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Segmental and Heterosegmental Effects of Repeated Transcutaneous Electrical Nerve Stimulation (TENS) on Voluntary Motor Functions in Spastic Hemiparetic Subjects

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ABSTRACT

We conducted two studies to examine the changes in voluntary motor functions in spastic hemiparetic muscles, their relationship to clinical spasticity and the reliability of these measures, as well as to investigate the effects of transcutaneous electrical nerve stimulation (TENS) on spasticity and voluntary motor functions in hemiparetic subjects. In our *first study*, the alterations in voluntary motor functions in the upper and lower limb muscles of spastic subjects were delineated through a comparative study with age-matched controls. Moreover, the test-retest reliability was evaluated for each measure. We noted a marked reduction in peak isometric torques, associated with a tendency towards an increase in antagonist co-contraction ratios for all the muscles tested in these spastic subjects. Of interest is that the elbow flexion torque was inversely related to the clinical severity of spasticity - especially that of its upper extremity score. Furthermore, the peak torque was the most reproducible measure. In our *second study*, the effects of 20 sessions of TENS applied to the radial nerve for 60 min every weekday over 4 weeks was investigated. In contrast to placebo stimulation, TENS produced a significant reduction in upper extremity spasticity after 4 weeks and a significant decrease in the tibialis anterior co-contraction ratio after 2 weeks of stimulation. Furthermore, 4 weeks of TENS, but not placebo stimulation, led to a significant improvement in elbow extension torque as compared with the control values in the majority (67%) of hemiparetic subjects. Such a reduction in spasticity and improvement in voluntary motor functions could have involved segmental reciprocal inhibitory mechanisms as well as non-segmental mechanisms via descending pathways.

RÉSUMÉ

Nous avons mené 2 études pour examiner l'altération des fonctions motrices volontaires de muscles hémiparétiques spastiques et sa relation avec la spasticité clinique et la reproduisibilité des paramètres de contraction maximale volontaire, et pour investiguer les effets de stimulations électriques transcutanées (SET) sur la spasticité et les fonctions motrices volontaires de sujets hémiparétiques. Dans notre première étude, les altérations des fonctions motrices volontaires de muscles du membre supérieur et inférieur ont été identifiées grâce à une étude comparative avec des sujets contrôles d'âge semblable. De plus, la reproduisibilité test-retest a été évaluée pour chaque mesure. Nous avons noté une réduction substantielle dans les torques isométriques maximaux en association avec une tendance vers une augmentation des ratios de co-contraction pour tous les muscles testés chez ces sujets spastiques. Il est intéressant de constater que le torque en flexion du coude était inversement relié à la sévérité de la spasticité clinique - en particulier celle du membre supérieur. En plus, le torque maximum était la mesure la plus reproduisible. Dans notre seconde étude, les effets de 20 sessions de SET appliquées au niveau du nerf radial pendant 60 min. chaque jour de semaine pendant 4 semaines ont été étudiés. Contrairement à la stimulation placébo, la SET a produit une réduction significative de la spasticité du membre supérieur après 4 semaines et une diminution significative du ratio de co-contraction du tibial antérieur après 2 semaines de SET. De plus, 4 semaines de SET mais non de stimulation placebo, ont amené une amélioration significative du torque en extension du coude en comparaison avec les valeurs contrôles chez la majorité (67%) des sujets hémiparétiques. Une telle réduction de la spasticité et amélioration des fonctions motrices volontaires impliquent probablement des mécanismes segmentaires d'inhibition réciproque et des mécanismes non-segmentaires via les voies descendantes.

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PREFACE

This thesis includes copies of two manuscripts in preparation for submission to *Journal of Neurology*. This option was chosen in accordance with the Guidelines Concerning Thesis Preparation (June 1994), Part B Section 2: Manuscripts and Authorship. The author has also obtained the approval of the Associate Director of Graduate Program, School of Physical and Occupational Therapy.

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REFERENCE LIST

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Chapter 1. Introduction and Literature Review

EPIDEMIOLOGY OF STROKE

Cerebrovascular accident (CVA), or stroke, is simply defined as the sudden onset of a focal neurologic deficit due to a presumed local disturbance in the blood supply to the brain (Dombovy et al., 1986). It is one of the leading causes of death and disability among elderly in North America. In Canada, a total death rate of 14,021 was reported for 1990 due to cerebrovascular disorders (Pan American Health Organization, 1992).

Over the past two decades, epidemiologic studies of stroke population have identified changing incidence and mortality rates in North America. In the 1970's, a decline in these rates was believed to be due to a more effective treatment of hypertension (Ostfeld and Wilk, 1990). Increasing use of computed tomography scans between 1980 and 1984 has allowed for improved diagnosis of stroke, resulting in the report of higher incidence rates (Broderick et al., 1989). A study in Quebec, Canada, however, noted an increasing hospitalization rate for patients with hemorrhagic strokes - beyond what could be attributed to a better detection of stroke alone (Mayo et al., 1991). Details aside, it appears that there *is* a growing reported incidence of stroke along with declining mortality rates in recent years.

Despite steady improvement in stroke survival rates through better detection and overall prevention (McGovern et al., 1992), stroke morbidity has remained constant through the last 20 years. Modan and Wagener (1992) speculated that the change in stroke classification and inefficient long-term treatment during this period might explain the discrepancy in these two trends. It has been documented that about 10% of stroke survivors require long-term institutionalization (Wade, 1992). Thus, the cost of stroke, in terms of rehabilitation, chronic care and loss of earnings, has a major socio-economical impact on

society. One of the primary goals of physiotherapy for these patients is to optimize the return of motor functions through various means such as appropriate physical modalities and therapeutic exercises. But this rehabilitative effort is often hindered by the development of spasticity in the affected muscles, that could aggravate any existent motor impairment.

PHYSIOLOGICAL BASIS OF SPASTICITY

1. Definition of Spasticity

In 1980, Lance defined spasticity as a motor disorder of the upper motoneuron syndrome, characterized by a velocity dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerks due to hyperexcitability of the stretch reflex. However, as it is discussed in Section 4 below, contribution to more chronic spasticity can also originate from non-neural factors. In fact, some studies have even suggested that the contribution of pathological changes in muscle fibers could be more significant than the abnormal activation of the muscles under certain circumstances (Dietz et al., 1981; Hufschmidt and Mauritz, 1985). Thus, spasticity may be considered as a neurological disorder caused by both neural and reactive non-neural factors, where the common feature is a change in muscle tone with a velocity dependent increase in the excitability of the stretch reflex (Fellows et al., 1989).

2. Clinical Characteristics of Spasticity

Clinically, spasticity is accompanied by several reflex signs (Ashby and McCrea, 1983; Bishop, 1977; Burke, 1988). For instance, phasic stretch reflexes, i.e. tendon jerks,

are exaggerated. Tonic stretch reflexes which partly underline the resistance of muscle to passive stretch are increased, such that the faster the velocity of stretch, the greater the reflex response. Clonus may be induced at the ankle or the wrist. The clasp-knife phenomenon may be present. These signs, though not always manifested together, collectively indicate the degree of hyperexcitability of the segmental reflex pathways. The mechanisms underlying such reflex disorders will be discussed in Section 4.

3. Spastic Hemiparesis

With the emergence of spasticity following a CVA, hemiparesis of the muscles on the side contralateral to the lesion is observed. It is known that the pyramidal tract innervation is denser for distal than proximal muscles of the forearm and hand in primates (Burke, 1988). Thus, the loss of fine motor control of the hand is a common feature of this upper motorneuron syndrome.

Reduced force output by the affected muscles may be considered the result of abnormalities in the agonist activation or the consequence of the restraint imposed upon by the antagonist muscle such as abnormal co-contraction and/or mechanical constraints (Bourbonnais and Vanden Noven, 1989). Indeed, several physiological changes in the characteristics of muscle fibers and the function of motor units in hemiparetic muscles have been reported. For example, the number of functioning agonist motor units were found to be decreased betweeen the second and sixth months following CVA, possibly due to transynaptic changes (Benecke et al., 1983; McComas et al., 1973). This suggested the possibility of denervation of muscle fibers that was found to be more prominant in distal

muscles (Brown and Snow, 1990). Muscle atrophy in hemiparetic limbs is observed frequently in chronic stroke patients. Human biopsy studies have demonstrated that spastic hemiparetic muscles showed evidence of selective atrophy of fast-twitch fibers in various muscles of upper and lower extremities (Edstrom et al., 1973). Since the fast-twitch fibers, typically referred to as Type II, are known to generate high twitch tension, selective loss of these fibers could certainly affect the overall force produced by the muscle. Further support for this finding was noted by Visser et al. (1985) when the contractile properties of motor units in hemiparetic patients were studied. The authors found that motor unit recordings from these patients demonstrated prolonged contraction times and tendencies toward increased fatiguability in ankle muscles. Another alteration in the function of the motor units associated with hemiparesis is thought to be a decrease in the firing rate of agonist motor unit. Lower firing frequencies were observed in the intrinsic muscles of the hand and tibialis anterior on the hemiparetic side (see Bourbonnais and Vanden Noven, 1989). It was suggested that an impairment in the recruitment and derecruitment pattern of agonist muscles contribute to deficits in voluntary muscle contraction (Sahrmann and Norton, 1977). Subsequently, Hammond et al. (1988a) reported that forearm muscles in hemiparetic subjects exhibited significantly slower agonist and antagonist recruitment times as compared to normals during isometric wrist contractions.

The net force output of the muscle could be reduced in hemiparetic limbs due to abnormal restraints counteracting the agonist muscle. It has been reported that changes in the mechanical properties of a muscle may contribute to its increased resistance to passive stretch (Dietz et al., 1981; Lee et al., 1987). In such cases, low net muscle force produced

by the agonist might be partly due to increased mechanical resistance from its spastic antagonist. Moreover, the antagonist could actively restrain the agonist via the development of hyperactive stretch reflex when it is stretched, and/or excessive co-contraction during voluntary effort, especially maximal isometric contraction (Berardelli et al., 1983; Hammond et al., 1988b; Knutsson and Martensson, 1980; Levin and Hui-Chan, 1994). The presence of abnormal antagonist co-contraction in spastic hemiparesis has been questioned on the basis that during isotonic and isometric elbow flexion against a load, the level of antagonist activity was within normal range even in severely impaired spastic subjects (Fellows et al, 1994a,b). However, during an active movement without load, overactivity of the antagonist muscle was apparent. These findings suggest that abnormal antagonist co-contraction could be present in spastic hemiparesis, but its magnitude may not be independent of the level of agonist activation. Certainly, we have demonstrated that the EMG co-contraction ratio in standing hemiparetic subjects, calculated as ratios of the antagonist (soleus) EMG area to the total agonist (tibialis anterior) plus antagonist EMG areas, is inversely correlated with the amount of dorsiflexing force produced by the paretic tibialis anterior ($r=-0.91$) (Levin and Hui-Chan, 1994).

4. Mechanisms of Spasticity

Among other motor signs, spasticity can be characterized by two parameters of the hyperactive stretch reflex: reduced reflex threshold and increased reflex gain. Investigators have debated as to whether the motoneurons are in a state of sustained depolarization leading to reduced threshold, or the reflex gain is abnormally increased. Variations in experimental

methods have made this delineation difficult. A study by Lee et al. (1987) found that when the excitability level of the motoneurons was controlled for in the elbow muscles by voluntary activation, joint stiffnesses were similar in the hemiparetic and non-affected arms. These investigators defined elbow joint stiffness during constant velocity extension as the slope of the relation between joint torque and angle. Since an increase in stretch reflex gain was not demonstrated by a change in stiffness, the results were taken to imply a reduced reflex threshold. This theory was further supported by Powers et al. (1988), who observed that the stiffness was of a stereotyped profile for a given hemiparetic subject, and it approached a constant value once the threshold angle was reached. On the other hand, Thilmann et al. (1991a) found a greatly prolonged and late electromyographic (EMG) activity in the biceps muscle in response to elbow extension in hemiparetic subjects. This EMG activity, which the authors attributed to muscle hypertonia, showed a positive linear correlation with the velocity of displacement. Moreover, the latency of this late activity did not vary in the majority of spastic subjects. Thus, they concluded that an increase in stretch reflex gain also contributed to the total increase in the magnitude of stretch reflex observed in spasticity. It is probable that once the motoneuronal threshold is reached, enhanced reflex gain could dominate, resulting in heightened stretch reflex response. Thus, both the reduced reflex threshold and increased reflex gain likely contribute to the hyperactive stretch reflex in spasticity.

Several neural mechanisms for the development of spasticity have been identified. The possibility of ***alterations in the intrinsic electrical properties of the alpha motoneuron***, such as its membrane conductance or the ionic mechanisms, have been proposed to explain

the enhanced alpha motoneuron excitability found in spasticity (see Katz and Rymer, 1989). Hounsgaard et al. (1984) observed, through intracellular recording from alpha motoneurons in decerebrate cats, that a brief stimulus to Ia afferents in the medial gastrocnemius nerve, induced an all-or-none plateau depolarization of the alpha motoneuron, leading to a sustained increase of its activity. Similar activity was induced by an intracellularly injected depolarizing current. Thus, the authors concluded that this enhanced excitability was due to altered intrinsic properties of the motoneurons rather than maintained synaptic excitation via the interneurons.

Adaptive changes such as ***denervation hypersensitivity*** and ***collateral sprouting,*** have been demonstrated in animal models after central nervous system (CNS) lesions. Bedard et al. (1979) showed that in a completely spinalized rat, injection of the serotonin precursor, 5-hydroxytryptophan or 5-HTP, was followed by an increase in spontaneous EMG activity of the paralyzed hindlimb muscles starting at approximately 4 days after the transection. The same dosage of 5-HTP produced a progressive increase in motor response over the following 30 day period. Hypersensitivity of 5-HTP receptors secondary to denervation was suggested as one of possible underlying mechanisms. Collateral sprouting is believed to be a compensatory mechanism resulting from transynaptic degeneration of the motoneurons (Benecke et al., 1983). These changes could lead to increased excitation of alpha motoneurons as the patient gradually progresses from the flaccid to the spastic state (Wainberg, 1988). The time course observed for the development of spasticity and return of voluntary motor functions seemed to correspond to that of this transynaptic degeneration process. Animal studies have demonstrated that the CNS of adult mammals was capable of

regeneration. Anatomical changes consistent with signs of collateral sprouting from the spared dorsal roots have been observed in partially hemisected cats in response to degeneration (Murray and Goldberger, 1974). Furthermore, these anatomical findings were accompanied by physiological changes such as recovery of spinal reflexes (Hultborn and Malmsten, 1983a,b).

One source of excitatory influence to the alpha motoneurons could be an enhancement of primary muscle spindle activity. ***Hyperactivity of the gamma efferent fibers*** leading to increased sensitivity of the muscle spindles to stretch was proposed in the past as a cause of spasticity (Rushworth, 1960), and its role has been under debate since. According to Hagbarth et al. (1973), recordings from muscle spindle afferents using microneurographic techniques in 2 spastic patients have shown no signs of increased dynamic spindle sensitivity. In contrast, Szumski et al. (1974), using similar recording technique in 15 normal and seven spastic patients, demonstrated that during muscle twitch and clonus, enhanced spindle activity was seen in the relaxation phase. Their claim, however, that this finding suggested increased dynamic spindle sensitivity, needs more direct experimental evidence. Nevertheless, one must bear in mind the predominance of alpha-gamma coactivation throughout the neural axis in both voluntary and pathological movements, such as in Parkinsonian tremor (Hagbarth et al., 1975).

Alpha motoneuron excitability could also be enhanced indirectly due to an overall reduced inhibitory control. Such mechanisms identified thus far include reciprocal, autogenic, recurrent and presynaptic inhibition. ***Reciprocal inhibition*** is known to result from Ia afferent volleys producing an inhibition of its antagonistic muscle during voluntary

contraction via Ia inhibitory interneurons. In spasticity, it has been suggested that the malfunctioning reciprocal inhibition may result in the occurrence of the stretch reflex in the antagonistic muscle during voluntary movement (Pierrot-Deseilligny and Mazieres, 1985). It was found that in the forearm muscles of hemiplegic subjects, the early phases of reciprocal inhibition were significantly reduced (Nakashima et al., 1989). In particular, the disynaptic phase of the inhibition was more reduced in patients with spasticity as compared to the patients with normal or flaccid muscle tone. These findings were later supported by Artieda et al. (1991). In contrast, reciprocal inhibition from ankle flexors to extensors was found to be increased in the ankle muscles of subjects with spinal spasticity (Boorman et al., 1991).

For a long time, ***autogenic inhibition*** was thought to be mediated via Ib afferents from Golgi tendon organs to Ib interneurons which inhibit the homonyous motoneuron pools during muscle contraction. However, Rymer and his collaborators (1979) provided experimental evidence to show that non-spindle group II, as well as small group III and IV muscle afferents do contribute to autogenic inhibition. In this context, a conditioning stimulus delivered to the gastrocnemius medialis nerve at an intensity which normally produces inhibition of the soleus H-reflex, resulted in facilitation of the H-reflex in hemiplegic subjects instead (Delwaide and Oliver, 1988). This finding thus suggested that a reduction in autogenic inhibitory mechanism may play a role in spasticity, at least in the triceps surae muscle (see Pierrot-Deseilligny, 1990).

It was once assumed that ***recurrent inhibition*** of the alpha motoneuron pool, mediated via Renshaw cells, was reduced in CNS lesions, thus contributing to exaggerated

stretch reflexes. Katz and Pierrot-Deseilligny (1982) used sophisticated H-reflex collision techniques to estimate the amount of recurrent inhibition in human subjects. They found that, contrary to what was assumed in the past, there was no evidence of a reduction in this inhibitory mechanism in the majority of spastic human subjects studied at rest. While some subjects demonstrated what appeared to be less recurrent inhibition, influence of other factors such as disinhibition of the soleus H-reflex could not be ruled out. However, they reported that during voluntary contraction of ankle flexors, facilitation of antagonist Renshaw cells normally seen in healthy subjects was not found in hemiplegic patients. A more recent study by Shefner et al. (1992) on spastic spinal cord injured (SCI) patients demonstrated that recurrent inhibition was increased at rest in these subjects as compared to healthy subjects. Hence, it was postulated that recurrent inhibition may be reduced in spasticity due to a modification in the excitability of the Renshaw cells from supraspinal control (Katz and Pierrot-Desilligny, 1982).

The excitability of the stretch reflex is also influenced by ***presynaptic inhibition***. As can be expected, the activity of the interneuron mediating this inhibition is modifiable by peripheral as well as descending pathways (Burke, 1988). In human, vibration of the muscle tendon or belly has been shown to result in discharges of homonymous Ia fibers and tonic contraction of the soleus muscle, known as the tonic vibration reflex (TVR). In addition, a concomitant suppression of the predominantly monosynaptic stretch reflex (H- or tendon jerk reflex) is observed. This is believed to be partly due to presynaptic inhibition of the Ia fibers by vibration-induced Ia volleys (Burke and Ashby, 1972). In spastic subjects, this suppression has been shown to be reduced as demonstrated by an increase in the H_{vib}/H_{ctl}

ratio (Ashby and Verrier, 1976). This observation suggsts that presynaptic inhibitory mechanism could be reduced in spasticity.

The role of ***disturbed supraspinal influences*** on the development of pathological reflex and voluntary motor functions must also be considered. Descending tracts (eg. corticospinal and lateral vestibulospinal tracts) could contribute to hypertonicity via direct, even monosynaptic excitatory projections to the lower motoneurons, or indirectly (eg. reticulospinal tract) by inhibition or facilitation of the interneurons mediating reflexes or voluntary movements (see Katz and Rymer, 1989; Messina, 1990). Thus, the net tonic excitatory synaptic input from the supraspinal tracts could change the baseline level of depolarization of the motoneurons, resulting in the increased alpha motoneuron excitability mentioned on page 6.

Experimental evidences have indicated that the ***alterations in mechanical properties*** of the muscle could significantly contribute to the development of chronic spasticity. Dietz and Berger (1983) observed that during ambulation, subjects with various CNS disorders demonstrated decreased EMG activities of triceps surae muscle group during the stance phase when compared to healthy subjects. Nevertheless, during passive stretch of relaxed triceps surae, the resistance to stretch was higher on the spastic leg despite its reduced EMGs. Similar results were observed in the study of reflex activity and tension development during elbow movements in patients with spastic paresis (Dietz et al., 1991).

A mechanism proposed to explain these results was possible degenerative changes in the muscle structure (Hufschmidt and Mauritz, 1985). It was postulated that the increased stiffness in triceps surae during slow, passive ankle dorsiflexion in hemiparetic subjects was

due to changes in the elastic properties of tendon and connective tissues secondary to alteration in collagen content (Thilmann et al., 1991b). While pathological changes in the mechanical properties of the spastic muscle itself could aggravate the manifestation of spasticity, such changes are more likely to be one of the consequences of abnormal muscle tone, rather than its cause. Furthermore, because the effects of sufficiently high velocity of stretch was not studied in the experiment by Thilmann et al. (1991b), possible contribution by stretch reflex activity cannot be excluded.

MEASUREMENTS OF SPASTICITY

It is evident that the pathophysiology of spasticity is complex, involving several different mechanisms. It follows, then, that several clinical and physiological measurements are required to adequately evaluate spasticity.

1. Clinical Measurements

Clinical assessments of segmental reflexes are generally quantified using scoring systems (Ashby et al., 1987). The ***Ashworth Scale,*** a standardized 5-point ordinal scale, is commonly used to grade the resistance felt by the examiner during passive manual stretching of a spastic muscle (Haley and Inacio, 1990). The muscle tone is rated from normal (0) to severe spasticity (4). High interrater reliability on the modified version of this measure (r=0.84) has been demonstrated between 2 evaluators in the elbow muscles of hemiplegic subjects (Bohannon and Smith, 1987). However, reliability was reported to be somewhat lower for the assessments of knee muscles (Sloan et al., 1992). Other similar clinical scales

have also demonstrated interrater reliability in the shoulder and wrist muscles of poststroke patients (Worley et al., 1991)

Tendon jerk response such as the Achilles tendon reflex, and measure of ankle ***clonus*** are used frequently to evaluate the excitability of the stretch reflex pathway. Hyperactive tendon jerks, mediated predominantly via a monosynaptic reflex pathway, are believed to be an indicator of increased sensitivity of the muscle spindles. Clonus is thought to be a manifestation of an ongoing oscillation in the stretch reflex arc (Burke, 1988). Significant relationships were reported between hyperreflexia (ankle and knee tendon jerk reflexes) and clonus, and between lower extremity weakness and muscle tone (Dohrmann et al., 1974). Though high correlations among these measurements are not always seen consistently (Ashby et al., 1987), Levin and Hui-Chan (1994) demonstrated a significant negative linear correlation ($r=-0.65$) between the force produced by maximum voluntary contraction (MVC) of the paralytic ankle dorsiflexors and the severity of spasticity in the plantarflexors. Another study by Levin and Hui-Chan (1993b) showed that clinical spasticity, composed of composite scores assessing the amount of resistance to passive stretch, Achilles tendon reflex excitability and ankle clonus on 4- or 5-point scales, showed high inter-session consistency ($r=0.87$) in seven hemiparetic subjects. Thus spasticity may be better estimated by a more global score.

Pendulum test is used to assess the angular displacement of a limb when it is left to oscillate freely or under controlled speed conditions (Haley and Inacio, 1990). Spastic limbs are observed to be typically limited in full angular excursion or the amplitude of oscillation such that a mathematical model may be used to evaluate the biomechanical characteristics.

While this method is recognized to be an easy and quick measure, fluctuation in the resistance of the limb during oscillation has been noted in this type of measurement, for example, due to the position of the subject (Bajd and Bowan, 1982). Furthermore, when using such an analysis, other variables such as the level of background contraction which could influence muscle stiffness have not been taken into account (Katz and Rymer, 1989). Nevertheless, a high reproducibility (r=0.96) of the pendulum test within the same testing session was demonstrated in 30 hemiplegic subjects, using a Cybex II isokinetic dynamometer (Bohannon, 1987).

2. Physiological Measurements

EMG and torque recordings are accepted as objective methods of measuring reflex responses and muscle activity during voluntary contraction. The Hoffman's or ***H- reflex*** is recognized as an indicator of the excitability of the predominantly monosynaptic stretch reflex (Angel and Hofmann, 1963), and is the electrical analogue of the tendon jerk response. Most commonly elicited in the soleus muscle by stimulating the tibial nerve, the H-reflex is conventionally normalized with respect to the maximum motor or ***M*** response. An M response is elicited when the motor axon is directly stimulated, and is a measure of the activity of the compound muscle action potential. Thus, the ratio of maximum H-reflex to maximum M response, H_{max}/M_{max}, is widely used to reflect the percentage of motoneurons in the soleus motoneuron pool that can be reflexly activated by an electrical stimulus optimal for exciting the group Ia fibres (Shahani and Cros, 1990). A CNS lesion resulting in an increased H_{max}/M_{max} ratio is considered to reflect an enhanced excitability of the

predominantly monosynaptic stretch reflex. Although an objective physiological measure, the H-reflex is reported to be quite variable in amplitude, latency and waveform, due to influences from factors such as the position of the limb, stimulus parameters, electrode placement and limb temperature (Arsenault et al., 1993; Delwaide, 1985; Maryniak et al., 1991; Shahani and Cros, 1990; Schieppati, 1987).

Mono- and polysynaptic ***stretch reflex*** has also been measured in muscle groups, for example, around the ankle and/or elbow joints, using hydraulic servo-motor or mechanical stretching devices that provide controlled ramp velocities (Kearney and Chan, 1982; Levin and Hui-Chan, 1993b; Thilmann et al., 1991b), or torque motor apparatus (Verrier et al., 1984). Characteristic features indicative of enhanced monosynaptic reflexes in subjects with upper motoneuron syndromes have included changes in soleus stretch reflexes, such as a shorter latency ($p<0.05$; Levin and Hui-Chan, 1993b), a longer duration as compared to age-matched normals, and increasing magnitude with increasing stretch velocity (Berardelli et al., 1983). The use of isokinetic dynamometers in measuring resistance to passive extension or flexion of the knee has also been implemented in an effort to quantify spasticity (Firoozbakhsh et al., 1993).

Surface EMG assessments have also been used to evaluate patterns of agonist and antagonist activation in hemiparetic subjects performing different ***motor tasks*** for example, force and/or displacement tracking tasks (McLellan and Hassan, 1982; Carey, 1990; Dietz et al., 1991), maximum voluntary isometric contractions (Levin and Hui-Chan, 1993b; Riddle et al, 1989), or gait (Dietz and Berger, 1983; Finch and Barbeau, 1986). Results from these studies have revealed that spastic hemiparesis is associated with abnormalities in rate

of movements, prolonged agonist activation and inappropriate antagonist co-activation. Thus, EMG techniques during static or dynamic motor functions are commonly used to detect such alterations in motor control and to measure the effects of treatment intervention.

Previously, it was thought that muscle testing or strength evaluations in patients with upper motoneuron disorders were not useful measures, because their motor output was presumably influenced, or sometimes masked, by factors such as spasticity. Nevertheless, recent studies have demonstrated the applicability of various force measurement methods in these patient populations. Riddle et al. (1989) reported that isometric strength measurements taken at various joints, using a hand-held dynamometer in patients with closed head injury or CVA, showed high intra- and inter-session reliability. Tripp and Harris (1991) concluded that knee torque in hemiparetic subjects could be evaluated reliably on different testing sessions with an isokinetic dynamometer. In a previous study, we examined maximum voluntary isometric contraction in the ankle muscles of hemiparetic subjects (Levin and Hui-Chan 1990; 1994). Parameters such as the force onset and peak force were reproducible in the same subjects tested on different days with r values ranging from 0.78 to 0.95, as was the EMG co-contraction ratio during maximum voluntary ankle dorsiflexion ($r=0.99$). Furthermore, the amount of force produced by the paretic dorsiflexors was inversely correlated with plantarflexor spasticity ($r=-0.65$). On the other hand, a positive relationship was found between strength deficits in the upper extremity, i.e. the shoulder medial rotator and elbow flexor, and spasticity in the agonist rather than the antagonist muscles (Bohannon et al, 1987). It is evident that the numerous tests available can be used in combination with each other to measure the various dimensions of spasticity. What remains to be of principal

concern is whether these tests are reliable for a given patient group and sensitive enough to be used in the evaluation of treatment intervention.

TREATMENTS OF SPASTICITY

1. Surgical Treatments

Selective dorsal rhizotomy is recognized as one of the most common surgical interventions used in the treatment of spasticity for selected patients. This procedure has been found to be effective in reducing spasticity in a variety of patient groups, with lasting effects for up to 14 years in some cases (Laitinen et al.,1983; Sindou et al.,1987). However, these studies used primarily clinical evaluations as the outcome measure. It was reported that in children with cerebral palsy (CP), selective dorsal rhizotomy followed by 4 weeks of intensive physiotherapy resulted in improved functional activities in spastic diplegic but not quadreplegic children (Dudgeon et al., 1994). ***Local injection of anesthetic***, such as phenol, into the peripheral nerves have also been shown to successfully reduce spasticity (Keenan et al., 1990). Despite their beneficial effects, such operative procedures tend to be unpredictable in terms of their treatment efficacy, while posing surgical risks to the patients. Consequently, pharmacological and physiotherapeutic methods have remained as the preferred choices in the management of spasticity.

2. Pharmacological Treatments

Several centrally and peripherally acting drugs have been shown to be effective in reducing spasticity in humans. However, long-term use of these drugs is limited by their

adverse side-effects. Among the centrally acting anti-spasticity drugs, ***benzodiazepines*** such as diazepam and librium have been under extensive investigations in various patient populations. These CNS depressants have become widely used for their ability to produce muscle relaxant effects (Glen and Whyte, 1990; see Merritt, 1981). The basic mechanism underlying the action of these drugs is believed to be an enhancement in presynaptic inhibition (Davidoff, 1985; Delwaide, 1985; Verrier et al., 1975).

Baclofen, a derivative of GABA, is known to stimulate $GABA_b$ receptors mainly at the spinal level to suppress the release of excitatory neurotransmitters (Milanov, 1992). Positive effects, such as decreased resistance to passive movement and reduction in painful spasms and clonus, have been found in multiple sclerosis (MS) patients (see Merritt, 1981). However, in chronic stroke patients, a daily dose of baclofen for approximately 19 to 40 days produced a reduction in muscle tone and F wave parameters but no changes in muscle strength or tendon reflexes (Milanov, 1992). Similar outcome was reported for other patient groups following intravenous administration of baclofen (Pedersen et al., 1974). More recently, intrathecal administration of baclofen was introduced, to better direct the drug to its site of action while minimizing the side-effects associated with long-term use. Immediate reduction in muscle tone, H-reflex and muscle spasms was observed in small groups of spinal cord injured subjects (Macdonell et al., 1989; Penn and Kroin, 1987). Based on a longer treatment duration, it has been demonstrated that intrathecal baclofen provided sustained relief from spasticity and spasms, and improved the quality of life for most patients with severe spasticity. However, these benefits were sometimes accompanied by serious complications such as meningitis and baclofen overdose (Patterson et al., 1994).

Cyproheptadine, a serotonergic antagonist, is thought to inhibit the excitability of the spinal neuron. This drug has been investigated for its therapeutic usefulness in reducing spinal spasticity by Wainberg et al. (1990). These authors found that in 6 SCI subjects, a 3 week course of cyproheptadine produced a reduction in episodes of involuntary movements in all the subjects and ankle clonus in 5 subjects, when compared to those who received placebo treatment. Furthermore, an improvement in locomotion pattern with respect to weight bearing ability and timing of EMG activity, particulary in the lower limb extensors, was observed in 2 subjects undergoing cyproheptadine therapy.

Dantrolene sodium is a peripherally acting drug, with its mechanism of action involving inhibition in the release of calcium ions from the sarcoplasmic reticulum. Thus, the activation of the contractile apparatus is prevented and the mechanical force of contraction is diminished (Davidoff, 1985). Joynt (1976) reported that, in the majority of 77 patients with various CNS disorders, a 2 year course of maintenance therapy resulted in improved segmental reflexes, but functional improvement was seen in less subjects. Positive results have been reported for mainly CVA and CP subjects (see Glen and Whyte, 1990). Thus, the results of drug treatment seem to vary depending on the specific neurologic disorder, the particular drug, the route of its administration and the duration of therapy.

3. Physiotherapeutic Treatments

In normal subjects, ***muscle cooling*** has been shown to result in diminished tendon but not the H-reflex (Bell and Lehmann, 1987). Cooling the spastic muscle for 10-45 min has been a common clinical practice in the management of spasticity. Immersion of the

lower leg in cold water for 10-30 min was used to relieve spasticity by Miglietta (1973). It was proposed that cold may have stimulated cutaneous receptors, hence decreasing the alpha and/or gamma extensor motoneuron excitability in accordance with the action of flexion reflex afferents (Lundberg, 1964). In addition, there could have been alteration in the contractile properties of the muscle. These findings were further supported by Lightfoot et al. (1975) in their study on the effects of 45 min of ice application to the calf muscle in 7 subjects with complete spinal cord lesion. They also observed that local cooling resulted in prolongation of the soleus twitch contraction and half-relaxation times as well as a significant reduction in the magnitude of the achilles tendon reflex.

Low amplitude, high frequency ***vibration*** of the antagonistic muscle belly or tendon is known to result in three phenomena: involuntary contraction of the vibrated muscle, termed the tonic vibration reflex or TVR, reciprocal inhibition of its antagonist and the inhibition of the phasic stretch reflex of the vibrated muscle (see Chan, 1986). A vigorous evaluation of the therapeutic effects of vibration has been scarce in the literature. Ageranioti and Hayes (1990) reported that immediately following 1 minute of vibration at 100 Hz frequency to wrist *extensor* tendons, a decrease in the passive resistive *flexor* torque concurrent with diminished integrated EMG activity was observed in CVA subjects. Thus, it appears that high frequency vibration of the muscle belly or tendon could be a therapeutic modality for spasticity.

Along with traditional therapeutic exercises usually employed in a treatment regime for spastic limbs (Wagenaar et al., 1990), ***prolonged passive stretching*** of the spastic muscles has been recognized as an integral part in the management of spasticity (Merritt,

1981). A study by Odeen (1981) showed that mechanically applied passive stretch for 30 minutes to hip adductors decreased the level of coactivation in lower extremity muscles during voluntary hip abduction. Furthermore, Odeen and Knutsson (1981) demonstrated that putting the plantarflexors on stretch along with weight bearing produced the most significant decrease in resistance to passive dorsiflexion of the ankle joint. It was speculated that the reduction in ankle spasticity might be due to a sustained autogenic inhibition. The effect of a single session of prolonged triceps surae muscle stretch via standing on a tilt table for 30 min was compared with a rest period of same duration in CP children (Richards et al.,1991). It was found that although a lower antagonist (tibialis anterior) activation was observed during the early part of the stance phase following stretching, a single session of such a stretching program did not significantly improve the children's spatiotemporal gait pattern. However, possible cummulation of inhibitory effects over repeated stretching sessions cannot be ruled out. For instance, daily, 30 min of tilt table standing over a 2 week period was found to reduce clinical spasticity in the lower extremity in one spinal cord injured subject (Bohannon, 1993). Of course, before any firm conclusion can be drawn, more controlled studies using additional quantitative measures need to be carried out in a much larger sample size. It was postulated that prolonged stretching could also decrease viscoelastic stiffness in the periarticular connective tissue, resulting in improved joint movement (Carey, 1990).

Electrical stimulation, both central and peripheral, has emerged as an important approach to the management of spasticity. Continuous spinal cord stimulation applied for at least 12 months via implanted electrodes in patients with various upper motoneuron

disorders has shown to produce positive effects on motor performance, bladder control and ankle clonus (Campos, 1981). However, a comparative study by Fredrikson et al. (1986) of the effects produced by 2 weeks of continuous transcutaneous stimulation and epidural spinal cord stimulation over 4-8 weeks in MS subjects, showed that although the bladder symptoms and motor functions improved significantly with both methods, the reduction in spasticity was non-significant. Stimulation of the anterior cerebellum and deep brain structures has been documented with some evidence of beneficial effects in humans (Davis et al., 1977). While no significant changes were observed in the neurophysiological tests performed immediately following 12-48 hours of cerebellar stimulation (McLellan et al., 1978), longer-term stimulation lasting between 2 to 7 days was reported to produce a reduction in muscle tone and H- and F-reflex amplitudes in CP subjects (Fisher and Penn, 1978).

Earlier stimulation of the peripheral nervous system involved stimulating the nerves innervating the spastic agonist or its paretic antagonist via implanted electrodes. Stimulation of the nerve or the paretic muscle is believed to produce reciprocal inhibition of its antagonist along with homonymous facilitation (Alfieri, 1982; see Chan, 1986). A study by Alfieri (1982) involving 115 spastic subjects showed that, with 10 min of electrical stimulation of various paretic muscle groups, an immediate decrease in spasticity lasting for an average of 1 hour was observed. However, the contribution of sham treatment was not studied, and the outcome measure used was clinical assessment only.

The use of ***transcutaneous electrical nerve stimulation (TENS)*** to reduce spasticity has also been investigated. In a study of six spinal cord injured subjects, a 20 min application of TENS to L3-4 dermatomes led to a decrease in spasticity in the knee

extensors, as measured by the pendulum test in 3 subjects (Bajd et al., 1985; however, see Vodovnik et al., 1984). But this effect was found to be short-lived, with the initial level of spasticity returning within two hours post-stimulation. Previous work in our laboratory (Hale and Hui-Chan, 1986) showed that after 9 sessions of 30 min treatments with conventional TENS to the low back, vibratory inhibition of the soleus H-reflex was enhanced in hemiplegic subjects. Although statistically non-significant, we observed a trend towards a decrease in the hyperactive stretch reflexes with negligible improvement in clinical spasticity. Our subsequent study showed that low-intensity TENS but not sham stimulation applied to the common peroneal nerve for 60 (rather than 30) min every weekday for 3 weeks (i.e. 15 sessions), produced a decrease in H_{vib}/H_{ctl} ratio ($p=0.02$), a reduction in clinical spasticity ($p<0.05$) and the magnitude of stretch reflexes in the spastic ankle plantarflexors ($p<0.05$), as well as an increase in the isometric force recorded in the paretic dorsiflexors ($p<0.05$) of hemiparetic subjects (Levin and Hui-Chan, 1992).

Such antispastic effects of TENS has also been shown to extend beyond local changes. Subcutaneous stimulation of the median and radial nerves on the contralateral side was shown to be capable of occasionally suppressing ankle clonus for up to 2 hours in some subjects with MS (Walker, 1982). When TENS was applied heterosegmentally to the contralateral wrist in spastic hemiparetic subjects, we noted that a single session of 45 min treatment could produce a prolongation of the stretch and H-reflex latencies in the spastic calf muscles for up to 60 min (Levin and Chan, 1989; Hui-Chan and Levin, 1993). Recently, immediate and long-term effects of TENS applied to 2 acu-points in patients with spinal spasticity was studied by Han et al. (1994). These authors reported that 30 min of

high frequency (100 Hz) TENS applied to the acu-points in the hand and ipsilateral lower leg regions produced a significant immediate reduction in clinically assessed muscle tone and clonus in the lower limbs bilaterally. In addition, a subgroup of 4 patients demonstrated longer-lasting therapeutic effects when the stimulations were applied to alternate sides and extended to twice a day for 3 months. But this study lacked an evaluation of properly controlled groups, not to mention the small sample size in their study of longer-term effects. Nonetheless, taken together all the findings hitherto, there appear to be some evidence for possible modulation of motor control by electrical stimulation via the diffuse effects of heterosegmental afferent stimulation.

PROBLEM FORMULATION

Although electrical stimulation of afferent nerve fibers or the spinal cord has initially been intended for treatment of pain, spasticity has also been observed by some investigators to be reduced through similar procedures. As previously reviewed in the literature, various types of electrical stimulation have been reported to be effective in reducing spasticity in certain neurological disorders. They include spinal cord or dorsal column stimulation, cerebellar stimulation, subcutaneous and transcutaneous stimulation of the peripheral nerves or the paretic muscles.

Dorsal column stimulation using low-intensity currents is thought to modulate the overactivity of the stretch reflex by releasing transmitter or modulator substances acting at presynaptic levels, interneuron sites or at the motoneurons themselves (Dimitrijevic, 1981). Peripherally, low intensity electrical stimulation of afferent nerve fibers have been shown

to inhibit Ia afferent excitation in the wrist flexors (Malmgren and Pierrot-Deseilligny, 1988a,b). The mechanism underlying such a phenomenon is believed to be due to influence on the activity of interneurons and/or alpha motoneurons via segmental and/or propriospinal pathways and involving presynaptic inhibition. In this context, low-intensity, high-frequency TENS (conventional TENS) has been shown by our previous study to excite mainly large diameter afferents (Levin and Chan, 1993a). Such afferent stimulation could modulate ongoing motoneuronal activity via segmental and possibly heterosegmental pathways. A question may therefore be raised as to whether similar conventional TENS, applied repeatedly over time at a site remote from the spastic muscle, can produce a significant reduction in clinical spasticity and an improvement in voluntary motor control. More specifically, to what extent will TENS applied to the radial nerve on the affected side produce effects on the remote ankle muscles as well as the local elbow muscles?

To investigate the therapeutic effects of TENS on spasticity, we conducted two main studies to address several important issues raised by the use of TENS to relieve spasticity and improve motor functions. In the *first study*, our aim was to examine the extent of alterations in voluntary motor functions associated with spastic hemiparesis. In Chapter 2, voluntary motor functions of the elbow and ankle muscles of CVA subjects were compared with those of normal control subjects, to delineate whether the physiological alterations such as reduced force output and abnormal antagonist co-contraction were indeed characteristic of spastic hemiparesis. More importantly, the relationship between changes in motor functions and the severity of clinical spasticity was investigated. Considering the wide within-subject variability in terms of reflex and voluntary motor functions that is well recognized in a

neurologically impaired population, we also addressed the reliability of the measures used.

Once the extent of spastictiy and impairments in motor functions were established with a satisfactory reproducibility of the chosen measurement parameters in these patients, we set out to investigate the effects of repeated application of conventional TENS in the *second study*. In Chapter 3, our first objective was to study the local effects of TENS applied to the radial nerve over a 4 week period. Our second objective was to delineate whether such stimulations would produce any effects at a remote site in the ankle muscles. We also mapped out the time course of the effects of TENS over the 4 week period, to investigate whether such longer-term treatment could produce any carry-over effects after the stimulation has ended. Findings from this study provided some insight into the possible mehanisms involved in modulation of spasticity and voluntary motor functions following peripheral afferent conditioning.

In Chapter 4, the main findings from these 2 studies are summarized and our overall conclusion is presented.

Chapter 2. Alterations in Voluntary Motor Functions Associated with Spastic Hemiparesis

SUMMARY

Previous experiment in our laboratory showed that the reduction in force during maximum voluntary contraction (MVC) of the hemiparetic ankle dorsiflexor during standing was inversely correlated with the amount of agonist/antagonist co-contraction ($r=-0.91$) and the severity of ankle spasticity ($r=-0.65$)(Levin and Hui-Chan, 1994). Such a relationship between voluntary motor deficits and spasticity has not been demonstrated in the affected upper limb muscles of hemiparetic subjects. The objectives of this study were 1) to compare the characteristics of voluntary motor functions in elbow and ankle agonist/antagonist muscle pairs during isometric MVC in spastic hemiparetic subjects with those of normal age-matched subjects; 2) to investigate the possible relationship between the alterations in motor functions and clinical spasticity; and 3) to establish the test-retest reproducibility of MVC parameters and clinically evaluated spasticity.

Ten cerebrovascular accident (CVA) patients with chronic spastic hemiparesis and 6 normal, age- and sex-matched subjects participated in this study. Each subject underwent isometric MVC tests of flexion and extension about the elbow and ankle joints during which the resultant force was recorded via a force transducer. Muscle activites were recorded electromyographically from the biceps, triceps, tibialis anterior and soleus. The severity of spasticity of each CVA patient was assessed by a single evaluator using a composite spasticity score. For the reproducibility test, the subjects were re-evaluated approximately 1 week later.

CVA subjects produced significantly less peak torques at both elbow and ankle joints ($p\leq0.01$), and demonstrated tendencies toward a prolonged half-rise time to peak torque and

a greater antagonist co-contraction in comparison to their normal counterparts. Of these parameters, only the voluntary elbow flexion torque was found to be inversely related to the total spasticity score ($r=-0.70$, $p=0.05$) as well as to the upper extremity subscore ($r=-0.82$, $p=0.01$). Another interesting finding was that the peak torque proved to be the most reliable measure (ICC=0.86 to 0.99) for both groups; while the half-rise time to peak torque, peak agonist EMG areas and EMG co-contraction ratios ranged from mildly to highly reproducible for the MVC tests across the two sessions (ICC=0.43 to 0.91, 0.64 to 0.94 and 0.20 to 0.99 respectively). The clinical spasticity score demonstrated high reproducibility between test and retest (ICC=0.78).

CVA subjects were thus distinguishable from the normals with respect to their marked reduction in muscle force output. The strength deficit in their spastic elbow flexor turned out to be the best indicator of the severity of their spasticity. Because the peak torques, MVC peak agonist EMG areas and clinical spasticity scores were highly reproducible between sessions, they could be used as very reliable measurement indexes for evaluating the effects of treatment over time in hemiparetic subjects.

INTRODUCTION

Hemiparesis of the contralateral side of the body is one of the major focal neurological symptoms arising from a cerebrovascular accident (CVA) (McGovern et al., 1992). Such a reduction in muscle strength has been attributed to alterations in motor functions as a result of disruption in descending motor command in upper motoneuron (UMN) lesions. Examples of these alterations include a reduction in the number of functioning motor units due to transynaptic degeneration of motoneurons (Benecke et al., 1983; Brown and Snow, 1990; McComas et al., 1973), selective atrophy of the muscle fiber types in the presence of spasticity (Edstrom et al., 1973), disuse atrophy in chronically affected muscles (Chokroverty et al., 1976), impaired recruitment and derecruitment pattern of agonist muscles (Sahrmann and Norton, 1977), and a reduction in their firing frequencies (Rosenfalk and Andreassen, 1980), as well as abnormal agonist/antagonist muscle co-activation (Hammond et al, 1988b; Levin and Hui-Chan, 1994; McLellan et al, 1985). In addition to reduced muscle force output, other functional motor impairments such as an increase in reaction time for knee extension (Nakamura and Sajiki, 1985), and prolonged time to reach peak torque during knee movements have been observed in hemiparetic subjects (Bohannon and Walsh, 1992), .

However, whether or not abnormal agonist/antagonist co-contraction really exists in spastic hemiparesis remains controversial. For example, Knutsson and Martensson (1980) demonstrated that diminished isokinetic flexion and extension at the knee joint was associated with antagonist co-activation in the majority of the spastic subjects examined. They observed that the antagonist activity was relatively higher during active than passive

knee movements at the same speed. In the upper limb, McLellan et al. (1982) also reported that spastic subjects manifested abnormal activation of elbow flexor during elbow extension, in the absence of any flexor muscle stretch during isometric force and position tracking tasks. Furthermore, during slow voluntary elbow flexion movement, long-lasting tonic co-contraction of the antagonist muscle was seen in >50% of the spastic hemiplegic patients. The latter was found to be enhanced with an increase in movement speed (El-Abd et al., 1993). In contrast, other authors observed that there was no significant antagonist co-activation in spastic elbow muscles as compared to normal subjects during isometric elbow flexion and extension (Fellows et al, 1994b; Tang and Rymer, 1981). The reason for the disparity in the extent of co-contraction found in spastic hemiparesis can be multifactorial. For instance, the amount of co-contraction is known to be dependent upon the nature (eg. isotonic or isometric) and complexity (eg. ballistc or tracking) of task (Smith, 1981). From a technical point of view, muscle co-contraction is difficult to quantify in a reliable fashion, because it is assessed primarily using electromygraphic (EMG) techniques with their inherent limitations. For example, when investigators compare raw EMG signals across subjects or sessions, the possibility of misinterpretation of the data should be considered.

Impairments in voluntary motor functions associated with spastic hemiparesis have been studied in muscles of the upper (Bohannon et al., 1987; El-Abd et al., 1993; Fellows et al., 1994a,b; Katz et al., 1992) and lower extremities (Bohannon and Walsh, 1992; Knutsson and Martensson, 1980) in patients with varying degrees of functional disability. However, systematic evaluations of the relationship between the impairments in voluntary motor functions in the agonist/antagonist muscle pairs and the severity of spasticity have

been scarce. In a previous study, we found that the voluntary motor impairment in the paretic ankle dorsiflexor of spastic hemiparetic subjects was related to the severity of ankle spasticity (Levin and Hui-Chan, 1994). Furthermore, voluntary motor functions of the ankle muscles in the standing position, in terms of peak isometric torque, co-contraction ratio and force onset, have been found to be reproducible across different sessions. To the best of our knowledge, similar investigations have not yet been carried out in the upper limb muscles. In addition, the wide variability between subjects certainly warrants that the reliability of these measures be established in a different subject group tested under new experimental conditions.

The objectives of this study are as follows: 1) To delineate the characteristics of voluntary motor functions in the agonist/antagonist muscles pairs of spastic hemiparetic subjects during voluntary isometric maximum contractions (MVC) at the elbow and ankle, and to compare the results obtained with those of the normal, age-matched controls. 2) To investigate if a systematic relationship exists between the alterations in these motor functions and the severity of clinical spasticity. 3) To establish the test-retest reproducibility of the MVC parameters and clinically assessed spasticity scores, with the view to develop reliable measurement tools for evaluating the effects of treatment over time.

SUBJECTS AND METHODS

Subjects

Six normal, adult subjects (median age=58.5 yrs) without a history of neurological or musculoskeletal disorders and 10 spastic, hemiparetic (CVA) subjects who met the

following inclusion criteria were recruited for this study: 1) a diagnosis of CVA with clinical manifestation of spasticity in the affected upper and lower limbs; 2) time since onset of the disease being greater than six months; 3) no history of previous neurological disorders; 4) no pain at rest or severe sensory impairments in the upper extremity, e.g. paraesthesia; 5) no severe aphasia or other perceptual deficits (i.e. They were able to comprehend instructions); 6) not receiving anti-spasmodic medications or other specific treatment for spasticity for the period of the experiment; 7) minimum passive ankle dorsiflexion to 90° (neutral position) and passive elbow extension to 120° on the affected side; 8) no cardiac pacemaker; 9) be ambulatory and capable of ascending and descending stairs with or without assistance. All subjects gave their written consent prior to participating in the study (Appendix I). Subjects' demographic data are summarized in Table 2.2.

For *objectives 1 and 2*, the two groups were matched with respect to age, sex and hand dominance. Thus, 8 CVA subjects (median age=53.5 yrs) consisting of 5 females and 3 males, were compared with 6 normal subjects (4 females and 2 males). All but 1 CVA subjects were right-handed. Three of the normals were tested on their dominant side to match with the affected side of 4 CVA subjects. For those subjects who underwent test-retest, the mean values of these two sessions were used for the between-group comparison. For *objective 3*, all the normal and 8 out of 10 hemiparetic subjects were tested on 2 separate occasions that were approximately 1 week apart, in order to evaluate the intersession reproducibility of the measurement parameters. All CVA subjects underwent clinical evaluation of spasticity, consisting of resistance to passive muscle stretch measured on a 5-point scale (doubly weighted since presumably they most closely reflect muscle tone), and

tendon jerk responses of the elbow and ankle muscles assessed on a 5-point scale, and ankle clonus on a 4-point scale (Levin and Hui-Chan, 1992,1993b). A single evaluator, who was an experienced neurologist, determined the overall severity of spasticity for each subject, and classified the latter into a mild, moderate or severe category according to the criteria presented in Table 2.1 (Table 2.1).

Subject Positioning and Fixation

The experimental set-up is illustrated in Fig. 2.1. For the upper extremity tests, the subject was seated at a custom-made table equipped with a steel forearm plate. Because initial muscle length is a known variable in the muscle tension produced (Vander et al., 1980), care was taken to standardize the upper and lower extremity joint positions. The shoulder joint was immobilized at approximately 75° of flexion with slight abduction, by means of straps and a firm foam wedge anchored to the table. The elbow joint was maintained at 90° of flexion and mid-supination by a sandsplint cast mounted on the forearm plate. For the lower extremity tests, the subject was placed in a semi-supine position with the hip and knee joints fixed at 30° of flexion by a partial sandsplint cast. The ankle joint was maintained at the neutral position by a foot plate.

Force and EMG Recording of Isometric MVC

Isometric MVCs generated in both the affected upper and lower limbs were measured, namely, elbow flexion (EF), and extension (EE), as well as ankle dorsiflexion (DF) and plantarflexion (PF). The subject was asked to give a MVC as fast as possible

following a "go" signal given by the experimenter, and to maintain the maximum contraction for approximately 3 sec. The duration of MVC used by other investigators ranged between 1 sec for knee extension (Yang and Winter, 1983) to 5 sec for elbow flexion (Colebatch et al., 1986). Three second duration was chosen for our experiment to allow ample time for the force development while minimizing the potential risk of fatique in our subjects. The subject received the "go" signal when the background agonist and antagonist EMG activities were sufficiently quiet, as monitored via a storage oscilloscope (Tektronix 5115). Three trials of each contraction were recorded. During the MVC trials, EMG activities were recorded from 4 muscle groups: biceps brachii (biceps), triceps brachii (triceps), tibialis anterior (TA), and soleus. After careful skin preparation, disposable silver-silver chloride surface electrodes (Medi-Trace 1801) were positioned 3 cm apart on each muscle as suggested by Basmajian and Blumenstein (1980). For the biceps, the electrodes were positioned over the belly of the muscle. For the triceps, the electrodes were placed on the medial head, at approximately 60% of the distance between the angle of the acromion and olecranon process. The electrodes were positioned longitudinally along the TA on the anterolateral aspect of the lower leg, two finger breadths inferior and lateral to the tibial tuberosity. For the soleus, the electrodes were placed 4 cm below the intersection of the two heads of the gastrocnemius muscle. The locations of all the recording electrodes were marked on the skin after the first session, and measured with references to surface landmarks such as the elbow crease, so that their placement could be repeated for the retest session. A Lebow 3132 force transducer, connected to the forearm plate between the wrist and the metacarpo-phalangeal joints, recorded the distractive (isometric elbow flexion) and compressive (isometric elbow

extension) forces. Note that elbow torque has been recorded at a similar location by other investigators (Tang and Rymer, 1981). Isometric dorsiflexion and plantarflexion forces were recorded in a similar fashion, approximately at the level of the metatarso-phalangeal joints. These forces were recorded in kilograms and converted to torques in Newton-meter (See ***Data Analysis*** section). The axis of rotation for elbow and ankle joints was located from surface landmarks, i.e. the lateral epicondyle, and the medial and lateral maleoli respectively for the elbow and ankle joints (Corrigan and Maitland, 1983).

Raw EMG signals from the four muscles were amplified at a gain of 2,000 and band-pass filtered at 10-1,000 Hz using Disa 15C 01 EMG amplifiers. These EMG and force signals were then sampled at 2.5 kHz by an Everex 486 computer and recorded from 120 msec before to approximately 3 sec following the trigger.

Data Analysis

Three MVC trials were analyzed and averaged off-line through a customized software from Lab Windows 2.2. Individual trials consisting of significant artifacts or cross-talks between agonist and antagonist muscles were discarded. The EMG signals were rectified and low-pass filtered at 75 Hz. Since torque is defined as, τ=force x $\perp$d (Lehmkuhl and Smith, 1983), the force recorded in kg was converted to torque (Nm), by multiplying the force value by the acceleration due to gravity (9.8 m/s^2) *and* the distance between the axis of rotation of the joint and the point of attachment of the force transducer. The onsets of EMG activity and torque were determined as the moment when the signals exceeded 3 S.D.

of their respective average baseline values. From the averaged torque trace, peak torque and half-rise time to peak torque were calculated. The peak EMG area was computed over a 500 msec window placed around the plateau phase of the torque trace (see Fig. 2.2). The EMG co-contraction ratio for each muscle was defined as the ratio expressed in percentage of peak EMG area of the muscle when it acts as an antagonist to that when it acts as an agonist (Knutsson and Martensson, 1980). For example,

$$\text{Co-contraction ratio of biceps} = \frac{\text{biceps EMG area during elbow } \textit{extension}}{\text{biceps EMG area during elbow } \textit{flexion}}$$

Comparisons of EMG co-contraction ratios and torque data between the normal and CVA groups were evaluated by a non-parametric statistical test (Mann-Whitney U). The inter-session reproducibility of MVC parameters for each group was evaluated using Wilcoxin signed ranks test as well as the interclass correlation coefficient (ICC). Correlations between the MVC parameters and clinical spasticity scores were tested using Pearson's product moment correlation coefficient (r). Significance level was set at 0.05 for all tests.

RESULTS

Comparison of Voluntary Motor Functions Between Normal and CVA Subjects

Peak torque during MVC. Examples of averaged MVC trials are illustrated in Fig. 2.2 for one subject from each group. Each ensembles of 3 traces consisted of agonist, antagonist EMG and the corresponding torque signals, where upward and downward deflections denote flexion and extension respectively. The difference in the relative

recruitment of agonist and antagonist muscles, and the resultant torque production between the normal (left traces) and CVA (right traces) subjects is notable. An example of when the peak MVC EMG area was calculated over a 500 msec window is marked by the shaded area.

A comparison of the MVC values between the normal and CVA groups are presented in Table 2.3. In the upper limb, peak EF and EE torques ranged from 43.4 to 135.3 Nm in the normal subjects and 0.3 to 85.8 Nm in the affected side of the CVA subjects. In the lower limb, ankle DF and PF peak torques ranged from 32.9 to 125 Nm and 2.2 to 49.6 Nm respectively for the normal and CVA subjects. As seen in Fig. 2.3A, the peak torques produced by all the muscles tested were significantly lower in the CVA as compared to the normal group ($p \leq 0.01$). We calculated the ratio of peak torque in the CVA group to that of the normal group for each MVC. In the upper limb, EF_{CVA}/EF_{normal} was 0.25 and EE_{CVA}/EE_{normal} was 0.23. In the lower limb, DF_{CVA}/DF_{normal} was 0.38 and PF_{CVA}/PF_{normal} was 0.33. Moreover, CVA subjects showed a tendency to take a longer half-rise time to reach their peak torques than normal subjects (Fig. 2.3B). For example, the half-rise time for EF and EE ranged from 90.2 to 576.6 msec in the normal group, as compared with 169.6 to 1002.8 msec in the CVA group (Table 2.3). For the ankle muscles, DF and PF half-rise times ranged from 150.4 to 451.4 msec in the normal, versus 127.6 to 643.2 msec in the CVA group. However, none of these values were significantly different between the two groups. For both groups, the half-rise time to peak torque in the PF was the longest (Fig. 2.3B).

Antagonist co-contraction ratio. Despite the marked weakness observed in CVA subjects for all the muscles tested, only the triceps co-contraction ratio was significantly

different between the two groups ($p<0.05$, Fig. 2.3C), where the value varied between 8.0 to 14.2% in normal subjects when compared with 4.4 to 289.4% in CVA subjects (Table 2.3). Nevertheless, all muscles showed a tendency towards greater antagonist co-contraction during isometric MVCs in the CVA group (Fig. 2.3C). We also found that in 1 or 2 subjects, the triceps and TA co-contraction ratios were above 100%. These results are summarized graphically in Fig. 2.3.

EMG - torque relationship. In normal subjects, there was no significant relationship between the agonist peak EMG area and peak torque for EF, EE or DF. One exception was the significant correlation found between soleus peak EMG area and PF torque ($r=0.99$, $p<0.001$). In contrast, significant positive linear relationships were observed between the two MVC parameters for biceps, triceps and TA muscles in the CVA subjects (Fig. 2.4A to C). Thus, with one exception of soleus EMG and PF torque (Fig. 2.4D), higher torque production was associated with greater agonist EMG areas in spastic hemiparetic muscles ($r=0.77$ to $r=0.92$).

Relationship Between MVC Parameters and Clinical Spasticity

The MVC parameters were also investigated in regard to possible correlations with clinical spasticity scores in CVA subjects. We found that only the EF torque was inversely related to total spasticity scores ($r=-0.70$, $p=0.05$, Fig. 2.5A). Other parameters did not demonstrate any significant relationship to spasticity. Thus, it appeared that the peak torque generated during MVC by the spastic elbow flexor was more closely related to the total severity of spasticity than either the co-contraction ratios or half-rise time to peak torque.

When the total spasticity score was divided into upper and lower extremity subscores for more meaningful correlations, the EF torque was inversely related to upper extremity subscores ($r=-0.82$, $p=0.01$). In other words, voluntary flexion torque generated at the elbow was negatively correlated with the upper extremity subscore consisting of biceps tonic stretch reflex and tendon jerk response. Furthermore, no significant relationship was observed between any of the MVC parameters for the ankle muscles and the lower limb subscore.

Reproducibility of Measurement Parameters

The test-retest reproducibility of the MVC parameters, EMG co-contraction ratios and clinical spasticity score are presented in Table 2.4. Due to the small sample size, non-parametric statistical test (Wincoxin signed ranks test) as well as the interclass correlation coefficients (ICC) were performed. For both groups, the peak torque, with ICC values above 0.86, was found to be highly reproducible. With one exception of PF peak torque in the CVA group ($p=0.02$), all other peak torque values were not significantly different from test to retest.

The half-rise time to peak torque for both the normal and CVA groups was not significantly different from test to retest, with the exception of the half-rise time to PF peak torque in the CVA group ($p=0.04$). The ICC values ranged from 0.43 to 0.91 in the normal group, with even higher values in the CVA group ($r=0.65$ to 0.88).

Because raw rectified EMG areas were to be used across different subjects for correlation analysis, the reproducibility of the agonist peak EMG area was also tested. We found that these EMG area values were also moderately to highly reproducible for both

groups, with ICC values ranging from 0.64 to 0.93 and 0.82 to 0.94 respectively for normal and CVA subjects.

The co-contraction ratios demonstrated varying degrees of reproducibility depending on the muscle studied. In the normal group, biceps (r=0.78) and soleus (r= 0.86) were more reproducible than either the triceps or TA (r=0.25 and 0.42, respectively); whereas in the CVA group, the opposite was observed. The co-contraction ratios of the triceps (r=0.90) and TA (r=0.99) were highly reproducible, while those of the biceps (r=0.36) and soleus (r=0.20) were less reliable. However, none of these values were statistically different across the two testing sessions. Finally, the clinical spasticity score was also found to be reproducible from one session to the next (r=0.78).

DISCUSSION

Comparison of Voluntary Motor Functions Between Normal and CVA Subjects

A comparison of the MVC parameters in all the muscles examined between normal and CVA groups demonstrated that spastic hemiparetic subjects produced significantly lower isometric torques in all the affected muscles ($p \leq 0.01$, Fig.2.3A). Moreover, they exhibited tendencies toward prolonged half-rise time to reach peak torque (Fig. 2.3B) and increased antagonist co-contraction ratio, with that in the triceps reaching statistical significance ($p<0.05$, Fig.2.3C). Further elaboration is hereby made with regards to the CVA group. The 10 CVA subjects were part of a total of 14 CVA patients (5 females, 9 males) recruited for the second part of the study. In order to compare the CVA with normal subjects, the two groups had to be comparable with respect to the variables that are known to affect force

production (see section on ***Subjects***). Therefore, from the total CVA group, all the 5 females and 3 randomly chosen males were used for the comparison between CVA and normal groups. This subgroup of 8 CVA subjects were comparable to the total group (n=14) in terms of the MVC parameters and severity of spasticity. More specifically, the median peak torque for the total CVA group ranged from 14.1 Nm for EE to 19.2 Nm for PF, the median half-rise time to peak torque ranged from 300.9 ms for EE to 436.7 ms for EF, and the antagonist EMG co-contraction ratio ranged from 28.5% for the triceps to 43.9% for the biceps - as compared with the data from the 8 CVA subjects in Table 2.3). Thus, we were assured that our subgroup of 8 CVA patients were representative of the total patient group.

A reduction in peak torques in the CVA group is expected since all our patients had some degree of hemiparesis in addition to spasticity. Alterations in motor unit functions have been identified as contributing factors to the motor deficits observed in hemiparetic muscles. Generally, a selective atrophy of fast-twitch fibers was found to be associated with the reduction in functioning motor units following upper motoneuron lesions (McComas et al., 1973). Furthermore, diminished firing rate of motor units has been demonstrated (Rosenfalk and Andreassen, 1980), resulting in decreased force output by the functioning motor units. It should be noted that the isometric MVC torque values for our small sample of normal subjects were comparable to the normative data reported by other investigators. For example, PF torques of 72 to 134 Nm were reported for healthy subjects between the ages of 50 to 59 years old (Fugl-Meyer et al., 1980). In the upper extremity, approximately 64 Nm EE torque was reported for normal subjects aged between 19 and 42 (Yamazaki et al., 1993). The ratio of peak torque in the CVA to that in the normal group indicated that the

upper limb muscles may have been somewhat more impaired (EF_{CVA}/EF_{normal}=0.25 and EE_{CVA}/EE_{normal}=0.23) than lower extremity muscles (DF_{CVA}/DF_{normal}=0.38 and PF_{CVA}/PF_{normal}=0.33). This finding might indicate a greater involvement of the middle cerebral artery in these CVA subjects (Brust, 1984). However, a common clinical belief that the extensors of upper extremity and the flexors of lower extremity tend to be 'weaker' than their spastic antagonists was not evident in our sample. Colebatch et al. (1986) also found that, contrary to the commonly believed "characteristic" distribution of weakness, the elbow flexors were relatively weaker than the extensors on the hemiparetic side in their patient sample.

Examination of the half-rise time to peak torque for isometric MVC showed that agonist recruitment was also altered in spastic hemiparesis. Although the two groups did not differ significantly, longer time tended to be required to fully activate the agonist for all the muscles tested. This finding is similar to what was reported for voluntary knee extension in hemiparetic patients (Bohannon and Walsh, 1992). Slower agonist and antagonist recruitment times were also observed through EMG recordings during voluntary isometric flexion and extension of the wrist (Hammond et al., 1988a). Single twitch contraction study on hemiparetic muscles also revealed that twitch contraction time was prolonged along with diminished maximum force in the ankle muscles (Visser et al., 1985). Thus, it appears that such temporal changes in force production also contribute to altered voluntary motor functions in spastic hemiparesis.

Relationship Between MVC Parameters and Clinical Spasticity

An intriguing question about such alterations in voluntary motor functions is the extent to which they could be related to the clinical manifestation of spasticity. In CVA subjects, we found that the EF torque was inversely related to the total spasticity score (r= -0.70, Fig.2.5), and to the upper extremity subscore to a slightly greater extent (r=-0.82). This result is similar to that of Bohannon et al. (1987) who also found that the strength deficit in shoulder medial rotators and elbow flexors were positively related to the agonist spasticity. In the lower limb, we have previously shown that the motor deficits in the paretic dorsiflexors was highly correlated with agonist/antagonist co-contraction ratio (r=0.91), and inversely related to clinical spasticity of the ankle plantarflexors (r=-0.65; Levin and Hui-Chan, 1994). One of the reasons for the lack of a significant relationship between the ankle muscle functions and clinical spasticity in the present study may be explained by the differences in the two experimental set-ups. In the previous study, the subjects were tested in standing; whereas in the present experiment, the subjects were examined in a semi-supine position. The functional demand for agonist/antagonist co-activation might be greater in the standing position for the purpose of maintaining balance. In addition, the position of the knee could have influenced the effectiveness of torque production at the ankle, and subsequently the extent of co-contraction. It has been reported that MVC for the PF can be reduced by up to 15% when the knee is flexed as compared to when it is extended with the body in supine position (Fugl-Meyer et al., 1980).

Motor reaction time was found to be significantly prolonged in spastic paraparetic subjects along with a reduction in the MVC force at their knee extensors (Nakamura and

Sajiki, 1985). In addition, this prolongation of motor reaction time was strongly correlated with the severity of spasticity ($r=0.795$, $p<0.05$). Thus, both the peak torque produced by MVC and the reaction time had been shown to be correlated with the extent of spasticity. From a functional point of view, the peak torque produced by MVC of the paretic knee extensor has been found to be a predictor of gait speed in stroke patients (Bohannon and Walsh, 1992).

Our finding that, compared to normal subjects, spastic patients demonstrated a tendency towards greater antagonist activation in both elbow and ankle muscle groups during isometric MVC was in agreement with those of other investigators who found a significant co-activation of antagonist muscles during isometric voluntary contractions in wrist and elbow muscles (Hammond et al., 1988b; El-Abd et al, 1993). On the other hand, some other studies reported no exaggerated antagonist co-activation in the elbow muscles of spastic subjects (Fellows et al., 1994a; Colebatch et al., 1986). Several reasons could account for this disparity: for example, differences in the methdology used. The degree of agonist activation in normal subjects has been shown to vary depending on the position of the limb being tested, the type of contraction performed, the degree of synergistic activity (Nakazawa et al., 1993), as well as the functional requirement of the limb (Falconer and Winter, 1985). It follows, then, that the extent of antagonist activation could be modified accordingly. Indeed, modification in the level of triceps antagonist activity was found in spastic subjects, depending on whether the elbow flexion was performed against a load (Fellows et al., 1994b). Another confounding factor could be the degree of paresis in the affected muscles. To elaborate, some of our severely affected patients had minimal agonist activity, thus

producing an extremely high co-contraction ratio value. On the other hand, more moderately involved subjects demonstrated these ratios to be within the range of the normal subjects. Wide between-subject variation is thus evident, and could account for the controversial reports in the literature.

A question may be raised as to the most appropriate method for quantifying EMG co-contraction. Investigators have used a variety of formulae with some of them demonstrating reliability over time (Falconer and Winter, 1985: Hammond et al, 1988b; Levin and Hui-Chan, 1994). Our choice of the formula presented under ***Data Analysis*** may be argued on the grounds that it did not take into account the agonist activity. But for the purpose of comparing relative antagonist activity across different subjects and different sessions, the ratio of antagonist activity normalized to its own MVC recorded during the same session, and through the same EMG electrodes and skin preparation, was considered to be an acceptable way to minimize variations.

Assuming that antagonist co-activation tends to be increased in hemiparetic subjects, one could question whether the degree of co-contraction is related to the severity of spasticity, and whether such an abnormality could interfere with motor functions. Our results indicated that EMG co-contraction ratios were not related to the severity of spasticity in the CVA subjects tested. Moreover, these ratios did not show significant relationship to peak torque or half-rise time to peak torque. Since the co-contraction ratios in these CVA subjects were not significantly greater than those of the normal subjects, it may be presumed that in this small sample of patients, abnormal antagonist co-activation during isometric MVC was not a functionally limiting factor.

Correlation analyses between EMG and peak torque revealed that, contrary to the negative findings in normal subjects, these two parameters were significantly and positively related for the biceps, triceps and TA muscles in the CVA group (Fig. 2.4). Several other studies have also reported such an abnormal relationship between force and EMG; i.e. for a given force level, greater EMG activity was observed in spastic hemiparetic muscles (Bourbonnais et al., 1989; Tang and Rymer, 1981). It may be speculated that in spastic hemiparetic muscles, other mechanisms which normally accompany agonist activation such as modulation of synergists and antagonist are altered. Hence, during MVC, the resultant force might be dependent mainly on the increasing activation of the agonist muscle alone rather than additional recruitment of the synergist muscles.

Reproducibility of MVC Parameters

The peak torques during isometric MVC were highly reproducible across the two testing sessions (ICC$\geq$0.86) in both subject groups. Furthermore, the half-rise time to peak torque (ICC=0.43 to 0.91) and co-contraction ratios (ICC=0.20 to 0.99) ranged from being mildly to highly reproducible (Table 2.4). Clinically evaluated spasticity score also demonstrated high test-retest reproducibility (ICC=0.78). The fact that PF torque was not as consistent from session to session in CVA subjects ($r=0.88$, $p=0.02$, Table 2.4) may be accounted for by the difficulty the patients had in isolating the PF contraction. Despite our instruction to the subjects not to compensate with other movements, several patients were unable to eliminate knee extension, for example. A majority of our subjects also had been wearing ankle-foot orthosis since the onset of stroke, hence it may have been difficult for

them to fully recruit the ankle muscles. Nonetheless, the fact that peak torques were, on the whole, reliable, was an indication that the subjects produced torques that were close to their maximum. It is recognized that raw EMG signals could vary greatly from session to session. Because we used raw EMG values in evaluating the relationship with torques, a certain degree of reliability was required. These values were found to be moderately to highly reliable for both groups (ICC=0.64 to 0.94), thus further supporting our assumption that each subject probably produced his/her maximum effort. It should be noted that the precaution we took in placing the electrodes on the same site besides careful subject fixation in each session (refer to ***Subject Positioning and Fixation*** section), also ensured better reproducibility of our EMG recordings.

The antagonist co-contraction ratios showed varying degrees of reproducibility. It appeared that since agonist peak EMG area of each muscle was moderately to highly reliable (ICC=0.64 to 0.94, Table 2.4), the variability in this ratio might be the result of inconsistency in the antagonist EMG activity within each subject. One may speculate on the reasons for the discrepancy in the reliability of co-contraction ratios among the 4 muscles between the two groups (Table 2.4). For example, in the normal subjects, more reproducible co-contraction ratios were found to be in the stronger muscles such as the biceps and soleus (ICC=0.78 and 0.86 respectively). Thus, these muscles could be co-activated to their maximum when acting as antagonists, resulting in better reproducibility in the normal subjects. In the CVA group, the opposite pattern was observed. For example, the antagonist co-contraction ratios were more reproducible in the paretic (ICC=0.90 and 0.99 respectively for the triceps and TA) as compared to the spastic muscles (ICC=0.36 and 0.20 respectively

for the biceps and soleus, Table 2.4). This may be due to the enhanced excitability level of the motoneuron pool in the latter muscles and insufficient reciprocal inhibitory mechanism from their antagonists, possibly resulting in more inconsistent EMG recruitment pattern.

To sum, our study demonstrated that spastic hemiparesis following CVA was characterized by a marked reduction in isometric MVC torques of the elbow and ankle muscle pairs, with those of the upper limb showing slightly greater deficits. This hemiparesis was accompanied by a tendency towards prolonged agonist recruitment time, which was reflected in a longer half-rise time to reach the peak torque, as well as a the tendency towards greater antagonist co-contraction during MVC in both the elbow and ankle muscles. However, these tendencies towards increased half-rise time to peak torque and antagonist co-contraction ratios observed in CVA subjects did not reach statistical significance. The extent of reduction in EF torque was related to the overall clinical severity of spasticity and specifically to the extent of elbow flexor spasticity. With few exceptions, the MVC parameters consisting of peak isometric torque, half-rise time to peak torque, peak agonist EMG area and antagonist co-contraction ratio, as well as clinical spasticity score demonstrated moderate to high reproducibility between test sessions. Of these parameters, peak torques, MVC peak agonist EMG areas and clinical spasticity scores were found to be very reliable measurement indexes for evaluating treatment efficacy over time in hemiparetic subjects.

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Table 2.1. Composite clinical spasticity score

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1) Resistance to passive stretch: Tonic stretch reflex

0 (0) - No resistance during elbow extension/ankle dorsiflexion
1 (2) - Slight resistance
2 (4) - Normal resistance
3 (6) - Moderately increased resistance
4 (8) - Maximally increased resistance

Upper extremity score - X/8
Lower extremity score - X/8

2) Tendon tap

0 - No tendon jerk elicited at biceps/Achilles tendon
1 - Minimal response (hypoactive tendon jerk)
2 - Normal response
3 - Moderately hyperactive response
4 - Maximally hyperactive response

Upper extremity score - X/4
Lower extremity score - X/4

3) Clonus at the ankle: Response to quick, maintained stretch

1 - No clonus elicited
2 - 1 to 2 beats of clonus, unsustained
3 - Greater than 2 beats of clonus, unsustained
4 - Sustained clonus

Lower extremity score - X/4

Total score - X/28

Mild spasticity : 1 - 13
Moderate spasticity : 14 - 21
Severe spasticity : 22 - 28

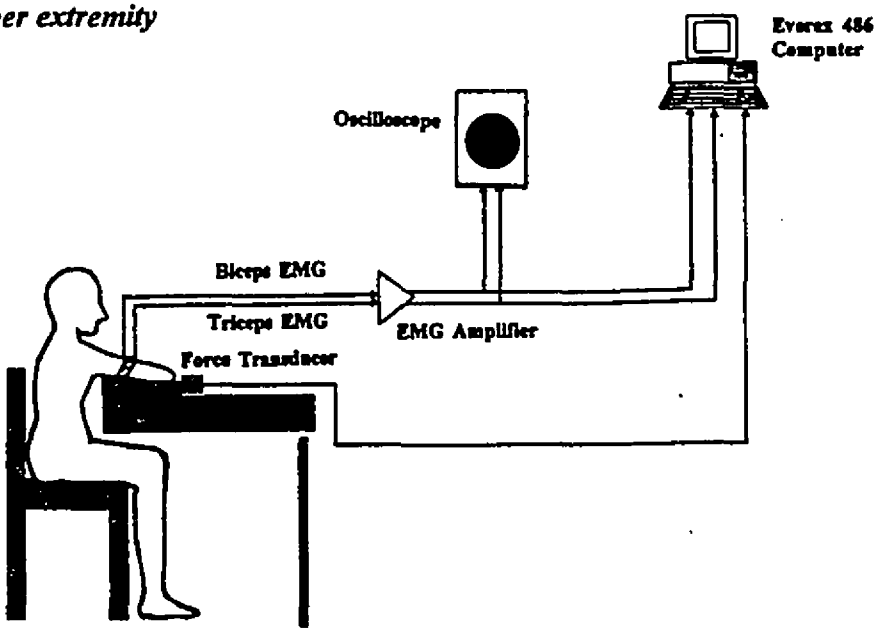
Upper extremity subscore=X/12; Lower extremity subscore=X/16.

Table 2.2. Demographic profile of normal age-matched and CVA subjects

Subject	Age (yrs)	Gender	Hand dominance	Side of hemiparesis	Diagnosis	Severity of spasticity	Duration of stroke (mos)
Normal							
1(WK)	61	F	R				
2(DT)	58	F	R				
3(HP)	59	F	R				
4(HE)	54	M	R				
5(BA)	62	F	R				
6(JK)	56	M	R				
Median	**58.5**						
CVA							
1(MS)*▲	76	M	L	dominant	R CVA	moderate	45
2(DK)*▲	57	F	R	dominant	L CVA	moderate	79
3(JS)*	73	M	R	non-dominant	R CVA	moderate	6
4(GD)▲	48	F	R	non-dominant	R CVA	severe	74
5(DL)*▲	48	F	R	dominant	L CVA	severe	16
6(RR)*▲	58	F	R	non-dominant	R CVA	severe	76
7(GR)*▲	37	M	R	non-dominant	R CVA	severe	17
8(MM)▲	75	M	R	non-dominant	R CVA	moderate	48
9(GW)*▲	50	F	R	dominant	L CVA	moderate	59
10(IL)*	39	M	R	dominant	L CVA	moderate	23
Median (▲)	**53.5**						**53.5**

* Subjects who participated in test-retest.
▲ Subjects who were compared with the normal group.

A) *Upper extremity*



B) *Lower extremity*

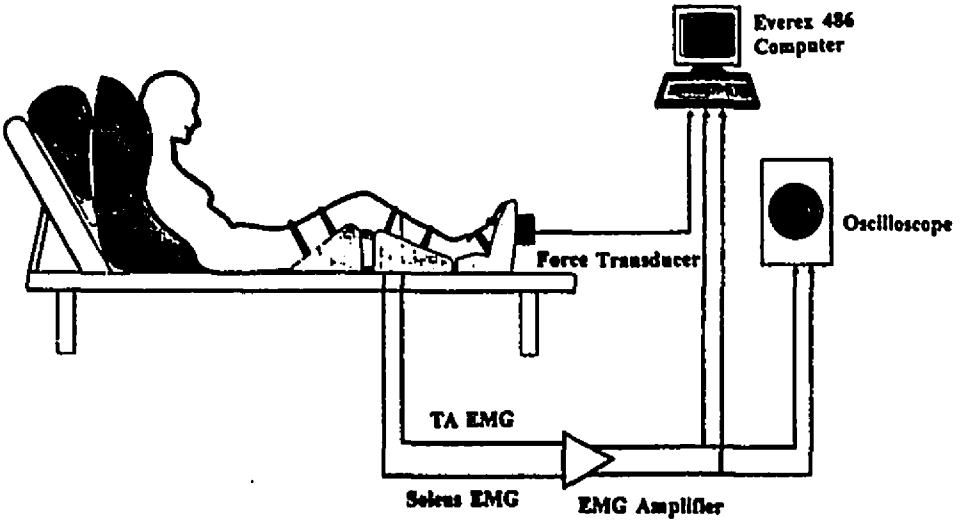


Fig. 2.1. Experimental set-up for recording of isometric maximum voluntary contraction (MVC).

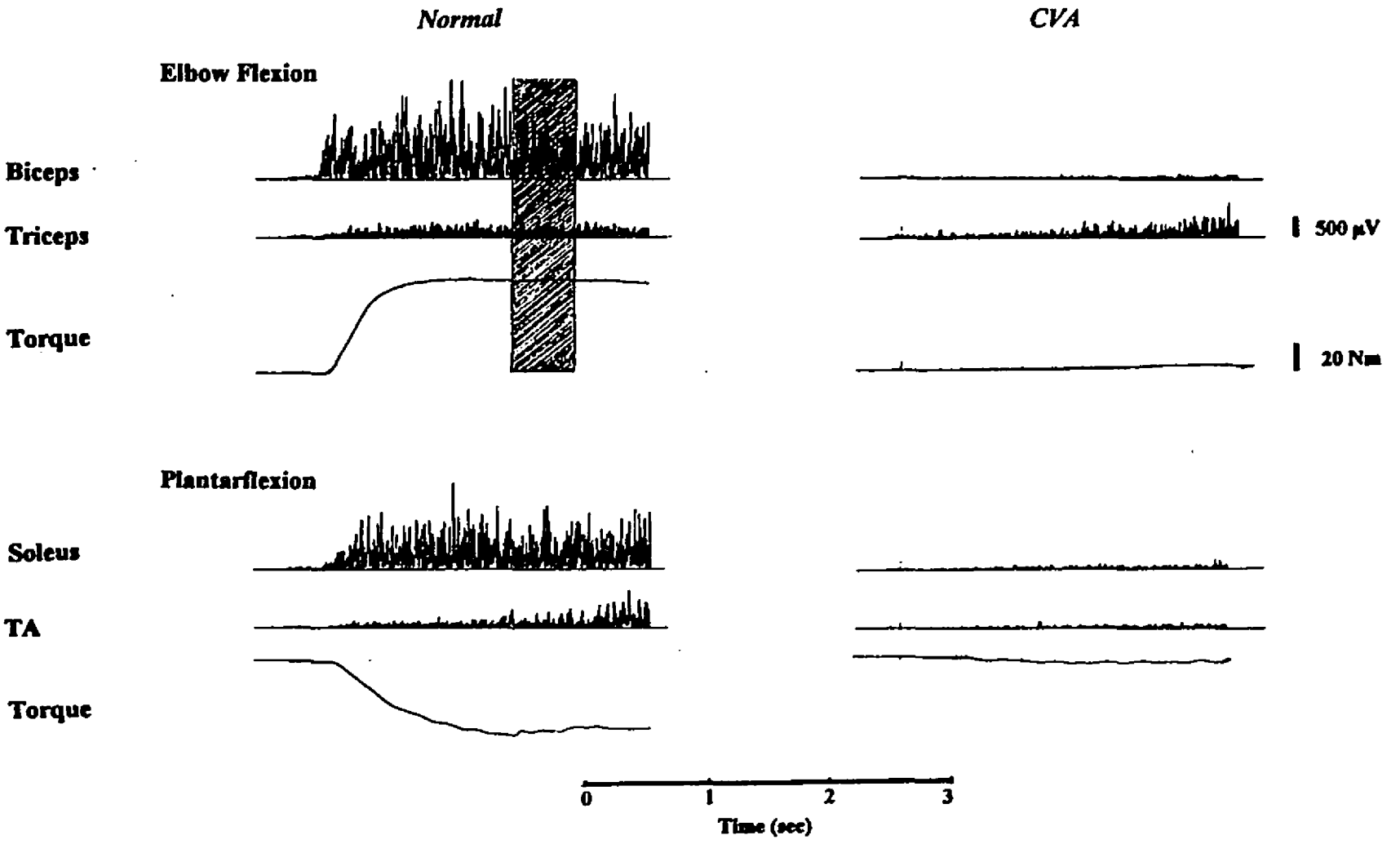


Fig. 2.2. EMG and torque recordings during maximum voluntary contraction (MVC) of elbow flexion (*upper 3 traces*) and ankle plantarflexion (*lower 3 traces*). The shaded area represents an example of when the peak MVC EMG area was claculated over a 500 ms window.

Table 2.3. Comparison of MVC parameters between normal and CVA subjects

		Normal	CVA	Mann-Whitney	
Peak torque (Nm)	EF	76.6 (62.5-135.3)	19.5 (1.7-85.8)	U=44.0	p=0.01
	EE	60.9 (43.4-115.5)	14.1 (0.3-46.1)	U=47.0	p=0.003
	DF	34.2 (32.9-88.5)	13.2 (2.5-24.0)	U=48.0	p=0.002
	PF	51.7 (52.9-125.0)	17.3 (2.2-49.6)	U=48.0	p=0.002
Half-rise time (ms)	EF	263.7 (196.4-576.6)	291.4 (175.0-1002.8)	U=17.0	n.s.
	EE	190.2 (90.2-450.8)	307.1 (169.6-716.0)	U=8.0	n.s.
	DF	169.6 (150.4-282.4)	286.0 (127.6-477.2)	U=8.0	n.s.
	PF	408.7 (234.0-451.4)	461.8 (191.4-643.2)	U=19.0	n.s.
Co-contraction ratio (%)	Biceps	26.4 (10.0-56.7)	38.9 (15.0-48.2)	U=14.0	n.s.
	Triceps	11.2 (8.0-14.2)	20.6 (4.4-289.4)	U=7.0	p=0.045
	TA	8.5 (3.1-31.9)	23.7 (1.8-192.2)	U=19.0	n.s.
	Soleus	18.5 (3.3-70.0)	43.0 (19.9-60.1)	U=13.0	n.s.

Note: Data are median values (range). EF=elbow flexion; EE=elbow extension; DF=dorsiflexion; PF=plantarflexion. n.s.=$p>0.05$.

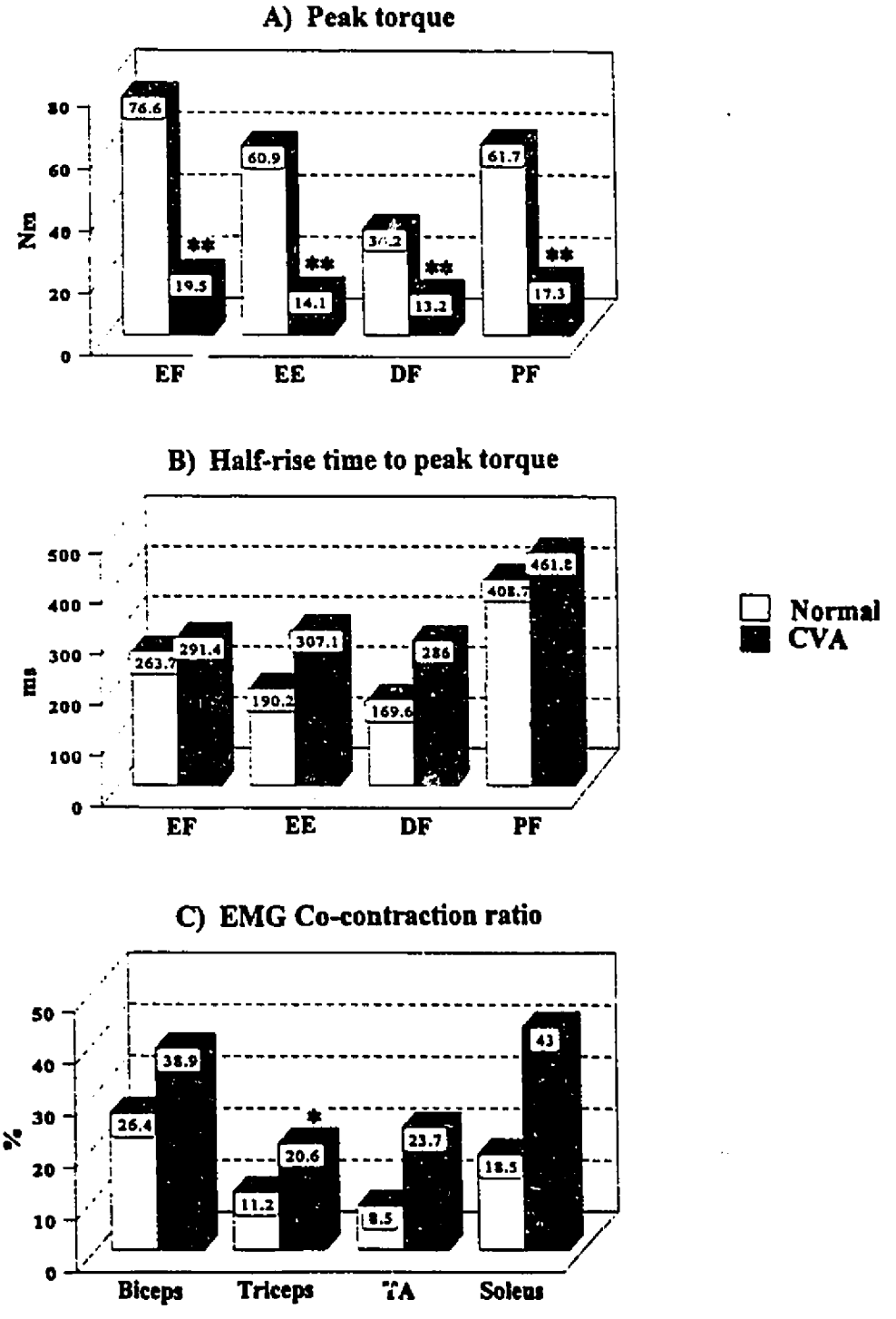


Fig. 2.3. Comparison of MVC parameters between the normal and CVA group. Each bar represents the group median value. EF=elbow flexion; EE=elbow extension; DF=dorsiflexion; PF=plantarflexion. *: $p<0.05$; **: $p<0.01$.

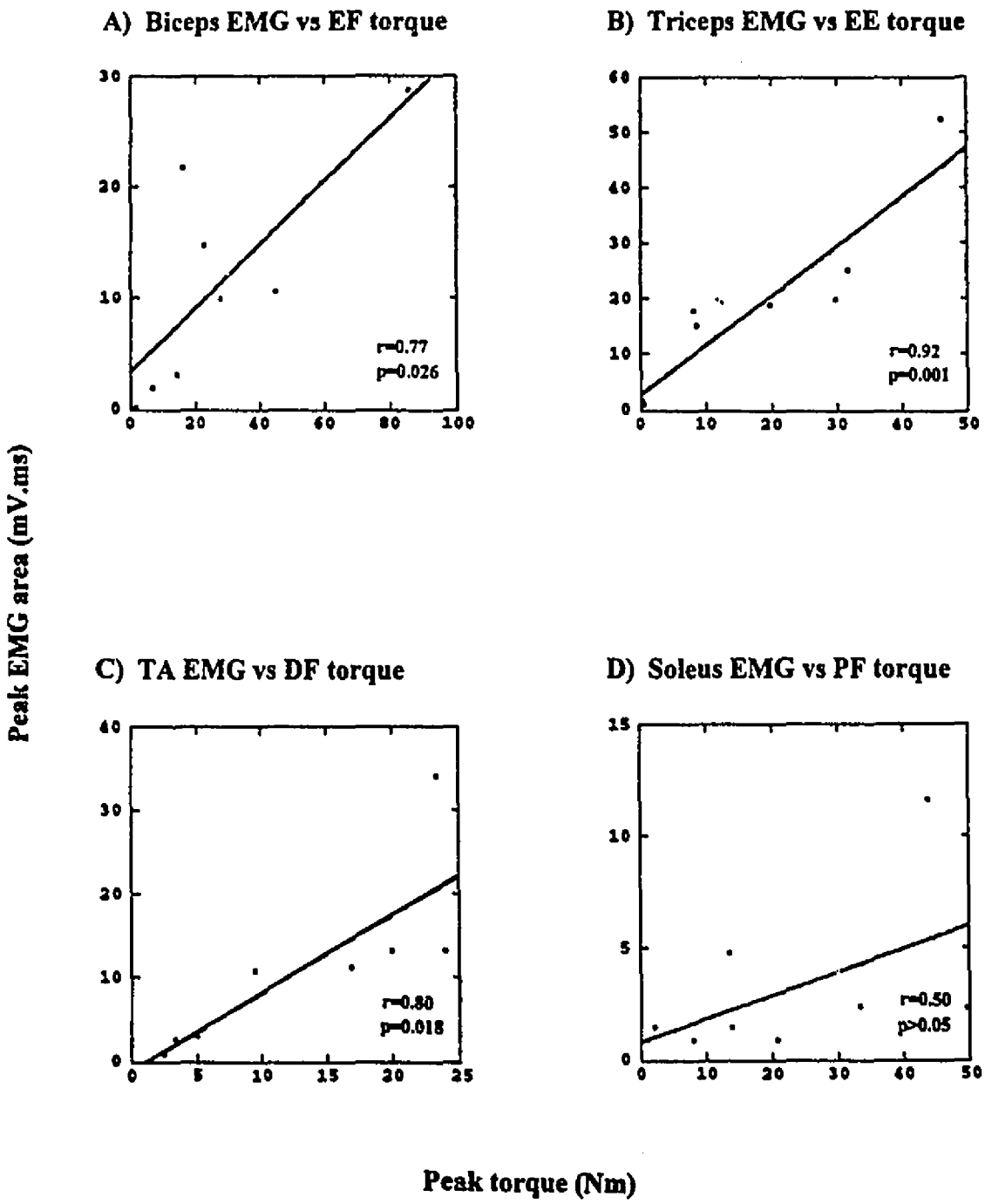


Fig. 2.4. Correlation between MVC peak EMG area (*y-axis*) and peak torque (*x-axis*) in CVA subjects. Each data point represents the mean of 3 trials of MVC for each subject.

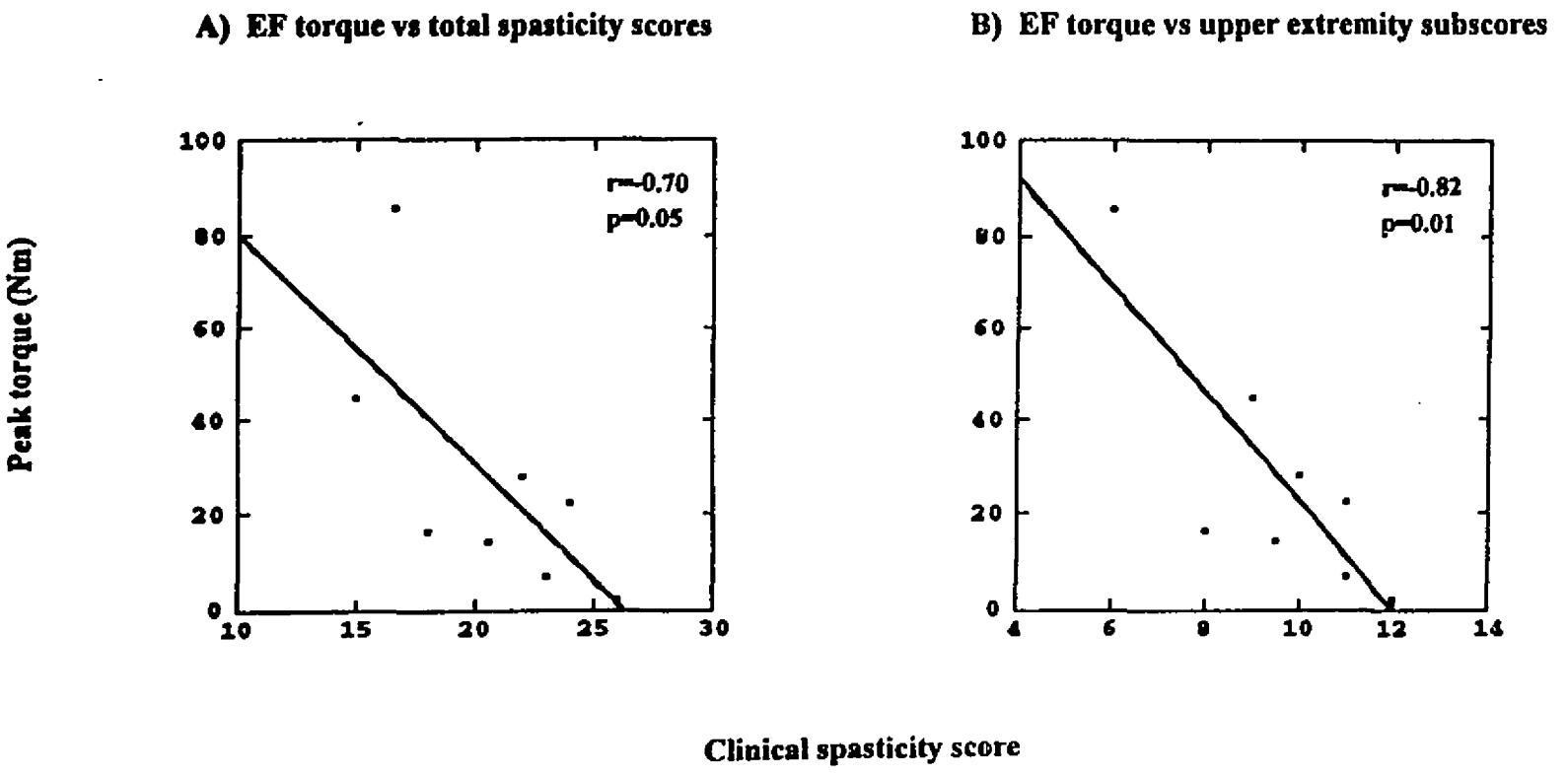


Fig. 2.5. Correlation between elbow flexion peak torque (*y-axis*) recorded during MVC and clinical spasticity scores (*x-axis*).

Table 2.4. Reproducibility of measurement parameters

		Normal (n=6)		*CVA (n=8)*	
		ICC	Wilcoxin p	ICC	Wilcoxin p
Peak torque	EF	0.96	n.s.	0.89	n.s.
	EE	0.99	n.s.	0.89	n.s.
	DF	0.96	n.s.	0.97	n.s.
	PF	0.86	n.s.	0.88	p=0.02
Half-rise time to peak torque	EF	0.79	n.s.	0.88	n.s.
	EE	0.91	n.s.	0.85	n.s.
	DF	0.43	n.s.	0.65	n.s.
	PF	0.73	n.s.	0.86	p=0.04
MVC peak EMG area	Biceps	0.64	n.s.	0.87	n.s.
	Triceps	0.82	n.s.	0.91	n.s.
	TA	0.67	n.s.	0.94	n.s.
	Soleus	0.93	n.s.	0.82	n.s.
EMG co-contraction ratio	Biceps	0.78	n.s.	0.36	n.s.
	Triceps	0.25	n.s.	0.90	n.s.
	TA	0.42	n.s.	0.99	n.s.
	Soleus	0.86	n.s.	0.20	n.s.
Clinical Spasticity Score				0.78	n.s.

Note: Wilcoxin p= p-value for Wilcoxin signed ranks test. n.s.= p>0.05. Abbreviations are as in Table 2.3.

Chapter 3. Segmental and Heterosegmental Effects of TENS on Clinical Spasticity and Voluntary Motor Functions in Hemiparetic Subjects

SUMMARY

Our previous studies have demonstrated that repeated applications of transcutaneous electrical nerve stimulation (TENS) to the common peroneal nerve for 3 weeks, significantly reduced the clinical spasticity of the spastic antagonist ankle plantarflexors ($p<0.05$), but not placebo stimulation, and improved the voluntary motor functions of the paretic agonist dorsiflexors ($p<0.05$) in spastic hemiparetic subjects. Two questions naturally arose; First, to what extent will similar results be found in the upper limb muscles? Second, will these effects be confined to segmental levels alone? Hence, the objective of the present study was to delineate both the segmental and heterosegmental effects of 4 weeks of TENS applications to the radial nerve on clinical spasticity and voluntary motor functions respectively at the elbow and ankle muscles of chronic spastic hemiparetic subjects.

Chronic CVA patients with appropriate inclusion and exclusion criteria were randomly allocated to either a TENS ($n=9$) or placebo ($n=5$) group. Twenty sessions of daily conventional TENS was applied for 60 min to the radial nerve on the hemiparetic arm over a 4 weeks period. Our measures consisted of clinical spasticity scores, peak torques generated during isometric maximum voluntary contractions (MVC) of flexion and extension about the elbow and ankle joints, as well as the respective electromyographic responses of the elbow (biceps and triceps) and ankle (tibialis anterior and soleus) muscles. Antagonist co-contraction ratios for each MVC tested were calculated. These measures were evaluated *before*, at 2 and 4 weeks *during*, as well as at 2 weeks *after* the stimulation period.

Our results indicated that TENS, but not placebo stimulation significantly reduced upper extremity spasticity score after 4 weeks ($p=0.05$) as well as reduced the tibialis anterior

co-contraction ratio after 2 weeks of stimulation ($p<0.01$). In addition, a greater proportion of subjects in the TENS group showed increases in peak torques at the elbow and ankle joints than the placebo group. Specifically, in 67% of subjects who received TENS for 4 weeks, a significant decrease in upper extremity clinical spasticity score ($p=0.04$) was found to be accompanied by a significant increase in elbow extension torque ($p<0.05$), when compared to the control values obtained before stimulation. However, no significant carry-over effect was observed at 2 weeks after the stimulation period. It is concluded that, in the majority of the spastic hemiparetic subjects, 4 weeks of conventional TENS applied to the ipsilateral radial nerve produced a significant reduction in upper limb spasticity as well as an improvement in voluntary elbow extensor torque. Of interest is the observation that the segmental effects produced were stronger than the heterosegmental effects in the ankle muscles. However, the emergence of some remote effects point to possible diffuse influence of long-term afferent conditioning via repeated TENS applications.

INTRODUCTION

Earlier studies have reported that chronic electrical stimulation of deep structures in the central nervous system (CNS), such as the cerebellum (Davis et al., 1977; Fisher and Penn, 1978), could reduce spasticity and improve voluntary motor functions in the majority of patients with various CNS disorders. The efficacy of peripheral electrical stimulation of the spastic agonist or its antagonist muscles in reducing spasticity has also been investigated, leading to the development of functional electrical stimulation in mainly spinal cord injured subjects (see Ragnarsson, 1992; Robinson et al., 1988). Furthermore, amelioration of spasticity in the antagonist muscle has been observed following electrical stimulations applied to predominantly the paretic agonist muscle, via either implanted or surface electrodes (Alfieri, 1981; Levine et al., 1952; Stepanovska et al., 1988; Vodovnik et al., 1984). Such a reduction in spasticity is thought to involve, in part, reciprocal inhibitory mechanisms at the segmental level.

Since the observation by Cook and Weinstein (1973) that spasticity and motor functions improved following chronic dorsal column stimulation (DCS) in multiple sclerosis (MS) patients, the potential role of afferent stimulation in the treatment of spasticity has surfaced. In this connection, Fredrikson et al. (1986) showed that transcutaneous and epidural spinal cord stimulation applied to the upper thoracic regions in MS patients significantly improved bladder dysfunction as well as voluntary motor functions at the knee. Although the underlying mechanisms for such a modulation remain unclear, its widespread nature suggested that heterosegmental as well as descending pathways might be involved. Dorsal column is known to contain mostly large diameter primary afferent fibers. We have

previously demonstrated that low intensity, high frequency transcutaneous electrical nerve stimulation (TENS) excited mainly large diameter afferent fibers (Levin and Hui-Chan, 1993). Thus, TENS applied peripherally could also be effective in relieving spastcity via similar pathways as DCS.

Therapeutic procedures such as the DCS have a disadvantage in that they require surgical approaches. On the other hand, TENS is a non-invasive method that patients could apply themselves with relative ease and without adverse effects. Preliminary evidence based on 6 patients with spinal cord injury showed that TENS applied to L3-4 dermatomes could reduce spasticity in the knee extensors in 3 subjects (Badj et al., 1985). More recently, Dewald et al. (1993) reported that 10 min of cutaneous stimulation at 20 Hz over the biceps muscle produced an immediate reduction in stretch induced torque in both elbow flexors and extensors of 7 hemiparetic subjects. However, the effect of placebo stimulations was not investigated in this study. Previous work in our laboratory (Levin and Hui-Chan, 1992) demonstrated that repeated daily applications of TENS for 60 min to the common peroneal nerve for 3 weeks, but not placebo stimulation, significantly reduced clinical spasticity of the ankle plantarflexors ($p<0.05$), soleus stretch reflex excitability ($p=0.05$) and improved voluntary ankle dorsiflexion force ($p<0.05$). Thus, peripherally applied surface electrical stimulation has been found to produce both immediate and longer-term local therapeutic effects.

Some evidence emerged pointing to the existence of remote effects as a result of such afferent conditioning. Walker (1982) showed that 1 hour of percutaneous electrical nerve stimulation applied to the right median, radial and saphenous nerves in MS patients

produced a bilateral inhibition in ankle clonus that could last for up to 2 hours following the termination of stimulation. Recently, Han et al. (1994) reported an immediate reduction in the Ashworth score denoting the degree of spasticity in the lower limb muscles as well as ankle clonus in patients with spinal spasticity following 30 min of TENS applied to two acupoints located respectively in the dorsal and palmer surfaces of the thenar muscles, and the lower lateral side of the knee joint at the top of the calf muscle. These changes were observed bilaterally and lasted for up to 10 min after the cessation of stimulation. Furthermore, longer-term improvements in clinical spasticity and ankle clonus were also observed when the stimulation was extended to twice daily to alternate sides for 3 months in 4 patients. Regretfully, this study lacked a proper control group. Furthermore, because the nerves in both the upper and lower extremities were stimulated, purely heterosegmental effects of TENS could not be delineated. On the other hand, we have previously demonstrated that, in 10 spastic hemiparetic subjects, 45 min of TENS applied either contralaterally to the median nerve or reciprocally to the common peroneal nerve resulted in prolonged soleus stretch reflex latency ($p<0.05$) which lasted for up to 60 min *after* the stimulation (Hui-Chan and Levin, 1993). Hence, peripheral afferent stimulation via TENS has also been found to produce remote or heterosegmental effects.

A few questions may be raised as to whether repeated TENS applications can have cumulative effects on spasticity and voluntary motor functions in the upper limb, and whether these effects will spread to the lower limb, and/or be maintained after treatment ends. If modification in clinical spasticity and/or motor functions are observed in the upper and lower limb muscles with a single site of stimulation, the results would suggest that

afferent conditioning may produce relatively diffuse effects involving both segmental and non-segmental mechanisms. Furthermore, the local and remote effects produced may be dependent on the total duration of treatment and/or differ in their relative magnitude.

Thus, three objectives were established for this study. Our first aim was to investigate the segmental and heterosegmental effects of repeated TENS applications to the radial nerve on clinical spasticity and voluntary motor functions respectively in the elbow and ankle muscles of spastic hemiparetic subjects. Our second objective was to determine whether a longer (4 weeks) stimulation period would produce greater effects than a shorter (2 weeks) period. Our final aim was to investigate whether any reduction in clinical spasticity score and/or improvement in voluntary motor functions at the elbow or ankle muscles would be maintained at 2 weeks after the cessation of stimulation.

SUBJECTS AND METHODS

Subjects

Fourteen CVA patients fulfilling the following inclusion criteria were recruited for this study. All subjects had no previous history of neurological disorders, with the onset of stroke being greater than 6 months. They manifested clinical spasticity in the upper and lower limb muscles, showed no significant pain, sensory impairment or aphasia, and were capable of minimum passive elbow extension to 120° and ankle dorsiflexion to neutral position on the affected side. These patients were not taking any anti-spasmodic medications or wearing a cardiac pacemaker. They were ambulatory with a cane and able to ascend/decend stairs with or without assisstance. Each subject's overall severity of spasticity

was evaluated by a single blind evaluator as described in the ***Evaluation Protocol and Data Recording*** section below.

After being stratified according to the severity, subjects were randomly assigned to either a TENS or placebo group with the exception of 1 subject who had previous experience with TENS for his shoulder pain. This patient was entered into the TENS group. One subject (#13), who initially participated in the placebo group, was enrolled in the treatment group following a sufficient wash-out period (3 months), after no significant changes in her clinical spasticity score and peak torque measurements was observed. Another subject was unavailable to continue with our study following his initial evaluation. Thus, 9 and 5 subjects participated in the TENS and placebo groups, respectively. Eleven out of 14 subjects were able to complete the follow-up evaluation at 2 weeks after the end of the stimulation period. Demographic profile of each subject is summarized in Table 3.1. The two groups were comparable in regards to the median age and the degree of spasticity. In the TENS group (4 females and 5 males), 4 subjects had moderate, and 5 had severe spasticity. In the placebo group (2 females, 3 males), 3 were moderately spastic while 2 subjects were severely affected. The median duration of stroke for the TENS group was 38 months while that of the placebo group was 59 months. This variable was not significantly different between the two groups ($p<0.05$).

Stimulation Protocol

Following an orientation session with detailed instructions on the proper use of the TENS unit and the stimulation protocol described below, the patient or a family member

applied TENS or placebo stimulation via a portable TENS unit (Staodyn Maxima III) at home. Two 4.5 x 4.5cm auto-adhesive electrodes (Staoderm C) were attached over the radial nerve distribution on the posterior surface of the hemiparetic arm, with the anode placed 3 cm above the olecranon process and the cathode approximately 4 cm proximal to the anode. Stimulation parameters consisted of 0.1 ms square pulses delivered at a frequency of 80 Hz and an intensity of 2-3 times the sensory threshold for the treatment group. The sensory threshold was determined as the intensity when the subject first reported a just noticeable tingling sensation in the cutaneous distribution of the radial nerve, along the back of the arm. This usually produced a 'moderate to strong but tolerable' sensation in our subjects. The subjects in the placebo group were provided with a sham TENS unit with the electrical circuit disconnected internally, but on which the parameter dials were to be set similar to those of the real treatment unit. Stimulation was applied continuously for 60 min per day (as previous reported by Levin and Hui-Chan, 1992), at 5 consecutive days per week for 4 consecutive weeks. Thus, all subjects underwent a total of 20 TENS or placebo stimulation sessions. The exception was 1 subject in the TENS group who reported that he had missed 1 day of stimulation. To ensure compliance with the treatment protocol, each subject was required to keep a daily log of the treatment record which was to be counter-signed by a family member. The record was then returned to the examiner on assessment days for verification.

Evaluation Protocol and Data Recording

Clinical assessment of spasticity and isometric maximum voluntary contractions

(MVC) during flexion and extension of elbow and ankle joints were recorded on 4 occasions: *before*, at 2 and 4 weeks *during*, as well as at 2 week *after* stimulation. Clinical assessment of spasticity was performed by a single blind evaluator with the subject seated comfortably on each of the testing sessions. The clinical measures consisted of resistance of the elbow and ankle muscles to passive stretch assessed on a 5-point scale (doubly weighted since presumably they most closely reflect muscle tone), biceps and Achilles tendon jerk responses on a 5-point scale, and ankle clonus on a 4-point scale (Table 2.1., Chapter 2). Each subject's severity of spasticity was then categorized as mild, moderate or severe.

Maximum voluntary contractions (MVC) for elbow and ankle flexion and extension were performed in the standarized positions illustrated in Fig. 2.1A and B and described in detail in Chapter 2, ***Subject Positioning and Fixation.*** Briefly, the upper extremity was tested with the subject seated at a custom-made table equipped with a steel forearm plate and partial cast. The joints were fixated to the forearm plate by means of velcro straps, with the shoulder immobilized in approximately 75° of flexion and slight abduction. The elbow joint was stabilized in 90° of flexion with the forearm in mid-supination. Similar position has been used by other investigators for force measurement in the elbow (Colebatch et al., 1986). For testing ankle muscles, each subject was placed in a semi-supine position with the lower limb fixated to partial casts by a series of straps, with the hip and knee joints held at approximately 30° of flexion and the ankle joint stabilized in neutral position by a foot plate. Care was taken to keep the limb positions constant from session to session, since initial muscle length is a known variable associated with tension produced by the muscle(see Vander et al., 1980).

Each subject was asked to give 3 trials of isometric MVC lasting for 3 sec for elbow flexion (EF) and extension (EE), as well as ankle dorsiflexion (DF) and plantarflexion (PF) in the positions described above following a "go" signal given by the experimenter. Isometric forces were recorded via Lebow 3132 force transducer connected to the forearm plate at approximately the level of the metacarpo-phalangeal joints and to the foot plate at the level of the metataso-phalangeal joints. The distance from the axis of rotation of the elbow and ankle joints to the point of attachment of the force transducer was recorded for each subject to be used in calculation of the torque. EMG activities were recorded simultaneously with the force mesurements from the biceps, triceps, tibialis anterior (TA) and soleus muscles, using surface electrodes attached to the locations as described by Basmajian and Bluemenstein (1980) and stated fully in Chapter 2, ***Force and EMG Recording of Isometric MVC***. The locations of all recording electrodes were marked and noted in the first session for use in all subsequent testing sessions.

Raw EMG signals were ampified at a gain of 2,000 and band-pass filtered at 10-1,000 Hz using a Disa 15C 01 EMG amplifier. The EMG and force signals were aquired at a sampling frequency of 2.5 kHz from 120 msec before to approximately 3 sec after the trigger by an Everex 486 computer.

Data Analysis

All EMG and torque signals were processed and analyzed off-line as described in Chapter 2, ***Data Analysis*** section. The force recorded in kg was converted to torque by using the formula: *Torque=Force x distance* (see Chapter 2, ***Data Analysis***). The MVC trials were

averaged and EMG signals were rectified and low-pass filtered at 75 Hz. The peak EMG area was computed over a 500 msec window placed around the plateau phase of the torque trace (see Fig. 2.2). Average peak torques and antagonist co-contraction ratios were determined for the isometric MVC of each of the muscles tested. The antagonist EMG co-contraction for each muscle was determined as the ratio of peak EMG area of the muscle when it acts as an antagonist to that when it acts as agonist (Knutsson and Martensson, 1980). The formula used for calculating this ratio has been presented in Chapter 2, ***Data Analysis.***

Due to the limited sample size and consequently, presumed non-homogeneity of variances between the groups, non-parametric tests were used for statistical analysis on each outcome measure. The effects of treatment were compared between the TENS and placebo groups at 2 and 4 weeks using Mann-Whitney Test. The data from subgroups from each experimental group consisting of those subjects who showed a tendency towards an increase in peak torque, were also analyzed. To test the effect of time course of TENS or placebo stimulation, each subgroup was examined separately for the 4 evaluation sessions using Friedman's Test for one-way repeated measures design. Correlations between peak torque and peak EMG area were tested with Pearson's product moment correlation coefficient (r). Unless otherwise stated, a significance level of $p \leq 0.05$ was used for all tests.

RESULTS

Changes in Clinical Spasticity Following TENS versus Placebo Stimulations

The effect of 2 and 4 weeks of TENS or placebo stimulations on spasticity is

illustrated in Fig. 3.1A to C. Each subject's score was normalized with respect to the control score obtained before any stimulation during the first evaluation session. The total spasticity score showed minimal change after 2 and 4 weeks of either TENS or placebo stimulation. However, when the total score was divided into its upper (UE) and lower (LE) extremity components (Table 2.1, Chapter 2), the UE subscore was significantly reduced after 4 weeks of TENS but not placebo stimulation ($p=0.05$), despite negligible changes in the LE subscore.

Changes in Voluntary Motor Functions Following TENS versus Placebo Stimulations

An example of the effects of TENS and placebo stimulations on isometric MVC is illustrated in Fig. 3.2. The traces represent the averaged MVC trial comprised of agonist, antagonist EMG responses and torque during EE for one subject from each of the TENS and placebo group recorded during the 4 evaluation sessions. Note the small increase in EE torque after 4 weeks of TENS (31.7, 27.7, 36.3 and 17.4 Nm for *before, 2, 4 weeks during* and *2 weeks after* stimulations, respectively) but not placebo stimulation (40.7, 30.1, 32.9 and 35.2Nm for *before, 2, 4 weeks during*, and *2 weeks after* stimulations, respectively) in these subjects. However, as a group, there was a tendency for a progressive increase in both EF and EE torque after 2 and 4 weeks of both TENS and placebo stimulation (Fig. 3.3A). The increase in EF torque was accompanied by an increase in triceps co-contraction ratio after 2 weeks of both TENS and placebo stimulation (Fig. 3.3B). Subsequently, following 4 weeks of TENS, the triceps co-contraction ratio remained above the control value, whereas the ratio tended to be reduced after 4 weeks of placebo stimulation. EE torque showed a similar increase at 4 weeks for both TENS and placebo stimulations which was accompanied

by a tendency for an increase in biceps co-contraction following 4 weeks of TENS stimulation and a tendency for a decrease in the co-contraction ratio after 4 weeks of placebo stimulation. However, it is important to note that these changes were not statistically significant.

In the lower limb, TENS produced a mild tendency for an increase in DF torque after 4 weeks, whereas the placebo stimulation resulted in initial increase in DF torque followed by a decrease in torque (Fig. 3.3A). The soleus antagonist co-contraction ratio tended to be diminished after 4 weeks of TENS, in contrast to that obtained after 4 weeks of placebo stimulation (Fig. 3.3B). Again, these changes were not statistically different between the two groups. Four weeks of TENS resulted in a tendency towards increasing PF torque whereas the placebo stimulation produced the opposite trend. Moreover, the TA co-contraction ratio was significantly reduced after 2 weeks of TENS but not placebo stimulations ($p<0.01$, Fig. 3.3B).

Subgroup Data

From the above group data, it could be seen that TENS, but not place stimulation, produced a statistically significant reduction in spasticity in the upper limb after 4 weeks and a significant reduction in TA co-contraction ratio after 2 weeks. A tendency toward a progressive increase was observed in the isometric torque production by elbow and ankle muscles with TENS, although these changes were not statistically different from those of placebo stimulation. However, due to the considerable between-subject variability and small sample size, some of the changes in peak torques or co-contraction ratios might have been

diluted when the effects of TENS versus placebo stimulation was compared. Thus, we extracted those subjects who demonstrated >10% increase in peak torques at either 2 or 4 weeks from both groups. The peak torque parameter was chosen for its high reproducibility even in a small sample (ICC≥0.88, see Chapter 2, **RESULTS**). The number of subjects showing such changes is presented in Table 3.2. Overall, a greater proportion of TENS group showed a measurable increase in peak torques at either 2 or 4 weeks than the placebo group. These subgroups were re-examined statistically. The individual data of these patients in the TENS group are illustrated in Fig. 3.4.

Fig.3.4 illustrates the individual data for the subgroup of patients who received TENS. The majority of subjects (7/9) showed a tendency towards an increase in EF torque, although as a group, a significant improvement was not found. In 4 of these 7 patients, the EF torque at the 2 week follow-up period also tended to be greater than before the stimulation began. In 2 of these 7 subjects, the increase in EF torque was accompanied by a tendency towards a decrease in triceps co-contraction (Table 3.3). On the other hand, TENS produced a significantly higher EE torque after 4 weeks as compared to before stimulation (Friedman's statistic=6.58, $p<0.05$; Fig. 3.4B), although this effect was not maintained 2 weeks after the stimulation ended. In this subgroup of patients, the increase in EE torque was associated with a significant decrease in UE spasticity subscore at 4 weeks as compared to before stimulation ($p=0.04$). Five of 6 subjects who demonstrated an increase in EE torque following TENS also showed a tendency towards a reduction in biceps co-contraction at 2 or 4 weeks which was statistically insignificant (Table 3.3).

At the ankle, 78% of patients showed a strong tendency towards progressive

improvement in DF torque (Friedman's test statistic=5.43, p=0.07; Fig. 3.4C). In 4 of these patients, the measurable increase in DF torque was associated with a decrease in soleus co-contraction ratio after 4 weeks of TENS, but these changes were not significantly different across the 4 testing sessions (Table 3.3). A small increase in PF torque after 4 weeks of TENS was observed in 5 subjects, with the exception of 1 subject who showed a marked improvement after 2 weeks of stimulation with the effect lasting up to the follow-up period. In general, the PF torque was greater at 2 weeks after the stimulation had ended than before. Corresponding TA co-contraction ratio also showed a tendency towards a decrease in all 5 subjects, especially at 2 weeks as compared with the control value (Table 3.3). However, these changes in PF torque or TA co-contraction ratio were not statistically significant.

A tendency towards an increase in peak torques was also observed in subjects who received placebo stimulation, despite such occurrences in an overall smaller proportion of subjects (Table 3.2). Within these subgroups, the increases in peak torques and the decreases in corresponding antagonist co-contraction ratios were not significantly different across the 4 testing sessions. Nonetheless, in one subject, 4 weeks of placebo stimulation produced a 69% improvement in PF torque as compared with the control value. Furthermore, when we compared the subgroups who showed an improvement following TENS with all the subjects who received placebo stimulations, there was no significant difference in peak torques at any of the sessions between these two groups.

The relationship between agonist EMG area and peak torque was examined for each of the 4 muscles separately in these subgroups of patients who received TENS (Fig. 3.5). There was a strong positive linear relationship between each agonist peak EMG activity and

peak torque before TENS, ranging from r=0.87 between soleus EMG and PF torque (p=0.05, in Fig.3.5D) to r=0.98 between biceps EMG and EF torque (p<0.001 in Fig. 3.5A). Because there was no significant reduction in antagonist co-contraction ratio for any of the muscles, even with a significant increase in EE peak torque following 4 weeks of TENS, we wondered if any change in torque was related to changes in relative agonist activity. Pearson's correlation analysis revealed that following 2 and 4 weeks of TENS treatment, biceps and EF torque maintained a significant (p<0.001) and strong linear relationship with r=0.97 and 0.95 respectively (Fig. 3.5A). However, triceps EMG was not significantly related to EE torque at 2 weeks but positively related at 4 weeks (r=0.86, p<0.05) to a slightly lesser extent than before the stimulation (r=0.95, p=0.003). In the ankle, the significant positive relationship between TA EMG and DF torque found before stimulation (r=0.90, p=0.006) was not maintained after TENS (r=0.45, p>0.05 and r=0.68, p>0.05 for 2 and 4 weeks, respectively). Soleus EMG showed no significant relationship to PF torque after 2 weeks, but a stronger correlation after 4 weeks (r=0.95, p=0.01) as compared to before TENS (r=0.87, p=0.05). Thus, it appeared that in some subjects, the relationship between peak EMG activities of triceps and TA and their corresponding torques were altered following 2 or 4 weeks of TENS.

DISCUSSION

Effects of TENS versus Placebo Stimulation on Clinical Spasticity and Voluntary Motor Functions

Our results indicated that 2 and 4 weeks of repeated daily conventional TENS

treatment to the radial nerve in hemiparetic arm produced a significant reduction in upper extremity spasticity subscore at 4 weeks ($p=0.05$, Fig.3.1B), as well as a significant decrease in the TA co-contraction ratio after 2 weeks ($p<0.01$, Fig. 3.3B). Furthermore, in the majority of subjects (55 to 78%), a tendency towards increasing peak torque was observed for all the 4 muscles tested with a significant improvement in EE torque ($p<0.05$, Fig. 3.4B) following 4 weeks of TENS but not placebo stimulation. In Chapter 2, we determined that these parameters were reliable across 2 separate test sessions, with ICC of 0.78 for clinical spasticity score and ICC of 0.99 for the TA co-contraction ratio. Biceps and soleus co-contraction ratios were less reproducible in the small sample of CVA subjects, thus changes in these ratios following 2 and 4 weeks of TENS or placebo stimulation may be due to random variation.

Several possible explanations for the lack of statistical difference between the effects of TENS versus placebo stimulation on the overall MVC parameters may be considered. One likely explanation is the tremendous between-subject variability in these parameters. Because the majority of subjects demonstrated minimal to moderate improvement, most changes could be lost within the between-subject variation. It was also possible that the subjects improved spontaneously with time. However, we recruited only those patients with at least 6 months duration of stroke to ensure that most of the spontaneous recovery had plateaued. Hence, this is not likely to be a major contributing factor. On the other hand, because most subjects had no previous experience with TENS, it may be assumed that sham TENS could produce a real placebo effect.

Because of wide between-subject variability, we examined the subgroups from each

subject group who showed appreciable increase in peak torques from the corresponding control value for each MVC. A criterion of >10% improvement from the control torque values was used for this comparison. We chose the peak torque because it was found to be the most reliable measurement parameter (ICC≥0.88), even in a limited sample size (n=8, see Chapter 2, Table 2.4). Thus, we examined the segmental and heterosegmental effects of TENS and placebo stimulations on peak torques in all the 4 muscles tested across the 4 test sessions in these subgroups of patients.

Segmental Effects of TENS

In 67% of hemiparetic patients, EE torque significantly improved following 4 weeks of TENS as compared to before stimulation (Fig. 3.4B). Such an increase in EE torque was associated with a decrease in upper extremity spasticity subscore for these particular patients at the 4 week period ($p=0.04$). However, this increase in EE torque was not accompanied by a significant decrease in biceps co-contraction. Furthermore, there appeared to be no significant maintenance of EE strength gain or reduction in upper limb spasticity 2 weeks after the stimulation ended. This segmental effect was comparable to the previous finding by Levin and Hui-Chan (1992). In their study, 15 daily TENS applications to the common peroneal nerve on the hemiparetic leg over a 3 week duration produced a significant reduction in the antagonist spasticity and an improvement in dorsiflexing force after only 2 weeeks of stimulation ($p<0.05$), followed by a decrease in DF agonist/antagonist co-contraction after the third week of TENS. It appeared that a similar pattern of segmental effect was observed between the two studies despite the difference in magnitude of the

results. One of the reasons might be the anatomical difference between the two nerves. In the posterior region of the arm, the radial nerve is situated deeper within the triceps muscle and the subcutaneous tissue of the upper arm so that it was more difficult to access transcutaneously. On the contrary, the common peroneal nerve in the lower limb is quite superficial as it descends around the fibular head. Thus, it is possible that the current reaching the nerve through surface electrodes was not as effective in exciting the large diameter fibers in the arm as it was in the lower leg.

Another factor to consider is the functional differences between the two limbs. All the subjects studied were ambulatory to varying degrees, so that it could be assumed that these subjects had to use their lower limb muscles on a regular basis. If any afferent conditioning is initiated in a repetitive manner, one could presume that any regular usage of the affected muscle is likely to provide further proprioceptive inputs (Musa, 1986) and possible maintenance of any improvement in motor functions. On the other hand, a hemiparetic upper limb tend to be left unused, since patient could compensate for its diminished functions by using the unaffected arm. This is especially true where the affected side happens to be the non-dominant side. Indeed, for the subjects in our TENS group, 55% of them were hemiparetic on the non-dominant side (Table 3.1), whereas only 1 of 5 subjects who received placebo stimulation was similarly affected. In the case where the TENS was applied to the non-dominant arm, it may have presented as an isolated treatment unless the patient contientiously exercised that arm or attempted to use it. The extent of regular usage of the affected upper limb was a factor we did not control, although each subject was encouraged to use the arm as much as possible during the experimental protocol. Thus, it

might be that the side affected was a confounding variable in the present study.

Heterosegmental Effects of TENS

In the ankle muscles, there was a tendency towards a progressive increase in DF and PF torques following 2 and 4 weeks of TENS without a significant reduction in the corresponding antagonist co-contraction ratios. Limited evidences are available in the literature for possible non-segmental effects of peripheral nerve stimulation. Walker (1982) used 60 min stimulation twice daily to the wrist for 1 week, and observed a suppression of ankle clonus bilaterally sometimes for up to 2 hours after treatment ended. But the stimulation was applied to the ipsilateral saphenous nerve as well, thus the effects could not be attributed to purely non-segmental mechanisms. In addition, the stimulations were delivered via indwelling electrodes. Thus, it is possible that the effectiveness of the current delivered together with more frequent treatments (ie. twice daily as opposed to once a day in our study) were the operative factors necessary to produce measurable effects at distant sites. Futhermore, our patients were assessed approximately 24 hours post-stimulations on each evaluation sessions. From the literature, the reported time course of lasting effects of TENS, local or remote, have rarely exceeded 2 hours (Walker, 1982; Hui-Chan and Levin, 1993). Hence, it is possible that cumulative effects of TENS may have gradually dissipated by the test day.

Mechanisms Underlying the Modifications in Antagonist Spasticity and Agonist Voluntary Motor Functions Following TENS

One may speculate on the possible underlying mechanisms associated with the changes in clinical spasticity and voluntary motor functions produced by long term afferent conditioning. The fact that UE spasticity subscore was significantly reduced following 4 week of TENS as compared to placebo stimulation could suggest a modulation in the biceps stretch reflex response. That is, repeated stimulation of the radial nerve may have reciprocally inhibited the spastic antagonist muscle. This may be argued on the basis that a significant reduction in antagonist co-contraction was not observed. However, antagonist co-contraction ratio was assessed during isometric contraction in the present study. Had we evaluated isotonic elbow contractions accompanied by passive muscle stretch, perhaps the extent of co-activation could have been altered following TENS.

Our results indicated that the tendency for an increase in peak torque either at the upper or lower extremity was not accompanied by a significant reduction in antagonist co-activation. One may speculate that the modulation in agonist, rather than the antagonist, activation may be the reason for the changes observed in the torque output. The relationship between the peak torque and agonist EMG area after TENS suggested that in both the elbow and ankle muscles, the paretic muscle activation (ie. triceps and TA) might be altered by TENS with respect to the torque produced in some subjects, but not the spastic muscles (biceps and soleus). On the other hand, reduction in co-contraction from other muscles such as brachioradialis, brachialis and gastrocnemius, may have resulted in the increase in torque production. That is, if TENS produces diffuse effects, it is possible that synergist muscles which may also be spastic could be modulated by the afferent conditioning. Since our EMG recordings were limited to one set of agonist and antagonist muscle pairs, contributions from

the neighboring muscles cannot be excluded. As mentioned in Chapter 2, although care was taken to fixate the limb being tested, variation in contraction pattern of each muscle could not be totally eliminated during maximum effort. For example, during isometric EF, the subject might also pronate the forearm to varying degrees, thus resulting in different EMG recruitment pattern despite similar net force. Bourbonnais et al. (1989) reported that in hemiparetic subjects, a marked disturbance in the EMG activities of biceps, triceps and brachioradialis during isometric elbow flexion and extension performed towards various directions orthogonal to the long axis of the forearm was observed on the affected side. Hence, it appears that alteration in agonist recruitment pattern may be present in hemiparesis.

One may query as to the possible mechanism underlying the remote effects of TENS. In our previous study, enhancement in presynaptic inhibition was postulated as one of the segmental mechanisms involved, because increased vibratory inhibition of the soleus H-reflex was observed following 3 weeks of TENS but not placebo stimulation to the comon peroneal nerve in hemiparetic subjects (Levin and Hui-Chan, 1992). Since our findings in the upper limb elbow muscles as a result of repeated long-term TENS application to the radial nerve parallel those found previously in the lower limb ankle muscles, it could be argued that presynaptic inhibitory mechanism may also be responsible for the reduction in spasticity in the upper limb.

With a few individual exceptions, significant carry-over effects at the 2 week follow-up period were not observed in the MVC parameters as a group after 4 weeks of TENS. This is expected especially if patients avoided the use of their affected upper limb. More intense stimulation regime, consisting of more frequent daily stimulations and/or longer treatment

duration, plus appropriate exercise programs may be warranted, in order to produce more lasting effects after the termination of stimulation.

Studying the effects of conditioning on spinal reflexes or voluntary motor functions is not new. Wolpaw has reported evidence of successful modulation of H-reflex through repeated mental conditioning in monkeys (Wolpaw et al., 1994). Thus, it appears that even the predominantly monosynaptic reflex can be modified through intense training over time. It follows, then, that voluntary motor functions, which presumably involve many more synapses, may be more readily modifiable via similar or even afferent conditioning. In fact, in spastic hemiparetic subjects, afferent conditioning via conventional TENS to the common peroneal nerve produced a significant improvement in agonist muscle force after 2 and 3 weeks of stimulation, whereas the soleus H-reflex excitability appeared to be much more resistant to modulation (Levin and Hui-Chan, 1992). Neilson and McCaughey (1982) also demonstrated that involuntary muscle activity at the elbow flexors could be self-regulated through repeated cognitive training in 4 cerebral palsy subjects. However, only 1 of these subjects demonstrated an improvement in performing a tracking task at the elbow following 18 months of training. Thus, it appears that the extent of functional improvement in the upper limb resulting from mental or afferent conditioning is difficult to anticipate.

In conclusion, conventional TENS applied for 4 weeks to the radial nerve has a potential therapeutic value in rehabilitating patients with spastic hemiparesis, in that it could reduce clinical spasticity of the antagonist muscle (biceps) and improve voluntary motor functions of the paretic muscle (triceps) at similar segmental levels, as well as produce minor improvements in motor functions of a remote paretic muscle (TA). With implementation of

sufficient treatment frequency and duration of TENS, we believe that further amelioration of spasticity and enhancement in voluntary motor functions could be possible, in both the affected upper and lower limbs.

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Table 3.1. Demographic profile of CVA subjects

Subject	Age (yrs)	Gender	Hand dominance	Side of hemiparesis	Diagnosis	Spasticity score	Duration of stroke (mos)
TENS group							
1(ms)	76	M	L	dominant	R CVA	21	45
2(dk)	57	F	R	dominant	L CVA	15	79
3(js)	73	M	R	non-dominant	R CVA	18	6
4(gd)	48	F	R	non-dominant	R CVA	26	74
5(dl)	48	F	R	dominant	L CVA	23	16
6(rr)	58	F	R	non-dominant	R CVA	22	76
7(gr)	37	M	R	non-dominant	R CVA	24	17
8(lb)	72	M	R	non-dominant	R CVA	20	38
9(sl)	66	M	R	dominant	L CVA	23	34
Median	**58**					**22**	**38**
Placebo group							
10(gw)	50	F	R	dominant	L CVA	17	59
11(hl)	73	M	R	dominant	L CVA	21	40
12(rr)	58	F	R	non-dominant	R CVA	22	72
13(il)	39	M	R	dominant	L CVA	21	23
14(wg)	58	M	R	dominant	L CVA	28	64
Median	**58**					**21**	**59**

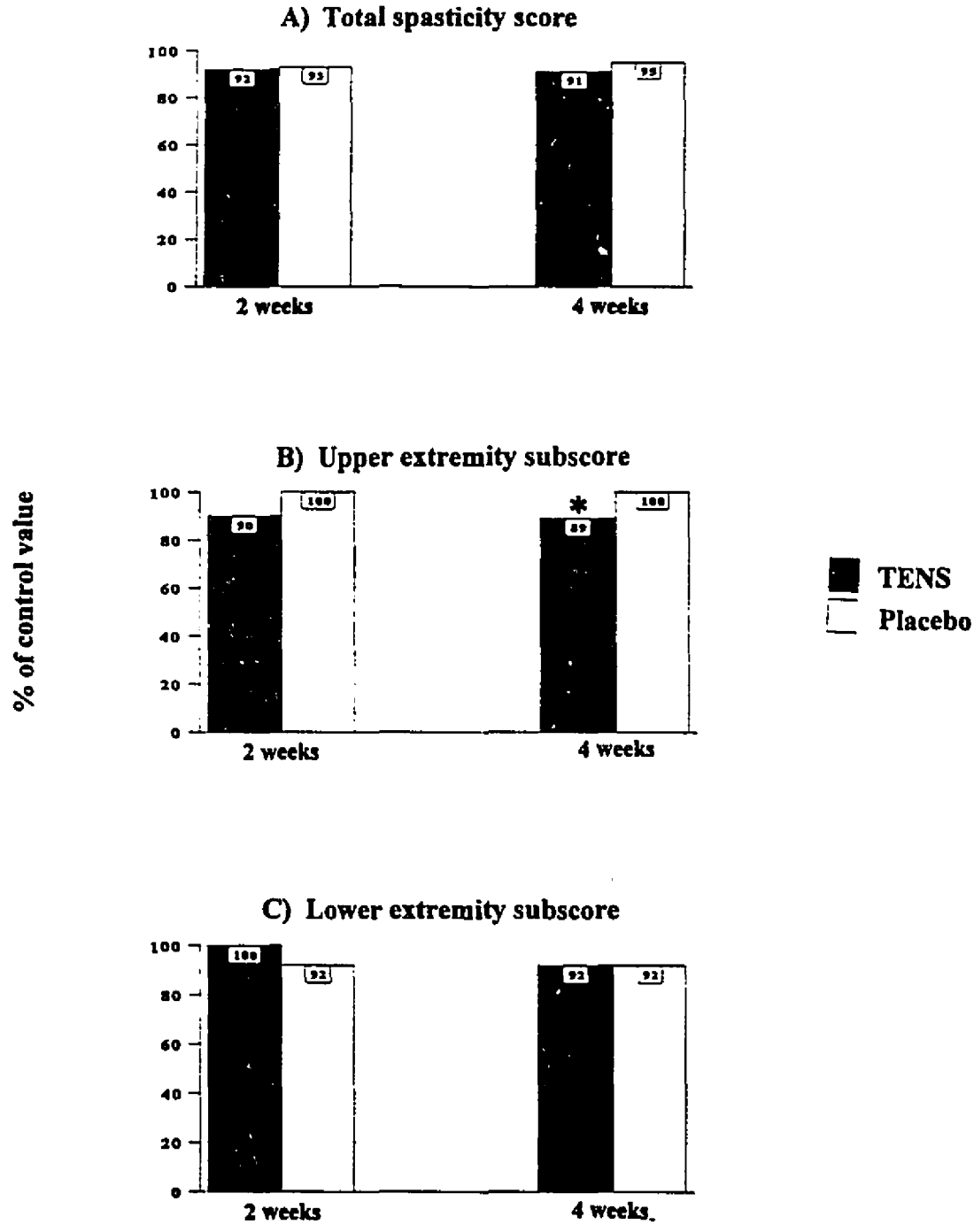

Fig.3.1. Changes in clinical spasticity scores following *2* and *4 weeks* of stimulation. Values are normalized to each subject's control score recorded in the first session. Each histogram represents the group median value. *: p=0.05

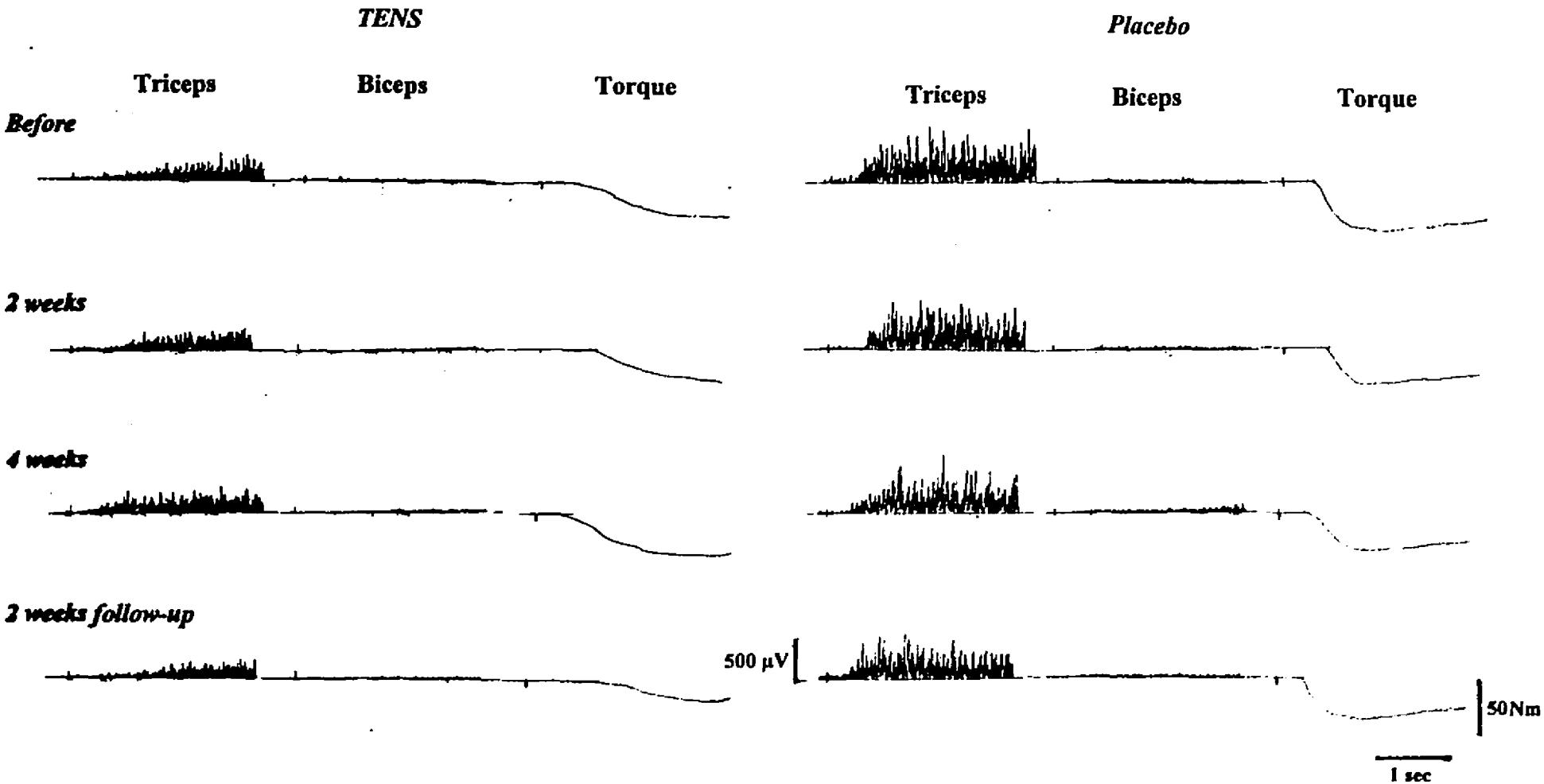

Fig. 3.2. Examples of averaged MVC trials for elbow extension *before*, *during 2* and *4 weeks* and *after 2 weeks follow-up* of stimulations for a different subject from the TENS (left traces) and placebo group (right traces).

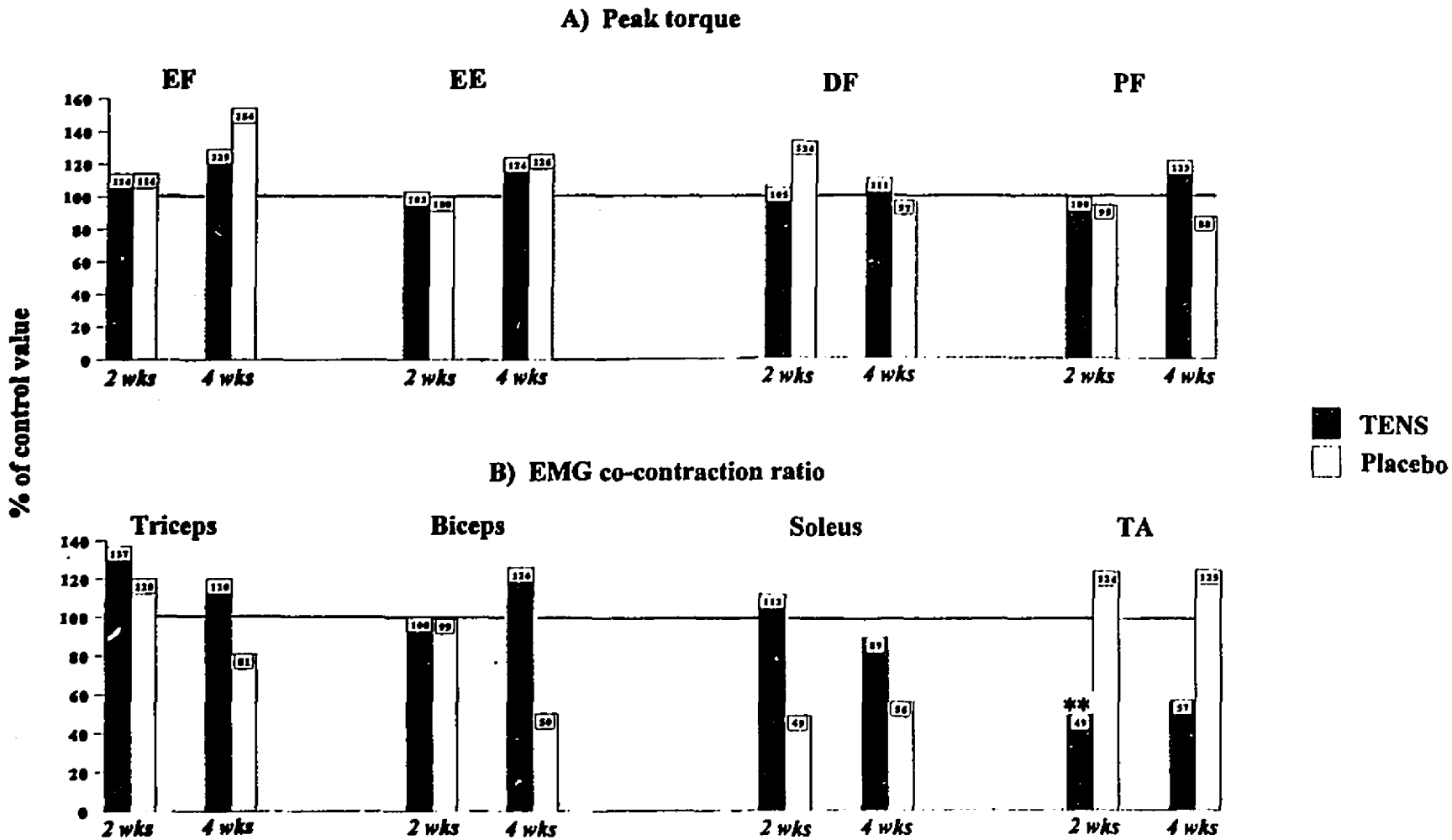

Fig. 3.3. Changes in peak torque and EMG co-contraction ratio following *2* and *4 weeks* of stimulation. Values are normalized to each subject's control value recorded in the first session. Each histogram represents the group median value. **: $p<0.01$

Table 3.2. Number of subjects showing measurable increases in peak torques

	TENS (n=9)	*Placebo* (n=5)
Elbow flexion	7 (78%)	3 (60%)
Elbow extension	6 (67%)	2 (40%)
Dorsiflexion	7(78%)	4 (80%)
Plantarflexion	5 (55%)	1 (20%)

Note: A criterion of **>10%** improvement from the control value was used to define 'measurable increase' in peak torques for each subject.

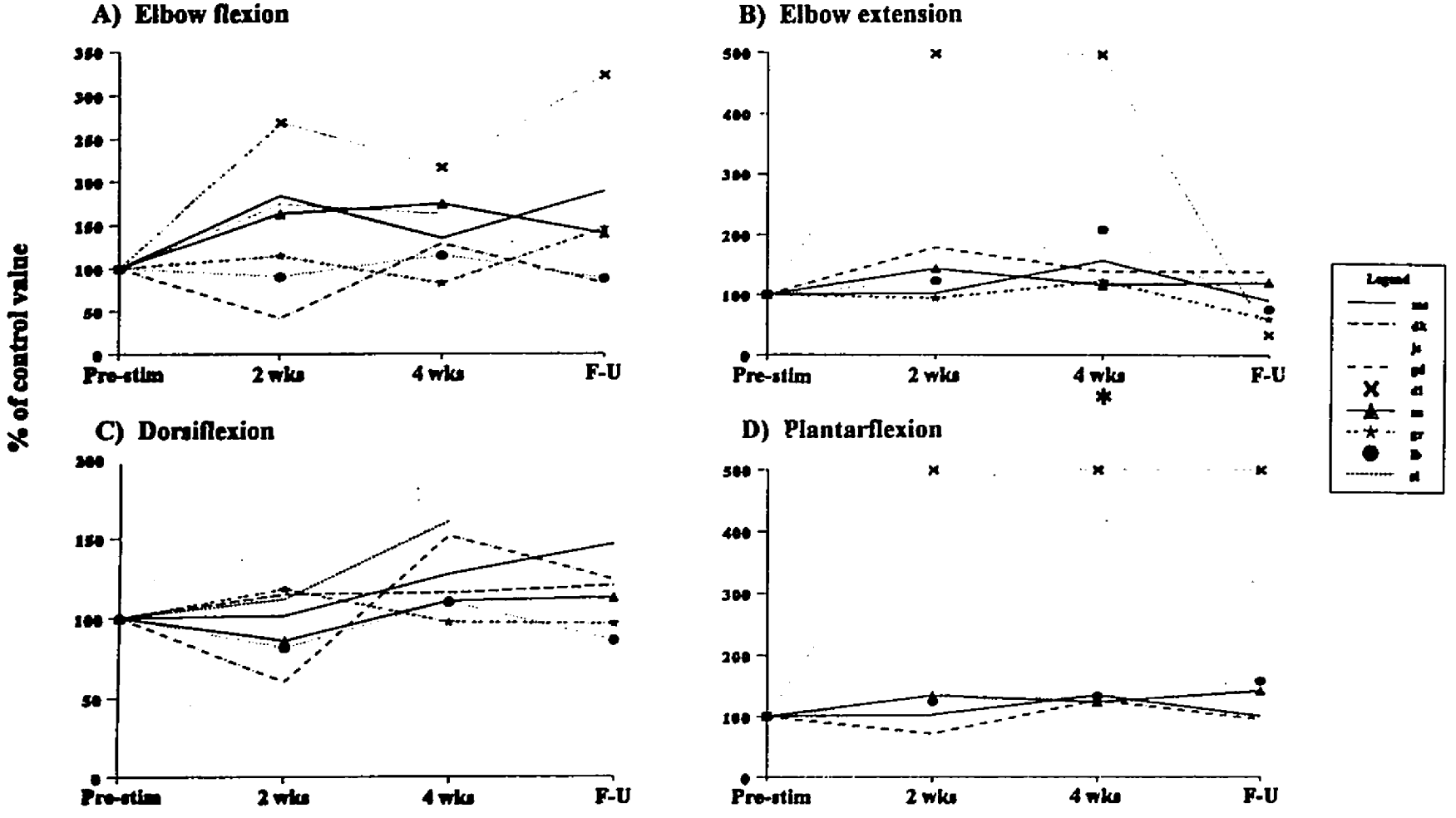

Fig. 3.4. Individual data for subjects who demonstrated a tendency towards increasing peak torque following either 2 or 4 weeks of TENS. Each point represents the mean of 3 MVC trials normalized to each subject's own control value. *: $p<0.05$

Table 3.3. EMG co-contraction ratios in % of control values (*before TENS*) of the subjects who showed a measurable increase in the peak torques recorded respectively in EF, EE, DF and PF after 2 or 4 weeks of TENS.

	Before TENS	*2 weeks*	*4 weeks*	*F-U*	*p value*
Triceps	100	41	62	56	n.s.
Biceps	100	88	85	71	n.s.
Soleus	100	112	62	236	p=0.06
TA	100	44	49	56	n.s.

Note: Group median values are presented. n.s.=p>0.05 for Friedman's statistic.

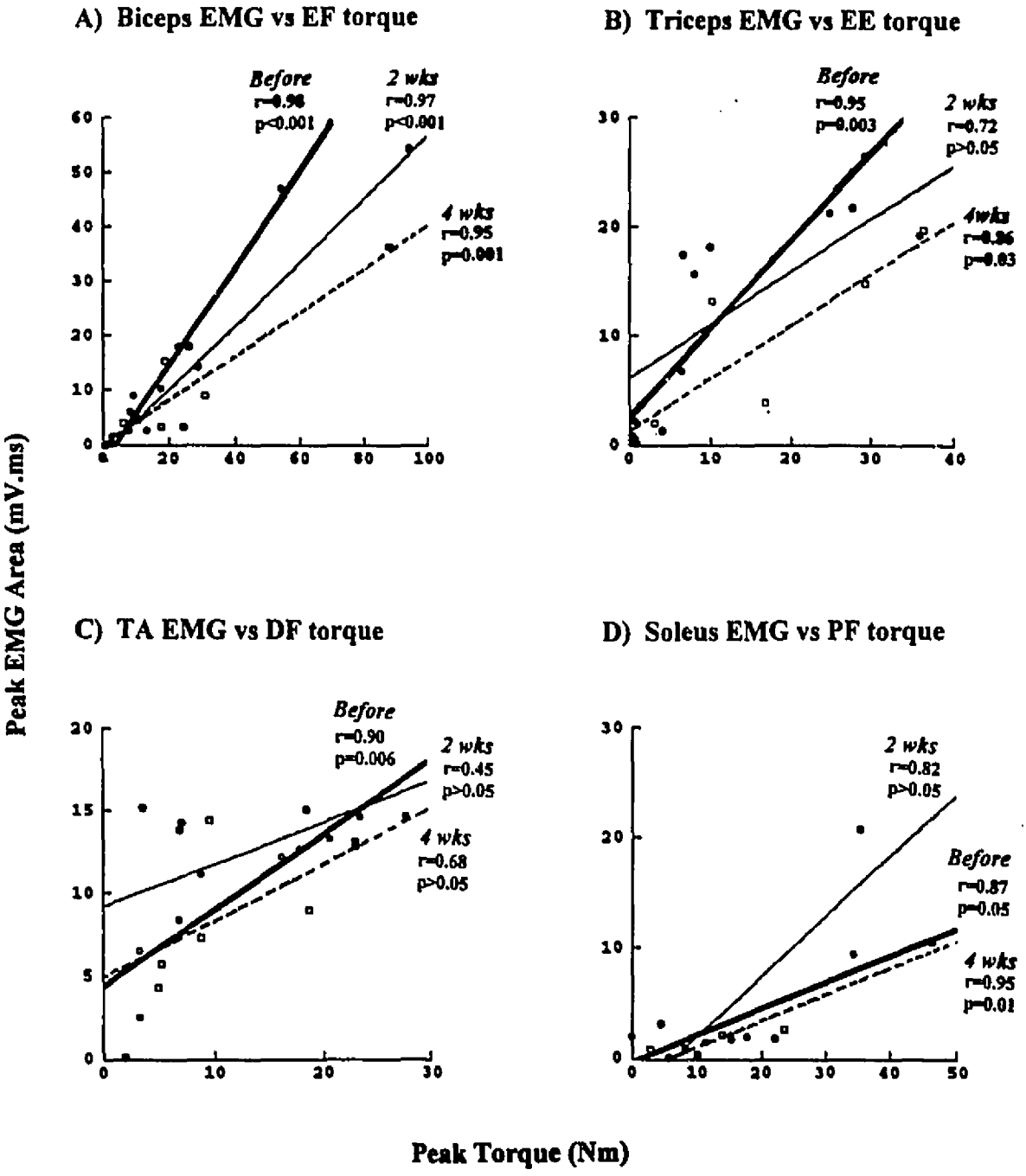

Fig. 3.5. Correlation between peak EMG area (*y-axis*) and peak torque (*x-axis*) during MVC in the subgroups of subjects who demonstrated measurable increases in peak torques. Each data point represents the mean of 3 MVC trials for each subject. ▬ before TENS; — following 2 weeks of TENS; - - - following 4 weeks of TENS.

Chapter 4. Summary and Conclusion

Previous studies in our laboratory demonstrated that a single session of 45 min of conventional TENS applied segmentally and heterosegmentally repeatedly to the peroneal and median nerve, increased soleus H- and stretch reflex latencies in the majority of spastic hemiparetic subjects for more than 60 min after the stimulation ended (Hui-Chan and Levin, 1993). Furthermore, we showed that repeated applications of 60 min of TENS to the common peroneal nerve for 3 weeks (15 sessions) reduced clinical spasticity and stretch reflex excitability in the spastic soleus muscle, as well as improved voluntary dorsiflexion force and decreased EMG agonist/antagonist co-contraction ratio during isometric ankle dorsiflexion in standing (Levin and Hui-Chan, 1992). Thus, we conducted two experiments to study the alterations in voluntary motor functions in spastic hemiparetic upper and lower limb muscles, their relationship to clinical spasticity and the reproducibility of these measures, as well as to investigate the segmental and possible heterosegmental effects of repeated TENS on spasticity and voluntary motor functions in hemiparetic subjects.

In our *first experiment*, the objective was to study the characteristics of voluntary motor functions in the agonist/antagonist muscle pairs of spastic hemiparetic upper and lower extremities and their relationship to clinical severity of spasticity in hemiparetic subjects. We compared the torque and EMG activities of the flexors and extensors of elbow and ankle joints in 8 spastic subjects with those of 6 normal controls. To the best of our knowledge, similar investigation has not yet been carried out in both limbs of the same patients. The main findings are as follows:

1) CVA subjects produced significantly smaller peak torques during both elbow and ankle MVCs ($p \leq 0.01$), with the group median torques ranging from 13.2 to 19.5 Nm

as compared to 34.2 to 76.6 Nm for normal subjects in the 4 muscles tested.

2) CVA subjects demonstrated tendencies toward a longer half-rise time to peak torque and a greater antagonist co-contraction ratio for all the muscles tested.

3) Of interest is that the elbow flexion torque in the CVA subjects was inversely related to the total spasticity score (r=-0.70) and to the upper extremity subscore (r=-0.82).

4) For both groups, the peak torque was the most reproducible MVC parameter (ICC=0.86 to 0.99). Moreover, the composite clinical spasticity score also demonstrated high reliability between sessions (ICC=0.78).

These results indicated that the spastic hemiparetic subjects could be distinguished from the normals with respect to their significantly lower peak torque production. The degree of weakness in their spastic elbow flexors was the strongest indicator of the severity of their spasticity. Of all the parameters examined, peak torques, MVC peak agonist EMG areas and clinical spasticity scores were found to be very reliable measurement tools for evaluating treatment efficacy over time.

The aim of the *second study* was to evaluate the local as well as possible remote effects of repeated daily 60 min applications of TENS to the radial nerve on the affected side for 4 weeks (20 sessions) in the hemiparetic subjects. Specifically, the changes in clinical spasticity and voluntary motor functions of the flexors and extensors of elbow and ankle joints were evaluated *before*, *during* 2 and 4 weeks, and at 2 weeks *after* TENS or placebo stimulations had ended. The main findings are:

1) In contrast to placebo stimulation, 4 weeks of TENS produced significant reduction in the upper extremity clinical spasticity subscore (p=0.05).

2) Two weeks of TENS resulted in a significant decrease in TA antagonist co-contraction ratio (48.6% of control value for the TENS versus 123.8% of control value for the placebo group, $p<0.01$).

3) In the majority (67%) of subjects who received TENS, the upper extremity spasticity score decreased significantly after 4 weeks of, as compared to before, stmulation ($p=0.04$). This was accompanied by an improvement in elbow extension torque ($p<0.05$).

The above findings indicated that repeated TENS applied to the radial nerve produced a significant reduction in the antagonist (biceps) spasticity accompanied by a mild improvement in the paretic agonist (triceps) muscle strength. The improvement in voluntary motor functions may be attributed to possible modulation of the agonist activity rather than a change in antagonist co-contraction.

In conclusion, repeated TENS to the nerve innervating the paretic muscle in hemiparetic subjects could reduce clinical spasticity in the antagonist and improve the motor functions in the agonist muscle. The segmental effects of such afferent stimulation seem to be stronger than the non-segmental effects. The time course of the observed changes (over a period of weeks) may suggest possible plastic changes within the nervous system. Further studies will investigate the influence of more frequent and longer period of stimulation, probably in conjunction with active training of the affected limbs, so as to maximize the effects of long-term afferent conditioning.

APPENDIX I

SCHOOL OF PHYSICAL AND OCCUPATIONAL THERAPY
McGILL UNIVERSITY

INFORMED CONSENT FORM

I, the undersigned, _____ agree to participate in the research project conducted by Yu Kyung Kim under the supervision of Dr. Christina Hui-Chan and entitled:

The segmental and heterosegmental effects of repetitive transcutaneous electrical nerve stimulation in spastic hemiparetic subjects

I have been satisfactorily informed as to the nature of my participation in this project which is briefly described below:

I am aware that I will be assigned to one of two treatment groups in a random order. Group 1 will receive moderate electrical stimulation to the arm for an hour a day for four weeks. Group 2 will receive faint stimulation to the arm for the same duration.

This study will evaluate the reflex responses in and my ability to voluntarily contract my elbow and ankle muscles. The evaluations will be done before, at two and four weeks after treatment commences, and at two week follow-up after the treatment ends. These sessions may last up to three hours. During these sessions, surface electrodes will be attached to the skin overlying my arm and ankle muscles. Electrical stimulation will be applied to the arm and the lower leg. Except for a brief moment when the maximal response is recorded, the electrical stimulation is not painful. My ankle then my elbow joint will be passively extended. There is little danger of risk associated with these techniques, which have been used in neurological evaluations.

I understand that no information which could influence my decision to participate in this study has been withheld from me. Any questions that I have concerning the study will be answered in person or over the phone by Dr. Hui-Chan at 398-4524.

For the duration of the project, I give my permission for Yu Kyung Kim or Dr. Hui-Chan to consult my medical chart, if the need should arise.

I understand that this treatment will in no way interfere with any treatment I may be currently receiving, that my anonymity will be fully respected, that I may withdraw from the study at any time, and that the study has been approved by the Ethics Committee of McGill University.

_____ _____

Signature of subject Signature of investigator

_____

Date

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