THE INFLUENCE OF TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION (TENS) ON HEMIPLEGIC SPASTICITY AND VOLUNTARY MUSCLE POWER

by

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ABSTRACT

These studies investigated possible relief of spasticity in hemiparetic subjects by transcutaneous electrical nerve stimulation (TENS) and its underlying mechanisms The first two studies quantified the disorders in reflex and voluntary motor functions and addressed the reproducibility of their measurement and their correlation with spasticity scores. Soleus stretch reflexes were enhanced and isometric voluntary contraction force was decreased linearly with increasing spasticity. The last two studies addressed the effects of single and repetitive TENS stimulation on spasticity, reflex and isometric voluntary contractions Compared to placebo stimulation, single 45 min sessions of TENS prolonged H and stretch reflex latencies for up to 60 min following stimulation Repetitive (15 daily, 60 min) applications significantly decreased spasticity scores, Hvib/Hctl ratios, stretch reflexes and co-contraction while improving dorsiflexion force. The improvement in spasticity and voluntary motor control may partly have been mediated by presynaptic inhibition and reduced hyperactive stretch reflexes thereby 'unmasking' descending control.

SOMMAIRE

Ces études portent sur la diminuation possible de la spasticité chez les sujets hemiparetiques par stimulation électrique transcutanée (TENS) ainsi que ses méchanismes sous-jacents. Les deux premières études portent sur la quantification des désordres des fonctions réflexes et volontaires ainsi que sur la reproductibilité de leurs mesures et leur corrélation avec les pointages de spasticité. Les réflexes d'étirements soléaire étaient augmentés et la force de contraction volontaire isométrique maximale était diminuée de façon linéaire avec l'augmentation de la spasticité. Les deux dernières études portent sur les effets d'une seule ou de plusieurs sessions de TENS sur la spasticité, sur les réflexes et sur les contractions voluntaires isométriques maximales. Comparativement à la stimulation placebo, une seule session de 45 min de TENS a entrainé une prolongation des latences des réflexes H et d'étirement et ce, jusqu'à 60 min suivant la stimulation. L'application répétitive (15 traitements de 60 min) a diminué significativement les pointages de spasticité, les ratios Hvib/Hctl, les réflexes d'étirements et la co-contraction tout en améliorant la force des dorsifléchisseurs. La diminution de la spasticité et l'amélioration du contrôle volontaire pourait avoir été partiellement modulées par inhibition présynaptique et par la réduction des réflexes d'étirement hyperactifs ayant donc ainsi 'demasqué' le contrôle descendant.

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PREFACE

According to section 7 of the Guidelines Concerning Thesis Preparation prepared by the Faculty of Graduate Studies and Research, McGill University, (March, 1989)*, the candidate has the option of including in the thesis manuscripts published or submitted to learned journals. This option has been taken in this thesis with the authorization of the Chairman, Department of Physiology

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* In accordance with stated requirements, section 7 of the Guidelines Concerning Thesis Preparation is cited in full below:

7 MANUSCRIPTS AND AUTHORSHIP
The candidate has the option, subject to the approval of the Department, of including as part of the thesis the text, or duplicated published text (see below), of an original paper, or papers. In this case the thesis must still conform to all other requirements explained in Guidelines Concerning Thesis Preparation. Additional material (procedural and design data as well as descriptions of equipment) must be provided in sufficient detail (e g in appendices) to allow a clear and precise judgement to be made of the importance and originality of the research reported. The thesis should be more than a mere collection of manuscripts published or to be published. It must include a general abstract, a full introduction and literature review and a final overall conclusion. Connecting texts which provide logical bridges between different manuscripts are usually desirable in the interests of cohesion

It is acceptable for theses to include as chapters authentic copies of papers already published, provided these are duplicated clearly on regulation thesis stationary and bound as an integral part of the thesis Photographs or other materials which do not duplicate well must be included in their original form In such instances, connecting texts are mandatory and supplementary explanatory material is almost always necessary

The inclusion of manuscripts co-authored by the candidate and others is acceptable but the candidate is required to make an explicit statement on who contributed to such work and to what extent, and supervisors must attest to the accuracy of the claims, e g. before the Oral Committee. Since the task of the Examiners is made more difficult in these cases, it is in the candidate's interest to make the responsibilities of authors perfectly clear Candidates following this option must inform the Department before it submits the thesis for review.

Chapter 1 provides a general introduction to and problem formulation of the present series of studies Chapters 2, 3, 4, and 5 are papers which have been submitted for publication. Their full authorship and titles are listed below These papers have been reformatted to provide consistancy throughout the thesis especially in the citing of references and in the sequencing of the main sections: Abstract, Introduction, Materials and Methods,

Results, and Discussion. Chapter 6 summarizes the main conclusions of the studies As well according to Section 6a of the Guidelines Concerning Thesis Preparation, Chapter 6 also includes statements concerning the original contributions to knowledge of this thesis All references have been collected at the end of thesis in the Bibliography section

REFERENCE LIST

Chapter 2 — Levin, M. F. and Chan, C W. Y Disorders in spastic hemiparesis I Characteristics of reflex responses Submitted to Brain

Chapter 3: — Levin, M. F and Chan, C W Y. Disorders in spastic hemiparesis II Maximal voluntary contractions in standing. Submitted to Brain

Chapter 4: — Chan, C. W Y and Levin, M F Repetitive electrical stimulation in spastic hemiparesis I Stretch reflex latency changes Submitted to Experimental Neurology

Chapter 5. — Levin, M F and Chan, C W Y Repetitive electrical stimulation in spastic hemiparesis· II Relief of spasticity is associated with improvement in reflex and voluntary motor control Submitted to Experimental Neurology

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CHAPTER 1

INTRODUCTION

SPASTICITY

The presence of spasticity is one of the principal factors affecting the rehabilitation of patients following cerebrovascular accidents (Twitchell, 1951; Moscowitz et al., 1972; Waylonis et al., 1973). In a traditionally accepted view, spasticity has been defined as hyperactivity of the stretch reflex arc manifested by a velocity dependent increase in tonic and phasic stretch reflexes, sometimes accompanied by clonus (Lance, 1980) Spasticity differs from the phenomenon of 'rigidity', which is characterized by a plastic resistance throughout the entire range of passive joint movement, equally distributed in flexor and extensor muscles (Denny-Brown, 1966). In contrast to rigidity, spasticity is found predominantly in one muscle group or synergy and is dependent on the velocity of stretch (Burke and Lance, 1973) and initial muscle length (Burke et al., 1970). Two types of spasticity have been defined, based on the lesion in the central nervous system (CNS). In spinal spasticity resulting from a lesion in the cord, hypertonicity is present predominantly in flexors more than extensor muscles (Riddoch, 1917; Kuhn, 1950, Shahani and Young, 1980) Lesions of the motor cortex and lower brain structures (see below) result in central (hemiplegic) spasticity, characterized by hypertonia in physiological extensors (i.e. antigravity muscles such as upper extremity flexors and lower extremity extensors) and weakness in physiological flexors (Pederson, 1974; Yanagisawa and Tanaka, 1978). The review below will focus on the anatomical and physiological basis of central spasticity and its related clinical signs and symptoms.

1. Anatomical Basis of Hemiplegic Spasticity

Hemiplegic spasticity with motor paresis was originally attributed to the disruption of corticospinal (pyramidal tract) fibres. This was based on the findings from post-mortem examinations of the spinal cord showing degeneration only in these fibres (Hines, 1960). However, Tower (1940) had demonstrated that lesions restricted to the bulbar pyramids in non-human primates resulted, not in hypertonia, but in hypotonia and hyporeflexia. Muscular tone was increased only after an additional lesion of the motor cortex. Considerable efforts

were made to determine the exact location of the lesion responsible for the disturbance in muscle tone and voluntary motor control similar to that in human hemiplegia The work of Kennard and Fulton (1933) established that removal of the pre-motor cortex (area 6) resulted in contralateral spasticity in monkeys The spasticity was maximal only when the lesions were bilateral and included both pre-motor and motor (area 4) areas It has subsequently been repeatedly demonstrated that spasticity results from the ablation of the primary motor cortex (Hines, 1936, 1937) The severity of spasticity and muscular weakness is enhanced following additional lesions to the ipsilateral supplementary motor area and the contralateral motor cortex (Mettler, 1943; Welch and Kennard, 1944, Travis, 1955a,1955b, Tasker et al , 1975) Purely cortical lesions appear to result in spasticity only when they are bilateral (Tasker et al , 1975). Interestingly, Fulton (1935) reported that bilateral ablation of both motor and supplementary motor areas, resulted in total and unrecoverable paralysis and spastic posturing However, if a portion of one motor area was spared, the animal showed some degree of recovery of voluntary function.

The investigation into the specific descending pathways contributing to spasticity began with Sherrington's work (1897, 1898) in the decerebrate cat Intracellular recordings in the spinal cord of the cat have shown considerable convergence of signals from segmental and descending pathways onto spinal interneurons and motoneurons (Baldissera et al , 1981, Rudomin et al , 1983; Alstermark et al., 1984; Rudomin et al., 1986) Two major centrifugal systems facilitate extensor motoneurons. The first is the reticulospinal pathway from the diencephalon to the medulla projecting bilaterally in the lateral funiculus (Eccles and Lundberg, 1958; Engberg et al., 1968). The second is the vestibulo-spinal tract from Dieter's nucleus descending ipsilaterally in the ventral funiculus (Hongo et al , 1969, Grillner et al , 1970). Counterbalancing these facilitatory effects is inhibitory output from the extrapyramidal cerebral cortex, the striatum, the ventromedial reticular formation and the anterior lobe of the cerebellum (Baldissera et al., 1981). This influence is channelled through the reticular inhibitory system, predominantly in the ipsilateral ventrolateral funiculus of the spinal cord (Lawrence and Kuypers, 1965; Goldberger, 1969; Kuypers, 1974) Another major output from the motor

cortex descends in the crossed lateral and uncrossed ventral corticospinal or pyramidal tracts. Excitatory and inhibitory effects of pyramidal tract stimulation on monosynaptic reflexes have been reported in a number of animal preparations (Preston et al., 1967; Gilman et al., 1971; Feldman and Orlovsky, 1972; Hultborn et al., 1976c; Chapman and Wiesendanger, 1982a; Keifer and Kalil, 1989). Pyramidal tract stimulation has been found to suppress monosynaptic reflexes in the cat (Preston et al., 1967; Hultborn et al., 1976c) and in *in vitro* hamster preparations (Keifer and Kalil, 1989). In the monkey, however, both facilitatory and inhibitory influences on stretch reflexes have been reported (Gilman et al., 1971; Chapman and Wiesendanger, 1982a).

Interruptions of descending pathways at the level of the brainstem or spinal cord upsets the balance of the descending control of muscle tone. Thus, in hemiplegia, hypertonia can partly be explained by the interruption of the inhibitory extrapyramidal pathways (Tasker et al., 1975). This would result in a release of stretch reflex activity from normal inhibitory control together with a net increase in descending excitation to segmental interneurons (Chapman and Wiesendanger, 1982b).

2. Physiological Basis of Spasticity

Both non-neural and neural factors may contribute to the hypertonia and hyperreflexia in spasticity. It is well established that changes occur in extrafusal muscle fibres following central nervous system lesions (Edstrom, 1970). In at least one report, it has been suggested that non-reflexogenic factors such as motor unit changes, may contribute to the hypertonia associated with locomotion (Dietz and Berger, 1983). These changes will be discussed in detail below in relation to voluntary movement. Neural factors such as enhanced spinal stretch reflexes are thought to contribute to hypertonia. Furthermore, the magnitude of short-latency stretch reflexes is found to be broadly correlated with the severity of spasticity (here defined as resistance to passive movement) in the wrist (Cody et al., 1987) and the ankle (Berardelli et al., 1983). The mechanisms underlying the hyperreflexia of spasticity are complex and more than likely involve a combination of pathological processes.

Enhanced and irradiating reflexes may result from altered segmental afferent input to propriospinal reflex circuitry or from abnormal processing of otherwise normal input from the periphery. To date however, there is no evidence indicating abnormally increased activity in cutaneous or muscular afferents in spasticity. Alternatively abnormal processing may result from altered central drive increasing 'gamma' and/or 'alpha' motoneuronal excitability (Foerster, 1927; Granit, 1955). However, given the formidable convergence on Ia interneurons and alpha motoneurons from descending pathways and from segmental and heterosegmental afferents (Hultborn et al., 1976a,b,c; Baldissera et al., 1981; Alstermark et al., 1984; Rudomin et al., 1986), other possibilities may also be considered. These include alterations in presynaptic, reciprocal and/or recurrent inhibition, changes in reflex thresholds and plastic changes in the central nervous system as a result of lesions. Each of these possible contributing factors will be discussed below.

(i) Gamma Motoneuronal Hyperexcitability

A quick stretch of the intrafusal muscle fibres excites primary (Ia) spindle afferents. These, in turn, have strong monosynaptic excitatory connections to homonymous alpha motoneurons in the ventral horn of the spinal cord. The result is a short latency contraction of the extrafusal muscle fibres (Liddell and Sherrington, 1924). One way to enhance alpha motoneuronal responsiveness would be to increase gamma motoneuronal drive, thus increasing the sensitivity of the Ia afferents (Granit, 1955). The hypothesis of enhanced gamma bias was supported by findings that 'selective' block of gamma efferents led to a reduction in spasticity and rigidity in the decerebrate cat (Matthews and Rushworth, 1957) and in man (Rushworth, 1960). Spasticity was therefore attributed to a selective disorder of dynamic fusimotor neurons and rigidity to a selective disorder of static fusimotor neurons (Jansen and Matthews, 1962; Rushworth, 1964; Dietrichson, 1971, 1973).

Several lines of evidence have put the hypothesis of enhanced gamma motoneuronal excitability in doubt. Firstly, this mechanism was implicated as the major contributor to spasticity since decreases in muscle tone were observed after 'selective' blockade of

fusimotor efferents by the injection of local anaesthetic (Rushworth, 1960). However, these findings should be interpreted with caution, since Burke (1983) has pointed out that injection of local anaesthetic into or around a motor nerve may not selectively block gamma motoneurons, especially in man Furthermore, similar studies attempting to block fusimotor activity using intrathecal and epidural injections of local anaesthetic or tibial nerve block did not alter spasticity (Landau et al , 1960, Gassel and Diamantopoulos, 1964) Secondly, direct spindle recordings from spastic hemiplegic monkeys indicated that spindle sensitivity decreased during the period of hypotonia but never increased to a level greater than normal even after the development of spasticity (Gilman et al., 1974). The advent of microneurographic recordings offered a more reliable and direct method of assessing spindle changes in man In the only study comparing a small number of spastic (n=2) with normal subjects (n=8), Hagbarth et al (1973) recorded from single Ia afferents in the medial gastrocnemius nerve They revealed no excessive spindle activity during dynamic and static stretch in triceps surae. On the other hand, Szumski et al. (1974) found a decreased latency of spindle responses during the relaxation phase of contractions induced by manual tendon taps during voluntary reinforcement (Jendrassik manoeuvre) in spastic patients. However, this heightened spindle activity at the onset of the tap and during relaxation of the reflex induced twitch, was qualitatively not different from that evoked in normal subjects at rest (Szumski et al , 1974) or during the Jendrassik manoeuvre (Hagbarth et al , 1975), although the responses were highly variable. Thus, equivocal evidence suggests that in spastic muscles at rest, spindle responses are not different from normal. Nonetheless, in the absence of spindle recordings from actively contracting spastic muscles, it would be premature to conclude that hyperreflexia is not the result of enhanced gamma motoneuronal activity. The bulk of the evidence to date, however, leads to reservations about this hypothesis.

(ii) Alpha Motoneuronal Hyperexcitability

Alpha motoneuronal hyperexcitability can result from an increased net descending excitatory drive due to the interruption of supraspinal pathways. To investigate this possibility,

Matthews (1959) analyzed the size of the tonic stretch reflex in the decerebrate cat He described a family of tension-length curves in the soleus muscle elicited by a variety of segmental reflexes with and without paralysis of gamma motoneurons He found that only the threshold of the stretch reflex changed while the slope of the tension-length relationship did not. Investigating the same question, Feldman and Orlovsky (1972) examined the effects of stimulation of various supraspinal structures (Dieter's nucleus, pyramidal tract, medial medullary reticular formation) in unanesthetized intercollicularly decerebrated cats They found that continuous stimulation (70 Hz) of Deiter's nucleus, which is excitatory to hindlimb extensors, resulted in a shift of the tension-length curve to the left, i e initial tension developed at a shorter muscle length. This suggested a lowering of the stretch reflex threshold. Combining the excitatory input (Dieter's nucleus stimulation) with that of different descending inhibitory systems resulted in a decrease of the stretch reflex threshold, but did not change the slope (reflex gain or stiffness) of the relationship. Similar results were obtained from the hindlimb flexors These findings suggested that an increased excitatory drive could lower the motoneuronal threshold, resulting in the their earlier activation for the same afferent input. Theoretically, such a shift in motoneuronal excitability may also be manifested in lowered stretch reflex thresholds (Feldman, 1966, 1986) and could account for all of the findings of hyperreflexia and hypertonia associated with spasticity The decrease in stretch reflex threshold is illustrated schematically in Fig. 1 The normal torque-angle relationship is shown by the thick solid line. Spasticity could arise from 1) a reduction in the stretch reflex threshold indicated by the thin solid line labelled **Lt**, 2) an increase in joint stiffness depicted by the dotted line, **S**; or 3) a combination of both disturbances, shown in the dashed curve **Lt,S**. Recent empirical evidence has lent support to this hypothesis (Lee et al., 1987; Powers et al , 1988, 1989). In a series of experiments on spastic elbow flexor muscles in hemiparetic subjects, stretch reflex thresholds were lowered while reflex gains were not different from normal (Powers et al , 1988, 1989). Thus, Powers et al (1988) found a negative linear relationship between the evoked elbow torque and the threshold angle of EMG activity, measured during stretch of the elbow flexors at 0.5 radians/sec There was no

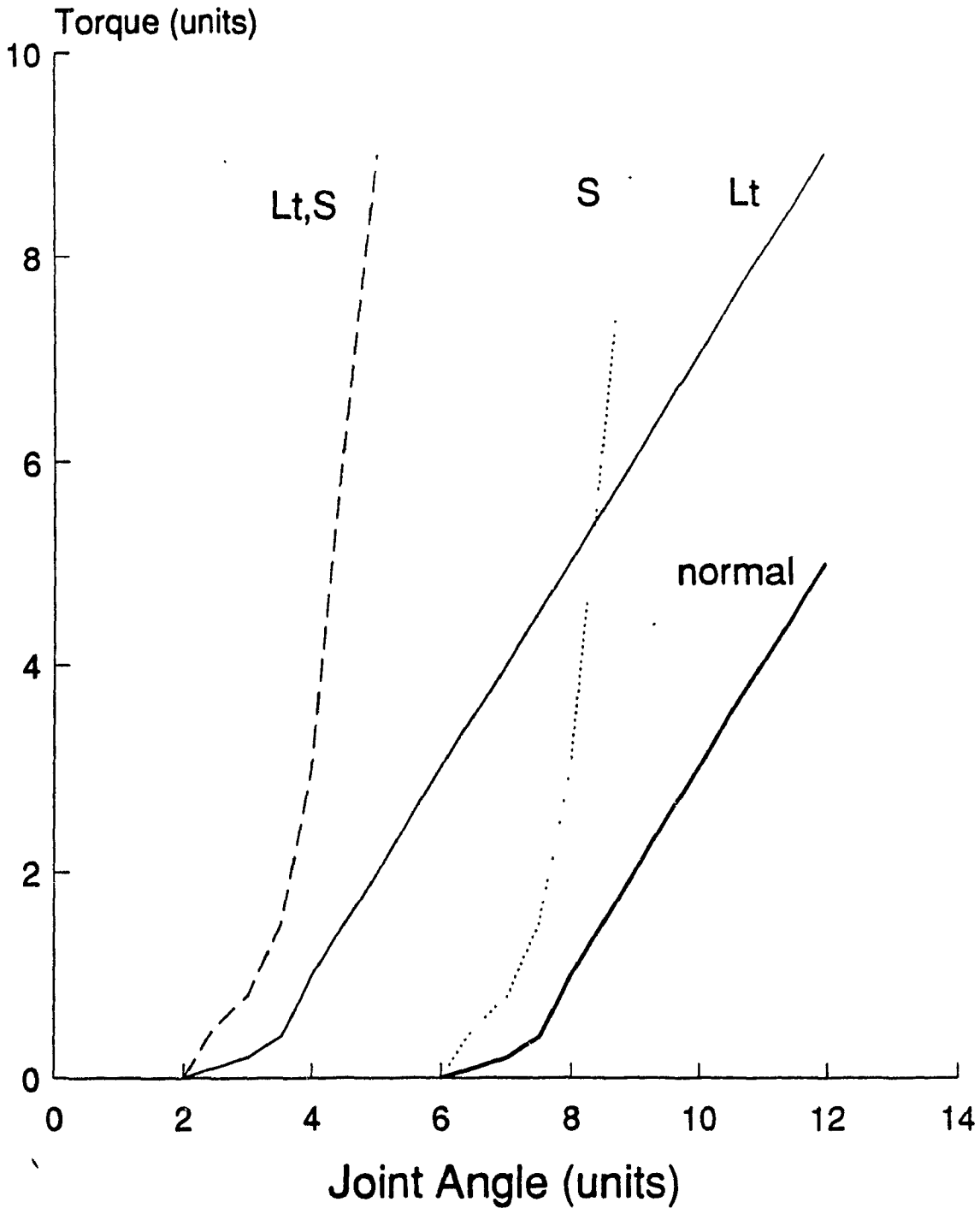


Fig. 1. The torque-angle relationship for eliciting the stretch reflex. The normal relationship is shown by the thick solid line. The theoretical changes in spasticity are depicted as a shift in stretch reflex thresholds (line **Lt**), an increase in joint stiffness (line **S**), or a combination of both (**Lt,S**).

systematic relation between stiffness and threshold angle Furthermore, when threshold influences were eliminated by requiring all subjects to generate a low level of active torque prior to stretch (thereby bringing most motoneurons above their threshold levels), they found a considerable overlap in the average dynamic and static stretch-evoked torque and EMG activity between spastic and normal subjects. This suggested that reflex gain was not enhanced in spasticity (Powers et al., 1988, 1989). Reflex threshold changes were also found to be correlated with the severity of clinical spasticity, although the calculated correlation coefficient was not reported. Thus, alpha motoneuronal excitability, as reflected by stretch reflex threshold levels, appears to be increased in spasticity However, the physiological mechanisms mediating this enhancement are, as yet, unclear

(iii) Presynaptic Inhibition

Excitability of the monosynaptic stretch reflex (MSR) is thought to be subject to presynaptic inhibition exerted via an axo-axonic synapse between an interneuron and an Ia afferent terminal prior to the latter's projection to the alpha motoneuron. The interneuron depolarizes the Ia afferent terminal, thereby reducing the amount of transmitter released by an impulse in this axon (Eccles, 1964). Axo-axonic GABAergic presynaptic contacts have been demonstrated by electron microscopy between Ia and Ib primary afferent fibres in Clarke's column (Walmsley et al., 1987), and on group Ia boutons in the motor nuclei of the cat (Curtis and Lodge, 1982; Fyffe and Light, 1984).

The presynaptic hypothesis is based on three types of observations in animals: 1) Conditioning volleys in the flexor nerve reduce the size of the monosynaptic excitatory post-synaptic potential (EPSP) in extensor motoneurons without changing the properties of the postsynaptic membrane (Eccles et al., 1961, 1962; Eide et al., 1968). 2) There exists a close relationship between the magnitude and time course of the inhibition, and the depolarization of the primary afferent (PAD) terminals (Eccles, 1964; Rudomin et al , 1983; Brink et al , 1984). 3) Depolarization of the presynaptic fibres during PAD reduces the presynaptic spike responsible for transmitter release (Eccles et al., 1962; Hubbard and Willis, 1962; Llinas,

1968).

Based on latency calculations, the presynaptic pathway is presumed to consist of a minimum of two interneurons, first proposed by Eccles et al (1961), and later identified by intra-axonal recordings and dorsal root potentials (Jankowska et al , 1981) Interneurons mediating PAD of cutaneous and group I muscular afferents have been located in separate laminae of the cat spinal cord (Jankowska et al., 1981). The relative effectiveness of pathways mediating PAD related to flexors and extensor muscles appears to be selectively controlled by peripheral and descending influences on these different last-order interneurons (Lundberg, 1964; Rudomin et al , 1983, 1986; Brink et al., 1984, Jimenez et al , 1988) For example, the low-threshold afferent evoked PAD from flexors to extensors in the cat may be differentially controlled by volleys in cutaneous nerves, stimulation of the ipsilateral reticular formation, the contralateral red nucleus or pyramidal tracts (Rudomin et al , 1983, 1986) Furthermore, spatial facilitation from various combinations of flexor and extensor Ia afferents produced larger dorsal root potentials than stimulation of either afferents alone (Brink et al , 1984). Similar convergence was demonstrated between flexor and extensor Ib, as well as flexor Ia and Ib, but not between extensor Ia and Ib afferents (Brink et al , 1984) That presynaptic control has been found to be mediated at the interneuronal level is not surprising, given the extensive convergence of peripheral and descending pathways onto common interneurons located in laminae III - VII of the spinal cord (Lundberg, 1964; Baldiserra et al , 1981, Rudomin et al., 1981, 1983; Brink et al., 1984)

Early investigations of presynaptic inhibition focused on the identification of PAD pathways mediated by Ia afferent fibres selectively activated by electrical stimulation. Subsequently, longitudinal low-amplitude, high-frequency vibration was found to be a powerful natural stimulus for the selective activation of primary muscle spindle endings in the cat (Brown et al., 1967, Gillies et al., 1969; Barnes and Pompeiano, 1970a). This was based on findings that vibration activated primary endings without significantly increasing the mean firing frequency of secondary spindle endings or Golgi tendon organs (Brown et al., 1967). In addition, inhibition of the MSR in the decerebrate cat was correlated with the appearance of

PAD and dorsal root potentials (Barnes and Pompeiano, 1970a,b) The vibration evoked inhibition was unaffected by removal of the skin or by section of the ventral roots, ruling out its mediation by cutaneous afferents or other muscular afferents activated by muscle contraction (Gillies et al , 1969) In these initial studies, it was further noted that, while monosynaptic reflexes of extensors could be inhibited by vibration of flexors, they were facilitated by vibration of extensor synergists (Barnes and Pompeiano, 1970a,b) This suggested a differential control over presynaptic inhibitory pathways to flexors and extensor motoneurons

In man, there is only indirect evidence for presynaptic inhibition evoked by muscle or tendon vibration. In contrast to the cat, a 2 mm amplitude vibratory stimulus of between 80-100 Hz applied to the homonymous Achilles tendon, was found to decrease the amplitude of soleus tendon jerks and H reflexes (DeGail et al , 1966, Rushworth and Young, 1966, Marsden et al , 1969, Desmedt and Godaux, 1978) The inhibition is not fully developed until 100 msec after vibration begins and may outlast it by several seconds (Somerville and Ashby, 1978), even though spindle responses are immediate (Burke et al , 1976) These findings suggested a central mechanism mediating the inhibition which may act at the segmental level, since the effect was still present in spinal cord injured subjects

In contrast to longitudinal vibration in the cat, perpendicularly applied vibration in man may be less selective for primary afferent fibers in the intact limb Using microelectrode recordings, Burke et al. (1976) showed that 1 5 mm amplitude vibration between 20 and 220 Hz activated spindle primary and secondary endings as well as Golgi tendon organs and Pacinian receptors. The relative selectivity of the stimulus for primary afferent excitation appears to be related to the frequency and amplitude of vibration Primary endings have been found to be much more sensitive than Golgi tendon organs or secondary endings to low-amplitude vibration (0 2 to 0.5 mm) in non-contracting muscles, the latter being relatively unresponsive (Roll et al., 1989). In addition, using either high- or low-amplitude vibration, primary endings were capable of following higher frequencies (up to 100 Hz) than secondary endings (Burke et al., 1976; Roll et al., 1989) These findings suggested that in man, a

relative stimulus for primary spindle endings consists of low-amplitude, high-frequency vibration.

In a further attempt to identify the mechanisms responsible for presynaptic inhibition, Ashby et al (1987) found that vibration applied to the homonymous muscle or tendon reduced the facilitation of voluntarily activated single motor units from low-threshold muscular but not cutaneous afferents Vibration alone however, did not alter the firing probability of soleus motor units, suggesting that the mechanism of the depression was likely to be presynaptic. However, in that study, spindle primary endings may not have been the dominant receptors activated This is suggested since the investigators used a large amplitude of vibration (6 mm), which is likely to stimulate more than just the primary afferents (Burke et al , 1976) Secondly, a significant contribution from Ib afferents cannot be ruled out, since the response to vibration has been found to increase greatly during contraction of the receptor bearing muscle (Roll et al., 1989). Furthermore, the inhibition of the MSR may be enhanced by the spread of vibration to antagonist muscles. For example, Dindar and Verrier (1975) found that the inhibition of the soleus MSR was decreased in man, when the Achilles tendon was vibrated during a complete block of the peroneal nerve innervating the muscles of the anterior compartment of the leg. This suggested that the inhibition was enhanced by the activation of receptors in the antagonistic flexor muscles

Thus, presynaptic inhibition may not be the only mechanism which contributes to the depression of monosynaptic reflexes during vibration in man. In fact, during prolonged vibration, other contributory factors may include refractoriness of the Ia fibres (Hagbarth, 1973), transmitter depletion of the Ia terminals (Katz et al., 1977), and postsynaptic non-reciprocal group I inhibition (Ia mediated Ib inhibition; Fetz et al., 1979). In other words, although the inhibition of the MSR evoked by vibration may in part be due to a presynaptic mechanism mediated by the activation of Ia afferents, additional contributions could originate from postsynaptic and reciprocal inhibition, as well as from mechanisms mediated by the activation of other muscular and cutaneous afferents.

An intriguing finding is that the amount of vibratory inhibition of the H reflex, expressed as a percentage of the control H reflex response (Hvib/H), is altered in patients with spasticity (Gillies et al , 1969, Burke and Ashby, 1972, Delwaide, 1973, Ashby and Verrier, 1975, 1976) More specifically, the Hvib/H ratios were found to be higher (64 3 $\pm$ S D 12 6%, Ashby and Verrier, 1976, 83 2 $\pm$ 20 6% Hale and Chan, 1986a) in chronic hemiplegic spasticity than in normals (41 5%, Ashby and Verrier, 1976, 44 6 $\pm$ 32 4% Hale and Chan, 1986a). Based on the mechanisms reviewed above, an increase in the Hvib/H ratio may partly result from a reduction in presynaptic inhibition Furthermore, diazepam, which has been found to increase presynaptic inhibition in animals (Stratton and Barnes, 1971), decreased Hvib/H ratios in spastic man (Delwaide, 1971, 1985) Consequently, indirect evidence suggests that reduced presynaptic inhibition, demonstrated by increased Hvib/H ratios and the response to diazepam, may be one factor contributing to spasticity in man

(iv) Plastic Changes

Following lesions in the central nervous system, new or altered synaptic connectivity may occur due to plastic changes. As early as 1911, Cajal presciently suggested 'na' prolonged morphological and physiological changes in synaptic connections between nerve cells could occur. Subsequently, plasticity has been defined as any persistent change in the functional properties of single neurons or neuronal aggregates (Tsukahara, 1981) This section will focus on the plastic mechanisms which may contribute to the development of spasticity.

Plastic changes associated with CNS lesions include altered effectiveness of synaptic usage due to 'unmasking' of latent synapses, release of transmission in existing reflex pathways, denervation supersensitivity and/or collateral sprouting resulting in the formation of new synapses. Each of these mechanisms may contribute to the development of spasticity Unmasking and release may occur immediately following CNS lesions, while denervation supersensitivity and sprouting appear within several days to weeks (Mendell, 1984)

Unmasking. Within several hours of spinal cord transection in the intact anesthetized cat, the population of motoneurons in the medial gastrocnemius responding to single Ia fibre stimulation increased from 80% to 99% (Nelson et al., 1979; Nelson and Mendell, 1979) These authors also reported an increase in EPSP amplitude that took hours to develop but returned to normal 5 days after transection The short time course of these changes in projection frequency and EPSP amplitude suggested the activation of already existing but previously 'masked' synapses. This mechanism could also explain the early finding of recovery of diaphragm paralysis due to cervical hemisection in the dog following transection of the contralateral phrenic nerve (Porter, 1895). This recovery may have resulted from the activation of a weak, normally ineffective, crossed descending pathway, caused by the sudden increase in respiratory drive. Unmasking may also have been the mechanism responsible for the immediate increase observed in reflex function following acute spinal transection in the cat (Wall, 1967; Mendell, 1972). Thus, unmasking appears to be a likely mechanism for immediate changes in reflex function which may contribute to spasticity. However, alterations in non-neuronal humoral mechanisms may also have contributed to these effects (Wall, 1988).

Release of Transmission in Reflex Pathways. There is also much evidence for 'switching' or release of transmission in reflex pathways following CNS lesions. This may result in changes in the adequate stimulus for evoking some reflex behaviour. For example, the normal pathway for bladder emptying in the cat consists of a spino-bulbospinal reflex initiated by a proprioceptive stimulus (distension). Following spinal transection interrupting this reflex arc, bladder emptying recovers but the pathway becomes a segmental one mediated by a cutaneous stimulation (Thor et al., 1986). Another example of reflex switching derives from flexor reflex afferent pathways (FRA). These afferents share a common polysynaptic reflex pathway which serves to predominantly facilitate the flexor and inhibit the extensor

motoneurons. However, transmission in these FRA pathways is under differential supraspinal control (Holmqvist and Lundberg, 1961; Baldissera et al , 1981) It is suppressed by descending monoaminergic and non-monoaminergic dorsal reticulospinal systems, and facilitated by the corticospinal and rubrospinal tracts. Lesions in the inhibitory dorsal reticulospinal tract and the pyramidal tract may 'release' the FRA from supraspinal control The relative degree to which the balance between inhibitory and facilitatory descending control is upset by supraspinal lesions may contribute to the appearance of either flexor or extensor hypertonicity Thus, the release from descending control may explain either the enhanced flexor tone reported in spinal spasticity (Kugelberg, 1962, Dimitrijevic and Nathan, 1968, Young, 1973), or the excessive extensor spasticity following brain lesions (Bobath, 1978).

Denervation Supersensitivity Denervation supersensitivity may result from changes in the physiology or morphology of presynaptic boutons responsible for neurotransmitter release or of postsynaptic receptors mediating transmitter action While several studies have demonstrated increased sensitivity to neurotransmitters following CNS lesions, conclusive evidence for either a presynaptic or postsynaptic locus of this effect is lacking Following lesions of the serotonergic and catecholeaminergic pathways in the rat spinal cord, the terminals of the descending fibres disappeared from the ventral horn This degenerative process developed during the initial two weeks following injury and was accompanied by an increased sensitivity to neurochemical agents such as the noradrenergic agonist, clonidine (Nygren et al., 1974). Similarly, in the first few days after spinal cord transection in the rat, an increased spontaneous hindlimb EMG activity was observed following the administration of 5-hydroxytryptophan. This sensitivity progressively increased by up to 1000% during the subsequent 30 days (Bedard et al., 1979). This suggested an enhanced sensitivity of serotonergic receptors. More direct evidence for a postsynaptic locus of denervation supersensitivity may be derived from binding studies. Nakata et al (1979) investigated the binding of ^{3}H-labeled substance P in deafferented rabbit spinal cord. They demonstrated an increased number of receptor sites while the affinity of these sites for substance P was unchanged

Denervation supersensitivity is a mechanism which has a similar time course as sprouting and may very well contribute to the development of spasticity

Sprouting. In the peripheral nervous systems, after partial transection of a motor nerve, collateral sprouts of intact motor fibres can reinnervate the deafferented muscle and re-establish functional connections (Edds, 1953; Brown and Ironton, 1987). Sprouting also occurs in the CNS, but it is far less prolific in the adult than in the neonate, and is restricted to specific neuronal pathways. For example, after destruction of the nucleus gracilis, the number of cells responding to forelimb stimulation in the ventral posterior lateral nucleus of the rat thalamus expanded to occupy almost 60% of the area previously representing the hindlimb (Wall and Egger, 1971). Sprouting has been described in noradrenergic bulbospinal (Bjorklund et al., 1971) and corticospinal fibres (Kalil and Reh, 1978) It is present in the hippocampus, the thalamus (Wall and Egger, 1971), the red nucleus (Tsukahara, 1981; Nieoullon and Dusticier, 1983), and the cerebral cortex (Purpura, 1961; Tsukahara, 1981) Sprouting has not been demonstrated in sensory relay nuclei such as spinal trigeminal nuclei (Kerr, 1972), nor in the rubrospinal fibres (Castro, 1978).

Evidence for sprouting may be derived anatomically, physiologically and functionally An increase in the number of afferent fibres on the affected side of the hemisected cord was originally demonstrated by light microscopy in adult rats, cats and primates (Liu and Chambers, 1958; McCouch et al., 1958). The finding of an increased density of dorsal root projections was later confirmed in cats (Murray and Goldberger, 1974) but not in rats (Malmsten, 1983; Rodin and Kruger, 1984), indicating some species differences. The original morphological evidence for sprouting awaited the development of higher resolution techniques for confirmation. Thus, it was found by electron microscopy that, in the rat septum, the sprouting axons made apparently functional morphological connections with vacated synaptic sites after interruption of fimbrial fibres (Raisman and Field, 1973). There is also some evidence for sprouting of the interrupted descending terminals following cord lesions (Prendergast and Misantone, 1980). That the new connections made in the spinal cord may be

functional has been demonstrated by an increase in the size of the cord dorsum potential (McCouch et al, 1958; Mendell et al., 1978), or an increase in the amplitude of the EPSP (Nelson and Mendell, 1979) associated with morphological evidence for sprouting

The slow time course of sprouting may be consistent with the gradual recovery of function simultaneously with the development of spasticity There are however, disagreements in the actual time course of sprouting between species and between different parts of the CNS. The rise in synaptic contacts in the rat septum occurred almost at once following fimbrial lesions and reached completion by one month (Raisman and Field, 1973) In the dorsal horn, however, the increased fibre count following midthoracic hemisections in the cat appeared only after a period of 2 weeks (McCouch et al, 1958) This is similar to the time course of recovery of motor function following spinal transection (Goldberger and Murray, 1978), although a degree of variability has been reported Some investigators noted the return of a certain level of motor control over a 4 to 21 day period (Hultborn and Malmsten, 1983), while others, only after a minimum of 2 weeks (Murray and Goldberger, 1974) The latter and not the former time course coincides with the time course of sprouting in several brain and spinal cord structures (Tsukahara, 1981) In contrast, the increase in segmental reflex excitability may precede the return of motor function Enhancement of spinal reflexes has been alternatively reported after periods of hours to days (Hultborn and Malmsten, 1983), and up to two weeks (Murray and Goldberger, 1974) following spinal hemisection or transection in the cat. On the other hand, polysynaptic reflexes (e.g. crossed extensor reflexes) were found to increase only after 7 days in the transected, hemi-deafferented cat. This increase appeared to be correlated with an increased dorsal root projection (Murray and Goldberger, 1974; Goldberger and Murray, 1974), suggesting a sprouting mechanism

From the findings to date, therefore, it seems likely that the gradual development of spasticity may be related to sprouting mediating some recovery of motor function and of polysynaptic reflexes rather than the mere return of segmental reflex activity.

(v) Other Mechanisms

In spasticity, other reflex pathways also undergo characteristic changes. Reciprocal inhibition mediated by a disynaptic pathway via the Ia inhibitory interneuron is altered. For example, in the lower limb of hemiplegic subjects, reciprocal inhibition from spastic ankle extensors to pre-tibial flexors is enhanced. This mechanism may contribute to the marked weakness in the latter muscle group (Yanagisawa et al., 1976, Tanaka, 1983). In the upper limb, Day et al. (1987) and Nakashima et al. (1989) used radial nerve conditioning of spastic wrist flexor H reflexes, to show that disynaptic reciprocal inhibition from extensors to spastic flexors of the forearm is reduced.

Recurrent (Renshaw) inhibition may also be altered in spasticity. Renshaw cells are small interneurons in the ventromedial horn of the spinal cord. They are monosynaptically excited by axonal recurrent collaterals and form inhibitory synapses with neighbouring motoneurons (Renshaw, 1941). One of the functions of Renshaw inhibition may be to limit the firing frequency of motoneurons and confine activity to a specified motoneuronal pool (Veale et al., 1973). In addition to their direct inhibitory effects on other motoneurons, Renshaw cells inhibit Ia inhibitory interneurons (Hultborn et al., 1971). This may cause an indirect disinhibition of the antagonistic motoneurons. Katz and Pierrot-Deseilligny (1982) compared the presumed Renshaw inhibition of conditioned M responses at rest and during voluntary activation between normal and spastic subjects. They used a complex methodology involving the conditioning of maximal M responses with a preceding H reflex stimulus timed to block the test motoneuronal antidromic volley. There was no evidence for a decrease in the excitability of Renshaw cells in spastic patients at rest, suggesting that a lack of recurrent inhibition may not contribute to hypertonicity. However, in contrast to normal subjects, Renshaw inhibition was absent during postural and voluntary contractions. Thus, although probably not contributing to the development of spasticity *per se*, altered recurrent inhibition may contribute to changes in voluntary muscular activation in patients with spasticity.

In summary, central projections to Ia inhibitory interneurons and Renshaw cells may

be disturbed following central nervous system lesions These alterations in the descending control of reflex pathways may contribute to the development of spasticity

(vi) Non-reflexogenic Contributions to Hypertonia

Although spasticity can largely be attributed to changed excitability in reflex pathways, altered mechanical properties and behavior of motor units may also be contributory Following upper motor neuron lesions, there may be a redistribution in the types of remaining motor units Mayer et al. (1984) examined the behaviour of individual gastrocnemius motor units via direct motoneuronal recording in chronic spinal cats up to 23 weeks following complete spinal transection. They found that all motor units, including FF (fast-fatiguable) type, exhibited some decreases in force output, mean fibre area, and isometric twitch contraction times They also found that the proportion of F (int; fast-intermediate) motor units was greater than normal FR (fast, fatigue-resistant) and S (slow-twitch) units were less numerous, while the proportion of FF units did not differ from normal. Histochemical examination revealed similar changes in the corresponding fibre types. In contrast, several studies have reported an equal decrease in the number of motor units of all histochemical types following spinal cord transection in cats and rats (Cope et al, 1986; Eidelberg et al., 1989).

In man, however, different patterns of motor unit changes occur depending on the location of the CNS lesion. In patients with spasticity due to complete spinal cord transection, an equal decrease in fast- and slow-twitch fibres has been reported (Edstrom et al, 1973). In contrast, in hemiparetic patients, Edstrom (1970) found a greater proportion of slow-twitch fibres in antigravity muscles (i e. ankle plantarflexors, elbow flexors) This was possibly due to a selective atrophy of fast-twitch fibres (McComas et al , 1973) Dietz et al (1986), while unable to demonstrate an altered proportion of motor unit types, similarly reported a selective atrophy in fast-twitch fibres in the gastrocnemius muscles of 4 hemipare-

tic subjects. These few studies in man classified the fibres only into fast or slow types Thus, the apparent discrepancy between animal and human findings may be attributable to changes in the number of F(int) fibre types, as suggested by Mayer et al. (1984), but this possibility has not yet been investigated in man.

In hemiplegic spasticity, the total number of functioning motor units was found to be decreased on the affected side to 50% of control in extensor digitorum brevis (McComas et al , 1973) and to 57% of control in soleus muscles (Sica and Sanz, 1976) This is consistent with recent results in the rat, indicating significant decreases (approximately 69% of control) in the total number of functioning motor units following bilateral ablation of the motor cortex (Eidelberg et al , 1989). Mean contraction times of the remaining fast-twitch units may also be slower in hemiparetic patients (Young and Mayer, 1982).

Mechanisms which may be responsible for motor unit and muscle fibre changes in spasticity include disuse atrophy (Edstrom et al., 1973, McComas et al., 1973), interconversion between slow- and fast-twitch muscle fibres (Lomo et al., 1980), and trans-synaptic degeneration of motoneurons induced by cortical lesions (McComas et al., 1973, Eidelberg et al., 1989).

The changed proportions of motor units may be partially responsible for the increased tone of spastic muscle. From animal experiments, it has been shown that slow-twitch muscle fibres themselves offer a small but slightly greater resistance to stretch than fast-twitch fibres, due to their viscoelastic properties alone (Browne, 1976). The increased proportion of slow-twitch muscle fibres found in spastic muscle could be, therefore, partly responsible for the production of increased muscular tension in spastic hemiplegia. Some support for this hypothesis derives from recent findings of increased Achilles tendon tension during the stance phase of gait (Dietz and Berger, 1983; Berger et al., 1984). Tension was recorded from the Achilles tendon by a laterally attached transducer. Compared to the unaffected side, tension in the tendon was augmented without concomitant increases in triceps surae EMG. The possibility that the increased tension may have been due to decreased co-contraction was ruled out by concomitant tibialis anterior EMG recordings. These findings suggest that

changes in tendon characteristics and/or muscle fibre types alone could augment muscle tone, but the extent of this possible contribution is unknown

Although changes in motor unit types and muscle fibres may contribute only a small amount to the increased resistance in spastic muscle, their possible contribution cannot be overlooked. As it will emerge below, alterations in the distribution and characteristics of motor unit types following upper motor neuron lesions may also contribute to problems in voluntary muscle activation.

VOLUNTARY MOTOR FUNCTION

Several abnormalities in muscle activation patterns have been described in patients with spasticity due to central lesions. Qualitative studies have reported an inability to maintain a steady motoneuronal discharge (Kranz, 1981) and, specifically, an impaired control of motor unit frequency (Petajan, 1983). These deficits may contribute to the reported impairment in whole muscle recruitment and termination during various active tasks (Benecke et al., 1983, Schieppati et al., 1985, Hammond et al., 1988b). Hammond and her group (1988b) studied maximal isometric contractions of wrist flexor and extensor muscles in hemiparetic subjects with the use of monopolar needle electromyography. They reported abnormally prolonged recruitment of EMG activity. Earlier termination of EMG activity was attributed to an inability to maintain a prolonged contraction. The duration of contraction in paretic wrist extensor muscles was reduced to half of that obtained in age-matched control subjects (3.08 sec compared to 5.94 sec for a 6 sec contraction) Although, in general, the ability to maintain prolonged contractions was better in spastic wrist flexors than in paretic extensors, it was nonetheless significantly less than that in controls (approximately 4.5 sec, Fitts et al., 1989) In a study of spastic amyotrophic lateral sclerosis patients performing quasi-isometric ankle plantarflexions, the termination of soleus EMG activity was delayed and this was associated with an abnormal facilitation of the soleus H reflex (Schieppati et al., 1985) This finding suggests that an inhibitory mechanism was reduced or absent in these patients Termination of muscular activity is also abnormally prolonged during rhythmic functional activities in

patients with spinal paraparesis. For example, in two separate studies using similar measurement techniques, lower limb extensors and flexors displayed enhanced and prolonged activity during normally quiescent phases of the bicycling and gait cycles (Benecke et al., 1983; Fung and Barbeau, 1989)

Normally, contraction of a muscle group is associated with reciprocal inhibition of its antagonists (Hultborn et al , 1976c). In spastic patients, abnormal co-contraction of agonist and antagonist muscles is frequently observed. However, some of the findings are contradictory and the mechanism(s) are unclear. Abnormal co-contraction in spasticity has been reported during some isolated movements in the upper (Prevo et al , 1982; Hammond et al , 1988a) and lower limb (McLellan, 1977, Knutsson, 1983), and during complex behaviours such as locomotion (Knutsson and Richards, 1979).

Co-contraction, expressed as the ratio of the antagonist to the total (agonist plus antagonist) EMG activity, was reportedly increased during both wrist extension and flexion Co-contraction ratios were 0.30 in spastic compared to 0.07 in normal controls for wrist extension, and 0 08 compared to 0.02 respectively for wrist flexion (Hammond et al., 1988a) Other studies have expressed co-contraction as the ratio of EMG area when the muscle acted as antagonist to its activity when acting as agonist (McLellan, 1977; Prevo et al , 1982). Abnormal co-contraction has also been described during isolated knee flexion and extension movements, and in the stance phase of gait in spinal cord injured (Fung and Barbeau, 1989) and in some hemiparetic subjects (Knutsson and Richards, 1979).

Several mechanisms may contribute to the abnormal motor control in spasticity. The deficit in voluntary motor control following cortical lesions has been partly attributed to alterations in the control of motor units following upper motor neuron lesions as discussed above. In decerebrate, dorsally hemisected cats, for example, the slope of the EMG/force relationship was found to be increased tourfold compared to control (Rymer et al , 1979). The changed relationship was attributed to a fall in the mean motor unit discharge rate so that the force output for each unit was substantially decreased. Thus, the production of a given level of force necessitated the recruitment of a greater number of motor units. These animal

findings were also extended to 17 hemiplegic subjects in whom, at least half had increased EMG/force relationships in spastic biceps-brachialis muscles (Tang and Rymer, 1981) Indeed, functional alterations in motor units may contribute to changes in EMG/force relationships in spastic muscle. However, these changes alone do not adequately explain the abnormalities in recruitment patterns of agonist and antagonistic muscles. Clearly, there are other factors involved.

In this connection, deficits in voluntary control of movement have been attributed to alterations in the organization of segmental reflex activity, such as enhanced stretch reflexes (McLellan, 1977; Knutsson and Martensson, 1980; Corcos et al , 1986), disordered reciprocal inhibition (Yanagisawa et al., 1976), and abnormal descending commands (Feldman, 1986) These possible contributory factors will now be discussed

The evidence that hyperactive reflexes interfere with voluntary movement is contradictory. Part of the controversy may be related to the possibility that the relationship between reflex and motor function may be differentially organized in the upper and lower limbs For example, Corcos et al. (1986) studied ballistic ankle dorsiflexions in the lower limbs of a mixed group of spastic subjects. Attempts to dorsiflex rapidly were impeded by abnormal antagonist EMG bursts in 3 out of 8 subjects The abnormal activity appeared to be reflex in origin, since it was velocity dependent and occurred at a latency consistent with stretch reflexes in the calf muscle (50 msec). Furthermore, the antagonist bursts may have contributed to reversals in movement direction evident in the position trace and reported previously by others (Dimitrijevic and Nathan, 1967). Evidence to the contrary has been found in the upper limb of spastic subjects. Sahrmann and Norton (1977) reported that isotonic elbow flexion and extension movements were slower and of smaller amplitude in spastic hemiparetic patients compared to normal controls. In these patients, EMG activity in the spastic elbow flexors during isotonic flexion movements was not correlated with hyperactive reflex activity evident in the EMG of the antagonist muscle triceps. This suggested that enhanced reflex activity did not contribute to the movement deficit. Instead, the deficit was associated with limited and prolonged recruitment and delayed termination of agonist contraction as well as

some degree of co-contraction. McLellen et al. (1985) also showed that the disorder in voluntary motor control may not be related to hyperactive stretch reflex activity. Their conclusion was based on the finding that pharmacological amelioration of reflex hyperactivity in the lower limb was not necessarily correlated with improved voluntary movement (Duncan et al., 1976, McLellan, 1977) However, in these studies, the reflex hyperactivity was measured at rest. It is well known that reflexes are modulated differently at rest from that during voluntary movement. In contrast to the resting condition, stretch reflex gains (measured as stiffness) are increased during voluntary movement, at least at low and intermediate force levels up to 50% maximal voluntary contraction in normal subjects (Marsden et al , 1976, Matthews, 1986; Gottlieb et al , 1970, Toft et al. 1989). In spasticity, reflex gains are similarly modified during voluntary effort and do not appear to differ from normal (Lee et al., 1987) Therefore, it is not surprising that a decrease in hyperactive stretch reflexes measured at rest did not result in an improvement in voluntary motor function in spastic subjects. In summary, the contribution of abnormal stretch reflexes to disturbed voluntary motor control in spasticity remains unclear

Along with the possible contribution of increased stretch reflexes, the deficit in voluntary activation in hemiparesis can also be ascribed to a disruption in descending commands. This may be expressed as a disordered supraspinal control of spinal interneurons responsible for reciprocal inhibition (see section (v) on Other Mechanisms), or as an imbalance between descending reciprocal and coactivation commands Two theories of motor control have emerged, based on early observations of reciprocal activity and coactivation Sherrington's (1909) work suggested that movements were organized in a reciprocal manner Later, Tilney and Pike (1925) proposed that muscular coordination depended primarily on synchronous coactivation of opposing muscle groups. Movements requiring precision or made at high velocities with heavy loads are characterized by some degree of co-contraction (Bouisset and Lestienne, 1974; Patton and Mortensen, 1971). On the other hand, reciprocal patterns of activation are more likely to accompany isometric contractions (Smith, 1981). A coordinated theory of motor control proposed by Feldman (1980a,b), based on these con-

cepts, suggests that movement is organized according to different combinations of reciprocal and/or co-contraction commands originating from higher centres Empirical support for this theory comes from the work in non-human primates. Overlapping regions of the pre-central motor cortex controlling reciprocal and coactivation commands for movements of the wrist, have been demonstrated (Humphrey and Reed, 1983) These control regions functioned independently of somatosensory feedback Similarly, other researchers have found that specific areas of the cortex (Cheney et al., 1982), cerebellum (Smith, 1981) and red nucleus (Cheney and Mewes, 1986) can be selectively activated during upper limb movements requiring reciprocal movement or coactivation Thus, in man, lesions of the pre-central cortex may result in disturbances of the proposed coordinated system between reciprocal and coactivation commands

In summary, disordered voluntary activation of spastic muscle in hemiplegic subjects may result from altered physiological properties of motor units, decreased stretch reflex thresholds leading to hyperactive and inappropriate stretch reflex activity, and/or disrupted descending commands resulting in increased co-contraction and decreased reciprocal inhibition.

Further research oriented towards a greater understanding of the mechanisms underlying spasticity is still needed. In addition, since spasticity is a complex phenomenon, future studies should incorporate comprehensive and representative measurement

MEASUREMENT OF SPASTICITY

It seems to be of general consensus that no single measure is a fully adequate descriptor of the changes associated with spasticity. As discussed above, the nature of spasticity is probably multifactorial. The relative contribution of each factor to the clinical manifestation of spasticity has not been clearly elucidated. Due to both the tonic and phasic nature of spasticity, recent investigators favour a barrage of measures, to achieve a composite index of spasticity (Dimitrijevic et al., 1983, Delwaide, 1985). This section will review commonly used clinical and physiological measures

1. Clinical Measures of Spasticity

Clinically measured hypertonia is by itself only one manifestation of spasticity, yet it is often used as the sole indication of this complex phenomenon. Muscle tone is measured as the resistance felt by the examiner to passive movement of the limb A widely employed three-point scale rates '1' for mildly, '2' for moderately, and '3' for severely increased tone (Ashworth, 1964) This resistance has been attributed to increased tonic stretch reflex activity, which varies linearly with the velocity of the ramp stretch over a wide range of velocities (80-400°/sec, Burke and Lance, 1973) Stretch reflex responses are also correlated with initial muscle length in the cat (Houk et al , 1981) and in man (Burke et al , 1970) Indeed, direct recordings of primary and secondary spindle afferents during ramp and hold stretches in the cat, revealed that both types of receptors responded to the product of muscle length and velocity of stretch (Houk et al., 1981). Thus, variability in clinical measurement of tone is related to the initial position of the limb being tested (Burke et al., 1970) and the velocity of the passive displacement (Burke and Lance, 1973; Meyer and Adorjani, 1980). Whether or not the velocity of displacement remains constant throughout the movement can be another contributing factor. As well, the position of the subject (Bobath, 1978), his alertness and the environmental conditions in the testing room such as temperature and noise (Stam and Tan, 1987), may also influence the reflex output. Finally, in subjective testing, factors such as the examiner's perception of the resistance being offered to the movement and the total time required for testing may contribute to the low reliability.

Other clinical measures used to assess spasticity include the excitability of tendon reflexes, the presence and severity of clonus, and clasp-knife reflexes. Tendon reflexes, evoked by a rapid stretch of the tendon via a hand-held reflex hammer, are employed clinically to assess the excitability of phasic stretch reflexes. Clinical evaluation consists of estimating the amplitude of the reflex response. This is expressed either qualitatively (i.e. 'sluggish' to 'brisk') or quantitatively via numerical rating scales. The amplitude of this reflex is reported to be proportional to the intensity of tendon percussion for soleus and quadriceps

(Stam and Tan, 1987), but not for biceps brachei (Stam and van Crevel, 1989) In these studies, the intensity of the stimulus was measured by a piezo-electric transducer attached to the hammer, which delivered a signal proportional to its deceleration during the tap The variability of the responses in soleus or quadriceps was found to be similar when using either a hand-held (coefficient of variation, CV = 17 9% and 25 5% respectively in the two muscles) or a mechanically-driven hammer (CV = 19 3% and 31 7% respectively) Clinical testing, however, should be done using maximal tendon percussion, since the examiner cannot reproduce a constant sub-maximal stimulus intensity

Clonus, a rhythmical (5-8 Hz) self-sustaining muscular contraction, is elicited by a sudden and maintained stretch. Conflicting evidence about the modifiability of clonus due to peripheral factors such as a change in the mass of the foot (Dimitrijevic et al , 1980, Rack et al., 1984) has been reported In the former study, no change in clonus frequency was found after a weight was added to the foot or an external viscous drag was created However, the location and effect of the imposed load on the foot was unclear These made the results difficult to evaluate. In the latter study, the external load was attached to the foot in such a way that the mass was increased, while the velocity of the perturbation evoking the clonus was unchanged Under these conditions, clonus frequency was reduced to 2 6 Hz with increasing loads These findings suggest that clonus can be influenced by peripheral factors Notwithstanding these results, it is generally agreed that clonus is due to a central mechanism such as a self-sustaining oscillation in the stretch reflex pathway (Dimitrijevic et al , 1980; Rack et al., 1984). Clinically, clonus is quantified by numerical scales indicating its presence or absence and the number of clonic beats elicited.

The clasp-knife phenomenon is an example of autogenic inhibition manifested by a steadily increasing resistance to passive stretch of the limb, which suddenly releases after a critical tension is reached (Burke and Lance, 1973). It has been demonstrated in lower limb extensors of the decerebrate cat, and is dependent on muscle length and initial force (Burke et al, 1970; Rymer et al., 1979). Findings in the cat suggest that clasp-knife reflexes are mediated by non-spindle group II, III and IV muscle afferents which are normally inhibited by

tonic activity in descending pathways (Rymer et al., 1979). Following upper motor neuron lesions, clasp-knife reflexes may be released from descending inhibitory control (Burke et al., 1972; Rymer et al., 1979). Clinical scales have been used to note the presence or absence of these reflexes.

Other clinical tests evaluate disturbances in voluntary motor activity due to spasticity. The electromyogram can be used to qualitatively analyze motor function in terms of the temporal patterns of muscular activity during functional tasks such as locomotion or bicycling (Knutsson and Richards, 1979). Measures such as functional scales (e.g. Barthel index, Mahoney and Barthel, 1965) are also commonly used. Such measures of overall motor performance are, however, difficult to interpret with respect to the quantification of abnormal muscle tone, as there is usually some degree of paresis or paralysis associated with spasticity.

2. Physiological Measures of Spasticity

Early studies of spasticity attempted, unsuccessfully, to quantify the separate contributions of reflexogenic and non-reflexogenic factors to abnormal muscle tone. Non-reflexogenic factors are defined as the passive resistance offered by spastic muscles to joint displacement due to muscle rheologic factors (inherent stiffness of muscle fibers) alone (Long et al., 1964; Nashold, 1966; Norton et al., 1972). Only recently has a method been developed to separate the passive properties from the reflex components of the stretch response in man (Sinkjaer et al., 1988), but it has not yet been applied to patients with spasticity.

More reliable approaches use torque- or servo-motor controlled limb displacements. These studies have focused on the quantification of the reflex behaviour of spastic muscles, largely due to exaggerated short and long-latency stretch reflexes (Chan et al., 1979; Gottlieb et al., 1978). Analysis of stretch reflex activity provides information about mono- and polysynaptic segmental and propriospinal pathways. Stretch reflex parameters are changed in hemiplegic spasticity. Thresholds are decreased (Powers et al., 1988), while reflex magnitudes are increased in terms of peak-to-peak amplitude, area and durations (Berardelli et

al., 1983; Hale and Chan, 1986a; Dichgans and Diener, 1987). Although the magnitude of stretch reflexes have been reported to be broadly correlated with the severity of spasticity (Berardelli et al., 1983; Cody et al., 1987), this relationship has not been convincingly quantified and presented. The stretch reflex response is dependent on the initial muscle length (Burke et al., 1970), the velocity of stretch (Burke and Lance, 1973) and the level of background EMG (Powers et al., 1988). Caution should be employed when interpreting changes in stretch reflexes evoked at rest, since the excitability of the population of motoneurons may not be at a uniform level. To avoid this possible source of variability, motoneuronal excitability could be brought to a constant level by requiring the subject to maintain a steady contraction. This, however, would preclude the study of stretch reflex threshold changes. Thus, although stretch reflexes are increased in spasticity, these changes must be interpreted with caution. As well, their relationship to the seventy of clinically measured spasticity is unclear.

Hoffmann (H) reflexes are related to phasic reflex activity and reflect the excitability of the motoneuronal pool via the activation of the presumed monosynaptic stretch reflex arc (Hoffmann, 1918; Schiepatti, 1987). At least the first component of the soleus H reflex is believed to be monosynaptic, but polysynaptic inputs from the activation of group Ib, II, and cutaneous afferents can also influence the waveform and magnitude of the response (Burke, 1983; Burke et al., 1983, 1984). Furthermore, the volley eliciting H reflexes in the calf is not limited to the activation of the afferents in the tibial nerve. It has also been shown to excite afferents from the intrinsic muscles and skin of the foot (Burke et al., 1983). The H reflex in the calf has traditionally been accepted as the electrical equivalent of the Achilles tendon jerk. There are, however, important differences in the electrically and mechanically evoked reflexes. H reflexes in the calf are inhibited when the ankle is passively dorsiflexed, whereas tendon jerks are enhanced (Burke et al., 1983). In addition, percussion of the Achilles tendon gives rise to a dispersed volley in soleus afferents which can begin 3.5-7.0 msec following percussion and last up to 30 msec. The percussion wave can spread to synergist and antagonist muscles, as well as the skin (Burke et al., 1983). In contrast, the afferent volley in

response to electrical stimulation is more synchronous and the spread of the current is limited (Burke et al., 1983). Thus, H reflexes and tendon jerks are neither entirely equivalent nor exclusively monosynaptic.

In normal individuals at rest, H reflexes can be evoked consistently in the calf muscles (Magladery and McDougal, 1950), quadriceps (Magladery et al., 1951), masseter (Godaux and Desmedt, 1975), extensor digitorum longus (Deschuytere and Rosselle, 1971) and some of the intrinsic muscles of the hand and foot (Thomas and Lambert, 1960; Upton et al., 1971). Whereas H reflexes have been repeatedly elicited in the tibialis anterior in patients with upper motoneuron lesions (Teasdall et al., 1952; Hohmann and Goodgold, 1961; Mayer and Mawdsley, 1965), they are rarely present in normal adults at rest (Deschuytere and Rosselle, 1971).

H reflex testing is susceptible to a large number of methodological influences. When used alone, they display a wide inter-subject variability and low reliability. Methodological issues contributing to this variability include: electrode placement, the anatomical distribution of sensory and motor fibres in the nerve being stimulated, the amount of subcutaneous tissue (Hugon, 1973; Ashby et al., 1974), and changes in baseline EMG level (Verrier, 1985). Other factors such as attention, affect, and the position of the subject (Paillard, 1955; Mayer and Mawdsley, 1965), as well as the degree of agonist and antagonist contraction or stretch (Magladery et al., 1951; Angel and Hofmann, 1963; Burke et al., 1983), also contribute to the variability of the H reflex amplitude. Therefore, attempts have been made to normalize H reflexes as H/M ratios. The maximal H reflex is expressed as a percentage of the maximal M response thought to represent the activation of the total motoneuronal pool and has been used as a more reliable measure of segmental motoneuronal excitability (Paillard, 1955; Landau and Clare, 1964; Ongerboer de Visser et al., 1989). In hemiplegic spasticity, H/M ratios are increased (Garcia-Mullin and Mayer, 1972; Ashby and Verrier, 1976; Hale and Chan, 1986a) although a large variability in this measure too, has been reported (i.e. 4.4% to 85.5% in 21 chronic hemiplegic patients; Garcia-Mullin and Mayer, 1972). Some studies have also shown a considerable overlap of the values obtained in spastic and normal limbs.

Therefore, their use as a measure of motoneuronal excitability has been disputed However, some of this variability may be due to the effects of age on H/M ratios (Delwaide, 1971, Ongerboer de Visser et al., 1989). Both normal and spastic subjects show a significant decline in H/M ratios with increasing age. In normal subjects, H/M ratios reportedly decrease from a mean of approximately 80% at age 25 to 40% at age 75 (Ongerboer de Visser et al , 1989). Thus, aside from methodological considerations, controlling for age should increase the reliability of this measure.

The amount of the H reflex inhibition during vibration, expressed as a percentage of its control value (Hvib/Hctl), has been used as an indicator of the amount of presynaptic inhibition of the presumed monosynaptic stretch reflex arc (Gillies et al , 1969). However, some caution is recommended in the interpretation of Hvib/Hctl ratios as a measure of presynaptic inhibition alone (Burke et al., 1976; and see discussion in section (iii) Presynaptic Inhibition). In spastic hemiplegic subjects, vibratory inhibition of the H reflex is reduced compared to normals. This finding is interpreted by some investigators to mean that presynaptic inhibition may be diminished in spasticity (Delwaide, 1971; Burke and Ashby, 1972). Although Hvib/Hctl ratios may be partial indicators of the amount of presynaptic inhibition, they have been found to correlate only poorly with the degree of spasticity (Hayat, 1979).

The above measures describe changes in segmental and plurisegmental reflex pathways during static conditions or at rest. Other physiological measures examining interneuronal pathways include flexor reflexes and H reflex recovery curves, conditioned by homonymous and/or heteronymous afferent input. Not surprisingly, none of these measures of static reflex function correlate very highly with the degree of clinically measured spasticity, possibly reflecting the more dynamic nature of the disorder. Indeed, measures of static reflex function alone provide little information about the extent to which changes in excitability of spinal circuitry affect everyday functional activity. Due to the diverse manifestations of upper motor neuron lesions with spasticity, recent investigators favour the use of multiple indicators which assess clinical, reflex and voluntary function simultaneously (Dimitrijevic et al., 1983, Delwaide, 1985).

Attempts to correlate spasticity with functional activity have likewise met with little success. This may be partly due to the heterogeneity of the spastic populations studied and the lack of comprehensive investigations. Some aspects of impaired voluntary motor function in spasticity have already been discussed (see section on Voluntary Motor Function). Here, the studies relating the deficit in voluntary function to the level of spasticity will be reviewed.

One of the features distinguishing the activation of spastic muscles has traditionally been the presence of an abnormal amount of co-contraction. Co-contraction normally occurs during movements requiring precision or made at high velocities with heavy loads (Bouisset and Lestienne, 1974; Patton and Mortensen, 1971). In some patients with spasticity, however, an abnormal degree of co-contraction has been found during both isometric (McLellan and Hazan, 1982) and isotonic movements (McLellan, 1977; Knutsson and Martensson, 1980). McLellan (1977) recorded the electromyograms from the quadriceps and hamstring muscles during active and passive cyclical knee flexion and extension movements. He found that most patients with mild to moderate spasticity showed little or no co-contraction during voluntary movement. Co-contraction was expressed as the area ratio of the EMG recorded when the muscle acted as antagonist to its activity when acting as agonist. Ratios in quadriceps were elevated in all 11 patients with spasticity (mean ratio approximately 48%) compared to normal (17%), but these values were not derived from movement performed at equal velocities. The effects of oral baclofen was contrasted with placebo in 6 patients. Co-contraction ratios were found to decrease in only half of the patients, despite a significant reduction in passive stretch reflexes and spasticity in all six. Thus, although spasticity was decreased, the amelioration did not appear to be related to an improvement in voluntary knee function in all subjects.

Complex behaviours such as bicycling (Benecke et al., 1983) and locomotion (Knutsson and Richards, 1979; Fung and Barbeau, 1989) have also been studied, in an attempt to correlate the degree of spasticity with functional impairment. In one study, three categories of disturbed gait in hemiparetic subjects were classified according to the patterns of movement and muscle activation. The authors found that differential response to therapeu-

tic interventions may be related to the type of motor disturbance (Knutsson and Richards, 1979). Using a dynamic index of spasticity, however, Benecke et al. (1983) and Fung and Barbeau (1989) recently reported the opposite finding. The dynamic index, which expressed the ratio of integrated EMG in a pre-determined 'off' window (when EMG is usually silent) of the normalized bicycling or gait cycle, to that in an 'on' window, was sensitive to improvements in spasticity following the administration of diazepam, and cyproheptadine respectively. Furthermore, dynamic indices during bicycling were correlated with the severity of spasticity in 62 spastic patients (Benecke et al., 1983). This index appears promising as a means of evaluating functional improvement during rhythmical movements in spastic patients.

In summary, evaluation of spasticity has traditionally focused on hyperactive mono- and polysynaptic reflex activity in the resting state, which addresses only one aspect of this multifaceted phenomenon. Both static and dynamic reflex activity and voluntary muscle activation are clearly disturbed in hemiplegic spasticity. To date, however, only a few studies have correlated these abnormalities with the severity of clinically measured spasticity. The latter would be desirable, especially in establishing the effectiveness of various pharmacologic and physiotherapeutic treatment regimes.

Despite the numerous investigations of reflex and voluntary motor function, the underlying mechanisms of spasticity remain controversial. Some clues may be derived from an understanding of the mechanisms underlying the relief of spasticity by therapeutic intervention.

PROBLEM FORMULATION

It is clear that the phenomenon of spasticity is complex and probably multifactorial. For example, it is characterized by both 'positive' symptoms, such as hyperactive reflexes and co-contraction, and 'negative' ones, such as weakness and loss of dexterity (Burke, 1988). One of the principal problems in understanding spasticity is that, to date, neither the cat nor the primate model adequately reflect the disorder in man. Furthermore, studies of spasticity in man raise other concerns. For example, measures used in the characterization of

spasticity range from the properties of motor units to polysynaptic reflexes to rhythmical movements such as gait. Several of these measures are clearly changed in spasticity, and an examination of their deviation from normal provides insights into the underlying mechanisms of the disorder However, the research in spasticity has also revealed a large variability in responses and, in some cases, contradictory findings. One source of variability may be due to the study of heterogenous patient populations with etiologies ranging from amyotrophic lateral sclerosis to brain tumours, all having some signs of 'spasticity' However, the pattern of hypertonicity and weakness may vary depending on the site of the lesion.

In spite of the large variability of responses and their often inconsistent correlation with the severity of spasticity, reflex and voluntary measures have, nevertheless, been used to measure the effects of therapeutic interventions on spasticity. However, little attention has been paid to their reproducibility, an issue that is particularly important when assessing the effects of treatment over a period of days or weeks. A brief overview of the treatment of spasticity is given in the next section.

Modifiability of Spasticity

Methods intended to reduce spasticity include pharmacological, surgical and physio-therapeutic treatment. Manipulation of muscular and/or cutaneous peripheral afferent input has been used to retrain motor pathways (Rood, 1956; Bobath, 1978). Indeed, low threshold afferent conditioning has been found to modulate ongoing motoneuronal activity through segmental, propriospinal and/or supraspinal pathways. For example, low-intensity electrical stimulation of the median nerve inhibited the Ia mediated excitation in oligo-synaptic pathways during voluntary wrist flexion (Malmgren and Pierrot-Deseilligny, 1988a,b). Similarly, low threshold afferent activation by vibration has been shown to augment voluntary power in paretic and normal muscles (Hagbarth and Eklund, 1968). A reduction in spasticity is reported following low-threshold afferent stimulation applied directly over antagonistic muscles (Duchenne, 1855; Levine et al., 1952; Alfieri, 1982; Vodovnik et al., 1984) or remotely over the dorsal columns of the spinal cord (dorsal column stimulation; Nashold and Friedman,

1972; Cook and Weinstein, 1973) An improvement in spasticity and voluntary motor control may also be achieved by a decrease in afferent input, such as a temporary nerve block with local anaesthetic, or local cooling of the spastic muscle (Dimitrijevic and Nathan, 1967, Knutsson, 1970b).

Several mechanisms have been proposed to explain these effects. Firstly, presynaptic inhibition could be involved, given the extensive convergence of descending pathways and of Ia, Ib and cutaneous afferents on common presynaptic inhibitory interneurons (Baldissera et al., 1981; Brink et al., 1984) Furthermore, Foreman et al (1976), studying the inhibitory effects of dorsal column stimulation on spinothalamic tract neurons in anaesthetized monkeys, suggested that it may be acting via a presynaptic inhibitory mechanism They demonstrated dorsal root potentials concurrently with inhibitory postsynaptic potentials in both high and low threshold spinothalamic tract neurons. If, indeed, presynaptic inhibition is decreased in spasticity (Ashby and Verrier, 1976), then enhancing low-threshold afferent input, as in dorsal column stimulation, may be one way of 'switching on' presynaptic inhibitory mechanisms.

Secondly, plastic changes can account for some of the reported changes In certain cases, the reduction of spasticity by repetitive electrical stimulation appeared to be long-lasting. For example, Alfieri (1982) reported that spasticity continued to improve with repeated (5 - 16 daily, 10 min treatments) stimulation of antagonist muscles. Also, the results of dorsal column stimulation suggest that the improvements develop slowly over time and may outlast the period of stimulation (Siegfried et al., 1978). The possibility of the occurrence of plastic changes in reflex pathways is reinforced by several findings of adaptive plasticity in the CNS For example, the vestibulo-ocular reflex, once thought to be 'hard-wired', can be modified following 2-3 weeks of altered vision conditions (Melvill Jones, 1983) Similarly, H reflex amplitudes in monkeys can be altered by 2-3 months of classical conditioning, resulting in what appear to be permanent changes in spinal cord responsivity (Wolpaw, 1987; Wolpaw and Lee, 1989). Finally, plastic mechanisms may be implicated, since the time course of the changes in motor function and spasticity following treatment are consistent with that needed for the development of sprouting in the CNS (Murray and Goldberger, 1974; Hultborn and

Malmsten, 1983).

Transcutaneous electrical nerve stimulation (TENS), a non-invasive afferent stimulation technique similar to dorsal column stimulation, has also been observed to affect spasticity and voluntary motor control According to clinical reports, TENS reduced subjective spasticity and improved bladder function in multiple sclerosis patients awaiting implantation of dorsal column stimulators (Fredriksen et al., 1986). Indeed, TENS may be acting via mechanisms similar to dorsal column stimulation. There is some evidence that TENS may be enhancing presynaptic inhibition. This was suggested by our previous finding of a significant increase in the amount of vibratory inhibition of the H reflex in spastic hemiparetic subjects following nine daily, 30 min TENS applications to the low back (Hale and Chan, 1986b) These findings also suggested the possibility of plastic changes due to the slow time course of the treatment effect. Lastly, TENS may trigger the release of inhibitory neuromodulators For example, TENS has been reported to release inhibitory neuromodulators or opioids in the cerebrospinal fluid and blood plasma of normal and pain patients (Almay et al., 1985; Salar et al, 1981). Thus, TENS may be acting via an augmentation of presynaptic inhibition, plastic changes, or the release of inhibitory neuromodulators. The latter may account for the delayed onset and prolonged effects observed for pain relief during and following TENS (Fredriksen et al, 1986; Chan and Tsang, 1987).

To date, the few studies investigating TENS do not fully describe its concurrent effects on spasticity, reflex and motor function. Indeed, a more comprehensive approach is needed. Thus, these studies were aimed at elucidating the effects of single (immediate) and repetitive (longer-term) applications of TENS on spasticity, reflex function and motor control in a homogeneous group of hemiparetic subjects. However, before studying the effects of TENS applied over a period of several weeks, preliminary studies were designed to address the problems of the reliability of and correlation between these measures The first study examined reflex responses and is described in Chapter 2. The purposes of this study were three-fold. The first aim was to compare an aggregate of reflex responses of the lower limb between spastic hemiparetic and normal subjects. These findings should provide insights into

the underlying mechanisms of spasticity by elucidating the possible differences in the organization of segmental reflex pathways The second goal was to examine the reliability of the reflex measures obtained from the same group of hemiparetic subjects on different days These results should help to determine which measures could confidently be used to compare the effects of treatment over time, e g. several weeks. The third goal was to correlate these measures with clinical spasticity to better understand the relationship between the different reflex pathways. The second paper, Chapter 3, examined the same issues with the added dimension of a measure of voluntary function namely, isometric ankle plantarflexion and dorsiflexion in the functional position of standing This could help to elucidate the relationship between reflex and voluntary pathways in spasticity

Once the reliability and characteristics of the measures were established, we undertook two further studies to elucidate the modifiability of spasticity in hemiparetic patients, as a result of manipulating somatosensory input The focus is on the use of low-intensity, high-frequency TENS which has been shown by our previous study to excite large diameter fibres (Levin and Chan, 1988) Chapter 4 reports on the third study undertaken to elucidate the influence of one (45 min) application of TENS on hemiparetic spasticity. The goals of this study were three-fold The first goal was to examine the possible changes in stretch reflex excitability following one application of TENS The second aim was to map out the time course of these changes. The third objective was to determine the role of segmental versus non-segmental mechanisms involved in mediating these changes

The final study, described in Chapter 5, examined the effects of longer-term TENS (after 15 daily, 60 min treatments) on spasticity, reflexes and voluntary control in hemiparetic subjects This study investigated whether repetitive TENS would lead to a reduction in clinical spasticity A second goal of the study was to discover whether this reduction was associated with a decrease in stretch reflex excitability and an improvement in voluntary motor function

The last chapter, Chapter 6, provides a summary of the studies and their major findings In it, the conclusions are reiterated and the contributions to original knowledge are indicated.

CHAPTER 2

DISORDERS IN SPASTIC HEMIPARESIS:

I. CHARACTERISTICS OF REFLEX RESPONSES.

SUMMARY

The underlying pathophysiology of the disturbed reflex functions in spasticity is poorly understood. The present study was thus aimed at elucidating the possible differences in segmental reflex function between spastic and normal states The second aim was to examine the reliability of these measures in spastic hemiparetic subjects to determine which ones could confidently be used to chart the effects of treatment over time The third aim was to correlate the possibly altered reflex function with spasticity, in order to delineate clinically meaningful physiological measures. This was achieved by comparing an aggregate of lower limb reflexes between ten spastic hemiparetic and seven normal subjects Lower limb reflexes examined were H/M ratios, Hvib/Hctl ratios and the soleus stretch reflexes (SR) in terms of latency, area and duration. Our results showed that, firstly, H and SR latencies were shorter ($p<0.05$), and reflex amplitudes were significantly greater (H/M ratios, $p<0.05$, SR/M areas, $p<0.005$) in spastic subjects Secondly, H/M ratios, Hvib/Hctl ratios, SR/M areas and SR onset angles showed high reproducibility. Thirdly, only some physiological measures showed consistent but non-significant relationships with clinical spasticity The findings of decreased reflex latencies and increased reflex responses in the hemiparetic subjects suggested that the underlying mechanisms of spasticity may be related to reduced reflex thresholds These physiological measures, together with clinically assessed tone, were both valid and reproducible when the same patients were tested on separate occasions Therefore, they can be used to evaluate the long-term effects of pharmacological or physiotherapeutic treatment Results of the correlational study between physiological and clinical measures further indicated that the severity of spasticity may not be fully described by static reflex measures alone

INTRODUCTION

The presence of spasticity is often one of the principal factors affecting the rehabilitation of patients suffering from upper motor neuron lesions, such as cerebrovascular accidents (Waylonis et al., 1973) According to the traditional view, spasticity is due to hyperactivity of the stretch reflex arc manifested by a velocity-dependent increase in tonic and phasic stretch reflexes, sometimes accompanied by clonus (Lance, 1980)

The multiple manifestations of this neurological disorder have been measured clinically and neurophysiologically, in order to describe how the integrity of various segmental and plurisegmental pathways may be altered in the spastic state. Indeed, many researchers now agree that no single measure is an adequate descriptor of spasticity They therefore purport the use of aggregate measures to describe concurrent changes in diverse pathways (Ashby and Verrier, 1976; Dimitrijevic et al., 1983; Delwaide, 1985). For instance, clinical measures could be employed in patient evaluation to assess the resistance to passive displacement of the limb (Ashworth, 1964) and changes in functional activity (e g. Bobath, 1978). More objective neurophysiological measurements provide quantitative indicators of alterations in segmental pathways (e g. H reflexes, tendon jerks, stretch reflexes, vibratory inhibition of monosynaptic stretch reflexes; Dimitrijevic and Nathan, 1967, Ashby and Verrier, 1976), inter-segmental pathways (e.g. irradiation of stretch reflexes, flexor reflexes, Dimitrijevic and Nathan, 1968; Dimitrijevic et al., 1983) and long-loop reflex pathways (e g functional stretch reflexes; Chan et al., 1979, Verrier et al., 1984).

Mapping of these reflex changes may provide more insight into the pathophysiological mechanisms underlying spasticity. To elaborate: H reflex and tendon jerk amplitudes are increased with respect to maximal M responses recorded in the spastic muscle These findings suggest that excitability in the monosynaptic stretch reflex arc is enhanced in hemiplegic spasticity (Angel and Hofmann, 1963; Ashby and Verrier, 1976). This enhanced excitability, according to some microneurographic findings, cannot be attributed to increased muscle spindle activity (Hagbarth et al., 1973, 1975; Burke, 1983; however, Szumski et al., 1974).

Nonetheless, the magnitude of the short-latency stretch reflex and its rate of increase with increasing velocity of stretch was found to be augmented in spasticity (Burke and Lance, 1973, Berardelli et al , 1983; Powers et al., 1989) Another observation was the diminished inhibition of the H reflex amplitude during vibration of spastic muscles It is thought to reflect reduced presynaptic inhibition on Ia fibres in the spastic state, though additional contributing factors are recognized (Delwaide, 1971, Burke and Ashby, 1972, Burke et al , 1976) Furthermore, exteroceptive polysynaptic (flexor) reflexes were reported to be altered in spasticity and their irradiation was often observed clinically (Dimitrijevic and Nathan, 1968, Dimitrijevic et al , 1983). This can probably be attributed to disrupted descending control of transmission through the flexor reflex afferents (FRA; See review in Chapter 1) Undoubtedly, certain reflex measures are changed in spasticity when compared to normal controls Yet, a comprehensive neurophysiological profile, based on concurrent measures of activity in various pathways has yet to emerge. Evaluation of concurrent changes may give us better insights into the pathophysiology of spasticity. This became the first objective of the present study

The reproducibility of these measures is an important issue, especially when they are used to assess the results of a given treatment over a period of weeks or months In a preliminary study, we examined the reproducibility of clinical spasticity scores and H reflex measures, on two separate occasions, in a small group of hemiparetic and normal subjects (n=3 each; Hale, 1987). Spasticity scores, H/M ratios, and the amount of vibratory inhibition of the H reflex (Hvib/Hctl) showed very high inter-session consistency with r=0 9, 1 0 and 1 0 respectively. The second goal of this study was to extend these findings to a larger population.

It appears, however, that isolated reflex measures do not adequately reflect the severity of clinically measured spasticity. Indeed, rather poor correlations have been reported to date, between clinical measures of tone and the magnitude of stretch reflexes For example, in a series of 84 spastic patients, Delwaide (1985) failed to find a systematic relationship between clinically measured spasticity (Ashworth scale) and physiological measures of myotatic reflex arc excitability (H/M ratio, vibratory inhibition of the H reflex, and

H reflex recovery at 100 ms). The amplitude of the stretch reflex in the wrist (Cody et al., 1987) and ankle (Berardelli et al., 1983) were reported to be correlated with tone. However, as pointed out by Cody et al. (1987), there was considerable intersubject variability and important exceptions, which further complicated meaningful interpretation of these findings. Thus, the third goal of the study was to correlate the activity in various reflex pathways with the severity of clinically measured spasticity.

To reiterate, the objectives of our study were three-fold. The first aim was to compare an aggregate of lower limb reflex responses between spastic hemiparetic subjects and normal age-matched controls. These findings should provide insights into possible differences in the organization of segmental reflex pathways between spastic and normal states. Our second aim was to examine the reproducibility of these reflex measures obtained in the same group of hemispastic subjects on different days. The results should help to determine which measures could confidently be used to examine the effects of treatment over time, e.g. several weeks. The third aim was to correlate the reflex activities with clinically measured spasticity, in order to delineate clinically meaningful physiological measures. A companion paper focuses on these same issues with regard to reflex and voluntary motor function in the lower extremity of a similar group of spastic hemiparetic patients. Some of these data have previously been published in abstract form (Levin and Chan, 1989).

METHODS

SUBJECTS

Ten patients with spastic hemiparesis (mean age = 56.2 $\pm$ S.D. 13.5 years) and 7 age-matched normal subjects (mean = 63.0 $\pm$ 14.7 years) participated voluntarily in the study. Of the normal subjects, three were female and four were male. All patients had spasticity in the lower extremity, a minimum of 10° of passive ankle dorsiflexion, no history of a previous stroke or other neurological disorder, no pain in the lower extremity, and no major

sensory impairment. They were ambulatory, and followed a stable pharmacological regime where applicable. Subjects were advised as to the nature of their participation and gave their informed consent.

Demographic data for the hemiparetic and normal subjects are presented in Table I together with separate scores of the three clinical measures of spasticity and their "spasticity scores" (by simple addition). The three clinical measures were measured while subjects were comfortably seated. They were recorded in the following manner: 1) Achilles tendon jerks were scored using a widely applied 5-point scale, where '0' denoted 'no response' and '4' indicated 'maximally hyperactive response'. 2) Resistance to full-range passive ankle dorsiflexion at a moderate speed was scored on a modified 5-point Ashworth Scale (Ashworth, 1964). Since this measure most closely represents 'tone' (Berardelli et al., 1983), it was doubly weighted. Thus, a score of '0' indicated 'no resistance', and a score of '8' corresponded to 'maximally increased resistance'. 3) Clonus was scored on a 4-point scale. where '1' indicated 'clonus not elicited' and '4' represented 'sustained clonus'. This evaluation was carried out to provide a composite (albeit subjective) index of spasticity. Based on our clinical experience, the computed 'spasticity scores' ranging from 0 to 9, 10 to 12 and 13 to 16 corresponded to 'mild', 'moderate' and 'severe' spasticity respectively.

EXPERIMENTAL PROTOCOL

Four of the normal subjects and all of the hemiparetic subjects were tested on at least 3 to 5 different days, with an interval of one week between sessions. The remainder of the normal subjects were tested once. Test battery consisted of the clinical evaluation as described above and three physiological measures. The latter involved recording the. 1) maximal amplitude of the H reflex as a percentage of the maximal M response, termed here the H/M ratio (Hoffmann, 1918; Schiepatti, 1987); 2) the amount of inhibition of the H reflex during vibration, expressed as a percentage of the control H reflex amplitude (Hvib/Hctl); and 3) the excitability of the soleus stretch reflex (SR) in terms of latency, duration and magnitude (SR/M area).

Table I. Demographic profile of hemiparetic and normal subjects

No.	Age	Sex	Etiology	Time since injury (mos)	Composite Spasticity Score: ATR	Resistance	Clonus	Spasticity score[a]	Degree of spasticity
Normal Subjects									
1.	72	F							
2.	64	F							
3.	64	M							
4.	72	F							
5.	71	M							
6.	68	M							
7.	30	M							
Mean=	63.0								
S.D.=	14.7								
Hemiparetic Subjects									
1.	67	F	L.CVA	56	1	2	1	4	mild
2.	48	F	R.CVA	11	4	2	1	7	mild
3.	49	F	L.CVA	26	2	4	3	9	mild
4.	43	M	L.CVA	7	3	4	3	10	moderate
5.	67	M	R.CVA	22	3	4	3	10	moderate
6.	67	M	R.CVA	37	4	4	2	10	moderate
7.	75	M	L.CVA	15	3	6	2	11	moderate
8.	31	M	R.CVA	24	4	6	3	13	severe
9.	57	M	L.CVA	50	3	7	4	14	severe
10.	58	M[b]	R.Trauma	15	4	8	4	16	severe
Mean=	56.2			26.3					
S.D.=	13.5			16.5					

[a] Spasticity score: 0-9 = mild spasticity
10-12 = moderate spasticity
13-16 = severe spasticity

[b] Subject on stable regime of anti-spasmodic medication (Dantroline Sodium)

ATR = Achilles tendon reflex
L./R.CVA = left/right cerebrovascular accident
F / M = female/male

SUBJECT FIXATION

Subjects reclined in a comfortable semi-supine position on a specially adapted treatment table (Fig. 1). Their thigh and calf were strapped into adjustable sandsplint casts, so that the knee was fixed at 30° flexion. The foot was attached to a footplate held in the neutral position (Hugon, 1973). The fixed position of the knee and ankle ensures that: 1) that the two-joint gastrocnemius muscle is relaxed, thus minimizing possible contributions from its afferents onto the soleus motoneuronal pool (Hugon, 1973). 2) The initial ankle angle was constant. The latter precaution reduced possible contributions from joint and muscle afferent stimulation consequent to changes in initial (soleus) muscle length (Brunia et al., 1973). The axis of the ankle joint was aligned with the axis of rotation of the footplate (Inman, 1976). Ankle joint angles were monitored and recorded with a custom made electrogoniometer (Beckman 5311 potentiometer, R5K L.5) which was mounted on the same axis.

STIMULATION PROCEDURES

H reflexes. H reflexes in the soleus muscle were elicited according to the procedure described by Hugon (1973). One msec square-wave pulses were delivered at 0.1 Hz via a cathode (a 2 cm Medi-Trace FC-26 surface electrode) placed over the posterior tibial nerve in the popliteal fossa, and an anode (a 20 cm^2 tin plate) positioned superior to the patella for selective stimulation of the nerve trunk (Hugon, 1973). For each stimulus intensity investigated, 10 consecutive responses were collected and averaged on-line by a laboratory developed program written for the PDP 11/23 plus computer. The intensity of the stimulation was gradually increased to record maximal H reflexes, termed here 'H', followed by maximal M responses ('M' or Mmax) The intensity was then decreased to register control H reflexes (Hctl) which were set at approximately 30% of the Mmax across all subjects. This procedure ensured that similar motoneuronal pools were being accessed by the stimulation, and that both increases and decreases in the excitability of the H reflex could be observed.

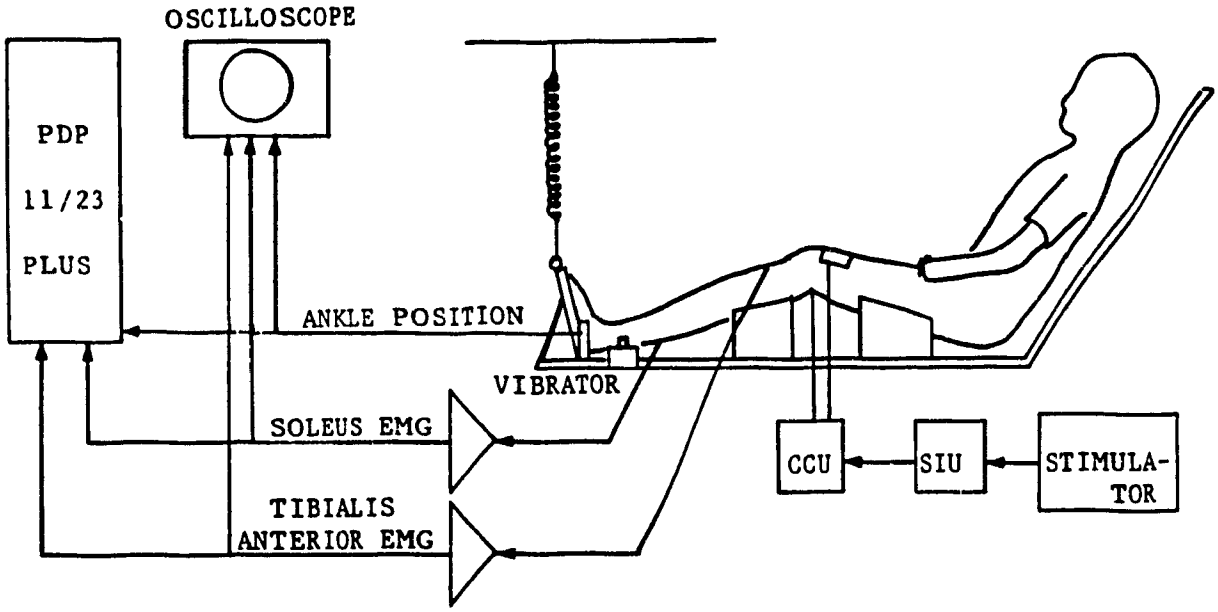


Fig. 1 Experimental set-up. Subjects reclined on an adjustable table with the knee and ankle angles fixed by posterior splints. See text for a full explanation.

Vibration. The effects of vibration of the Achilles tendon on control H reflex amplitudes were investigated by applying a vibrator (Ling Dynamics 101) on the skin at a right angle to the inferior third of the Achilles tendon. Vibration with a maximal amplitude of 2 mm was applied at 100 Hz to preferentially activate Ia afferent fibres (Hagbarth, 1973, Burke et al., 1976; Desmedt and Godaux, 1978, Roll et al , 1989). However contributions from the activation of cutaneous and other muscular afferents cannot be completely avoided (Burke et al., 1976). Following a one-minute accommodation period, during which the response to vibration reached a steady state, 10 H reflexes were elicited and collected on-line, while the vibration was continued. After the cessation of vibration, H reflexes were monitored until they returned to at least 90% of the control value before continuing with the experiment

Stretch Reflexes. To assess stretch reflex activity evoked in the soleus, the ankle was rapidly dorsiflexed by a mechanical stretching device at a velocity greater than 360°/sec through a ramp of 30° This was done while subjects were given the instruction "Do not intervene voluntarily" (Asatryan and Feldman, 1965). The mechanical stretching device consisted of a footplate attached to an overhead bar by 50 lb springs, and a mechanical stop which arrested ankle dorsiflexing movement at 10° past the neutral position of the joint The procedure for evoking stretch reflexes was as follows: The footplate and ankle were manually displaced to 20° plantarflexion past the neutral position and maintained for 10 sec During this time, soleus and tibialis anterior EMG were monitored on the oscilloscope The subject was instructed to eliminate any active muscle contraction. When the background EMG was sufficiently quiet, the computer data collection program was triggered and the footplate was released 500 msec later. This was done in order to have adequate baseline EMG for subsequent analysis. Movement beyond the experimental range (past 10° dorsiflexion) was prevented by a chain connecting the distal end of the footplate to the table To allow sufficient recovery in the reflex pathways, at least 30 sec of rest was permitted between trials. In order to ensure that the testing procedures remained constant across days, we assessed the reproducibility of the stretch perturbations presented to the subjects The mean

velocities of these stimuli, delivered to hemiparetic subjects on five separate testing sessions, ranged from 450 2 ± 58.8°/sec to 511.0 ± 77 5°/sec, and were not significantly different across days ($p>0.10$). Mean maximal displacements also did not differ across days (range = 31.4 ± 2.2° to 34.0 ± 3 6°; $p>0$ 10). In addition, there was no difference in the values obtained between normal and hemiparetic subjects ($p>0.10$). These findings thus demonstrated the consistency with which the mechanical input was presented across different sessions and subject groups.

EMG RECORDING

After preparing the skin, disposable silver-silver chloride surface electrodes (Medi-Trace 1801) were positioned on the soleus and tibialis anterior muscles of the right (for normal subjects) or the affected (for hemiparetic subjects) lower extremity. For soleus EMG, the electrodes were placed 3 cm apart, 4 cm below the intersection of the medial and lateral heads of gastrocnemius and the Achilles tendon (Hugon, 1973). For tibialis anterior EMG, the electrodes were oriented longitudinally along the muscle bulk, 3 cm apart, 7 cm below and 5 cm lateral to the antero-superior border of the tibia. A common reference electrode was positioned over the head of the fibula. Soleus and tibialis anterior EMG signals were amplified with a gain of 1,000 for H reflex and of 5,000 for stretch reflex trials, and filtered (10 to 500 Hz) by Disa 15CO1 amplifiers. They were then monitored on a storage oscilloscope (Textronix R5115) before being digitized at 2,000 and 1,250 Hz respectively for H and stretch reflexes, and stored in a PDP 11/23 plus microprocessor. In order to have adequate baseline values, soleus EMG activity was recorded for 200 msec following the H reflex stimulation. The EMG activity from the soleus and tibialis anterior muscles, as well as the ankle displacement, were recorded from 500 msec before and up to 900 msec following the stretch perturbation.

DATA ANALYSIS

H reflexes and M responses. Individual and mean peak-to-peak H reflex and M response amplitude values were calculated on-line. Maximal M response areas were computed off-line, by rectifying and integrating the M wave within a window, determined from the response onset to its offset (the point at which the trace exceeded, or returned to, 3 standard deviations of the baseline). Since EMG values can vary according to skin preparation and electrode placement in the same subject on different days, a means of normalizing EMG amplitude and area values was sought. The maximal M response is presumed to represent the total motoneuronal pool activated by a maximal stimulus (Schiepatti, 1987) Assuming that recording conditions remain constant, it should display a strong intra-session stability. EMG amplitude and/or area values were therefore expressed as ratios of the appropriate parameter of the maximal M response (i.e. H/M amplitude, SR/M area) The amplitude of the H reflex during vibration was calculated as a percentage of the control H reflex amplitude (Hvib/Hctl). These normalization procedures were done so that mean values could be compared across subjects.

Stretch Reflexes. Individual stretch reflex trials were analyzed off-line for latency, onset angle, response duration, and area Trials were screened qualitatively prior to inclusion in the analysis, to eliminate those in which the subject intervened voluntarily or was unable to relax completely. Rejected trials included those which had inappropriate transients in the displacement trace or a large amount of background EMG respectively EMG signals were first rectified and background baseline activity was removed. Figure 2 shows a typical stretch reflex trial. EMG latency was determined from the onset of displacement (i e when the displacement surpassed 2° or approximately 7% of total displacement), to the time when the EMG signal exceeded 3 standard deviations of the baseline value. The latency was then used to determine the onset angle from the displacement trace. Figure 2 also shows the duration of the stretch reflex, calculated from the EMG onset (defined above) to the time when the EMG returned to 3 standard deviations from the baseline Finally, the areas of the

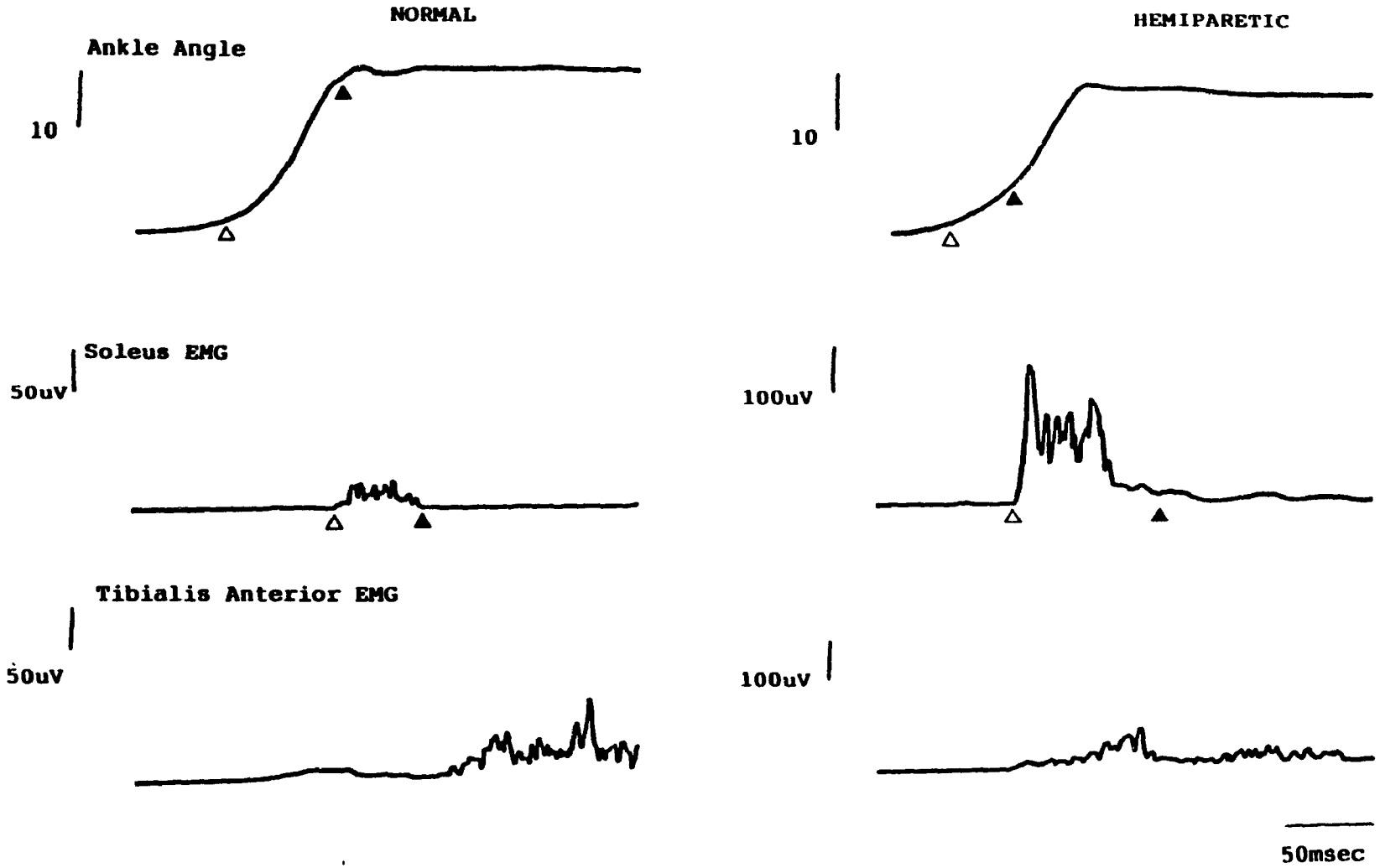


Fig. 2. Typical stretch reflex responses recorded in a normal subject (left) and a spastic hemiparetic subject (right). From top to bottom: angular displacement of the ankle (dorsiflexion indicated by upward deflection), soleus EMG, tibialis anterior EMG. The stretch reflex latencies were measured from the onset of the displacement (open arrow in top trace) to the onset of the soleus EMG (open arrow in middle trace). Stretch reflex onset angles were extrapolated from the displacement trace (filled arrows in top traces) at the point where soleus EMG activity began (open arrows in middle traces). The duration of the soleus stretch reflex was measured from the EMG onset (open arrow) to EMG offset (closed arrow) as shown in the middle traces.

soleus and tibialis anterior responses (when the latter were present) were calculated by a computer algorhythm that determined the maximal integral of the EMG over the 150 msec following its onset. These were expressed as percentages of the maximal M response areas evoked in the same muscles.

Statistical Analysis. H/M ratios, vibratory inhibition of the H reflex and parameters of the stretch reflex were compared between the normal and hemiparetic group Non-parametric statistics (Mann-Whitney U test) were used due to the non-homogeneity of variances in the two groups. Reproducibility of the data was evaluated by interclass correlation coefficients which take into account the proportion of the variance of an observation due to subject-to-subject variability (Fleis, 1986) Pearson's correlations were computed between the clinical and physiological measures of spasticity in the hemiparetic subjects. A significance level of 0.05 was used for all two-tailed tests.

RESULTS

CHARACTERISTICS OF REFLEX RESPONSES IN SPASTIC HEMIPARETIC AND NORMAL SUBJECTS

H reflexes. Figure 3 shows electromyographic reflex responses recorded in one normal (Fig. 3, left column) and one moderately spastic hemiparetic subject (Fig 3, right column). Ten maximal H reflex responses (Fig. 3, first row) were elicited, followed by ten maximal M responses (Fig. 3, second row). In this example, the H/M ratios were 49 2% in the normal and 88.2% in the spastic subject. In Fig. 3 (third row), recordings of the H reflex during vibration are superimposed on their control H reflexes. These examples reflect the extremes in the range of responses, such that the normal subject had an Hvib/Hctl ratio of 6.2%, while the hemiparetic subject had a much higher ratio (76 5%), denoting a markedly reduced amount of H reflex inhibition during vibration (but see Table II below)

The means of 10 responses (H reflex latencies, H/M and Hvib/Hctl ratios) for each of the hemiparetic and normal subjects recorded in one session are listed in Table II H reflex

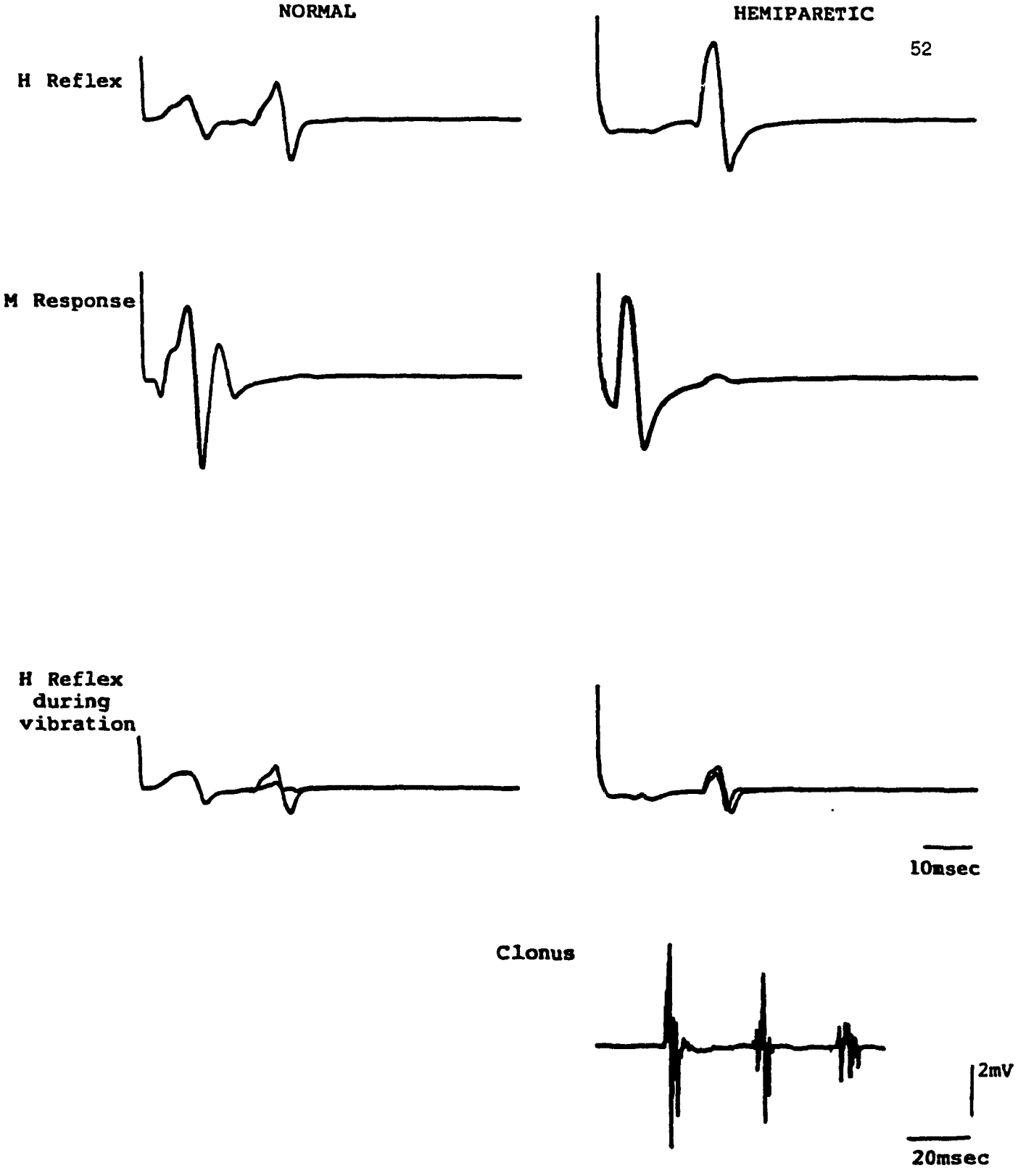


Fig. 3. Examples of maximal soleus H reflexes (first row), maximal M responses (second row), and H reflex during vibration (third row) in one normal (left column) and one spastic hemiparetic subject (right column). Maximal H reflexes were expressed as a percentage of the maximal M responses (H/M). For these subjects, the H/M ratios were 49.2% and 88.2% respectively. H reflex responses during vibration are superimposed on control H reflexes in the third row of traces. These values were 6.2% and 76.5% respectively in the normal and hemiparetic subjects. An example of clonus elicited by the H reflex stimulus is shown for the same subject in the bottom trace.

Table II. Reflex profile of hemiparetic and normal subjects

No.	H reflex latency (msec)	H/M (%)	Hvib/ Hctl (%)	Stretch Reflex (SR) Response Parameters: Onset latency (msec)	Onset angle (deg)	Duration (msec)	SR/M area (%)
Normal Subjects							
1.	30.2	23.3	50.0	70.0	30.0	48.0	2.9
2.	26.7	42.1	49.3	66.6	31.4	79.6	42.0
3.	30.9	51.8	6.2	63.2	34.0	44.5	15.7
4.	31.0	35.3	55.5	72.4	29.8	53.4	19.5
5.	32.2	21.1	79.3	45.6	20.1	77.6	32.0
6.	31.0	68.1	14.5	44.7	30.1	58.6	12.4
7.	30.0	53.6	72.1	77.6	30.1	40 8	14.0
Mean =	30.3	42.2	46.7	62.9	30.1	57.5	19.8
S.D. =	1.7	17.0	27.3	12.9	4.7	15.5	13.1
Hemiparetic Subjects*							
1.	28.0	100.0	27.4	34.8	14.0	58.8	62.0
2.	28.4	65.9	40.0	42.4	15.5	61.8	25.0
3.	29.4	83.8	34.5	30.1	8.6	71.7	46.0
4.	28.2	17.5	17.4	70.5	32.1	49.3	27.0
5.	25.5	76.5	33.3	45.0	12.4	76.0	48.0
6.	31.0	50.9	81.9	85.5	23.1	63.4	41.0
7.	27.9	16.4	55.3	37.6	7.0	99.5	46.0
8.	28.5	78.7	-	44.1	19.9	93.5	63.0
9.	30.4	90.0	64.4	38.6	15.2	88.9	44.0
10.	27.7	88.2	76.5	-	7.3	82.1	59.0
Mean =	28.6*	66.8*	47.9	47.6*	15.5*	74.5*	47.1**
S.D. =	1.6	29.5	22.7	18.2	7.8	16.4	13.1

* Subjects are listed in order of increasing spasticity as in Table I
* Mann-Whitney U test, $p < 0.05$
** Mann-Whitney U test, $p < 0.005$

latencies were shorter in the hemiparetic subjects ($p<0.05$, $U=14.8$), and H/M ratios were significantly increased ($\bar{x}$ = 66.8 ± S.D. 29.5%, $p<0.05$, $U=1.0$, Mann-Whitney U test), when compared to the control group ($\bar{x}$ = 42.2 ± 17.0%). In contrast to the individual responses shown in Fig. 3 (third row), the amount of vibratory inhibition of the H reflex was not different between our normal and hemiparetic subjects, possibly due to the wide range of responses in both groups.

Stretch Reflexes Four parameters of stretch reflexes were measured: latency, onset angle, duration, and SR/M area (Fig. 2). Figure 2 shows that SR latencies and onset angles were significantly smaller in hemiparetic than in normal subjects (compare the time between the open arrows in Fig. 2. A,B for latencies, and the closed arrows for onset angles). As a group, the data from Table II shows that SR latencies were significantly shorter in hemiparetic (47.6 ± 18.2 msec) than normal subjects (62.9 ± 12.9 msec; $p<0.05$). Since latency and onset angle are highly correlated, it was not surprising that onset angles showed a similar relationship. The duration of the stretch reflex was slightly longer in the hemiparetic patients (74.5 ± 16.4 msec) compared to normal subjects (57.5 ± 15.5 msec; $p=0.05$). Finally, SR/M area values were significantly ($p<0.005$) larger in the hemiparetic (47.1 ± 13.1%) than the normal group (19.8 ± 13.1%).

In all ten hemiparetic subjects, fast ramp stretch of the plantarflexors resulted in a shortening or Westphal reaction in the antagonist tibialis anterior which was consistently seen on repeated testing days (Fig. 2, bottom right trace). These shortening reactions were also present in 4 of the 7 normal subjects.

Three of the 10 hemiparetic subjects had sustained clonus that was triggered by the stretch perturbation and, in one case, by the H reflex stimulus (Fig. 3, bottom trace). The frequency of this stretch-evoked clonus was in the order of 3 to 5 Hz.

REPRODUCIBILITY OF MEASURES

Table III shows that a high degree of inter-session consistency was found in the measures from hemiparetic subjects tested on three separate occasions Clinical ratings of spasticity (r=0 87), H/M ratios (r=0 94), Hvib/Hctl ratios (r=0 91) and SR onset angles (r=0 93) and areas (r=0.71) showed high reliability through interclass correlation coefficients Stretch reflex latencies (r=0.44) and durations (r=0.20), however, did not demonstrate significant day-to-day stability.

CLINICAL CORRELATES

Intercorrelations between clinical and physiological measures of spasticity are shown in Table IV. Correlations were calculated on all the measures recorded in the same subjects on three different days. For clarity, only the results of two analyses are presented in the Table. Correlations equal to or greater than 0.63 and 0 71 were significant ($p<0.05$) respectively for the first (top number) and second group of values (bottom number) From Table IV, it is apparent that high correlations between certain measures of spasticity could have occurred by chance alone. For example, H/M ratios and Achilles tendon jerks (ATR) were negatively correlated on one occasion (-0.35), but were highly positively correlated on the other day (0.77). Therefore, only those values which showed consistency over two testing days were considered to be meaningful.

Our findings on the clinical measures of spasticity were that the severity of clonus varied with that of the resistance to passive stretch (r=0.82 and 0 65) Contrary to traditional expectations, another commonly used clinical indicator, the ATR, was not associated with any other measure. The total spasticity score, derived from simple addition of the three clinical measures, was more dependent on the resistance to passive stretch and clonus than on the Achilles tendon reflex.

Not surprisingly, high correlations (0.90 and 0.92) were found between two physiological measures of stretch reflex excitability (latency and onset angle). However, stretch reflex latencies showed only weak negative associations with other measures resistance to passive

Table III. Reproducibility of spasticity and reflex measures recorded in the same group of spastic hemiparetic subjects on three different days

Measures	Day X	Day Y	Day Z	r[a]
Spasticity	10.4 (3.4)[b]	10.0 (3.3)	10.0 (3.4)	0.87 n=10
H/M (%)	68.9 (39.8)	61.8 (34.9)	74.2 (39.6)	0.94 n= 9
Hvib/Hctl (%)	48.7 (25.0)	55.8 (26.8)	46.9 (21.0)	0.91 n= 7
SR latency (msec)	43.0 (9.7)	40.5 (9.4)	38.3 (10.5)	0.44 n= 9
SR onset angle (deg)	19.3 (7.1)	16.5 (5.5)	17.6 (5.3)	0.93 n= 9
SR duration (msec)	75.0 (26.8)	71.5 (14.5)	74.5 (14.7)	0.20 n= 9
SR/M area (%)	45.6 (18.5)	41.5 (19.4)	41.8 (23.0)	0.71 n= 8

[a] = interclass correlation coefficient
[b] = values are Mean (± S.D.)
SR = stretch reflex
deg = degree

Table IV. Correlation matrix between clinical and physiological measures of spasticity based on scores from two different testing days

	ATR	Resist-ance	Clonus	Spast-icity score	H reflex latency (msec)	H/M (%)	Hvib/ Hctl (%)	SR onset latency (msec)	SR onset angle (deg)	SR dura-tion (msec)
Resist-ance	0.41 0.36									
Clonus	0.25 0.55	0.82 0.65								
Spast-icity[a]	0.60 0.65	0.94 0.89	0.85 0.86							
H reflex latency	0.42 -0.03	0.08 0.51	-0.08 0.05	0.32 0.16						
H/M	-0.35 0.77	-0.06 0.09	0.01 0.20	-0.18 0.27	0.32 -0.45					
Hvib/ Hctl	0.31 0.42	0.48 0.41	0.23 0.50	0.42 0.43	-0.01 0.38	-0.34 0.22				
SR latency	0.13 -0.24	-0.37 -0.54	-0.16 -0.27	-0.13 -0.41	-0.20 0.13	-0.54 -0.50	-0.34 -0.01			
SR angle	0.20 -0.49	-0.44 -0.55	-0.06 -0.33	-0.30 -0.54	-0.13 0.01	-0.28 -0.60	-0.36 0.06	0.90 0.92		
SR duration	-0.04 -0.60	0.59 -0.31	0.41 -0.76	0.47 -0.53	0.09 0.14	-0.04 -0.54	0.39 -0.58	0.63 0.32	0.31 -0.73	
SR/M	-0.45 0.55	-0.01 0.6	0.07 0.44	0.55 0.46	0.52 0.11	0.76 0.75	-0.16 0.44	-0.53 -0.84	-0.73 -0.73	0.30 -0.55

[a] Spasticity score = Achilles tendon reflex (ATR) + resistance + clonus
See Table I

SR = stretch reflex

stretch (-0.37, -0.54), H/M (-0.54, -0.50) and SR/M area ratios (-0.53, -0.84). Interestingly, SR/M areas varied significantly with H/M ratios (0.76, 0.75) and SR onset angles (-0.78, -0.78).

Although not statistically significant, clinical spasticity scores bore fairly consistent relationships only with Hvib/Hctl ratios (0.42, 0.43), SR/M areas (0.55, 0.46) and SR onset angles (-0.30, -0.54).

DISCUSSION

COMPARISON OF RESPONSES BETWEEN HEMIPARETIC AND NORMAL SUBJECTS

In spastic hemiparetic subjects, H and stretch reflex latencies were shorter, H/M ratios and SR/M areas were greater and stretch reflex durations were longer than in normal controls (Table II). Except for H reflex latencies, these relationships have previously been reported by separate investigators (Ashby and Verrier, 1976; Berardelli et al., 1983; Hale and Chan, 1986a). These results agree with previous reports of enhanced motoneuronal excitability in the spastic state (Angel and Hofmann, 1963; Pierrot-Deseilligny and Mazieres, 1985; Schiepatti, 1987).

Specifically, reduction of H and stretch reflex latencies could be due to decreased reflex thresholds, leading to an earlier firing of motoneurons (Powers et al., 1988). These findings in the lower limb muscles are consistent with recent reports in the upper limb muscles of spastic hemiparetic subjects (Lee et al., 1987; Powers et al., 1988, 1989), although the latter studies investigated only stretch but not H reflexes. Reduced reflex thresholds in spasticity may be due to several mechanisms (Burke, 1988). In the following paragraphs, two possibilities: 1) enhanced peripheral afferent input and 2) increased central motoneuronal drive, will be discussed.

One can argue that the increased reflex activity in spasticity is due to abnormal segmental afferent input such as enhanced fusimotor drive (Dietrichson, 1973). Abnormalities in some segmental pathways have been identified e.g. reciprocal inhibitory pathways

(Yanagisawa et al , 1976). However, there is mounting evidence to suggest that at least group Ia afferent input to the spinal cord is essentially unaltered in spasticity The latter is based on findings from a primate model of hemiplegia (Gilman et al , 1971, 1974) and from microneurographic recordings in man (Hagbarth et al , 1973, 1975)

An alternate explanation for hypertonia may be derived from the lambda hypothesis of motor control elaborated by Feldman (1966, 1986) According to this hypothesis, a shift in the average resting membrane potential of alpha motoneurons, caused by a net increase in descending excitation (central command), would result in the earlier activation of motoneurons Such a shift in resting membrane potential could lead to lowered H and stretch reflex thresholds which could account for all the changes described in this study In support of this interpretation, Powers et al. (1988, 1989) proposed that increased motoneuronal excitability (lowered threshold) may have been the mechanism responsible for the steep velocity dependence of the stretch-evoked EMG activity in initially inactive human spastic elbow flexors. Assuming a lowered motoneuronal threshold in spasticity, H reflexes could have shorter latencies, since the motoneurons could be recruited earlier by the electrical stimulus, and the response could be larger due to recruitment of more motoneurons Similarly, stretch reflexes could occur at a shorter initial muscle length, resulting in a decreased stretch reflex latency and a reduced onset angle As well, more motoneurons could be recruited at a shorter length, causing an increase in the EMG response (SR/M area). An increased after-discharge due to a maintained stimulus, and/or a tendency to more asynchronous firing, could contribute to the prolongation of the stretch reflex in spasticity This hypothesis for the changes in reflex responsivity in spasticity warrants further investigation

In contrast to previous reports (Delwaide, 1985), the amount of vibratory inhibition of the H reflex was not different between the normals and our group of hemiparetic patients In normal subjects, inhibition of the soleus H reflex has been reported to be maximal when a 2 mm amplitude vibratory stimulus of between 80 and 100 Hz is applied to the homonymous Achilles tendon (Desmedt and Godaux, 1978). Using these parameters of vibration, the

inhibition of the H reflex is believed to be partially mediated by presynaptic inhibition of the Ia terminals (Gillies et al , 1969, Burke et al., 1976) Thus, our findings of a lack of difference between groups could indicate that our patients did not have a deficit in presynaptic inhibitory processes. An alternate explanation could be that the difference was not apparent, due to the high inter-subject variability of our samples.

REPRODUCIBILITY OF MEASURES

The highly consistent clinical spasticity scores, H/M ratio, vibratory inhibition of the H reflex, and SR/M area measures shown in Table III, may reflect both the reproducibility of our experimental paradigm as well as the chronicity of our patient population Our results and those of our previous study (Hale, 1987) thus indicated that these measures are valid and reliable indicators of spasticity in hemiparetic subjects. Consequently, they can be used to assess the effects of treatment interventions repeated over days or weeks However, soleus stretch reflex latency and duration did not appear to display high reproducibility across testing days (Table III) Although care was taken to ensure that subjects remained completely relaxed throughout the testing session by monitoring the background EMG, the variation in onset latency could be attributed to different degrees of resting motoneuronal excitability in the same subjects on different testing days (Lee et al., 1987; Powers et al 1988, 1989) In order to bring all of the motoneurons to the same level of excitability, subjects could have been required to actively contract the soleus muscle to a pre- determined percentage of maximal voluntary force (Lee et al., 1987). However, this would, in fact, preclude the possibility of measuring threshold changes. Our results and these considerations suggest that inter-session changes in stretch reflex latencies and durations measured in relaxed subjects should be interpreted with caution.

The stretch reflex onset angle appeared to be a more stable indicator of stretch reflex excitability, as it showed a correlation of 0.93 across three testing sessions (Table III). This may possibly be explained by the fact that the calculation of the onset angle depended only on the determination of the onset of EMG activity. The latency calculation, however, was also

dependent on the onset of displacement and thus, took into consideration the rise time as a function of the velocity of the displacement (see Fig 2) The possibility that either onset measure may have been correlated with the total displacement, velocity or acceleration of the perturbation was not investigated in the present study.

CLINICAL CORRELATES

Some correlations were found between stretch reflex excitability, vibratory inhibition of the H reflex and the clinical assessment of spasticity, but many of these were non-significant (Table IV). These correlational data are consistent with previously reported findings on H reflexes and their modulation by vibration (Ashby and Verrier, 1976, Hale and Chan, 1986a)

Stretch reflex amplitudes in the relaxed limb have been correlated with tone measured at the ankle (Berardelli et al , 1983), and at the wrist, (r=0 77, Cody et al , 1987) However, our results showed that stretch reflex areas correlated only weakly with the spasticity score (0.55, 0 46; Table IV). This finding suggested that this measure alone did not adequately represent clinically assessed tone Although not significantly related to spasticity, stretch reflex areas (SR/M) were highly correlated with the amplitude of the H reflex (H/M) This observation suggested that the magnitude of these two reflexes may, to a large extent, be determined by reflex excitability involving similar segmental pathways

The stretch reflex onset angle also showed a consistent, if not significant, relationship with clinically measured resistance to passive stretch (r=-0.44, -0 55) This finding agreed with the recent report of a broad negative correlation between reflex threshold and clinically measured tone (Powers et al., 1988). However, stretch reflex onset angles showed a much stronger correlation with stretch reflex areas (r=-0.78, Table IV) This is in keeping with the suggestion of lowered stretch reflex thresholds in spasticity Lowered thresholds could account for both the earlier onset of the stretch reflex and the recruitment of more motoneurons resulting in a larger response

The weak correlation between reflex and clinical measures was not surprising Indeed, if spasticity can be attributed to a decrease in stretch reflex threshold, a more rigorous

clinical measure of this parameter must be designed. None of the three clinical measures commonly in use is particularly sensitive to threshold changes. Rather, they are more indicative of response magnitudes. These results pointed to the need for more specific clinical testing to be developed.

CHAPTER 3

DISORDERS IN SPASTIC HEMIPARESIS:

II. MAXIMAL VOLUNTARY CONTRACTIONS IN STANDING.

SUMMARY

The underlying pathophysiology of the disturbed reflex function and motor control in spasticity is poorly understood. In spite of this, measures of reflex and voluntary motor function are often used to investigate the effects of long-term therapeutic intervention in the control of spasticity. In this study, reflex and voluntary EMG and force measurements from the lower limbs were compared between thirteen spastic hemiparetic and seven normal subjects. In addition, the reproducibility of the measures and their correlation with clinical spasticity manifested in the hemiparetic subjects was also investigated. H and stretch reflexes were first elicited in the calf. Then, subjects were required to generate maximal isometric plantarflexion and dorsiflexion force in the standing position. The results showed that maximal agonist EMG areas and forces were significantly decreased in the affected leg of hemiparetic subjects. During dorsiflexion, agonist EMG and force were decreased to 39% and 33% of the non-affected limb respectively. For plantarflexion, agonist EMG was 63% of the non-affected leg while force was decreased to 59%. Measures of maximal and mean force, force onset and dorsiflexion co-contraction ratios were highly reproducible (r=0.78 to 0.99), while raw and normalized EMG area measures were less reliable. Good correlations were found between the degree of clinically measured spasticity and the function of the dorsiflexors on the affected side (r=-0.65). The decreased force of the dorsiflexors was related even more strongly to the amount of co-contraction (r=0.91), but not to the hyperactive reflexes in the calf. The high reproducibility of the force measurements suggested that they could be used to evaluate the effects of therapeutic intervention over time. The findings also suggested that in hemiparetic subjects, the motor deficit in the non-spastic dorsiflexors was a reliable and valid indicator of the severity of spasticity. However, plantarflexion function and reflex measures in the calf were not. The changes in voluntary and reflex function of the leg muscles suggested that the motor deficit in spasticity may be related to altered descending commands.

INTRODUCTION

Spastic hemiparesis resulting from cerebrovascular accidents may be associated with hyperactive phasic and tonic reflexes, clonus, as well as disordered sensory and motor function (Burke, 1988) The disorganized motor control in spasticity is typically characterized by altered electromyographic activity e.g. prolonged EMG recruitment and derecruitment patterns, as well as abnormal agonist/antagonist co-contraction (Conrad et al , 1985, Hammond et al , 1988a,b) Despite extensive investigation, the origins of these motor deficits remain controversial. They may result from impaired supraspinal control (central command) of spinal interneurons. Alternatively, they may be due to hyperactive stretch reflexes, independent of central voluntary commands. The hypothesis that the central command may be altered in hemiparetic spasticity is supported by findings of abnormal co-contraction in flexors and extensors of the upper extremity during isometric force tracking tasks (McLellan et al , 1985). Since the spastic muscles were not stretched under isometric conditions, the reported motor deficit may not have been related to excessive stretch reflex activity On the other hand, there is evidence to suggest that hyperactive stretch reflexes could also be partly responsible for movement deficits relating to uniarticular motor activity at the knee (McLellan, 1977) and ankle (Corcos et al., 1986) joints, as well as multiarticular motor control such as bicycling (Benecke et al., 1983) and gait (Knutsson, 1970a, Knutsson and Richards, 1979, Fung and Barbeau, 1989).

A previous study focused on the measurement of segmental reflex functions mediated primarily by muscle stretch receptors (Levin and Chan, 1990a) Measures of segmental and plurisegmental stretch reflexes generally correlate poorly with the severity of clinical spasticity (Ashby and Verrier, 1976; Lee et al., 1987; Hale and Chan, 1986a, Levin and Chan, 1990a) Measures of reflex function are significantly increased in spasticity, yet these measures alone provide little information about the origins of the deficits in voluntary motor control Since the presence of spasticity is often associated with disordered motor control, a more comprehensive approach would be to use multi-system measures (Dimitrijevic et al , 1983, Delwaide,

1985). These measures could simultaneously assess reflex as well as voluntary function. Furthermore, measures of spasticity are often carried out without attention to their reliability, a matter that must be addressed when assessing the effects of long-term pharmacological and physiotherapeutic intervention (but see Delwaide, 1985; and Levin and Chan, 1990a).

Having resolved these questions for reflex measures in spasticity in the previous paper, we turned our attention to voluntary motor functions. Our objectives were three-fold. The first aim was to examine the underlying pathophysiology of the disturbed voluntary motor control. This was done by comparing EMG and force measurements of the lower extremity during maximal isometric voluntary contractions between spastic hemiparetic and age-matched normal subjects in the functional position of standing. The second aim was to examine the reliability of these measures. The third aim was to correlate aspects of voluntary motor activity with clinically measured spasticity on the one hand, and reflex function on the other. The correlation data will help to delineate clinically meaningful physiological measures of spasticity. The latter results could provide some insight into how changes in stretch reflex excitability may affect voluntary motor control.

METHODS

SUBJECTS

Thirteen patients with spastic hemiparesis (mean age = 59.1 $\pm$ S.D. 13.6 yr) and seven age-matched normal subjects (mean age = 63.0 $\pm$ 14.7) participated in the study. Criteria for inclusion of the hemiparetic subjects were the same as those outlined in the previous Chapter. All subjects were given details about the nature of their participation before signing an informed consent form.

Demographic and clinical data for the spastic hemiparetic subjects are presented in Table I. Note that the clinical assessment of their spasticity consisted of the three commonly used measures already described in detail in the previous Chapter (Levin and Chan, 1990a).

Table I. Demographic profile and clinical features of spastic hemiparetic subjects

Subject	Age (yr)	Etiology	Time since injury (mos)	Spasticity score*	Degree of spasticity
1. M	75	L.CVA	18	6	mild
2. F	49	L.CVA	27	9	mild
3. M	67	L.CVA	8	9	mild
4. M	31	L.CVA	25	10	moderate
5. F	76	R.CVA	43	10	moderate
6. M	43	L.CVA	8	11	moderate
7. M	67	R.CVA	23	12	moderate
8. M	58	L.CVA	50	12	moderate
9. M	57	L.CVA	85	13	severe
10. M	73	R.CVA	26	13	severe
11. M	67	R.CVA	37	13	severe
12. M	58	R.CVA	16	15	severe
13. M	47	L.CVA	11	16	severe
Mean=	59.1		29.0	11.5	
S.D.=	13.6		21.2	2.7	

* The spasticity score is based on 3 clinical measures of spasticity:
1) Achilles tendon reflex
2) resistance to passive stretch
3) clonus

L./R. CVA = left/right cerebrovascular accident
F / M = female/male

EXPERIMENTAL PROTOCOL

Normal subjects were tested once and hemiparetic subjects at least twice, one week apart. The test battery consisted of five measures, four of which have been described in detail in the previous Chapter (Levin and Chan, 1990a). Briefly, they involved recording: 1) the clinical score of spasticity; 2) the maximal amplitude of the H reflex as a percentage of the maximal M response (H/M ratio); 3) the amount of inhibition of the H reflex during vibration, expressed as a percentage of the control H reflex amplitude (Hvib/Hctl); 4) the excitability of the soleus stretch reflex (SR) in terms of its latency, response duration and magnitude (SR/M area); and 5) the maximal isometric force generated by voluntary ankle plantarflexion and dorsiflexion in the standing position.

For all hemiparetic subjects, spasticity about the ankle joint was assessed at the beginning of each testing session. Subjects then practised making single sustained, two second maximal isometric contractions in response to a response signal, which was preceded by a warning signal after a fixed brief interval (500 msec). In each ensemble of six trials, two 'catch trials' were randomly interspersed. During a 'catch trial', no response signal was presented following the warning signal, so that only baseline EMG and force were recorded. Since it was not known when the 'catch trials' would occur, subjects could not anticipate the response signal. Upon hearing the response signal, subjects made the appropriate muscular contraction as forcibly as possible. Most subjects required between 3 to 6 practice trials, to voluntarily generate contractions with consistent force profiles in terms of onset and the maximal force attained. Generally, more practice trials were required for the affected than the non-affected leg in the hemiparetic subjects. All in all, four dorsiflexing and four plantarflexing maximal isometric contractions were collected from the right leg of the normal subjects, as well as from both the affected and non-affected legs of the hemiparetic subjects.

Following the recording of voluntary contractions, reflex data were collected in the manner described in the previous Chapter. They were recorded last because the time consuming procedure could have caused varying degrees of fatigue in our patients. Fatigue was closely controlled since it could result in variability of the maximal voluntary contractions.

Note that the duration of the entire testing protocol was approximately two and a half hours.

SUBJECT FIXATION

For the voluntary contraction task, subjects stood on a standing platform shown in Fig. 1. The platform had a fixed back support to which the subject's trunk was centred and secured by a wide canvas strap. This procedure helped to ensure that the subject's weight was equally distributed on each leg. Subjects stood without shoes. Both feet were fixated by heel cups and velcro straps to aluminum footplates 30.5 cm apart with ankle joints in the neutral position between plantar- and dorsiflexion (90°). The height of the standing platform was adjusted so that the ankle joint aligned coaxially with the axis of rotation of the footplate (Inman, 1976). The footplates were free to rotate due to frictionless bearings at each axis. Movement of either plate could be prevented, however, by a transverse bar that fixed the footplate to a force transducer (see below) mounted below it on an immovable platform The rigid steel bar transmitted compressive (plantarflexing) or distractive (dorsiflexing) torque generated at the ankle to the force transducer Positioning the bar under the right or the left footplate allowed for independent evaluation of plantarflexion or dorsiflexion force generated by either leg.

Subjects then reclined in a semi-supine position with the affected leg fixated in the manner described in the previous Chapter, for eliciting soleus H and stretch reflexes (Levin and Chan, 1990a).

EMG RECORDING

After preparing the skin overlying the soleus and tibialis anterior muscles, disposable silver-silver chloride surface electrodes (Medi-Trace 1801) were applied. For recording the soleus EMG, the electrodes were positioned 3 cm apart, 4 cm below the intersection of the medial and lateral heads of gastrocnemius and the Achilles tendon (Hugon, 1973). For tibialis anterior EMG, the electrodes were oriented longitudinally along the muscle bulk, 3 cm apart, 7 cm below and 5 cm lateral to the antero-superior border of the tibia. A common reference electrode was placed over the head of the fibula.

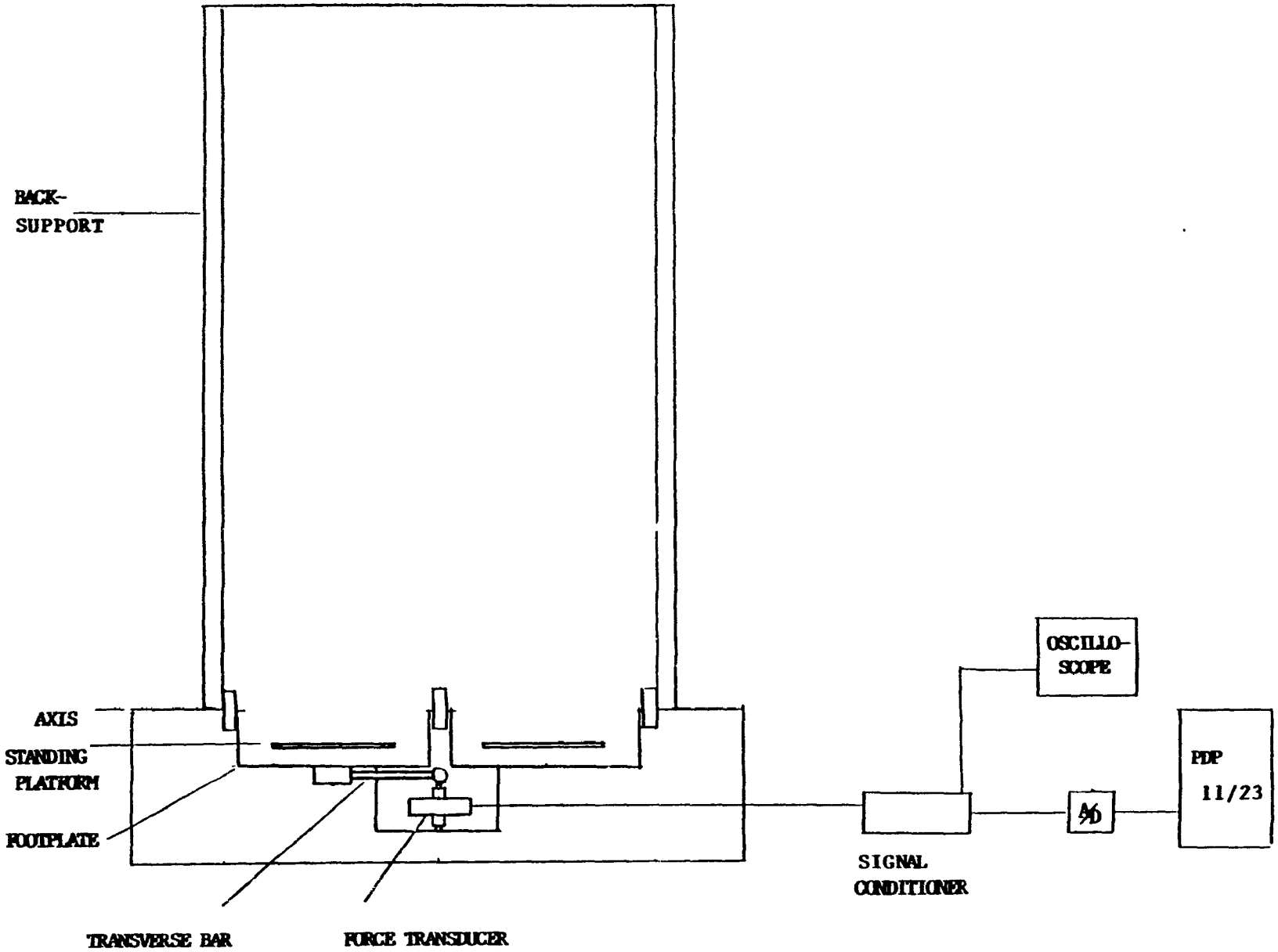


Fig. 1. Experimental apparatus for recording maximal contraction force produced by voluntary ankle plantarflexion and dorsiflexion in the standing position. See text for a full description.

For the voluntary contraction trials, EMG signals were amplified with a gain of 5,000 and filtered (10 to 500 Hz) by Disa amplifiers. They were monitored on a storage oscilloscope (Textronix R5115) before being digitized (1,250 Hz) and stored on computer disks. In order to obtain adequate baseline values, soleus EMG, tibialis anterior EMG, plantarflexion and dorsiflexion force were recorded from 500 msec before to 2,000 msec following the response signal.

EMG signals from reflex measures were processed as described in the previous Chapter (Levin and Chan, 1990a).

FORCE RECORDING

Compressive or distractive forces applied to the footplate were transmitted by a rigid transverse steel bar to the force transducer (Lebow 3132) whose maximal range was ± 225 kg. The signal from the 4 arm strain gauge (wheatstone bridge) of the load cell was amplified by a strain gauge conditioner (Daytronic model 3170) with a gain of 10,000 and then sampled on-line at 1,250 Hz by a PDP 11/23 plus computer (Digital). Force data were considered proportional to torques, since for our apparatus, the distance from the axis of rotation to the site of force recording was fixed for all subjects regardless of the point of application of the force.

DATA ANALYSIS

H reflexes, M responses and stretch reflexes were analysed in the same way as previously described (Levin and Chan, 1990a).

Individual trials of voluntary contraction were analyzed off-line. Analysis included maximal and mean agonist and antagonist EMG areas, maximal and mean force, force onset, and time to half-maximal force. Trials were screened qualitatively prior to inclusion in the analysis, to eliminate those in which force development was inconsistent.

A specially designed computer program was employed for the data analysis. Soleus and tibialis anterior EMG were first full-wave rectified. Their baseline activity, obtained during

quiet standing was then removed. Figure 2 shows an example of typical EMG (top two traces) and force records (bottom trace) registered during a voluntary ankle plantarflexion (Fig. 2A) and a catch trial during quiet standing for one normal subject (Fig. 2B). The maximal and mean area values of the agonist (soleus) and antagonist (tibialis anterior) EMG response were calculated over a 500 msec window placed where the force attained a plateau, as shown by the shaded areas in Fig. 2A. This time window was chosen for analysis instead of the dynamic phase of force production, due to the high variability of the latter phase in hemiparetic subjects. The plateau in the force recording usually included the maximal force obtained. However, some hemiparetic subjects could not maintain the maximal force on the affected leg for more than a few milliseconds.

Co-contraction ratios were calculated from the maximal agonist and antagonist EMG areas defined by the above windows for active contraction (Fig. 2A) and for quiet standing (Fig 2B) It was recognized, however, that area and amplitude values of raw EMG signals may have varied between subjects and sessions according to skin preparation and electrode placement. Thus, individual EMG signals obtained on the same day were normalized by expressing the antagonist EMG area as a ratio of the total agonist plus antagonist EMG areas:

$$\text{Co-contraction ratio} = \frac{\text{Antagonist EMG area}}{\text{Agonist + Antagonist EMG area}}$$

This technique permitted comparison of data obtained on different days for each subject, or between different subjects.

The force trace was further analyzed over the 500 msec window denoted in Fig. 2A to extract 1) the mean and maximal force, 2) the latency of the force onset, defined as the time lapse from the response signal to when the force exceeded three standard deviations from the baseline; and 3) the rate of force development, taken as the time from the onset of force to half-maximal force. The half-maximal instead of the maximal force latency was used since force development was often quite prolonged in the affected leg of hemiparetic subjects In some cases, it occurred later than the force plateau. Prior to recording, the force transducer was recalibrated to zero to eliminate the subjects' body weight.

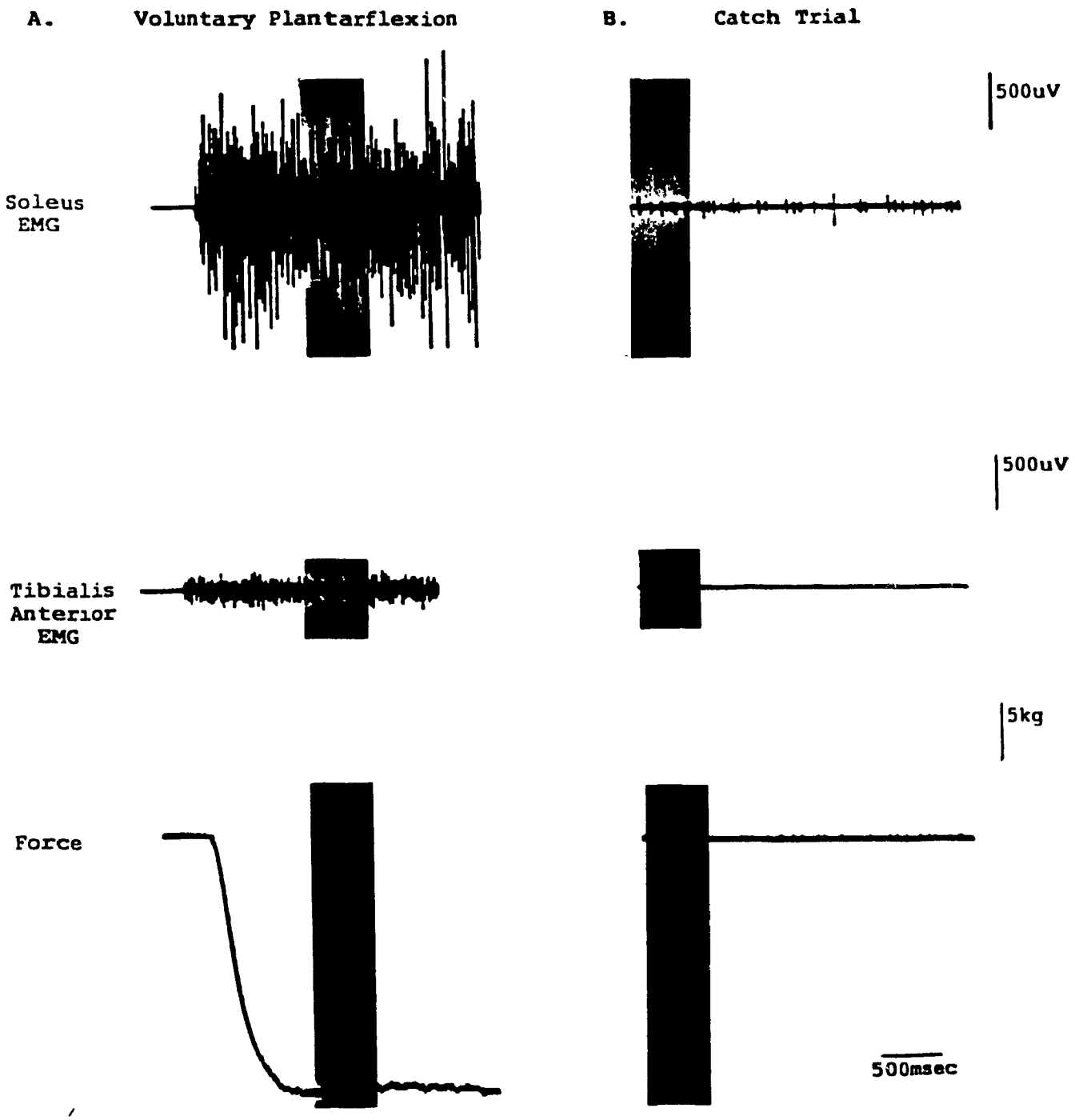


Fig. 2. Typical raw soleus EMG (upper traces), tibialis anterior EMG (middle traces) and force records (lower traces) obtained during (A) voluntary isometric ankle plantarflexion, and (B) a catch trial in one normal subject. During maximal voluntary contraction, mean EMG and force values were calculated over a 500 msec window when the force attained a plateau (shown by the shaded area in A). This was done after subtraction of baseline activity computed from a similar window during a corresponding catch trial (shown by the shaded area in B).

Statistical Analysis. Agonist EMG and force distributions were determined by constructing frequency histograms with appropriate class intervals Comparisons of data between the two subject groups were made via two-tailed t-tests The reliability of the voluntary contraction force and EMG data was determined by interclass correlation coefficients Correlations between clinical, physiological and EMG measures were computed by Pearson's correlation statistics. A significance level of 0 05 was used for all two-tailed tests

RESULTS

COMPARISON BETWEEN NON-AFFECTED LEGS OF HEMIPARETIC SUBJECTS AND NORMAL SUBJECTS

Examples of the raw EMG and force recorded during plantarflexion in the non-affected leg of one hemiparetic subject are shown in Fig. 3A. Compare these values to those obtained from a normal subject, shown in Fig. 2A on a different scale The maximal plantarflexion force was 21 4 kg and 24 0 kg respectively for the non-affected and the normal leg In fact, the ranges of forces and the mean forces generated by the non-affected legs of the hemiparetic subjects were not different from normal controls for both plantar- and dorsiflexion These relationships are graphically depicted in the histograms of Fig 4 and the values are listed in Table II For the normal and non-affected legs, mean maximal forces were 29 14 and 25 71 kg respectively for the plantarflexion task, and 13.65 and 10 36 kg respectively for the dorsiflexion task However, the non-affected leg did differ from normal subjects in two of the characteristics measured 1) an increased amount of raw antagonist EMG during plantarflexion but not dorsiflexion, and 2) a prolonged time to half-maximal force during both tasks.

COMPARISON BETWEEN NON-AFFECTED AND AFFECTED LEGS OF HEMIPARETIC SUBJECTS

Given the overall similarity between normal and non-affected legs, data from the hemiparetic subjects were compared to their non-affected legs, instead of normal control legs.

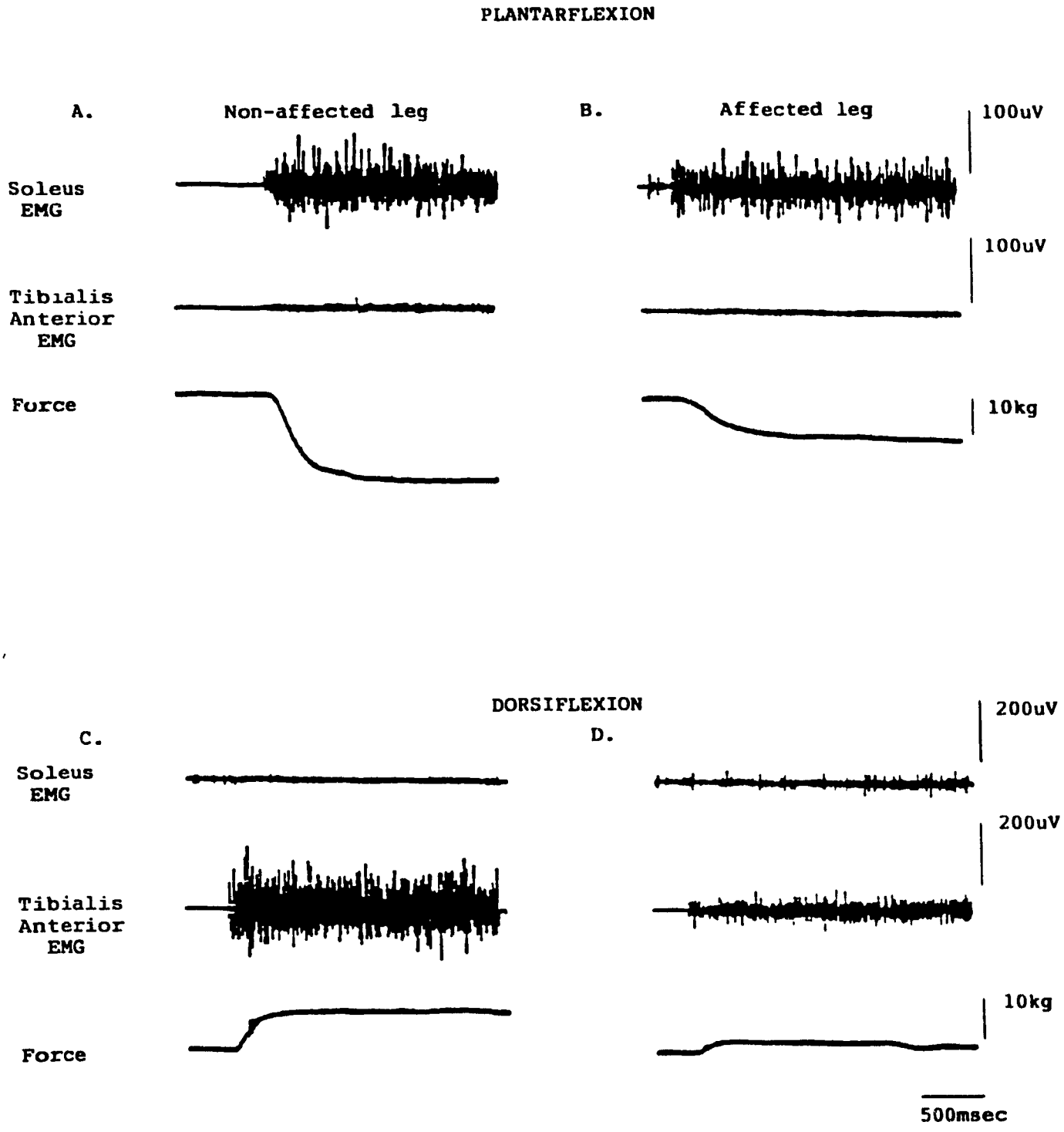


Fig. 3. Typical raw soleus (upper traces) and tibialis anterior (middle traces) EMG and force (lower traces) records for the non-affected (A,C) and affected legs (B,D) of one moderately spastic hemiparetic subject. Plantarflexing contractions are depicted in A and B, while dorsiflexing contractions are shown in C and D

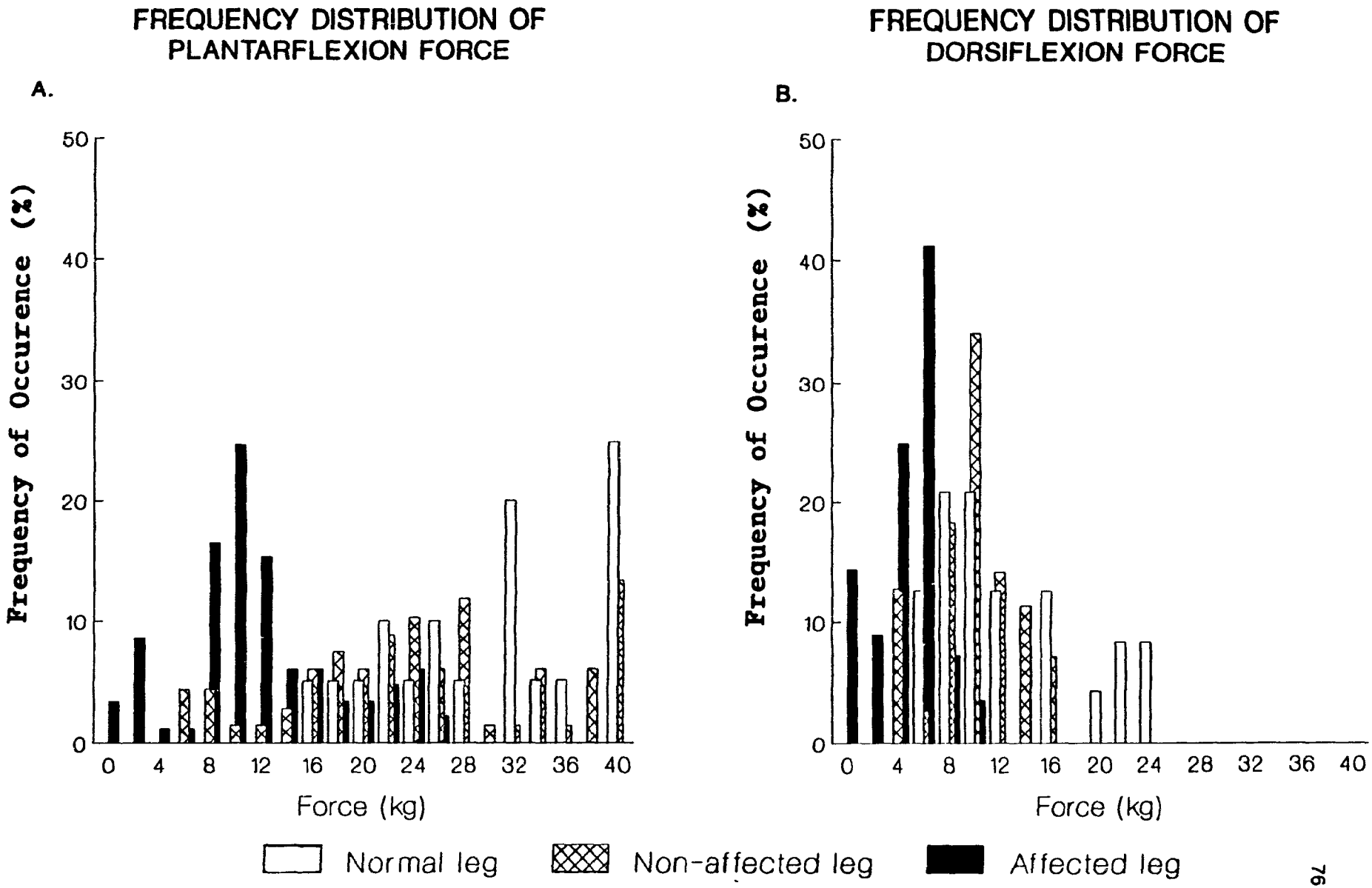


Fig 4 Frequency distributions of A) plantarflexing and B) dorsiflexing force generated in age-matched normal subjects (open bars), as well as in the non-affected (hatched bars) and affected (filled bars) legs of hemiparetic subjects. The ranges of forces recorded in non-affected legs were similar to those of normal subjects, whereas those in the affected legs were shifted towards lower values during both tasks.

This is because data comparison carried out among a matched group of muscles having similar length and mass (non-affected and affected legs of the same subjects) is more valid than that among a non-matched group (hemiparetic legs in one group of subjects and legs from a different group of normal subjects).

Examples of raw agonist and antagonist EMG and force records obtained from the non-affected and affected legs of one hemiparetic subject with moderate spasticity are shown in Fig. 3 A,B for the plantarflexion task, and in Fig 3 C,D for the dorsiflexion task Note the remarkable decrease in the amount of plantarflexion and dorsiflexion force on the affected leg (Fig. 3 B,D), and the increased co-contraction during dorsiflexion (Fig 3D) when compared to the non-affected leg (Fig. 3C).

These comparisons showed that the group mean maximal force was significantly smaller in the affected than the non-affected legs, being 15 05 and 25.71 kg respectively for plantarflexion, and 3.40 and 10.36 kg respectively for dorsiflexion (Table II) This relationship is also depicted by the leftward shift towards reduced maximal forces generated in the affected legs by both voluntary plantar- and dorsiflexion in Fig. 4 A and B (filled histograms) The temporal characteristics of force production also showed abnormalities in the affected legs Force onsets were prolonged for both tasks (Table II) For plantarflexion, the mean force onset was 369.9 $\pm$ 128.6 msec for the affected leg compared to 282 8 $\pm$ 72 53 msec for the non-affected leg ($p<0.001$). For dorsiflexion, the mean force onset was 409 3 $\pm$ 199 1 msec compared to 280.9 $\pm$ 67.7 msec respectively for the affected and non-affected legs ($p<0.001$). Thus, force onsets were prolonged by 131% and 146% for plantarflexion and dorsiflexion respectively. Lastly, the time to half maximal force was similarly prolonged for both plantarflexion (299.3 $\pm$ 67 8 msec compared to 209.3 $\pm$ 37 5 msec, 143%, $p<0$ 001) and dorsiflexion (238.5 $\pm$ 234 6 msec compared to 156.0 $\pm$ 76 2 msec; 153%, $p<0$ 001)

Co-contraction Ratios During Voluntary Effort

The affected leg of the hemiparetic subjects showed decreased agonist EMG compared to the non-affected leg for both voluntary plantarflexion (mean area = 51 2 $\pm$ 18 2

Table II. Comparison of maximal voluntary contractions of the ankle muscles between the normal subjects and the non-affected and affected legs of hemiparetic subjects

	Normal control leg (n=20)	Non-Affected leg (n=68)	Affected leg (n=85)
Plantarflexion			
Agonist EMG area (uV.s)	95.75 (36.52)[NB]	81.43 (28.97)	51.20 (18.15)*
Antagonist EMG area (uV.s)	20.40 (1.91)	34.48 (25.05)**	20.47 (14.01)*
Co-contraction ratio (%)	21 30 (7.00)	28.20 (8.00)	26.30 (9.00)**
Maximal force (kg)	29.14 (8.51)	25.71 (10.05)	15.05 (6.90)*
Force onset (msec)	268.10 (83.57)	282.80 (72.53)	369.90 (128.60)*
Time to half maximal force (msec)	111.80 (27.53)	209.30 (37.48)***	299.30 (67.84)*
Dorsiflexion			
Agonist EMG area (uV.s)	168.00 (119.90)	161.10 (46.30)	63.47 (33.88)*
Antagonist EMG area (uV.s)	26.74 (25.59)	24.85 (8.64)	28.30 (21.43)
Co-contraction ratio (%)	12.40 (5.00)	13.80 (5.00)	42.10 (26.00)*
Maximal force (kg)	13.65 (6.04)	10.36 (3.22)	3.40 (2.90)*
Force onset (msec)	299.60 (80.68)	280.90 (67.69)	409.30 (199.10)*
Time to half maximal force (msec)	79.89 (28.71)	156.00 (76.16)**	238.50 (234.60)*

[NB] = Values are Mean (± S.D.)
* = p< 0.001 compared to non-affected legs
** = p< 0.05 compared to normal control legs
*** = p< 0.001 compared to normal control legs

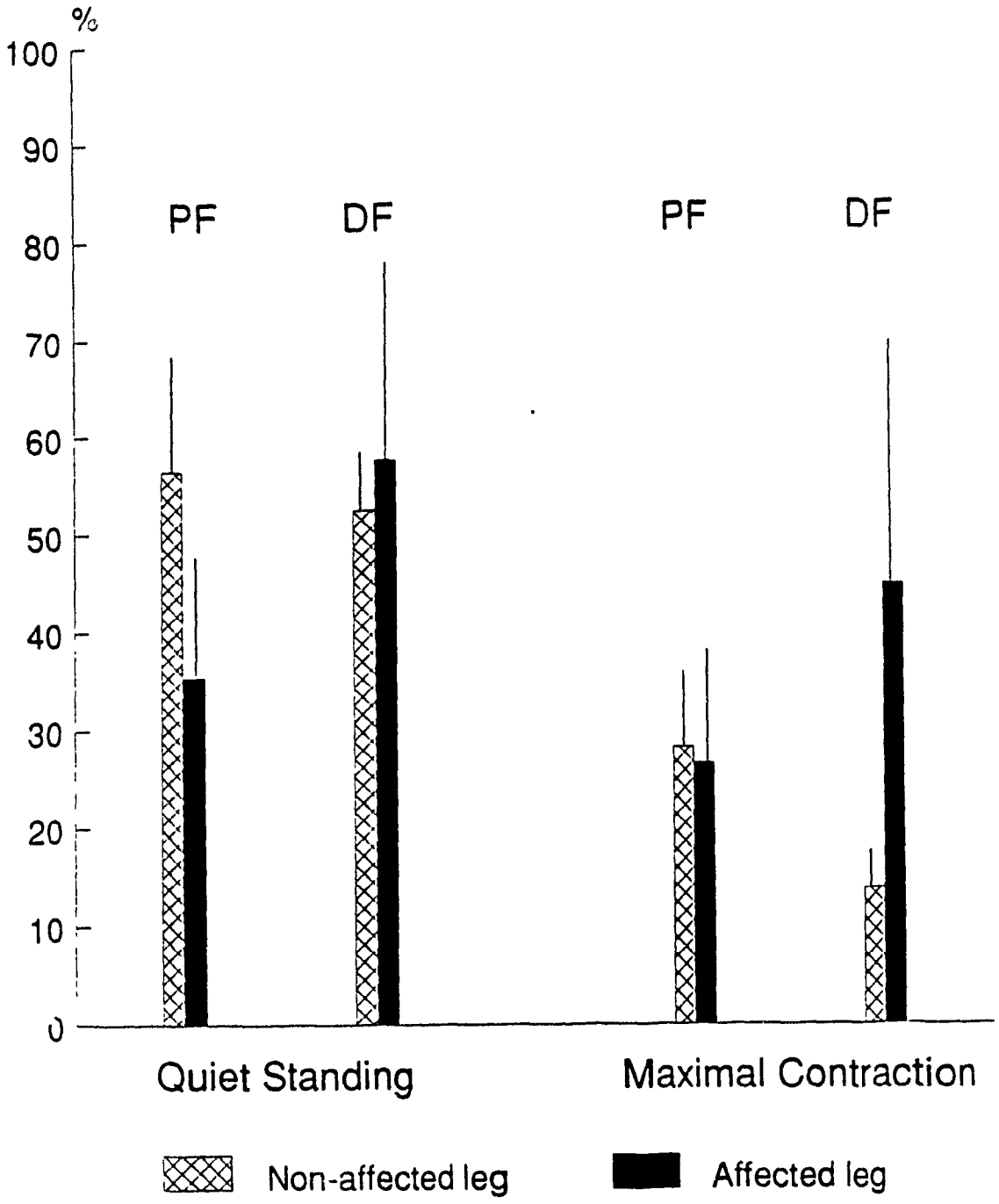
uV.s compared to 81.4 ± 29.0 uV.s; 63%, p<0.001) and dorsiflexion (63 5 ± 33.9 uV.s compared to 161.1 ± 46.3 uV.s; 39%, p<0.001, Table II). Antagonist EMG areas were also decreased for plantarflexion but remained similar for dorsiflexion Consequently, co-contraction ratios were unchanged during plantarflexion, being 26.3 ± 9 0% and 28.2 ± 8.0% respectively for the affected and non-affected leg (Fig. 5, third histogram) However, they were markedly increased from 13.8 ± 5.0% in the non-affected leg to 42.1 ± 26.0% in the affected leg, that is, by 305% (p<0 001) during dorsiflexion (Table II and Fig. 5, fourth histogram). This was not due to a difference in co-contraction ratios during quiet standing. Indeed, when the subject's 'motor set' (Friedli et al., 1984) was to dorsiflex, there was no difference between co-contraction ratios in the non-affected and the affected legs during quiet standing (Fig 5, first and second histograms).

Figure 6 describes the relationship between the mean co-contraction ratios and maximal voluntary force for each leg and each movement direction. As expected, there was no relationship between co-contraction and maximal force either in the non-affected or the normal control legs (not shown) for both tasks. However, a clear relationship existed between these parameters in the affected leg of hemiparetic patients during ankle dorsiflexion and is depicted by the linear regression line in the figure (r=0 91). Thus, subjects with the largest co-contraction ratios generated the least dorsiflexing force Indeed, three subjects who could produce only plantarflexion force when attempting to dorsiflex the ankle had the highest co-contraction ratios. These are depicted as negative forces in the figure. Despite quite similar co-contraction ratios during ankle plantarflexion (Table II), greater forces were generated by the non-affected leg of the hemiparetic subjects than the affected leg (see also Fig. 6).

Temporal Characteristics of Force Generation

Affected legs required more processing time to generate maximal forces (Table II). Furthermore, maximal forces were generally smaller than the non-affected leg for each movement direction. However, correlational analysis revealed no relationship between the

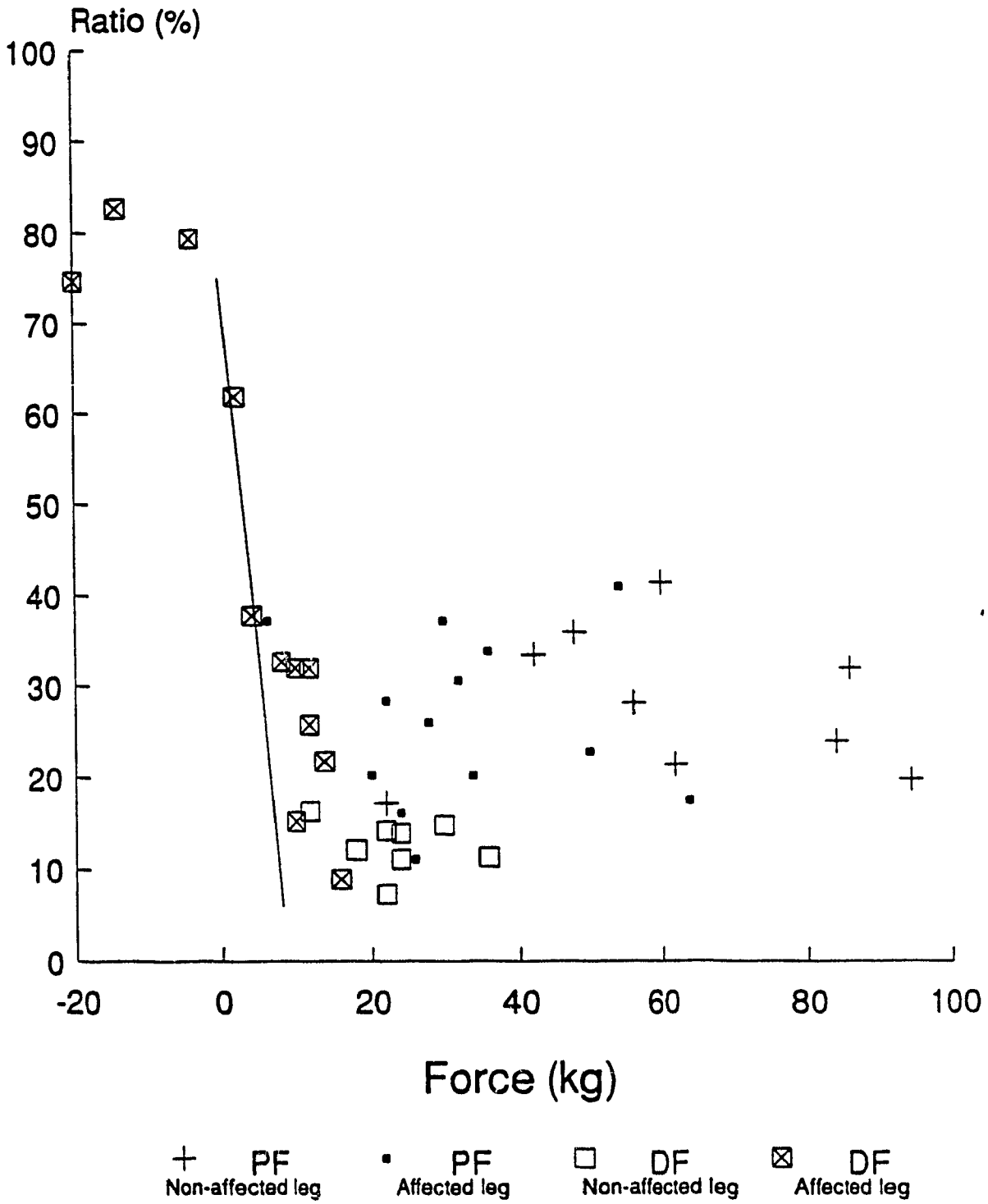
CO-CONTRACTION RATIOS* IN HEMIPARETIC SUBJECTS



*antagonist /(agonist + antagonist EMG)

Fig. 5. Co-contraction ratios during quiet standing (left) and maximal voluntary contractions (right) in non-affected (hatched bars) and affected hemiparetic legs (filled bars). The amount of co-contraction was expressed as the ratio of the antagonist/agonist + antagonist EMG here and in Fig. 6. Note that the co-contraction, normally present at rest is still apparent, but reduced, during isometric contractions in both plantarflexing (PF) and dorsiflexion (DF) directions. Compared to non-affected legs, co-contraction ratios were increased during dorsiflexion in hemiparetic legs.

CO-CONTRACTION RATIO* vs MAXIMAL FORCE



*antagonist /(agonist + antagonist EMG)

Fig. 6. Relationships between co-contraction ratios and maximal force generated by voluntary ankle plantarflexion (PF) and dorsiflexion (DF) in non-affected (+,□) and affected (•, ⊠) legs. The linear relationship (df=11, y=0.75 - 0.09x, r=0.91, p<0.05) between force and co-contraction ratios during dorsiflexion is depicted by the solid line. The graph shows that despite quite similar co-contraction ratios, more force was generated by the non-affected than the affected legs of hemiparetic subjects particularly during plantarflexion.

processing time and the magnitude of force for plantar- and dorsiflexion for either the affected or non-affected legs A significant relationship did exist between force onset and the time to half maximal force during dorsiflexion ($r=0.72$, $p<0.05$) but not during plantarflexion ($r=0.16$). Thus, the more rapid the onset of dorsiflexing force, the shorter the force development time

REPRODUCIBILITY OF THE PARAMETERS OF MAXIMAL VOLUNTARY CONTRACTION

Our second aim was concerned with the reproducibility of the EMG and force data recorded in the hemiparetic subjects. Parameters of the maximal voluntary contractions recorded on two different days during ankle plantarflexion and dorsiflexion are shown in Table III and IV respectively. Values for each parameter are the means of four trials recorded per session. For both tasks in both legs, maximal and mean force recordings were highly stable with interclass correlation coefficients ranging from 0.78 to 0.97. Force onset was also highly reproducible in the affected and in the non-affected leg, with respective values being 0 79 and 0.75 during plantarflexion (Table III), and 0.83 and 0 73 during dorsiflexion (Table IV). The other temporal characteristic, the time to half maximal force, however, was not reliable for plantarflexion (0 21 for the affected and 0.23 for the non-affected leg; Table III) nor for dorsiflexion in the affected leg (0 57; Table IV).

In spite of the well-known cautions in comparing raw EMG area values recorded on different days, raw tibialis anterior (agonist) EMG areas were surprisingly reproducible during dorsiflexion, the r values being 0 91 and 0.77 respectively for the affected and non-affected legs (Table IV) Computation of the co-contraction ratios further yielded a high correlation of 0.99 (Table IV) for dorsiflexion in the affected leg. In sum, measures of magnitude and timing of force generation by the same hemiparetic patients were highly reproducible across days for both movement directions However, raw agonist EMG area values and co-contraction ratios were largely stable only during dorsiflexion but not plantarflexion in the affected leg.

Table III. Reproducibility of maximal **plantarflexion** force and EMG characteristics recorded on two different days from the affected and non-affected legs of the same hemiparetic subjects

Measure	Affected Leg		Non-Affected Leg	
	Day X	Day Y	Day X	Day Y
Maximal force (kg)	13.1 (5.9)[a]	11.7 (6.1)	27.0 (12.1)	26.1 (9.4)
	r = 0.78[b]		r = 0.97	
Mean force (kg)	11.7 (5.6)	10.7 (6.0)	25.5 (11.9)	24.4 (9.2)
	r = 0.87		r = 0.95	
Force onset (msec)	387.0 (133.1)	365.7 (183.2)	330.7 (92.8)	246.0 (74.0)
	r = 0.79		r = 0.75	
Soleus[c] EMG area (uV.s)	51.8 (17.5)	54.2 (32.5)	76.0 (29.3)	81 2 (26.3)
	r = 0.27		r = 0.71	
Tibialis[d] Anterior EMG area (uV.s)	22.8 (13.6)	19.4 (12.7)	28.2 (21.4)	40.5 (30.7)
	r = 0.62		r = 0.23	
Co-contraction ratio (%)	30.4 (12.6)	25.2 (9.5)	26.4 (10.8)	31.1 (11.8)
	r = 0.53		r = 0.16	
Time to half maximal force (msec)	302.1 (120.2)	311.9 (95.5)	215.2 (52.8)	213 0 (41 6)
	r = 0.21		r = 0.23	

[a] values are Mean (± S.D.)
[b] interclass correlation coefficient
[c] agonist muscle
[d] antagonist muscle

Table IV. Reproducibility of maximal **dorsiflexion** force and EMG characteristics recorded on two different days from the affected and non-affected legs of the same hemiparetic subjects

Measure	Affected Leg		Non-Affected Leg	
	Day X	Day Y	Day X	Day Y
Maximal* force (kg)	5.2 (2.5)[a]	4.4 (2.4)	10.6 (3.0)	10 8 (3 6)
	r = 0.95[b]		r = 0.92	
Mean* force (kg)	4.5 (2.4)	3.2 (2.0)	9.8 (2.9)	10.1 (3.7)
	r = 0.87		r = 0.94	
Force* onset (msec)	369.3 (152.6)	277.6 (57.7)	304.0 (89.1)	280.9 (64.7)
	r = 0.83		r = 0.73	
Tibialis[c] Anterior EMG area (uV.s)	48.6 (42.1)	59.0 (46.5)	153.6 (44.2)	157.9 (38 4)
	r = 0.91		r = 0.77	
Soleus[d] EMG area (uV.s)	25.7 (11.7)	38.0 (23.8)	25.9 (9.0)	22.1 (8.2)
	r = 0.04		r = 0.28	
Co-contraction ratio (%)	47.6 (33.4)	47.9 (31.9)	15.1 (5.2)	12.4 (4.6)
	r = 0.99		r = 0.53	
Time to half maximal force (msec)	184.4 (311.1)	142.1 (153.3)	147.7 (69.1)	161.3 (95.6)
	r = 0.57		r = 0.85	

* does not include negative or zero values
[a] values are Mean (± S.D.)
[b] interclass correlation coefficient
[c] agonist muscle
[d] antagonist muscle

CLINICAL CORRELATES

Intercorrelations between reflex measures, parameters of maximal voluntary contraction and the degree of clinically measured spasticity (Tables I, II and V) were calculated for the two complete sets of data collected from the same hemiparetic subjects on different days. Because high correlations among the various data may have occurred by chance (Levin and Chan, 1990a), only those relationships which showed significant correlations on both testing days were considered to be meaningful and are highlighted below.

As previously reported (Levin and Chan, 1990a), the total spasticity score showed consistent but non-significant relationships with physiological measures of reflex function. However, in the affected leg, spasticity in the plantarflexors was significantly related to the ability of their antagonists, the pre-tibial flexors, to generate EMG and force during dorsiflexion. Specifically, it varied inversely with the maximal dorsiflexion force (-0 65, $p<0.05$, Fig 7A) and increased linearly with increasing amount of co-contraction recorded in the agonist/antagonist muscle pair (0 68, $p<0.05$, Fig. 7B). The findings suggest that the greater the degree of spasticity in the plantarflexors, the greater the degree of co-contraction in the ankle muscles during dorsiflexion and the smaller the dorsiflexing force Indeed, the degree of co-contraction was also highly correlated with the maximal force generated by voluntary ankle dorsiflexion ($r=0.91$, $p<0.05$; see also Fig. 6). In contrast, no relationship was found among spasticity, co-contraction ratios and maximal force during voluntary ankle plantarflexion in the affected leg. Nor was there a relationship between co-contraction ratio and maximal force during either task in non-affected legs of hemiparetic and normal control subjects. Moreover, parameters of maximal voluntary contraction of the dorsiflexors was not correlated with any reflex measures in the plantarflexors of the affected leg in hemiparetic subjects.

Table V. Reflex and isometric maximal voluntary force profile of spastic hemiparetic subjects

	Reflex Profile				Maximal Voluntary Contraction	
	H/M (%)	Hvib/ Hctl (%)	SR onset (msec)	SR/M area (%)	Plantar-flexion force (kg)	Dorsi-flexion force (kg)
1.	28.1	22.0	25.5	59.0	16.1	5.0
2.	100.0	17.0	41.0	60.0	16.7	7.3
3.	17.2	99.4	58.9	35.0	10.7	4.2
4.	100.0	51.9	32.0	59.0	22.4	5.8
5.	11.5	71.7	37.2	98.0	10.4	7.9
6.	21.9	21.8	39.8	13.0	28.9	1.4
7.	100.0	15.8	53.5	66.0	23.8	6.4
8.	94.2	74.5	28.5	53.0	9.5	1.2
9.	100.0	89.1	35.8	65.0	3.1	0.0
10.	50.7	30.4	29.9	85.0	12.4	0.0
11.	89.5	64.9	34.1	61.0	13.5	4.4
12.	26.3	90.1	31.3	28.0	10.5	1.2
13.	100.0	87.6	31.5	92.0	17.6	0.0
Mean=	64.6	56.7	36.8	59.5	15.0	3.4
S.D.=	38.3	31.6	9.7	24.3	6.9	2.9

SR = stretch reflex

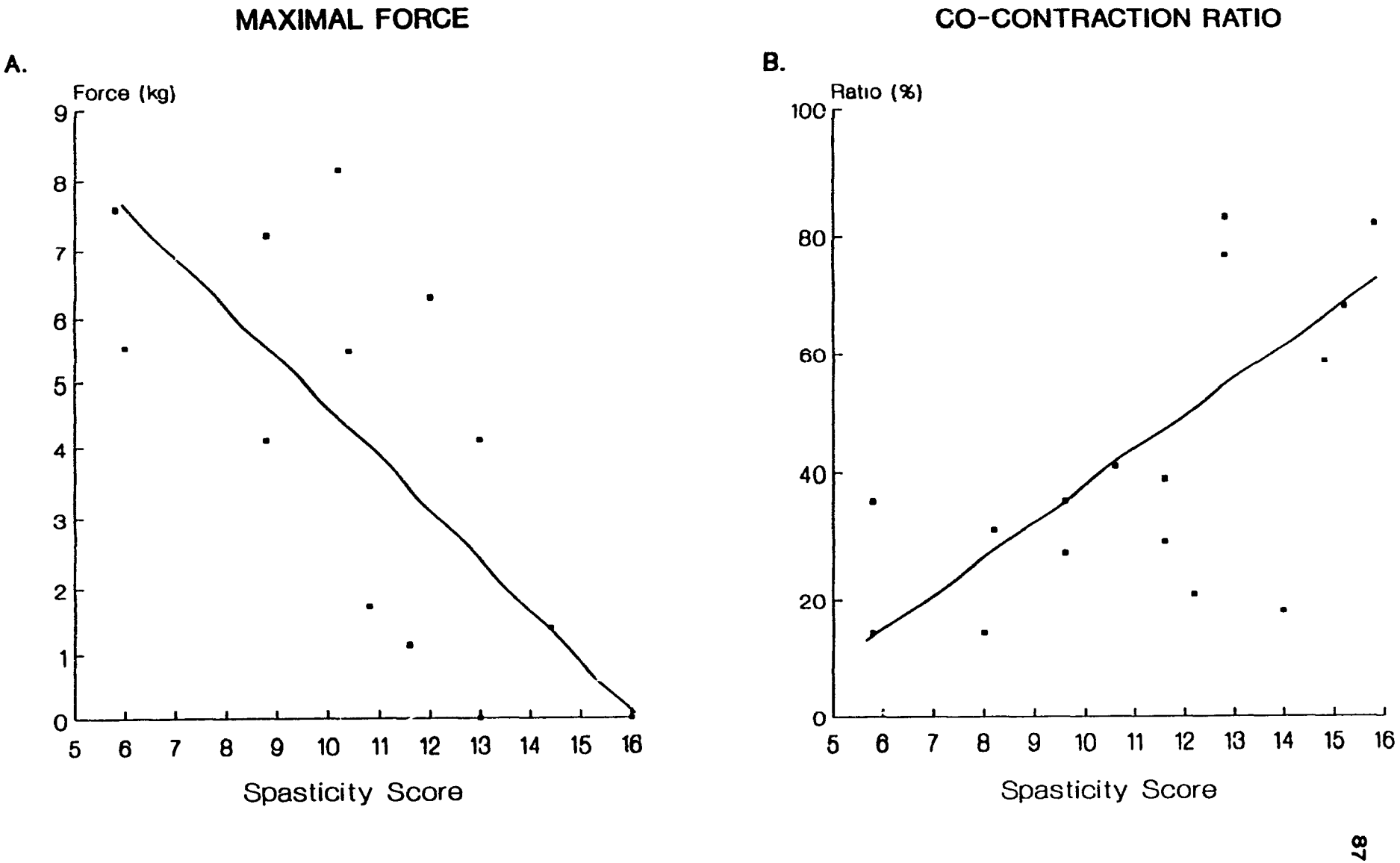


Fig. 7. Relationships between the severity of spasticity and A) maximal dorsiflexing force (df=11, y=11.48 - 0.7x, r= -0.65, p<0.05), and B) the co-contraction ratios (df=11, y=1.23 - 0 06x, r= 0.68, p<0.05) during voluntary ankle dorsiflexion in spastic hemiparetic subjects.

DISCUSSION

COMPARISON BETWEEN NON-AFFECTED LEGS OF HEMIPARETIC SUBJECTS AND NORMAL LEGS

The morphological and physiological properties of motor units on the non-affected side of hemiparetic subjects are not different from normal subjects (McComas et al , 1973, Sica and Sanz, 1976). This has lent justification to the use of non-affected limbs of hemiparetic subjects as appropriate matched controls in studies investigating motor unit properties (McComas et al , 1973) and gross motor behaviour (Lee et al , 1987, Bourbonnais et al , 1989). In our hemiparetic subjects, the activity in the non-affected plantarflexors and dorsiflexors did not differ from age-matched normals in terms of agonist EMG areas, co-contraction ratios or the ability to generate maximal force (Table II). Thus, we felt confident in comparing the activity of the affected legs with that of non-affected legs from the same group of patients. This was preferable to comparisons with potentially more heterogeneous limbs from a different group of normal subjects.

The non-affected legs did differ from normal legs in demonstrating a significantly prolonged time to half maximal force during both voluntary ankle plantar- and dorsiflexion (Table II). This has been previously reported in the upper limb by Hammond et al (1988b) However, since all other parameters of force and EMG were similar to normal (with the exception of antagonist EMG area during ankle plantarflexion), the delayed force development time may not have been related to changes in motor unit properties in non-affected limbs of hemiparetic patients. An alternative explanation may be that the hemiparetic leg was unable to provide adequate stabilization for rapid force generation on the non-affected side during standing. Thus, deficits of postural stability in stroke patients (Bobath, 1978, Horak et al., 1984) may well have contributed to the longer recruitment times

CHARACTERISTICS OF VOLUNTARY CONTRACTION IN HEMIPARETIC LEG MUSCLES

Changes in motor unit properties in the affected limb of hemiparetic subjects could

have contributed to the disordered motor function (see below). However, changes in the gain of stretch reflexes during voluntary movement could also have contributed to the motor deficit. On the other hand, the decreased agonist recruitment (39% of the non-affected leg; Table II) and impaired inhibition of antagonists (114% of the non-affected leg; Table II) in the dorsiflexors further suggested that descending commands may be modified in central spasticity Thus, alterations in motor unit properties, stretch reflexes, and/or descending commands could all have contributed to the motor deficits in central spasticity Each of these considerations will now be discussed in light of the findings in our present study.

Altered Motor Unit Properties

Alterations in motor unit properties, such as the number and types of remaining motor units as well as changes in their discharge rates, may partially explain the altered voluntary function. At the motor unit level, the interference pattern of the EMG is proportional, at least to the number of recruited units and to their discharge rates (Fuglsang-Frederiksen et al., 1977, 1987). In hemiplegic spasticity, there is a selective loss of fast twitch motor units predominantly in antigravity muscles (i.e. ankle plantarflexors, elbow flexors; Edstrom, 1970). The total number of functioning motor units is decreased on the affected side to 50% and 57% of control values in the extensor digitorum brevis (McComas et al., 1973) and the soleus muscles respectively (Sica and Sanz, 1976). Mean contraction times of the remaining fast twitch motor units may also be slower in hemiparetic patients (Young and Mayer, 1982). These functional alterations, no doubt, help to explain our findings of decreased surface EMG and prolonged recruitment times They do not, however, adequately describe the changes in agonist/antagonist recruitment patterns.

Hyperactive Stretch Reflexes

The activity in several reflex pathways is disturbed in spasticity and may be a factor contributing to the motor deficits (Burke, 1988). One such pathway is that mediating reciprocal inhibition. Reciprocal inhibition from pre-tibial flexors to extensors is decreased in spastic

hemiparesis while it is marked from extensors to flexors (Yanagisawa et al., 1976). The latter finding may partly explain the pronounced weakness in the dorsiflexor muscles of hemiparetic patients (Yanagisawa et al., 1976). The reported changes in reciprocal inhibition would, in addition, argue for increased co-contraction during plantarflexion. During dorsiflexion, co-contraction would be decreased. In fact, our findings suggested the opposite. Co-contraction was unchanged during plantarflexion while it was markedly increased by 305% during dorsiflexion. Thus, it seems unlikely that changes in reciprocal inhibition alone could account for the motor deficits in our subjects.

Alterations in other segmental pathways may also contribute to the disrupted motor control in spasticity. Measures of reflex function are clearly increased in spasticity (Delwaide, 1985; Levin and Chan, 1990a). The relationship between increased reflexes and disordered motor control, however, is unclear. Significant correlations were not demonstrated between these variables in our hemiparetic subjects or by other investigators (e.g. Knutsson and Martensson, 1980; McLellan et al., 1985). The soleus muscle was not stretched during isometric dorsiflexion. Thus, the co-contraction may not have been related to hyperactivity in segmental pathways driven by peripheral afferents. Rather, these findings suggested that peripheral feedback mechanisms may have been impaired at the interneuronal level.

It is generally agreed that measures of segmental reflex excitability at rest may be poor indicators of the amount of disruption of voluntary motor pathways (McLellan et al., 1985). Stretch reflex gains are normally modulated during voluntary movement (Marsden et al., 1976; Toft et al., 1989). One explanation for the changed motor control in spasticity, may be abnormal or increased stretch reflex gains during voluntary movement (McLellan et al., 1985). Recent evidence, however, has suggested that while reflex gains in spasticity are indeed modified during voluntary movement, they do not appear to differ from normal (Lee et al., 1987).

Thus, the motor deficit in spasticity may partly be due to altered reciprocal inhibitory mechanisms. However, it is unlikely that it is related to the enhanced reflex activity at rest or enhanced reflex gains during voluntary movement.

Changes in Central Commands

A coordinated theory of motor control suggests that movement is organized according to different combinations of either reciprocal or co-contraction commands originating from higher centres (Feldman, 1980a,b). This theory has received empirical support from work in primates (Humphrey and Reed, 1983). They demonstrated overlapping regions of the pre-central motor cortex controlling reciprocal and co-activation commands for movements of the wrist, which were independent of somatosensory feedback. Lesions of the pre-central cortex, often occurring after cerebrovascular accidents, may result in disturbances of the coordination between the reciprocal and coactivation command systems. The decreased agonist recruitment and increased co-contraction during voluntary ankle dorsiflexion in the lower limb of our subjects is consistent with similar findings in the upper and lower limbs of hemiparetic patients studied by other investigators (Knuttson and Martensson, 1980; McLellan and Hassan, 1982; Hammond et al., 1988a). It is likely that the disturbed motor function arose from disordered descending commands, since activity in afferents mediating stretch reflexes should not have affected voluntary EMG and force during isometric contractions. Thus, our findings of decreased agonist recruitment during isometric ankle plantar- and dorsiflexion, along with increased co-contraction, supports the hypothesis of altered descending commands in spasticity.

REPRODUCIBILITY OF MEASURES

According to our experimental paradigm, measures of maximal and mean force, force onset and dorsiflexion co-contraction ratios were highly reproducible (0.73 to 0.99; Table III and IV). These results suggested that these measures could be used with confidence in comparing the results of treatment over several days or weeks. To our knowledge, this issue has not been addressed by previous investigators.

Raw EMG recorded from different subjects on different days is generally not considered reliable. Variability in recording conditions due to changes in skin resistance and

electrode placement cannot always be avoided. Despite these limitations, efforts were made to duplicate EMG recording conditions in each testing session as closely as possible Surprisingly, raw EMG area values generated in the tibialis anterior muscle during dorsiflexion of the affected leg were highly consistent when the same hemiparetic subjects were tested across two different sessions (r=0 91, Table IV) Soleus EMG areas however, were less stable (Table III). One explanation for the discrepancy may be that tibialis anterior contributed a larger percentage towards dorsiflexing force than did soleus towards the total plantarflexing force. For example, during ankle dorsiflexion, extensor hallucis longus and extensor digitorum longus may have contributed a small amount of force in comparison to tibialis anterior During plantarflexion, however, gastrocnemius, tibialis posterior and flexor hallucis longus may have contributed a somewhat larger percentage of the force in comparison to soleus (Kendall et al., 1971). Therefore, presuming a selective electrode technique and the lack of significant volume conduction (DeLuca and Merletti, 1988), the relative contribution of the soleus muscle to plantarflexing force may have been more variable than the tibialis anterior's contribution to dorsiflexing force. Another possibility is that a surface recording technique may adequately pick up a significant proportion of the muscle action potentials generated in the superficially located tibialis anterior, but it would be less adequate for the more deeply located soleus (Basmajian, 1978). This view is supported by the finding that when the EMG potentials were maximal (tibialis anterior acting as an agonist), the raw EMG values displayed more inter-session reliability (r=0.91, 0 77; Table IV) than when their activity was sub-maximal (r=0.62, 0 23; tibialis anterior acting as an antagonist, Table III)

CLINICAL IMPLICATIONS

Maximal agonist EMG area was significantly decreased in the affected leg of hemiparetic subjects during both plantarflexion and dorsiflexion (to 63% and 39% of the non-affected limb respectively, c.f. Table II) Maximal force for each task was also significantly lower in the affected than non-affected limbs (59% and 33% respectively) These findings of the decreased agonist recruitment and force along with increased co-contraction ratios during

voluntary dorsiflexion suggested impaired inhibition of the spastic antagonist (soleus). Since no relationship was found between voluntary ankle function and hyperactive reflex activity in the calf at rest, it is further suggested that the motor deficit may be related to impaired descending voluntary commands However, our data does not rule out the possibility that enhanced reflex activity during voluntary effort may also have contributed to the motor deficit.

This study also showed that maximal force, mean force and force onset during both plantarflexion and dorsiflexion, and co-contraction ratios in the affected leg during dorsiflexion were highly reproducible accross testing sessions (r=0.73 to 0.99, Tables III and IV). An important clinical finding was that the increased co-contraction and decreased force during maximal voluntary ankle dorsiflexion correlated highly with the severity of spasticity such that the more severe the spasticity, the greater the co-contraction and the lower the force developed by the antagonist to the spastic muscle. These findings suggested that reliable measures of force and co-contraction for muscles with residual function may be valid instruments of charting therapeutic improvement..

CHAPTER 4

REPETITIVE ELECTRICAL STIMULATION IN SPASTIC HEMIPARESIS:

I. STRETCH REFLEX LATENCY CHANGES.

SUMMARY

Repetitive low-intensity electrical stimulation of the dorsal column reportedly decreases spasticity, although the mechanisms mediating this effect are unclear. A question arises whether activation of large diameter fibres through transcutaneous electrical nerve stimulation (TENS) would also decrease spasticity Thus, the objectives of this study were (1) to examine possible changes in stretch reflex excitability following 45 min of TENS via both latency and magnitude (amplitude or area) measurements, (2) to map out the time-course of possible post-stimulation effects, and (3) to determine the role of segmental versus non-segmental mechanisms involved in mediating these changes The effects of 45 min of segmentally and heterosegmentally applied TENS on lower limb reflexes in ten spastic hemiparetic subjects were contrasted with those resulting from placebo stimulation Our main finding was that, in contrast to placebo stimulation, both segmentally and heterosegmentally applied TENS caused an immediate increase in the latencies of soleus H and stretch reflexes that was evident for up to 60 minutes following the cessation of stimulation These results suggested that manipulation of segmental and hetero-segmental afferents for 45 min may lead to a decrease of the otherwise augmented stretch reflex excitability accompanying hemiparetic spasticity Such a finding has important implications for the rehabilitation of patients with spasticity

INTRODUCTION

According to the traditional view, spasticity is due to hyperactivity of the stretch reflex arc manifested by a velocity dependent increase in tonic and phasic stretch reflexes, sometimes accompanied by clonus (Lance, 1980). This hyperactivity could result from either abnormal segmental afferent input to proprioceptive reflex circuits in the spinal cord, or from abnormal processing of otherwise normal input from the periphery, or both However, findings from a primate model of hemiplegia (Gilman et al., 1974) and from patients (Hagbarth et al , 1973; 1975) both suggest that afferent input to the spinal cord is essentially unaltered in spasticity. On the other hand, an increase in the average resting membrane potential of alpha motoneurons, caused by a net increase in descending excitation, could result in an earlier activation of motoneurons (Feldman, 1966, 1986). This could lead to a decrease in stretch reflex threshold and the enhanced reflex activity reported in spasticity (Ashby and Verrier, 1976, Levin and Chan, 1990a)

As demonstrated by Dimitrijevic and Nathan (1968) and Dimitrijevic et al. (1983), another principal sign of spasticity is irradiation of reflexes. Consequently, **remote or hetero-segmental** afferents may play an important role in driving spasticity. In this connection, clinical reports indicate that peripheral nerve blocks (Dimitrijevic and Nathan, 1967) and repetitive electrical stimulation of antagonistic muscles (Duchenne, 1855; Levine et al , 1952; Alfieri, 1982, Vodovnik et al , 1984) could both lead to immediate reductions in spasticity. Similarly, large diameter afferent conditioning via dorsal column stimulation has been found to decrease spasticity (Nashold and Friedman, 1972; Cook and Weinstein, 1973).

While dorsal column stimulation requires surgical exposure of the spinal cord, an alternative technique - transcutaneous electrical nerve stimulation (TENS), is non-invasive At low-intensity, high-frequency stimulation, it is thought to predominantly activate large diameter afferents In fact, using recording of evoked sensory potentials and measurements of conduction velocity, we have shown that such kind of stimulation excited large diameter fibres in the Aαß range (Levin and Chan, 1988) It is thus noteworthy that, in a clinical study of 49 multiple sclerosis patients, two weeks of continuous TENS applied heterosegmentally were found to produce a moderate but meaningful reduction in

subjective spasticity, associated with an improvement in the motor performance of knee flexors and extensors (Fredriksen et al., 1986).

While the underlying mechanisms remain unclear, an interesting observation is that very brief (several seconds of) dorsal column stimulation could have prolonged effects (up to minutes), which cannot be explained solely by simple synaptic mechanisms. For example, in decerebrate cats, Chapman et al. (1983) found that the suppression of static but not dynamic stretch reflexes outlasted the period of dorsal column stimulation (1 - 10 min) for 5 to 20 min. In three spastic patients, Siegfried et al (1978) reported an elevation of H reflex thresholds for up to 3 min following only one 300 msec conditioning train applied to the dorsal column Indeed, longer applications of TENS may have even more prolonged effects For example, Chan and Tsang (1987) found long-lasting inhibition of the lower limb flexion reflex in normal subjects, in some cases for more than one hour, following 30 min of low-intensity TENS applied segmentally to the low back. These findings open up the possibility that TENS may also generate prolonged depression of reflex excitability.

In an earlier study, we investigated the immediate effects of 30 min of **segmentally** applied TENS on the reflex measures of the spastic soleus in hemiparetic patients (Hale and Chan, 1986a) TENS applied to the low back of these patients produced no significant change in the amplitude of H and stretch reflexes. However, the extent to which reflex amplitudes or gains reflect the severity of spasticity has lately been questioned. Recent investigations of stretch reflex activity in the spastic elbow flexors of hemiparetic subjects suggested that spasticity may be characterized more appropriately by a decrease in the stretch reflex threshold than by an increase in gain (Lee et al., 1987; Powers et al., 1988). In these studies, a reduced threshold was implied by the appearance of EMG activity after a smaller elbow joint angle deflection, while stretch reflex gain or stiffness in these patients was not found to be significantly different from the non-affected limb or from normal subjects.

Since threshold changes may be reflected in appropriate latency changes, we re-examined the immediate effects of 45 min of TENS (versus 30 min in the previous study; Hale and Chan, 1986a) on the latency and magnitude characteristics of both the monosynaptic and polysynaptic stretch reflexes in the spastic calf muscles of hemiparetic patients. In an added attempt to determine

the time course of possible post-stimulation effects, measurements of stretch reflex excitability were repeated at 20 min intervals for up to 60 min after the cessation of TENS. To further delineate the respective contribution of segmental versus non-segmental (e.g. propriospinal and descending) mechanisms, the effects of segmentally applied TENS on stretch reflex excitability were contrasted with heterosegmental and placebo stimulation. To reiterate, the objectives of the present study were. (1) to examine possible changes in stretch reflex excitability following 45 min of TENS via both latency and magnitude (amplitude or area) measurements, (2) to map out the time-course of possible post-stimulation effects, and (3) to determine the role of segmental versus non-segmental mechanisms involved in mediating these changes. Some of these data have previously appeared in abstract form (Levin and Chan, 1989).

METHODS

SUBJECTS

Ten patients with spastic hemiparesis (mean = 56.2 $\pm$ S.D. 13.5 years) participated voluntarily in the study. Specific inclusion criteria, method of subject fixation, stimulation and recording procedures have all been described in detail in a previous publication (Chapter 1; Levin and Chan, 1990a). Table I summarizes the demographic data for these hemiparetic subjects. As previously described (Chapter 1; Levin and Chan, 1990a), the evaluation of spasticity consisted of 1) Achilles tendon reflexes, 2) resistance to passive ankle dorsiflexion, and 3) amount and duration of ankle clonus. It provided a composite (albeit subjective) index of spasticity. Based on our clinical experience, the computed 'spasticity scores' ranging from 0 to 9, 10 to 12, and 13 to 16 corresponded to 'mild', 'moderate' and 'severe' spasticity respectively.

EXPERIMENTAL PROTOCOL

Subjects returned for three randomly ordered sessions in which they received either 45 min of 1) **segmentally** or 2) **heterosegmentally** applied TENS, or 3) placebo stimulation, to be described

Table I. Clinical features of spastic hemiparetic subjects

Subject	Age	Etiology	Time since injury (mos)	Spasticity score[a]	Degree of spasticity
1. F	67	L.CVA	56	4	mild
2. F	48	R.CVA	11	7	mild
3. F	49	L.CVA	26	9	mild
4. M	43	L.CVA	7	10	moderate
5. M	67	R.CVA	22	10	moderate
6. M	67	R.CVA	37	10	moderate
7. M	75	L.CVA	15	11	moderate
8. M	31	R.CVA	24	13	severe
9. M	57	L.CVA	50	14	severe
10. M[b]	58	R.Trauma	15	16	severe
Mean =	56.2		26.3	10.4	
S.D. =	13.5		16.5	3.4	

[a] The spasticity score is based on 3 clinical measures of spasticity:
1) Achilles tendon reflex
2) resistance to passive stretch
3) clonus.
Scores ranging from 0-9, 10-12 and 13-16 respectively were classified as mild, moderate and severe spasticity.

[b] Subject on stable regime of anti-spasmodic medication (Dantrolene Sodium)

L./R. CVA = left/right cerebrovascular accident

F / M = female/male

below. Since no single measure has been definitively correlated with changes in the severity of spasticity, we used multiple indicators to investigate the effects of TENS Pre- and post-stimulation test batteries consisted of the clinical evaluation as described above and three physiological reflex measures. For reflex testing, subjects reclined in a semi-supine position with the knee fixated at 30° flexion and the ankle supported in the neutral position. A full description of the testing procedures have been described (Chapter 1; Levin and Chan, 1990a). Briefly, they involved recording 1) the maximal amplitude of the H reflex as a percentage of the maximal M response, termed here, the H/M ratio (Hoffmann, 1918; Schieppati, 1987); 2) the amount of inhibition of the H reflex during vibration, expressed here as a percentage of control H reflex amplitudes (Hvib/Hctl), and 3) the excitability of the soleus stretch reflex (SR) evoked at rest, computed as the SR/M area ratio. To further assess the time course of post-stimulation effects, these measures were repeated at three 20 min intervals after the cessation of TENS or placebo stimulation.

TENS AND PLACEBO STIMULATION

TENS and placebo stimulation were applied via a Selectra 7720 stimulator (Medtronic) for a period of 45 min. Two rectangular rubber surface electrodes (3 8 cm x 5.1 cm) were coupled to the skin with electric conductive gel and hypoallergenic tape. Stimulation consisted of continuous high-frequency (99 Hz), square 0.125 msec electrical impulses delivered at low intensity (twice the sensory threshold) for TENS and at essentially zero intensity (0.1 x threshold) for placebo At the beginning of each testing session, sensory threshold was determined by gradually increasing the intensity of the stimulation to a level when the subject first reported a faint tingling sensation The intensity was then decreased until no sensation was felt. The average of three such trials was used to determine the threshold intensity for each session. TENS was applied to two sites: 1) the common peroneal nerve (L4-S2) located just posterior to the head of the fibula, which supplies the muscles antagonistic to the spastic calf muscles; or 2) the volar aspect of the contralateral wrist over the median nerve (C6-T1). Placebo stimulation was applied only to the first site The two sites were chosen in order to determine the differential effects of **segmental** versus **heterosegmental** mechanisms in the possible modification of stretch reflex excitability in spastic hemiparesis

EMG RECORDING AND DATA ANALYSIS

Procedures for recording and anlayzing H/M ratios, Hvib/Hctl ratios and stretch reflexes have previously been described in detail (Chapter 1; Levin and Chan, 1990a). Briefly, EMG from soleus and tibialis anterior muscles were recorded via disposable surface electrodes. Maximal peak-to-peak H reflex amplitudes were expressed as a percentage of maximal M response amplitudes. The amount of inhibition of the H reflex during vibration was calculated as a percentage of the control H reflex amplitude which was approximately 30% of the maximal M response. Stretch reflex area values were normalized by expressing them as ratios of maximal M response areas. Other parameters analyzed were stretch reflex latencies, onset angles and durations.

Statistical Analysis. Changes in H reflex latencies, H/M and Hvib/Hctl ratios, as well as parameters of the stretch reflex were expressed as percentages of their corresponding pre-stimulation control values for each subject. Changes in each 20 min post-stimulation time interval were compared between treatments. Occasionally, post-stimulation changes in the the three time periods were pooled. Two-way ANOVAs compared the effects of the segmental and heterosegmental TENS stimulation with placebo treatments on each reflex measure. Differences between individual pairs of means were determined by a post-hoc test (least significance difference test). A significance level of 0.05 was used for all two-tailed tests.

RESULTS

CHARACTERISTICS OF REFLEX RESPONSES

H/M ratios were generally elevated in our spastic hemiparetic patients. Examples of H/M and Hvib/Hctl ratios for two subjects are illustrated in Fig. 1. The subject shown in Fig. 1 (A-C) was a 48 year old female with left hemiparesis and mild spasticity. This subject had an H/M ratio of 65.9% and an Hvib/Hctl ratio of 40.0%. In contrast, the subject in Fig. 1 (D-F) was a 57 year old male with right hemiparesis and severe spasticity, who had an H/M ratio of 90.0% and an Hvib/Hctl ratio of 64.4%. In spite of the apparent correlation between the H/M ratios and the degree of clinical

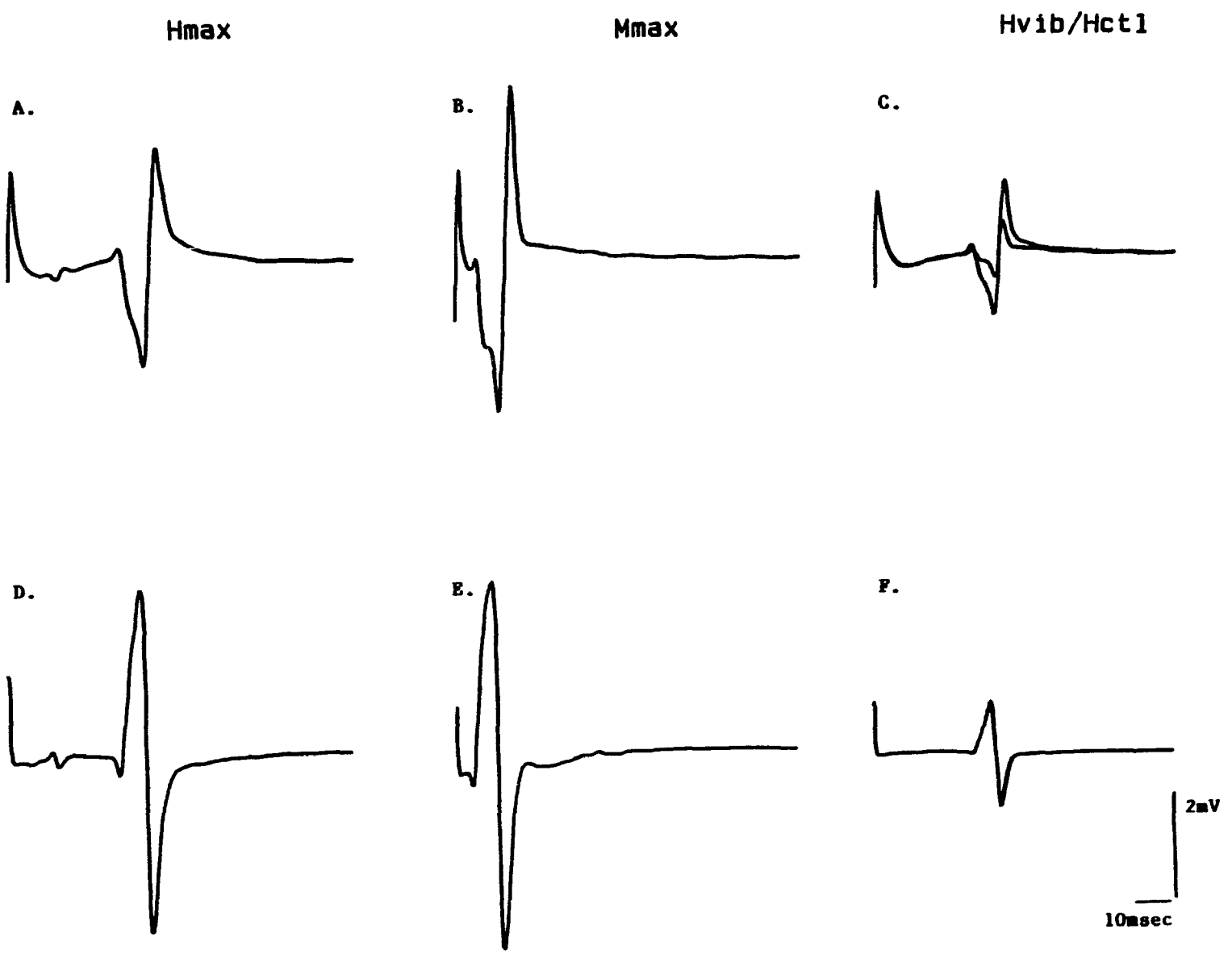


Fig. 1 Examples of maximal H reflex (Hmax, A & D), maximal M responses (Mmax; B & E), and vibratory inhibition of the H reflex (Hvib/ Hctl; C & F) in two hemiparetic subjects with mild (A-C) and severe (D-F) spasticity For these subjects, the H/M ratios were 65 9% and 90 0%, while the Hvib/Hctl ratios were 40 0% and 64 4% respectively

spasticity (mild versus severe) in the two subjects shown in Fig. 1, this was not the case for all subjects. As reported in a previous paper (Chapter 1; Levin and Chan, 1990a), the total spasticity score did not show any consistent relationship with H/M or Hvib/Hctl ratios (r=0.27, 0.43 respectively). Similarly, the magnitude of H/M and Hvib/Hctl ratios were not correlated with each other (r=0.22, Chapter 1; Levin and Chan, 1990a).

EFFECTS OF TENS ON H REFLEXES

Due to the large inter-subject variability of H reflex measures, we expressed the post-stimulation effects as percentages of the control values, in order to compare the results of each treatment across subjects. Figure 2 shows the group mean changes in H reflex latencies, H/M and Hvib/Hctl ratios in the three 20 min post-stimulation time periods (P1, P2, P3) after TENS application to the lower extremity (filled bars), or to the upper extremity (hatched bars), and after placebo stimulation to the lower extremity (open bars). Placebo stimulation had no effect on H reflex latencies in the hemiparetic patients (mean change of the three post-stimulus intervals was 99.6 $\pm$ 8.3%). In contrast, Fig. 2 (left panel) shows that segmental and heterosegmental TENS produced a significant increase in H reflex latencies which was evident in each of the 20 min time intervals following TENS. The mean post-stimulus change in latency was 106.5 $\pm$ 8.7% ($p<0.02$) following TENS to the lower extremity, and 105 7 $\pm$ 6.2% ($p=0.02$) after TENS to the upper extremity.

No significant effects of segmental, heterosegmental or placebo TENS were found on the magnitude of either H/M ratios (Fig. 2, center panel) or Hvib/Hctl ratios (Fig. 2, right panel), although segmental TENS tended to decrease H/M ratios. The large inter-subject variability of Hvib/Hctl ratios may have masked any possible treatment effect. However, no effect was found even after examining the results of those subjects who initially had low (<50%) or high Hvib/Hctl ratios (>50%).

EFFECTS OF TENS ON STRETCH REFLEXES

Neither TENS nor placebo stimulation had any consistent effect on stretch reflex durations, areas, or on stretch-evoked clonus. However, both latencies and onset angles were significantly increased following TENS but not placebo stimulation ($F=7.36$, $p=0.001$). An example of the effect of

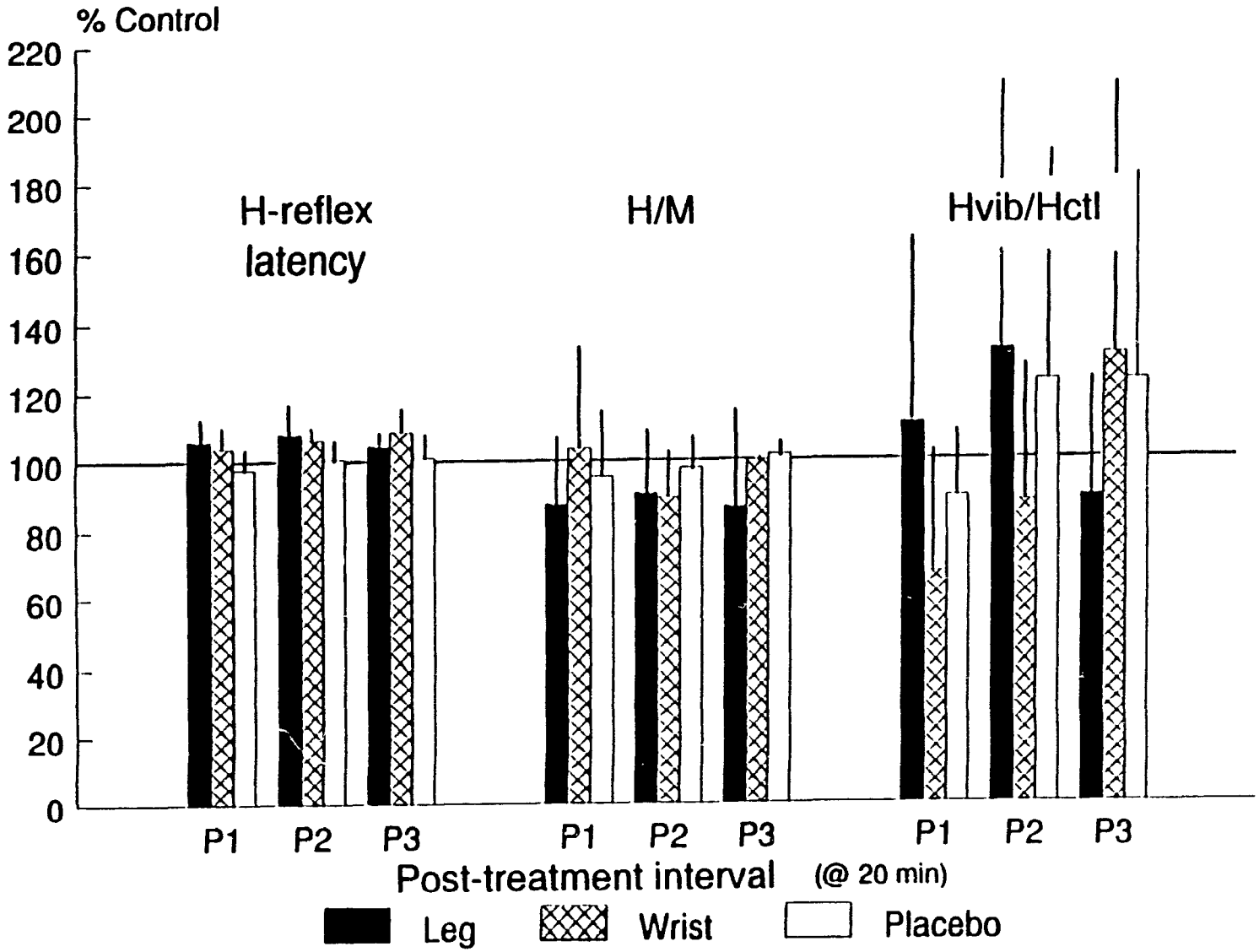


Fig. 2. Histograms of the means and standard deviations of post-stimulation changes in H reflex latencies (left), H/M ratios (middle), and Hvib/Hctl ratios (right) for each of the three treatment procedures Solid bars denote TENS treatment to the common peroneal nerve of the leg. Hatched bars represent TENS treatment to the contralateral wrist Open bars indicate placebo stimulation to the leg Post-stimulus changes at three 20 min intervals (P1, P2, P3) are expressed as percentages of the control values Compared to placebo stimulation, the mean H reflex latencies were significantly prolonged after TENS to either site (Post-Hoc test, $p < 02$)

TENS on the soleus stretch reflex latency is shown in Fig. 3A-D for one subject with moderate spasticity. The mean values of ten stretch reflexes (solid line) and their standard errors (dotted line) are displayed on the same time scale along with the corresponding mean ankle displacement (dashed line) before stimulation (Fig 3A), 20, 40, and 60 minutes (Fig 3B-D) after 45 minutes of TENS stimulation to the common peroneal nerve. The prolongation of stretch reflex latencies is clearly seen in this example, as an increased distance from the vertical line aligned with the onset latency of the control response in Fig. 3A. Group effects are summarized in the histograms of Fig. 4 showing the mean values of stretch reflex latency changes, expressed as a percentage of the control, in the three 20 min time intervals following the applications of TENS or placebo stimulation The means of all three post-stimulation periods for stretch reflex latencies were 110 5 $\pm$ 4.5% for TENS applied to the contralateral upper extremity, and 109 8 $\pm$ 9 2% for TENS applied to the ipsilateral lower extremity. These were significantly longer than the value obtained following placebo stimulation (90 8 $\pm$ 7 7%, $p<0$ 05). It should further be noted that the increase in stretch reflex latencies was evident for at least 60 min post-TENS stimulation.

DISCUSSION

Of all the aspects of segmental reflex circuitry investigated in our spastic hemiparetic subjects, only H and stretch reflex latencies showed any improvement (5 7% to 10.5%) immediately following 45 min of low-threshold afferent conditioning. Of particular interest was that the prolongation of the onset measures was evident after both segmentally and heterosegmentally applied TENS, but not after placebo stimulation. Furthermore, the effect outlasted the period of stimulation for at least 60 min.

TENS or placebo treatment had no significant effects on the magnitude of either H/M ratios or Hvib/Hctl ratios (Fig 2). Since the former reflects the amount of excitability in the alpha motoneuronal pool (Hugon, 1973; Schieppati, 1987), our findings may suggest that 45 min of TENS had no immediate effects on motoneuronal excitability. Nevertheless, H/M ratios showed a tendency to decrease following segmental TENS stimulation, and Hvib/Hctl ratios appeared to be depressed for

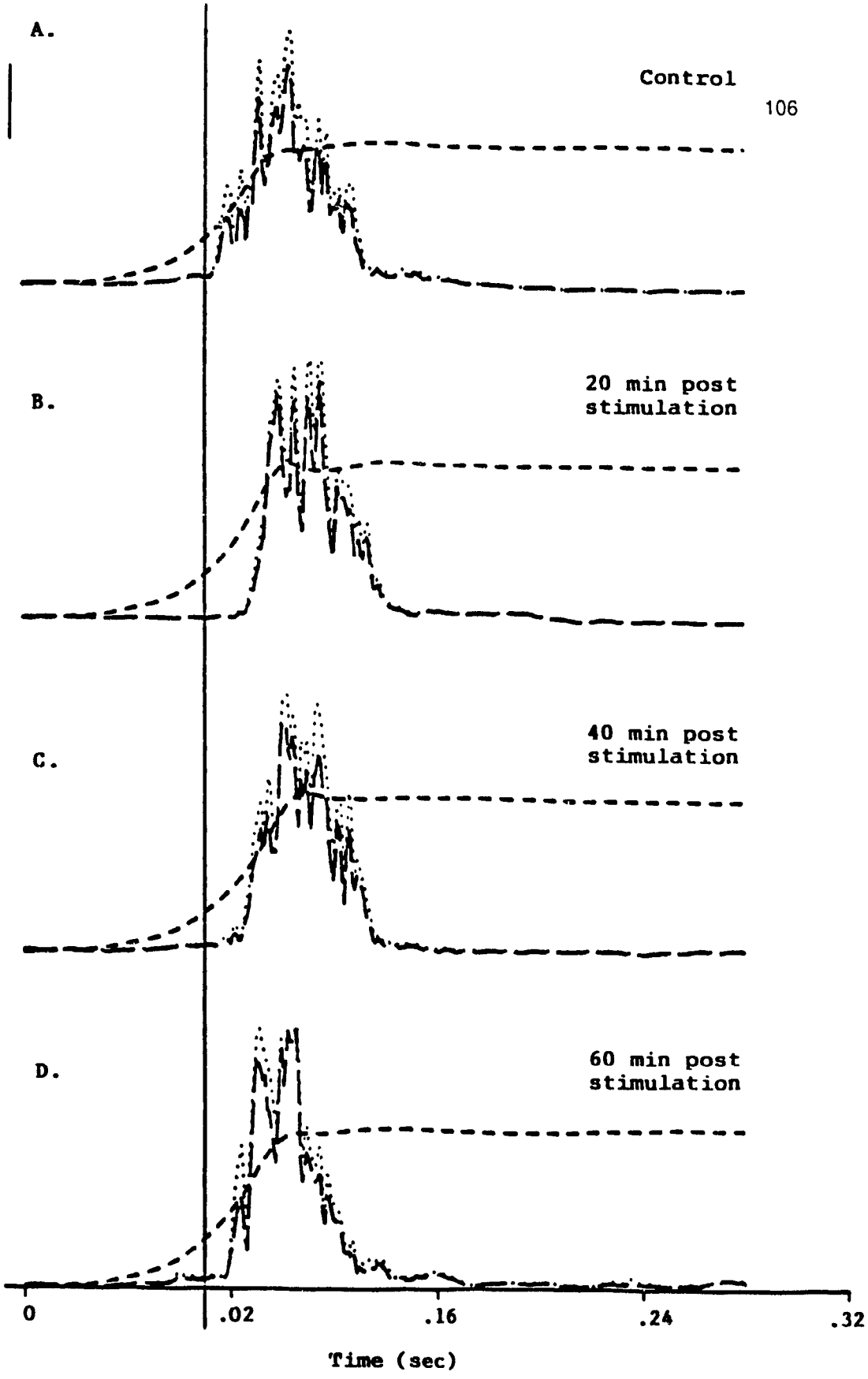


Fig. 3. Soleus stretch reflexes in one subject with moderate spasticity (A) before, (B) 20, (C) 40 and (D) 60 min after 45 min of TENS to the common peroneal nerve. Mean EMG values of ten trials are denoted by solid lines and standard errors by dotted lines. Stretch reflex responses are shown on the same time scale as the ankle displacement denoted by dashed lines. Vertical line indicates the control stretch reflex latency The prolongation of onset latencies in each post-stimulus time interval is clearly seen as an increased distance from this line

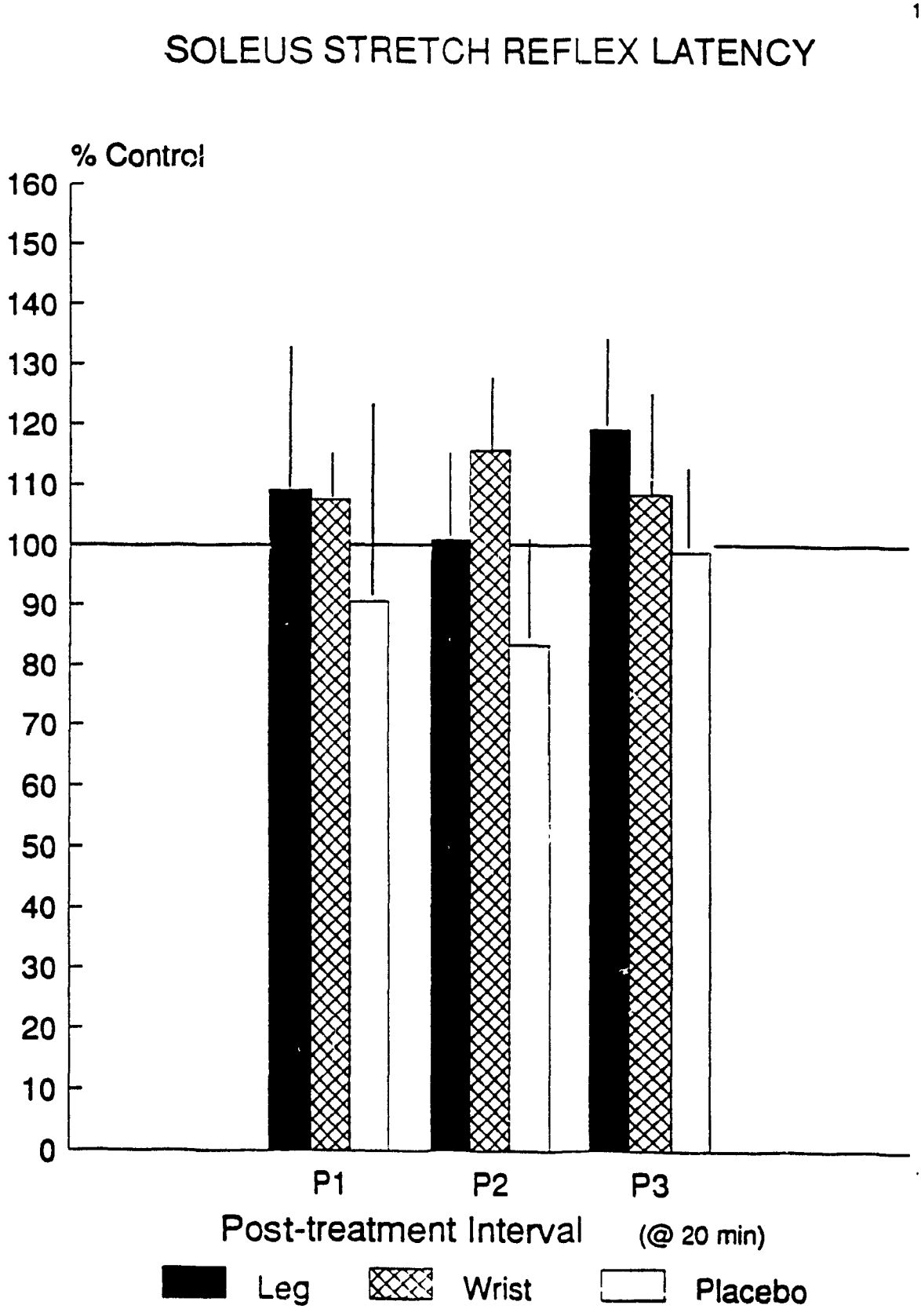


Fig. 4. Histograms of the means and standard deviations of soleus stretch reflex onset latencies in each 20 min interval for each treatment procedure. Legends are the same as for Fig. 2. Note that, in contrast to placebo stimulation, TENS applied to the leg or wrist significantly prolonged stretch reflex latencies (Post-Hoc test, $p<.05$).

up to 40 min following heterosegmental TENS stimulation (Fig 2). H/M ratios would not be altered if the maximal H and M responses increased or decreased together Therefore, in an effort to determine if TENS affected them in parallel, we measured the changes in each response over time in individual subjects Both of them were found to increase together slightly regardless of TENS or placebo stimulation. Possible explanations for the increasing trends include changes in limb temperature, skin or electrode resistance (Brunia et al , 1973) However, these factors would not be important in the interpretation of findings in Hvib/Hctl ratios, since control H reflexes were chosen as a constant percentage of the maximal M response evoked in each successive 20 min time interval

EFFECTS OF SEGMENTAL TENS

Segmental mechanisms may have contributed to the prolongation of reflex latencies observed in this study. A likely mechanism could be reciprocal inhibition It is well documented that repetitive low-threshold afferent stimulation immediately inhibits spinal reflex activity segmentally, via the activation of reciprocal inhibitory pathways (Eccles and Lundberg, 1958, Tanaka, 1983) Extensive excitatory and inhibitory convergence from segmental, as well as supraspinal systems onto Ia inhibitory interneurons, has been established by direct interneuronal recording in cats (Hultborn et al , 1976a,b,c). In normal man, reciprocal inhibition from pre-tibial flexors to extensors is present during voluntary activation of the dorsiflexors, as evidenced by suppression of the H reflex amplitude in the antagonist at latencies consistent with a disynaptic pathway (Tanaka, 1983). Reciprocal inhibition is present, although weak, in patients with hemiplegia (Yanagisawa et al , 1976) Thus, one possible explanation for the effects of segmentally-applied TENS could be that repetitive large diameter afferent conditioning may have resulted in an inhibition of the excitability of extensor alpha motoneurons mediated by Ia reciprocal inhibitory pathways Our findings of increased H and stretch-reflex latencies are consistent with the view that reciprocal inhibition may modulate the threshold, and consequently the latency, rather than the amplitude of the soleus H reflex in man (Davies, 1985).

EFFECTS OF HETEROSEGMENTAL TENS

TENS applied to the wrist prolonged H and stretch reflex latencies in the contralateral lower

limb by the same order of magnitude as segmental stimulation (Figs. 2 and 4). This heterosegmental stimulation also depressed Hvib/Hctl ratios (see Fig. 2) for up to 40 min post-stimulation, but the effect was not significant ($p>0.05$). Since both segmental and heterosegmental stimulation affected lower extremity reflexes to a similar extent, it is not likely that these results can be explained by purely reciprocal mechanisms discussed above. Furthermore, the prolonged effects of 45 min of TENS suggested that repetitive electrical stimulation may have triggered the release of long-lasting inhibitory neuromodulators to be discussed below

The immediate effects of remote, heterosegmental conditioning of low-threshold afferents on lower limb reflexes in man has not been previously described, although Walker (1982) observed a prolonged suppression of clonus in the lower extremity of multiple sclerosis patients following percutaneous stimulation of the contralateral radial/median nerve with implanted electrodes. In intact rats, a gradual enhancement of inhibition in spinal lumbar interneurons has been reported following repeated electrical cutaneous conditioning of the ipsilateral hindlimb (MacDonald and Pearson, 1979). In this study, the inhibition outlasted the stimulation from 0.5 sec to 7 min in intact but not spinal rats, suggesting that the development of inhibition depended on descending influences.

Possible mechanisms which may explain the results of remote afferent stimulation on reflex latencies could include 1) an increase in presynaptic inhibition, 2) a non-specific release of inhibitory neuromodulators, or 3) an augmentation of descending inhibition via propriospinal pathways, as it will emerge below.

Presynaptic Inhibition. In the present study, both segmental and heterosegmental afferent conditioning were found to have no significant effect on Hvib/Hctl ratios in spastic hemiparetic patients. In normal subjects, inhibition of the soleus H reflex is maximal when a 2 mm amplitude vibratory stimulus of between 80 to 100 Hz is applied to the homonymous Achilles tendon (Desmedt and Godaux, 1978). Under these conditions, inhibition of the H reflex is believed to be partially mediated by presynaptic inhibition of the Ia terminals onto the presumed monosynaptic stretch reflex arc (Gillies et al., 1969, Burke et al , 1976). Vibratory inhibition of the H reflex has been reported to be decreased in spastic hemiplegic subjects (Ashby and Verrier, 1976), suggesting that presynaptic

inhibition may be diminished in spasticity. One of the mechanisms proposed to be responsible for the decrease in spasticity during dorsal column stimulation is an enhancement of presynaptic inhibition at the segmental level (Phillips, 1981) The evidence supporting this contention, however, is quite indirect. Our findings that TENS did not decrease Hvib/Hctl ratios may have been related to the fact that only half of our subjects had Hvib/Hctl ratios that were larger than normal (>50%) However, even in the patients with elevated ratios (n=5), the mean post- stimulus effects of segmental and heterosegmental TENS were not significantly different (p>0 05) from placebo stimulation, being 83 9 $\pm$ 23 0%, 89.1 $\pm$ 33 7% and 96 2 $\pm$ 33 5% respectively. Paradoxically, TENS treatments tended to increase the Hvib/Hctl ratios in the remaining subjects with low initial ratios when compared to placebo, the respective values being 124.6 $\pm$ 67 8%, 130 7 $\pm$ 72.5% and 91.5 $\pm$ 65 8%. However, these results were not significant due to the high intersubject variability Despite the difficulty in interpreting these results due to the small size of our sample, the insignificant decrease in the group mean Hvib/Hctl ratio is not consistent with an immediate enhancement of presynaptic inhibition following a single session of TENS stimulation.

Release of Inhibitory Neuromodulators. The prolonged increase in reflex latencies for periods outlasting the TENS stimulation may point to the possible involvement of inhibitory neuromodulators. In this connection, TENS applications for pain control have been reported to increase opioid concentrations in the plasma and cerebrospinal fluid of normal human subjects (Facchinetti et al., 1984; Salar et al , 1981). Furthermore, morphine sulphate injected in the intrathecal space overlying the spinal cord has been found to produce a striking relief of clinical spasticity (Erickson et al , 1989). Thus, the release of neuromodulators triggered by TENS stimulation may be a powerful inhibitory mechanism which could explain the prolonged increase of reflex latencies

Increase in Descending Inhibition. Our results also support the hypothesis that low-threshold afferent stimulation may have raised the threshold of motoneuronal excitability at the segmental level via activation of propriospinal and/or descending inhibitory pathways Assuming that stretch reflex thresholds are decreased in spasticity (Powers et al , 1988), possibly by an increase in

segmental motoneuronal excitability produced via descending pathways (Feldman, 1966; 1986), stretch reflex onset latencies would be shorter in spastic hemiparetic subjects. Similarly, one would expect an increase in H/M and SR/M ratios. This indeed was the case in our patient group compared to normal age-matched control subjects (Chapter 1; Levin and Chan, 1990a). Since both repetitive segmental and heterosegmental stimulation increased stretch reflex latencies, it seems unlikely that the effects were mediated strictly by segmental mechanisms. Rather, non-segmental mechanisms appear to be involved. Feldman and Orlovsky (1972) have shown that stimulation in specific areas of the brainstem of decerebrate cats (Dieter's nucleus, pyramidal tract, reticular formation) resulted in a net inhibition of thresholds but not stiffness or magnitude of stretch reflexes in ankle extensor muscles Similarly, our repetitive stimulation may have caused a net inhibitory influence at the segmental level via the activation of propriospinal and/or descending pathways, and/or via a triggered release of long-lasting inhibitory neuromodulators. Further investigation of these possible contributing mechanisms seems warranted.

CLINICAL IMPLICATIONS

Our results suggested that peripherally applied TENS may increase reflex latencies via non-segmental mechanisms, since changes of similar magnitude were found following segmental or heterosegmental stimulation. It was not evident, however, that the increase in latencies reflected a concomitant decrease in clinical spasticity. Indeed, clinical measures of spasticity were not correlated with measures of static reflex function in the lower extremities of our patients (Chapter 1; Levin and Chan, 1990a). The lack of correlation however, was not surprising, since none of the clinical measures is particularly sensitive to threshold changes, but rather more indicative of response magnitudes Also, the possible inhibitory effects of a single TENS application on clinically measured spasticity, indeed, may have been subclinical.

Given the encouraging effects on reflex latencies from a single session of TENS, we speculated that prolonged treatment with repetitive low-threshold afferent stimulation may be of therapeutic importance in the reduction of hemiplegic spasticity A companion paper therefore attempts to elucidate possible longer-term effects of afferent manipulation in the management of spasticity.

CHAPTER 5

REPETITIVE ELECTRICAL STIMULATION IN SPASTIC HEMIPARESIS: II. RELIEF OF SPASTICITY IS ASSOCIATED WITH IMPROVEMENT IN REFLEX AND VOLUNTARY MOTOR CONTROL

SUMMARY

In a previous study, we found that single, 45 min applications of transcutaneous electrical nerve stimulation (TENS) prolonged H and stretch reflex latencies in hemiparetic subjects. In addition, repeated TENS applications (9 daily 30 min treatments) enhanced vibratory inhibition of the H reflex and tended to decrease hyperactive stretch reflexes. This suggests that longer term TENS may also be effective in the reduction of hemiparetic spasticity. However, the effects of TENS on motor control remain inconclusive. The objectives of this study were: 1) to determine whether longer-term repetitive TENS stimulation would lead to a reduction in clinical spasticity in hemiparetic subjects; and 2) to examine whether such a reduction may be associated with a decrease in stretch reflex excitability and an improvement in voluntary motor function. In this study, the effects of fifteen 60 min TENS treatments to the affected lower limb on clinical spasticity scores, reflex measures and maximal voluntary isometric plantarflexion and dorsiflexion of the ankle in standing were contrasted with those of placebo stimulation in similar groups of hemiparetic subjects. Repeated applications of TENS decreased clinical spasticity ($p<0.05$), increased vibratory inhibition of the H reflex ($p=0.02$), and decreased the magnitude of stretch reflexes ($p=0.05$) in the spastic ankle extensors. These changes occurred concomitantly with a dramatic improvement in voluntary dorsiflexion but not plantarflexion force (up to 920%) and a decrease in co-contraction ratios ($p<0.05$). These results indicated that repeated applications of TENS can reduce clinical spasticity and improve control of reflex and motor function in hemiparetic subjects. Furthermore, the mechanism of the improvement may be partly related to an enhancement in presynaptic inhibition, and a possible 'disinhibition' of descending voluntary commands to flexor motoneurons.

INTRODUCTION

Motor dysfunctions associated with upper motor neuron lesions appear to result from a lack of the coordination between homo- and heteronymous reflex systems on the one hand, and descending supraspinal mechanisms on the other, at least in the cat (Nichols, 1989) The underlying causes of these disorders are, as yet, unclear However, indirect evidence from spastic subjects suggests that it may be partly related to a loss of presynaptic inhibitory mechanisms acting on the muscle spindle afferent terminals (Ashby and Verrier, 1976, Burke, 1988).

Pathophysiological mechanisms aside, there is abundant evidence that low threshold afferent input can reduce the ongoing activity in interneurons and/or alpha motoneurons via segmental, proprio-spinal or supraspinal pathways (Pierrot-Deseilligny and Mazieres, 1984) Such a possibility has been demonstrated in the cat where descending commands were modified by activity in cervical proprio-spinal neurons during target-reaching tasks (Alstermark et al., 1981) Similarly, electrical stimulation (0.6 x motor threshold) of low threshold afferents from the median and ulnar nerves has been found to inhibit Ia afferent mediated excitation in reflexly and voluntarily activated wrist flexor muscles (Malmgren and Pierrot-Deseilligny, 1988a,b).

Furthermore, dorsal column stimulation has been shown to inhibit transmission in spinothalamic tract pathways via both pre-and postsynaptic inhibitory mechanisms (Foreman et al., 1976) Indeed, there is considerable supraspinal and peripheral afferent convergence onto spinal interneurons mediating presynaptic inhibition (Baldissera et al., 1981). If presynaptic inhibition is indeed diminished in spasticity (cf. Ashby and Verrier, 1976; Burke, 1988), then segmental input arising through natural or electrical stimuli may be one way of 'switching on' presynaptic inhibitory mechanisms

Now, remote subcutaneous electrical stimulation of the contralateral wrist has been found to suppress ankle clonus in spastic multiple sclerosis patients (Walker, 1982) This inhibition developed gradually (an hour after 60 min of stimulation) and outlasted the period of stimulation for up to three hours in some instances (Walker, 1982). According to other clinical reports, low-intensity transcutaneous electrical nerve stimulation (TENS) also reduces spasticity and improves motor function in

patients with spinal spasticity. These effects are reported whether TENS is applied directly over spastic muscles (Bajd et al., 1985) or remotely on the skin overlying the dorsal columns of the spinal cord (Fredriksen et al., 1986). The mechanisms by which TENS may be exerting these effects are, as yet, unclear. However, there is some evidence that it may be acting via a combination of several mechanisms. Possible enhancement of presynaptic inhibition was suggested by the finding of a significant increase in the amount of vibratory inhibition of the H reflex in spastic hemiparetic subjects following nine daily, 30 min TENS applications to the low back (Hale and Chan, 1986b). Alternatively, the release of inhibitory neuromodulators or opioids may account for the prolonged influence of TENS (Almay et al., 1985; Salar et al., 1981).

Based on these findings, we recently studied the effects of 45 min of TENS, applied either segmentally to the ipsilateral common peroneal nerve or heterosegmentally to the contralateral median nerve in spastic hemiparetic subjects. As described in the previous chapter (Chan and Levin, 1990), we found a significant and long-lasting (up to 60 min post-stimulation) prolongation of H and stretch-reflex latencies in the spastic calf muscles regardless of the site (segmental or heterosegmental) of stimulation. These findings suggested that a single session of TENS could lead to a prolonged decrease in hyperexcitable stretch reflexes in hemiparetic spasticity, that could be independent of segmental reciprocal inhibitory mechanisms.

Considering that the disorder in spasticity may be partly related to enhanced stretch-reflex excitability (Feldman, 1986; Powers et al., 1988), the above finding led us to speculate that repeated TENS applications over a period of time (weeks) could result in a significant reduction of clinical spasticity. We set out to investigate this possibility in the present study. The effects of a long period of TENS stimulation (fifteen daily 60 min treatments) on subjective spasticity, hyperactive reflexes and maximal voluntary isometric ankle contractions were studied in spastic hemiparetic subjects. These effects were compared with those of placebo stimulation applied for the same period to a similar group of hemiparetic subjects, in an attempt to monitor possible changes in these measures due to mental set and/or time alone. To elaborate, the objective of the present study was to investigate whether repetitive low-threshold afferent stimulation (TENS) over two or three weeks would lead to a reduction in clinical spasticity in hemiparetic subjects. A further objective was to find out whether such a

reduction was associated with a decrease in stretch reflex excitability and an improvement in voluntary motor function.

METHODS

SUBJECTS

Thirteen patients with spastic hemiparesis (mean age = 59.1 ± S.D 13.6 yr) participated in the study. Criteria for inclusion of the hemiparetic subjects, method of subject fixation, stimulation and recording procedures have all been described in detail in the previous chapters (Levin and Chan, 1990a,b; Chan and Levin, 1990). For the clinical assessment of spasticity, an evaluation form consisting of three commonly used measures was developed. As already described (Levin and Chan, 1990a), it consisted of: 1) Achilles tendon jerk; 2) resistance to passive ankle dorsiflexion; and 3) amount and duration of ankle clonus. This evaluation provided a composite though subjective index of spasticity. Based on our clinical observations, total spasticity scores ranging from 0-9, 10-12, and 13-16 corresponded to mild, moderate and severe spasticity respectively (Table I). Hemiparetic subjects were stratified according to the level of spasticity thus 'computed' in the affected lower leg. Initially they were randomly allocated to either a treatment or a placebo group. Seven patients were thus assigned to the treatment group and six to the placebo group (mean age 64 7 ± 10.6 yr). Since the placebo stimulation was later found to have no effect, four of the six patients in the placebo group then underwent a further three weeks of TENS stimulation. This increased the final number of patients in the treatment group to a total of *eleven* (mean age 58.5 ± 14.7 yr). Baseline clinical, reflex and maximal voluntary force data for all subjects are presented in Table I.

EXPERIMENTAL PROTOCOL

Most subjects were tested on two occasions, with at least one week apart, to acquire baseline measurements. The test battery consisted of five measures which have been described in detail previously (Levin and Chan, 1990a,b) They were: 1) the clinical spasticity scores; 2) the maximal amplitude of the H reflex as a percentage of the maximal M response (H/M, Hoffmann, 1918); 3) the

Table I. A comparison of clinical features, reflex profile and maximal voluntary force between spastic hemiparetic subjects in TENS treatment and placebo groups

Clinical Features				Reflex Profile			Maximal Contraction		
Age (yr)	Etiology	Time since injury (mos)	Spasticity score[a]	H/M (%)	Hvib/Hctl (%)	SR onset (degree)	SR/M area (%)	PF force (kg)	DF force (kg)
TENS Treatment Group									
75	L.CVA	18	6	17.1	53.4	7.0	37.0	16.1	5.0
49	L.CVA[b]	27	9	98.1	17.0	16.9	82.0	16.7	7.3
67	L.CVA[b]	8	9	22.3	80.9	29.5	27.0	10.7	4.2
31	L.CVA[b]	25	10	94.7	43.2	20.3	53.0	22.4	5.8
76	R.CVA[b]	43	10	19.8	81.7	11.5	29.0	10.4	7.9
43	L.CVA	8	11	19.9	24.2	12.1	16.0	28.9	1.4
67	R.CVA	23	12	88.6	29.8	23.2	51.0	23.8	6.4
57	L.CVA[b]	85	13	100.0	96.3	13.5	60.0	3.1	0.0
73	R.CVA[b]	26	13	57.9	30.1	11.4	100.0	12.4	0.0
58	R.CVA[b]	16	15	77.9	96.3	11.4	48.0	10.5	1.2
47	L.CVA[b]	11	16	100.0	81.4	10.5	100.0	17.6	0.0
Mean=58.5		26.4	11.2	63.3	57.7	15.2	50.3	15.7	3.6
S.D.=14.7		21.9	2.9	36.6	30.3	6.6	25.7	7.3	3.1
Placebo Group									
67	L.CVA[b]	8	9	22.3	80.9	29.5	37.0	11.0	3.1
76	R.CVA[b]	43	10	19.8	81.7	11.5	65.0	12.3	0.0
58	L.CVA	50	12	85.9	76.9	8.2	49.0	9.5	1.0
67	R.CVA[b]	37	13	60.2	75.6	10.6	53.0	13.5	5.1
73	R.CVA[b]	26	13	57.9	30.1	11.4	100.0	9.0	5.0
47	L.CVA[b]	11	16	100.0	84.3	10.5	100.0	14.0	0.0
Mean=64.7		29.2	11.8	57.7	71.6	13.6	68.0	11.6	2.4
S.D.=10.6		17.2	2.5	32.5	20.6	7.9	27.8	2.1	2.4
ns		ns	ns	ns	ns	ns	ns	ns	ns

[a] Spasticity score: 0-9 = mild spasticity
10-12 = moderate spasticity
13-16 = severe spasticity

[b] Four patients participated in both placebo and treatment groups after no placebo effect was demonstrated.

SR = stretch reflex
PF/DF = plantarflexion/dorsiflexion
L/R CVA = left/right cerebrovascular accident
ns = non-significant

amount of inhibition of the H reflex during vibration (Hvib/Hctl); 4) the excitability of the soleus stretch reflex in terms of latency, response duration and magnitude (SR/M area); and 5) maximal voluntary isometric plantarflexion and dorsiflexion of the ankle (EMG and force) in standing.

The testing procedure was as follows: Spasticity about the ankle joint was assessed at the beginning of each experimental session. Subjects then performed the maximal voluntary isometric contractions in the functional position of standing. Four such contractions in the dorsiflexing and plantarflexing directions were obtained from both the affected and non-affected legs of the hemiparetic subjects. This was followed by reflex data measurements with the subjects in a semi-supine position. The duration of the entire testing protocol was approximately two and a half hours

Following the initial testing session(s) and the allocation to either the treatment or placebo group, subjects and/or their family members were instructed in the use of a portable TENS stimulator. The stimulation (or placebo) was applied for 60 min per weekday during a three week period, for a total of fifteen treatments. The 60 min treatment time was considered optimal based on findings from previous studies investigating the effects of repetitive electrical stimulation in spastic patients (Walker, 1982; Hale and Chan, 1986b; Chan and Levin, 1990). Compliance with the treatment protocol was verified by the examiner via inspection of a log book kept by the subject or subject's family. To assess the time course of the effects of stimulation, the five measures described above were repeated after two and three weeks of stimulation (Days 11 and 16).

STIMULATION PROCEDURES: TENS and Placebo Stimulation

TENS or placebo stimulation was applied via a Selectra 7720 stimulator (Medtronic) and was the same as already described in Chapter 4 (Chan and Levin, 1990). Briefly, low-intensity, high-frequency TENS at twice sensory threshold, or placebo stimulation at 0.1 x sensory threshold, was applied over the common peroneal nerve located just posterior to the head of the fibula on the hemiparetic leg. This nerve supplies the skin and muscles antagonistic to the spastic calf muscles. Correct positioning of the electrodes was confirmed by the subject reporting a tingling sensation in the cutaneous distribution of the nerve along the anterior part of the leg and dorsum of the foot.

EMG RECORDING AND DATA ANALYSIS

The procedures for recording and analyzing H reflexes, M responses, stretch reflexes, and maximal voluntary EMG and force were the same as previously described (Levin and Chan, 1990a,b). Briefly, soleus and tibialis anterior EMG was recorded via surface electrodes. Individual and mean peak-to-peak H reflex and M response amplitude values were calculated on-line. The stretch reflex onset was defined as the angle of ankle displacement corresponding to the onset of the soleus stretch reflex EMG (Levin and Chan, 1990a). Stretch reflex area was calculated by rectifying and integrating the soleus EMG in the 150 msec following its onset. It was expressed as a percentage of the area of the maximal M response recorded in the same muscle by the same electrodes. For maximal voluntary isometric contractions of the ankle muscles, soleus and tibialis anterior EMG, as well as plantarflexion and dorsiflexion force, were measured from 500 msec before to 2 sec after the response onset. EMG areas, maximal and mean force were calculated in a 500 msec window placed where the force trace reached a plateau. EMG areas were used to calculate co-contraction ratios such that antagonist EMG areas were expressed as a percentage of the total agonist plus antagonist EMG areas.

Statistical Analysis. Differences between the baseline data from the two groups of subjects were tested by Student's t-tests. Post-stimulation changes for each of the above measures were expressed as raw data or computed as percentages of the control values for each subject. The effects of TENS on each measure were compared with pre-stimulation control values or with placebo stimulation, using two-way ANOVAs. Differences between individual pairs of means were determined via 'least significant difference' tests. A significance level of 0.05 was used for all tests.

RESULTS

CHARACTERISTICS OF SPASTIC HEMIPARETIC SUBJECTS

Based on our clinical evaluation of the subjects comprising the treatment group, three had mild, four had moderate and four others had severe spasticity (Table I). In the placebo group, one subject

had mild, two had moderate and three had severe spasticity. The mean control composite spasticity scores did not differ between the two groups of subjects (11.2 $\pm$ 2.9 and 11.8 $\pm$ 2.5 respectively, t=-0.102 p>0.90, Fig. 1). There were no initial differences in control H/M, Hvib/Hctl, and stretch reflex values between the TENS and placebo groups (p>0.10, Table I). For maximal voluntary contractions, the mean control values of plantarflexion and dorsiflexion force were not significantly different from those of the placebo group (p)0.05, Table I). Mean control co-contraction ratios during ankle dorsiflexion also did not differ between the TENS and placebo groups (45.2 $\pm$ 25.5% and 53.7 $\pm$ 31.1% respectively, p>0.05).

EFFECTS OF TENS AND PLACEBO STIMULATION ON SPASTICITY SCORES AND H REFLEXES

The mean control and post-stimulation spasticity scores after two and three weeks of TENS (filled columns) or placebo (open columns) stimulation for each group are presented in Fig 1. The improvement in spasticity was evident after two weeks of TENS but not placebo stimulation. However, an additional week of TENS stimulation did not lead to a further reduction in spasticity scores. Of clinical importance is the finding that the reduction in spasticity following two and three weeks of TENS was significant when contrasted with placebo stimulation (F=4.66, p<0.05). This result is particularly remarkable in view of the consistancy of the spasticity scores after 2 and 3 weeks of placebo stimulation (Fig. 1).

Neither TENS nor placebo stimulation had any significant effect on the H/M ratios, despite the latter's tendency to decrease after two weeks of TENS (Fig. 3). On the other hand, Hvib/Hctl ratios did show significant trends after TENS stimulation. Examples of Hvib/Hctl ratios are shown in Fig. 2 for one subject with severe spasticity who received both TENS (subject 9; Table I) and placebo (subject 5; Table I) treatments. Hvib/Hctl ratios in this subject were highly consistent when measured on two occasions, one week apart (30.4% and 29.7%, Fig. 2A and B). Furthermore, they showed a significant reduction following TENS but not placebo stimulation (Fig. 2). It is noteworthy that this improvement was evident in 7 of the 11 subjects receiving TENS treatment, but in none of the subjects receiving placebo stimulation. Table II contrasts the effects of stimulation on the reflex measures between treatment and placebo groups. In two subjects of the treatment group, the reduction in Hvib/Hctl ratios

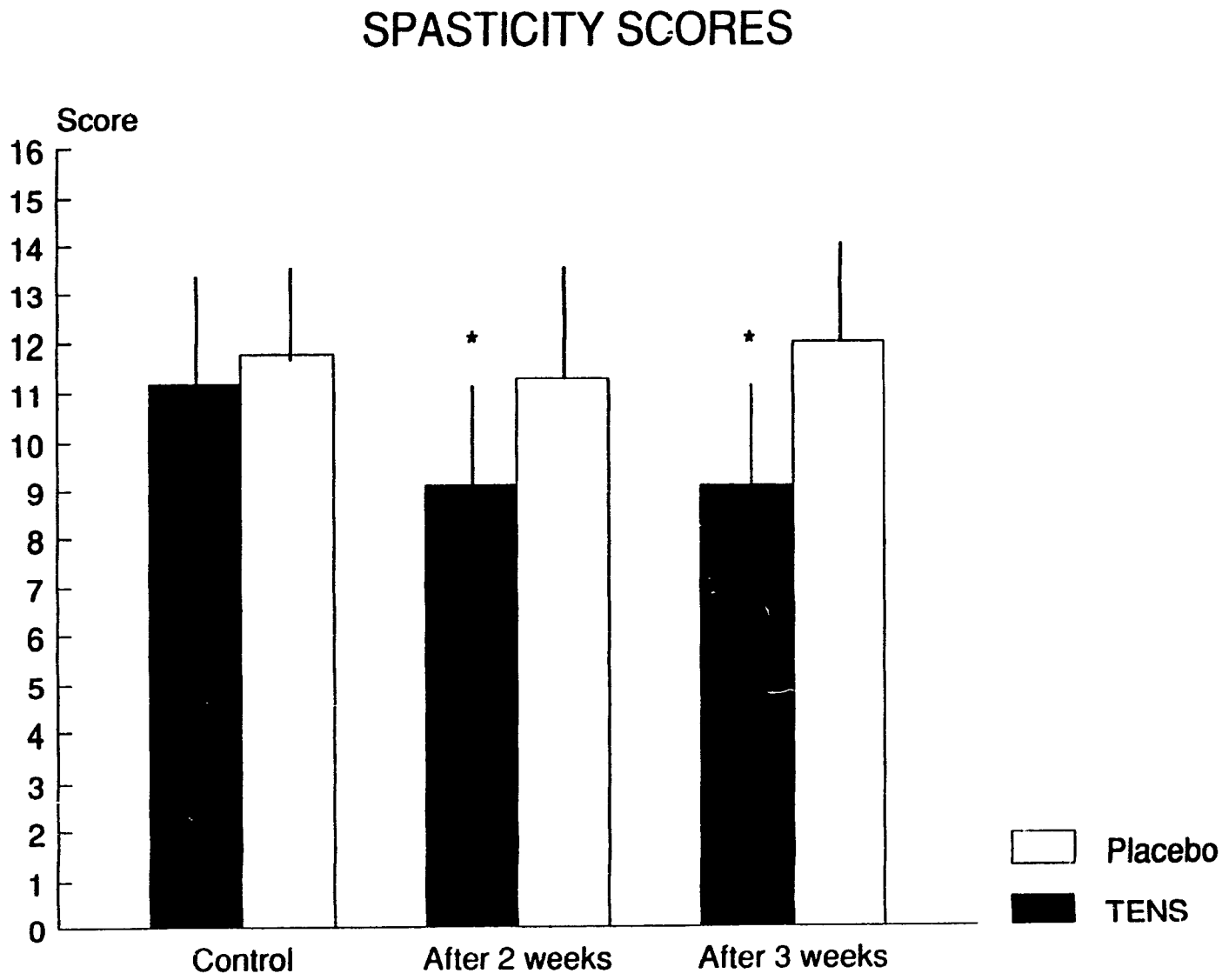


Fig. 1. Means and standard deviations of composite spasticity scores before (Control), two- weeks and three weeks after TENS (filled columns) or placebo stimulation (open columns) Note that TENS but not placebo stimulation resulted in a significant improvement in clinical spasticity ($\bar{p}<0.05$).

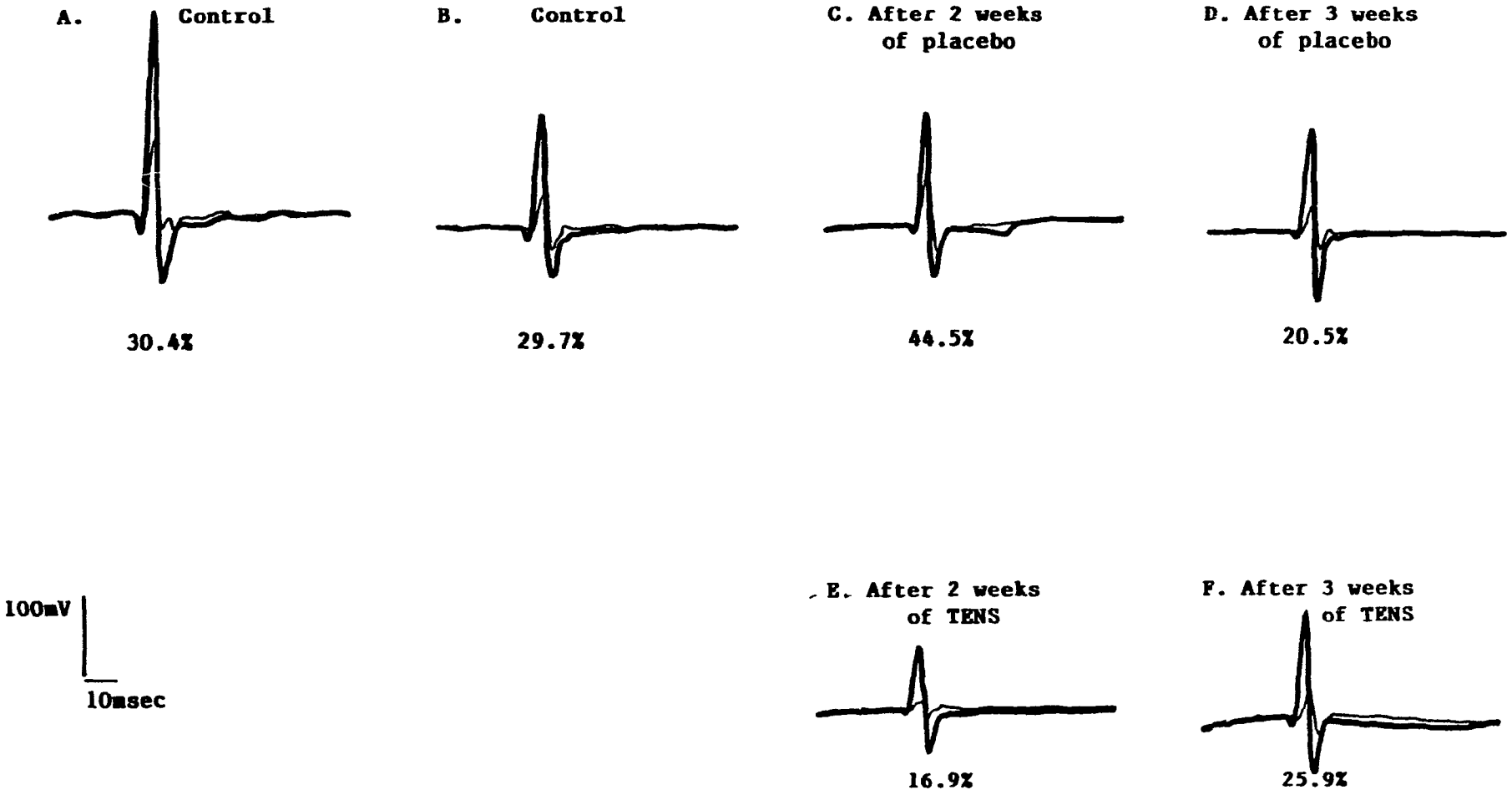


Fig. 2. Vibratory inhibition of the H reflex in one severely spastic hemiparetic subject H reflex responses during vibration (thin line) are superimposed over control reflexes (thick line). From top left Two control responses recorded one week apart were stable (A, 30.4%; B, 29.7%). Hvib/Hctl ratios are shown after two and three weeks of placebo (C, 44.5%; D, 20.5%) and TENS stimulation (E, 16.9%; F, 25.9%)

Table II. A comparison of reflex responses before and after 2 and 3 weeks of TENS and placebo stimulation

Subject	Hvib/Hctl			SR/M Area		
	Control	2 weeks	3 weeks	Control	2 weeks	3 weeks
TENS Treatment Group						
1.	53 4	53.3	-	37.0	-	10.0
2.	17.0	17.7	4.3	82.0	84.0	67.0
3.	80.9	92.9	86.4	27.0	20.0	28.0
4.	43.2	38.6	52.9	53.0	148.0	30.0
5.	81.7	-	54.8	29.0	29.0	18.0
6.	24.2	19.6	19.7	16.0	34.0	17.0
7.	29.8	22.2	3.1	51.0	63.0	45.0
8.	96.3	94.7	103.2	60.0	42.0	44.0
9.	30.1	16.9	25.9	100.0	66.0	66.0
10.	96.3	3.5	2.7	48.0	71.0	21.0
11.	81.4	36.5	72.2	-	-	-
Mean =	57.7	39.6*	42.5*	50.3	61.9	34.6**
S.D. =	30.3	31.8	36.7	25.7	38.8	20.2
Placebo Group						
1.	80.9	88.3	99.6	37.0	34.0	-
2.	81.7	46.8	82.3	65.0	21.0	42.0
3.	76.9	90.9	77.0	49.0	73.0	58.0
4.	75.6	80.8	78.2	53.0	66.0	-
5.	30.1	44.5	20.5	100.0	85.0	69.0
6.	84.3	74.7	50.7	104.0	118.0	105.0
Mean =	71.6	71.0	68.1	68.0	66.2	68.5
S.D. =	20.6	20.5	28.1	27.8	35.1	26.7

* p=0.02
** p=0.05

was marked (from 29.8% to 3.1% in subject 7; and from 96.3% to 2.7% in subject 10; Table II). For the four subjects in whom these ratios did not change, one was among the oldest subjects (75 yr., subject 1), one had very long-standing hemiplegia (85 mo., subject 8), and one had variable responses (subject 4). The fourth subject (subject 3 in the treatment group and subject 1 in the placebo group) had very consistent results in all 6 testing sessions.

Table II showed that the mean group Hvib/Hctl ratios were significantly decreased ($F=7.08$, $p=0.02$) following TENS (from 57.7% to 39.6% and 42.5%) but not placebo stimulation (from 71.6% to 71.0% and 68.1%). These changes are graphically depicted in the histograms of Fig. 3 as percentages of their respective control values. In the figure, the mean Hvib/Hctl ratios following two and three weeks of TENS stimulation were 70.3 $\pm$ 35.0% and 68.9 $\pm$ 40.6% respectively compared to placebo stimulation (104.7 $\pm$ 30.3% and 92.6 $\pm$ 23.8% respectively).

EFFECTS OF TENS AND PLACEBO STIMULATION ON STRETCH REFLEXES

TENS, but not placebo stimulation, increased the onset angle and decreased the magnitude of stretch responses. Following three weeks of TENS treatment, stretch reflex onset angles were increased by 134.6 $\pm$ 69.7% compared to placebo stimulation (105.9 $\pm$ 31.1%). The apparent prolongation of stretch reflex onsets following TENS however, was non-significant ($p=0.11$), possibly due to the high inter-subject variability in this measure. On the other hand, SR/M areas were significantly reduced, from 50.3 $\pm$ 25.7% to 34.6 $\pm$ 20.2% after three weeks of TENS treatment compared to placebo stimulation (from 68.0 $\pm$ 27.8% to 68.5 $\pm$ 26.7%; $F=4.03$, $p=0.05$, Table II). Note however, that this reduction was not apparent after two weeks of treatment.

EFFECTS OF TENS AND PLACEBO ON MAXIMAL ISOMETRIC VOLUNTARY CONTRACTIONS

In a previous study, it was found that overall EMG and force data recorded from the non-affected leg of hemiparetic subjects, did not differ from that obtained in the legs of normal subjects (Levin and Chan, 1990b). Therefore, we felt justified in comparing the effects of TENS and placebo stimulation on these measurements between the affected and non-affected legs of our hemiparetic subjects

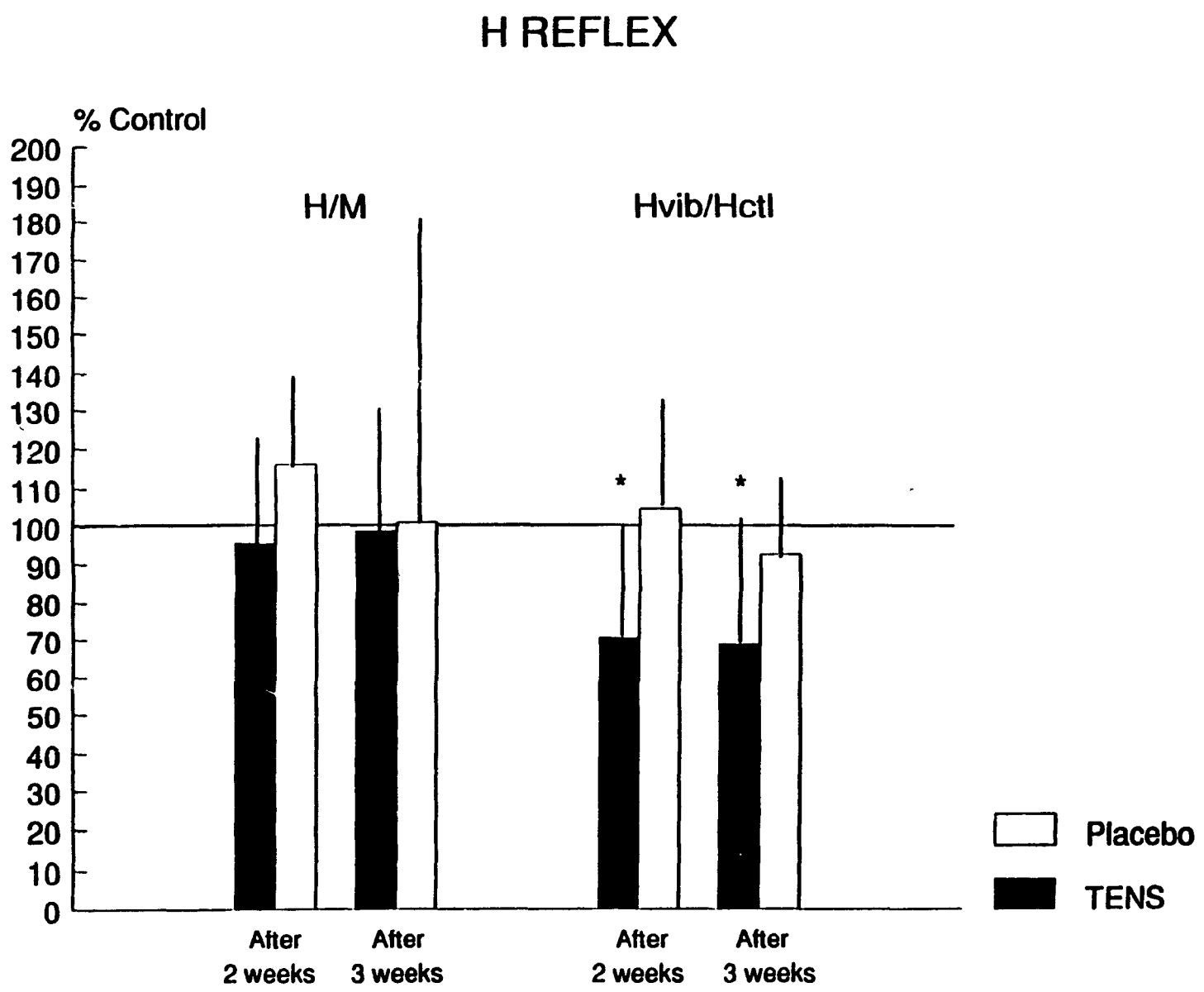


Fig 3. Histograms of the effects on H/M (left) and Hvib/Hctl (right) ratios expressed as a percentage of pre-stimulation control values after two and three weeks of TENS (filled columns) and placebo stimulation (open columns) *p=0.02.

The most striking result of our TENS treatment was a marked improvement in dorsiflexion force in the affected legs of hemiparetic subjects. This effect is illustrated by data from one subject in Fig 4 It was apparent that the significant improvement in dorsiflexion force was accompanied by a decrease in co-contraction of the antagonistic soleus muscle For example, in this subject, the mean control co-contraction ratio was 38% and the mean maximal force 1 4 kg After 2 weeks of treatment, the co-contraction ratio did not change (38%), but the mean maximal force increased to 3 4 kg By the end of three weeks of treatment, the co-contraction ratio was decreased to 18% along with an even greater increase in force to 7 4 kg.

Following three weeks of TENS stimulation, mean maximal dorsiflexing force had increased to 5.5 $\pm$ 2.9 kg in the TENS group but only to 3.7 $\pm$ 2.9 kg in the placebo group. Compared to control, this improvement was significant for the TENS ($F=4.40$, $p<0.05$) but not the placebo group ($F=1.09$, $p=0.37$). Figure 5 shows the changes in maximal plantar- and dorsiflexion force as percentages of their pre-stimulation control values for both groups. For dorsiflexion, the improvement in force was remarkable for the affected but not the non-affected leg, and ranged from 105% to 920% of control values. Although plantarflexion force showed improvement following TENS and placebo stimulation in both affected and non-affected legs, the magnitude of the improvement was similar for both stimulations, with no significant difference being found between group means.

Since we had previously found that EMG co-contraction ratios were quite stable across days for dorsiflexion ($r=0.99$) but not for plantarflexion ($r=0\ 53$; Levin and Chan, 1990b), only the former ratios were considered here. After two weeks of TENS stimulation, co-contraction ratios did not change for either TENS (44.0 $\pm$ 25.0%) or placebo (53.0 $\pm$ 26.0%) stimulation However, a marked reduction was evident in co-contraction ratios after three weeks of TENS (33.7 $\pm$ 23 8%, $F=4\ 13$, $p<0.05$), but not after three weeks of placebo stimulation (43.5 $\pm$ 26.1%; $F=1\ 57$, $p=0\ 25$). For plantarflexion, co-contraction ratios of the affected legs were not different from those of the non-affected legs, nor were they affected by either type of stimulation.

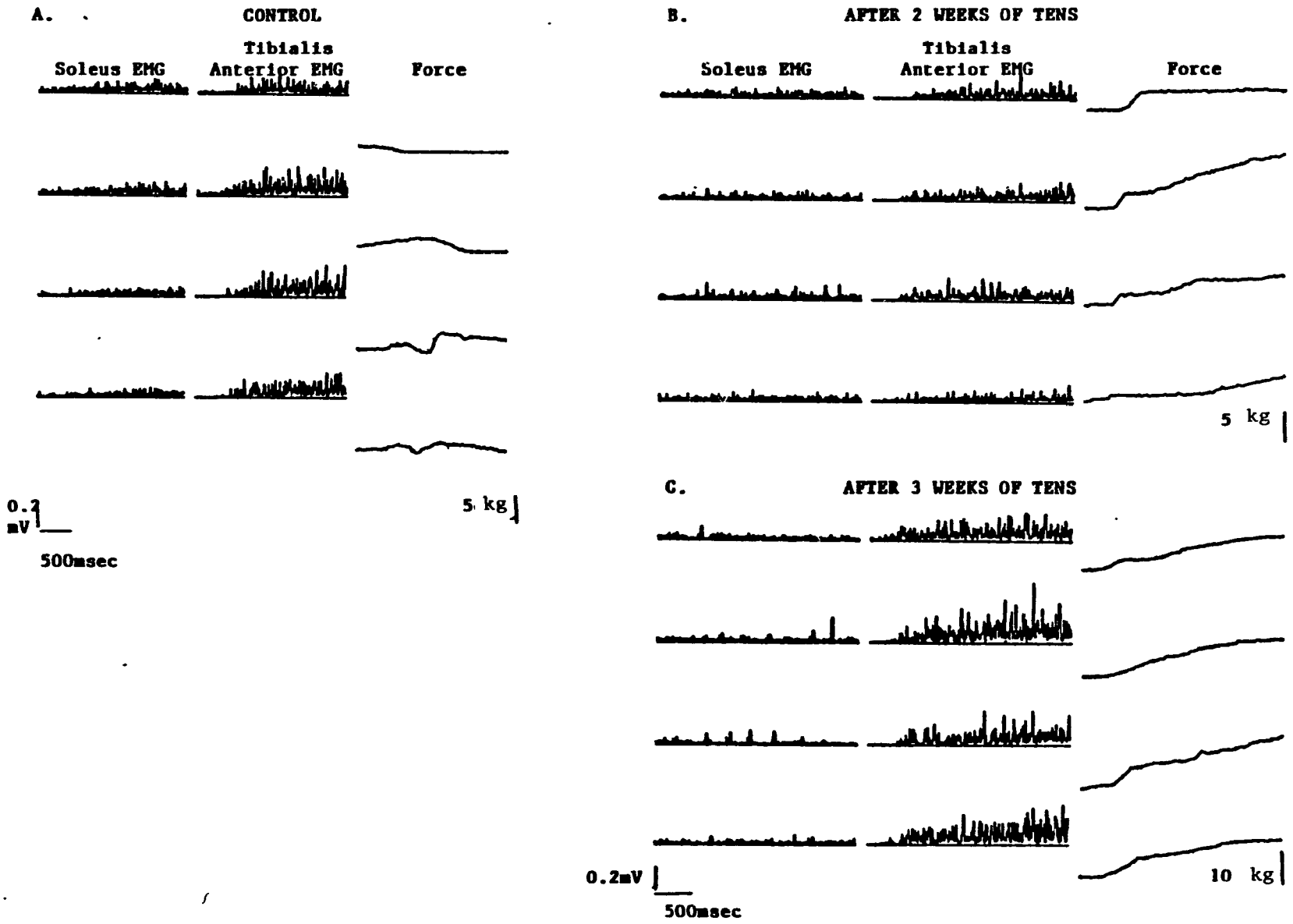


Fig 4. Four dorsiflexion trials in one subject with moderate spasticity A) control, B) after two and C) three weeks of TENS stimulation. In this subject, co-contraction ratios decreased from a mean of 38% to 18% while the maximal isometric force generated by the dorsiflexors increased from a mean of 1.4 to 7.4 kg after three weeks of treatment.

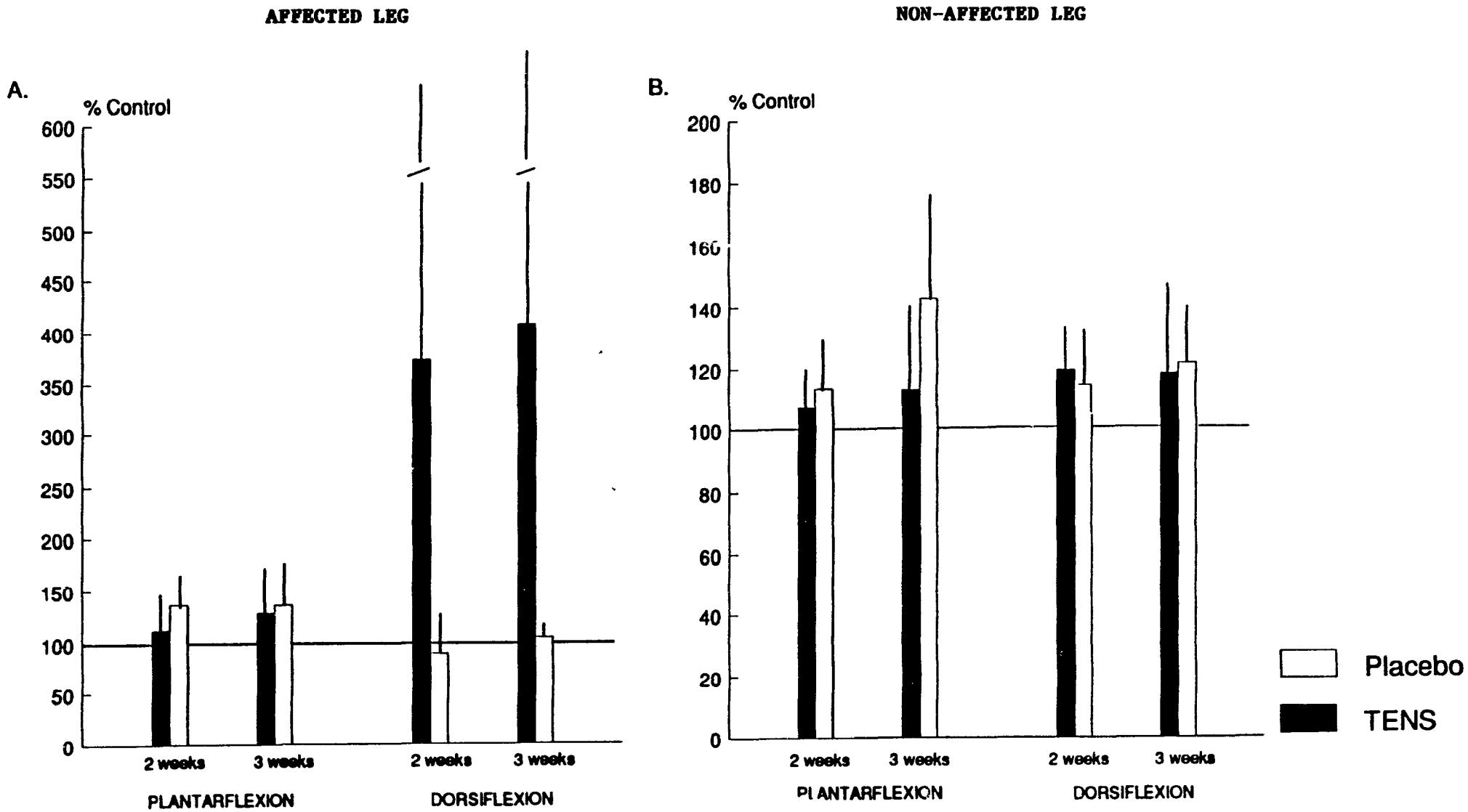


Fig. 5. Changes in plantarflexion and dorsiflexion force in the A) affected and B) non-affected legs of hemiparetic subjects after two and three weeks of TENS (filled columns) or placebo (open columns) stimulation Only dorsiflexion force was significantly increased following TENS treatment.

DISCUSSION

Our main findings from this study demonstrate that repeated TENS applications significantly improved subjective spasticity concomitantly with reflex and voluntary motor control in spastic hemiparetic subjects. Specifically, TENS reduced spasticity scores, increased vibratory inhibition of the H reflex, decreased the magnitude of soleus stretch reflexes, and improved dorsiflexion force with a simultaneous decrease in EMG co-contraction ratios. The results of this study confirmed earlier findings in spastic hemiparetic subjects, of enhanced vibratory inhibition of the H reflex following nine daily 30 min TENS treatments to the low back (Hale and Chan 1986b). In that study, although non-significant, trends towards improved H/M ratios and reduced stretch reflex magnitude measures were also reported. Our two studies in patients with central spasticity, agree with two previous reports of therapeutic TENS interventions in spinal spasticity. In one report, 20 min of TENS applied segmentally over the L3/4 dermatome in spastic spinal cord injured subjects, resulted in a marked immediate decrease in knee extensor spasticity as measured by pendulum testing (Bajd et al., 1985). The reduction in spasticity outlasted the period of stimulation for up to two hours. Similarly, hetero-segmental TENS stimulation on the skin overlying the dorsal columns of the spinal cord (low cervical, high thoracic region) applied continuously for 2 weeks decreased spasticity and improved maximal voluntary flexor and extensor knee torque in 49 multiple sclerosis patients (Fredriksen et al., 1986).

Spasticity has been attributed to hyperactivity and abnormal organization in mono- and polysynaptic reflex pathways (Lance, 1980; Nichols, 1989). Among other factors, this may result from a lowering of stretch reflex thresholds in spastic muscles (Feldman, 1986; Powers et al., 1988). Indeed, H and stretch reflex latencies, which may reflect thresholds, are decreased in spasticity, while stretch reflex magnitude measures (H/M ratios and SR/M areas) are enhanced (Ashby and Verrier, 1976; Hale and Chan, 1986a; Levin and Chan, 1990a).

Despite the obvious hyperactivity in stretch reflexes, we had found neither latency nor magnitude measures to be correlated with the severity of clinical spasticity in spastic hemiparetic patients in previous studies (Hale and Chan, 1986a; Levin and Chan, 1990a). However, a significant correlation was found between the severity of spasticity and the reduction in dorsiflexion force (Levin and Chan,

1990b). This relationship suggested that an amelioration of spasticity could be manifested by an improvement in voluntary dorsiflexion This indeed was what we found in the affected leg of hemiparetic subjects after 3 weeks of TENS application to the common peroneal nerve As it will emerge below, this finding also provided some insights into the mechanisms underlying the improvement of spasticity and voluntary control following TENS but not placebo stimulation.

EFFECTS OF REPETITIVE TENS APPLICATIONS IN SPASTIC HEMIPARETIC SUBJECTS

Large diameter afferent (Group A; via dorsal column stimulation) mediated suppression of C-fibre evoked transmission in spinothalamic tract pathways has been described in primates (Foreman et al , 1976). This mechanism may explain the suppression in perceived pain during this type of stimulation. However, the effects of longer-term low-threshold afferent stimulation on transmission in pathways mediating spasticity have not previously been investigated. The TENS parameters (low intensity, high frequency) used in the present study had been shown previously to activate large diameter afferents (Levin and Chan, 1988) Taken together with our present findings, repetitive stimulation of large diameter afferents via TENS over a period of time (weeks) could lead to a reduction in spasticity simultaneously with an improvement in voluntary motor control More specifically, TENS applied to the common peroneal nerve increased vibratory inhibition of the H reflex in the antagonist extensor muscle in chronic hemiparetic subjects. This effect was not evident after a single session of TENS (cf. Chapter 4), but only after two weeks of daily stimulation and seemed to plateau after that time period (Fig. 3). These results confirmed our earlier findings in spastic hemiparetic subjects of enhanced vibratory inhibition of the H reflex following nine, daily 30 min TENS treatments to the low back (Hale and Chan, 1986b). Although the evidence is indirect, vibratory inhibition of the H reflex has been attributed to presynaptic inhibition in group Ia terminals (Gillies et al , 1969, Burke et al , 1976) Thus, increased vibratory inhibition of the H reflex by repetitive TENS may have been exerted via an enhancement of presynaptic inhibition which has been shown to be suppressed in hemiplegic spasticity (Ashby and Verrier, 1976).

In addition, an enhancement of reciprocal inhibition from the flexors to extensors could contribute to the decreased extensor muscle spasticity and the improvement in flexor muscle function However,

the results of the study reported in the previous chapter in which TENS was found to produce similar effects on reflex latencies independent of the site of application (segmental versus heterosegmental), makes this interpretation unlikely. Taken together, these results suggested instead, that repetitive TENS applications may indeed be increasing presynaptic inhibition, but that this effect is only evident after a critical length of time (see below).

Repetitive stimulation of low-threshold afferents may also have caused the release of inhibitory neurotransmitters mediating the decreased spasticity and reflexes, and the recovery of voluntary motor function. Indeed, dramatic reductions in spasticity and improvements in motor control have been reported following the administration of opioids in spastic patients (Erickson et al , 1989) In addition, repetitive TENS increased protein and opioid levels in the cerebrospinal fluid and blood plasma of normal subjects and pain patients (Almay et al., 1985; Facchinetti et al., 1984; Salar et al , 1981). Thus, our findings may partially be explained by the triggered release of opioids or other inhibitory neuromodulators. We suggest that this would provide an interesting subject for further investigation.

It was most surprising that TENS treatment also resulted in a striking improvement in the strength of the dorsiflexors but not that of the plantarflexors. The improvement, however, was incomplete, being still well below the mean dorsiflexion force generated in the same standing position by the non-affected legs (Levin and Chan, 1990b). This improvement in dorsiflexor function cannot be explained by a training effect, since all subjects were long past the time in which the majority of recovery of function occurs (Moscowitz et al., 1972). Certainly, placebo stimulation had no effect on these parameters (Fig. 5). Furthermore, none of the subjects was undergoing other treatment or training during the study period. The improvement also cannot be explained by alterations in motor unit properties known to be changed in spastic extensor but not weak flexor muscles (Edstrom, 1970; Sica and Sanz, 1976). At least two concurrent mechanisms may contribute to the reflex and voluntary abnormalities in spasticity. On the one hand, decreased stretch reflex thresholds may result in hyperactive segmental reflex excitability. On the other, it may be assumed that part of the motor deficit in the weak dorsiflexors in hemiplegia is related to a lack or decrease of descending excitation to flexor motoneurons (Burke, 1988). Thus, in spasticity, hyperactive segmental activity could effectively 'mask' or override any underlying descending motoneuronal excitation. This would result in an even

more marked decrease in dorsiflexion force. Repetitive TENS stimulation may have improved dorsiflexor function by decreasing plantarflexion (soleus) stretch reflex hyperexcitability, thereby 'disinhibiting' or 'unmasking' underlying neural pathways to dorsiflexor motoneurons At the same time, as our results indicate, the recovery of force would not be complete since the descending command would remain impaired.

The time course of these improvements cannot be judged based on the few studies to date However, these results concur with the suggestion that there may be a critical duration or therapeutic threshold for disinhibition or restitution of function following multimodal stimulation (Walsh and Cummins, 1976). The critical time period is unknown Single 30 or 45 min TENS treatments applied to similar segmental sites, had no immediate effects on Hvib/Hctl ratios or stretch reflex magnitudes (Hale and Chan, 1986a; Chan and Levin, 1990). However, reflex thresholds in terms of latencies were already prolonged after only a single 45 min session of TENS stimulation to the common peroneal nerve (Chan and Levin, 1990). According to our results and those of a previous study (Hale and Chan, 1986b), it appeared that three weeks of stimulation were necessary, at least before changes in both reflex magnitudes (Fig. 3 and Table II) and co-contraction ratios during maximal voluntary contractions became evident (Fig.4). These changes appeared to be preceded by increased presynaptic inhibition and improved clinical spasticity, which became significant after only two weeks of stimulation (Table II and Fig. 1). In summary, these results suggest that the initial improvements in spasticity and dorsiflexion force evident after two weeks of TENS stimulation may have been due to an enhancement in presynaptic inhibition. Further improvements in dorsiflexing force appeared to have resulted from decreased stretch reflexes associated with decreased co-contraction, only evident after three weeks of stimulation

Considering the time course of improvement being in terms of weeks, the changes may have been mediated by several plastic mechanisms. Possibilities include sprouting of intact descending pathways making new synapses with motoneurons (Goldberger and Murray, 1978) and/or unmasking or reorganization of somatosensory-motor cortical connections (Bach-y-Rita, 1981)

CLINICAL IMPLICATIONS

Low-intensity TENS is a clinically accessible, non-invasive electrical stimulation technique currently used in the physiotherapeutic treatment of pain disorders. This study reports that repeated applications of TENS decreased clinical spasticity and hyperactive reflexes in lower limb plantarflexors, and improved motor function of dorsiflexors in chronic spastic hemiparetic subjects. It is important to note that these changes were directly a result of the TENS intervention, since no effects were evident following placebo stimulation. Furthermore, these patients had been stable, showing no improvement prior to TENS intervention. The use of TENS therefore, appears to be an effective adjunct in the clinical approach to the treatment of spasticity and the retraining of sensorimotor functions in hemiparetic patients.

CHAPTER 6

SUMMARY AND STATEMENT OF ORIGINAL CONTRIBUTIONS

In accordance with Section 6a of the Guidelines Concerning Thesis Preparation, contributions to original knowledge are indicated by asterisks in the summary of the principal findings listed below.

1 As stated in Chapter 1. INTRODUCTION, these experiments were concerned with elucidating the immediate (after one session) and longer-term (after 15 sessions) effects of TENS on spasticity, reflex organization and voluntary motor control. Prior to examining the effects of TENS, clinical spasticity scores, reflex responses and maximal voluntary contractions of the ankle were compared between normal and spastic hemiparetic subjects. In particular, their reproducibility as stable, repeatable measures was investigated in the hemiparetic population.

2. Since a mechanical stretching device was used in the Methodology, the question of the consistency of the input stretch stimulus was addressed in the first study. In spite of the mechanical nature of the device and the presumed difference in muscle tone between normal and spastic limbs, the velocity and total displacement of the input were not different between the two subject groups, nor across the various testing sessions The mean velocities of the perturbations ranged from 450.2 to 511.0°/sec and the mean displacements ranged from 31.4 to 34.0 degrees.

*3. In the hemiparetic group, individual spasticity scores, H/M ratios, Hvib/Hctl ratios, stretch reflex onset angles and areas were highly reproducible across days The interclass correlation coefficients for these measures were. r=0 87, 0 94, 0 91, 0 93, and 0.71 respectively. However, stretch reflex latencies and durations were not reproducible over different testing sessions (r=0 44, 0.20). These results indicated that, with the latter two exceptions, clinical spasticity and reflex measures could be reliably compared when recorded in the same patients on different days.

4. Comparisons of soleus reflex measures between spastic hemiparetic and age-matched normal subjects revealed the presence of spasticity

*a) H reflex latencies were significantly shorter (28.6 ± 1.6 msec compared to 30.3 ± 1.7 msec; p<0 05).

b) Stretch reflex latencies were significantly shorter (47 6 ± 18.2 msec compared to 62 9 ± 12.9 msec; p< 0.05).

c) H/M ratios were significantly increased (66.8 ± 29.5% compared to 42.2 ± 17.0%; p<0.05), whereas Hvib/Hctl ratios were unchanged in this group of patients.

d) Stretch reflexes durations were longer (74.5 ± 16 4 msec compared to 57 5 ± 15.5 msec; p<0.05) and areas (SR/M area) were significantly larger than normal (47 1 ± 13 1% compared to 19.8 ± 13 1%; p< 0 005)

5. In examining the degree of correlation among the three clinical spasticity measures, an interesting finding emerged. Namely, the severity of clonus varied significantly with the resistance to passive stretch (r=0.82, 0.65*) Among the physiological measures, only H/M and SR/M ratios were significantly correlated (r=0 76, 0 75*) Furthermore, spasticity scores showed non-significant though fairly consistent relationships with Hvib/Hctl ratios (r=0.42, 0.43), SR/M areas (r=0.55, 0.46) and SR onset angles (r=-0 30, -0 54)

Our results are thus in accordance with the findings of previous investigators that the changes in segmental reflex excitability were not well correlated with the degree of clinical spasticity. These observations implied that reflex measures alone may not be adequate indicators of the severity of spasticity Consequently, they are unlikely to reflect changes in

clinical spasticity due to therapeutic interventions.

*6. The second study reports, for the first time, a comparison of voluntary ankle muscle activation between age-matched normal and hemiparetic subjects in the functional position of standing.

*7. Agonist EMG area, co-contraction between agonist and antagonist muscle pairs, and force generated by maximal isometric contractions of the ankle muscles in non-affected legs of hemiparetic subjects were not different from those of normal subjects. The only significant differences were in the amount of antagonist EMG during plantarflexion and the time to develop maximal force. Therefore, data obtained from the non-affected legs were used as control values, instead of the potentially more heterogeneous data obtained from normal subjects

*8. Maximal and mean force generated by voluntary isometric contraction of the affected ankle muscles were highly reproducible when the same hemiparetic subjects were tested on two different days, with r=0 78 and 0.87 respectively during plantarflexion and r=0.95 and 0.87 during dorsiflexion. However, EMG areas and co-contraction ratios generated during voluntary plantarflexion of the affected leg were variable. In contrast, agonist EMG area (r=0.91) and co-contraction ratios (r=0.99) generated during voluntary dorsiflexion were highly stable measures in the affected leg. Therefore, force measurements for both directions of ankle contractions, and EMG measures during dorsiflexion, are reliable indices for purposes of comparison over time.

*9. Comparisons of maximal voluntary isometric contractions in the standing position between the affected and non-affected legs of spastic hemiparetic subjects revealed marked deficits which are outlined below. For both plantar- and dorsiflexion, agonist EMG areas in the affected leg were significantly reduced (x=51.2 compared to 81.43 uV.s for

plantarflexion, $p<0.001$, $\bar{x}=63.5$ compared to 161.1 uV.s for dorsiflexion, $p<0.001$) Antagonist EMG was not changed during plantarflexion, but was increased during dorsiflexion ($p < 0.001$). These changes in agonist and antagonist EMG areas led to altered co-contraction ratios. The latter were significantly increased for the dorsiflexion task ($\bar{x}$ =42.1% compared to 13.8%, $p<0.001$) For both tasks, maximal force production was reduced to approximately half of that generated by the non-affected leg Force onset, as well as the time to develop maximal force were prolonged ($p<0.001$) in affected legs of the spastic hemiparetic group.

*10. The presence of spasticity may be more significantly related to the deficit in voluntary motor control than to abnormalities in reflex pathways This study reports for the first time, a significant relationship between the level of spasticity and the amount of co-contraction during isometric ankle dorsiflexion in the standing position ($r=-0.68$, $p<0.05$) Furthermore, the level of spasticity was also significantly and inversely related to the maximal dorsiflexion force developed by the affected leg ($r=-0.65$, $p<0.05$) These findings also have important implications for the measurement of spasticity when evaluating the effects of treatment interventions.

*11. The last two (third and fourth) studies investigated the effects of repetitive transcutaneous electrical nerve stimulation (TENS) on spasticity, reflex and voluntary motor control in spastic hemiparetic subjects. The main goal of these studies was to investigate the mechanisms of possible changes due to TENS intervention

1. The third study was concerned with the immediate effects of one, 45 min TENS treatment The effects of TENS applied to two locations was compared to placebo stimulation. This study revealed that both segmentally and hetero-segmentally applied TENS caused an immediate and long-lasting (up to 60 min) prolongation of H and stretch reflex latencies The latter finding may be taken to reflect an increase in stretch reflex thresholds. These results further suggested that:

a. the mechanism for the increase in latencies is likely to be non-segmental since segmental and heterosegmental stimulation were found to be equally effective.

b. repetitive electrical stimulation may be triggering the release of long-lasting inhibitory neuromodulators.

2. The fourth study investigated the longer-term effects of repetitively applied TENS (15 daily, 60 min sessions over a period of 3 weeks). This study demonstrated that longer-term TENS reduced clinical spasticity, Hvib/Hctl ratios and SR/M areas. Associated with the improvements in clinical and reflex measures was an increase in dorsiflexion force and a decrease in co-contraction. These results suggested that:

a. the improvement in voluntary motor function may be related to a decrease in spasticity.

b. the mechanism of the improvement may be an increase in presynaptic inhibition, the release of inhibitory neurotransmitters and/or plastic changes. This could result in decreased reflex excitability which 'unmasked' underlying descending excitatory pathways to motoneurons.

*12. The overall conclusion of these studies is that repetitive TENS stimulation decreases the excitability of segmental reflexes and improves dorsiflexion function in spastic hemiparetic subjects. One of the contributing mechanisms to these improvements is likely to be an enhancement of presynaptic inhibition leading to an 'unmasking' of residual motor control.

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