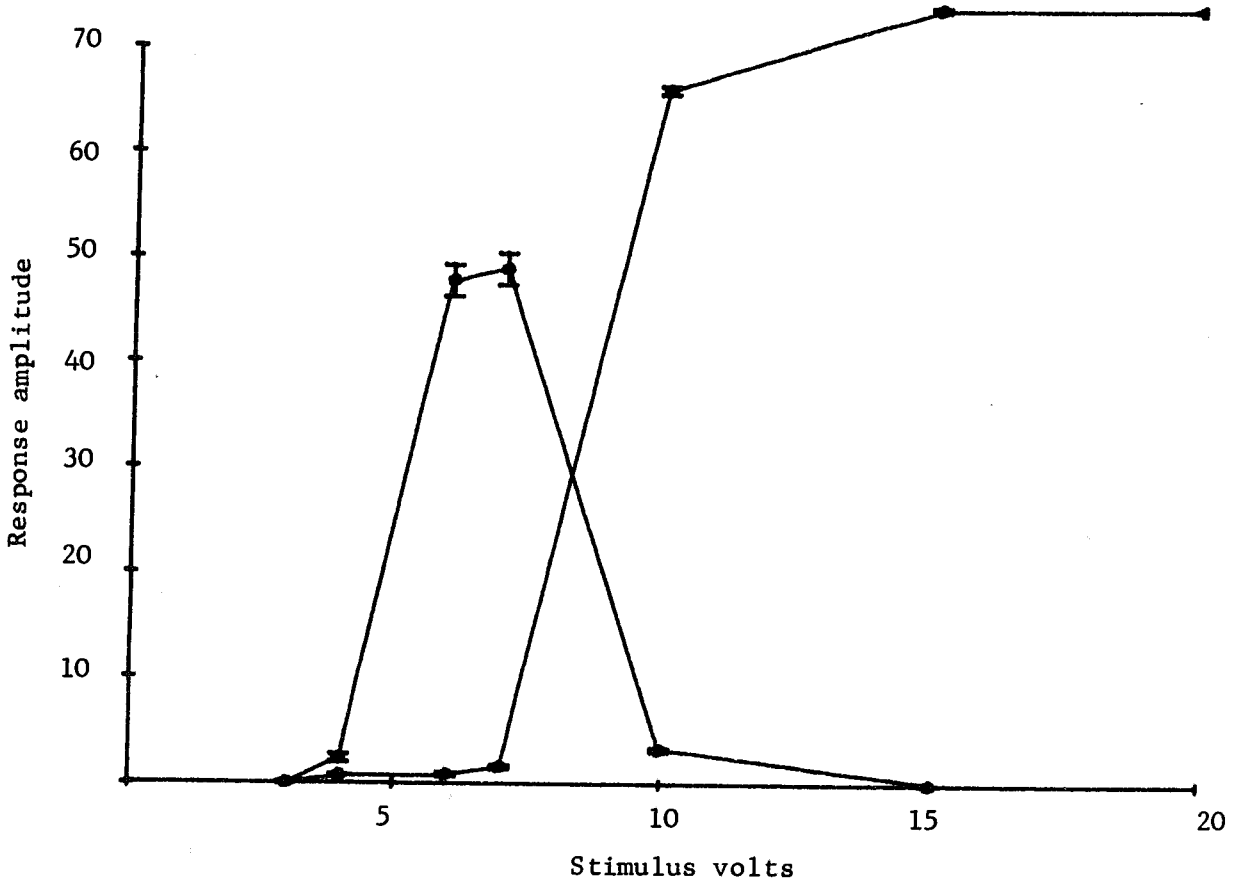


Fig. 84 Recruitment curve of case 1, MS, a subclinical case of dystrophia myotonica. The H-reflex was of normal amplitude (Mean ± SD).

in this group. Functional disabilities ranged from walking with aids to wheel chair bound. Frontal baldness was seen.

The ankle jerk was absent in all patients and knee jerk was reduced, as well as a flexor planter response.

Electromyographic studies showed the typical myotonic discharge and a breaking up of motor unit potentials.

I SUBCLINICAL GROUP

In this group there is only one patient (M.S.) who is 9 years of age. His father suffers from dystrophia myotonica . This patient suffers mainly from myotonia in his masseter muscles during chewing and in the lower limb muscles during walking H-reflex studies showed the following results.

The maximum amplitude of H-reflex was 5.8 m V . This value was within normal limits (Mayer et al 1973). $^{H}/_{M}$ ratio was 66.3% (Table 22) which is also a normal value. The recruitment curve (Fig 84) showed a normal pattern. The recovery curve was lower than normal value (Fig 85). The test reflex recovers after an inhibition period which lasted for 55 msec. It showed a very slow recovery with an amplitude of only 39% of the control at 300 msec. The test reflex was 78% of the unconditioned reflex at 1000 msec. After 1000 msec. interval the test reflex began to recover, from the abnormally long inhibition, with a value of 80% at 2000 msec. This curve differs from cerebellar type in that its recovery time started relatively early.

Cooling of the calf muscle for 5 minutes produces a reflex facilitation to 126.2% of the control (Table 22). Measuring the MN recovery after 5 min. cooling showed a dramatic change towards

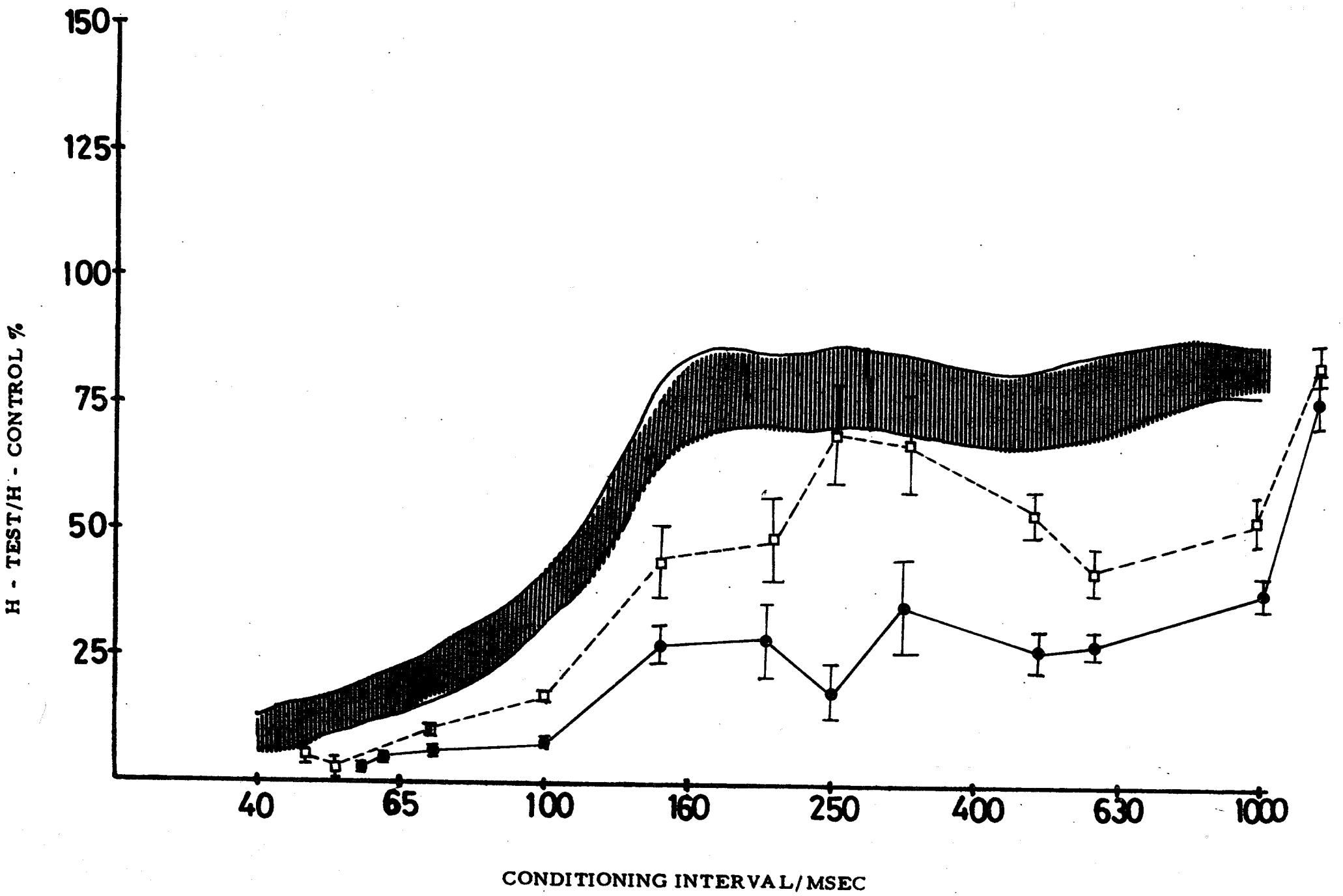


Fig. 85 Recovery curve of case 1, MS, subclinical dystrophia myotonica, before (●) and 15 min. after (□) cooling of the calf muscle. (Mean ± SD).

the normal pattern (Fig 85). The test reflex after cooling recovered 10 msec. earlier than before cooling and showed a recovery time after inhibition for 45 msec. The test reflex recovered faster and with a larger amplitude, to reach a mean value of 71% of the control at 250 msec. The curve showed an apparent 2 ^{ry} inhibition period similar to that in normal curves. The test reflex recovered to high normal value (80%) at 2000 msec. after a long period of inhibition.

Vibration of the tendoachilles produced a reflex inhibition to a mean value of 35.9% of the control (Table 22). The inhibition was consistent in all records with no visible reflex fluctuation. There is no published data on the degree of reflex inhibition by vibration in such a young age. Compared with normal adults there was slight disinhibition of the reflex by vibration. The test reflex was slightly facilitated after vibration stopped for a short time.

Scrubbing the sole of the foot produced a reflex inhibition to 8% of the control (Table 22). It was significantly smaller than the normal value. However, the normal standard of the H-reflex inhibition by scrubbing sole of the foot was taken from normal adults. A normal standard for children aged 10-15 years is needed before classifying the finding in this patient as abnormal.

Table 22 H-reflex and the parameters measured in dystrophia myotonica

Patient Name	Age	Group	H/R Amplitude mV.	$H_{/M}$ ratio	Vibration mean ($\frac{\text{H-test}}{\text{H-control}}$ %)	Scrubbing $\frac{\text{H-test}}{\text{H-control}}$ %	Cooling $\frac{\text{H-test}}{\text{H-control}}$ %
M.S.	9	S*	5.8	66	36	8	126
S.M.	37	C‡	7.88	45	47	64	-
J.H.	43	C	5.4	46	19	66	-
E.M.	29	C	3.25	37	81	42	94
A.A.	34	C	4.5	62	53	41	174
H.O.	51	I‡‡	< 0.3	60(..)	83	64	-
P.	47	I	< 0.1	4	-	-	-
L.R.	25	I	0.125	29	-	68	66
M.A.	47		0.125	15	95	69	143

* S = Subclinical ‡ C = Clinical ‡‡ I = Incapacitated
(..) M response = 0.58 mV.

It is safe to say that, in this patient there was mild reduction of the inhibition produced by vibration. The discharge of muscle spindles largely contributes to the inhibition of the test reflex in normal subjects.

II CLINICAL GROUP

In this group there are four patients with ages ranging from 29 to 43 years, three males and one female. They showed a normal reflex amplitude ranging from 3.25 to 7.88 and with a mean value of 5.3 ± 2. (Table 22). There was a direct relationship between the reflex amplitude and the severity of the complaints in this group. The most affected (or incapacitated) patient showed the smallest reflex amplitude. The reflex was triphasic in these patients with no feature of asynchronism

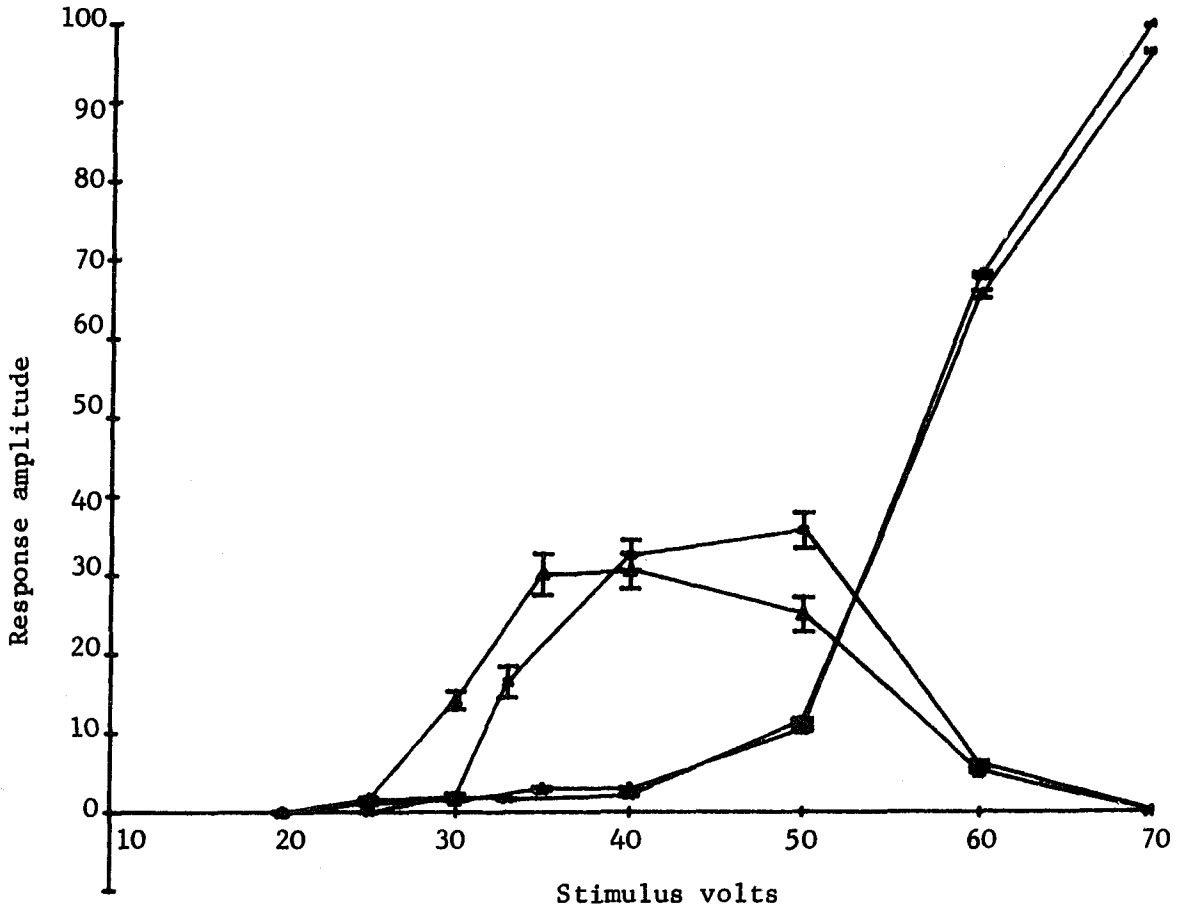


Fig. 86 Recruitment curve of one patient of dystrophia myotonica (SM) from the clinical group. The maximum H-reflex was significantly small compared to the maximum M-response. The curves showed slight change from the control (▲) after 15 min. cooling (x). (Mean ± SD).

of MNs firing. The $^{H}/_{M}$ ratio was relatively small. It ranged from 37% to 61.7% with a mean value of 47.5 (Table 22). Fig. 86 shows an example of a recruitment curve, of one patient, from this group. The test reflex showed a normal recruitment of MNs with incremental stimuli.

In the recovery curve the test reflex showed variable changes. In two patients the test reflex was relatively smaller with a slower recovery. There was an early recovery after 35 and 40 msec. (Fig 87). In these patients tightness in the muscles (the myotonia) was the major complaint. No weakness or muscle wasting were noticed. In the other two patients the converse was true. The test reflex recovered later than in normal value i.e. at 50 and 80 msec., with a faster reflex recovery. The test reflex was larger than in the control, between 100 and 500 msec., in one patient and between 200 and 300 in the other. The 2^{ry} inhibition period was clear in these patients. It was not completely similar to spastic curve, as the late reflex recovery and the prominent 2^{ry} inhibition period being different. In these patients muscle weakness was noticed in muscles of UL and neck accompanied by myotonia. The muscle weakness was not such as to cause incapacitation. Cooling of the soleus muscles for 10-15 min. in the last two patients showed a reflex facilitation to 174% (Table 22). In one patient who was considered to be an advanced clinical type, the reflex showed mild inhibition to 93.6% with cooling.

The recovery curve showed peculiar changes with cooling. In one patient the curve showed a dramatic return to the normal pattern. In the other patient the curve was more hyperactive than that before cooling. The change was not significant in the latter case.

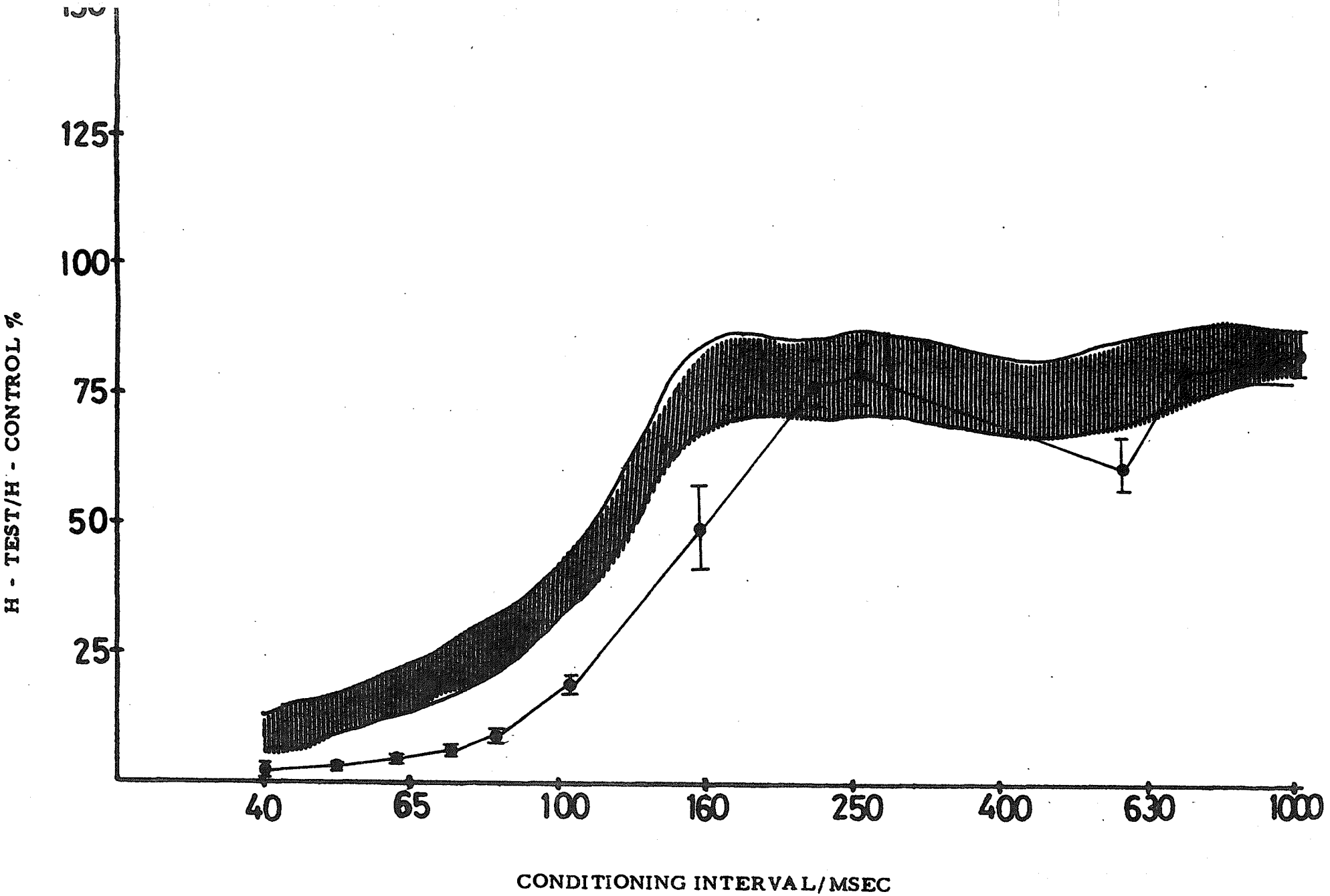


Fig. 87 Recovery curve of one patient with dystrophia myotonica (clinical group). The test reflex was significantly smaller than normal (Hatched curve). (Mean ± SD).

The effect of vibration of the tendoachilles in these cases was different from normal findings. The reflex amplitude during vibration ranged from 19.2 to 80.8% of the control, with a mean value of 49.8 $\pm$ 25.2 (Mean $\pm$ S.D) (Table 22). In one patient the test reflex was 19.2% of the control, which is a nearly normal value. In the other three patients the test reflex ranged from 46.7 to 80.7% of the control with a mean value of 60 $\pm$ 10.5. The change was significant at the 5% level. This shows the disinhibition of the reflex by vibration in the clinical group. It is interesting to note that the test reflex was stable and did not show significant fluctuations. The effect of vibration was consistent in all records.

Of more importance is that, in the most advanced case of this group (E.M.) the test reflex showed the largest amplitude with vibration i.e. greatest disinhibition. In the cases that noticed a mild weakness in the muscles, they exhibited significant disinhibition by vibration. This is evidence for the progression of the disease to involve the muscle spindle, and most likely the large afferent. This was associated, in a second stage, to involve the peripheral nerves and again most likely the Ia afferent fibres. This was strongly supported by the abnormally small reflex amplitude as well as the small $^{H}/_{M}$ ratio.

The effect of mechanoreceptor stimulation by scrubbing sole of the foot was studied. The test reflex ranged from 41 to 67% of the control with a mean value of 53 $\pm$ 13.5 (Mean $\pm$ SD) (Table 22). It was of a normal value when compared with previously tested normal subjects.

It was clear from patients grouped as clinical cases that the reflex amplitude, $^{H}/_{M}$ ratio, and vibration disinhibition effects

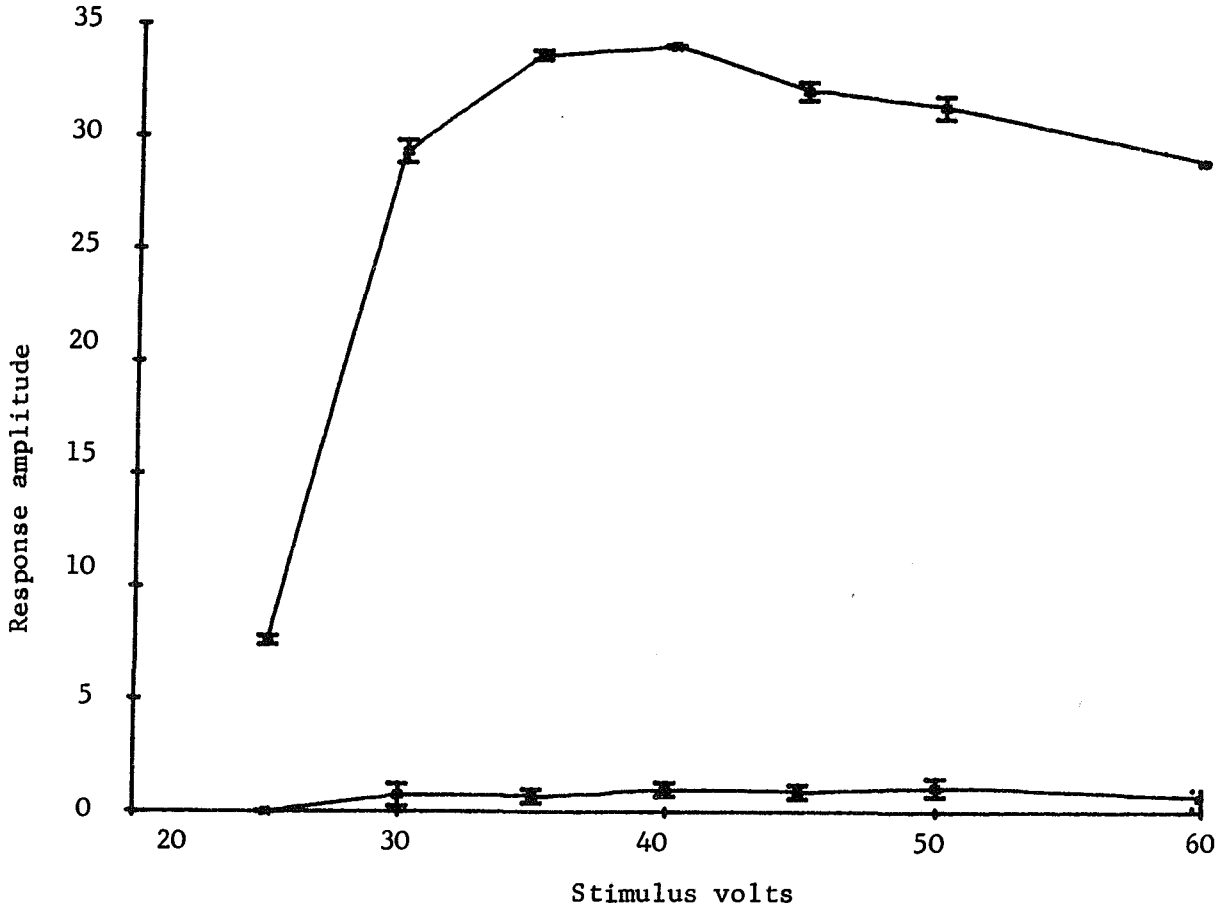


Fig. 88 Recruitment curve of one patient of dystrophia myotonica, from the incapacitated group (MRP). H-reflex is significantly small while the M-response was still of large amplitude. (Mean ± SD).

coincided with the progress in the clinical condition. In advanced cases a smaller reflex amplitude, with a smaller $^{H}/_{M}$ ratio were characteristic findings, with a larger reflex amplitude when the tendo-achilles was vibrated.

III INCAPACITATED GROUP

There are four patients in this group with ages ranging from 25-51 years. Three females and one male were tested. The reflex amplitude was significantly small in all patients and ranged from 0.1 - 0.3 mV., with a mean value of 0.16 $\pm$ 0.1 (M $\pm$ S.D) (Table 22). It was polyphasic in shape with long duration (longer than normal) which shows the a synchronism in motor unit functions. The muscle action potential was of nearly normal value in three out of four patients. (Fig. 88) shows the recruitment curve of one patient from this group. In the 4th patient the disease was so well advanced that significant muscle weakness was observed as well as muscle wasting. This manifested itself in the very small M-response of 0.6 mV.

The small reflex amplitude in conjunction with normal musculature gave a smaller $^{H}/_{M}$ ratio than normal value. It ranged from 4-59.8% with a mean value of 27 $\pm$ 24 (M $\pm$ S.D) (Table 22). It was significantly smaller than the normals at the 1% level. In three out of four the $^{H}/_{M}$ ratio ranged from 4 to 28.8% In the last (or 4th) patient, who showed severe incapacitation the 59.8% of the $^{H}/_{M}$ ratio was not due to the large reflex amplitude, but due more to the very small M response. Because of the small reflex amplitude the recovery curve was plotted with difficulty for these three patients. We were unable to measure the recovery curve in the 4th patient because of the extensively small amplitude. In the three patients tested for reflex recovery, they

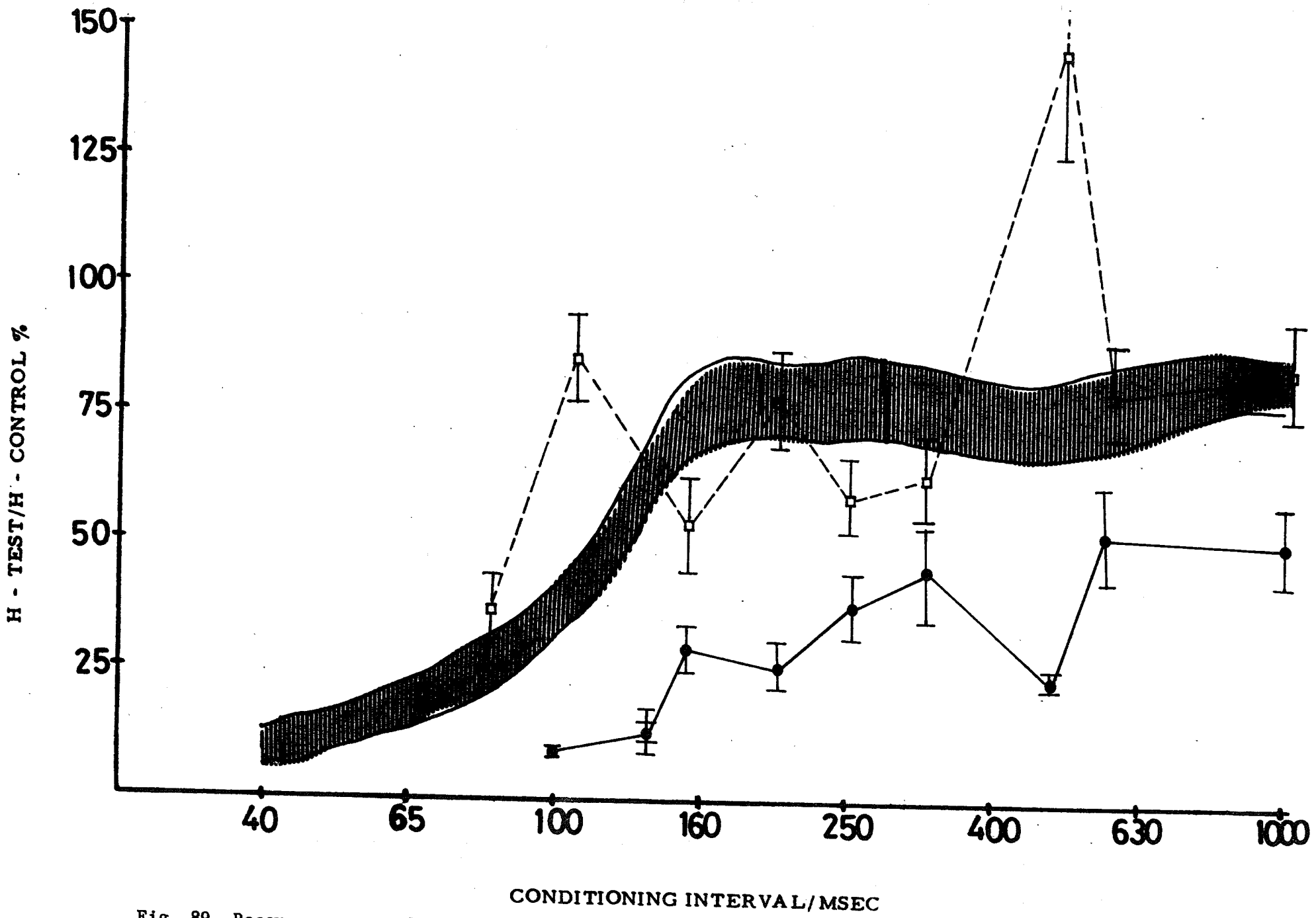


Fig. 89 Recovery curve of one case of dystrophia myotonica (Incapacitated group) before (●) and after (□) 15 min. cooling of the calf muscle. (Mean ± SD).

recovered after a longer inhibition period than normal. The reflex recovered slowly with a smaller amplitude. This is shown in the recovery curve of the patient in Fig.89 . The degree of reflex inhibition in the recovery curve was related to the functional disabilities of the patient.

Cooling of the muscles for 10 to 15 min. in three patients showed interesting results. The test reflex was inhibited in two patients. In one of them the test reflex becomes 66.3% of the control (Table22). In the other, it was difficult to measure the reflex amplitude after cooling as it was so small (0.1 mV.) even before cooling was applied. In the third patient of this group, the reflex showed facilitation to 143% of the control (Table22).

During recording it has been noticed that the test reflex showed facilitation with cooling in the less incapacitated patients. In more advanced cases the reflex was inhibited with cooling. In all cases M-response did not show significant changes. The recovery curve showed a dramatic change to normal pattern with cooling (Fig.89). This was consistent in all cases tested for this manoeuvre. The test reflex showed more fluctuations with cooling but was of higher value than that before cooling.

Of more importance, was the earlier recovery time of the test reflex which was seen in all subjects tested. The test reflex recovers 10 to 20 msec. earlier than that before cooling.

The muscle spindle dysfunction was very apparent in these cases and was shown by the effect of vibration for the tendoachilles. In two patients out of four the mean reflex amplitude was 82.8% and 94.6% of the control during vibration (Table 22). In the other two cases tested for this manoeuvre, we were not able to measure the reflex

amplitude from the background noise produced by the vibrator. It was clear that the test reflex in those patients did not show significant inhibition by vibration. The disinhibition of the reflex by vibration was greater in advanced cases and was more significant in the incapacitated group than in the clinical group.

Scrubbing the sole of the foot produced a nearly normal value compared to normal young subjects. The reflex amplitude ranged from 64 to 68.8% of the control, in three patients, with a mean value of 66.8 ± 2.5 ($M \pm S.D$) (Table22). Again the small reflex amplitude restricts the recording of changes as a result of scrubbing sole of the foot in the 4th patient.

In this group the parallelism between reflex amplitude, $^{H}/_{M}$ ratio and the disinhibition effect of vibration appeared to relate to the degree of functional disorders of the patient. This was the case as long as the muscle fibres did not show dramatic changes in severely advanced cases. In the latter condition, which was seen in one patient of 51 years with long history of illness, all the previous parameters showed the same changes but the $^{H}/_{M}$ ratio increased again. The latter was due mainly to the decrease in the motor units normally functioning with stimulation. The polyphasic shape of the reflex support this evidence on the peripheral level. The changes in reflex shape and duration were not observed in subclinical or in clinical cases and was hardly seen in incapacitated patient of good condition.

Discussion

Dystrophia myotonica is a multisystem disease which involves the CNS both in the brain (Refsum 1959, 1967) and the spinal cord (Papapetropoulos 1972) as well as the PNS (Woolf & Coers 1974). The purpose of this study was to explore the neural aspect of this disease and the relative contribution of this neural involvement to the neuromuscular dysfunction. Tests for the muscle spindle, afferent fibres, central spinal mechanism as well as the muscle fibres themselves were involved.

The H-reflex recovery curves of myotonic dystrophy patients suggest disturbances in the spinal segmental mechanism. Changes in the muscle spindles have been demonstrated and they appear to be less responsive to vibration. In the late stage, muscle spindle dysfunction is assumed to be followed by degeneration in the peripheral afferent fibres and which contributes to the reduction of the H-reflex amplitude and $^{H}/_{M}$ ratio. These stages will be discussed in some detail with histological and electrophysiological evidence.

A. Evidence for spinal cord dysfunction

The recovery curve demonstrated significant changes from normal with increasing inhibition in most cases whether in the subclinical, clinical or incapacitated groups. One could argue that these may be due to changes in the recurrent discharge of the muscle spindle evoked by the conditioning pulse. In fact this is very unlikely, as in such cases the changes should be noticed only in the recovery turnover part of the curve i.e. 2^{ry} facilitation period between 100 and 300 msec. (McLeod et al 1967).

However in most cases studied reflex inhibition was demonstrated at all intervals of the time course, associated with late and slow recovery. This provides evidence for a central factor working in the disease. It is difficult to identify exactly what are these central factors, but the MN is assumed to be the site of one or more of them (McComas et al 1965). McComas et al (1965) demonstrated polysynaptic potentials attributed to motor unit activity and recorded from the muscles of dystrophic mice. These potentials were not present after severing of the peripheral nerve and were therefore ascribed to MN activity.

It is interesting to note that reflex recovery was later than normal in all incapacitated cases as well as in the other two patients from the clinical group. This provides further support to our suggestion of central factor working in this disease. It may be due to increase of the inhibitory mechanism from supraspinal centres (Gassel 1970, Taborikova 1973, Taborikova et al 1969). This is unlikely, because no changes have been reported from the brain stem centres. However an alternative assumption is that these changes in the recovery time could be due to degeneration in some of the MNs especially in advanced cases. This degeneration is most likely to be of the small tonic MNs which usually showed higher excitability with early recovery when measured by SFEMG previously in this thesis. Brook et al (1969) in their studies of histographic analysis of human muscle biopsies reported a very strong association between myotonic dystrophy and the selective atrophy of type I (tonic) muscle fibres. These changes were found in 80% of biopsies taken from gastrocnemius muscle and have been confirmed by other

authors (Dubowitz et al 1973). The type I MNs exhibited degeneration in elderly subjects (refer to age related changes). It is tempting to think that this degeneration was secondary factor to the changes in the CNS affecting the MN connected to type I fibres and possibly related to the trophic substance.

B. Evidence for spindle dysfunction

The remote effect of the central spinal disturbances was assumed to reflect primarily on the muscle spindle. This stems from the findings that the muscle spindles were not responding to vibration in all patients tested including the subclinical groups. Inhibition of the H-reflex by vibration is a normal finding shown before in this study as well as by other workers (Hagbarth et al 1966). It was attributed, in normal subjects, to presynaptic inhibition of the @ MNs (Gillis et al 1969, Delwaide 1973). As the vibration is a selective stimulus to the spindle primaries (Bianconi et al 1963) it can be seen that this part of the system was affected in all cases in the three groups tested. The less responsive Ia fibres were present in all patients with varying degrees, increasing with the advance of the disease. The reflex inhibition by vibration was marked in the incapacitated > the clinical > the subclinical cases, a finding which shows progressive derangement in the muscle spindles. However one could argue whether the Ia fibres are affected primarily in the muscle spindle level in the nerve trunk or in the cord. The answer to this question could be extracted by comparing these results with the reduction of H-reflex amplitude at rest. The latter will be accounted for by a reduction in the Ia fibres in the nerve trunk or in the spinal cord.

In the subclinical case the reflex amplitude was normal while it still showed mild unresponsiveness to vibration. In the clinical group the H-reflex demonstrated mild reduction in amplitude but the muscle spindles were clearly not responding to vibration. A dramatic reduction in the reflex amplitude was seen in the incapacitated patients, which was associated with muscle spindles not responding at all to vibration. This provides evidence that the primary defect was within the spindle primaries itself making it less responsive to vibration. The changes in the primary spindle afferents seem to preceed those occurring in the peripheral nerve trunk. This tallies with the histological changes found by Swash (1972) and Daniel & Strich (1964) who demonstrated progressive changes in the muscle spindle primarily in its motor innervation followed by the helical structure of the primary sensory endings.

It seems probably that the muscle spindle exhibits dysfunction before even any histological changes. Swash (1972) reported abnormalities in the innervation of the muscle spindles of all his seven autopsies. Differentiation between sensory and motor innervation was difficult. Motor innervation showed changes before the sensory one, with an increase in number of the end plates accompanied by multi innervation of the intrafusal muscle fibres. The abnormal motor innervation was found to be followed by longitudinal splitting in the intrafusal muscle fibres, a process considered to be unique to dystrophia myotonica. The differentiation between nuclear bag and nuclear chain muscle fibres was lost with aggregation of a large number of thin fibres within the lumen of the spindle. This was usually followed by abnormalities in the sensory innervation

especially in the helical structure of the primary sensory endings. These changes in the muscle spindles were found to be of patchy distribution within the affected muscle. A correlation was found between the presence of abnormality in the muscle spindle and the degree of abnormality in the extra-fusal fibres within a part of a muscle. Of importance was the decrease in the total number of muscle spindles in autopsies of old patients more than the young ones, with fibrosis of the split intrafusal muscle fibres so that spindles with a large number of fibres similar to those of young persons was not found.

All the previous findins were demonstrated even more clearly in the elegant histological description of Daniel & Strich (1964) in five autopsies taken from human myotonic dystrophy. Moreover they described muscle spindles filled with inflammatory, largely mononuclear, cells, a finding which was considered unique for dystrophia myotonica. The changes in the muscle spindle were so severe that motor innervation disturbances could not be ascribed to sprouting of spindle ɣ-fibres or interference from extrafusal @-motor innervation.

Swash (1972) and Daniel & Strich (1964) in their autopsy studies were investigating muscle spindles from advanced cases, whereas in this study muscle spindle dysfunction was found in all cases, even in the subclinical and clinical patients who were working and did not suffer from significant muscle weakness. This raises the interesting question of whether the changes in the muscle spindle were due to local or remote cause. This question cannot be answered from this scanty data. However a suggested explanation is put, based

on electrophysiological evidence, for a factor central and affecting the muscle spindle, working in this disease. This was extracted from the changes seen in the recovery curve as explained previously.

Moreover the changes exhibited in the peripheral nerves seem to be secondary to the central and muscular changes. The reflex recovery and muscle spindle changes were early findings in this disease and the reduction in the reflex amplitude comes in later stages.

C. Evidence for peripheral nerves dysfunction

In the clinical group the reflex amplitude was slightly smaller than normal but in the incapacitated patients it was dramatically small, a finding which provides evidence for a progressive reduction occurring in the peripheral nerves. However one could argue about the involvement of the MN degeneration, postulated before, in the reduction of the reflex amplitude in advanced cases. This could be one of the factors associated with the reduction, but the fact that abnormalities in the large primary afferents of the muscle spindles (Swash 1972), the small intramuscular nerve terminals (Danial et al 1964) and in the nerve trunk outside the muscle (Harris et al 1971) as well as the abnormalities in the terminal innervations of the muscles (Coers & Woolf 1959 , Woolf & Coers 1974) make the reduction of the H-reflex amplitude more likely to be due to degeneration of the Ia afferent fibres. This is supported by McComas et al (1965) who postulated a peripheral defect in the nerve axons in these cases. Moreover Harris et al (1971) found a decreased number of myelinated nerve fibres in the nerve to the tibialis anterior muscle in dystrophic mice.

Another piece of evidence which emphasized the changes in the peripheral nerves, especially the afferent fibres, was the small $^{H}/_{M}$ ratio in these cases, a finding which supports the idea of degeneration somewhere in the reflex arc, but not in the extrafusal muscle. This again could be either in the peripheral nerves or in the MNs. In this case the latter is unlikely as the maximum muscle AP (M-response) was virtually normal in most cases studied, may be due to collateral sprouting of the healthy nerve terminals (Woolf 1962 a, b, Woolf & Coers 1974). In table 22 the $^{H}/_{M}$ ratio gets smaller as the patient progressed from the clinical to the incapacitated condition, until changes started to occur in the muscle fibres which lead to a decrease in the functioning units. Only at such time the $^{H}/_{M}$ ratio exhibited a higher value again. This is shown in one of the incapacitated patients "HO" who had a maximum H-reflex amplitude of 0.3 mV. and maximum M-response of 0.58 mV. and an $^{H}/_{M}$ ratio of 60% value. This perhaps is strong evidence which supports a neural more than a muscular disturbance in the dystrophia myotonica.

Not least of importance was the reflex shape as it was polyphasic in most advanced cases. This is due to a synchrony of the MNs during reflex action (Milner-Brown et al 1973). However the terminal nerve sprouting and enlargement of the motor unit could account for the polyphasic reflex (Campbell et al 1973). The latter increases the reflex duration more than increasing its phasic components. However Buchthal et al (1963) showed that the individual motor unit potential duration was reduced by 20 to 60% below normal in dystrophia myotonica patients.

Cooling of the muscle caused reflex facilitation in three out of five patients. This may be mainly due to increased accessibility of the MNs to a Ia volley but the reason for this has not been established. Moreover it showed an increase in the excitability of the MNs in the recovery cycle in most dystrophic patients even in those which did not show reflex facilitation by cooling. This suggests a central disturbance more than a peripheral one, affecting the MN excitability level and unmasked by cooling.

Indeed, in spite of the multiple regulation of the contractile properties of the striated muscles (Gutmann 1976) the neural influence forms an important aspect (Gutmann et al 1975, Close 1972, Buller et al 1969, Hanzlikova et al 1974). This neural influence would be either in the form of neurotrophic substance (Miledi 1960, Buller et al 1960) or of nerve impulses i.e. frequency pattern or degree of activity (Jones & Vrbova 1971, Lomo & Rosenthal 1972). The myogenic influence on the muscle fibres is either developmental (Sreter et al 1972) or hormonal (Hanzlikova & Gutmann 1974).

It is unwise to ascribe the dysfunction in dystrophia myotonica to only one cause. However it is important to discover the primary disturbances taking consideration of the hierarchy of this control system. A central disturbance, although it is minute and unnoticable, could reflect on the subordered part of the system with even a great malfunction.

Perhaps our results support the concept of sick MNs put forward by McComas et al (1971) and related it to the trophic substance which it is suggested is liberated by the MNs for maintenance of the contractile properties of the muscle fibres (Buller et al 1960, 1965).

In this work we postulate that central changes found in our studies may occur and may result due to abnormalities in the trophic substance. This may be the primary cause of the disease followed by a secondary change in the muscle spindles and muscle fibres. Changes have been noticed in the @ -MNs in murine muscular dystrophy by Papapetropoulos et al (1972). It is worth noting that murine muscular dystrophy of the Bar-Harbor strain of mice discovered by Michelson et al (1955) was found to correspond closely to clinical dystrophia myotonica (McIntyre et al 1959). Perhaps other evidence which supports changes in the MN stems from the findings of Rageb (1971) who showed a significant decrease in the synaptic vesicle population in the nerve terminals in the neuromuscular junction of the very young dystrophic mice.

However there is evidence, in our work, against this assumption. The change in the muscle was progressive from mild to advanced cases and the changes in the central factors were expected to be progressive as well. This was not the case, as no direct relationship was found between the advance of the disease and the degree of reflex inhibition in the recovery curves. However in the most advanced case studied showed the slowest recovery after a longer inhibition period. Furthermore two of the cases studied exhibited hyperactive recovery. This may be due to the mechanism and type of abnormality of this trophic material which may lead to slight recovery changes accompanied by significant muscle spindle and fibre derangement as was seen in some advanced cases. These findings are strongly supported by Salafski's experiments (1971) who showed that minced muscle transplanted from a normal mouse to a dystrophic one did not grow

well, while the dystrophic muscle grows normally if it is transplanted to a healthy mouse.

In our hypothesis the degree of MN sickness or abnormality depends upon the mechanism and type of changes in the trophic substance. However I do not think that the MN disturbance in these cases resulted from overactivity as reported by McComas et al (1965). The MNs in this study exhibited less activity than normal.

However one could argue about the second factor in the neural influence, over the muscle i.e. nerve impulses frequency and pattern, as a factor of MN abnormality. This could be one of the factors combined with the trophic substance (Buller 1970). It is unlikely that the nerve impulse frequency contributes solely to the MN abnormality especially when we consider the myotonic dystrophy as a systemic disease affecting the endocrine system as well as serum immunoglobulin (Walton et al 1974).

In conclusion most workers who studied the problem of the dystrophia myotonica before did not look at the reflex changes in this systemic disorder. Disturbances within the muscle fibres do not exclude other disorders in the peripheral nerves or in its MN, even as a primary site of disturbance. Moreover Refsum et al (1959, 1967) found in dystrophic patients who are not incapacitated for work, enlargement in the 3rd ventricle, when they studied by pneumoencephalography. Most myotonic dystrophy patients showed an abnormal EEG (Barwick et al 1965). However Michelson et al (1955) found no central or peripheral nervous system abnormalities in dystrophic mice. On the other hand, McComas et al (1967) demonstrated electro-

physiologically the presence of denervated fibres in murine muscular dystrophy. Recently McComas et al (1970a, b), Campbell et al (1970) provided evidence for the neuronal factor in dystrophia myotonica. However all of these studies as well as other histological findings (Swash 1972, Harmans et al 1963, MacDermot 1961) discussed the peripheral factors either in the muscle or the peripheral nerves, but not the central ones. In this work central factors were seen early, perhaps before peripheral changes. Few histological studies were done on the changes in the spinal cord in myotonic dystrophy. Papapetropoulos et al (1972) found that the spinal MNs increased in number in dystrophic mice more than the control. Though there is no decrease in the number of spinal MNs in dystrophic mice, as was expected, this does not exclude the suggested abnormality in the trophic influence of the MN on the muscle fibres. A considerable body of evidence for this trophic substance has been developed by cross innervation experiments (Buller et al 1960 , 1965, Close 1965, Romanul et al 1967, Yellin 1967, Guth et al 1968, Rubbins et al 1969). It has been shown by Korr et al (1967), in autoradiographic studies, that neuroplasmic protein component passes from the motor nerve endings to the muscle fibre. Bloom et al (1970) isolated a number of these proteins in adrenergic nerves. However if these types of proteins determine the functional properties of the muscle fibre (Buller et al 1960, 1965), it is likely that abnormalities in this protein derived from a sick MN (McComas et al 1971) will result in derangement such as those found in dystrophic mice as well as in man.

It is possible to ascribe the changes found by McComas et al

(1965) and Conrad et al (1961) in the resting membrane potential and Conrad et al (1964), Katz et al (1957), McComas et al (1965), in the miniature end plate potential by long term effect of the trophic substance on the ionic pump of the muscle fibre membrane (Aidley 1971 pg. 74). This is supported by the finding that single muscle fibre potentials excited with less frequency after nerve interruption or after neuromuscular transmission blocking. It is pertinent to ask whether these muscle fibre potentials existed for a long time after denervation and nerve blocking i.e. after complete depletion of the long term effect of this trophic material. Buller et al (1965) emphasized that for changes in the muscle fibre to occur, a sufficient time needed to elapse. This indicates the long term effect of this trophic material.

However these speculations have to await the isolation of this trophic substance and more work is needed to confirm our hypothesis at the central and peripheral level. The exploration of the trophic material, its proper function in the neuromuscular interaction in combination with other factors will be extremely profitable.

GENERAL DISCUSSION

GENERAL DISCUSSION

The control of excitability of the MN is a complex mechanism by which mysterious smoothness, tension, delicacy and co-ordination of the contracting muscle are expressed. In this work the MN excitability was studied using the electrically elicited monosynaptic H-reflex to escape from the complexed mechanisms of the supraspinal centres as the spinal reflexes are responsible about the moment to moment reaction of movement (Matthews 1972, pg. 320).

Regarding other spinal mechanisms which inhibit the volleys at the entrance of the cord or inside it, before reaching the synaptic junction i.e. presynaptic inhibition, it would be better to use the H-reflex amplitude as a measure for MSR excitability. However Decandia et al (1968) described an escape of the MSR of the gastrocnemius-soleus MNs from presynaptic inhibition established in the spinal segment of posterior biceps-semitendenosus muscle after using train of pulses for its nerve.

To make the results more acceptable the excitability cycle of the MNP was used as a measure for MN excitability, while the H-reflex amplitude denotes the accessibility of the MNs to peripheral stimuli in addition to measuring MSR excitability. These measurements were applied to study different mechanisms affecting the MNP either by testing the whole population of the pool or only one single unit, i.e. single MN. This came about from the fact that for a certain reaction of the spinal centres to external demand a large fraction of the MNP is triggered in the motor act. However a skillful motor act conceals highly integrated and complex mechanisms which are easier to explore at the unitary level in order to escape from the

interference of the other working units. This is a simplifying method for such a complex problem especially when we take into consideration the hierarchy of the CNS in man. However the difficulty in experimenting in man hitherto with the persisting needs to solve these problems may urge the use of such simple methods. These points should be borne in mind while interpreting results of experiments on humans.

1. Spinal mechanisms controlling the MN output

It is possible, perhaps, to extract some information about the spinal controlling mechanism for the MN output, from the previous results. The skin receptors either cold or mechanoreceptors have a segmental effect, mostly suppression, on the MN discharge possibly by increasing presynaptic inhibition (See Nathan 1976). This supports the pattern theory of cutaneous sensibility which was proposed by Weddell and his colleagues at Oxford (1955). In this theory the many differences in the discharge characteristic of peripheral nerve fibres and of nerve fibres of the CNS connected to them are the source of the various kinds of sensation we experienced. Moreover a certain group of fibres contributes to more than one kind of sensation. It includes the concept that differences in quantity of peripheral nerve fibre discharge could give rise to differences in quality of sensation.

Not only the cutaneous receptors modulate the MN excitability but the muscle receptors, especially the Ia's, also suppressed it by increasing the presynaptic inhibition.

There must be an association between muscle receptors and skin receptor firing, at such instances the supraspinal centres are called

into operation. One of the supraspinal pathways conducting these impulses is the long loop reflex of the spinobulbospinal pathways (Shimamura et al 1964).

It seems probable that the sensation of each specific modality is the function of the higher centres and is different from the moment to moment modulation of the MN excitability by the same sensory pathways which is the prime function of the spinal centres. Nathan 1976 wrote elegantly about Head's application of Jackson's concepts of the evolution and dissolution in the nervous system, for cutaneous sensation. According to this conception, when the nervous system disintegrates, the higher controlling or inhibiting level disintegrates first, leaving the next level manifesting itself in an uncontrolled and excessive manner. The neural organization of every level is supposed to be controlling the neural organization of the lower level.

The MSR excitability modulation by the skin and muscle receptors was a continuous process as long as the natural stimuli were used. No fatigue of the spinal centres was seen. However when electrical pulses were used for the spindle primaries fatigue of the spinal centres was observed and revealed in a period of primary inhibition for up to 50-70 msec. after the conditioning pulse. This was ascribed to deficiency of the transmitter substances at the synaptic knobs (Curtis & Eccles 1960, Taborikova et al 1969). It is important to stress that the electrical stimulus is not a natural signal to be decoded by the nervous system and the latter's reaction does not convey the true response as if it is subjected to

a natural stimulus. When the spinal centres failed to continue discharging the MNs the supraspinal centres were recalled to compensate so that the MNs could cope with the external demands. The LLR could play this role by mediating the supraspinal modulation mechanism for the MNs.

The spinal controlling mechanisms have within their disposal different types of MNs (see SFEMG section for references) with various physiological functions (Henneman et al 1965). Each of these neurones controlled a definite muscle apparatus well adapted for a particular function (Burke 1973). However the situation is not clear cut as any motor unit could be transformed to another type when subjected to a long history of new requirements. Barnard et al (1970) reported that motor units may undergo transition between categories analogous to types FF and FR of Burke (1967), depending on the exercise history of the animal. These operating instruments switched on according to the external demands so that fast powerful and short duration reflex movements recruited large phasic before small tonic motor units. These quick movements are impractical for use all the time and moreover it is functionally difficult, as the large motor units fatigue quickly (Burke 1967, Burke et al 1973). During isometric and isotonic contraction of the muscle switching on the opposite order usually occurs as the tonic recruits before the phasic motor unit (refer to SFEMG for references). It is difficult to locate the site of the switching on mechanism; however it is unlikely to be in the spinal cord. The stereotyped order of recruitment proposed by Henneman et al (1965)

is no longer tenable, as it makes the nervous system incompetent to deal with some external requirements. Henneman noted in the international conference of "The control of movement and posture" (Granit & Burke 1973) that he and his colleagues were unable to produce clear variations in recruitment order among motor units voluntarily. It is pertinent to ask whether this hypothesis fits with different muscles. This is therefore one problem indicated by the present results in need of further investigation. Moreover it is important to stress here that the SFEMG technique in recording the AP from single MN through the H-reflex is a powerful technique and very promising. It is conceivable, however, that this method will open a new era in the field of experimental and clinical neurophysiology in man. However it needs further refinement for study of the more complicated mechanisms. This perhaps will be one of the important steps in future work.

2. Possible changes in spinal mechanisms in ageing and diseased states

The ageing process is associated with changes in the neuromuscular system (see Gutmann & Hanzlikova 1972). However this is a blank spot in such a young science of experimental gerontology. In this work significant changes have been noticed in old aged people which indicate not only selective degeneration of the large diameter peripheral nerve fibres but also small tonic MNs in the spinal cord (and possibly fibres of spinobulbospinal pathways!). These small tonic MNs are the highly excitable and frequently utilized neurones in daily movement (Henneman 1974) and are more liable to be affected

by the ageing process and disease states (Brooke & Engel 1969b, Dubowitz & Brooke 1973). This is one point that could be quickly checked subsequently by SFEMG. Moreover histological studies are needed to confirm such findings, but this should be performed on human, possibly post-mortem subjects.

The results of Gutmann & Hanzlikova (1966) are not convincing as they found significant loss of muscle fibres, motor units, but not of nerve fibres. They concluded that no loss of motor nerve cells could be seen in old aged rats judged by their results of nerve fibres counts.

The degeneration postulated in some @-MNs, in our results, was associated with a decrease in the excitability of the other MNs; this in conjunction with a decrease in the synthesis, release and re-uptake of the transmitter substances at the synaptic knobs. This point could be further studied using SFEMG technique. One point has to be taken into consideration for doing such studies that the propagation velocity inside the muscle fibre has to be estimated first before further steps toward testing transmitter changes as the former is expected to be deviated from normal in old subjects.

Our results perhaps illustrate the importance of using age matched controls for clinical investigations. One has to assert the primary deficiency in old aged people before judging the departure from normal.

In diseased states namely dystrophia myotonica neuromuscular disturbances occur as well as malfunction of other systems in the body. However the main question was whether it is a primarily muscle or neurological disease. In my opinion, the approach to

such a problem was wanting as it ignored two important facts, firstly that the disease is a systemic one and the second the different levels in the hierarchy of the nervous system. Changes in the nervous system need not be dramatic to affect the muscle. For example, abnormalities in the trophic material (Buller et al 1960, Gutmann 1976) is enough to produce dramatic changes in the muscle fibres (Buller et al 1965, Buller 1972). In later stages of such a disease small MNs were shown to be degenerated by electrophysiological techniques (refer to dystrophia myotonica section) as well as by histological ones (Brooke et al 1969b, Dubowitz et al 1973). Following the disturbances in the spinal mechanisms, the lower controlled level i.e. the muscle spindle and muscle fibres, suffered also.

It is possible to explain the findings shown in the muscle fibres in this disease by disturbances occurring centrally according to the hypothesis discussed in the text. However one has to stress that such hypothesis needs further investigation especially a histological one at the level of the spinal cord, which has not been studied. Moreover isolation and discovery of the mechanistic properties and functions of the trophic material is a persistent need, not only for this disease but also to assign the disturbances in other diseases possibly caused by abnormalities in this substance.

3. Conventional methods for improving spinal mechanisms

Disturbances in the spinal mechanisms are either loss of sensory feedback (Illis et al 1976), the discharging cephalocaudal pathways, or in the final executing unit i.e. the MNs. One has to assign the deficiency in order to identify the appropriate method

for its improvement. Spinal cord stimulation proved to be an appropriate method for improving spinal disturbances which affects the primary supraspinal conducting pathways. We don't know exactly what are the pathways we are stimulating except that the dorsal columns tracts are involved. Moreover it is difficult to assign the mechanism of functional improvement by SCS. However the functional improvement is probably attained by activating pathways either not or little used before the stimulation (Illis 1967, 1973a, b and c). In the recovery curves, the hyperactive spastic type showed decrease towards normal i.e. reduction in the MN excitability, while those of hypoactive cerebellar type demonstrated facilitation towards normal i.e. increase in the MN excitability. It is perhaps the most interesting finding in SCS that the long term after effect was noticed by all patients. One patient (Mrs. SE) reported, at the time of writing this discussion i.e. more than 8 months after removal of the spinal cord electrodes, she still has the bladder sensation which recovered during SCS. Surprizingly enough was the regression of the muscular improvement at the time of keeping bladder function normal. Moreover the recovery curve in this case did not return to the pre-stimulation level for up to two months after removal of the electrodes.

There are a number of questions of clinical and academic interest. If SCS enhances the functional improvement by using pathways little used before stimulation, it is pertinent to ask why these pathways stopped transmitting information after SCS stopped. If it was still transmitting impulses for a considerable time in the voluntary nervous system after removal of the

electrodes, what are the causes of its re-dysfunction? Moreover why should such pathways for the autonomic nervous system, i.e. bladder, still function properly for eight months, while other pathways stopped?

These are a set of questions from many needing to be answered in order to improve the technique and to use all its potentialities for functional improvement.

It seems that electrical stimulation of the nervous system heralds a new era of functional application. Papakostopoulos et al (1976), Brindley et al (1976a, b), Cooper (Personal communication) reported functional improvement in torticollis by upper cervical spinal cord stimulation and in epilepsy and cerebral palsy by cerebellar stimulation. However these are still under experimental evaluation and many questions need to be answered by further application at the clinical level.

CONCLUDING SECTION

GENERAL SUMMARY AND CONCLUSION

The monosynaptic reflex and motoneurone excitability were studied in normal subjects and in multiple sclerosis patients, treated by spinal cord stimulation, as well as a group of patients suffering from dystrophia myotonica. The electrically elicited monosynaptic 'H' reflex, recorded from the soleus muscle, was used as a measure for monosynaptic reflex and motoneurone excitability after standardization of the technique. The reliability of this measurement was supported by the reproducibility of the measurements. Further support was obtained by using single fibre EMG technique to record the action potential of a single motoneurone, from single muscle fibre, through the monosynaptic reflex arc.

Control and experimental studies

In normal subjects, the modulation of the monosynaptic reflex excitability by skin and muscle receptors was studied using natural stimuli. Skin mechanoreceptors were stimulated using scrubbing brush which was scrubbed up and down the limb over different skin areas including the sole of the foot. A pain relieving spray which produces a feeling of intense cold was used to stimulate the cutaneous cold receptors. Both stimuli produced inhibition of the 'H' reflex during application with an abrupt return to the former value when the conditioning stimulus ceased. Significant effects were found when stimuli were applied over the soleus muscle and the sole of the foot. It is difficult to claim that the effects demonstrated are entirely segmental reflexes as the stimulus continued for up to 30 seconds and in that time any supra-segmental pathways could be recruited. However the fact that the most effective dermatomes are

innervated by the same roots as in soleus that is L_5 $S_{1,2}$ the major effect possibly is segmental and mediated by an interruncial mechanism. However the supraspinal control of these interneurones which has been proposed by other workers, seems to modify the inhibition. With cooling of the skin and muscle underneath for 30 minutes the 'H' reflex was enormously facilitated to over 300% of the control especially with cooling of the calf area. Cooling for such a long time will anaesthetise the skin nerves including the cutaneous cold receptors, blocking their discharge. Thus the reflex facilitation was explained as due to increase in the motoneurone's discharge after liberation from the ongoing inhibitory effects of the skin receptors. These results were different from those obtained by other workers who used noxious and electrical stimuli and this discrepency is discussed in the text. Our stimuli were natural and applied on relaxed subjects.

Muscle receptors were stimulated using vibration of the Achilles tendon and reflex inhibition was found confirming previous works. It has been shown to be due to an increase in presynaptic inhibition and this is discussed in the text.

Motorneurone excitability was studied by the 'H' reflex recovery curves. In these curves the primary inhibition period was studied with the following recovery, as it seems to be important clinically. Evidence has been presented for the deficiency of the chemical transmitter at the central synapse, by the conditioning pulse, to account for this inhibition period. However this does not exclude the well-known recurrent inhibition of the Renshaw cells.

Interestingly, this work gives evidence that recurrent discharge of the muscle spindle and golgi tendon organs does not significantly affect this inhibition period. It was concluded that the reflex inhibition depends mainly upon the degree of deficiency of the synaptic transmitter, while the reflex recovery was attributed to motoneurone activation by a long loop reflex mediated possibly by spinobulbo-spinal pathways. Moreover reflex recovery depends upon the type of motoneurones in the pool, either tonic or phasic, and this was further studied by the single fibre EMG technique.

Furthermore these recovery curves were studied in normal young and old subjects and significant differences were noted. Longer reflex latency with significantly small polyphasic potentials, as well as a longer inhibition period in the recovery curves were shown in old subjects. These were attributed to degeneration in the large diameter nerve fibres as well as alpha-motoneurones in the spinal cord.

Study of the single unit of the motoneurone potential was needed to confirm previous findings and to proceed to further study, with minimal interference from other individuals of the pool. This study provides evidence for two types of motoneurones forming the pool of the soleus muscle. One type considered to be the more phasic while the other the more tonic motoneurones. Different characteristics of these motoneurones studied by single fibre EMG was given and discussed in the text. With incremental stimuli it was found that the more phasic motoneurones recruited first followed by the more tonic ones. This was further confirmed by decrementing

stimuli and from these results a new hypothesis was developed which goes against the size principle hypothesis and the stereotyped recruitment order of Henneman et al (1965). The new hypothesis presumes that the functional requirement determines the order of recruitment of the motoneurones. During slow isometric and isotonic contraction of the muscles, the tonic followed by the phasic motoneurones fulfils the functional requirements of the movement. However with fast movement as well as reflex activity the recruitment order should be reversed, so that the phasic motoneurones are recruited first before the more tonic ones, in order to cope with the external demands. A switching mechanism, to determine the appropriate recruitment order is proposed and further discussed in the text.

In addition to the main experimental results summarized above, numerous other supporting studies were also done. These involved the study of the blocking order of the motoneurones with high amplitude pulses as well as the inhibition order of the motoneurones by mechanoreceptors stimulation. The results from these supporting experiments support the results from the primary experiments.

Studies of motoneurone excitability as temporal and spatial summation, using single fibre EMG technique were found to be helpful in the understanding of the recovery curves. These studies illustrate the potentiality of this technique for exploring different integrative mechanisms at the motoneurone on the unitary level and revealed many important problems which need to be resolved.

Clinical studies

Clinically, these measurements were applied in patients with multiple sclerosis and motoneurone disease treated by spinal cord stimulation. Dramatic changes in the recovery curves towards normal values were noticed in those patients who showed clinical functional improvement. Moreover patients with sensory paraesthesia noticed amelioration with spinal cord stimulation the reflex tested against segmental mechanoreceptors stimulation demonstrated significant recovery towards normal values.

Further studies for the mechanism of functional improvement by spinal cord stimulation was done using different types of stimuli delivered to the spinal cord through the implanted electrodes. These experiments further support the increase in the motoneurones discharge possibly by using pathways not or little used before spinal cord stimulation. An increase in the sensory feedback was assumed and these interpretations were further discussed in the text. This is considered preliminary work which needs more elaboration in the future. However these basic studies suggest a number of possible ways for exploration of the mchanisms of the spinal cord stimulation in the amelioration of disease and for study of the integrative activity of the nervous system.

Patients with dystrophia myotonica were studied using the 'H' reflex. Significant changes were noted in the reflex amplitude, shape as well as $^{H}/_{M}$ ratio, reflex inhibition by vibration and the recovery curves. 'H' reflex recovery curves showed significant changes before any other dystrophic changes were apparent, a finding which

suggests a central neural defect, as a primary factor in the disease. Another piece of evidence was seen in the unresponsiveness of spindles to vibration. A speculative assumption, based on the previous findings is that in dystrophia myotonica neural changes precede the muscular one. The dystrophia may then result from abnormalities in the trophic substance liberated by the motoneurones which have been presumed by previous workers. The neural changes and mechanistic derangement of the neuro-muscular system in relation to the proposed assumption was further elaborated and discussed in the text.

It is interesting to note that the type of motoneurones assumed to degenerate in old age are the same group as thought to be affected in dystrophia myotonica and more liable to defects in other diseased states. These are the highly excitable small tonic motoneurones which recovered first and are most frequently used in daily life.

Concluding remarks

Of the results reported in this study, four are considered to be of more importance than others. These are:-

I Clinically

1. The neural evidence as a primary factor in dystrophia myotonica disease.
2. The age related changes in the neural apparatus.

II Physiologically

1. The recruitment order of the motoneurones during voluntary and reflex activity with the switching mechanism of the order to fulfil the functional requirement of the motor act.

2. Using natural stimuli Hagberth's concept of the pattern of skin areas is no longer tenable and shows a more complex mechanism for the modulation of the monosynaptic reflex excitability.

These results in normal subjects enable more detailed examination of similar mechanisms in diseased states and the following points emerge:-

1. Dystrophia myotonica is considered to involve primarily the neural apparatus before the muscular one during the course of the disease.
2. The importance of age matched controls especially when investigating elderly people.
3. There are disturbances in spinal and supraspinal centres in upper motor neurone diseases which affect the switching mechanism and the recruitment order of the different motoneurones which may be one of the factors in movement disturbance in these cases.
4. In sensory paraesthesias the decrease in the modulation of the motoneurone excitability may affect the discharging properties of these neurones. This may account to some extent for the poor control of voluntary movements and ataxia shown in these cases.
5. 'H' reflex measurement proved to be useful for pathophysiological investigations as well as an objective measure of the amelioration of the neurological diseases by treatment.

6. Deep cooling was found to increase the accessibility of the motoneurones to peripheral stimuli and does not decrease it as previously thought. Thus this new fact has to be considered in re-evaluating the use of deep cooling in physiotherapy and cryotherapy in various diseased states.

Finally the author believes that methodology and technology has progressed to the point where meaningful pathophysiological experiments can be done safely and without significant discomfort in humans. It is regretted that so little research effort can presently be applied in this field for without it our understanding of fundamental problems in human neurophysiology will remain limited and the application of such understanding to the vast number of sufferers from neurological disease will not ensue.

FUTURE STUDIES

This study indicates the need for further experiments to elaborate the previous results and further detailed study of the problem of MN excitability from other aspects.

It is perhaps one of the criticisms of this thesis that it covers a wide range of topics concerning the problem of MSR and MN excitability in man. For example SFEMG studies are an important step forward in deep analytical studies of the MN excitability on the unitary level after investigating the whole MNP. However it would be better to focus research studies on a critical point analyzing all its variables and looking for the parameters that affect it. It is safe to say that this thesis creates a sound base for future work stemming from the different topics of its content. In my opinion a solid base of SFEMG studies has been created in this work which needs more elaboration in future. Study of the recruitment order of MNs in a number of typically mixed muscles e.g. Gastrocnemius needs to be investigated. The recruitment order is expected to be altered during H-reflex facilitation with contraction of the calf. Study of such an alteration will explore one aspect of the integrative mechanisms of the CNS.

Moreover the study of the interaction between natural stimuli at the MNs is worthwhile. This could be elaborated by its application to patients suffering from UMNL. I was always surprised by the dramatic differences in the reaction to these stimuli in those few cases I studied and I would like to attack the question of what fundamental elements underly these changes. This would form the core of experimental studies in future work.

In spite of the fact that in this thesis the γ-system was not studied I feel an inclination towards studying its role in control of movement. The role of single muscle and nerve fibres recording will be of great importance in these studies especially if it is used on conjunction with the technique of Dietrecheson (1973) who used $^{T}/_{H}$ ratio for γ-system studies.

The pathophysiological aspects of future work are interesting. Disturbances in diseases of @ and γ-system excitability form a comprehensive aim. However alteration of these systems in various types of spasticity and rigidity is of particular interest. Single muscle and nerve fibre recording in conjunction with data handling by computer will be of great importance.

Spinal cord stimulation is shown to be very effective in this preliminary report and the discovery of its mode of action is of clinical and physiological interest.

It is perhaps with respect to the last point that the author would like to stress the urgent need to use recent advanced in technology and methodology in order to obtain more reliable information from humans and to develop therapeutic procedures.

APPENDIX

Schumacher's Criteria for Diagnosis of Multiple Sclerosis

Clinical criteria

The following criteria are essential to diagnose the disease as clinically "definite multiple sclerosis".

a. Must be objective abnormalities of the CNS.

b. Must fulfil the "multiplicity" of the lesions with involvement of two or more separate parts of the CNS.

c. The lesions must reflect predominantly white matter involvement i.e. fibre tract damage with probably minor proportion of signs of lower motor neurone lesions.

d. The CNS involvement must have occurred temporally in one or the other of the following patterns:

   1. In two or more episodes of worsening, separated by a period of one month or more, each episode lasting at least 24 hours.
   2. Slow or stepwise progression of signs and symptoms, over a period of at least six months.

e. The ages of the patient at the onset of the disease must fall within the range of 10 to 50 years, inclusive.

f. The patient's signs and symptoms cannot be explained better by some other disease process, a decision which must be made by a physician competent in clinical neurology.

BIBLIOGRAPHY SECTION

BIBLIOGRAPHY

Abdel-Hamid, T. (1967) "The evoked and reflex potentials in electromyography". A thesis of M.D. Ain Shams University, Cairo.

Adams, R.D. (1969) "Pathological reactions of the skeletal muscle fibre in man" in "Disorders of voluntary muscle", 2nd edition J. Walton (Ed.) 143-202. Churchill-London.

Adams, R.D., Denny-Brown, D. & Pearson, C.M. (1962) "Diseases of muscle", a study in pathology, 2nd edition, (New York: Hoeber).

Adie, W.J. & Greenfield, J.G. (1923) "Dystrophia myotonica-Myotonica atrophica" Brain 46, 73-127.

Adrian, E.D. (1928) "The basis of sensation. The action of the sense organs" Christophers, London.

Adrian, E.D. & Bronk, D.W. (1929) "The discharge of impulses in motor nerve fibres. Part II. The frequency of the discharge in reflex and voluntary contraction". J. Physiol. 67, 119.

Aidley, D.J. (1975) "The physiology of excitable cells", Cambridge University Press.

Anastasijevic,R. Anojcic, M., Todorovic, B. & Vuco, J. (1968) "The differential reflex excitability of -motoneurones of decerebrate cats caused by vibration applied to the tendon" Brain Res. 11, 336-346.

Andersen, P., Eccles, J.C. & Schmidt, R.F. (1962) "Presynaptic inhibition in the cuneate nucleus", Nature (London) 194, 741-793.

Andersen, P., Eccles, J.G., Schmidt, R.F. & Yokota, T. (1964) "Slow potential waves produced in the cuneate nucleus by cutaneous volleys and by cortical stimulation". J. Neurophysiol. 27, 78-91.

Andersen, P., Etholm, B. & Gordon, G. (1968) "Presynaptic depolarization of dorsal column fibres by adequate stimulation". J. Physiol. 194, 83-84.

Angel, R.W. & Hoffmann, W.W. (1963) "The H-reflex in normal, spastic and rigid subjects" Arch. Neurol. 8, 591-596.

Arcangel, C.S., Johnston, R. & Bishop, B. (1971) "The achilles tendon reflex and the H-response during and after tendon vibration" . Phys. Ther. 51 (8), 889-902.

Ashby, P., Verrier, M. & Lightfoot, E. (1974) "Segmental reflex pathways in spinal shock and spinal spasticity in man". J. Neurol. Neurosurg. Psychiat. 37, 1352-1360.

Ashworth, B., Grimby, L. & Kugelberg, E. (1967) "Comparison of voluntary and reflex activation of motor units - Functional organization of motor neurones", J. Neurol. Neurosurg. Psychiat. 30, 91-98.

Baker, N., Blahd, W.H. & Hart, P. (1958) "Concentrations of K. and Na in skeletal muscle of mice with a hereditary Myopathy (Dystrophia muscularis) Amer. J. Physiol. 193 (3), 530-533.

Barnard, R.J. Edgerton, V.R. & Peter, J.B. (1970), "Effect of exercise on skeletal muscle" I. Biochemical & histochemical properties. Amer. J. Physiol. 28, 762-766.

Barrett, J.N. & Crill, W.E. (1971) "Specific membrane resistivity of dye-injected cat motorneurons" Brain Res. 28, 556-561.

Barron, D.H. & Matthews, B.H.C. (1935) "Intermittent conduction in the spinal cord". J. Physiol. 85, 73-103.

Barron, D.H. & Matthews, B.H.C. (1938) "The interpretation of potential changes in the spinal cord". J. Physiol. 92, 276-321.

Barwick, D.D., Osselton, J.W. & Walton, J.N. (1965) "Electroencephalographic studies in hereditary Myopathy". J. Neurol. Neurosurg. Psychiat. 28, 109-114.

Basmajian, J.V. (1962) "Muscle Alive : Their functions revealed by electromyography". Williams & Wilkins - Baltimore.

Basmajian, J.V. (1963) "Control and training of individual motor units" Science 141, 440-441.

Bathien, N. & Hugon, M. (1964) "Etude chez l'homme de la depression d'un reflexe monosynaptique par stimulation d'un nerf cutane". J. Physiol (Paris) 56, 285-286.

Batten, F.E. & Gibb (1909) "Myotonica atrophica". Brain 32, 187.

Beranek, R. (1961) "Intracellular electromyography in man" Physiol. Bohemoslov. 10, 94.

Besson, P. & Perl, E.R. (1969) "Responses of cutaneous sensory units with unmyelinated fibres to noxious stimuli" J. Neurophysiol. 32, 1025-1042.

Bianconi, R. & Van Der Meulen, J.P. (1962) "The response to vibration of the end organs of mammalian muscle spindles" J. Neurophysiol. 26, 177-190.

Bianconi, R., Granit, R., & Resis, D.J. (1964) "The effects of extensor muscle spindles and tendon organs of mammalian muscle spindles". J. Neurophysiol. 26, 177-190.

Bigland, B. & Lippold, O.C.J. (1954) "Motor unit activity in the voluntary contraction of human muscle". J. Physiol. 125, 322.

Birren, J.E. & Wall, P.D. (1956) "Age changes in conduction velocity, refractory period, number of fibres, connective tissue space and blood vessels in sciatic nerve of rats" J. Comp. Neurol 104, 1-16.

Bjork, A. & Kugelberg, E. (1953a) "Motor unit activity in the human extraocular muscles" EEG. Clin. Neurophysiol. 5, 271-

Bjork, A. & Kugelberg, E. (1953b) "The electrical activity of the muscles of the eye and eyelids in various positions and during movement" EEG Clin. Neurophysiol. 5, 595.

Bloom, F.E., Iversen, L.L. & Schmidt, F.O. (1970) "Macromolecules in synaptic function". A report based on an NRP work session. Neuroscience Res. Prog.Bull. 8, 329-455.

Bodian, D. (1966) "Development of fine structure of spinal cord in monkey fetuses. I. The motoneurone neuropil at the time of onset of reflex activity" Bull. John Hopk. Hosp. 119, 129-149.

Boes, M.C. (1962) "Reduction of spasticity by Cold". J. Amer. Phys. Ther. Assoc. 42, 29-32.

Bonsett, C.A., Abreu, B.E. & Ralston, J.D. (1961) "Skeletal muscle studies by means of combined electromyography and needle biopsy. I. The electromyographic myotome". Texas Rep. Biol. Med. 19, 749.

Bosemark, B. (1966) "Some aspects of the crossed extensor reflex in relations to MNs supplying fast and slow contracting muscles" in Granit Nobel Symposium I, Muscular afferents and motor control. pp. 261-268 (Almqvist & Wiksell - Stockholm).

Bourne, G.H. & Golarz, M.N. (1963) "Muscular dystrophy in man and animals" (Karger-Basel).

Braddom, R.I. & Johnson, E.W. (1974) "Standardization of H-reflex and diagnostic use in S_1 radiculopathy". Arch. Phys. Med. Rehabil. 55, 161-166.

Bradley, K. & Eccles, J.C. (1953) "Analysis of fast afferent impulses from thigh muscles". J. Physiol. (Lond.) 122, 462-473.

Brindley, G.S., Falconer, M.A. Fenton, G.W., Fenwick, P.B.C. Rushton, D.N. (1976) "Chronic cerebellar stimulation in the treatment of generalized Epilepsy: A case report" EEG. Clin. Neurophysiology E.E.G. Clin. Neurophysiol. 4, 539 .

Brindley, G.S., Falconer, M.A., Fenton, G.W., Fenwick, P.B.C. Polkey, C.E. & Rushton, D.N. (1976) "Immediate effects of cerebellar stimulation in an epileptic patient" EEG Clin. Neurophysiol. E.E.G. Clin. Neurophysiol. 3, 539.

Brody, A. (1955) "Organization of the cerebral cortex. III A study of ageing in the human cerebral cortex". J. Comp. Neurol. 102, 511-556.

Brooke, M.H. & Engel, W.K. (1969a) "The histographic analysis of human muscle biopsies with regard to fibre type. I Adult male and female" Neurol. 19, 221-233.

Brooke, M.H. & Engel, W.K. (1969b) "The histographic analysis of human muscle biopsies with regard to fibre type. III Mytonias, myasthesia gravis and hypokalemic periodic paralysis" Neurol. 19, 469-497.

Brooks, V.B. & Wilson, V.J. (1959) "Recurrent inhibition in the cats spinal cord". J. Physiol. (Lond.) 146, 380-391.

Brown, G.L. & Harvey, A.M. (1939) "Congenital myotonia in the goat" Brain 62, 341-363.

Buchthal, F. (1957) "An introduction to electromyography" Gyldendel, Copenhagen.

Buchthal, F., Madsen, A. (1950) "Synchronous activity in normal and atrophic muscle" EEG Clin. Neurophysiol. 2, 425.

Buchthal, F., Guld, C. & Rosenfalck, P. (1955) "Innervation zone and propagation velocity in human muscle". Acta Physiol. Scand 35, 174-190.

Buchthal, F., Guld, C. & Rosenfalck, P. (1957b) "Multielectrode study of the territory of a motor unit". Acta Physiol. Scand. 39, 83-104.

Buchthal F., Guld, C. & Rosenfalck, P. (1957) "Volume conduction of the spike of the motor unit potential investigated with a new type of multielectrode". Acta Physiol. Scand. 38, 331-354.

Buchthal, F. & Rosenfalck, P. (1963) "Electrophysiological aspects of Myopathy with particular reference to progressive muscular dystrophy" in Muscular dystrophy in man and animals by Bourne & Golarz (Eds). 193-262. (Karger-Basel).

Buchthal, F. & Schmalbruch, H, (1970a) "Contraction times and fibre types in intact human muscle" Acta Physiol. Scand. 79, 435-452.

Buchthal, F. & Schmalbruch, H., (1970b) "Contraction times of twitches evoked by H-reflexes" Acta Physiol. Scand. 80, 378-382.

Buchthal, F. & Rosenfalck, P. (1973) "On the structure of motor units" New develop. in EMG. clin. Neurophysiol. J. Desmedt (Ed.), I, pp. 71-85 (Karger-Basel).

Bugaj, R. (1975) "The cooling, analgesic and rewarming effects of ice massage on localized skin" Phys. Ther. 55 (1), 11-19.

Buller, A.J. (1970) "The neural control of the contractiel mechanism in skeletal muscle" Endeavour 29, 107-111.

Buller, A.J., Dornhorst, A.D. Edwards, R., & Kerr, D. (1959) "Fast and slow muscles in mammals" Nature 183, 1516-1517.

Buller, A.J., Eccles, J.C., & Eccles, R.M. (1960) "Interactions between motoneurones and muscles in respect to the characteristic speeds of their responses". J. Physiol. 150, 417-439.

Buller, A.J. & Lewis, D.M. (1965) "Functional differences between mammalian fast twitch and slow twitch skeletal muscle fibres" In "Research in muscular dystrophy" Proc. 3rd synpos. of the muscular dystrophy group (London) pp. 271-285.

Buller, A.J., Mommaerts, W.H.F. & Seraydarian, K. (1969) "Enzymic properties of myosin in fast and slow twitch muscles of the cat following cross-innervation". J. Physiol. 205, 581-597.

Burke, R.E. (1967a) "Motor unit types of cat triceps srae muscle" J. Physiol., 193, 141-160.

Burke, R.E. (1967b) "Composite nature of monosynaptic excitatory postsynaptic potential" J. Neurophysiol. 30, 1114-1137.

Burke, R.E. (1968a) "Group Ia synaptic input to fast and slow twitch motor units of cat triceps surae". J. Physiol. 196, 605-630.

Burke, R.E. (1968b) "Firing patterns of gastrocnemius motor units in decerebrate cat" J. Physiol 196, 631-654.

Burke, R.E. (1973) "On the central nervous system control of fast and slow twitch motor units" New Develop. in EMG Chin. Neurophysiol. Desmedt (Ed), III, 69-94, (Karger-Basel).

Burke, R.E., Jankowska, E. & Bruggencate, G. Ten (1970) "A comparison of peripheral and rubrospinal synaptic input to slow and fast twitch motor units of triceps surae". J. Physiol. 207, 709-732.

Burke, R.E. Levine, D.N., Zajac, F.E. III, Tsairis, P., & Engel, W.K. (1971) "Mammalian motor units, physiological-histochemical correlation in three types in cat gastrocnemius" Science 174, 709-712.

Burke, R.E., Tsairis, P., Levine, D.N. & Zajac, F.E. III (1973) "Direct correlation of physiological and histochemical characteristics in motor units of cat triceps surae muscle" New Develop. in EMG. Clin. Neurophysiol. J. Desmedt (Ed.), I, 23-30 (Karger-Basel).

Burton, H. (1975) "Responses of spinal cord neurones to systematic changes in hindlimb skin temperatures in cats and primates" J. Neurophysiol. 38 (5), 1060-1077.

Cajal, R.Y.S. (1899) "Textura del sistema nervioso del hombre ye de los vertebrados", N. Moya, Madrid.

Campa, J.F. & Engel, W.K. (1970) "Histochemistry of motor neurones and interneurones in the cat - lumber spinal cord" Neurol. (Minn) 20, 559-568.

Campbell, M.J., McComas, A.J., & Sica, R. (1970) "Electrophysiological study in dystrophia myotonica" J. Physiol. 209, 28-29.

Campbell, M.J., McComas, A.J. & Petito, F. (1973) "Physiological changes in ageing muscle" J. Neurol. Neurosurg. Psychiat. 36, 174.

Carlson, K.E., Alton, W., & Feldmann, D.J. (1964) "Electromyographic study of ageing in skeletal muscle" Am. J. Phys. Med. 43, 141-145.

Castaigne, P., Held, J.P, Cathala, H.P, Pierrot-Deseilligny, E., Bussel, B. & Morin, C. (1972) "Reflex changes induced by cutaneous stimulation in hemiplegics with variously situated lesions" Revue Neurol. 126 (6)

Caughey, J.E. & Myrianthopoulos, N.C. (1963) "Dystrophia myotonica and related disorders" (Thomas, Springfield, Illinois).

Cauthen, J.C. (1975) "Transcutaneous and peripheral nerve stimulation for chronic pain states", Surg. Neurol. 4, 102-104.

Cazzato, G. (1970) "Myopathic changes in denervated muscle. A study of biopsy material in various neuromuscular diseases" Exempta Medica. Int. Congr. Ser. No. 199. 392-401

Clamann, H.P., Gillies, J.D., Skinner, R.D. & Henneman, E. (1974a) Quantitative measures of output of a motoneurone pool during monosynaptic reflex" J. Neurophysiol. 37, 1328-1337.

Clamann, H.P., Gillies, J.D. & Henneman, E. (1974b) "Effects of inhibitory inputs on critical firing level and rank order of motoneurones" J. Neurophysiol. 37, 1350-1360.

Clarke, A.M. (1966) "The effect of stimulation of certain skin areas on the extensor motoneurones in the phasic reaction of a stretch reflex in normal human subjects" EEG. Clin. Neurophysiol. 21, 185-93.

Clark, W.K. (1975) "Electrical stimulation of the nervous system for control of pain: University of Texas Southwestern Medical School experience". Surg. Neurol. 4, 164-166.

Clendenin, M.A. & Szamski, A.J. (1971) "Influence of cutaneous ice application on single motor units in humans" Phys. Ther. 51, 166-175.

Close, R. (1965) "Effect of cross union of motor nerves to fast and slow skeletal muscles" Nature 206, 831-832.

Close, R.I. (1972) "Dynamic properties of mammalian skeletal muscles" Physiol. Rev. 52 (1), 129-197.

Close R.I. (1972) "Les variations structurelles normales et pathologique de la jonction neuro musculaire". Acta neurol. belg. 55, 741.

Coers, C. (1965) "Histology of the myoneural junction in myopathies" In Muscle by Paul, Daniel, Kay & Monckton (Eds.), p. 453 (Pergamon Oxford, N.Y.).

Coers, C. & Woolf, A.L. (1959) "The innervation of muscle" (Blackwell-Oxford).

Collins, W.F., Nulsen, F.E. & Shealy, C.N. (1966) "Electrophysiological studies of peripheral and central pathways conducting pain". In Knighton, R.S. & Dunske, P.R. (Eds.) Pain. (Little Brown & Co.).

Conrad, J.T. & Glasier, G.H. (1961) "Bioelectric properties of Dystrophic mammalian muscle. A.M.A. Arch. Neurol. 5, 46-59.

Conrad, J.T. & Glasier, G.H. (1964) "Spontaneous activity at myoneuronal junction in dystrophic muscle" AMA Arch. Neurol. 11, 310-316.

Cook, A.W. (1974a) "Stimulation of the spinal cord in the motor neurone disease (letter) Lancet II, 7874, 230.

Cook, A.W. (1974b) "Electrical stimulation of the spinal cord (letter) Lancet I, 7862, 869.

Cook, A.W. & Weinstein, S.P. (1973) "Chromic dorsal column stimulation in multiple sclerosis" NY State J. Med. 73, 2868-2872.

Cook, A.W. (1976) "Electrical stimulation in multiple sclerosis" Hosp. Practice 11 (4), 51-58.

Cook, A.W. (1976) "Electrostimulation of the spinal cord in multiple sclerosis". The application of electronics in medicine. Proceedings of the Institution of Electronic and Radio Engineers. University of Southampton, England.

Coombs, J.S., Eccles, J.C. & Fatt, P. (1955) "Excitatory synaptic action in motoneurones" J. Physiol. 130, 374-395.

Coombs, J.S., Eccles, J.C. & Fatt, P. (1955) "Excitatory synaptic in motoneurones" J. Physiol. 130, 374.

Cooper, S. & Eccles, J.C. (1930) "Isometric responses of mammalian muscles" J. Physiol. 69, 337.

Cooper, R. (1976) "Personal Communication".

Corrie, W.S. & Hardin, W.B.J.R. (1964) "Post-tetanic potentiation of H-reflex in normal man". Arch. Neurol. 11, 317-323.

Cottrell, L. (1940) "Histological variations with age in apparently normal peripheral nerve trunk" Arch. Neurol. Psychiat. 43, 1138-1150.

Creed, R.S., Denny-Brown, D., Eccles, J.C., Liddell, E.G.T. & Sherrington, C. S. (1932) "Reflex activity of the spinal cord" Humphrey Milford-London.

Critchely, M. (1942) "Problems of Ageing" by Cowdrey (Ed.) pp. 518. Williams ¾ Wilkins - Baltimore.

Curtis, D.R. & Eccles, J.C. (1960) "Synaptic action during and after repetitive stimulation. J. Physiol. (Lond.) 150, 374-398.

Daniel, P.M. & Strich, S.J. (1964) "Abnormalities in the muscle spindles in dystrophia myotonica". Neurol. 14, 310-316.

Darian-Smith, I., Johnson, K.O, & Dykes, R.D. (1972a) "Cold fibre population innervating palm and digital skin of the monkey: responses to cooling pulses". J. Neurophysiol. 36, 325.

Darian-Smith, I., Johnson & Lamotte, C., (1972b) "Warming and cooling the skin. Peripheral neural determinants of perceived changes in skin temperature". In Kornhuber, H.H. (Ed.): The somatic sensory system".

Decandia, M. Gasteiger, E.L. & Mann, M.D. (1968) "Escape of the extensor monosynaptic reflex from presynaptic inhibition" Brain Res. 7, 317-319.

De Gail, P., Lance, J.W., & Neilson, P.D. (1966) "Differential effects on tonic and phasic reflex mechanisms produced by vibration of muscles in man" J. Neurol. Neurosurg. Psychiat. 29, 1-11.

Delwaide, P.J. (1969) "Approche de la physiopathologie de la spasticite: Reflexe de Hoffmann et variations appliquees sur la tendon d"Achille." Rev. Neurol. 121, 72-74.

Delwaide, P.J. (1971) "Etude experimentale de l'hypereflexie tendineuse en clinique neurologique (Arascia, Bruxelles).

Delwaide, P.J. (1973) "Human monosynaptic reflexes and presynaptic inhibition" New Develop. in EMG. Clin. Neurophysiol. J. Desmedt (Ed.), III, 508-522 (Karger-Basel).

Delwaide, P.J. & Hugon, M. (1969) "H-reflex depression by soleus sinusoidal stretching and facilitation by voluntary contraction" Experentia 25, 1152-1153.

Delwaide, P.J., Hugon, M. & Thiriet, E. (1970) "Slow stretching of human triceps surae by a pneumatic device" Electromyography 4, 399-405.

Delwaide, P.J. & Delbecq, P. (1973) "Vestibular influences on proprioceptive reflexes of the lower limb in normal man" New Develop. EMG. Clin. Neurophysiol. Desmedt (Ed.), III, 336-341. (Karger-Basel).

Denny-Brown, D. (1928) "On inhibition as a reflex accompaniment of the tendon jerk and of other forms of active muscular response" Proc. Roy. Soc. B103, 321-336.

Denny-Brown, D. (1929) "On the nature of postural reflexes" Proc. Roy. Soc. B. 104, 252-301.

Denny-Brown, D. & Nevin, S. (1941) "The phenomenon of myotonia" Brain 64, 1-18.

Deschuytere J. & Rosselle, N. (1973) "Diagnosic use of monosynaptic reflexes in L_5 and S_1 root compression". New Develop. EMG. Clin. Neurophysiol. J. Desmedt (Ed.), III, 360-366. (Karger-Basel).

Desmedt, J. and others (1973) "A discussion of the methodology of the triceps surae T- and H-reflexes" New Develop. in EMG. Clin. Neurophysiol. by J.E. Desmedt (Ed.) III 773-780 (Karger-Basel).

Devanandan, M.S., Eccles, R.M., Lewis, D.M. & Stenhouse, D. (1966), cited in: Eccles, J.C. (1966). Atti Accad. med. lombarda 21, 158-176.

Diamantopoulos, S. & Zander-Olsen, P. (1965) "Motoneurone excitability in normal subjects and patients with abnormal muscle tone" Proceedings of the 6th International Congress EEG. Clin. Neurophysiol. New York, 621-623. (Elsevier).

Diamantopoulos, E. & Zander Olsen, P. (1967) "Excitability of motor neurones in spinal shock in man". J. Neurol. Neurosurg. Psychiat. 30, 427-431.

Douglas, W.W. & Malcolm, J.L. (1955) "The effects of localized cooling on conduction in the cat nerves". J. Physiol 130, 53-71.

Douglas, W.W. & Ritchie, J.M. (1959) "The sensory functions of the non-myelinated nerve fibres from the skin" in "Pain & Itch Nervous mechanisms". Ciba Symposium No. 1, 26-39, Churchill, London.

Dietrichson, P. (1973) "The role of the fusimotor system in spasticity and Parkinsonian rigidity" New Develop. in EMG Clin. Neurophysiol. J. Desmedt (Ed.) III, 496-507 (Karger-Basel).

Drachman, D.B. & Farnbrough, D.M. (1976) "Are muscle fibres denervated in myotonic dystrophy" Arch. Neurol. 33, 485-488.

Dubowitz V & Brooke, M.H. (1973) "Muscle Biopsy: a modern approach" Saunders.

Eccles, J.C. (1931) "Studies on the flexor reflex III. The central effects produced by an antidromic volley" Proc. Roy. Soc. Med. B. 107, 557-585.

Eccles, J.C. (1953) "The neurophysiological basis of mind: The principles of neurophysiology". Clarendon- Oxford.

Eccles, J.C. (1957) "The physiology of nerve cells" John Hopkins - Baltimore.

Eccles, J.C. (1966) "Long loop reflexes from the spinal cord to the brain stem and cerebellum" Atti Accad. Med. lom. 21, 1-19.

Eccles, J.C. (1973) "The understanding of the Brain" McGraw-Hill, New York.

Eccles, J.C. & Sherrington, C.S. (1931) "Studies on the flexor reflex. VI Inhibition Proc. Roy. Soc. B. 109, 91-113.

Eccles, J.C. & Pritchard, J.J. (1937) "The action potential of motoneurones". J. Physiol. 89. 43-45.

Eccles, J. & Rall, W. (1951) "Effects induced in monosynaptic reflex path by its activation". J. Neurophysiol. 14, 353-376.

Eccles, J.C., Fatt, P. and Koketsu, K. (1954) "Cholinergic and inhibitory synapses in a pathway from motor axon collaterals to motoneurones". J. Physiol. (Lond.) 126, 524-562.

Eccles, J.C., Eccles, R.M. & Lundberg, A. (1957a) "Synaptic actions on motoneurones in relation to the two components of the group I muscle afferent volley". J. Physiol. 136, 527-546.

Eccles, J.C., Eccles, R.M. & Lundberg, A. (1957b) "Synaptic actions on motoneurones caused by impulses in golgi tendon organ afferents". J. Physiol. 138. 227-252.

Eccles, J.C., Eccles, R.M. & Lundberg, A. (1958). "The action potentials of the alpha motoneurones supplying fast and slow muscles". J. Physiol. 142, 275-291.

Eccles, R.M. & Lundberg, A. (1959a) "Synaptic actions in motoneurones by afferents which may evoke the flexion reflex". Archs. Ital. Biol. 97, 199-221

Eccles, R.M. & Lundberg, A. (1959b) "Supraspinal control of interneurones mediating spinal reflexes". J. Physiol. 147(3), 565-584.

Eccles, J.C., Eccles, R.M., Iggo, A. Ito, M. (1961) "Distribution of recurrent inhibition among motoneurones". Acta. Physiol. Scand. 50, 32.40.

Eccles, J.C., Kostyuk, P.G. & Schmidt, R.D. (1962) "Presynaptic inhibition of the central actions of flexor reflex afferents. J. Physiol. 161, 258-281.

Eccles, J.C., Magni, F. & Willis, W.D. (1962b) "Depolarization of central terminals of group I afferent fibres from muscle". J. Physiol. 160, 621-693.

Eccles, J.C., Schmidt, R.F. & Willis, W.D. (1963) "Depolarization of the central terminals of cutaneous afferent fibres". J. Neurophysiol. 26, 646-661.

Echlin, F. & Fessard, A. (1938) "Synchronized impulse discharges from receptors in the deep tissues in response to a vibratory stimulus". J. Physiol. (Lond.) 93, 312-334.

Edstrom, L. & Kugelberg, E. (1968) "Histochemical composition, distribution of fibres and fatiguability of single motor units". J. Neurosurg. Psychiat. 31, 424-433.

Ekholm, J. & Skoglund, S. (1964) "Possible factors influencing the demonstration of post-tetanic of the H-reflex as studied in cat". Exp. Neurol. 9, 183-197.

Ekstedt, J. (1964) "Human single muscle fibre action potentials" Acta physiol. scand. 61, suppl. 226, 1-96.

Ekstedt, J. & Stalberg, E. (1963) "A method of recording extracellular action potentials of single muscle fibres and measuring their propagation velocity in voluntary activated human muscles" Bull. Amer. Ass. EMG Electrodiagn. 10, 16 (1963).

Ekstedt, J., Haggqvist, P. & Stalberg, E. (1969) "The construction of needle multi-electrodes for single fibre EMG" EEG. Clin. Neurophysiol. 27, 540-543.

Ekstedt,J. & Stalberg, E. (1973) "Single fibre electromyography for the study of the Microphysiology of the human muscle" New Develop. EMG. Clin. Neurophysiol. Desmedt (Ed.), I, 89-112 (Karger-Basel).

Ekstedt, J. Nilsson, G. & Stalberg, E. (1974) "Calculation of the electromyographic jitter". J. Neurol. Neurosurg. Psychiat. 37, 526-539.

Eldred, E. & Hagbarth, K.E. (1954) "Facilitation and inhibition of gamma efferents by stimulation of certain skin areas". J. Neurophysiol. 17, 59-65.

Eldred, E., Lindsley, D.F. & Buchwald, J.S. (1960) "The effect of cooling on mammalian muscle spindles". Exp. Neurol. 2, 144-147.

Ellis, R.S. (1920) "Norms for some structural changes in the human cerebellum from birth to old age". J. Comp. Neurol. 32, 1-33.

Engel, W.K. (1973) in "The control of movement and posture" by Granit, R. & Burk, R. Brain Res. 53, 1-28.

Erb, W. (1875) Berl. klin. Wschr. no. 26. quoted by Sherrington 1906.

Erb, W. (1975) Arch. Psychiat. Nervenkr. V. 792 quoted by Sherrington 1906.

Erlanger, J. & Gasser, H.S. (1937) "Electrical signs of nervous activity", University of Pennsylvania, Philadelphia.

Fatt, P. & Katz, B. (1951) "An analysis of the end plate potential recorded with an intracellular electrode". J. Physiol. (Lond), 115, 320-369.

Fedina, L. & Hultborn, H. (1972) "Facilitation from ipsilateral primary afferents of interneuronal transmission in the Ia inhibitory pathway to motoneurones" Acta physiol. scand. 86 (1), 59-81.

Fleck, H. (1962) "Action potentials from single motor units in human muscle" Arch. phys. Med. Rehab. 43, 99.

Floyd, W.F., Kent, P. & Page, F. (1955) "Electromyographic study of myotonia" EEG. Clin. Neurophysiol. 7, 621-630.

Foreman, R.D. Beall, J.E. Applebaum, A.E., Coulter, J.D. & Willis, W.D. (1976) "Effects of dorsal column stimulation on primate spinothalamic tract neurons". J. Neurophysiol.

Fox, J.L. (1974) "Dorsal column stimulation for relief of intractable pain: problems encountered with neuropacemakers" Surg. Neurol. 2, 59-64 (1974).

Freund, H.J., Wita, C.W. & Srung, C. (1972) "Discharge properties and functional differentiation of single motor units in man" in Neurophysiology studied in man by Somjen (Ed.), 305-313. (Exerpta Medica - Amesterdam).

Freund, H.J., Dietz, V., Wita, C.W. & Kapp (1973) "Discharge characteristics of single motor units in normal subjects and patients with supraspinal motor disturbances" New Develop. EMG. & Clin. Neurophysiol. Desmedt (Ed.), III, 242-250 (Karger-Basel).

Freund, H.J., Budingen, H.J. & Dietz, V. (1975) "Activity of single motor units from human forearm muscles during voluntary isometric contractions". J. Neurophysiol. 38 (4). 933-946.

Frubel-Osipova, S.I. (1969) in "Bases of Gerontology" by Cebotarev, Malkovaski & Fulkis (Eds.), 128 (Meditaina - Moskow).

Fujita, S. & Cooper, I.S. (1971) "Effect of L-Dopa on the H-reflex in parkinsonism". J. Amerc. Geriat. Soc. 19 (4), 289-295.

Garcia-Mullin, R., Mayer, R.F. (1972) "Acute and chromic hemiplegia II H-reflex studies". Brain, 95, 559-572.

Gardner, E. (1940) "Decrease in human neurones with age". Anat. Rec. 77, 529-536.

Gassel, M.M. (1969) "Monosynaptic reflexes (H-reflex) and motoneurone excitability in man" Develop. Med. Child. Neurol. 11 (2), 193-197.

Gassel, M.M. (1970a) "A critical review of evidence concerning long-loop reflexes excited by muscle afferents in man" J. Neurol. Neurosurg. Psychiat. 33, 358-362.

Gassel, M.M. (1970b) "The role of skin areas adjacent to extensor muscles in motoneurone excitability; evidence bearing on the physiology of Babinski response". J. Neurol. Neurosurg. Psychiat. 33, 121-126.

Gassel, M.M. & Ott, K.M. (1970a)"Local sign and late effects on motoneurone excitability of cutaneous stimulation in man". Brain 93, 95-106.

Gassel, M.M. & Ott, K.M. (1970b) "A critical review of evidence concerning long loop reflexes excited by muscle afferents in man". J. Neurol. Neurosung. Psychiat. 33, 358-362.

Gasser, H.S. (1943) "Pain producing impulses in peripheral nerves" Assoc. Res. Nervous Mental Disease 23, 44-62.

Gatz, A., Fudema, J. & Ostery (1960) "A comparative study of muscular dystrophy". Anat. Rec. 136, 196.

Gerilowsky, L. & Tsekov. T.S. (1975) "Preparation of monosynaptic reflex excitability for voluntary movement in man" EEG. Clin. Neurophysiol. 39 (6p), 674.

Gerhandt, B.E. & Shimamura, M. (1961) "Mechanisms of interlimb reflexes in cat". J. Neurophysiol. 24, 665-676.

Gernandt, B.E. & Megirian, D. (1961) "Ascending propriospinal mechanisms". J. Neurophysiol. 24, 364-376.

Geschwind, N.A. & Simpson, J.A. (1955) "Procaine amide in the treatment of myotonia". Brain 78, 81-91.

Gillies, J.D., Burke, D.J. & Lance, J.W. (1971) "The supraspinal control of the tonic vibration reflex". Proc. Aust. Assoc. Neurol. 8, 143-146.

Gillies, D., Lance, J.W., Neilson, P.D. & Tassinari, C.A. (1969) "Presynaptic inhibition of the monosynaptic reflex by vibration" J. physiol. (Lond.) 205, 329-339.

Godaux, E. & Desmedt, J. (1975) "Human masseter muscle: H. and tendon reflexes, their paradoxical potentiation by muscle vibration". Arch. Neurol. 32, 229-234.

Golarz, M.N. & Bourne, G.H. (1963) "The histochemistry of muscular dystrophy" in muscular dystrophy in man and animals" by Bourne and Golarz (Eds.), 89-157 (Karger-Basel).

Goldberger, M.E., Murray, M. (1974) "Restitution of function and collateral sprouting in the cat spinal cord: the deafferentated animal". J. Comp. Neuroo. 158, 37-54.

Goodgold, J. & Eberstein, A. (1972) "Electrodiagnosis of neuro-muscular diseases" Williams & Wilkins, Baltimore.

Gottlieb, G.L., Agarwal, G. & Stark, L. (1970) "Interaction between voluntary and postural mechanism of the human motor system". J. Neurophysiol 33, 365-381.

Gottlieb, G.L., Agarwal, G. (1971) "Effects of initial conditions on the Hoffmann reflex" M. Neurol. Neurosurg & Psychiat. 34, 226-230.

Gottlieb, G.L., Gyan, C. & Agarwal, G.C. (1973a) "Modulation of postural reflexes by voluntary movement. I. Modulation of the active limb." J. Neurol. Neurosurg. Psychiat. 36, 529-539.

Gottlieb, G.L. & Agarwal, G.C. (1973b) "Modulation of postural reflexes by voluntary movement. II Modulation at an inactive joint". J. Neurol. Neurosurg. Psychiat. 36, 540-546.

Gottlieb, G.L. & Agarwal, G.C. (1976) "Extinction of the Hoffmann reflex by antidromic conduction". EEG. Clin. Neurophysiol. 41, 19-24.

Gottlieb, G.L., Agarwal, G. & Stark, L. (1970) "Interactions between voluntary and postural mechanism of the human motor system". J. Neurophysiol. 33, 365-381.

Grant, R.E. (1964) "Massage with ice (cryokinetics) in the treatment of painful conditions of the musculoskeletal system". Arch. Phys. Med. Rehabil. 45, 223-238.

Granit,R. (1950) "Reflex regulation of muscle contraction and autogenetic inhibition". J. Neurophysiol. 13, 351-372.

Granit, R. (1955) "Receptors and sensory perception", Yale University - New Haven.

Granit, R. (1970) "The Basis of Motor control". Academic.

Granit, R. & Lundberg, A. (1947) "Heat and cold sensitive mammalian muscle fibres. Acta physiol. scand. 13 (4), 334-346.

Granit, R. & Henstsch, H.D. (1956) "Gamma control of dynamic properties of muscle spindles". J. Neurophysiol. 19, 356-366.

Granit, R. Henatsch, H.D. & Steg, G. (1956) "Tonic and phasic ventral horn cells differentiated by post-tetanic potentiation in cat extensors". Acta physiol. scand. 37, 114-126.

Granit, R., Kellerth, J.O. & Szumski, A.J. (1966) "Intracellular autogenetic effects of muscular contraction on extensor motoneurones: The silent period". J. physiol. 182, 484-503.

Granit, R. & Burke, R. (1973) "The control of movement and posture" conference report, Brain Res. 53, 1-28.

Grillo, P.J., Yu, H.C. & Patterson, R.H. (1974) "Delayed intraspinal haemorrhage after dorsal column stimulation for pain". Arch. Neurol. 30, 105-106.

Grimby, L. & Hannerz, J. (1968) "Recruitment order of motor units on voluntary contraction changes induced by proprioceptive afferent activity". J. Neurol. Neurosurg. Psychiat. 31, 365-573.

Grimby, L. & Hannerz, J. (1970) "Differences in recruitment order of motor units in phasic and tonic reflex in spinal man". J. Neurol. Neurosurg. Psychiat. 33, 562-570.

Grimby, L. & Hannerz, J. (1973) "Tonic and phasic recruitment order of motor units in man under normal and pathological conditions". New Develop. EMG. Clin. Neurophysiol. Desmedt (Ed.) III, 225-233 (Karger-Basel).

Grimby, L. & Hannerz, J. (1976) "Disturbances in voluntary recruitment order of low and high frequency motor units on blockades of proprioceptive afferent activity". Acta. Physiol. Scand. 96, 207-216.

Growe, A. & Matthews, P.B.C. (1964) "The effects of stimulation of static and dynamic fusimotor fibres on the response to stretching of the primary endings of muscle spindles". J. Physiol. (Lond.) 174, 109-131.

Guihenenc, P. & Ginet, J. (1971) "Hoffmann's reflex significance of the interval between the M and H-responses and value of its measurement". CR. Soc. Biol. (Paris), 165, 1783-1766.

Guihenenc, P. & Ginet, J. (1974) "Study of the Hoffmann's reflex obtained at the level of the quadriceps muscle of normal human subjects" EEG. Clin. Neurophysiol. 36; 225-231.

Guillery, R.W. (1974) in "Essays on the nervous system" by R. Ballairs & E.G. Gray (Eds.) 299, Oxford.

Grillner, S. & Udo, M. (1971) "Recruitment in the tonic stretch reflex". Acta physiol. Scand. 81, 571-573.

Guth, L, Watson, P.K. & Brown, W.C. (1968) "Effects of Cross-reinnervation on some chemical properties of red and white muscles of rat and cat". Exp. Neurol 20, 52-69.

Gutmann, E. (1970) "Nervous & hormonal mechanisms in the ageing process". Exp. Geront. 5, 357-366.

Gutmann, E. (1976) "The multiple regulation of contractile and histochemical properties of cross-striated muscle" in the motor system: Neurophysiology and muscle mechanisms" M. Shahani (Ed.). Elsevier.

Gutmann, E. & Hanzlikova, V. (1965), "Age changes of motor end plates in muscle fibres". Gerontologia 11, 12.

Gutmann, E. & Hanzlikova, V. (1966) "Motor unit in old age", Nature, Lond. 209, 921-922.

Gutmann, E., Hanzlikova, V. & Jakoubek, B. (1968) "Changes in the neuromuscular system during old age". Exp. Geront. 3, 141-146.

Gutmann, E. & Hanzlikova, V. (1972) "Age changes in the neuro-muscular system". Scientechnica - Bristol.

Gutmann, E., Carlson, M.B. (1975) "Contractile and histochemical properties of regenerating cross-transplanted fast and slow muscles in the rat". Pflugers Arch. 353, 227-239.

Gydikov, A. & Kosarov, D. (1972) "Studies on the activity of @-MNs by means of a new electromyocraphic method". In Neurophysiology studied in man". Somjen (Ed.) 321-329. Exerpta medica. Amsterdam.

Haase, J., Cleveland, S. & Ross, H.G. (1975) "Problems of post-synaptic autogenous and recurrent inhibition in the mammalian spinal cord". Rev. Physiol. Biochem. Pharmacol. 73, 73-129.

Hagbarth, K.E. (1952) "Excitation and inhibition of flexor and extensor skin area". Acta physiol. scand. 26, suppl. 94, 1-58.

Hagbarth, K.E. (1960) "Spinal withdrawal reflexes in the human lower limbs". J. Neurol. Neurosurg. Psychiat. 23, 222-227.

Hagbarth, K.E. (1962) "Post tetanic potentiation of myotatic reflexes in man". J. Neurol. Neurosurg. Psychiat. 25, 1-10.

Hagbarth, K.E. (1973) "The effect of muscle vibration in normal man and in patients with motor disorders". New Develop. in EMG. Clin. Neurophysiol., J. Desmedt (Ed.), III, 428-443.

Hagbarth, K.E. & Naess, K. (1950) "The autogenetic inhibition during stretch and contraction of the muscle", Acta physiol. scand. 21, 41-53.

Hagbarth, K.E. & Finner, B.L. (1963) "The pasticity of human withdrawal reflexes to noxious stimuli in lower limbs". Prog. Brain. Res. 1, 65-78.

Hagbarth, K.E & Eklund, G. (1966a) "Tonic vibration reflexes (T.V.R.) in spasticity". Brain. Res. 2, 201-203.

Hagbarth, K. & Eklund, G. (1966b) "Motor effects of vibratory stimuli in man" in Granit Nobel Symposium 1, Muscular afferents and motor control, 177-186 (Almqvist & Wiksell, Stockholm).

Hagbarth, K.E. & Eklund, G. (1968) "The effect of muscle vibration in spasticity rigidity and cerebellar disorders". J. Neurol. Neurosurg. Psychiat. 31, 207-213.

Hakansson, C.H. (1956) "Conduction velocity and amplitude of the action potential as related to circumference in the isolated fibre of frog muscle". Acta physiol. Scand. 37, 14.

Hakansson, C.H. (1957) "Action potentials recorded intra and extracellularly from the isolated frog muscle fibre in Ringer's solution and in air". Acta physiol. Scand. 41, 1.

Hales, S. (1730) as quoted by Sherrington, 1906.

Hall, M. (1833) "On the reflex function of the medulla oblongata and medulla spinalis". Philosophic. Trna. Roy. Soc. Lond. 123, 635.

Hannerz, J. & Grimby, L. (1973) "Recruitment order of motor units in man. Significance of pre-existing state of facilitation". J. Neurosurg. Psychiat. 36, 275-281.

Hanzlikova, V. & Gutmann, E. (1974) "The absence of androgen - sensitivity in the grafted soleus muscle innervated by the pudendal nerve". Cell. Tiss. Res. 145, 121-129.

Hardy, J.D., Wolff, H.G. & Goodell, H. (1940) "Studies on pain. A new method for measuring pain threshold: Observations on the spatial summation of pain". J. Clin. Invest. 19, 649.

Harman, P.J., Tassoni, J.P., Curtis, R.L. & Hollinshead, M.B. (1963) "Muscular dystrophy in mouse" in Muscular Dystrophy in man and animals by Bourne and Golarz (Eds.), 407-456 (Karger-Basel).

Harms, W. (1924) "Morphologische und experimentelle Untersuchungen an alternden Hunden". Zeit. Anat. 71, 319-381.

Harris, J. & Wilson, P. (1971) "Denervation in murine dystrophy". Nature 229, 61-62.

Harris, J., Wallace, C. & Wing, J. (1972) "Myelinated nerve fibre counts in the nerves of normal and dystrophic mouse muscle". J. Neurol. Sci. 15, 245-249.

Hartviksen, K. (1962) "Ice therapy in spasticity". Acta Neurol. Scand. 38/Suppl. 3, 79-84.

Hayden, C. (1964) "Cryokinetics in early treatment program", Med. J. Aust. 2, 612-614.

Hazouri, L.A. & Mueler, A.D. (1950) "Pain threshold studies in paraplegic patients". Arch. Neurol. Psychiat. 64, 607.

Hedenberg, L.A.R.S. (1970) "Functional improvement of the spastic hemiplegic arm after cooling". Scand. J. Rehabil. Med. 2 (4), 154-158.

Henneman, E. (1957) "Relation between size of neurones and their susceptibility to discharge". Science 126, 1345-1347.

Henneman, E. (1974) "Peripheral mechanisms involved in the control of muscle" in Medical Physiology. V. Mountcastle (Ed.) 617-635. (Mosby-Saint Louis).

Henneman, E. & Olson, C.B. (1965) "Relations between structure and function in the design of skeletal muscles". J. Neurophysiol. 28, 581-598.

Henneman, E. Somjen, G. & Carpenter, D.O. (1965a)"Functional significance of cell size in spinal motoneurones". J. Neurophysiol. 28, 560-580.

Henneman, E. Somjen, G. & Carpenter, D. O. (1965b) "Excitability and inhibability of motoneurones of different sizes". J. Neurophysiol. 28, 599-620.

Henneman, E. Clamann, H.P., Gillies, J.D. &Skinner, R.D. (1974) "Rank order of motoneurones within a pool: Law of combination." J. Neurophysiol. 37, 1338-1349.

Hensel, H. & Bowman, K.K. (1960) "Afferent impulses in cutaneous sensory nerves in human subjects". J. Neurophysiol. 23, 564-578.

Hermian, R. & Byck, R. (1964) "Differential peripheral nerve blockade by procaine and local cold". Clin. Pharmacol. Ther. 5-6 part 2: 848-851.

Hess, A. (1961) "The structure of slow and fast extrafusal muscle fibres in the extra occulor muscles and their nerve endings in guinea pigs." J. Cell. Comp. Physiol. 58, 63-79.

Hodes, R. (1953) "The innervation of skeletal muscles". A Rev. Physiol. 15, 139-164.

Hodes, R. Gribetz, I. (1962) "H-reflexes in normal human infants: Depression of these electrically induced reflexes (EIRs) in sleep". Proc. Soc. exp. Biol. Med. 110, 577-580.

Hodge, C.F. (1894) "Changes in ganglion cells from birth to senile death. Observations on man and honey-bee". J. Physiol. (Lond.) 17, 129.

Hoffmann, P. (1918) "Uber die Beziehungen der Sehnenreflexe zur Willkurlichen Bewegung and zum Tonus". Z. Biol. 68, 351-570.

Hoffmann, P. (1919) "Uber die relative unermudbarkeit der Sehnen reflexe". Z. Biol. 69, 517-528.

Hoffmann, P. (1920) "Uber die Beziehungen der Hautreflexe zu den Sehnenreflexen". Z. Biol. 73, 101-106.

Hoffmann, P. (1920) "Versuche uber Bahnung und Hemmung im menschlichen Ruckenmark". Med. Kinik 16, 677-678.

Hoffmann, P. (1920b) "Demonstration cines Hemmungsreflexes in meschlichen Ruckenmark". Z. Biol. 70, 515.

Hoffmann, P. (1922) "Untersuchungen uber die Eigenreflexe (Sehnenreflexe) Menschlichen Muskeln." Berlin: Springer.

Hoffmann, P. (1924) "Untersuchungen uber die refraktare Periode des menschlichen Ruckenmarkes." Z. Biol. 81, 37.

Holmgren B., Merton, P.A. (1954) "Local feedback control of motoneurones". J. Physiol. 123, 47-48p.

Hongo, T., Jankowska, E. & Lundberg, A. (1969) "The subrospinal tract. I. Effects on -motoneurones innervating hindlimb muscles in cats". Exp. Brain Res. 7, 344-364.

Hongo, T., Jankowsa, E, & Lundberg, A. (1969b) "The rubrospinal tract II facilitation of interneuronal transmission in reflex paths to motoneurones". Exp. Brain Res. 7, 365-391.

Horvath, B. & Proctor, J.B. (1960) "Muscular dystrophy. Quantitative studies on the composition of dystrophic muscle". Res. Pub. Ass. nerv. ment. Dis. 38, 740-766.

Houke, J.C., Singer, J.J, & Goldman, M.R. (1970) "An evaluation of length and force feedback to soleus muscles of decerebrate cats". J. Neurophysiol. 33, 784-811.

Howland, B., Lettvin, J.Y., McCulloch, W.S., Pitts, W.H. & Wall, P.D. (1955) "Reflex inhibition by dorsal root interaction". J. Neurophysiol. 18, 1-7.

Hugon, M. (1973) "Methodology of the Hoffmann reflex in man". New Develop. in EMG. Clin. Neurophysiol. J. Desmedt (Ed.), III, 277-293. (Karger-Basel).

Hultborn, H. (1972) "Convergence on interneurones in the reciptorcal Ia inhibitory pathway to motoneurones". Acta physiol. Scand. Suppl. 375, 5-42.

Hultborn, H. & Udo, M. (1972) "Convergence of large muscle spindle (Ia) afferents of interneuronal level in the reciprocal Ia inhibitory pathway to motoneurones". Acta Physiol. Scand. 84 (4), 493-499.

Hunt, C.C. (1952) "The effect of stretch receptors from muscles on the discharge of motoneurones". J. Physiol. 117, 359-379.

Hufschmidt, H.J. (1960) "Wird die silent Period nach direckter Musckelreizung durch Golgi-Sehenorgane ausgelost?" Pflugers Arch 271, 35-39.

Hufschmidt, H.J. (1961) "Bausteine motorischen Regelung Schweiz". Arch. Neurol. Psychiat 87, 260-280.

Hufschmidt, H.J. (1962) "Golgi-sehnenorgane und spinale Koordination der Motorik beim Karninchen." Pflugers Arch. 275, 121-133.

Hufschmidt, H.J. (1966) "The demonstration of autogenic inhibition and its significance in human voluntary movement". In "Muscular afferent and motor control" Nobel Symposium I, 269-274. Granit (Ed.). Stockholm. Almquist and Wiksell.

Illis, L.S. (1964) "Spinal cord synapses in the cat: The reactions of the Boutons Termineaux at the motoneurona surface to experimental denervation." Brain 87, 555.

Illis, L.S. (1967a) "The relative densities of monosynaptic pathways to the cell bodies and dendrites of the cat ventral horn". J. Neurol. Sci. 4, 259-270.

Illis, L.S. (1967b) "The motor neuron surface and spinal shock" in Modern trends in Neurology". D. Williams (Ed.), 4, Butterworths.

Illis, L.S. (1969) "Enlargement of spinal cord synapses after repetitive stimulation of a single posterior root". Nature 223, 76-77.

Illis, L.S. (1973a) "Regeneration in the CNS" Lancet, 1035-1037.

Illis, L.S. (1973b) "Experimental model of regeneration in the CNS". I Synaptic change". Brain 96: 47-60.

Illis, L.S. (1973c) "Experimental model of regeneration in the CNS. II. The reaction of glia in the synaptic zone". Brain 96, 61-68.

Illis, L.S., Patangia, G.N. & Cavanagh, J.B. (1966) "Boutons termineaux and tri-orth. cresyl phosphate neurotoxicity". Exp. Neurol. 14, 160-174.

Illis, L.S., Mitchell, J. (1970) "The effect of tetanus toxin on Boutons terminaux". Brain Res. 18, 283-295.

Illis, L.S., Taylor, F.M. (1971) "Neurological and electroencephalographic sequalae of tetanus". Lancet, 826-830.

Illis, L.S. Oygar, A.E. Sedgwick, E.M. & Sabbahi, Awadalla,M.A. (1976) "Dorsal-column stimulation in the rehabilitation of patients with multiple sclerosis". The Lancet, 17973, 1383-1386.

Ioko, M. Ogawa, M. & Jinnai, D. (1971) "Studies on facilitation of the H-reflex in spasticity and rigidity" Electronmyography 11, 11-23.

Isaacs, E.R., Szunski, A.J. & Suter, C. (1968) "Central and peripheral influence on the H-reflex in normal man". Neurol. (Minn.) 18, 907-914.

Jabbur, S.J. & Banna, N.R. (1968) "Presynaptic inhibition of cuneate transmissions by widespread cutaneous inputs". Brain Res. 10, 273-276.

Jabbur, S.J. & Banna, N.R. (1970) "Widespread cutaneous inhibition in dorsal column nuclei". J. Neurophysiol. 33, 616-624.

Jackson, J.H. (1958) Selected writings: Vols. I & II, Taylor, J. (Ed.), Staples - London.

Jack, J.J.B., Miller, S., Porter, R. & Redman, S.J. (1970) "The distribution of group Ia synapses on lumbosacral spinal MNs in the cat." in Andersen & Jansen. "Excitatory synaptic mechanisms", 199-205 (Universitetsforlaget - Oslo).

Jack, J.J.B., Miller, S., Porter, R. & Redman, S.J. (1971) "The time course of minimal excitatory post-synapstic potentials evoked in spinal MNs by group Ia afferent fibres". J. Physiol. 215, 353-380.

Jankowska, E. & Smith, D.O. (1973) "Antidromic activiation of Renshaw cells and their axonal projections" Acta Physiol. Scand. 88, 198-214.

Jasper, H. & Ballem, G. (1949) "Unipolar electromyograms of normal and denervated human muscle". J. Neurophysiol. 12, 231.

Johnson, M.A. Polgar, J. Weightman, D. & Appleton, O. (1973) "Data on the distribution of fibre types in thirty-six human muscles - An autopsy study". J. Neurol. Sci. 18, 111-129.

Johnson, K.O., Darian-Smith, I., & Lamotte, C. (1973) "Peripheral neural determinants of temperature discrimination in man: a correlative study of responses to cooling skin". J. Neurophysiol. 36, 347.

Jolly, W.A. (1911) "On the time relations of the knee-jerk and simple reflexes". Q. Jl. exp. Phsyiol. 4, 67-87.

Jones, R., Vrbova, G. (1971) "Can denervation hypersensitivity be prevented". J. physiol. 217, 67-75.

Kato, M. & Tanji, J. (1972) "Conscious control of motor units of human finger muscles" in "Neurophysiology studied in man" Somjen (Ed.) 330-342 exerpta medica. Amesterdam.

Katz, B. & Thesleff, S. (1957) "On the factors which determine the amplitude of the miniature end-plate potential". J. physiol. (Lond.) 137, 267.

Kendutsch, A.A. & Russell, A.E. (1958) "Creative and creatinive in tissues and urine of mice with hereditary muscular dystrophy" Amer. J. physiol. 194, 553-556.

Kernell, D. (1965) "The limits of firing frequency in cat lumbo-sacral motoneurones possessing different time course of after hyperpolarization". Acta physiol. Scand. 65, 87-100.

Kernell, D. (1966) "Input resistance, electrical excitability and size of ventral horn cells in the cat spinal cord". Science 152, 1637-1640.

Kleeman, F.J. Partridge, L.D. & Glaser, G.H. (1961) "Resting potential and muscle fibre size in mouse muscular dystrophy". Amer. J. Phys. Med. 40, 183.

Knutsson, E. & Mattsson, E. (1969) "Effects of local cooling on monosynaptic reflexes in man". Scand. J. Rehabil. Med. 1 (313) 126-132.

Knutsson, E. (1970) "On effects of local cooling upon motor functions in spastic Paresis". Prog. phys. Ther. 1, 124-131.

Knuttson, E. (1971) "Tropical cryotherapy in spasticity" Scand. J. Rehabil. Med. 2 (4), 159-163.

Koketsu, K. (1956) "Intracellular potential changes of primary afferent nerve fibres in spinal cords of cats". J. Neurophysiol. 19, 375-392.

Korr, I.M., Wilkinson, P.N. & Chornock, F.W. (1967) "Axonal delivery of neuroplasmic components to muscle cells". Science 155, 342-345.

Krassoivitch, M.M. Delwaide, P.J. & Hugon, M. (1972) "Modification of the Hoffmann reflex by stretching. Control of soleus muscle" EEG. Clin. Neurophysio. 32 (5), 465-470.

Krott, H.M. & Jacobi, H.M. (1972) "Neurophysiological investigations of the disturbances of monosynaptic reflexes in Adie's Syndrome". Arch. Psychiat. Nervenker 215 (4) 338-361.

Kugelberg, E. & Edstrom, L. (1968) "Differential histochemical effects of muscle contractions on phosphorylase and glycogen in various types of fibres: relation to fatigue". J. Neurol. neurosurg. Psychiat. 31, 415-423.

Kuno, (1959) "Excitability following antidromic activation in spinal motoneurones supplying red muscles". J. Physiol. 149, 374-393.

Kuno, M. & Miyahara, J.T. (1969) "Analysis of synaptic efficacy in spinal motoneurones from quantum aspects". J. Physiol. 201, 479-493.

Lahouda, F. (1972) "Simultaneous registration of temperature and action potentials in human skeletal muscles". Biomed. Tech. 17 (2), 70-73.

Laitinen, L.V. (1970) "Effects of thalamic stimulation and thalamotomy on the H-reflex" EEG. Clin. Neurophysiol. 28, 586-591.

Laitinen, L.V. & Ohno, Y. "H-reflex in parkinsonism". Confin. Neurol. 32, 88-92.

Lanari, A. (1946) "Mechanism of myotonic contraction" Science 104, 221.

Lance, J.W. (1965) "The mechanism of reflex irradiation". Proc. Austr. Ass. Neurol. 3, 77-82.

Lance, J.W., De Grail P., & Neilson, P.D. (1966) "Tonic & phasic spinal cord mechanisms in man". J. Neurol. Neurosurg. Psychiat. 29, 535-544.

Lance, J.W., Neilson, P.D. & Tassimari, C.A. (1968) "Suppression of the H-reflex by peripheral vibration". Proc. Austr. Assoc. Neurol. 5, 45-49.

Lance, J.W., Burke, D. & Andrews, C.J. (1973) "The reflex effects of muscle vibration. Studies of tendon jerk irradiation, Phasic reflex inhibition, and the tonic vibration reflex". New Develop. in EMG. Clin. Neurophysiol, J. Desmedt (Ed.), III, 444-462 (Karger-Basel).

Lance, J.W., McLeod, J.G. (1975) "The tendon jerk and other spinal reflexes" in "A physiological approach to clinical neurology" Lance & McLeod (Eds.) 3, 81-102 (Butterworth).

Landau, W.M. (1951) "Comparison of different needle leads in EMG recording from a single site" EEG Clin. Neurophysiol. 3, 163.

Landau, W.M. (1952) "The essential mechanism in myotonia", Neurol. (Minn.), 2, 369-388.

Landau, W.M. & Clare, M.H. (1964a) "Fusimotor function. IV Reinforcement of the H-reflex in normal subjects". Arch. Neurol. (Chic.) 10, 117-23.

Landau, W.M. & Clare, M.H. (1964b) "Fusimotor function VI Reflex tendon jerk and reinforcement in hemiplegia". Arch. Neurol. (Chic.) 10, 128-134.

Languth, H.W., Teasdall, R.D. & Magladery, J.W. (1952) "Electrophysiological studies of nerve and reflex activity in patients with lesion of nervous system. III. Motoneurone excitability following afferent nerve volleys in patients with rostrally adjacent spinal cord damage". Bull. J. Hopk. Hosp. 91, 257-266.

Laporte, Y. & Lloyd, D.P.C. (1952) "Nature and significance of the reflex connections established by large afferent fibres of muscular origin. Am. J. physiol. 169, 609-621.

Lapriesle, J. & Milhaud, M. (1964) "Pathologie du fuseau neuro-musculaire". Revue neurol. 110, 97-122.

Larson, S.J., Sancas, A.J.R., Riegel, D.H. Meyer, G.A., Dallmann, D.E. & Swiontek, T. (1974) "Neurophysiological effect of dorsal column stimulation in man and monkey". J. Neurosurg. 41, 217-223.

Lashley, K.S. (1938) "Factors limiting recovery after central nervous lesions". J. nerv. ment. Des. 88, 733.

Lele, P.P., & Wedell, G. (1956) "The relation between neurohistology and corneal sensibility". Brain 79, 119-154.

Lennman, J.A.R. (1963) "Microelectrode studies in muscle disease" in Research in muscular dystrophy, 230-239 (Pitman Medical - London).

Lidell, E.G.T. (1934) "Spinal shock and some features in isolation - alteration of the spinal cord in cats". Brain 57, 386.

Lipicky, R.J. & Bryant, S.H. (1973) "A biophysical study of the human myotonias". New Develop. EMG. Clin. Neurophysiol. J. Desmedt (Ed.), I, 451-463 (Karger-Basel).

Lippold, O.C.J., Redfearn, J.W.T. & Vuco, J. (1957) "The rhythmical activity of groups of motor units in the voluntary contraction of muscle". J. physiol. 137, 473.

Lippold, O.C., Nichollis, J. & Redfearn, J.W.T. (1960) "A study of the afferent discharge produced by cooling mammalian muscle spindle". J. physiol. 153, 218-231.

Lloyd, D.P.C. (1941) "A direct central inhibitory action of dromically conducted impulses". J. Neurophysiol. 4, 184-190.

Lloyd, D.P.C. (1943a)"Reflex action in relation to pattern and peripheral source of afferent stimulation.". J. Neurophysiol. 6, 111-120.

Lloyd, D.P.C. (1943b) "Neuron patterns controlling transmission of ipsilateral hindlimb reflexes in cat". J. Neurophysiol. 6, 293-315.

Lloyd, D.P.C. (1946a)"Integrative pattern of excitation and inhibition in two neurones reflex arcs". J. Neurophysiol. 9, 439-444.

Lloyd, D.P.C. (1946b) "Facilitation and inhibition of spinal motoneurones". J. Neurophysiol. 9, 421-438.

Lloyd, D.P.C. (1949) "Posttetanic potentiation of response in monosynaptic reflex pathways of spinal cord". J. Gen. physiol. 33, 147-170.

Lloyd, D.P.C. (1951) "After currents, after potentials, excitability and ventral root electrotonus in spinal motoneurones". J. Gen. Physiol. 35, 289-321.

Lloyd, D.P.C. (1956) "Monosynaptic reflex response of individual motoneurones as a function of frequency". J. Gen. Physiol. 40, 435-450.

Lloyd, D.P.C. (1959) "Early and late post-tetanic potentiation and post tetanic block in a monosynaptic reflex pathway. J. Gen. Physiol. 42, 475-488.

Lomo, T. & Rosenthal, J. (1972) "Control of Arch Sensitivity of muscle in the rat". J. Physiol. 221, 493-513.

Long, D.L. (1973) "Electrical stimulation for relief of pain from chronic nerve injury". J. Neurosurg. 39, 718-722.

Lorente De No'r (1935) "The synaptic delay of the motoneurones". Am J. physiol. 111, 272-282.

Lorente de No, R. (1938) "Limits of variation of the synaptic delay of motoneurones". J. Neurophysiol. 1: 187-194.

Lorente de No, R. (1947) "A study of nerve physiology. Studies from the Rockefeller Institute, Vol. 132, Ch. 16.

Lowdon, B.J., Moore, R.J. (1975) "Determinants and nature of intramuscular temperature changes during cold therapy". Amer. J. phys. Med. 54 (5), 223-233.

Ludin, H.P. (1970) "Microelectrode study of normal human skeletal muscle". Europ. Neurol. 3, 116-121.

Ludin, H.P. (1973) "Action potential of normal and dystrophic human muscle fibres. New Develop. EMG. Clin. Neurophysiol. Desmedt (Ed.), I, 400-406 (Karger-Basel).

McComas, A.J. & Mossaway, S.J. (1965a)"Electrophysiological investigation of normal and dystrophic muscles in mide" in Research in muscular dystrophy. Proceeding of the 3rd symposium of the muscular dystrophy group, 317-342. (London).

McComas, A.J. & Mossaway, S.J. (1965b) "Electrophysiological studies on muscle fibres in dystrophic mice". J. physiol. (Lond.) 177, 69.

McComas, A. & Payan, J. (1967) "Motoneurone excitability in the Holmes-Adie syndrome" in Control & Innervation of skeletal muscles, by Andrew (Ed.), 182-195, London, Livingstone.

McComas, A.J. & Mrozek, K. (1967) "Denervated muscle fibres in hereditary mouse dystrophy". J. Neurol. Neurosurg. Psychiat. 30, 526-530.

McComas, A.J., Sica, R.E.P. & Curries (1970) "Muscular dystrophy evidence for a neural factor". Nature 226, 1263-1264.

McComas, A.J. & Sica, R.E.P. (1970) "Muscular dystrophy: Myopathy or neuropathy?". Lancet 1, 1119.

McComas, A., Sica, R.E.P., Campbell, J.J. (1971) "Sick motoneurones - a unifying concept of muscle disease". Lancet I, 321-325.

McComas, A.J., Campbell, M.J. & Sica, R.E.P. (1971) "Electrophysiological study of dystrophia myotonica". J. Neurosurg. Psychiat. 34, 132-139.

McDonald, W.I. (1974) "Pathophysiology in multiple sclerosis". Brain, 97, 179-196.

McIntyre, A.R. Bennett, A.L. & Brodkey, J.S. (1959) "Muscle dystrophy in mice of the Bar Harbor strain". Arch. Neurol. Psychiat. (Chic.) 81, 678-683.

McLeod, J.G. & Van der Meulen, J.P. (1967) "Effect of cerebellar ablation on the H-reflex in the cat". Arch. Neurol. (Chic.) 16, 421-432.

McLeod, J.G. (1969) "H-reflex studies in patients with cerebellar disorders". J. Neurol. Neurosurg. Psychiat. 32, 21-27.

McPhedran, A.M. Wuerker, R.B. & Henneman, E. (1965) "Properties of motor units in homogeneous red muscle (soleus) of the cat". J. Neurophysiol. 28, 71-84.

MacDermot, V. (1961) "The histology of neuromuscular junction in dystrophia myotonica", Brain 84, 75-84.

Magladery, J.W. (1955) "Some observations on spinal reflexes in man". Pflugers Archiv. 261, 302-321.

Magladery, J.W. (1959) "Neurophysiology of Ageing in Handbook of ageing and individual" by Birren, J.E. (Ed.) 173 (University of Chicago, Chicago).

Magladery, J.W. & McDougal, D.B. (1950) "Electrophysiological studies of nerve and reflex activity in normal man. I. Identification of certain reflexes in EMG and the conduction velocity of peripheral nerve fibres". Bull, J. Hopk. Hosp. 86, 265.

Magladery, J.W., McDougal, D.B. & Stoll, J. (1950) Electrophysiological studies of nerve and reflex activity in normal man. II The effect of peripheral ischaemia". Bull. J. Hopk. Hosp. 86, 291-312.

Magladery, J.W., McDougal, D.B. & Stoll, J. (1950). Electrophysiological studies of nerve and reflex activity in normal man. III The post ischaemic state". Bull, J. Hopk. Hosp. 86, 313-340.

Magladery, J.W., Porter, W.E., Park, A.M. & Teasdall, R.D. (1951). Electrophysiological studies of nerve and reflex activity in normal man IV The two neurone reflex and identification of certain action potential from spinal roots and cord". Bull J. Hopk. Hosp. 88, 499-519.

Magladery, J.W., Teasdall, R.D., Park, A.M. & Porter, W.E. (1951) "Electrophysiological studies of nerve and reflex activity in normal man. V Excitation and inhibition of two neurone reflexes by afferent impulses in the same nerve trunk". Bull J. Hopk. Hosp. 88, 520-537.

Magladery, J., Teasdall, R.D., Park, A.M. & Languth, H.W. (1952) Electrophysiological studies of reflex activity in patients with lesions of the nervous system. I. A comparison of spinal motoneurone excitability following afferent nerve volleys in normal persons and patients with upper motor neurone lesions." Bull. J. Hopk. Hosp. 91, 219-244.

Magladery, J.W. & Teasdall, R.D. (1958) "Effects of age on planter flexor and superficial abdominal reflexes in man". J. Gerontol. 13 (3), 282-288.

Manikal, M.D. & Simpson, J.A. (1973) "Evaluation of spinal inhibitory activity in epilepsy by the H-wave recovery curve". Epilepsia 14, 311-321.

Mark, R.F. & Coquery, J.M. & Paillard, J. (1968) "Autogenetic effects of slow or steady stretch of the calf muscles in man". Exp. Brain. Res. 6, 130-145.

Marsden, C.D., Merton, P.A., & Morton, H.B. (1971) "Servoaction and stretch reflex in human muscles and its apparent dependence on peripheral sensation". J. physiol. 216, 21-22p.

Marsden, C.D., Merton, P.A. & Morton, H.B. (1972) "Servo action in human voluntary muscle". Nature 238, 140-143.

Masland, W.S. & Ariz,T.(1972)"Facilitation during the H-reflex recovery cycle". Arch. Neurol. (Chic.) 26 (4), 313-319.

Matsuoka, S., Waltz, J.M., Terada, C., Ikeda, T. & Cooper, I.S. (1966). "A computer technique for evaluation of recovery cycle of the H-reflex in the abnormal movement disorders". EEG. Clin. Neurophysiol. 21, 496-500 (1966).

Matthews, P.H.C. (1933) "Nerve endings in mammalian muscles". J. physiol. (Lond.) 78, 1-53.

Matthews, B.H.C. (1934) "Impulses leaving the spinal cord by dorsal roots". J. Physiol. 81, 29-31.

Matthews, P.B.C. (1966a) "Reflex activation of the soleus muscle of the decerebrate cat by vibration". Nature, Lond., 209, 204-205.

Matthews, P.B.C. (1966b)"The reflex excitation of the soleus muscle of the decerebrate cat caused by vibration applied to its tendon". J. Physiol. (Lond.) 184, 450-472.

Matthews, P.B.C. (1972) "Mammalian muscle receptors and their central actions". Edward Arnold.

Matthews, W.B. (1970) "The clinical implications of the H-reflex and other electrically induced reflexes" in Modern Trends of Neurology by D. Williams (Ed.), 5, 241-253 (Butterworths).

Mayer, R.F. & Mawdsley, C. (1965a) "Studies in man and cat of the significance of the H-wave". J.Neurol. Neurosurg. Psychiat. 28, 201-211.

Mayer, R.F. & Mawdsley, C. (1965b) "Parameters of the H-reflex in pathological status". 6th International Congress of EEG. Clin. Neurophysiol. 635-638.

Mayer, R.F. & Mosser, R.S. (1973) "Maturation of human reflexes". New Develop. EMG. Clin. Neurophysiol. J. Desmedt (Ed.). III 294-307 (Karger-Basel).

Mecomber, S. & Herman, R.M. (1971) "Effects of local hypothermia of reflex and voluntary activity" 51 (3), 271-282.

Melzack, M. (1973) "The puzzle of pain" Harmondsworth, England, Penguin Education.

Melzack, M. & Wall, P.D. (1962) "On the nature of cutaneous sensory mechanisms". Brain 85, 331-356.

Melzack, M. & Wall, P.D. (1965) "Pain mechanisms: a new theory" Science, New York, 150, 971-979.

Mendell, L. & Wall, P.D. (1964) "Presynaptic hyperpolarization: a role for fine afferent fibres". J. Physiol. 172, 274-294.

Mendell, L.M. & Henneman, E. (1971) "Terminals of single Ia fibres: location density and distribution within a pool of 300 homony-mouse motoneurones". J. Neurophysiol. 34, 171-187.

Merrill, E.G., Wall, P.D. (1972) "Factors forming the edge of a receptive field: the presence of relatively ineffective afferent terminals". J. Physiol. 226, 825-846.

Merton, P. (1953) "Speculations on the servo-control of movement, in Malcolm, Gray & Wolstenholme. The spinal cord, Ciba Foundation Symposium, London, 247-260. Churchill - London.

Messina, C. & Cotrufo, R. (1976) "Different excitability of type I and type II @-motoneurones". J. Neurol. Sci. 28, 57-63.

Meulen, V-Der (1973) in "The control of movement and posture" by Granit, R. & Burk, R. Brain. Res. 53, 1-28.

Michelson, A.M., Russell, E.S. & Harman, P.J. (1955) "Dystrophia muscularis: a hereditary primary myopathy in the house mouse". Proc. the Acad. Sci. 41, 1079-1084.

Miglietta, O. (1971) "Spinal motoneurone excitability in normal subjects and hemiplegic patients". Arch. Phys. Med. Rehabil. 51, 696-670.

Miglietta, O. E. (1962) "Evaluation of cold in spasticity". Amer. J. phs. Med. 41, 148-151.

Miledi, R. (1960) "Properties of regenerating neuromuscular synapses in the frog". J. physiol. 154, 190-205.

Milner Brown,H.S., Stein, R.B., & Yemm, R. (1973) "The orderly recruitment of human motor units during voluntary isometric contractions". J. physiol. 230, 329-370.

Milner-Brown, H.S., Stein, R.B. & Lee, R.G. (1975) "Synchronization of human motor units; possible roles of exercise and supraspinal reflexes". EEG. Clin. Neurophysiol. 38, 245-254.

Mizuno, Y., Tanaka, R., Yanagisawa, N. (1971) "Reciprocal group I inhibition on triceps surae motoneurone in man". J. Neurophysiol. 34, 1010-1017.

Monakow, C. von (1902) quoted by Sherrington 1906.

Mongia, S.K. (1972a) "H-reflex from quadriceps and gastrocnemius muscles". EMG. Clin. Neurophysiol. 12, 179-190.

Mongia, S.K. (1972b) "Significance of certain evoked responses in cases of neurogenic disorders". EMG. Clin. Neurophysiol. 12, 191-211.

Mountcastle, V.B. (1974) "Medical physiology". Mosby (Saint Louis).

Mountcastle, V.B., Talbot, W.H. & Kornhuber, H.H. (1966) "The neural transformation of mechanical stimuli delivered to the monkey's hand. In de Reuck, A.V.S. & Knight, J. (Eds.), Ciba Foundation Symposium on touch, heat and pain, London, J. & A. Churchill.

Moyer, E.K. & Kalyszewski, B.F. (1958) "The number of nerve fibres in motor spinal nerve roots of young, mature and aged cats". Anat. Rec. 131, 681-700.

Murakami, M. (1971) "Evoked electromyogram (M and H waves) in rats with special reference to the characteristics and time analysis of the H-wave in relation to the distribution in nerve fibres in rats" Nippon IKa Daigaku Zasshi 38, 1-8.

Nachmias, V.T. & Padykula, H.A. (1958) "A histochemical study of normal and denervated red and white muscles of the rat". J. biophys. biochem. cytol. 4, 47-54.

Nashold, B.S. Jr. & Friedman, H. (1972) "Dorsal column stimulation for control of pain. Preliminary report on 30 patients" J. Neurosurg. 36, 590-597.

Nathan, P. (1976) "The Gate-Control Theory of pain: A critical review" Brain 99, 123-158.

Nielson, K.D., Watts, C. & Clark, W.K. (1976) "Peripheral nerve injury from implantation of chronic stimulating electrodes for pain control". J. Surg. Neurol, 4, 51-53.

Nielson, K.D., Adams, J.E. & Hosobuchi, Y. (1975) "Experience with dorsal column stimulation for relief of chronic intractable pain, 1969-1973", Surg. Neurol. 4, 148-152.

Norris, F.H. (1962) "Unstable membrane potential in human myotonic muscle". EEG. Clin. Neurophysiol. 14, 197-201.

Norris, A.H., Shock, N.W. & Wagman, I.H. (1955) "Age changes in the maximum conduction velocity of motor fibres of human ulner nerves". J. appl. physiol. 5, 589-593.

Novikova, V.P. (1970) "A comparative analysis of H and M responses and of general muscular electrogenesis in spasticity". Electromyography 10 (2), 145-152.

O'Leary, J.L. (1956) "Speculative trends in electrophysiology. Lessons in humanity derived from a survey of our historic continuity with the past". A.M.A. Arch. Neurol. Psychiat. 76, 187.

Ogata, T. & Mori, M. (1964) "Histochemical study of oxidative enzymes in vertebrate muscles". J. histochem. cytochem. 12. 171-182.

Olsen, Z. P. & Diamantopoulos, E. (1967) "Excitability of spinal motor neurones in normal subjects and patients with spasticity, Parkinsonian rigidity and cerebellar hypotonia". J. Neurol. Neurosurg. Psychiat. 30. 325-331.

Olsen, C.B. Carpenter, D.O. & Henneman, E. (1968) "Order recruitment of muscle action potentials". Arch. Neurol. (Chic.) 19, 591-597.

Ovsyanikov, A.V. (1972) "Motor present state in humans during motor immersion." Fiziol. Zh. SSSR IM IM Sechenova 58 (3), 303-310.

Paillard, J. (1955) "Reflexes et regulations d'origin proprioceptive Chez 1'homme-Etudes neurophysiologique" (Arnette, Paris).

Paillard, J. (1955b) "Reflexes et regulations d'origine proprioceptive chez le'homme Etude Neurophysiologique et psychophysiologique. Librairie Arnette: Paris.

Papakostopoulos, D., Cooper, R. Cumins, B. & Winter, A. (1976) "Evoked and intrinsic activities in the cerebellum of conscious man". EEG. Clin. Neurophysiol. EEG Clin. Neurophysiol 41, 537.

Papapetropoulos, T.A. & Bradey, W.G. (1972) "Spinal motor neurones in murine muscular dystrophy and spinal muscular atrophy". J. Neurol. Neurosurg. Psychiat. 35, 60-65.

Park, A.M., Teasdall, R.D. & Magladery, J.W. (1951) "Electrophysiological studies of nerve and reflex activity in normal man VIII. Certain effects of brief stretch". Bull. J. Hopk. Hosp. 88, 549-561.

Patel, A.N., Lalitha, V.S. & Dastur, D.K. (1968) "The spindle in normal and pathological muscle". Brain 91, 737-750.

Petajan, J. & Watts, N. (1962) "Effect of cooling on the triceps surae reflex" Amer. J. phys. Med. 51, 240-251.

Peterson, I. & Kugelberg, E. (1949) "Duration and form of action potential in the normal human muscle". J. Neurol. Neurosurg. Psychiat. 12, 124-128.

Pierrot-Deseilligny, E. (1966) "Etude par la reflexe monosynaptique (reflex H) de certains mecanismes dans la regulation tonique posturale normale et pathologique". These med. Paris.

Pierrot-Deseilligny, E. Lacert, P. & Cathala, P. (1971) "Monosynaptic reflexes amplitude and variability before voluntary movement". Physiol. Rev. 7 (4), 495-508.

Pierrot-Deseilligny, E., Lacert, P. (1973a)"Amplitude and variability of monosynaptic reflexes prior to various voluntary movement in normal and spastic man". New Develop. in EMG. Clin. Neurophysiol. J. Desmedt (Ed.), III, 538-549. (Karger-Basel).

Pierrot-Deseilligny, E., Bussel, B. & Morin, C. (1973b) "Supraspinal control of the changes induced in H-reflex by cutaneous stimulation, as studied in normal and spastic man". New Develop. in EMG. Clin. Neurophysiol. J. Desmedt (Ed.) III, 550-555. (Karger-Basel).

Pierrot-Deseilligny, E., Bussel, B., Sideri, G., Cathela, H.P. & Castaigne, P. (1973c) "Effect of voluntary contraction on H-reflex changes induced by cutaneous stimuli in normal man" EEG. Clin. Neurophysiol. 34, 185-92.

Pierrot-Deseilligny, E., Bussel, B., Held, J.P., & Katz, R. (1976) "Excitability of human motoneurones after discharge in a conditioning reflex". EEG. Clin. Neurophysiol 40, 279-287.

Porter, R. & Horse, J. (1969) "Time course of minimal cortico-motoneuronal excitatory post-synaptic potentials in lumber MNs of the monkey". J. Neurophysiol. 32, 443-451.

Prestige, M.C. (1966) "Initial collaterals of motor axons within the spinal cord of the cat". J. Comp. Neurol. 126, 123-136.

Preston, J.B. & Whitlock, D.G. (1963) "A comparison of motor cortex effects on slow and fast muscle innervations in the monkey". Exp. Neurol. 7, 327-341.

Pruzanski, W. (1966) "Variants of myotonic dystrophy in pre-adolescent life (the syndrome of myotonic dysembyroplasia)." Brain 89, 563.

Coquery, J.M. (1962) "Les variations 'spontanees' du Reflexe de Hoffmann". Doctorat these - Universite d'Aix - Marseille.

Ragab, A.H.M.F. (1971) "Motor end plate changes in mouse muscular dystrophy". Lancet 2, 815.

Raisman, G. (1969) "Neuronal plasticity in the spatial nuclei of the adult rat". Brain Res. 14, 25-48.

Rall, W., Burke, R.E., Smith, T.G. Nelson, P.G. & Frank, K. (1967) "Dendrite location of synapses and possible mechanisms for the monosynaptic EPSP inMNs". J. Neurophysiol 30, 1169-1193.

Refsum, S. Engeset, A. & Lonnum, A. (1959) "Pneumoencephalographaic changes in dystrophia myotonica". Acta psychiat. Neurol. Scand. Suppl. 137, 34, 98.

Refsum, S. Lonnum, A. Sjaastad, O. & Engeset, A. (1967) "Dystrophia myotonica repeated pneumoencephalographic studies in ten patients" Neurol. (Minn) 17, 345-348.

Renshaw, B. (1940) "Activity in the simplest spinal reflex pathways". J. Neurophysiol. 3: 373.

Renshaw, B. (1941) "Influence of discharge of motoneurones upon excitation of neighbouring motoneurones". J. Neurophysiol. 4, 167-183.

Renshaw, B. (1946) "Central effects of centripetal impulses in axons of spinal ventral roots". J. Neurophysiol 9, 191-204.

Rexed, B. (1944) "Contributions to knowledge of postnatal development of peripheral nervous system in man; study bases and scope of systematic investigations into fibre size in peripheral nerves". Acta psychiat. neurol. suppl. 33, 1-206.

Rexed, B. & Therman, P.O. (1948) "Calibre spectra of motor and sensory nerve fibres to flexor and extensor muscles". J. Neurophysiol. 11, 133-140.

Rockstein, M. (1967) "Cellular age changes in insects". Symp. Soc. exp. Biol. 21, 337-349.

Romanul, F.C.A. (1964) "Enzymes in muscle. I. Histochemical studies of enzymes in individual muscle fibres". Arch. Neurol. 11, 355-368.

Romanul, F.C.A. & Meulen, J.P. Van-Der (1967) "Slow and fast muscles after cross innveration. Enzymatic and physiological changes". Arch. Neurol. 17, 387-402.

Rosman, N.P. & Kakulas, B.A. (1966) "Mental deficiency associated with muscular dystrophy. A neuropathological study". Brain 89, 769.

Rosenberg, M.E. (1970) "Synaptic connexions of alpha extensor motoneurones with ipsilateral and contralateral cutaneous afferents". J. Physiol. 207, 231-255.

Rothman, S. (1954) "Physiology and Biochemistry of the skin". Chicago University Press.

Rowe, R.W.D. (1969) "The effect of senility on skeletal muscles in the mouse". Exp. Geront. 4, 119-126.

Rubbins, N., Kaparti, G. & Engel, W.K. (1969) "Histochemical and contractile properties in the cross innervated guinea pig soleus muscle". Arch. Neurol. 20, 318-329.

Rudomin, P. & Madrid, J. (1972) "Changes in correlation between monosynaptic responses of single motoneurones and in information transmission produced by conditioning volleys to cutaneous nerves". J. Neurophysiol. 35, 44-64.

Rudomin, P., Burke, R.E. Nunez, R. Madrid, J. & Dutton, H. (1975) "Control by presynaptic correlations: A mechanism affecting information transmission from Ia fibres to motoneurones". J. neurophysiol. 38.

Rushworth, G. & Young, R.R. (1966) "The effect of vibration on tonic and phasic reflexes in man". J. physiol. (Lond.) 185, 63-64 (1966).

Ryall, R.W., Piercey, M.F. & Polosa, C. (1971) "Intersegmental and intrasegmental distribution of mutual inhibition of Renshaw cells". J. Neurophysiol. 34, 700-707.

Sabbahi, Awadalla,M.A. & Sedgwick, E.M. (1973) "Excitability changes in human motoneurones measured by the H-reflex and produced by local cooling of the skin". J. Physiol. (Lond.) 232, 58p.

Sabbahi Awadalla, M.A. & Sedgwick, E.M. (1976) "H-reflex modulation by natural stimulation of the skin". EEG. Clin. Neurophysiol. E.E.G. Clin. Neurophysiol. 41, 537.

Saint Ambrogio, G., Frazier, D., Reed, R.I. & Boyarsky, L. (1961) "Alterations in central letency, motoneurone number and blood volume of spinal cord of the ageing rat". Am. J. physiol. 200, 927-931.

Salafski, B. (1971) "Functional studies of regenerated muscles from normal and dystrophic mice". Nature (Lond.) 229, 270-272.

Scheibel, M.E. & Scheibel, A.B. (1971) "Inhibition and the Renshaw cells. A structural critique". Brain Behav. Evol. 4, 53-93.

Schmidt, R.F. (1965) "Prasynaptische Hemmung im Nucleus Cuneatus der Katze". Pflugers Archiv fur die gesamte physiologie des Menschen und der Tiere 278, 78-79.

Schmidt, R.F. (1971) "Presynaptic inhibition in the vertebrate central nervous system". Ergebn. physiol. 63, 20-101.

Schmalbruch, H. (1970) "Die quergestreiften Muskelfasern des Menschen. Ergebn. EntwGesch. 43, 1-75.

Schumacher, G.A., Beebe, G., Kibler, R.F., Kurland, L.T., Kurtzke, J.F., McDowell, F., Nagler, B., Sibley, W.A., Tourtellotte, W.W. & Willman, T.L. (1965) "Problems of experimental trials of therapy in multiple sclerosis: Report by the panel on the evaluation of experimental trials of therapy in multiple sclerosis". Ann. Ny. Acad. Sci. 122, 552-568.

Schwartz, M.S. & Stalberg, E. (1975) "SFEMG studies in myasthenia gravis with repetitive nerve stimulation". J. Neurol. Neurosurg. Psychiat. 38, 678-682.

Setschenow, J. (1863). Physiol. Studien ud. Hemmungsmach f.d. Reflexthat. d. Ruckenur. U. Gehirn d. Frosch. Berlin.

Shealy, C.N. Mortimer, J.T. & Reswick, J.B. (1967) "Electrical inhibition of pain by stimulation of the dorsal columns. Preliminary clinical report". Anesth Analg. (Cleveland) 46, 489-491.

Shealy, C.N., Mortimer, J.T., Hagfors, N.R. (1970) "Dorsal column electroanalgesia". J. Neurosurg. 32, 560-564.

Shealy, C.N. (1975) "Dorsal column stimulation: Optimization of application". Surg. Neurol. 4, 142-145.

Sherrington, C.S. (1906) "The integrative action of the nervous system". Yale University.

Shimamura, M., & Akert, K. (1965) "Peripheral nervous relations of propriospinal and spinobulbospinal reflex systems". Jap. J. Physiol. 15, 638-647.

Shimamura, M. & Livingstone, R.B. (1963) "Longitudinal conduction systems serving spinal and brain stem co-ordination". J. Neurophysiol. 26, 258-272.

Shimamura, M., Mori, S., Matsushima, S. & Fujimori, B. (1964) "On the spinobulbospinal reflex in dogs, monkeys and man". Jap. J. Physiol. 14, 411-421.

Showman, J., Wedlick, L.T. (1964) "The use of cold instead of heat for the relief of muscle spasm". Med. J. Aust. 2: 612-614.

Somjen, G. (1972) "A comment concerning the recruitment of motor units". In "Neurophysiology studied in man", G. Somjen (Ed.) 343-344 (Exerpta Medica - Amsterdam).

Somjen, G., Carpenter, D.O. & Henneman, E. (1965) "Responses of motoneurones of different sizes to graded stimulation of supra-spinal centres of the brain." J. Neurophysiol. 28, 958-965.

Spira, R. (1974) "Contribution of the H-reflex to the study of spasticity in adolescents". Dev. Med. Child. Neurol. 16, 150-157.

Sreter, F.A., Gergely, J. Salmons, S. & Romanul, F. (1973) "Synthesis by fast myosin-light chains characteristic of slow muscle in response to long term stimulation". Nature. New Biol. 241, 17-19.

Stalberg, E. (1966) "Propagation velocity in human muscle fibres in situ". Acta physiol. Scand. 70, Suppl. 287, 1-112.

Stalberg, E., Trontelj, J.V. (1970) "Demonstration of axon reflexes in human motor nerve fibres". J. Neurol. Neurosurg. Psychiat. 33, 571-579.

Stalberg, E., Ekstedt, J. & Browman, A. (1971) "The elctromyographic jitter in normal human muscles". EEG. Clin. Neurophysiol. 31, 429-438.

Stalberg, E. & Thiele, B. (1972) "Transmission block in terminal nerve twigs A-SFEMG finding in man". J. Neurol. Neurosurg. Psychiat 35, 52-59.

Stalberg, E. & Ekstedt, J. (1973) "Single fibre EMG and micro-physiology of the motor unit in normal and diseased human muscle". New develop. EMG. Clin. Neurophysiol. Desmedt (Ed.) I, 113-129. (Karger-Basel).

Stalberg, E. & Thiele, B. (1973) "Discharge pattern of motoneurones in Humans - A single fibre EMG study". New Develop. EMG. Clin. Neurophysiol. Desmedt (Ed.), III, 234-241. (Karger-Basel).

Stalberg, E., Schwartz, M.S. & Trontejl, J.V. (1975) "Single fibre EMG in various processes affecting the anterior horn cell". J. Neurol. Sci. 24 (4), 403-415.

Stalberg, E., Schwartz, M.S. & Thiele, B. (1976) "The normal motor unit in man - A SFEMG multielectrode investigation". J. Neurosci. 27, 291-301.

Stein, J.M. & Padykula, H.A. (1962) "Histochemical classification of individual skeletal muscle fibres of the rat". Amerc. J. Anat. 110, 103-124.

Steinert, H. (1909) "Myopathologische beitrage I. Uber das Klinische und anatomische bild des muskelschwunds der myotoniken". Dtsch. Z. Nervenheilk 37, 58.

Stelter, W.J., Spaan, G. & Klussman, F.W. (1969) "Der Einfluss der spinalen und peripheren Temperatur auf die Reflexspannung roter und blasser Muskeln". Pflugers Arch. Ges. Physiol. 312, 1-17.

Stephanis, C.N. & Matsouoka, S. (1965) "Spinal motoneurone hyper-excitability in patients with parkinsons's disease as revealed by the recovery curve of the H-reflex". 6th international congress of EEG. Clin. Neurophysiol. 625-626.

Sterling, W. (1874). Ludwigs Arbeiten, 245. Leipzig.

Stimson, C.W. Kheder, N., Hicks, R.G. & Orlando, R. (1969). Nerve conduction velocity and H-reflex studies in two groups of severely retarded children". Arch. Phys. Med. Rehabil. 50, 626-631.

Swash, M. (1972) "The morphology and innervation of the muscle spindle in dystrophia myotonica". Brain 95, 357-368.

Swash, M. Fox, K. (1972) "The effect of age on human skeletal muscle. Studies of the morphology and innervation of the muscle spindles". J. Neurol. Sci. 16, 417-432.

Synder, C.D. (1910) "The latency of the knee jerk response in man as measured by the thread galvanometer". Am. J. physiol. 76, 474-482.

Szentagothai (1968) "Structure and function of inhibitory neuronal mechanisms". Skoglund von Euler & Sodersberg (Eds.) 15-31 (Pergamon - Oxford).

Taborikova, H. (1966) "Fraction of the MNP activated in the monosynaptic H-reflex in man". Nature (Lond.) 209, 206-207.

Taborikova, H. (1973) "Supraspinal influences on H-reflexes". New Develop. in EMG. Clin. Neurophysiol., J. Desmedt (Ed.), III, 328-335. (Karger-Basel).

Taborikova, H., Provini, L. & Decandia, M. (1966a) "Evidence that muscle stretch evokes long-loop reflexes from higher centres". Brain Res. 2, 192-194.

Taborikova, H., Provini, L & Decandia, M. (1966b) (Unpublished observations) cited in: Eccles, J.C. (1966), Atti. Accad. Med. Lombarda 21, 158-176.

Taborikova, H. & Sax, D.S. (1968) "Motoneurone pool and the H-reflex" J. Neurol. Neurosurg.. Psychiat. 31, 354-361.

Taborikova, H. & Sax, D. (1969) "Conditioning of H-reflexes by a preceding subthreshold H-reflex". Brain 92, 203-212.

Takahashi, K. (1965) "Slow and fast groups of pyramidal tract cells and their respective membrane properties". J. Neurophysiol. 28, 908-924.

Takamori, M. (1967) "H-reflex study in upper motor neurone disease". Neurol. (Minn.) 17, 32-40.

Talbot, W.H., Darian Smith, I., Kornhuber, H.H. & Mountcastle, U.B. (1968) "The sense of flutter-vibration: Comparison of the human capacity with response patterns of mechanoreceptive afferents from the monkey hand". J. Neurophysiol. 31, 301.

Tanaka, R. (1972) "Activation of reciprocal Ia inhibitory pathway during voluntary motor performance in man". Brain Res. 43, 649-652.

Taylor, A. (1962) "The significance of grouping of motor unit activity". J. Physiol. 162, 259.

Teasdall, R.D., Park, A.M. Porter, W.E. & Magladery, J.W. (1951) "Electrophysiological studies of nerve and reflex activity in normal man. VI. Excitation and inhibition of two neurone reflexes by impulses in other nerves". Bull, J. Hopk. Hosp. 88, 538-548.

Teasdall, R.D., Park, A.M., Langruth, H.W. & Magladery, J.W. (1952) "Electrophysiological studies of reflex activity in patients with lesions of the nervous system. II Disclosure of normally suppressed monosynaptic reflex discharge of spinal motoneurones by lesions of lower brain-stem and spinal cord". Bull. J. Hopk. Hosp. 91, 245-256.

Teasdall, R.D., Languth, H.W. & Magladery (1952) "Electrophysiological studies of reflex activity in patients with lesions of the nervous system IV A note on the tendon jerk. Bull. J. Hopk. Hosp. 91, 267.

Thomas, J.E. & Lambert, E.H. (1960) "Ulnar nerve conduction velocity and H-reflex in infants and children". J. Appl. Physiol. 15, 1-9.

Thomasen, E. (1948) "Thomsen's Disease, Paramyotonia, Dystrophia Myotonica" (Universitetsforlaget. Aarhus).

Timires, P.S. & Vernadakis, A. (1972) "Structural, biochemical and functional ageing of the nervous system in Developmental physiology and ageing", 502-526 (Macmillan - New York).

Tokizane, T. & Shimazu, H. (1964) "Functional differentiation of human skeletal muscles. Corticalization of movement". University of Tokyo, Tokyo.

Trontelj, J.V. (1968) "H-reflex of single motoneurones in man". Nature, Lond. 220, 1043-1044.

Trontelj, J.V. (1969) "Latency variation of single human motoneurones in the H-reflex" EEG. Clin. Neurophysiol. 27, 723.

Trontelj, J.V. (1970) "Reflex facilitation and inhibition of single motoneurones in man". Ingoslav, Physiol. Pharmacol. Acta 6 (1), 119-124.

Trontelj, J.V. (1973) "A study of the H-reflex by single fibre EMG". J. Neurol. Neurosurg. Psychiat. 36, 951-959.

Tsukahara, N. & Ohye, C. (1964) "Polysnaptic activation of extensor motoneurones from group Ia fibres in cat spinal cord", Experientia 20, 628-629.

Tzavellas, O., Gabriel, E. & Friedel, B. (1972) "The H-reflex in patients with parkinsonism syndrome before and after stereotoxic procedures and during administration of L-Dopa". Confin. Neurol. 34, 295-298.

Urbscheit, N. & Bishop, B. (1970) "Effects of cooling on the ankle jerk and H-response". Phys. Ther. 50 (7), 1041-1049.

Urbscheit, N., Johnston, R. & Bishop, B. (1971) "Effects of cooling on the ankle jerk and H-response in hemiplegic patients". Phys. Ther. 51 (9), 983-989.

Vallbo,A.B. & Hagbarth, K.E. (1967) "Impulses recorded with microelectrodes in human muscle nerves during stimulation of mechanoreceptors and voluntary contractions". EEG. Clin. Neurophysiol. 23, 392.

Vallbo, A.B. & Hagbarth, K.E. (1968) "Activity from skin mechanoreceptors recorded percutaneously in awake human subjects". Exp. Neurol. 21, 270-289.

Vasin, N. Ya., Shakhnovich, A.R. Iliyinsky, I.A. & Milovanova, L.S. (1971). "H-reflex and capsular effect in stereotoxic operations on the ventrolateral thalamic nucleus". VOPR NEIROKHIR 3, 6-10.

Veale,J.L., Mark, R.F. & Rees, S.M. (1971) "Differential stimulation of the human ulnar nerve". Proc. Austr. Phys. Pharm. Soc. 2, 85.

Veale, J.L., Mark, R.F. & Rees, S. (1973a) "Differential sensitivity of motor and sensory fibres in human ulner nerve". J. Neurol. Neurosurg. Psychiat. 36, 75-86.

Veale, J.L. & Rees, S. (1973b) "Renshaw cell activity in man". J. Neurol. Neurosurg. Psychiat. 36, 674-683.

Veale, J.L., Rees, S. & Mark, R.F. (1973c) "Renshaw cell activity in normal and spastic man". New Develop. in Clin. Neurophysiol., J. Desmedt (Ed.), III, 523-537 (Karger-Basel).

Vernik, A. Ya., & Starobinets, M.K.H. (1972) "The H-reflex and F-wave in the differential diagnosis of spinal shock and lesions of the caudal region of the spinal cord". Vopr. Neirokhir 36, 36-39.

Wager, E.W. Buerger, A.A. (1974) "A linear relationship between H-reflex latency and sensory conduction velocity in diabetic neuropathy". Neurol. (Minn.) 24, 711-714.

Wagman, I.H. & Lesse, H. (1952) "Maximum conduction velocities of motor fibres of ulnar nerve in human subjects of various ages and sizes". J. Neurophysiol 15. 235-244.

Walberg, F. (1965) "Axoaxonic contacts in the cuneate nucleus, probable basis for presynaptic depolarization". Exp. Neurol. 13, 218-231.

Wall, P.D. (1970) "The sensory and motor role of impulses travelling in the dorsal columns towards cerebral cortex". Brain 93, 505-524.

Wall, P.D. (1958) "Excitability changes in afferent fibre terminations and their relation to slow potentials". J. Physiol. 142, 1-21.

Wall, P.D. (1962) "The origin of a spinal cord slow potential". J. Physiol. 164, 508-526.

Wall, P.D. (1964) "Presynaptic control of impulses at the first central synapse in the cutaneous pathway". Progress in Brain Res. 12, 92-115.

Wall, P.D., Egger, M.D. (1971) "Formation of new connexions in adult rat brains after partial deafferentation". Nature 232, 542-545.

Walthead, K.M. & Tchicaloff, M. (1968) "Motor points" in Electrodiagnosis and electromyography" by S. Licht (Ed.), 153-170 Waverly - Baltimore.

Walton, J.N. & Gardner-Medwin, D. (1974) "Progressive muscular dystrophy and the myotonic disorders" in Disorders of voluntary muscle by J. Walton (Ed.) (Churchill).

Warmolts, J.R. & Engle, W.K. (1973) "Correlation of motor unit behaviour with histochemical myofiber type in humans by open-biopsy electromyography". New Develop. EMG. Clin. Neurophysiol. Desmedt (Ed.), I, 35-40 (Karger-Basel).

Wayner, M.J. & Emmers, R. (1958) "Spinal synaptic delay in young and aged rats". Am. J. Physiol. 194, 403-405.

Weddell, G., Palmer, E. & Burgess, P.R. (1955) "Nerve endings in mammalian skin" Biological Reviews 30, 159-195.

Weinstock, I.M., Epstein, S. & Milhorat, A.T. (1958) "Enzyme studies in muscular dystrophy. III In Hereditary muscle dystrophy in mice. Proceeding Soc. Exper. Biol. Med. 99, 272-276.

Westphal, C. (1875) "Uber einige Bewegunserscheinungen an gelahmten Gliedern." Arch. F. Psychiat. 5, 803.

Whytt, R. (1755) as quoted by Sherrington 1906.

Wirski, J. (1971) "Observations on the variability of the H-reflex in patients with spinal cord lesion". Chir Narzadow Rochu ortop. Pol. 36, 379-383.

Wirski, J. (1973a) "Value of H-reflex in the evaluation of the spinal cord function". Chir. Narzadow Ruchu ortop. Pol. 38, 97-103.

Wirksi, J. (1973b) "The effect of skin stimulation on modification of Hoffmann's reflex in patients with spinal shock" J. Neurol. Neurochir. Pol. 7 (1), 39-45.

Wohlfart, G. (1951) "Dystrophia myotonica and myotonia congenita histopathologic studies with special reference to changes in the muscles". J. Neuropath. exp. Neurol. 10, 109-124.

Wolf, S.L. & Basmajian, J.V. (1973) "Intramuscular temperature changes deep to localized cutaneous cold stimulation". Physical Therapy 53 (12), 1284-1288.

Woolf, A.L. & Coers, C. (1974) "Pathological anatomy of the intramuscular nerve endings" in Disorders of voluntary muscle by J. Walton (Ed.) 274-309 (Churchill, London).

Woolf, A.L. (1962a) "The theoretical basis of clinical electromyography". Parts I and II. Ann. Phys. Med. 6, 189-241.

Woolf, A.L. (1962b) "Muscle biopsy" in Modern Trends in Neurology D. Williams (Ed.), 3rd edn. (Butterworth, London).

Wright, E.A. & Spink, J.M. (1959) "A study of the loss of nerve cells in the central nervous system in relation to age". Gerontologie 3, 277-287.

Wuerker, R.B., McPhedran, A.M. & Hennemann, E. (1965) "Properties of motor units in a heterogenous pale muscle (muscle gastrocnemius) of the cat". J. Neurophysiol. 28, 85-99.

Wyman, R.J., Waldron I. & Wachtel, G.M. (1974) "Lack of fixed order of recruitment in cat MNPs". Exp. Brain. Res. 20, 101-114.

Yamanaka, T. (1964) "Effect of high frequency vibration on muscle spindle in the human body". J. Chiba med. Soc. 40, 338-346.

Yap, C.B. (1967) "Spinal segmental and long loop reflexes in spinal motoneurone excitability in spasticity and rigidity" Brain 90, 887-896.

Yellin, H. (1967) "Neural regulation of enzymes in muscle fibres of red and white muscle". Exp. Neurol. 19, 92-103.

Young, H.L., Young, W. & Edelman, I.S. (1959) "Electrolyte and lipid composition of skeletal and cardiac muscle in mice with hereditary muscular dystrophy". Amer. J. Physiol. 197 (2), 487-490.

Zotterman, Y. (1953) "Special senses: thermal receptors". Ann. Rev. Physiol. 15, 363.