Treatment of upper limb paresis by transcutaneous electrical nerve stimulation and task-related training during chronic stroke

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2008

CERTIFICATE OF ORIGINALITY

The idea of the present investigation originated from Professor Christina W.Y. Hui-Chan, the design of the study and the planning of the experiment result from discussions between the author and Professor Christina W.Y. Hui-Chan.

All experiments in the present investigations were completed solely by the author.

The author declares that the work presented in this thesis is, to the best of the author's knowledge and belief, original, except as acknowledged in the thesis, and the material has not been submitted previously, either in whole or in part, for a degree at this University.

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August 2008

ABSTRACT

This thesis consists of 2 inter-related studies. The objectives of **study 1** were (1) to delineate the characteristics of spasticity, associated reactions, muscle strength, reaction time, and functional performance of the paretic upper limb in patients with chronic stroke, (2) to determine the extent to which they differed from normal subjects, and (3) to delineate the relationships among quantitative variables and clinical assessments of the motor deficits in the paretic UL. The global aim of the main study (**study 2**) was to examine the effectiveness of a program combining TENS with task-related training (TRT) in promoting motor recovery in the upper extremity of patients with chronic stroke.

Ninety-eight stroke survivors participated in **study 1**. Twenty normal subjects also participated. The quantitative measures included maximum isometric voluntary contraction (MIVC) force of elbow flexors, extensors and hand grip of the affected arm, EMG co-contraction ratios during MIVC of elbow flexors and extensors, associated reactions in the paretic elbow muscles recorded as IEMG during non-paretic hand grip, and reaction time of the paretic wrist in extension and flexion. The clinical assessments included Composite Spasticity Index (CSI), Associated Reaction Rating Score (ARRS), and Wolf Motor Functional Test (WMFT).

In the clinical CSI, ARRS and WFMT tests, the intraclass correlation coefficients (ICCs) were very high, with 0.978 for CSI, 0.912 for ARRS, and 0.987 for functional ability and 0.872 for time score of the WFMT, and *P* values <0.001 for all. The quantitative variables including MIVC force, IEMG and RTs also showed relatively high ICCs ranging from 0.802 to 0.928. The ICCs for MIVC of the elbow extensors and flexors and for hand grip force ranged from 0.804 to 0.863. The ICCs for the IEMG ranged from 0.802 to 0.928. The reaction time for wrist flexion and extension in patients with stroke ranged from 0.863 to 0.883. These results all had *P* values <0.001.

Our findings showed that the affected UL in patients with stroke produced significantly smaller force during MIVC of elbow flexors, extensors and hand grip than those of their non-affected UL and of normal subjects ($P<0.01$). There were no significant differences in the co-contraction ratio of maximum isometric voluntary

(MIV) elbow flexion and extension among the affected and unaffected sides of the stroke survivors, and the normal subjects. When the stroke survivors performed a maximum grip using their non-paretic hand, associated reaction was manifested as elbow flexion (62.2 %), elbow extension (27.6%), or no elbow movement (11.2 %) in the paretic arm. Reaction time (RT) of wrist flexion and extension in the stroke survivors' affected hands were significantly longer than that in the normal subjects and their unaffected hands (P<0.01 for both).

Statistically significant correlations were found between MIVC force recorded during elbow flexion in the affected arm and ARRS (negatively; ρ=-0.321, P=0.001), and WMFT functional ability (ρ=0.380, P<0.001) and time score (negatively; ρ=-0.389, P<0.001). MIVC force recorded during elbow extension in the affected arm was found to produce similar results. It correlated with ARRS (negatively; ρ=-0.291, P=0.004), and with WMFT functional ability (ρ=0.277, P=0.006) and time score (negatively;

ρ=-0.302, P=0.002). Maximum hand grip force in the affected arm correlated moderately with CSI (negatively; ρ= -0.425, P<0.001), ARRS (negatively; ρ=-0.430, P<0.001), and with WMFT functional ability (ρ=0.658, P<0.001) and time score (negatively; ρ=-0.630, P<0.001).

There were no significant associations between the co-contraction ratios during MIV elbow flexion and the CSI, ARRS, and WMFT results. However, the co-contraction ratio during MIV elbow extension correlated moderately but significantly with CSI (ρ=0.227, P<0.05), ARRS (ρ=0.377, P<0.001), and with WMFT functional ability (negatively; ρ=-0.358, P<0.001) and time score (ρ=0.360, P<0.001).

Moderate but statistically significant correlations were also found between the paretic biceps IEMG recorded as an index of associated reaction during non-paretic hand grip and CSI (ρ= 0.418, P<0.001), ARRS (ρ=0.557, P<0.001), and with WMFT functional ability (negatively; ρ=-0.561, P<0.001) and time score (ρ=0.559, P<0.001). Although the paretic triceps IEMG recorded as an index of associated reaction during non-paretic hand grip correlated marginally with CSI (ρ=0.199, P=0.05); like the biceps IEMG, it correlated moderately with ARRS (ρ=0.371, P=0.001), and with

WMFT functional ability (negatively; ρ=-0.378, P<0.001) and time score (ρ=0.403, P<0.001).

The wrist flexion RT correlated moderately with CSI (ρ=0.412, P<0.001) and ARRS (ρ=0.341, P<0.001), and with WMFT functional ability (negatively; ρ=-0.531, P<0.001) and time score (ρ=0.504, P<0.001). Similarly the wrist extension RT correlated moderately with CSI (ρ=0.429, P<0.001), ARRS (ρ=0.374, P<0.001), and with WMFT functional ability (negatively; ρ=-0.531, P<0.001) and time score (ρ=0.486, P<0.001).

In summary, our findings from **study 1** showed that all the quantitative measures and clinical assessments were reliable, with ICCs ranging from 0.802 to 0.987. Moreover, MIVC force of the affected elbow flexors, extensors and hand grip in patients with chronic stroke was significantly smaller, and RT of their wrist flexion and extension was significantly longer than those of their non-affected UL and of normal subjects. During non-affected hand grip, associated reaction was mainly manifested as elbow flexion (62.2%) in the paretic UL. These 3 quantitative parameters were further found to be correlated moderately but significantly with the clinical scales of CSI (except for MIVC force of elbow flexors and extensors), ARRS, and WMFT functional ability and time scores, in either a positive or negative manner. These findings suggest that both quantitative and clinical assessments could serve as reliable and valid assessment tools to measure treatment effectiveness in patients with stroke over time in study 2.

The research design of **study 2** was a randomized, controlled trial involving 77 subjects being randomly allocated to 4 groups. One group received TENS alone (n=20), another p-TENS + TRT (n=20), a third received TENS + TRT (n=18), and there was also a control group which received no active treatment (n=19). Outcome measures were recorded in the paretic arm as follows: (1) the composite spasticity index (CSI), (2) maximum isometric voluntary contraction (MIVC) force of elbow flexors and extensors, and hand grip, (3) reaction times (RT) of wrist flexion and extension, and (4) functional ability and time scores of the Wolf Motor Function Test (WMFT). Assessments were carried out before treatment on day 1 (baseline

assessment), at week 4 (mid-way through the treatment), at the end of the 8-week treatment program, and at follow-up 4 weeks after treatment ended.

Significant differences between groups were found in time domains but not muscle change strength in the UL. After 8 weeks of treatment, the TENS+TRT group showed a significantly greater percentage decrease in the reaction time of wrist flexion (-16.8%) when compared with the TENS group (22.5%, $P<0.05$) and the control group (26.5%, $P<0.05$), and the p-TENS+TRT group had a significantly greater percentage decrease in the reaction time of wrist extension (-12.1%) when compared with the TENS group (19.3%, $P<0.05\%$). However, at follow-up 4 weeks after treatment ended, only the TENS+TRT group had a significantly greater percentage decrease in wrist flexion RT (-11.6%) when compared with the control group (31.1%, $P<0.05$), and of wrist extension RT (-11.5%) when compared with the TENS group (26.5%, $P<0.05$). With regard to WMFT, the 2 groups receiving TRT (i.e. p-TENS+TRT and TENS+TRT) showed a significant percentage decrease of the WMFT time when compared with the control group after 8 weeks of treatment.

In conclusion, our findings from **study 2** showed that the 2 groups receiving TRT had significantly faster RT for either wrist flexion or extension, and faster WMFT time scores after 8 weeks of intervention. In the TENS+TRT group, the percentage decrease of wrist flexion RT compared with the control group and of wrist extension RT compared with the TENS group can even be carried over to the follow-up at week 12. The faster RT and motor functional performance plus the presence of carry over effects in the combined treatment group suggest that combing TRT with TENS would be superior to TENS alone, or no active treatment in patients with chronic stroke.

Publications arising from the thesis:

毕胜 Christina Hui- Chan. Wolf 运动功能测试量表的标准效度和评定者内部信度研究. 中国康复医学杂志, Chinese Journal of Rehabilitation Medicine. Vol. 21, No.12 pp1084-1086 (2006)

毕胜 许云影. 偏瘫上肢联合反应分级量表内部一致性与信度研究, 中国康复医学杂志, Chinese Journal of Rehabilitation Medicine. Vol. 22, No.7 pp626-627 (2007)

Bi Sheng, MD. Christina W Y Hui-Chan, PhD. Treatment of Upper Limb Paresis by Transcutaneous Electrical Nerve Stimulation and Task-related Training during Chronic Stroke A Randomized Placebo-Controlled Trial ACRM-ASNR Washington, DC 3 - 7 October 2007.

ACKNOWLEDGEMENTS

I wish to thank the many people without whom this study would not have been possible.

First, I gratefully acknowledge the instruction of my chief supervisor, Christina W.Y. Hui-Chan, Chair Professor of the Department of Rehabilitation Sciences. She helped me greatly with her scientific advices, continuous guidance and high standards in research. Under her guidance, I not only learned logical thinking and logical writing, but also really came to understand that the most important thing in research is to obtain original findings, the soul of scientific progress. After receiving her training in scientific research, I am confident that I am able to transform myself from a clinician to a rehabilitation scientist. Her instructions go beyond my PhD study and will undoubtedly benefit the rest of my career.

I appreciate all the patients who participated in this work. I could not have completed the thesis without their kindness and patience during the whole process of the research.

I gratefully thank Professor Chetwyn Chan who is the Chair of the department of Rehabilitation Sciences and Professor Gabriel Ng, the Chair of the Doctoral Research Committee for their support throughout my studies.

I also would like to express my sincere gratitude to the following persons for their contributions to my studies. Thanks for Dr. Shamay Ng, Dr. William Tsang, Dr. Margaret Mak, Dr. Stephanie Au-Yeung and Dr. Amy Fu for sharing their knowledge and experience with me. Thanks also go to the research therapists for their contributions to the study, and to Mr. Peggo Lam and Mr. Raymond Chung who provided me with their professional advice on statistical analyses.

Finally, I express my deepest gratitude to my wife and my daughter for their encouragement and support during my studies in Hong Kong.

This project was supported by a grant from the Hong Kong Polytechnic University to Prof. Christina W.Y. Hui-Chan and a studentship to me.

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LIST OF ABBREBIATION

ANOVA	analyzed of variance
ARRS	Associated Reaction Rating Score
CIMT	constraint-induced movement therapy
CNS	central nervous system
CSI	Composite Spasticity Index
ICC	intraclass correlation coefficient
IEMG	integrated EMG
$IEMG_{AS}$	IEMG of associated reaction
LL	lower limb
LOCF	last observation carried forward
M1	primary motor cortex
MVC	maximum voluntary contraction
MIV	maximum isometric voluntary
MIVC	maximum isometric voluntary contraction
MT	movement time
p-TENS	placebo-TENS
RT	reaction time
S1	primary sensory cortex
S2	secondary sensory cortex
SMA	supplementary motor area
SPSS	Statistical Package for Social Sciences
TENS	transcutaneous electrical nerve stimulation
TMS	transcranial magnetic stimulation
TRT	task-related training
UL	upper limb
UMN	upper motor neuron

WMFT Wolf Motor Function Test

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CHAPTER 1

INTRODUCTION

1.1 Introduction to stroke

1.1.1 Definition and categories

Stroke is defined as a focal abnormality of brain function caused by altered cerebral circulation that lasts longer than 24 hours. When neurological signs or symptoms last for less than 24 hours, the event is defined as a "transient ischemic attack." Strokes are categorized as either ischemic (caused by blockage of blood flow) or hemorrhagic in origin (caused by rupture of a cerebral vessel). Ischemic strokes are further divided into thrombotic – due to thrombus developed at the site of blockage, or embolic – due to thrombus developed proximally then travelling downstream to the site of the blockage.

1.1.2 Incidence

In the United States, more than 700,000 people suffered from stroke each year, with a prevalence of approximately 3 per million (Broderick et al. 1998). It is the third leading cause of mortality, accounting for 150,000 deaths per year. There are 3 millions stroke survivors with varying degrees of neurological impairments, making it the most common cause of disability requiring rehabilitation (Prescott 1994). It has been estimated that the cost of acute and chronic stroke care, plus the loss of income, amount to 30 billion dollars per year (Matchar et al. 1994). In Hong Kong, there were more than 26,000 hospital admissions with a diagnosis of stroke in 2002 (Hospital Authority 2004). The mortality rate of cerebro-vascular disease was 33.2 per 100,000 of population, and it was ranked as the third highest cause of death (Hospital Authority 2004). In China, according to an epidemiological study of cerebraovascular disease carried out in 1986, the prevalence and incidence were respectively 159.9/100,000 and 115.6/100,000 (Li 1998).

1.2 Motor deficits after stroke

The most common motor deficit following stroke is hemiparesis, affecting >80% of acute subjects and >40% of chronic subjects (Gresham et al. 1995). In the past, the motor problems resulting from lesions of the central nervous system (CNS) were categorized as either positive or negative. Positive impairments included abnormal postures, increased stretch reflexes and spasticity, and increased cutaneous reflexes. Negative impairments included those that represented a loss of pre-existing function, such as loss of muscle strength and dexterity. Furthermore, because the impairments caused by brain damage take some time to resolve, secondary impairments such as contracture could arise as adaptations to the primary impairments.

1.2.1 Spasticity

Spasticity is one of the features of upper motor neuron (UMN) syndromes, together with hyperactive tendon reflexes, clonus and flexor spasms. Lance (1980) defined spasticity as “a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes (muscle tone) with exaggerated tendon jerk.” He reiterated this definition later by adding that “spasticity does not include impaired voluntary movement and an abnormal posture.” (Lance 1990). A key factor of spasticity is thus a velocity-dependent increase in resistance of a muscle to passive stretch. Spasticity results from injury to decending pathways from the brain which leads to loss of descending inhibitory input. Loss of descending inhibitory input from the brain can cause abnormal reflexes, including overactivity of the alpha motor neuron pool, overactivity of (Group Ia) spindle and flexor reflex afferents, alteration of synaptic activity and reduction of presynaptic Ia inhibition (Brown 1994, Mayer 1997).

Spasticity is a well-recognized complication of upper motor neuron injury. A few studies have investigated the prevalence of spasticity after stroke. In a systematically

identified cohort of patients who had been admitted to hospital, the prevalence of spasticity at 12 months after stroke was found to be 38% by Watkin et al. (2002). Another study showed that spasticity was present in only 19% of the patients earlier after stroke at 3 months, and was more frequently found in upper than lower extremities (Smomerfeld et al. 2004). Contralateral to the site of brain lesion, a gradual increase in the magnitude of the stretch reflex to imposed displacement occurs. One year after stroke, stretch reflex amplitude was found to reach a level significantly larger than that of normal subjects (Thilmann & Fellows 1991). Another study showed that tonic spasticity was particularly noticeable at 6 months after stroke (Ju et al. 2000). For example, patients with stroke frequently develop flexor spasticity of the upper limb. Spastic posture and contracture of the affected limb could be disabling, as they may impair motor function when patients need to reach or manipulate objects with their affected hand and arm.

Using a targeted meta-analytic approach, Francis et al. (2004) demonstrated that reducing spasticity in the arm was associated with a significant improvement in arm function. Spasticity thus seems to contribute to motor impairments and activity limitations and may be a severe problem for some patients after stroke (Smomerfeld et al. 2004). The Drawing Test, a quantitative index of upper limb movement ability, was found to be correlated highly with the Ashworth Scale in patients with stroke (Eder et al. 2005). But raising the hemiparetic arm to reach a target while extending the elbow seem to reflect a problem in motor control rather than spasticity alone (Zackowski et al. 2004).

Therefore, there is still no agreement on the role of spasticity in the reduction of motor function following stroke. Because activation of the stretch reflex is velocity-dependent, spasticity could limit a patient's ability to move quickly. Excessive co-activation of the antagonist muscle has been described as "antagonist restraint"

(Bobath 1990, Davies 1985) or “spastic restraint” (Knutsson & Richards 1979). However, a number of studies showed that one primary cause for disorders of motor control following a CNS lesion is inadequate recruitment of agonist motor neurons, not just increased activity in the antagonist (Bohannon & Andrews 1990, Tang & Rymer 1981). Thus paresis of movement, abnormality of reciprocal inhibition of agonist and antagonist, and abnormal muscle synergies may contribute more to deficits of motor control than simple spasticity alone (Katz & Rymer 1989).

1.2.2 Muscle weakness

Muscle strength is described as the ability to generate sufficient tension in a muscle for the purposes of posture and movement (Smidt & Rogers 1982). It is determined by the musculoskeletal properties of the muscle itself in addition to the neural activation of that muscle. Weakness is defined as a lack of ability to generate normal levels of force. It is a major impairment of motor function in many stroke patients. Paralysis or paresis of movement is partly the result of decreased voluntary motor unit recruitment, an inability to recruit sufficient skeletal motor units to generate intended muscle torque or movement (Gracies 2005). Paresis is caused by a lesion within descending motor pathways, which hinders the central excitatory drive to motor units. Hemiplegia (or hemiparesis) is weakness affecting one side of the body, which is most commonly found in patients with stroke (Shumway-Cook & Woollacott 2007).

In recent years, muscle strength has been extensively examined in patients with stroke. The initial thinking was that strengthening exercises could exacerbate any tendency for increased muscle tone. Therefore, most muscle groups were not examined (Eng et al. 2002, Greson et al. 2000, Hsu et al.2002, Pohl et al. 2000). A number of studies have shown that stroke patients were weak during isometric contraction (Andrews and Bohannon 2000, 2003, Canning et al. 1999, Chae et al.2002, Levin et al.

2000, Newham and Hsiao 2001). Distal muscles seemed to be more affected than proximal ones (Frascarelli et al. 1998), and flexors more than extensors (Andrews and Bohannon 2000). The muscle weakness found soon after stroke suggested that it was not caused by inactivity alone (Andrews and Bohannon 2000, 2003, Newham and Hsiao 2001). Harris et al. (2001) also found reduced force being generated by externally stimulated quadriceps in the first week after stroke. Their results suggested that at least some of the muscle weakness was a direct (and rather long-lasting) consequence of brain lesion. Furthermore, muscles weakness was also found on the "non-paretic' side very soon after stroke (Hsaio & Newham 1999). The number of motor units recruited is one of the main determining factors in the power developed by a muscle (Gracies 2005). Reduced descending drive was thought to cause a failure to recruit higher threshold motor units, and to reduce the ability to modulate or increase motor unit discharge rate when patients tried to increase their voluntary force output (Gracies 2005).

1.2.3 Muscle co-contraction

Co-contraction (co-activation) is defined as the simultaneous activity of agonist and antagonist muscles crossing the same joint, and involves opposing muscles contracting at the same time to increase the stiffness of a joint (Damiano 1993). A number of conflicting results have been reported in studies investigating isometric co-activation of the affected muscles after stroke. Co-contraction in stroke patients has been reported by some investigators to be similar to rather than different from the controls (Davies et al. 1996, Fellows et al.1994, Gowland et al. 1992, Newham & Hsiao 2001, Tang & Rymer 1981). However, using EMG methods, other investigator have found that upper limb muscles were more affected by excessive co-contraction of agonists and antagonists in patients with stroke than in normal subjects (Kamper &

Rymer 2001). Furthermore, the degree of co-contraction was shown to be significantly correlated with motor impairment and physical disability in the affected upper limb (Chae 2002). Nevertheless, it should be noted that co-contraction is not a necessary result of impairment of motor function, because healthy individuals could show co-contraction during the early stages of learning (Shumway-Cook & Woollacott 2007).

1.2.4 Associated reactions

Walshe (1923) defined associated reaction as released postural reactions deprived of voluntary control on the affected body part, triggered by the voluntary effort exerted by patients on the non-affected body part. Associated reaction was found in 80% of a group of stroke patients in conjunction with yawning, coughing, and sneezing and in functional activities that required some efforts (Mulley 1982). It was thought to accompany spasticity throughout the affected muscles, especially in the paretic upper extremity, where it appeared in a typical flexor pattern (Bobath 1990, Hastings 1965). Lazarus (1992) hypothesized that associated reactions in patients with hemiplegia resulted from a loss of supraspinal inhibitory mechanisms that normally suppress the coupling of intralimb and interlimb movements. There were significant differences in the onset of biceps EMG activity and in the elbow flexion angle between the affected side and non-affected side of stroke and of control subjects during single-leg stance (Dickstein et al. 1995). EMG levels in the hemiparetic subjects were significantly higher in the affected upper limb (UL) muscles during contralateral non-affected hand grips than during ankle exertions (Boissy et al. 2001). A direct relationship was found between levels of effort induced in the non-paretic forearm and the associated reactions elicited in the paretic forearm of post-stroke patients (Dvir et al. 1996). With increasing grip force of the non-affected hand, substantial increases of shoulder flexion and

internal rotation and elbow flexion torques were found in the affected upper limb of subjects with severe stroke (Boissy et al.1997). However, associated reaction was not confined to patients with severe spasticity; they can be present in people with minimal spasticity (Bhakta et al.2001). Another study showed that associated reactions were not necessarily associated with contracture (Ada & Q'Dwyer 2001).

1.2.5 Reaction time and movement time

Timing problems in patients with stroke include abnormal reaction time and abnormal movement time. Reaction time is defined as the time between the patient's decision to move or the onset of an external response signal and the initiation of the movement itself. It could be modified by neuromuscular and cognitive factors. Neuromuscular factors that affect reaction time include inadequate and/or decreased rate of force generation, insufficient range of motion, and abnormal postural control (Shumway-Cook & Woollacott 2007). Movement time is the time from movement initiation to movement completion. Patients with hemiparesis following stroke demonstrated longer movement times (Levin 1996).

1.2.6 Loss of dexterity

Loss of dexterity refers to a loss of the coordination of various voluntary muscle activities to meet environmental demands and is not restricted to manual dexterity alone. It is difficult to measure loss of dexterity because measures of dexterity (which are typically measures of muscle function) are usually confounded by muscle weakness, since patients need to have a prerequisite amount of muscle strength to perform the test. However, Ada et al. (1996) showed that upper limb (UL) dexterity and muscle strength were not correlated (Ada et al. 1996). Canning et al. (2000) investigated the muscle activation characteristics associated with loss of dexterity after stroke, and found that

low dexterity performance was characterized by abnormal muscle activation to reach movement target.

1.3 Physiotherapeutic management of stroke

Rehabilitation approaches appeared to be more effective in promoting functional recovery in the lower limb than in the upper limb (Basmajian 1989). However, upper limb function was found to be important for independent living and self-esteem (Balliet et al.1986, Granger et al.1989).

Following a cerebrovascular accident, spontaneous recovery of upper limb motor function is generally thought to be limited to the first six months (Bard & Hisschberg 1965, Parker et al. 1986). During this period, rehabilitation approaches such as EMG biofeedback (Basmajian et al. 1982, Ince et al. 1987), and positional feedback with electrical stimulation (Bowman et al. 1979) promoted motor recovery beyond that achieved by conventional therapy such as neurofacilitatory physical therapy (Basmajian et al.1987). For the purpose of this thesis study, the following physiotherapeutic approaches will be highlighted.

1.3.1 Electrical stimulation for management of spasticity

Effect of electrical stimulation on spasticity has been investigated in a case study on 4 subjects by Levine et al (1952) who showed that stimulating muscle antagonistic to the spastic muscle resulted in relaxation of the spastic muscle. Transcutaneous electrical nerve stimulation (TENS) produced a significant reduction in elbow flexor spasticity and a significant improvement in elbow extension torque after 4 weeks of application (Kim 1994). Low levels of cutaneous electrical stimulation over the biceps muscle for a period of 10 minutes produced significant reduction in spasticity of the

flexors and extensors of the elbow in hemiparetic patients with stroke (Dewald et al. 1996).

Electrophysioligic measurements of H-reflex and stretch reflex latencies in the form of transcutaneous electrical nerve stimulation (TENS) over the common personal nerve on the affected low leg were made before and after 3 weeks of daily stimulation (Levin & Hui-Chan 1992, 1993) These studies suggested that stretch reflex latencies and vibratory inhibition of H-reflex were increased after applying TENS at 5 times a week for 3 weeks. Other studies have even demonstrated the effects of electrical stimulation on stretch reflex (Stefanovska et al. 1988) and reflex torque (Dewald 1996) in paretic patients with stroke. A short-term attenuation of the stretch reflex was also found while stimulating the antagonistic muscle groups in the lower extremity (Apkarian & Naumann 1991). Short-term post-stimulation inhibitory effects could be produced on hyperactive stretch reflex activity in spasticity of cerebral origin, when TENS was applied peripherally to the sural nerve (Potisk et al.1995). However, TENS failed to produce significant effects on H-reflex amplitude in spinal spasticity, but there was a significant decrease in the Achilles tendon reflex and Modified Ashworth Scale (Goulet et al. 1996).

Some mechanical measurements to quantify alterations in spasticity following electrical stimulation were carried out (Bajd et al. 1985, Robinson et al.1988, Vodovnik et al. 1987). There were changes in the torque output immediately following stimulation over the antagonistic muscle, compared with the pre-stimulation torque output in response to slow ramp perturbations of the affected elbow in hemiparetic patients (Given & Dewald 1991). It was postulated that the mechanism underlying spasticity-reducing effects by electrical stimulation could involve modification of synaptic circuitry (Hugenholtz et al. 1988).

1.3.2 Electrical stimulation for rehabilitation of upper limbs

One of the treatment techniques used to enhance upper limb function in patients with chronic stroke involves electrical stimulation. Afferent feedback cues from electrically stimulated movements of the affected limb was thought to be effective because appropriate afferent pathways from joint and muscle receptors of the affected limbs are activated. The first study on a device that electrically stimulated a target muscle when triggered by amplified-low voluntary EMG signals from that muscle, hereby termed “EMG-stim”, reported improvement in the range of motion of the wrist joint (Van 1979). Fields et al. (1987) also reported an improvement in the ROM and in extensor EMG activity of the wrist in patients with chronic stroke receiving EMG-stim as part of an intensive physical therapy programme. Another study by George et al. (1992) reported that certain rehabilitation techniques improved function of the arm and hand in patients with chronic hemiplegia. Briefly, subjects receiving proprioceptive neuromuscular facilitation training improved their Fugl-Meyer scores by 18%. Those receiving low-intensity electrical stimulation of wrist extensors combined with voluntary contractions improved their score by 25%. However, those receiving EMG-stim improved by 42%. When combining such an active neuromuscular stimulation (EMG-stim) with repetitive training, motor capabilities of the affected muscles were found to be also improved in patients with stroke (Cauraugh and Kim 2003). However, since none of the studies used randomized controlled trials to directly compare the various treatment methods, there is no concrete evidence that EMG-stim is indeed more effective than non EMG-stim approaches. Another type of electrical stimulation is predominantly sensory electrical stimulation. In subjects with chronic stroke, mesh-glove stimulation administrated to the patients daily was found to improve voluntary wrist extension movement (Dimitrijevic et al. 1996).

1.3.3 Acupuncture and stroke rehabilitation

Acupuncture has been suggested to be a promising treatment for stroke rehabilitation. However, the effectiveness of acupuncture has not been proved unequivocally, and the mechanisms underlying the use of acupuncture for stroke rehabilitation are not well understood. To examine the effectiveness of acupuncture in patients with stroke, a number of studies had used meta-analysis to systematically review randomized controlled trials of acupuncture as a treatment approach for stroke rehabilitation (Park et al. 2001, Sze et al. 2002, Wu et al. 2006). Park et al. (2001) reviewed 9 randomized controlled trials involing 538 patients with stroke. Six studies showed promising results, and 3 yielded negative outcomes. However, the only 2 studies reaching the standard of best methodological trials demonstrated no significant effect of acupuncture on patients with stroke. Sze et al. (2002) summarized 14 trials with a total sample size of 1,213 patients. The results of this meta-analysis indicated that acupuncture had no supplementary effect on motor recovery, but had a slightly positive effect on the disability of patients with stroke. However, it may be a result of a true placebo effect. Wu et al. (2006) reviewed 5 randomized controlled trials (368 patients). Four studies indicated that the odds of an increase in global neurological deficits in the acupuncture group were higher than that in the control group. However, due to substantial heterogeneity of the study population, this claim may not be valid. Only 1 study demonstrated that improvement of motor function was insignificant between the real acupuncture group and the sham acupuncture group. Therefore, the benefits of acupuncture on patients with sub-acute or chronic stroke have yet to be proven.

Though there are no obvious effects of acupuncture on motor recovery, several studies have shown positive effects on spasticity, one type of motor impairments after stroke. For example, Moon et al. (2003) carried out a study to compare the

effectiveness of electro-acupuncture and of moxibustion on the spasticity caused by stroke. Spasticity in the electro-acupuncture group was significantly reduced when compared with that of the moxibustion and control groups, 1 and 3 hours after treatment of 20 min, and even on the 5th day after acupuncture and thereafter. This study indicated that electro-acupuncture can temporarily reduce spasticity, and that it can maintain the reduction in spasticity if applied repeatedly. Another study showed that 40 minutes of electro-acupuncture followed by 30 minutes of strengthening exercises twice a week for 6 weeks significantly reduced spasticity, as measured by averaged speed-dependent stretch reflex torque and Modified Ashworth Scale scores in the wrist joint (Mukherjee et al. 2007).

1.3.4 Task-related training: theory and principle

According to Horak (1991), task-related training (task-oriented training) is a contemporary approach which assumes that the CNS is hierarchically organized. Following CNS damage, patients make an effort to compensate for the damage so as to achieve functional performance. In other words, the goal of recovery from CNS damage is to realize functional performance. Because of uniqueness in personal characteristics and in performance contexts, there could be variations in the sequence of recovery from CNS damage. Personal characteristics of patients including psychological, sensorimotor and cognitive attributes interact with their performance contexts such as physical, socio-cultural and economic factors to call for different behavioural changes (Mathiowetz & Haugen 1994). A solution to appropriate training is that the essential elements within each task in a given environment context must be fully comprehended. Therefore, a therapist should provide various levels of difficulty during task-related training that are based on personal characteristics and performance

contexts, coupled with motor learning strategies such as behavioural shaping techniques to promote skill development (O'Sullivan & Schmitz 2007).

On conducting task-related training, a therapist needs to consider the patient's past history, health status, age and experience, so as to design appropriate, interesting and stimulating activities. The principles of task-related training are: (1) Tasks to be selected are important to the patients for independent function. (2) Tasks possess potentials for patient achievement based on their abilities and level of recovery. (3) Repetitive and extensive practices are provided to patients; and the practice of variable behaviours to facilitate adaptation is encouraged. (4) Samples of task performance are presented to guide the patient to successfully carry out initial movements. (5) Supervised and unsupervised practices are used; feedback and reward are given when patients obtain small improvements in task performance. (6) Finally, hands-on therapy is minimized by emphasizing the role of the therapist as a training coach (O'sullivan & Schmitz 2007).

1.3.4.1 Task-related training in stroke rehabilitation of upper limbs

Task-related training (TRT) was thought to provide optimal control strategies for alleviating patients' motor problems (Gentile 2000). Some studies, for example, Winstein et al. (2004) showed that task-related training was more effective than other conventional therapies for patients with acute stroke. Physiotherapy treatment using motor relearning with task-oriented training was thought to be preferable to the Bobath approach in the rehabilitation of acute stroke (Langhammer and Stanghelle 2000). Additional task-related training of upper limb or mobility tasks was found to improve the functional outcome during in-patient stroke rehabilitation (Blennerhassett and Dite 2004).

Beneficial training effects of task-related practice have been noted for the subset of stroke survivors who have some voluntary control of the wrist and hand (Duncan et al. 2003). More affected subjects with chronic stroke seemed to benefit the most from TRT (Thielman et al. 2004). One trial randomized patients within 1 month of a stroke to receive up to 5 months of home-based therapy with an occupational therapist or no therapy. The outcomes measures recorded by blinded assessors revealed significant gains made by the group who received home-based therapy. Instrumental ADLs were clearly better and patients' handicap decreased (Walker et al. 1999). A well-defined approach for patients with mild residual hemiparesis in the affected UL, known as Arm Ability Training, employs practice in activities such as aiming, tapping, writing, turning over coins, tracking through a maze, picking up bolts, and placing small and large objects (Platz et al. 2001). The results showed that the AAT group was significantly faster in performing a series of functional outcome tasks for the upper extremity than the conventional therapy group and the benefits even persisted a year later. Constraint-induced movement therapy for 2 weeks was also found to be beneficial to patients with chronic stroke in performing most daily tasks (Taub 2000, Wolf et al.2007). This is a form of intensive TRT for patients who have at least modest motor function of the upper extremity.

In sum, various TRT forms of in the UL has been found to improve functional outcome or daily task performance of the affected UL, but it appears to require prolonged period of intensive treatment.

1.4 Possible underlying mechanisms

1.4.1 Brain plasticity after stroke

Stroke recovery in the first few days may be due to resolution of edema or reperfusion of the ischemic penumbra. Much of the recovery after the initial 2 weeks

can probably be attributed to brain plasticity, with some areas of the brain taking over the functions previously performed by the damaged regions. Brain plasticity refers to the brain's ability to undergo neurochemical and/or structural change resulting in functional improvement of the affected body parts. Furthermore, it can be altered by the environment or by training. Three proposed mechanisms of recovery have been investigated in animal and human studies.

The first mechanism is sprouting of collateral fibers from the surviving neurons with formation of new synapses (Ivanco et al. 2000). The second mechanism is unmasking of previously existing but functionally inactive pathways (Aizawa et al. 1991, Jenkins & Merzenich 1987, Nudo et al. 1996). The third mechanism is redundancy of brain circuitry with parallel pathways performing similar functions in such a way that an alternative pathway may replace the one that has been damaged (Frost et al. 2003, Weiller et al. 1992, 1993). These will be discussed in greater details below.

The initial change of brain plasticity is neurochemical. It has been suggested that modification of the synaptic strength of horizontal connections was one mechanism that mediates functional changes in the cerebral cortex. The occurrence of long-term potentiation and long-term depression in the rat hippocampus or cerebral cortex was the most broadly researched model for exploring synaptic mechanisms underlying learning and memory (Hess & Donoghue 1996). LTP is one of the most likely neuronal mechanisms by which synapses and groups of neurons encode new information for a new movement skill. It develops from repeated associated inputs projecting to the neurons in the motor cortex, called Hebbian synaptic learning (Edeline 1999). The concept of Hebbian learning is an important one in providing a framework for analyzing interactions between neural and behavioural levels. Two neurons or groups of neurons that have been disconnected by a lesion may become reconnected if they are

repeatedly activated at the same time. Recent results by Ivanco et al. (2000) showed that altered dendrite morphology and increased spine density correlated with LTP induction in the neocortex.

Structural alteration in the brain follows in due course. Several studies have examined brain reorganization after small lesions of primary motor cortex (M1) or the primary sensory cortex (S1). For example, following small infarcts of S1 in owl monkeys, the skin surface formerly represented by the infarcted zone became represented topographically in the surrounding cortical region (Jenkins & Merzenich 1987). However, the movement formerly represented in the infracted zone did not reappear in the adjacent cortical regions in monkeys not receiving post-infarct training. In addition, the areas adjacent to the infracted cortical area which previously represented the digit were further reduced (Nudo & Milliken 1996). In contrast, after monkeys received rehabilitative training following the infarct, the cortical region had a preserved hand territory, and in some cases, the hand territory even expanded to the elbow and shoulder representation areas (Nudo et al. 1996). These findings demonstrated that functional recovery after small cortical infarct may be related to the adjacent intact cortical area taking over the function of the damaged cortex. Though a few monkeys could recover their functions without post-infarct training, it is assumed that lost functions by the adjacent undamaged motor cortex are to some extent use-dependent. Other cortical or subcortical motor areas may also contribute to functional recovery. For example, after a focal lesion of the primary motor cortex (M1), pre-movement activity in the supplementary motor area (SMA) reappeared to replace the function of M1. Neurons in the SMA were usually active before limb movement, but such pre-movement activity was no longer observed after the movement was over-learned (Aizawa et al. 1991). Movement became more difficult after M1 lesion, leading to reappearance of SMA activity. According to Frost et al. (2003),

reorganization of more remote cortical areas could occur following cortical injury. Findings from neuroanatomical tract tracer methods suggested that M1 injury results in axonal sprouting near the ischemic injury and in establishment of novel connections in a more distant target.

Human studies showed that motor recovery may be mediated by the use of alternative cortical areas. The role of alternative motor pathways in functional recovery received support from PET studies in patients with good recovery from striatocapuslar infarcts (Weiller et al. 1992, 1993). The adjacent cortex can also take over the function of the damaged pathways. For example, in patients with lesions limited to the posterior limb of the internal capsule, recovered hand movement was found to be associated with motor cortical activation that extended laterally to the face area, suggesting that hand representation shifted toward the face area (Weiller et al. 1993). PET studies showed increased activation of the contralateral sensorimotor area with finger movement in patients with subcortical infarct when compared to that of normal subjects (Wassermann 1995). This finding suggested that the undamaged sensorimotor cortical area could even compensate for the damaged subcortical area.

To conclude, animal and human studies showed that plastic changes occurred spontaneously in the brain after brain injuries. Neurochemical changes appear first in the form of LTP, and are followed by structural changes in the brain such that adjacent or more distant brain areas will take over the function of the damaged cortical areas to underpin certain spontaneous recovery of the affected body part (UL) in a use-dependant manner.

1.4.2 Brain plasticity and training

In recent years, studies using neuroimaging methods revealed that training of the affected arm promoted more plastic changes in the brain. Nelles et al. (2001) used serial

positron PET to study training-induced brain plasticity after severe hemiparetic stroke. Before treatment, all stroke patients revealed bilateral activation of the inferior parietal cortex. After treatment, the training group revealed relatively more activation bilaterally in IPC and premotor areas, and in the contralateral sensorimotor cortex. In other words, task-oriented arm training induced functional reorganization in cortical areas both bilaterally and contralaterally. Johansen-Berg et al. (2002) showed that therapy-related improvement of hand function was associated with increases in fMRI activity after 2 weeks of home-based therapy with progressive training for the affected limb plus restraint of the unaffected limb in patients with stroke. fMRI activity was found in the premotor cortex and secondary somatosensory cortex contralateral to the affected hand, and in the superior posterior regions of the cerebellar hemispheres bilaterally. These results indicate that successful motor rehabilitation could cause activity changes in the brain both bilaterally and contralaterally. Jang et al. (2004) investigated the effect of task-oriented training on the cortical activation pattern in 6 hemiparetic patients with chronic stroke. Functional status of the affected hand and fMRI were assessed before and after the training program. The main cortical activation changes accompanying functional recovery were an increase in the affected primary sensorimotor cortical activities and a decrease in the unaffected primary sensorimotor cortical activities.

The effect of constraint-induced movement therapy (CIMT) has also been investigated extensively. In 2001, Levy et al. examined the neural correlates of recovery with fMRI in 2 subjects treated with CIMT. Before treatment, subject 1 showed fMRI activity of scattered regions in the posterior parietal and occipital cortices ipsilateral to the affected hand. Subject 2 demonstrated that there were almost no areas of significant fMRI activity. Following CIMT training, subject 1 demonstrated fMRI activity bordering the lesion, in the primary motor cortex ipsilateral to the affected hand, and in the association motor cortices bilaterally. Subject 2 demonstrated fMRI activity

near the lesion site. These results showed that CIMT caused substantial functional improvement in the upper limb as well as cortical reorganization. In another study, Schaechter et al. (2002) used fMRI to examine brain activation after CIMT. Pre-intervention fMRI revealed a lower laterality index (LI) during affected hand movements in patients with stroke when compared to that of controls, due to a trend towards increased ipsilateral motor cortical activation. Motor function testing showed that patients made significant gains in functional use of the affected upper extremity and significant reductions in motor impairment immediately after CIMT. These effects persisted even at 6-month follow-up.

In sum, neuroimaging methods in patients with stroke showed that intensive TRT or CIMT of the affected UL promoted functional recovery of the UL, as well as greater reorganization of the adjacent and undamaged cortical areas ipsilaterally, contralaterally and/or bilaterally.

1.4.3 Brain plasticity consequent to electrical stimulation

It has been suggested that peripherally applied electrical stimulation may have a direct effect on the excitability of cortical (Golaszewski et al. 1999, Han et al.2003) and subcortical brain centers (Spiegel et al. 1999). Conventional transcutaneous electrical nerve stimulation (TENS) at low intensity and high frequency has been shown by Levin and Hui-Chan (1992) to excite large sensory and motor fibers. Recent fMRI studies have demonstrated that electrical stimulation or proprioceptive input activated M1 and S1 areas (Alary et al. 1998, Spiegel et al. 1999, Weiller et al. 1996). When electrical stimuli were delivered unilaterally to the median nerve and to the tibial nerve, activation was observed by fMRI in the post-central gyrus, the posterior parietal cortex, and the mesial pre-frontal region contralaterally, and in the supratemporal region bilaterally (Del Gratta et al. 2000). These findings implied that electrical stimulation

may have an important role in stimulating (largely but not exclusively) contralateral cortical (sensory) areas to promote recovery of motor function. For example, when TENS was combined with task-related training, it was found to be more effective than TENS alone in improving patients' lower limb muscle strength and walking performance (Ng & Hui-Chan, 2007).

Furthermore, a dose-response relationship between peripheral nerve stimulation and activation of selected brain regions, such as the primary motor cortex (M1), the primary sensory cortex (S1), the secondary sensory cortex (S2), and the cingulate gyrus have also been shown (Backes et al. 2000, Davis et al. 1995, Smith et al. 2003). In patients with stroke, repetitive movements produced by electrical stimulation were found to be effective in producing increased primary sensory cortical activity even ipsilaterally (Kimberley et al. 2004).

Afferent input, produced by electrical stimulation of peripheral nerve, reduced the level of intracortical inhibition (Ridding & Rothwell 1999), and this reduced inhibition was thought to be directly responsible for the changed motor map (Jacobs & Donoghue 1991). Indeed, prolonged stimulation of afferent nerves in humans had been shown to increase the excitability of the motor cortex and the size of cortical maps of muscle representation (Mckay et al. 2002, Ridding et al. 2000). This nerve stimulation, when paired with transcranial magnetic stimulation (TMS) of the motor cortex and repeated over successive days, can cause such changes to persist for several days even after cessation of stimulation (Mckay et al. 2002). Khaslavskaia et al. (2002) also showed that electrical stimulation of the common peroneal nerve for 30 min led to an increase the motor evoked potentials elicited by TMS in the tibialis antenior muscle.

The frequency of nerve stimulation also affected brain excitability in that prolonged depression of corticospinal excitability was caused by low frequency stimulation and prolonged facilitation of corticospinal excitability was caused by high frequency

stimulation (Pitcher et al. 2003). TENS to the forearm muscles can lead to transient reciprocal inhibitory and facilitatory changes in the corticomotoneuronal excitability of forearm flexor and extensor muscles lasting several minutes (Tinazzi et al. 2005). In other words, TENS could regulate impairment of the excitatory and inhibitory balance between agonist and antagonist.

The review above suggested that transcutaneous electrical nerve stimulation could augment agonist muscle activation, probably by increasing cortical motor neuronal excitability as well as the size of cortical representation of the affected side through stimulation-induced sensory (and motor) input.

1. 5 Rationale and objectives of the study

1.5.1 Rationale

Stroke is an upper motor neuron (UMN) syndrome which is divided into positive and negative features. Positive features are characterized by muscle overactivity, either excessive muscle contraction or some sort of abnormal muscle activity, including spasticity, clonus, increased tendon reflexes and abnormal muscle co-contraction… etc. Some abnormal features could contribute to motor dysfunction. Negative features of the UMN syndrome are characterized by a reduction in motor activity. This can cause muscle weakness, loss of dexterity and easy fatigueability. It is also associated with disability. Though some studies have investigated certain characteristics of these abnormalities (Boissy et al.1997, 1998, 2000), possible relationships among these characteristics have not been explored (Boissy et al.1997, 1998, 2000). Furthermore, these studies examined only a small sample of subjects which put the validity of their findings to question.

Previous studies from our research group showed that transcutaneous electrical nerve stimulation (TENS) decreased ankle spasticity and significantly improved the

voluntary dorsoflexing force in patients with chronic stroke (Levin and Hui-Chan 1993). Furthermore, when TENS was combined with task-related training, it was found to be more effective than TENS alone in improving patients' lower limb muscle strength and walking performance (Ng and Hui-Chan 2007). Based on these findings, we hypothesize that combining TENS with TRT of the upper limb would also promote greater motor recovery of the upper limb than either treatment (TENS or TRT) being administrated alone to patients with chronic stroke. Therefore, the main aim of our research was to investigate the effectiveness of a novel rehabilitation program which combined transcutaneous electrical nerve stimulation with task-related training to promote motor recovery in the upper extremity of patients with chronic stroke.

1.5.2 Objectives

Global objective

To characterize the motor disorders and to investigate the effectiveness of a novel rehabilitation program which combined transcutaneous electrical nerve stimulation (TENS) with task-related training to promote motor recovery in the upper extremity of patients with chronic stroke.

Specific aims

(1) To delineate the characteristics of spasticity, associated reactions, muscle strength, reaction time, and functional performance of the paretic upper limb in patients with chronic stroke, and to determine the extent to which they different from normal subjects similar in age, gender, height and weight. Did any relationships exist among these variables?

(2) To compare the effectiveness of combining TENS with task-related training versus either treatment alone or no active treatment (control) on the motor recovery of the paretic upper extremity in patients with chronic stroke.

CHAPTER 2

METHODOLOGY

Summary

This thesis consists of 2 studies to address the 2 specific aims outlined in the last chapter: In **study 1**, 98 patients with stroke and 20 healthy normal subjects meeting a set of inclusion-exclusion criteria were recruited. Five sets of variables were measured in the non-affected side and affected side of patients and the dominant side of normal subjects: (1) Abnormal muscle tone by Composite Spasticity Index (CSI) and associated reaction by Associated Reaction Rating Score (ARRS), (2) EMG co-contraction ratios and force of maximum isometric voluntary contraction (MIVC) of elbow flexors and extensors of paretic UL, and maximum voluntary grip force of paretic hand (3) Integrated EMG of the affected biceps and triceps during maximum voluntary non-affected hand grip as a measure of associated reaction ($IEMG_{AS}$), (4) reaction time (RT) of wrist extension and flexion, and (5) Wolf Motor Function Test (WMFT).

A number of statistical methods in the Statistical Package for Social Sciences (SPSS) version 14.0 were utilized to analyze the results. To test the reproducibility of measurement protocols, the mean score of each outcome measure between days were analyzed. Correlations among relevant measurements were examined by computing Pearson correlation coefficients or Spearmman correlation coefficients, depending on whether the data tested displayed normal distribution or non-normal distribution, respectively.

In **study 2**, a double-blind, randomized, placebo-controlled design was carried out. Seventy-seven patients with stroke meeting carefully selected inclusion-exclusion criteria were recruited. The sample size, as calculated by using “Java applets for power and sample size” software, was actually 64 in total. In anticipation of drop-out, 77 patients were examined. All subjects were randomly allocated to 4 groups: (1) TENS, (2) placebo-TENS plus task-related training (p-TENS+TRT), (1) TENS +TRT,

and (4) control without active treatment. Patients received treatment daily, at 5 days a week, for 8 weeks. The following 4 outcome measures of study 2 included: (1) Composite Spasticity Index, (2) MIVC of elbow flexors and extensors and of paretic hand grip, (3) reaction time of paretic wrist flexion and extension, and (4) Wolf Motor Function Test.

Outcome measurements of CSI, MIVC of elbow flexors and extensors and of paretic hand grip, RT of wrist flexion and extension, and WMFT were analyzed with repeated measure of variance (ANOVA) to compare the main effects. The between-subject factor was the 4 subjects groups. The within-subject factor was the 4 assessment intervals. One-way ANOVA followed by multiple comparisons (post-hoc tests) was used to compare treatment effects among the 4 groups. Taking into consideration, patients' drop-out factor, the intention-to-treat analysis was conducted. The significant level was set at 5%.

Our preliminary study examined the intra-rater reliability in 10 patients with stroke. High test-restest repeatability was found for the CSI, ARRS and the WMFT scores on different days. The ICCs for the CSI between days were 0.978 (P<0.001)., The ICCs for the ARR scores were 0.912 (P<0.001). The ICCs for the Wolf test were 0.987 for functional ability and 0.872 for time (P<0.001). The ICCs for MIVC of the elbow extensors and flexors and of hand grip ranged from 0.804 to 0.863 (P<0.01). The ICCs for IEMG measures of the affected biceps and triceps during MIVC of elbow flexors and extensors and during maximum voluntary grip of the non-affected hand as a measure of associated reaction ranged from 0.802 to 0.928 (P<0.01). The ICCs for RT of wrist flexion and extension in the stroke patients ranged from 0.863 to 0.883 (P<0.01). All the data in our study demonstrated good to very good intra-rater reliability.

2.1 Study 1: Motor impairments of the upper limbs following stroke and inter-relationships among motor parameters

2.1.1 Subjects

Inclusion criteria

The inclusion criteria were:

(1) age between 45-75 years old;

(2) at least 12 months after a unilateral stroke;

(3) ability to follow simple instructions;

(4) some volitional control of the paretic arm, having at least grade 2 strength of the paretic shoulder, elbow and wrist, and ability to flex the fingers a little on the affected side ;

(5) having been discharged from all rehabilitation services at least 1 month before the treatment program commenced.

Exclusion criteria

The exclusion criteria were:

(1) having a brain lesion located in either the brain stem or cerebellum;

(2) symptomatic cardiac failure or unstable angina, uncontrolled hypertension;

(3) significant orthopaedic or chronic pain conditions;

(4) pre-existing neurological disorders such as multiple sclerosis, Parkinson's disease, dementia;

(5) Abbreviated Mini-Mental State Examination score (Appendix Ⅱ) of less than 8 (Sze et al. 2000);

(6) previous neurosurgery and/or orthopaedic surgery of the upper extremity.

Ninety-eight patients with stroke and 20 healthy normal subjects meeting the above inclusion-exclusion criteria were recruited.

Five variables were recorded in the non-affected side and affected side of patients and the dominant side of normal subjects as follow: (1) Abnormal muscle tone by Composite Spasticity Index (CSI) and associated reaction by Associated Reaction Rating Score (ARRS), (2) EMG co-contraction ratios and force of maximum isometric voluntary contraction (MIVC) of elbow flexors and extensors, and maximum isometric voluntary contraction of paretic hand grip, (3) $IEMG_{AS}$ of the affected biceps and triceps during maximum voluntary hand grip of the non-affected hand as a measure of associated reaction, (4) reaction time (RT) of wrist extension and flexion, and (5) Wolf Motor Function Test (WMFT). The rationale and the method for recording each of there variable described below.

2.1.2 Spasticity and associated reaction

Spasticity is characterized by a velocity-dependent increase in tonic stretch reflexes, which could be manifested together with hyperactive tendon reflexes with or without clonus (Sheean 2002). Chan (1986) and Levin and Hui-Chan (1992) designed a Composite Spasticity Scale for testing the lower leg to comprise of Achilles tendon jerks, resistance to passive ankle dorsiflexion, and the amount and duration of ankle clonus. The evaluation was a 4-point scale for “clonus,” and a 5-point scale for the other 2 indexes. The score for “resistance to passive dorsiflexion” was doubly weighted because it closely represented muscle tone (Levin and Hui-chan 1992). Scores ranging from 0-9, 10-12 and 13-16 corresponded to mild, moderate and severe spasticity respectively (Levin and Hui-chan 1992). A high ICC of 0.87 was found (Levin and Hui-Chan 1993). The Cronbach’s α coefficient revealed a good level of internal

consistency with a value of 0.70 (Nadeau et al. 1998). Based on principal-component analysis, Achilles tendon jerks and clonus items explained 67.9% of the total variance (Nadeau et al. 1998).

A Composite Spasticity Index (Appendix **III**) to measure spasticity of the UL was developed by Kim (1994) and Levin and Feldman (1994). It consists of 3 parts: (1) Biceps jerks were scored on a scale from 0 for 'no response' to 4 for 'maximally hyperactive reflex'. (2) Resistance to full-range passive elbow extension at fast speed was scored with 0 indicating 'no resistance' and 8 indicating 'maxmally increased resistance'. (3) Wrist clonus was assessed on a scale from 1 indicating 'no clonus' to 4 indicating 'sustained clonus'. Scores of 0-4, 5-8, 9-12 and 13-16 corresponded to no spasticity, mild, moderate and severe spasticity. This CSI was adopted in the present thesis with the patient sitting in a chair and his affected arm relaxed. The examiner tested the biceps tendon jerk, resistance to passive elbow extension, and wrist clonus using the scale described above.

Associated Reaction Rating Score (Appendix **IV**)

The Associated Reaction Rating Score has been created as a clinical tool to assess the severity of associated reactions in the hemiplegic upper limb (Macfarlane et al. 2002). The scale includes 4 characteristics related to the severity of associated reactions: (1) Excursion of the associated reaction (AR) and duration after the effort ceases. (2) Extent of AR in the affected limb. (3) Ability of the subject to release the AR. (4) Effect of the AR during functional performance. Inter-rater reliability and intra-rater reliability have been tested and they were found to be encouraging (kappa values=0.43-0.85 and 0.61-0.87 respectively; Macfarlane et al. 2002). The procedure for this assessment was to ask the patients to stand from a chair and to observe the reactions of their affected arm. The examiner recorded the patient's score using the

captioned scale described here.

2.1.3 Maximum isometric voluntary contraction (MIVC) force and EMG co-contraction ratio of the paretic elbow flexors and extensors and maximum voluntary grip force of the paretic hand

During this test, subjects sat with the arm fixed in a specially designed frame. The shoulder joint was kept in slight abduction (10°) and the elbow joint at 90º of flexion in the frame. The wrist joint was kept in supination with velco straps. A load cell attached to the wrist frame was used to measure the force exerted. The subject was asked to give a MIVC of the affected and non-affected elbow flexors and extensors and to maintain the maximum contraction for approximately 2-3 sec (Fig. 2.1). A load cell recorded the force. The test was repeated 3 times with a rest of 4-5 sec in between.

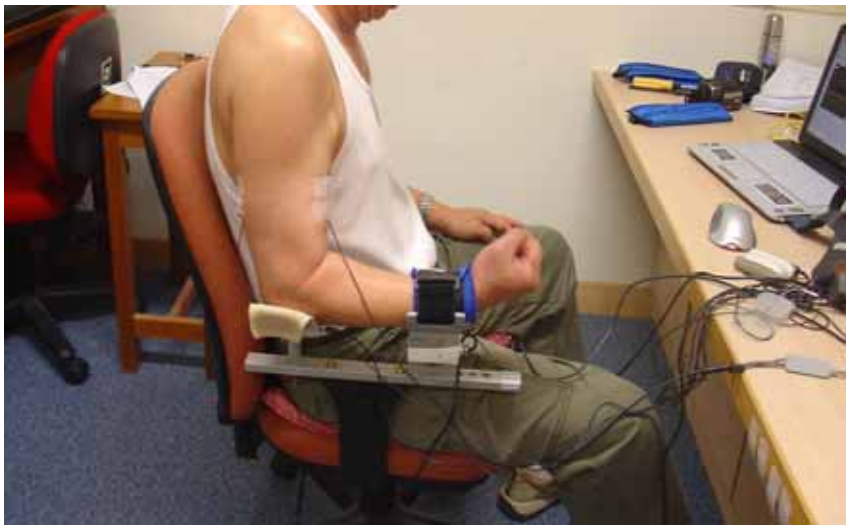


Fig. 2.1 Experimental set-up for recording of MIVC of the affected elbow flexors and extensors

Maximum grip strength of affected hand:

During this test, subjects sat with the affected arm fixed in a specially designed frame. The shoulder joint was kept in slight abduction (10°), the elbow joint at about 100º of flexion in the frame, and the wrist joint at a middle position with velco straps.

A load cell was placed in the patient's hand to measure the maximum voluntary grip force produced by affected hand (Fig. 2.2).

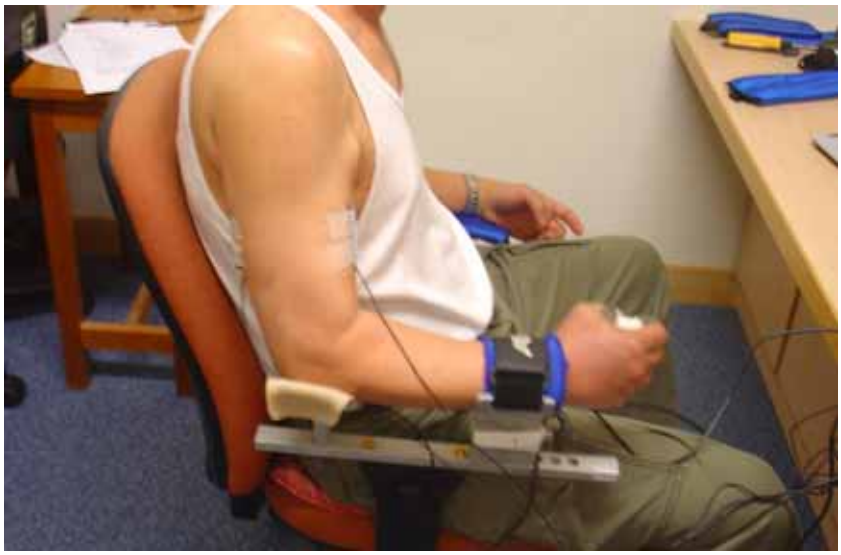


Fig. 2.2 Recording of maximum hand grip strength on the affected side

During MIVC trials, EMG activities were recorded from the biceps brachii (biceps) and trips brachii (triceps) as follow: (1) Biceps: two active AG- AGCL electrodes (2 cm apart) were placed parallel to the muscle fibers in the center of the muscles mass (Cram et al. 1998). (2) Triceps: two active AG-AGCL electrodes (2 cm apart) were placed parallel to the muscle fibers, 2 cm medial from the midline of the arm, at approximately 50% of the distance between the acromion and the olecranon or elbow (Cram et al.1998).

To ensure good electrical contact, the skin was shaved and the electrode sites were cleaned with alcohol. The electrodes (diameter = 8 mm) were attached with an inter-electrode distance of 22 mm by using adhesive pads and electrode gel. The gain of the pre-amplifers on the electrodes was 330. EMG signals were sampled at a frequency of 1000 Hz per channel. Raw EMG data were stored and later digitized with a 12 bit analog-to-digital (A/D) converter. Brief training on how to produce MIVC was given to

the subjects at each session before recording. Six trials were recorded from each muscle during each assessment session, 3 each for elbow flexor and extensor. EMG signals were full-wave rectified and the EMG area was calculated over a 500 msec window placed where the peak force attained a plateau (Fig. 2.3). Co-contraction ratio was calculated as Antagonist EMG area/Agonist + Antagonist EMG area according to Levin and Hui Chan (1994).

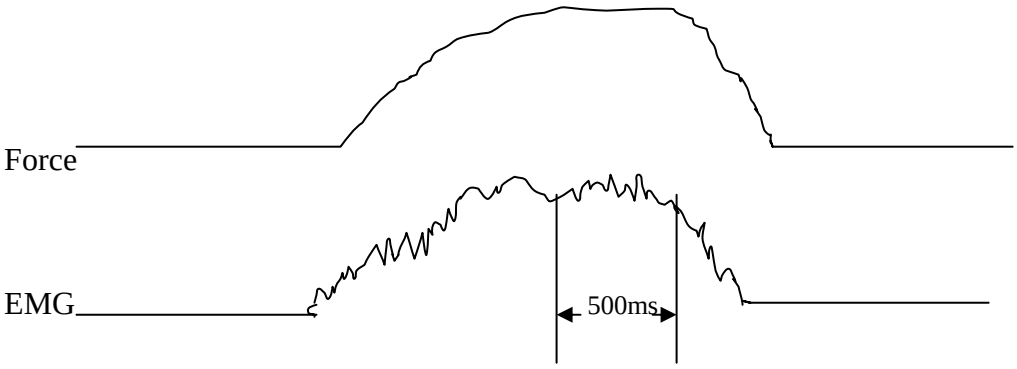


Fig. 2.3 EMG area was calculated over a 500 msec window placed where the peak force attained a plateau

2.1.4 Associated reactions: $IEMG_{AS}$ of affected biceps and triceps during maximum voluntary grip of the non-affected hand

During this test, subjects sat with the affected arm fixed in a specially designed frame (Fig.2.4). The shoulder joint was kept in slight abduction (10°), the elbow joint at about 100º of flexion in the frame, and the wrist joint at a middle position with velco straps. A load cell was placed in the patient's hand to measure the maximum voluntary grip force produced by the non-affected hand (Fig. 2.4). The subject was asked to maintain the maximum voluntary grip force for approximately 2-3 sec. Integrated EMG (IEMG) is the total amount of electrical activity in which the value is proportional to the area under the EMG envelop (Bouisset & Maton 1970). $IEMG_{AS}$ (IEMG of

associated reaction) were recorded from the biceps brachii (biceps) and trips brachii (triceps) on the affected side during non-affected hand grip (Fig.2.4). The test was repeated 3 times with a rest of 4-5 sec between each test. $IEMG_{AS}$ was then normalized with respect to the MIVC of its corresponding muscle (Lehman & McGill 1999), either the affected biceps or triceps. Elbow flexion or extension force of the affected UL induced as "associated reaction" by maximum voluntary non-affected hand grip was recorded by another load cell attached to the part of frame below the wrist joint.

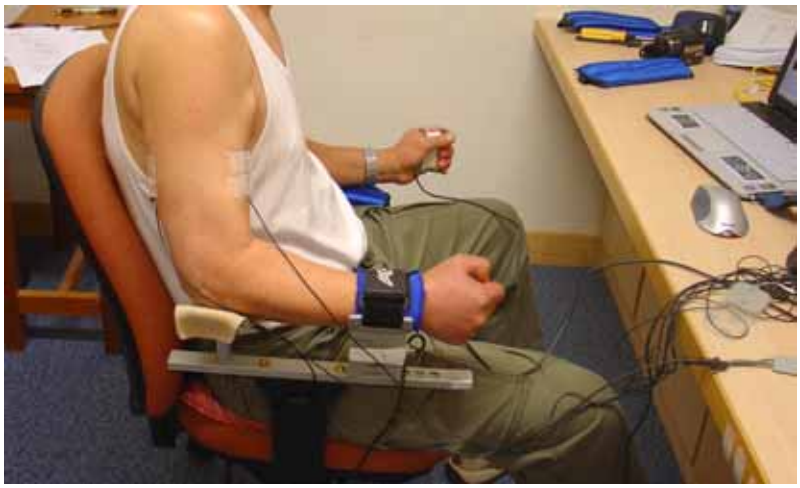


Fig. 2.4 Recording of maximum voluntary grip force produced by the non-affected hand, and EMG of the affected biceps and triceps as a measure of associated reaction

2.1.5 Reaction time (RT) of wrist flexion and extension

The subject was asked to flex or extend the affected and non-affected wrist as fast as possible, following an auditony "go" signal (frequency = 100 Hz) given by a beeper that lasted 200 msec. An auditory warning signal (frequency = 80 Hz) was provided 1000 msec before the "go" signal for approximately 2-3 sec. An electrogoniormeter attached to the wrist measured wrist flexion and extension angle (Fig.2.5). RT was defined as the time from the "go" signal to a change in wrist angle denoting movement onset (3 SD from baseline). (Fig.2.6).

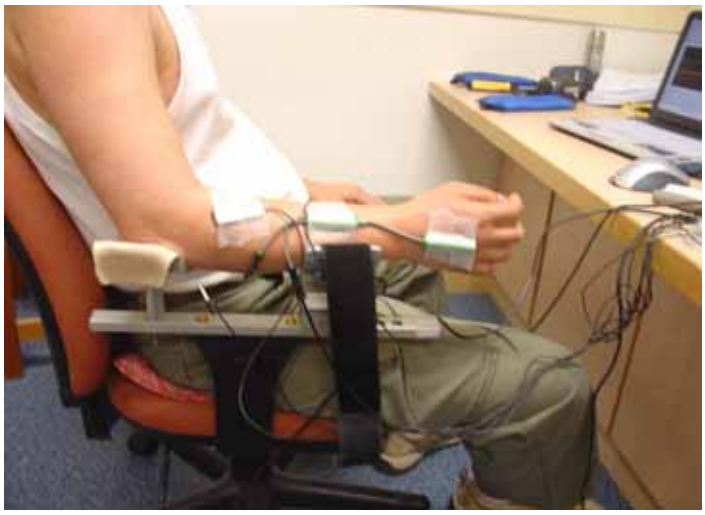


Fig. 2.5 Recording of wrist flexion and extension angle by an electrogoniormeter attached to the wrist

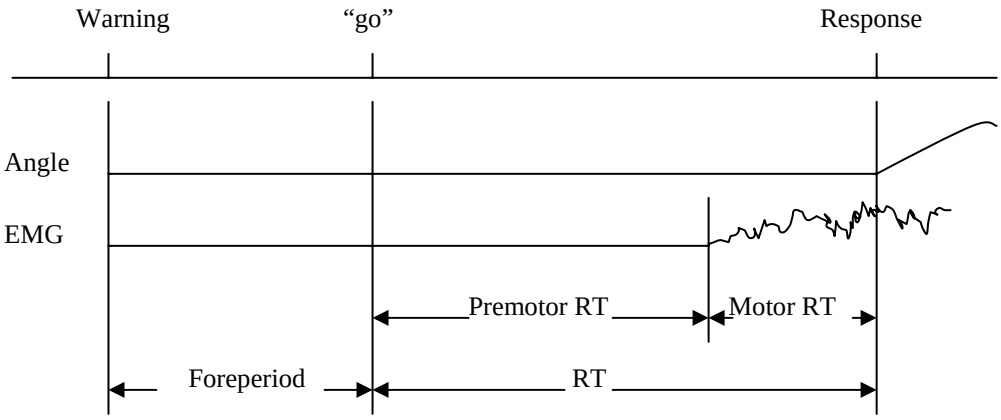


Fig. 2.6 The reaction time (RT) paradigm and definitions of RT, premotor and motor RT

2.1.6 **Fugl-Meyer assessment** (Appendix Ⅴ)

The Fugl-Meyer assessment of sensorimotor recovery after stroke (FMA) evaluates changes in sensormotor function in 6 areas: sensation, pain, joint range of

motion, UL motor function and coordination, lower limb (LL) motor function and coordination, and balance (Fugl-Meyer et al. 1975). Motor function items for the extremities are based on Brunnstrom's stages of motor recovery, which assumed that motor recovery proceeds in a sequence from mass flexion or extension movement patterns to movements that combine parts of the 2 patterns, and then to voluntary, isolated movements at each joint. Items are scored on a 3-point ordinal scale from 0 to 2, yielding a total of 66 points for UL function and 34 points for LL function. Fugl-Meyer and Jaasko (1980) tested the construct validity of this scale. Excellent inter-tater and intra-rater reliability has been demonstrated (Duncan et al. 1983, Sanford et al.1993). Preliminary evidence suggests that the Fugl-Meyer assessment is responsive to change (Wood-Dauphinee et al. 1990). Limitations of the motor domain include a ceiling effect, omission of some potentially relevant items, and greater weighting of the arm than the leg. The purpose of using this scale is to measure the general UL motor function of patients with stroke. In the present project, only the 66 points for UL function were recorded in patients with chronic stroke.

2.1.7 **Wolf Motor Function Test** (Appendix VI)

The Wolf Motor Function Test (WMFT) was developed by Wolf (1989) to examine the effects of constraint-induced movement therapy for survivors of stroke and traumatic brain injury. It was further elaborated for use as an outcome measure in constraint-induced movement therapy (Morris et al. 1997, Taub et al. 1993, Uswatte and Taub 1999). The original version of the test consisted of 21 simple tasks sequenced according to the joints involved and level of difficulty. In the current version, which contains 17 tasks, several tasks were dropped from original the testing protocol. Two of the tasks were simple measures of muscle strength. Because their performance was not rated and not included in the total performance time or functional ability score on the

test, they were not included. The inter-test and inter-rater reliability, internal consistency and stability of the test were high for both functional ability and the performance time rating scale measures, ranging from 0.88 to 0.98, with most of values close to 0.95 (Morris et al. 2001).

2.1.8 Statistics

In this study, a number of statistical methods in the Statistical Package for Social Sciences (SPSS) version 14.0 were utilized to analyze the results. Descriptive statistics for subjects' relevant characteristics were conducted first. Prior to that, the we used a non-parametic test, 1-Sample K-S Test, to examine all the data to determine whether they followed normal distribution. To test the reproducibility of measurement protocols, the mean score and ICC of each outcome measure between 7 days were analyzed. Correlations among relevant measurements were examined by computing Pearson correlation coefficients or Spearman correlation coefficients, depending on whether the data tested displayed normal distribution or non-normal distribution, respectively.

2.2 Study 2: Effects of TENS and TRT in promoting upper limb motor function after stroke

2.2.1 Subjects

The inclusion criteria and exclusion criteria had been described in section 2.1.1. Seventy-seven patients with stroke were recruited for this study.

2.2.2 Sample size and study power

Sample size was calculated using "Java applets for power and sample size" software (Lenth 2007). The effect size was based on a paper on constraint-induced movement therapy in patients with chronic stroke (Miltner et al.1999), and was set at

1.02 for the Wolf Motor Function Test. Statistical significance was set at 5% (alpha level=0.05) and power was set to equal 80% (beta level=0.2). From this, the number of patients per group was calculated and estimated to be 16. Four groups of patients made for 64. Supposing that there would be 10-15% of patients who might drop-out during treatment, an extra 8 patients were recruited. The sample size was thus adjusted to 72, with 18 for each of the 4 groups (Table 2.1).

Table 2.1 Power analysis and sample size estimated for the study

Total subjects	Subjects per group	Effect size	Alpha level	Study power
72	18	0.96	0.05	0.80
64	16	1.02	0.05	0.80
56	14	1.10	0.05	0.81
48	12	1.20	0.05	0.81

In study 2, 623 subjects were recruited, 104 patients fulfilled the inclusion criteria and 77 patients joined the research project.

2.2.3 Randomization procedure

A computer program of stratified randomization, called “Minimize” (Jensen 1991), was used to minimize differences in known variables among groups. The stratification in this study included age (2 sub-groups of 45-60, 61-75 years of age) and spasticity level as determined by Composite Spasticity Index (4 sub-groups of CSI of 0-4, 5-8, 9-12, 13-16 corresponding to normal, mild, moderate and severe.

Each subject was admitted to the study after signing an informed consent form (Appendix I). The aforementioned variables of age and CSI were entered into the computer program “Minimize” which assigned the subjects randomly to 1 of the 4

groups described below. Subjects could not be changed to another group after randomization by the computer.

2.2.4 Treatment protocols

Subjects received the treatment according to the groups they were randomly allocated to:

Group 1: TENS alone (60 min)

Group 2: TENS (60 min) plus task-related training (60 min)

Group 3: p-TENS (60 min) plus task-related training (TRT) (60 min)

Group 4: control with no active treatment

The treatment of the subjects in Groups 1, 2 and 3 was conducted by a physiotherapist. A doctor (the author) who was blinded to the treatment received by the patients conducted the assessment procedures for all 4 groups.

2.2.5 Transcutaneous electrical nerve stimulation

The model Cefar Tempo TENS stimulator with 4 channels was used to deliver TENS and p-TENS. The electrical circuit in the device used for placebo stimulation was disconnected inside. Four surface electrodes (3.81 cm × 4.45cm) were placed on the following acupuncture points: Shousanli LI10, Waiguan SJ5 (on the wrist extensor), Naohui SJ13, and Tianjing SJ 10 (on the elbow extensor) (Fig.2.7), chosen according to Guo (2003). The rationale for choosing these acupuncture points was that they were all located on the extensor muscles of the UL alongside the radial nerve. It is thought that appropriate electrical stimulation intensity would have stimulated the extensors in the upper limb and through reciprocal inhibition could reduce the spasticity of the elbow flexors (Levin & Hui-Chan 1992, 1993, Tinazzi et al.2005).

TENS stimulation consists of 200 μs square pulses, applied continuously at an intensity of 2 times the sensory threshold and a frequency of 90 Hz. It was given 60 minutes per treatment sessions per day, 5 days a week for 8 weeks.

For placebo stimulation, the TENS device, stimulation parameters, electrode location and treatment protocol were the same as those in the TENS group. The only difference was that the electrical circuit in the device used for placebo stimulation was disconnected manually inside.

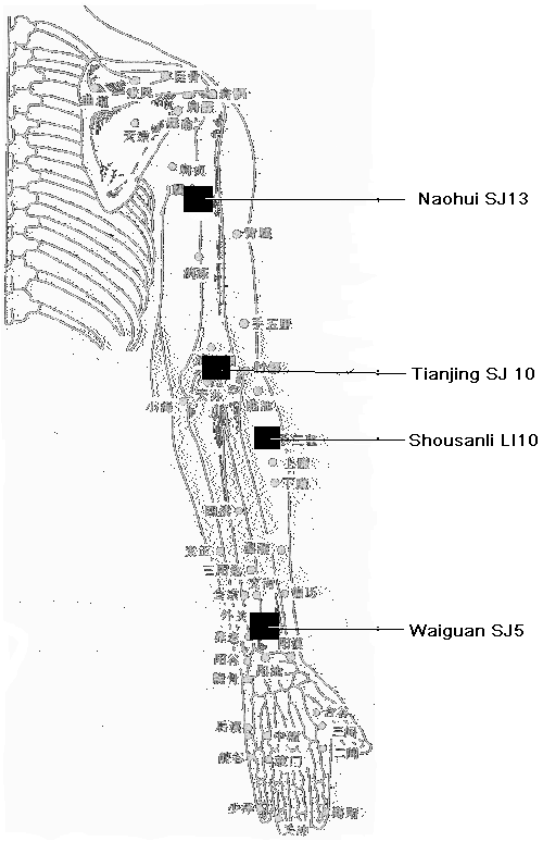


Fig. 2.7 Acupuncture points on the upper limb (adapted from Guo 2003.)

2.2.6 Task-related training

Task-related training was divided into 4 parts and the level of difficulty for each part was adjusted according the patient's capability.

Table 2.2 Task-related training in patients with stroke

Time	Task	Description
1st-2nd week 15 minutes	Soft tissue stretching of the affected UL	• Brief passive stretch of affected upper limb muscles immediately before an exercise session to decrease muscle tightness. Hold stretch for approximately 20 s. Relax. Repeat 4-5 times. • Brief stretch of affected hand with the body leaning on the out-stretched hand placed horizontally on a wall or vertically on a table top. • Manual stretch of long finger flexors, wrist flexors, and thumb adductor by a physiotherapist. • Brief manual stretch of the elongated forearm pronator with the patient's forearm on a table top by a physiotherapist. • Brief manual stretch of adductors and internal rotators of the glenohumeral joint with arm abducted, externally rotated, and elbow extended by a physiotherapist with the patient seated.
15 minutes	Reaching	• Forward: flexion of glenohumeral joint. • Sideways: Abduction of glenohumeral joint.

		• Backward: extension of glenohumeral joint.
15 minutes	Grasping	• Extension of wrist and fingers with abduction and conjunct rotation of carpometacarpal joint of thumb and other flexion of fingers around objects.
15 minutes	Releasing	• Abduction and extension of carpometacarpal joint of thumb.
3 nd -4th week	Soft tissue	• Same as above.
20 minutes	stretching	• Resistance exercises with elastic band for shoulder flexors, abductors, external rotators, and elbow flexors and extensors. Ten repetitions for each muscle for 3 times.
10 minutes	Arm strengthing	
10 minutes	Forearm pronation and supination	• Nylon velcro for training forearm pronation and supination
10 minutes	Finger pointing	• Patient's fingers pointing to a target on a touch screen placed at a distance of 20 cm and 30 cm above a table where the hand initially rested
5 th -6 th week		
30 minutes	Stretching	• Soft tissue stretching, forearm pronation and

	and strengthing	supination, and arm strengthing exercises as described above.
10 minutes	Bolt and nut	• Pick up bolts and nuts and screw nuts on bolts.
10 minutes	Placing small objects	• Place small wooden and iron objects on top of each other at different positions on the work platform.
10 minutes	Maze tracking	• Perform slow, continuous, and visually guided movements using an abacus on a curved iron wire along a frame (see picture below). 
7th-8th week 30 minutes	Functional training	• Pick up bolts and nuts. Place small objects and do maze tracking as described above.
30 minutes	ADL training	Bimanual practice: • Pour water from jug to cup/glass and back. • Fold a towel, remove the lid from a can. • Hold newspaper, turn the pages over with the newspaper on a table. • Progress to simultaneously holding

		newspaper and turning pages.

2.2.7 Outcome measurements

Four variables of muscle tone and motor function of the paretic upper limb were recorded as follow:

(1) Composite Spasticity Index

(2) MIVC of elbow flexors and extensors and of hand grip

(3) Reaction time (RT) of wrist flexion and extension

(4) Wolf Motor Function Test (WMFT)

2.2.8 Assessment schedule

Outcome measurements were recorded before treatment on day 1 (baseline assessment), at week 4 (mid-way through treatment) and week 8 (end of treatment) of the 8-week treatment, and at follow-up 4 weeks after treatment ended.

2.2.9 Statistics

Since a randomization program was used, it was assumed that the variances of subjects were in equal distribution among the 4 groups before treatment. Descriptive statistics for subjects' relevant characteristics were conducted first. Prior to that, the we used a non-parametic test, 1-Sample K-S Test, to examine all the data to determine whether they followed normal distribution. The main statistical test was repeated measure of variance (ANOVA). Outcome measurements of CSI, MIVC of elbow flexors and extensors, maximum hand grip strength, RT of wrist flexion and extension, and WMFT were analyzed with repeated measure of variance (ANOVA) to compare the main effects. The between-subject factor was the 4 subjects groups: TENS alone,

p-TENS + TRT, TENS + TRT, and control with no active treatment. The within-subject factor was the 4 assessment intervals: pre-treatment, at week 4 and week 8 during the 8-week treatment, and at follow-up 4 weeks after treatment ended. One-way ANOVA followed by multiple comparisons (post-hoc test) was used to compare treatment effects among the 4 groups. The study was carried out over a 12-week period. During this period, some patients had dropped out from the study. To take into consideration this factor, analysis of outcome measures was based on the intention-to-treat (ITT) approach, which included all the patients who had baseline data and had received at least one assessment. In the ITT analysis, the last observation carried forward (LOCF) model was used. Using LOCF, the missing data were analyzed as if they were fully recorded .The significant level was set at 5%.

2.3 Ethical considerations

The two studies involving chronic stroke patients were conducted in The Hong Kong Polytechnic University. Ethical approval was obtained from the University before subjects were recruited. Subjects were required to sign an informed consent from (Appendix I) prior to starting the study. They were informed that TENS and task-related training are regular modalities employed in stroke rehabilitation with no report of notable side-effects when properly administered. They could withdraw from the study at any time without any justification. Any personal information in this study was kept confidential and their personal identity was not disclosed in any form.

2.4 Preliminary study: Reliability of the outcome measures

2.4.1 Rationale

In clinical research, data reliability is the first prerequisite and at the heart of all measurements. If a subject can produce consistent responses under set conditions on

different days, then an investigator can repeat the tests and get consistent outcomes over time. Test-retest reliability is demonstrated by keeping all test conditions and methods as invariable as possible while the same sample of subjects is examined on 2 at least separate occasions. The intraclass correlation coefficient (ICC) is the preferred index of test-retest reliability because it reflects both correlation and agreement (Portney & Watkins 2000).

Before launching study 1 and study 2, we examined the intra-rater reliability of CSI, ARRS and WMFT clinical scales, as well as the quantitatively using measures of IEMG, force and reaction time in a preliminary study described below.

2.4.2 Subjects

10 patients with stroke who met the inclusion criteria described in section 2.1.1 participated in this part of the study. The subjects were 47 to 64 years old (average age = 58.3 years), with 8 men and 2 women, 6 having been diagnosed with ischemia and 4 with hemorrhage. The average time from stroke onset to the first session of assessment was 42.6 months.

2.4.3 Procedure

Subjects were assessed twice on different days within a 7 day span by the same examiner. The methods and procedures for measuring the outcome variables were as described in sections 2.1.2-2.1.5 and 2.2.5. Each subject was assessed on each occasion in terms of the composite spasticity index (CSI), his or her associated reaction rating score (ARRS), and the Wolf Motor Function Test (WMFT). MIVC of elbow extensors and flexors and hand grip force were measured, and $IEMG_{AS}$ of the affected biceps and triceps were recorded during MIVC of the elbow flexors and during extensors and maximum voluntary grip with the unaffected hand as a measure of the associated

reaction. Reaction times (RTs) were also measured for wrist extension and flexion. The mean score and ICC between days were analyzed for each outcome measure.

2.4.4 Results

Table 2.3 presents the intra-rater reliability results for the CSI, ARRS and the WMFT scores on different days. High test-restest repeatability was found. The ICCs between days for the CSI were 0.978 (P<0.001). The ICCs for the ARRS scores were 0.912 (P<0.001). The ICCs for the WMFT were 0.987 for functional ability and 0.872 for time (P<0.001) (Table 2.3).

Table 2.3 Mean scores and ICCs in test-retest evaluation of CSI, ARRS, and WMFT in patients with chronic stroke

	Mean scores ± S.D.		ICC	P value
	Day X	Day Y	between days	
CSI score	6.0±1.6	5.9±1.5	0.978	<0.001
ARRS	1.0±1.7	1.3±1.8	0.912	<0.001
WMFT				
Functional ability	3.5±0.8	3.5±0.8	0.987	<0.001
Time score (s)	4.6±2.7	4.4±2.4	0.872	<0.001

S.D.: standard deviation

Table 2.4 shows the reliability results for MIVC force of the elbow extensors and flexors and hand grip of affected UL. The ICCs for these variables ranged from 0.804 to 0.863 (P<0.01).

Table 2.4 Mean scores and ICCs for MIVC force of elbow flexors and extensors and of hand grip of paretic UL in patients with chronic stroke

	Mean scores ± S.D.		ICC	P value
	Day X	Day Y	between days	
Elbow flexion				
Force (N)	146.7±74.9	131.1±109.7	0.804	P=0.01
Elbow extension				
Force (N)	78.0±44.4	74.7±21.3	0.846	P=0.005
Hand grip				
Force (N)	81.4±20.6	75.4±18.8	0.863	P=0.002

S.D.: standard deviation

Table 2.5 presents the reliability of the IEMG measures of the affected biceps and triceps during MIVC of elbow flexors and extensors and during maximum voluntary non-affected hand grip as a measure of associated reaction. The ICCs ranged from 0.802 to 0.928 (P<0.01).

Table 2.6 shows the test-retest reliability of reaction time measurements for wrist flexion and extension in patients with stroke. The ICCs of the variables ranged from 0.863 to 0.883 (P=0.001).

Table 2.5 Mean scores and ICCs of IEMG measured on the affected biceps and triceps during MIVC of the elbow flexors and extensors and during maximum voluntary grip with the unaffected hand

	Mean scores ± S.D.		ICC	P Value
	Day X	Day Y	between days	
Elbow flexion				
Biceps IEMG (mV.s)	23.2±16.5	24.6± 18.4	0.888	P=0.001
Triceps IEMG (mV.s)	2.2± 0.5	2.4± 0.7	0.856	P=0.002
Elbow extension				
Biceps IEMG (mV.s)	3.9± 3.7	3.9± 3.1	0.837	P=0.004
Triceps IEMG (mV.s)	11.5± 8.3	12.5± 9.4	0.829	P=0.007
Hand grip				
Biceps$IEMG_{AS}$ (mV.s)	4.8±1.9	5.2±2.0	0.802	P=0.009
Triceps$IEMG_{AS}$ (mV.s)	2.8±1.8	2.8±1.7	0.928	P<0.001

S.D.: standard deviation

Table 2.6 Mean scores and ICCs for RT of wrist extension and flexion in patients with stroke

	Mean scores ± S.D.		ICC	P Value
	Day X	Day Y	between days	
Wrist flexion				
Reaction time (ms)	305.8±69.9	305.1±77.1	0.883	P=0.001
Wrist extension				
Reaction time (ms)	328.2±86.0	319.6±31.9	0.863	P=0.001

S.D.: standard deviation

2.4.5 Discussion and conclusion

The results of all the tests demonstrated high intraclass correlation coefficients. In the clinical CSI, ARRS and WFMT tests, the coefficients were very high, with 0.978 for CSI; 0.912 for ARRS; and 0.987 for functional ability and 0.872 for time of the WFMT, and with all the *P* values <0.001. These findings are similar to those reported by previous investigators.

The reliability of the Composite Spasticity Score for the lower limb has previously been examined by Levin and Hui-Chan (1993) and by Nadeau et al. (1998). Levin and Hui-Chan (1993) found a high ICC of 0.87. Cronbach's α coefficient revealed a good level of internal consistency with a value of 0.70 (Nadeau et al. 1998). Achilles tendon jerks and clonus items explained 67.9% of the total variance in a principal-component analysis (Nadeau et al. 1998). The CSI for the upper limb was studied previously by Kim (1994) and by Levin and Feldman (1994). Kim reported an ICC of 0.78 for the CSI of the upper limb which was less than the ICC value of 0.978 found by us (Table 2.3). The inter-rater reliability (kappa values 0.43-0.85) and intra-rater reliability (kappa values 0.61-0.87) of the ARRS have been examined by Macfarlane et al. (2002), who found to them to be acceptable. For the WMFT, Morris et al. (2001) reported high inter-test and inter-rater reliability, and high internal consistency and stability for both the functional ability and performance time measures. Similar to our findings in Table 2.2, their values ranged from 0.88 to 0.98, with most of the values being close to 0.95.

In this study, all the quantitative variables including force, IEMG and RTs showed relatively high ICCs ranging from 0.802 to 0.928 (P<0.01; Tables 2.4-2.6). ICCs for maximum voluntary isometric contraction of the elbow extensors and flexors and for hand grip force ranged from 0.804 to 0.863 (P<0.01; Table 2.4). The ICCs of the IEMG ranged from 0.802 to 0.928 (P<0.01; Table 2.5). The reaction time for wrist flexion and extension in patients with stroke ranged from 0.863 to 0.883 (P<0.01; Table 2.6).

The above findings are similar to previous studies which examined the reliability of force and torque measurements in the affected UL of patients with stroke. Kim (1994), for example, found an ICC of 0.89 for the peak torque of elbow flexion and extension in the affected UL with 8 patients with stroke. Dynamometer measurements of sustained squeezing and repetitive squeezing using 23 subjects with stroke and 12 elderly controls have shown excellent inter-rater (r = 0.99) and intra-rater (r = 0.97) reliability (Cramer et al.1997). Another study tested the reliability of maximum voluntary grip force, and demonstrated good reliability (ICC >0.86) and low standard error (Boissy et al. 1999). Furthermore, the reliability coefficients for strength measurements of 5 UL muscle groups have been found to be in the range of 0.81-0.97, with standard errors of measurements accounting for 4% to 20% of the group means in patients with stroke (Bertrand et al. 2007).

Another previous study investigated the root mean square and mean frequency reliability of surface electromyography during an endurance test consisting of repetitive maximum concentric knee extensions. The ICC was good for the absolute RMS of the rectus femoris (ICC≥0.80), vastus medialis (ICC≥0.88) and vastus lateralis (ICC≥0.82) and for the mean frequency (MNF) of the rectus femoris (ICC≥0.82) and vastus medialis (ICC≥0.83) (Larsson et al. 2003). However, EMG recordings of 50% MIVC showed better reproducibility than those of 100% MIVC (Kollmitzer et al. 1999). There have been few studies on the reliability in surface EMG measurements and the reaction times of the affected UL in patients with stroke. Kim (1994) examined IEMG of the biceps and triceps during MIVC of elbow flexion and extension using 8 stroke subjects and found an ICC of 0.87 for the mean frequency of the biceps IEMG, and of 0.91 for the triceps IEMG. Ng and Hui-Chan (2004) examine the test-retest ICCs for peak force, peak torque and IEMG results of the agonists during ankle dorsiflexion and

plantarflexion and found ICC of 0.63 to 0.99 respectively in patients with stroke and 0.95 to 0.98 respectively in healthy elderly controls.

Using subjects with healthy ankle joints, intra-class correlation coefficients ranging from 0.17 for the electromechanical delay of the peroneus longus to 0.89 for maximum inversion speed have been found in experiments on the test-retest reliability of RT measurements during a sudden ankle inversion while standing (Eechaute et al. 2007). Another study assessed the reliability of RT estimates in brain-damaged patients and controls using the Kendall coefficient of concordance. Concordance coefficients were computed for simple and choice RT tests. The values were acceptable by Godefroy et al. (1994).

The ICC reflects both a degree of correspondence and an agreement among ratings. As a general guideline, ICC values above 0.75 suggest good reliability (Portney & Watkins 2000). So all the data in our study demonstrated good to very good intra-rater reliability. Having shown our measures to be repeatable, we embarked on study 1 to delineate the motor impairments in patients with stroke, and to determine the extent to which the various motor performance criteria could be inter-related.

CHAPTER 3

STUDY 1

MOTOR IMPAIRMENTS OF THE UPPER LIMBS FOLLOWING STROKE AND INTER-RELATIONSHIPS AMONG MOTOR PARAMETERS

Summary

Ninety-eight stroke survivors participated in this study. The mean age of the subjects was 59.53±7.47 years. There were 67 men and 31 women. The mean duration since the stroke was 48.47±33.43 months. Seventy of the subjects had suffered ischemic stroke and 28 cerebral hemorrhage. Twenty normal subjects also participated. The mean age of these 8 men and 12 women was 59.30±9.80 years. The quantitative measures included force during MIVC of elbow flexors, extensors and hand grip of the affected arm, co-contraction during MIVC of elbow flexors and extensors, associated reactions in the paretic elbow muscles during non-paretic hand grip, and reaction time of the paretic wrist in extension and flexion. The clinical assessments included Composite Spasticity Index (CSI), Associated Reaction Rating Score (ARRS), and Wolf Motor Functional Test (WMFT).

Our findings showed that the affected UL in patients with stroke produced significantly smaller force during MIVC of elbow flexors, extensors and hand grip than those of their non-affected UL and of normal subjects ($P<0.01$). There were no significant differences in the co-contraction ratio of maximum isometric voluntary (MIV) elbow flexion and extension among the affected and unaffected sides of the stroke survivors, and the normal subjects. When the stroke survivors performed a maximum grip using their non-paretic hand, associated reaction was manifested as elbow flexion (62.2 %), elbow extension (27.6%), or no elbow movement (11.2 %) in the paretic arm. Reaction time (RT) of wrist flexion and extension in the stroke survivors' affected hands were significantly longer than that in the normal subjects and their unaffected hands ($P<0.01$ for both).

Statistically significant correlations were found between MIVC force recorded during elbow flexion in the affected arm and ARRS (negatively; $\rho=-0.321$, $P=0.001$), and WMFT functional ability ($\rho=0.380$, $P<0.001$) and time score (negatively; $\rho=-0.389$,

P<0.001). MIVC force recorded during elbow extension in the affected arm was found to produce similar results. It correlated with ARRS (negatively; ρ=-0.291, P=0.004), and with WMFT functional ability (ρ=0.277, P=0.006) and time score (negatively; ρ=-0.302, P=0.002). Maximum hand grip force in the affected arm correlated moderately with CSI (negatively; ρ= -0.425, P<0.001), ARRS (negatively; ρ=-0.430, P<0.001), and with WMFT functional ability (ρ=0.658, P<0.001) and time score (negatively; ρ=-0.630, P<0.001).

There were no significant associations between the co-contraction ratios during MIV elbow flexion and the CSI, ARRS, and WMFT results. However, the co-contraction ratio during MIV elbow extension correlated moderately but significantly with CSI (ρ=0.227, P<0.05), ARRS (ρ=0.377, P<0.001), and with WMFT functional ability (negatively; ρ=-0.358, P<0.001) and time score (ρ=0.360, P<0.001).

Moderate but statistically significant correlations were also found between the paretic biceps IEMG recorded as an index of associated reaction during non-paretic hand grip and CSI (ρ= 0.418, P<0.001), ARRS (ρ=0.557, P<0.001), and with WMFT functional ability (negatively; ρ=-0.561, P<0.001) and time score (ρ=0.559, P<0.001). Although the paretic triceps IEMG recorded as an index of associated reaction during non-paretic hand grip correlated marginally with CSI (ρ=0.199, P=0.05); like the biceps IEMG, it correlated moderately with ARRS (ρ=0.371, P=0.001), and with WMFT functional ability (negatively; ρ=-0.378, P<0.001) and time score (ρ=0.403, P<0.001).

The wrist flexion RT correlated moderately with CSI (ρ=0.412, P<0.001) and ARRS (ρ=0.341, P<0.001), and with WMFT functional ability (negatively; ρ=-0.531, P<0.001) and time score (ρ=0.504, P<0.001). Similarly the wrist extension RT correlated moderately with CSI (ρ=0.429, P<0.001), ARRS (ρ=0.374, P<0.001), and with WMFT functional ability (negatively; ρ=-0.531, P<0.001) and time score (ρ=0.486, P<0.001).

In conclusion, our findings from study 1 showed that MIVC force of the affected elbow flexors, extensors and hand grip in patients with chronic stroke was significantly smaller, and RT of their wrist flexion and extension was significantly longer than those of their non-affected UL and of normal subjects. During non-affected hand grip, associated reaction was mainly manifested as elbow flexion (62.2%) in the paretic UL. These 3 quantitative parameters were further found to be correlated moderately but significantly with the clinical scales of CSI (except for MIVC force of elbow flexors and extensors), ARRS, and WMFT functional ability and time scores, in either a positive or negative manner. These findings suggest that both quantitative and clinical assessments could serve as reliable and valid assessment tools to measure treatment effectiveness in patients with stroke over time in study 2.

3.1 Characteristics of motor impairments of the upper limb following stroke

3.1.1 Force during MIVC of elbow flexors, extensors and of paretic hand grip

Muscle weakness is defined as a lack of ability to generate normal levels of force. It is a major impairment of motor function in many stroke patients. Paralysis or paresis of movement is partly the result of decreased voluntary motor unit recruitment, an inability to recruit sufficient skeletal motor units to generate intended muscle torque or movement (Gracies 2005). Paresis is caused by a lesion within descending motor pathways, which hinders the central excitatory drive to motor units. Hemiplegia (or hemiparesis) is weakness affecting one side of the body, which is most commonly found in patients with stroke (Shumway-Cook & Woollacott 2007).

In recent years, muscle strength has been extensively examined in patients with stroke. A number of studies have shown that stroke patients were weak during isometric contraction (Andrews and Bohannon 2000, 2003, Canning et al. 1999, Chae et al.2002, Levin et al. 2000, Newham and Hsiao 2001). Distal muscles seemed to be more affected than proximal ones (Frascarelli et al. 1998), and flexors more than extensors (Andrews and Bohannon 2000). The muscle weakness found soon after stroke suggested that it was not caused by inactivity alone (Andrews and Bohannon 2000, 2003, Newham and Hsiao 2001). Harris et al. (2001) also found reduced force being generated by externally stimulated quadriceps in the first week after stroke. Their results suggested that at least some of the muscle weakness was a direct (and rather long-lasting) consequence of brain lesion. Furthermore, muscles weakness was also found on the “non-paretic’ side very soon after stroke (Hsaio & Newham 1999). The number of motor units recruited is one of the main determining factors in the power developed by a muscle (Gracies 2005). Reduced descending drive was thought to cause a failure to recruit higher threshold motor units, and to reduce the ability to modulate or increase motor unit discharge rate when patients tried to increase their voluntary force

output (Gracies 2005). Though muscle weakness in patients with stroke have been widely investigated, few studies examined its relationship with spasticity (Bohannon et al. 1987), associated reactions, and motor functional performance in their affected upper limbs. This formed one of our objectives in the study.

3.1.2 Co-contraction during MIVC of elbow flexors and extensors

Co-contraction (co-activation) is the simultaneous activity of agonist and antagonist muscles crossing the same joint, and involves opposing muscles contracting at the same time to increase the stiffness of a joint (Damiano 1993). Healthy individuals often show co-contraction during the early stages of learning new tasks (Shumway-Cook & Woollacott 2007), or when doing familiar tasks under challenging conditions (Buchanan et al. 1986). During voluntary movements in normal subjects, co-contraction of agonist and antagonist muscles appears during isometric contraction related to reciprocal patterns of activation (Flanders & Cordo 1987), and the antagonist not only opposes the force of the agonist but also provides stability and stiffness to a joint movement (Ait-Haddou et al. 2000). In subjects with upper motor neuron lesions, muscle weakness may cause a decrease of central control of the muscle. The weakness could be caused by unwanted activation of the antagonist, which could limit the agonist muscle contraction (Fellows et al.1994).

Conflicting results have been reported in studies investigating isometric co-activation of the affected muscles after stroke. A number of investigators have reported co-contraction in stroke patients to be similar to the activity in controls (Davies et al. 1996, Fellows et al.1994, Gowland et al. 1992, Newham & Hsiao 2001, Tang & Rymer 1981). In contrast, Kamper & Rymer (2001) found that the upper limb (UL) muscles in patients with stroke were more affected than other muscles and showed excessive co-contraction of agonists and antagonists. Furthermore, the degree

of co-contraction was demonstrated to be significantly correlated to motor impairment and physical disability in the affected UL (Chae 2002). However, these previous studies have not thoroughly investigated the relationship between co-contraction rations and clinical measures of spasticity, associated reactions and motor functional performance in stroke survivors. Therefore, part of the 2 objectives of the present study were (1) to examine differences in EMG co-contraction ratios during maximum isometric voluntary contraction (MIVC) of the elbow flexors and extensors between normal subjects and stroke survivors, and (2) to determine the relationships between these co-contraction ratios and CSI, ARRS and WMFT scores.

3.1.3 Associated reaction in the paretic upper limb

Associated reactions (ARs) are involuntary movements often seen in patients after stroke during stressful activities, most noticeably in the UL (Carr & Shepherd 2003). Riddoch and Buzzard (1921) described associated reactions as, “automatic activities which fix or alter the posture of a part or parts when some other part of the body is brought into action by either voluntary effort or reflex stimulation.” Walshe (1923) defined associated reactions as released postural reactions deprived of voluntary control, triggered by a voluntary effort exerted by the patient, and he found that their magnitude was related to the degree of hypertonicity in that side of the body.

After stroke, associated reactions have been observed in the paretic arm after movement of other parts of the body (Bobath 1990, Brunstrom 1970). Clinical ordinal rating scales have been developed to measure them (Macfarlane 2002) to supplement quantitative assessments such as joint angle measurements (Dvir 1993), EMG readings (Boissy et al. 2000, Cernacek 1961, Diskstein 1995, Green 1967, Hwang et al. 2005), and associated reaction force measurements (Bhakta et al. 2001, Boissy et al.1997, Nelles et al. 1998). Some studies have demonstrated that patients with associated

reactions show more serious motor deficits than those without associated reactions (Hwang et al.2005, Nelles et al. 1998). Based on clinical observation, associated reactions have been shown to be more commonly elicited when spasticity is present (Cornall et al.1991). On the other hand, they are occasionally found in patients who have little or no spasticity in the responding limb. So these reactions are not always associated with spasticity and may not be a valid indicator of spasticity (Ada and O'Dwyer2001).

Thus, the 2 objectives of the present study were also (1) to examine possible presence of associated reactions in patients with chronic stroke, and (2) to explore the relationships among associated reactions measured by quantitative assessments of EMG activity of the paretic elbow muscles during non-paretic hand grip and clinical measures of CSI, ARRS, and WMFT scores in stroke survivors.

3.1.4 Reaction time of the paretic wrist in extension and flexion

Reaction time is, "a measure of the time from the arrival of a suddenly presented and unanticipated signal to the beginning of the response to it" (Schmidt & Lee 1999). As illustrated in Fig. 2.6 of Chapter 2, RT has two components: "central" and "peripheral" (Weiss 1965), called "premotor RT" and "motor RT" respectively. Premotor RT refers to the interval between the signal and the first response detectable in an EMG. It corresponds to the central component, including signal perception and the decision to move. Motor RT is the interval between EMG onset and the start of the movement, which represents the peripheral component related to the muscle and force production (Jahanshahi 2003, Schmidt & Lee 2005). The total RT is the time interval from signal onset to movement onset (Schmidt & Lee 1999), and it is thought to be an index of ability in both preparation and execution of movement.

RT as a measurement in the study of movement disorders has been used for a long time. It has been used most extensively with Parkinson's disease (Chan 1986, Jahanshahi et al.1992, Talland 1963), Huntington's disease (Girotti et al. 1988, Jahanshahi et al.1993), and Alzheimer's disease (Pirozzolo et al. 1981, Gordon & Carson 1990). Brain injury could also have an effect on RT, because RT is related to brain cognitive and motor processes. Brain-injured patients are normally significantly slower than normal controls (Blackburn & Benton 1955). As long ago as 1983, Dickstein et al. (1983) showed conclusively that the RT of the paretic UL in patients with stroke was slower than in a control group. They found that the RTs in the affected wrist flexor and extensor were significantly longer than those of the unaffected side. Furthermore, premotor RT in both wrist flexion and extension on the affected side has been shown to be inversely correlated with the Medical Research Council (MRC) score for muscle strength (Miscio 2006).

The previous studies have compared RT between normal subjects and patients with neurological disease and examined the correlation between premotor RT and muscle strength in patients with stroke. The present study was designed not only to compare the RTs of the unaffected and affected sides in stroke survivors, but also to compare them with those of normal subjects, and to explore the relationships among wrist flexion and extension RT on the affected side and the motor deficits of the UL as measured by clinical CSI, ARRS, and WMFT scores.

3.2 Methods

3.2.1 Subjects

Ninety-eight hemiparetic stroke survivors participated in this study. Their mean age was 59.5±7.5 years (Table 3.1). There were 67 men and 31 women, and the mean duration since stroke was 48.5±33.4 months. Seventy of the subjects had suffered an

ischemic stroke and 28 had survived a cerebral hemorrhage. The inclusion and exclusion criteria have been described in Chapter 2, section 2.1.1. Twenty normal subjects also participated. Their mean age was 59.3±9.8 years old. There were 8 men and 12 women. All subjects gave written informed consent to participate in the study, which was approved by an ethics committee of The Hong Kong Polytechnic University before the subjects were recruited. Fugl-Meyer score of the affected UL was carried out for screening purpose.

Table 3.1 Relevant characteristics of the subjects

	Normal subjects	Stroke survivors
Number	20	98
Age (years), mean±S.D.	59.3±9.8	59.5±7.5
Gender: Male (N)	8	67
Female (N)	12	31
Affected side: Right (N)	20 (dominant side)	44
Left (N)		54
Type of stroke: Ischemic		70
Hemorrhagic		28
Time since stroke (months), mean±S.D.		48.5±33.4
CSI score, mean±S.D.		7.3±1.7
Fugl-Meyer score, mean±S.D.		35.6±12.5

3.2.2 Measurements

The following measurements were recorded on the dominant side of the normal subjects, and on the unaffected and affected sides of the stroke subjects, unless otherwise indicated. Please refer to the descriptions of methods in Chapter 2 (sections 2.1.2-2.1.6).

(1) Abnormal muscle tone was assessed using the Composite Spasticity Index (CSI), and associated reaction using the Associated Reaction Rating Score (ARRS). (2) The maximum isometric voluntary contraction (MIVC) of the elbow flexors/extensors and

hand grip, and the co-contraction ratio of MIVC the elbow flexors/extensors were assessed by EMG. (3) IEMG measurements of the associated reaction in the biceps and triceps of the affected UL were recorded during maximum voluntary grip of the unaffected hand. (4) Reaction time for wrist extension and flexion was measured together with (5) WMFT functional ability and time scores of the affected UL.

3.2.3 Statistics

A number of the statistical methods available in the Statistical Package for Social Sciences (SPSS) version 14.0 were used to analyze the results. Descriptive statistics for the subjects' relevant characteristics were computed first. The nonparametic 1-sample K-S test was used to determine whether the data conformed to the normal distribution. Normally distributed data were analyzed using analysis of variance (ANOVA), while the K-W H test was used for non-normally distributed data. Correlations were assessed by computing Pearson's correlation coefficient for normally distributed data or Spearman's correlation coefficient for non-normally distributed data. Body mass index (BMI) was a confounding factor for muscle strength, so co-variance analysis and partial correlation were applied to analyze the elbow MIV flexion and extension and hand grip force data. The significance level was set at 5%.

3.3 Results

3.3.1 Differences between subject groups

3.3.1.1 MIVC force of elbow flexors and extensors and of paretic hand grip

The results showed that the force recorded during MIVC of elbow flexors, extensors and hand grip of the affected arm were significantly smaller than those of the non-affected arm in patients with stroke and of normal subjects ($P<0.01$). There were

no significant differences in there force data between the non-affected arm in patients with stroke and the normal subjects (Table 3.2, Fig. 3.1).

Table 3.2 Force during MIVC of elbow flexors, extensors and hand grip in normal subjects and subjects with stroke

	Normal	Subjects with stroke	
		Unaffected side	Affected side
	(n=20)	(n=27)	(n=27)
Elbow flexor force (N)	322.7±112.1	305.1±121.5	145.4±69.0#
Elbow extensor force (N)	168.3±57.1	161.9±68.6	101.6±73.0#
Hand grip force (N)	442.0±156.9	442.2±167.7	124.1±86.1#

significant difference at the $P<0.01$ level when compared with the normal group and the unaffected side of subjects with stroke, using BMI as a co-variate in the analyses.

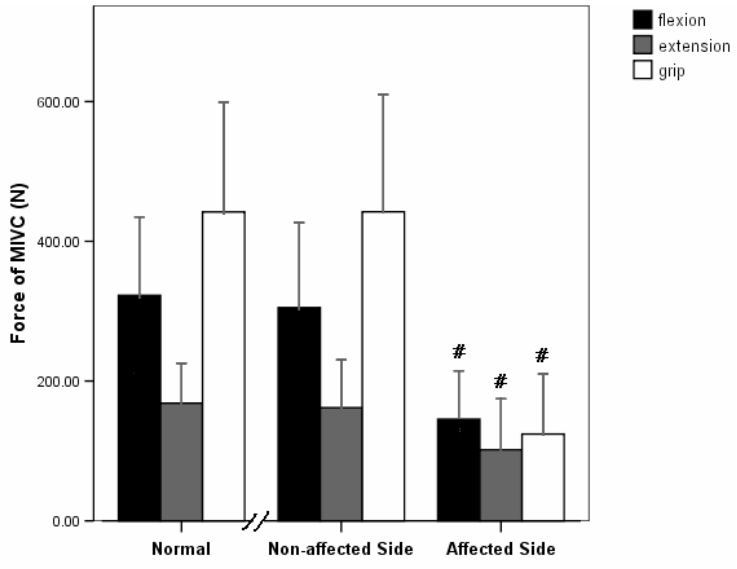


Fig. 3.1 Force recorded during MIVC of elbow flexors, extensors and hand grip in normal subjects and subjects with stroke # significant difference at the $P<0.01$ level when compared with the normal group and the unaffected side of subjects with stroke

3.3.1.2 Co-contraction ratio during MIVC of the elbow flexors and extensors

The results showed no significant differences in the EMG co-contraction ratios during MIVC of elbow flexors and extensors among the normal subjects, the unaffected side and the affected side of the stroke survivors (P>0.05) (Table 3.3).

Table 3.3 Co-contraction ratios during MIVC of elbow flexors and extensors in normal subjects and subjects with stroke

	Normal	Subjects with stroke	
		Unaffected side	Affected side
	(n=20)	(n=27)	(n=27)
Elbow flexor co-contraction ratio (%)	13.4±8.7	9.0±4.8	12.5±5.9
Elbow extensor co-contraction ratio (%)	43.1±23.1	32.8±18.2	33.1±22.6

3.3.1.3 Associated reaction in the paretic upper limb

There was no elbow movement and no EMG activity in the biceps or triceps in the non-paretic arm during maximum hand grip of the paretic hands in stroke survivors. Control measurements during maximum grip tests with the normal subjects gave similar results. There was, however, elbow flexion (62.2 %), elbow extension (27.6%), and no elbow movement (11.2 %) of the paretic arm when the stroke survivors performed a maximum grip using their non-paretic hand.

3.3.1.4 Reaction time for paretic wrist flexion and extension

All the reaction times were analyzed using one-way ANOVA. The results showed that there were no significant differences in any of the variables between normal subjects and the unaffected sides of the stroke patients. The stroke survivors' affected hands, however, showed significant differences from the normal subjects ($P<0.01$) and from their unaffected hands ($P<0.01$) (Table 3.4, Fig. 3.2).

Table 3.4 RT for wrist flexion and extension in normal subjects and subjects with stroke

	Normal	Subjects with stroke	
		Unaffected side	Affected side
	(n=20)	(n=27)	(n=27)
Wrist flexion RT	209.5±61.4	292.9±94.2	464.3±206.5#
Wrist extension RT	201.4±51.9	274.4±106.6	310.8±164.6#

significant difference at the $P<0.01$ level when compared with the normal group and the unaffected side of subjects with stroke

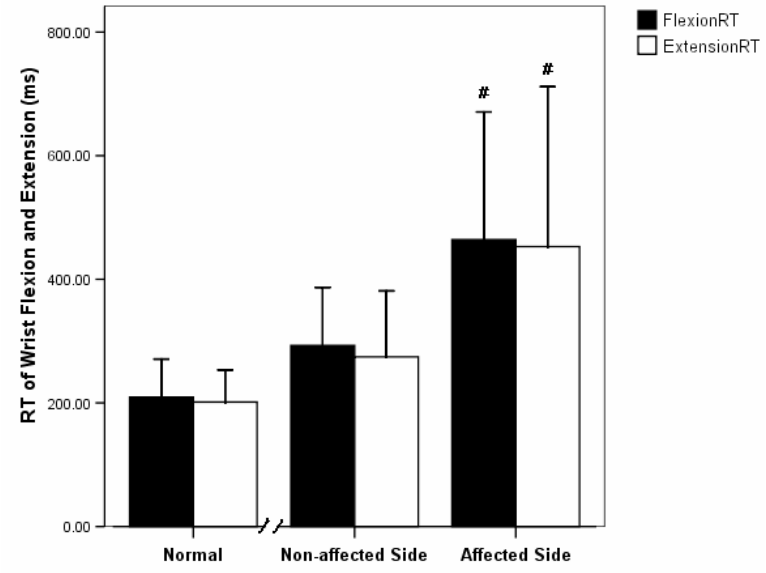


Fig 3.2 Reaction time of wrist flexion and wrist extension in normal subjects and stroke survivors. # significant difference at the $P<0.01$ level when compared with the normal subjects and the unaffected side of stroke survivors

3.3.2 Correlations among quantitative measurements and clinical assessments

3.3.2.1 MIVC force of elbow flexors and extensors and of paretic hand grip

Table 3.5 and Fig. 3.3 show that statistically significant correlations were found between the MIVC force recorded during elbow flexion in the affected arm and ARRS (negatively; ρ=-0.321, P=0.001), and WMFT functional ability (ρ=0.380, P<0.001) and time score (negatively; ρ=-0.389, P<0.001). The MIVC force recorded during elbow extension in the affected arm was found to produce similar results. It correlated with ARRS (negatively; ρ=-0.291, P=0.004), and WMFT functional ability (ρ=0.277, P=0.006) and time score (negatively; ρ=-0.302, P=0.002). The MVC (maximum voluntary contraction) force recorded during hand grip in the affected arm correlated moderately with CSI (negatively; ρ= -0.425, P<0.001), ARRS (ρ=-0.430, P<0.001), and WMFT functional ability (ρ=0.658, P<0.001) and WMFT time (negatively; ρ=-0.630, P<0.001).

Table 3.5 Correlation of MIVC recorded force during elbow flexion/extension and maximum hand grip with CSI, ARRS, and WMFT values in the paretic arm of patients with stroke

		Elbow flexion	Elbow extension	Hand grip
CSI	ρ	- 0.175	- 0.083	- 0.425#
	P	0.085	0.416	<0.001#
ARRS	ρ	- 0.321#	- 0.291#	-0.430#
	P	0.001#	0.004#	<0.001#
WMFT				
FAS	ρ	0.380#	0.277#	0.658#
	P	<0.001#	0.006#	<0.001#
Time	ρ	-0.389#	- 0.302#	- 0.630#
	P	<0.001#	0.002#	<0.001#

ρ denotes Spearman's correlation coefficient , # significant difference at the 0.01 level

(A) Elbow flexion (B) Elbow extension (C) Hand grip

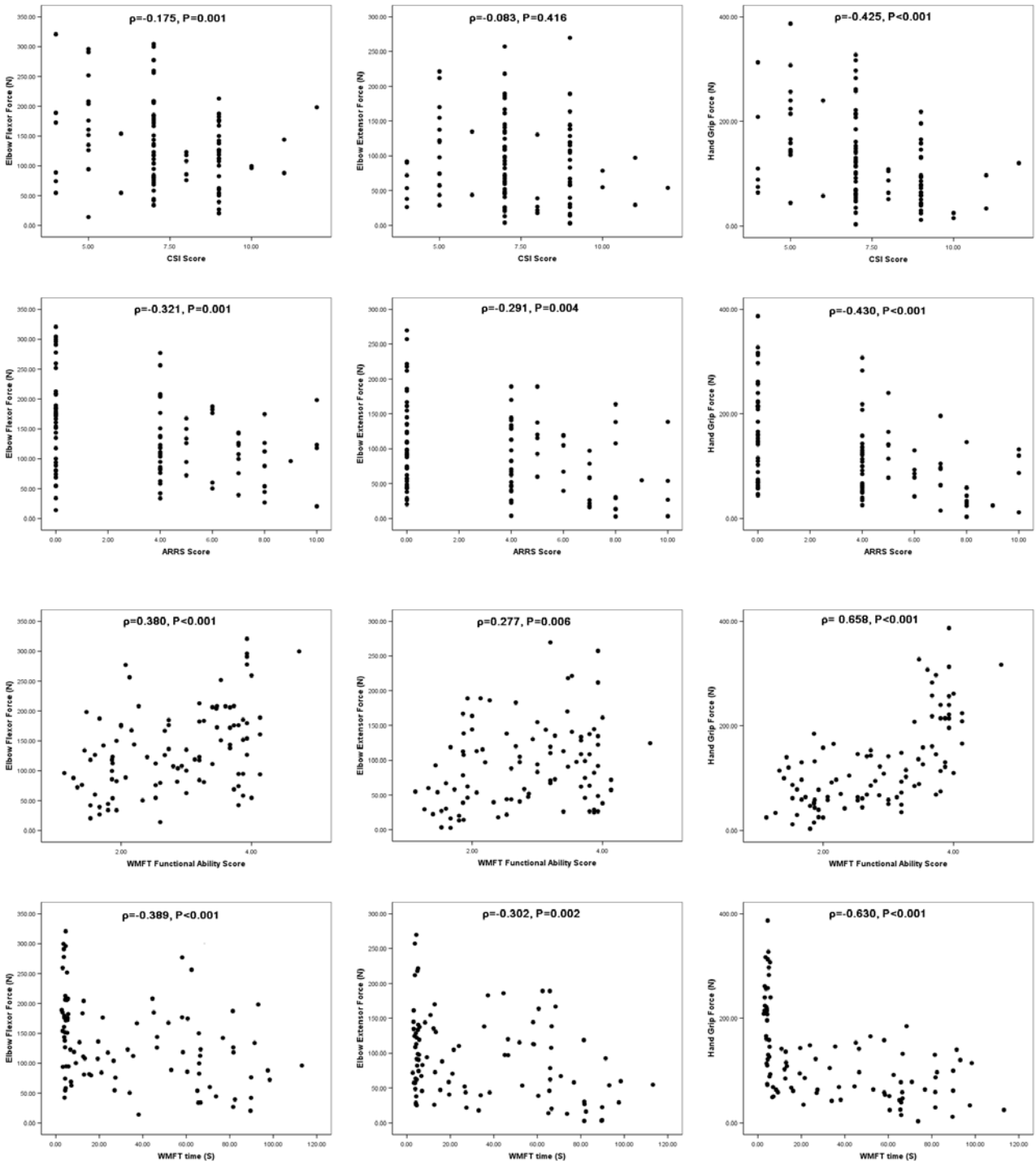


Fig. 3.3 Correlation of MIVC force during (A) elbow flexion, (B) extension and (C) hand grip with CSI, ARRS, and WMFT values in the paretic arm of patients with stroke

3.3.2.2 Co-contraction during MIVC of elbow flexors and extensors

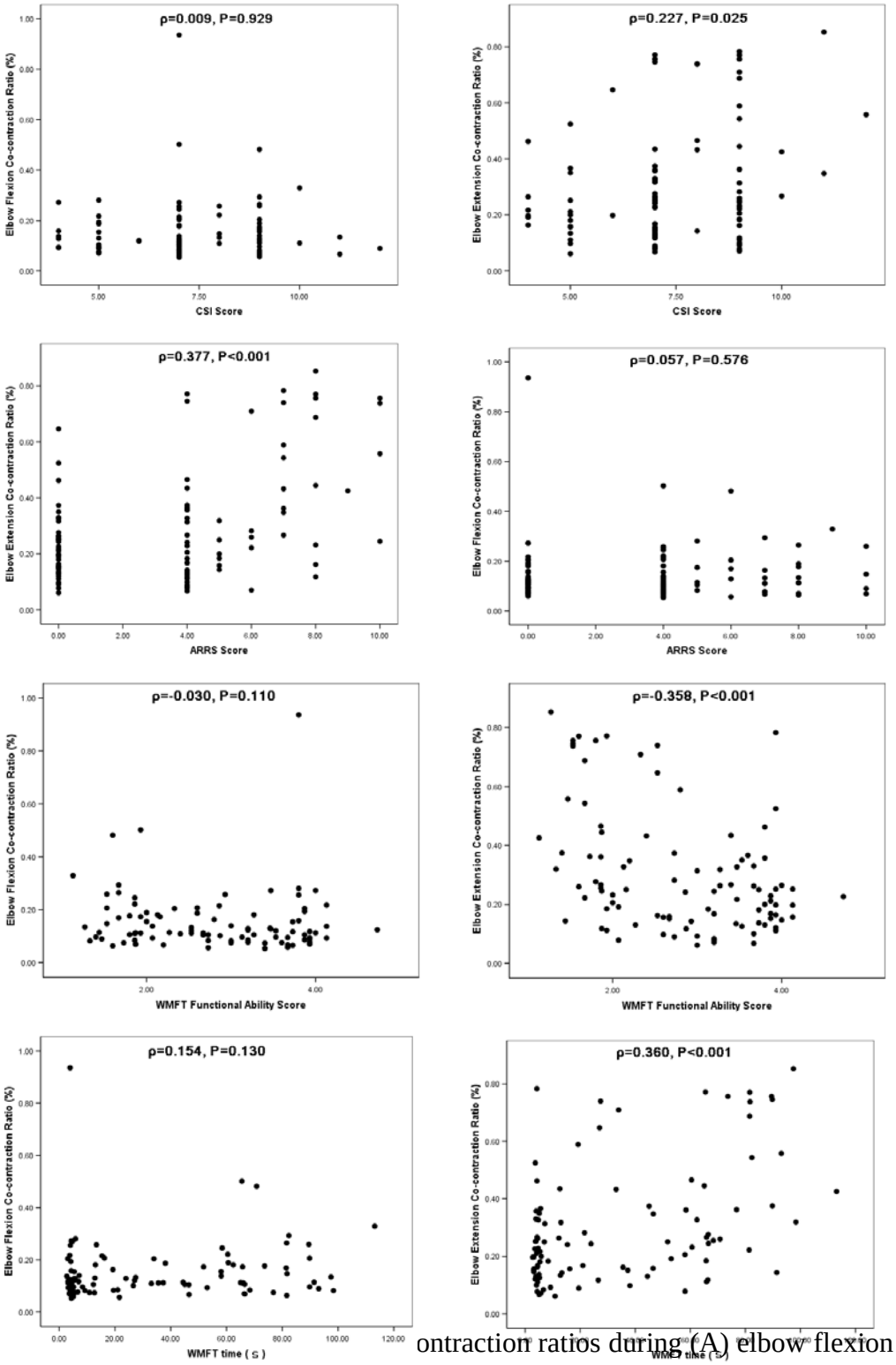
Spearman correlation analyses showed that there were no significant associations between the EMG co-contraction ratio during MIVC of elbow flexors and the CSI, ARRS, and WMFT results. However, the co-contraction ratio during MIVC of elbow extensors correlated moderately with CSI (ρ=0.227, P<0.05), ARRS (ρ=0.377, P<0.001), and WMFT functional ability (negatively; ρ=-0.358, P<0.001) and time score (ρ=0.360, P<0.001) (Table 3.6, Fig 3.4).

Table 3.6 Correlation of EMG co-contraction ratios during elbow flexion and extension with CSI, ARRS, and WMFT values in the paretic arm of stroke survivors

		Elbow flexion co-contraction ratio (%)	Elbow extension co-contraction ratio (%)
CSI	ρ	0.009	0.227*
	P	0.929	0.025*
ARRS	ρ	0.057	0.377#
	P	0.576	<0.001#
WMFT			
FAS	ρ	-0.030	-0.358#
	P	0.110	<0.001#
Time	ρ	0.154	0.360#
	P	0.130	<0.001#

ρ denotes Spearman's correlation coefficient ,* significant difference at the 0.05 level , # significant difference at the 0.01 level

(A) Elbow flexion (B) Elbow extension



ontraction ratios during (A) elbow flexion and (B) extension with CSI, ARRS, and WMFT values in the paretic arm

3.3.2.3 Associated reaction in the paretic upper limb

Table 3.7 and Figure 3.5 show that statistically significant correlations were found between the affected biceps normalized $IEMG_{AS}$ recorded during non-paretic hand grip as an index of associated reaction and CSI (ρ= 0.418, P<0.001), ARRS (ρ=0.557, P<0.001), and WMFT functional ability (negatively) (ρ=-0.561, P<0.001) and time score (ρ=0.559, P<0.001). Although the affected triceps $IEMG_{AS}$ recorded during non-paretic hand grip correlated marginally with the CSI (ρ=0.199, P=0.05), they correlated moderately with ARRS (ρ=0.371, P=0.001), and WMFT functional ability (negatively; ρ=-0.378, P<0.001) and time score (ρ=0.403, P<0.001).

Table 3.7 Correlation of the normalized $IEMG_{AS}$ of the paretic biceps and triceps recorded during non-paretic hand grip with CSI, ARRS, FM and WMFT scores in the paretic arm of stroke survivors

			Biceps normalized IEMG	Triceps normalized IEMG
CSI		ρ	0.418#	0.199*
		P	<0.001#	0.050*
ARRS		ρ	0.557#	0.371#
		P	<0.001#	<0.001#
WMFT	FAS	ρ	- 0.561#	- 0.378#
		P	<0.001#	<0.001#
	Time	ρ	0.559#	0.403#
		P	<0.001#	<0.001#

ρ denotes Spearman's correlation coefficient ,* significant difference at the 0.05 level , # significant difference at the 0.01 level

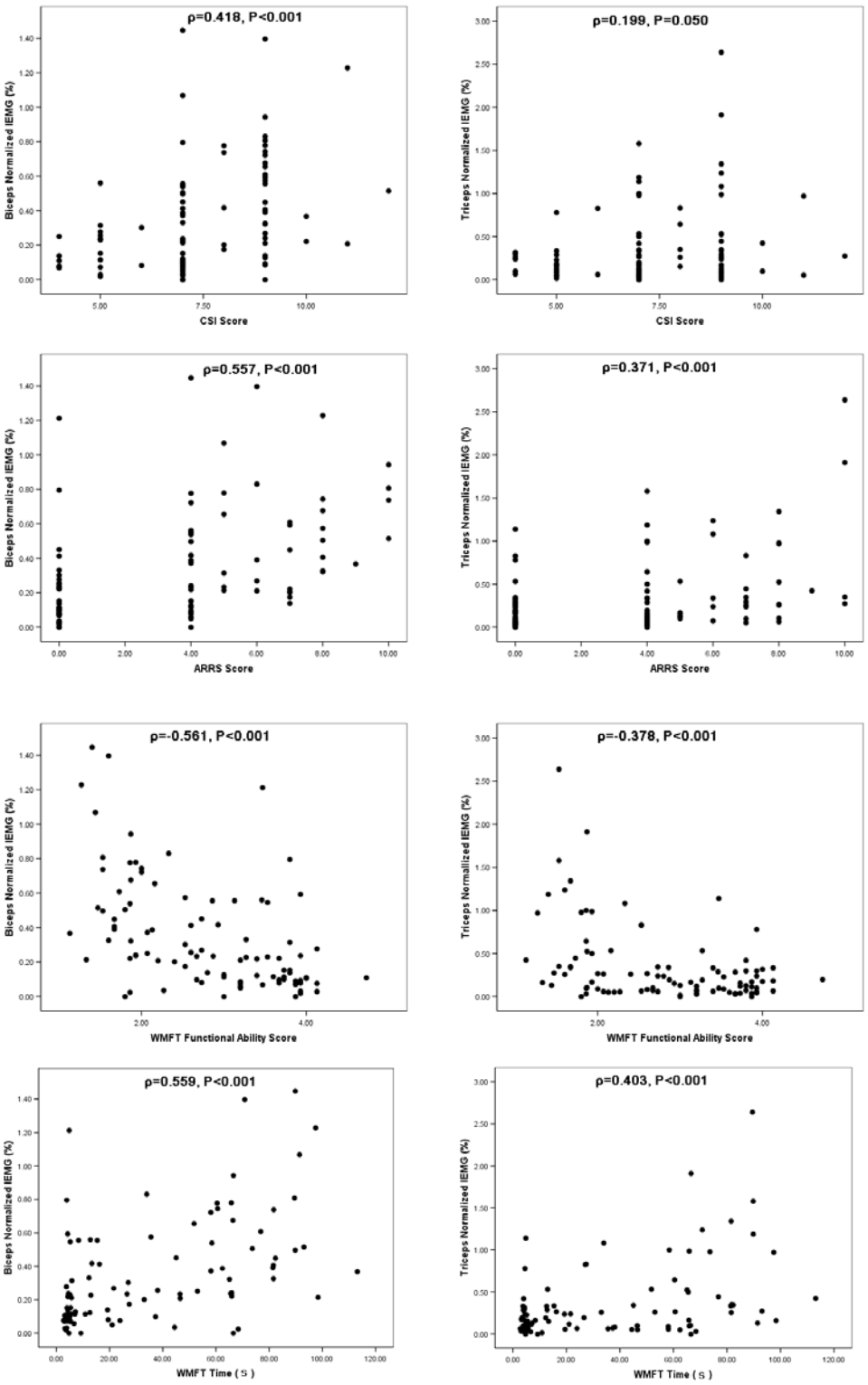


Fig. 3.5 Correlation of normalized $IEMG_{AS}$ of the paretic (A) biceps and (B) triceps during non-paretic hand grip with CSI, ARRS, FM and WMFT scores in the paretic arms of stroke survivors

3.3.2.4 Reaction time for flexion and extension of the paretic wrist

The wrist flexion RT correlated moderately with CSI (ρ=0.412, P<0.001) and ARRS (ρ=0.341, P<0.001), and moderately but negatively with WMFT functional ability (ρ=-0.0.531, P<0.001), and moderately with WMFT time score (ρ=0.504, P<0.001). The extension RT correlated similarly with CSI (ρ=0.429, P<0.001), ARRS (ρ=0.374, P<0.001), and WMFT functional ability (ρ=-0.0.531, P<0.001) and time score (ρ=0.486, P<0.001) (Table 3.8, Fig. 3.6).

Table 3.8 Correlation between wrist flexion and extension reaction time and CSI, ARRS, and WMFT values in the paretic arm of stroke survivor

		Wrist flexion RT	Wrist extension RT
CSI	ρ	0.412#	0.429#
	P	<0.001#	<0.001#
ARRS	ρ	0.341#	0.374#
	P	<0.001#	<0.001#
WMFT			
FAS	ρ	- 0.531#	- 0.531#
	P	<0.001#	<0.001#
Time	ρ	0.504#	0.486#
	P	<0.001#	<0.001#

ρ denotes Spearman's correlation coefficient , # significant difference at the 0.01 level

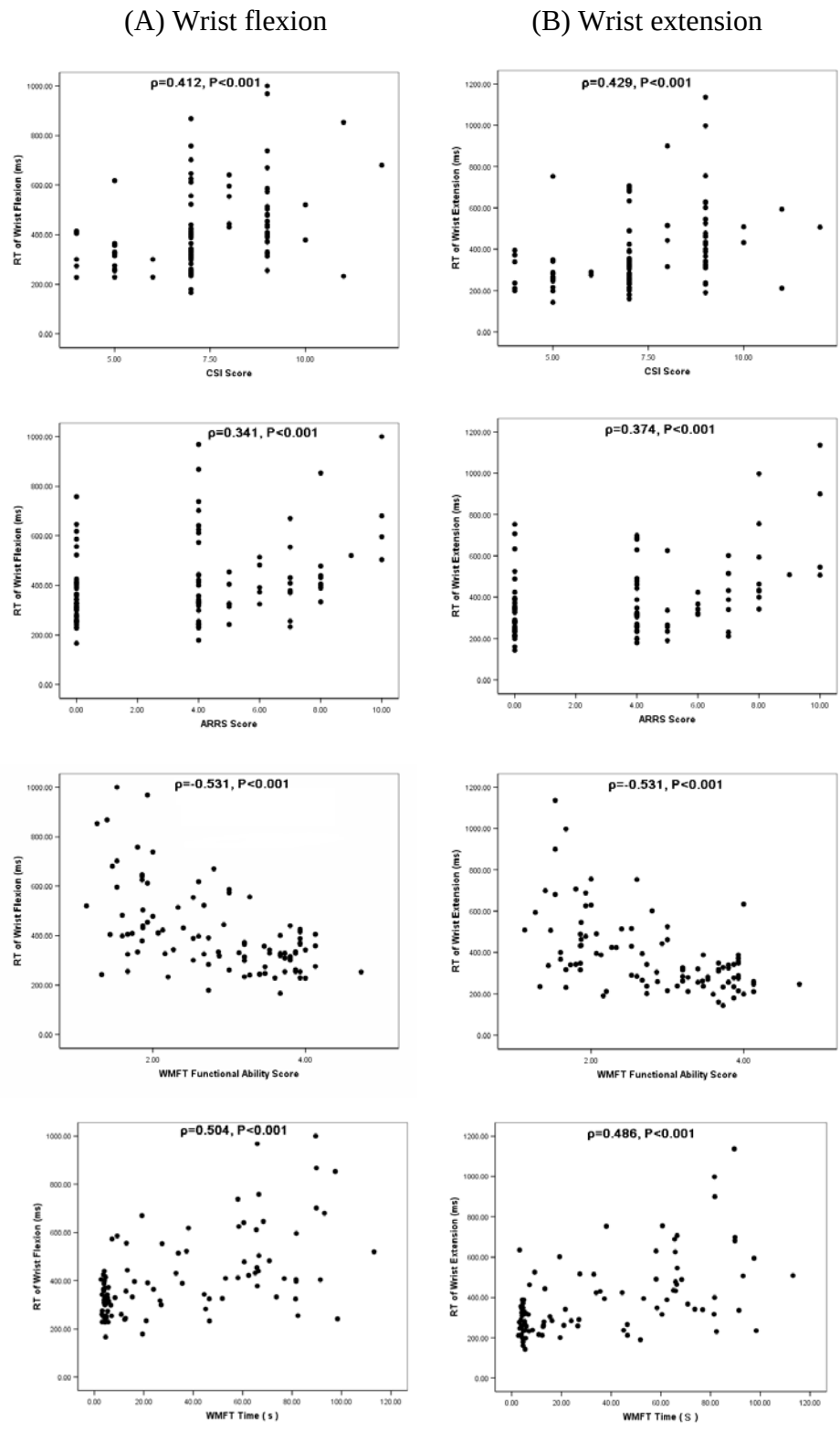


Fig. 3.6 Correlation of (A) wrist flexion and (B) extension RTs with CSI, ARRS, and WMFT scores in the paretic arm of stroke survivors

3.4 Discussion

3.4.1 MIVC force of elbow flexors and extensors and of paretic hand grip

The results showed that the force recorded during MIVC of elbow flexors, extensors and hand grip of the affected arm were significantly smaller than those of the non-affected arm in patients with stroke and of the normal subjects. There were no significant differences in these force data between non-affected arm in patients with stroke and the normal subjects (Table 3.2, Fig. 3.1). Statistically significant correlations were found between elbow flexion and extension MIVC force and ARRS and WMFT functional ability and time score. Furthermore, maximum hand grip force in the affected arm correlated moderately with CSI, ARRS, and WMFT functional ability and time score (Table 3.5, Fig. 3.3).

In our study, elbow flexor strength decreased to 45% and extensor strength decreased to 60% of that of the normal subjects. However hand grip strength decreased the most to 28%. The results were in line with the Frascarelli's study (1998) which showed the distal muscles to be more affected than the proximal ones. This study demonstrated that the first recruited motor unit showed a lower baseline firing rate in the distal muscles, and that they appeared significantly earlier in the affected distal than proximal locations. These findings suggest that the central nervous system in hemiplegic patients were unable to modulate the frequency of firing during minimal voluntary movements, thus distal muscles tend to behave like proximal muscles (Frascarelli et al. 1998). Our results further showed that there were no significant differences between the non-affected arm in patients with stroke and the normal subjects. These findings were different from those of Hsaio & Newham's (1999) who examined patients with acute rather than chronic stroke and measured maximal

movement velocity of both quadriceps and hamstrings in the affected lower rather than upper limb.

In our study, only hand grip strength was found to be correlated with the CSI score. A previous study found shoulder medial rotator and elbow flexor strength to be correlated with the spasticity of the agonist muscles measured by Ashworth scale (Bohannon et al. 1987). Note that the CSI score includes a measure of tendon jerk and clonus in addition to the resistance felt in response to passive muscle stretch as measured by the Ashworth scale. The different measuring tasks may partly explain why our results were different from those of Bohannon (1987). Interestingly, muscle strength of elbow flexor and extensor and hand grip strength demonstrated moderate but negative correlation with the ARRS assessing associated reactions.

Our study demonstrated that grip strength of the paretic hand was closely associated with motor functional performance in patients with stroke (Table 3.5). Other studies obtained similar results (Boissy et al. 1999, Sunderland et al.1989). In addition, table 3.5 showed that hand grip strength more strongly correlated with motor functional performance than elbow flexion or extension strength. This result was in line with the study of Mercier and Bourbonnais (2004). In conclusion, our results that UL muscle weakness especially that of hand grip strength may have a moderate impact on UL functional performance in patients with chronic stroke.

3.4.2 Co-contraction during MIVC of elbow flexors and extensors

The results of this study demonstrate that elbow flexion and extension co-contraction ratio in stroke survivors was not significantly different on the affected side than that on the unaffected side and from normal subjects (Table 3.3). These results are similar to those found in previous studies that the co-contraction ratios after stroke were similar to those of normal controls (Davies et al. 1996, Fellows et al.1994,

Gowland et al. 1992, Newham & Hsiao 2001, Tang & Rymer 1981). However, they differed from those of Kamper and Rymer (2001) who examined co-contraction of the extensor muscles of the metacarpophalangeal (MCP) joint in subjects with chronic hemiplegia, and found significant differences between the affected and non-affected side. Despite the lack of significant difference from the normal subjects, the co-contraction ratio during elbow extension correlated with the CSI, ARRS, and WMFT functional ability and time scores (Table 3.6). Activation of antagonist muscle pairs during a voluntary movement is largely reciprocal in nature (Gottlieb et al.1989), and co-activation of a muscle pair is normal when subjects perform isometric movements (Corcos et al.1990). The co-contraction ratio is modulated by two neural factors: agonist and antagonist activity. Both reducing the agonist activity and increasing the antagonist activity could cause the co-contraction ratio to increase. Following stroke, a lesion of the descending motor pathways either from the cerebral cortex, the subcortical white matter, the internal capsule, or the brainstem could decrease central excitation of the motor units (Shammy-Cook & Woollacott 2007). This could decrease the number of voluntary motor units recruited and the rate of their discharge to generate the amount of intended muscle torque or movement (Shammy-Cook & Woollacott 2007). Another reason could be a loss of inhibitory control causing hyperexcitability of the spinal motor neuron pool, which could also contribute to muscle weakness through reducing reciprocal inhibition of the affected antagonist (Heckman 1994).

Our results show that the EMG co-contraction ratio in elbow extension correlated moderately with CSI, ARRS, and WMFT functional ability and time scores (Table 3.6, Fig 3.4). The moderate correlation with CSI could be because the generation of elbow extension torque generation was coupled with a stretch-induced reflex in the spastic elbow. Our results are similar to those reported by Chae et al. (2002) in that

co-contraction in the affected UL muscles correlated significantly with motor impairment and physical disability. Though the pathophysiology of abnormal co-contractions of agonist and antagonist muscles is not thoroughly understood, the results might be explained as follows. Positive signs or stereotyped abnormalities appear following upper motor neuron injury. Abnormal co-contractions in hemiparesis are the clinical manifestation of such stereotyped abnormalities. In spastic muscles, loss of descending inhibitory input from the brain can cause impaired spinal segmental reflexes, including hyperactivity of spindle (Ia) and flexor reflex afferents, reduction of presynaptic Ia inhibition, alteration of synaptic activity and hyperactivity of the alpha motor neuron pool (Brown 1994, Mayer 1997). Abnormal co-contraction in spastic muscles might be caused by decreased reciprocal Ia inhibition. During a voluntary contraction of a spastic muscle, a lack of normal increase in reciprocal inhibition will increase antagonist co-activation (Morita et al. 2001). Therefore, decreased reciprocal inhibition and presynaptic inhibition of the Ia fibers might play a prominent role in abnormal co-contraction (Gracies 2005). In addition, loss of descending inhibitory input may cause increased dependence on the undamaged vestibulospinal, reticulospinal, and tectospinal pathways. These brainstem pathways may generate abnormal activation patterns through extensive branching, innervating neurons over many spinal segments. These may alter the torque patterns produced in the paretic arm of patients after stroke (Dewald et al. 1999, 2001).

3.4.3 Associated reaction in the paretic upper limb during non-paretic hand grip

Most reports on associated reactions in hemiparetic patients have been based on clinical observations or observed rates of recurrence (Brunnstrom 1970, Gelhom 1964, Michels 1970,. Mulley 1982, Walshe 1923). Associated reactions tend to occur in the same direction as the movement evoking the responses. That is, flexion tends to evoke

flexion reactions and extension tends to evoke extension reaction. According to Simon (1923), gripping an object with the normal hand usually evokes associated reactions on the affected side. MIVC of the unaffected hand grip may be the optimal movement to elicit associated reactions in UL muscles on the affected side (Boissy et al. 2000). After stroke, increasing the level of unaffected hand grip force has been observed to evoke increased shoulder flexion, internal rotation and elbow flexion on the affected side, accompanied by increased EMG activity of the biceps bracii, brachioradialis and triceps brachii muscles (Boissy et al. 1997).

The results of our study are partly consistent with many of the above findings. However, not all hemiplegic patients demonstrate associated reactions. About 11% of the patients did not produce significant force in the paretic elbow during maximal non-paretic hand grip. These results are similar to the clinical observations of Mulley (1982) that 80% of stroke patients manifested associated reactions in the hemiplegic arm. But they are not identical to the results of other studies, such as Boissy's (1997), in which all patients were found to produce elbow flexion torque. This may be due to Boissy's small sample. In our study, 62.2% of the patients generated secondary elbow flexion force. This agrees with previous observations by Brunnstrom (1970) that elbow flexion was the dominant associated reaction in the paretic UL.

Normalized $IEMG_{AS}$ readings from the paretic biceps and triceps during non-paretic hand grip were found to be correlated with both CSI and ARRS ratings, indicating that associated reactions were correlated with spasticity (Table 3.7, Fig.3.5). Other studies have obtained similar results (Hwang et al.2005, Nelles et al. 1998). Associated reactions were more prominent in spastic limbs than in the flaccid arm muscles of hemiplegia. Indeed, they are thought to exist only in the presence of some degree of spasticity and to be directly related to spasticity in magnitude (Cornall 1991). Previous studies based on clinical signs have given similar results. A number of

researchers have thought of associated reactions as widespread spasticity throughout the affected body side, especially in the paretic UL, appearing in a typical flexor pattern (Bobath 1990, Davies 1985, Hastings 1965). Although these studies were based on clinical observations, they were similar to those observed using EMG recordings in the paretic elbow muscles in our experiments. On the other hand, other studies have suggested that AR is not confined to patients with severe spasticity and that AR in the UL may occur with minimal spasticity as measured by the modified Ashworth scale (Bhakta 2001).

However, Ada and O'Dwyer (2001) found that associated reactions were not associated with spasticity and were not a valid indicator of spasticity. These studies assessed associated reactions by using a 50% MVC contraction of contralateral muscles rather the MVC as we had used here, and the incidence of associated reactions was found to be only 29%. Spasticity was measured in terms of tonic stretch reflex hyperactivity, unlike the other studies (Bhakta et al. 2001, Boissy et al.1997, Dickstein et al.1995, Dvir et al. 1993, 1996). In our study, spasticity was measured in terms of the more comprehensive CSI instead of tonic stretch reflex hyperactivity alone. These differences may partly account for the differences in findings among the various studies.

Spasticity and associated reactions are both results of upper motor neuron lesions. Associated reactions are one type of involuntary movement expressed as a result of so-called motor irradiation (Hwang et al.2005). Motor irradiation is the result of diffused or stereotyped radiation to other parts of the body during voluntary effort (Carson 2005). Patients with stroke could be unable to block the radiation and the overflow of excitation due to a lack of spatial and temporal inhibitory control from supraspinal control systems. Thus, they may require more effort to complete a task thereby activating propriospinal interneurons or contralateral motoneurons causing

motor irradiation (Wiesendanger 1991). A key feature of spasticity is a velocity-dependent increase in the resistance of a muscle or muscle group to passive stretch. The neural mechanism underlying spasticity is an abnormality within the segmental stretch reflex due to changes in descending control. A loss of descending inhibitory control could result in hyperexcitability of the alpha motorneuron pool, which could enhance stretch reflex activity (Mayer 1997).

Therefore, the 2 abnormalities, spasticity and associated reactions may have a similar pathological foundation: a lesion of an upper motor neuron causing a loss of upper neuron control, resulting in abnormal signs. This can explain why the associated reaction, as measured quantitatively in $IEMG_{AS}$ of the patient's elbow muscles during unaffected hand grip, was moderately correlated with spasticity (Table 3.7). The final finding that $IEMG_{AS}$ of the paretic elbow muscles recorded during unaffected hand grip were significantly correlated with WMFT functional ability and time score indicated that ARs, a motor impairment, have moderate relationship with functional disability in patients with stroke.

Though many studies have explored associated reactions following stroke, a number of unresolved questions remain, such as the reliability and validity of the clinical scales, suitable quantitative measures, and whether these reactions are indicators of muscle tone alone or of motor function as well. The results of our study showed that both the clinical ARRS and the quantitative $IEMG_{AS}$ measures of the patient's biceps and triceps recorded during non-affected hand grip were reliable, with ICC being 0.912 (P<0.001, Table 2.2), and 0.802 and 0.928 (P<0.01, Table 2.4), respectively. Furthermore, some 90% of our stroke sample manifested the AS as either elbow flexion (62.2%) or elbow extension (27.6%). The fact that the quantitative $IEMG_{AS}$ measure correlated with CSI, ARRS and WMFT scores suggest that the former is a valid indicator of muscle tone and motor functional performance in patients

with chronic stroke. The mechanisms underlying the associated reactions are subjects for future investigation.

3.4.4 Reaction time for paretic wrist flexion and extension

Reaction times of wrist flexion and extension on the stroke survivors' affected side were significantly longer than those on the unaffected side and those of the normal subjects. Because these RT measurements also have high intra-rater reliability (Table 2.5), they will serve as valid and reliable outcome measures for examining treatment efficacy in subjects with stroke. Our results further showed that wrist flexion and extension RT correlated moderately with CSI and ARRS and inversely with motor functional performance in the UL (Table 3.8).

The neuronal mechanism of simple reaction time has been investigated by Kansaku et al. (2004). In simple reaction time, sensory input project to multimodal sensory brain areas to be sent for motor processing. The shared neural substrate controlling movements produced by different body parts share an important role in mediating sensory inputs and motor output. Therefore, lesions of sensory input and motor output regions in the brain could both affect the reaction time of wrist movements on the affected side after stroke, the later being demonstrated by our findings of prolonged RTs in the paretic wrist (Table 3.4; Fig 3.2).

In normal people, various factors can affect RTs. For example, greater force output increases RT (Nagasaki et al.1983). In subjects with stroke, RT for both wrist flexion and extension on the affected side have been shown to be inversely correlated with the Medical Research Council score for muscle strength, but they were not correlated with the Ashworth scores for spasticity (Miscio 2006). However, wrist flexion and extension RT were found in our study to be correlated with spasticity as measured by the CSI (Fig. 3.6). Daly et al. (2006) found that the cortical planning time,

measured by motor-related cortical potential, was highly related to motor impairments after stroke. The longer the cortical planning time, the more severe the motor impairments. Cortical planning time is a component of reaction time, which consists of time for scheduling and planning in the central nervous system (CNS) and for signal transmission to the peripheral muscle involved (Fang et al. 2007). Preparing a difficult or novel motor task requires more time than an easier task (Schreiber et al. 1983). Wrist flexion or extension in the affected UL is more difficult in more severely affected patients, so the more severe patients may need a longer cortical planning time to complete the task. This may explain why the RT for flexion or extension of the affected wrist correlated moderately with motor impairment in UL as measured by CSI and ARRS in our study.

3.5 Conclusions

This chapter assessed some motor impairment of the upper limbs following stroke including EMG co-contraction ratios, associated reactions and reaction time. Our findings from **study 1** showed that MIVC force of the affected elbow flexors, extensors and hand grip in patients with chronic stroke was significantly smaller, and RT of their wrist flexion and extension was significantly longer than those of their non-affected UL and of normal subjects. During non-affected hand grip, associated reaction was mainly manifested as elbow flexion (62.2%) in the paretic UL. These 3 quantitative parameters were further found to be correlated moderately but significantly with the clinical scales of CSI (except for MIVC force of elbow flexors and extensors), ARRS, and WMFT functional ability and time scores, in either a positive or negative manner. These findings suggest that both quantitative and clinical assessments could serve as reliable and valid assessment tools to measure treatment effectiveness in patients with stroke over time in study 2.

CHAPTER 4

STUDY 2

TRANSCUTANEOUS ELECTRICAL NERVE STIMULATION AND TASK-RELATED TRAINING FOR PROMOTING UPPER LIMB MOTOR FUNCTION AFTER STROKE

Summary

The global aim of the main study was to examine the effectiveness of a program combining TENS with task-related training (TRT) in promoting motor recovery in the upper extremity of patients with chronic stroke. The research design was a randomized, controlled trial involving 77 subjects being randomly allocated to 4 groups. One group received TENS alone (n=20), another p-TENS + TRT (n=20), a third received TENS + TRT (n=18), and there was also a control group which received no active treatment (n=19). TENS, p-TENS or TRT was administrated 60 min a day one week for 8 weeks. Outcome measures were recorded in the paretic arm as follows: (1) the composite spasticity index (CSI), (2) maximum isometric voluntary contraction (MIVC) force of the elbow flexors and extensors, and hand grip, (3) reaction times (RTs) for wrist flexion and extension, and (4) functional ability and time scores of Wolf Motor Function Test (WMFT). Assessments were carried out before treatment on day 1 (baseline assessment), at week 4 (mid-way through the treatment), at the end of the 8-week treatment program, and at follow-up 4 weeks after treatment ended.

No significant differences were found in all the outcome measures at baseline, indicating homogeneity among the 4 subjects groups. Furthermore, there were no significant differences in the CSI and MIVC force of elbow flexion and extension and hand grip among the 4 groups at any assessment interval. However, significant differences between groups were found in the time domain. After 8 weeks of treatment, the TENS+TRT group showed a significantly greater percentage decrease in the reaction time of wrist flexion when (-16.8%) compared with the TENS group (an increase of 22.5%, $P<0.05$) and control group (an increase of 26.5%, $P<0.05$). The p-TENS+TRT group presented a significantly greater percentage decrease in the reaction time of wrist extension (-12.1%) when compared with the TENS group (an increase of 9.3%, $P<0.05$). At follow-up 4 weeks after treatment ended, only the

TENS+TRT group presented a significantly greater percentage decrease in wrist flexion RT (-11.6%) when compared with the control group (31.1%, P<0.05), and in wrist extension RT (-11.5%) when compared with the TENS group (26.5%, *P*<0.05). With regard to WMFT, the 2 groups receiving TRT (i.e. p-TENS+TRT and TENS+TRT) showed a significant percentage decrease of the WMFT time when compared with the control group after 8 weeks of treatment, being -26.1% and -28.0% respectively (*P*<0.05 for both).

In conclusion, the 2 groups receiving TRT showed significant improvements in UL motor function by having faster RT of either wrist flexion or extension, and faster WMFT time scores after 8 weeks of intervention. In TENS+TRT group the percentage decrease of wrist flexion RT in the compared with the control group and of wrist extension RT compared with the TENS group could even be carried over to the follow-up at week 12. The finding demonstrated the presence of carry over effects in the combined treat group.

4.1 Introduction

Previous studies have shown that transcutaneous electrical nerve stimulation (TENS) applied to the peroneal nerve can alleviate ankle spasticity and improve voluntary dorsiflexion in subjects with chronic stroke (Levin and Hui-Chan 1993). Electrical stimulation is known to bring about sensory and motor cortical reorganization (Golazewski et al. 2004, Kaelin-Lang et al. 2002, Wu et al. 2005) and was shown to promote paretic hand grip force (Conforto et al. 2002, Wu et al.2006). Other studies have shown that task-related training (TRT) was more effective than conventional therapies such as the Bobath approach for promoting motor function in patients with acute (Langhammer and Stanghelle 2000, Winstein et al.2004) and chronic stroke (Thielman et al. 2004).

More recently, investigators have begun to explore the combined effect of electrical stimulation and motor training on patients with stroke. Ng and Hui-Chan (2007) showed that TENS combined with TRT was generally significantly more effective than TENS alone in improving patients' lower limb muscle strength and gait velocity. The extent to which findings from the lower limb can be generalized to the upper limb is questionable. First, cortical representation of the lower limb is located on the medical hemisphere supplied by the anterior cerebral artery. In contrast, cortical representation of the hand and upper limb is located on the lateral hemisphere supplied by the middle cerebral artery, which is a common site for cerebral vascular accidents. Secondly, walking - except for its start and stop being under cortical control - is a rhythmical movement largely controlled by a central pattern generator located at the level of spinal cord (Pearson 2000). In contrast, the control of UL dexterity function is much more complex and is presumed to be predominantly under cortical control (Shumway-Cook & Woollacott 2007).

Following somatosensory electrical stimulation of the median nerve and motor training, Conforto et al. (2007) found that the improvement in motor performance was significantly greater than after control stimulation at intensity below that eliciting paresthesia. Celnik et al. (2007) also demonstrated that somatosensory electrical stimulation could enhance the effects of hand training in patients with stroke. In another study, McDonnell et al. (2007) showed that patients with stroke receiving afferent stimulation combined with task-specific training performed significantly better in a grip-lift task than those receiving sham stimulation with task-specific training. But there was no statistically significant difference in the Action Research Arm Test or Fugl-Meyer Assessment scores between the 2 groups.

These results suggest that combining TENS with TRT for the upper limb may promote greater recovery in motor performance than either treatment alone in patients with chronic stroke. However, some of the studies used the same training protocol to assess the patients (Celnik et al. 2007, Conforto et al. 2007). Thus, learning effect cannot be excluded when using the same tool to assess the treatment effect. As for the study by McDonnell et al.(2007), the location of electrical stimulation was on the first dorsal interosseous and abductor pollicis, muscles which were in involved with the grip-lift task. But in clinical assessment such as the Action Reach Arm Test and Fugl-Meyer Assessment, no significant difference was found between the 2 groups. Furthermore, this study did not include a pure electrical stimulation group, thus the effect of pure electrical stimulation could not be determined.

Therefore, this study was designed to compare the treatment effects among 4 groups (TENS, p-TENS+TRT, TENS+TRT and control group). Patients with stroke received a training protocol in this study which was different from the assessment protocol to exclude the learning effect. We also carry out more sensitive clinical assessment scale i.e. WMFT functional ability and time scores, and other quantitative

measures such as force and RT to obtain more comprehensive results. The main aim of this research was to compare the effectiveness of a program combining TENS with task-related training in promoting motor recovery in the upper extremity of patients after stroke with either TENS or p-TENS+TRT treatment or no treatment (control).

4.2 Methods

4.2.1 Study design

A randomized, controlled trial was designed to compare 3 treatments with a control receiving no treatment. The sample size was calculated using the "Java applets for power and sample size" software described in Chapter 2 (section 2.2.3). Fig.4.1 showed the total of 623 candidates were screened, and 104 subjects who fulfilled the inclusion criteria were selected. Please refer to the inclusion and exclusion described in Chapter 2 (sections 2.1.1). Twenty-seven of the subjects withdrew before treatment. The 77 remaining subjects were divided into 4 groups using the randomization procedure described in Chapter 2 (section 2.2.3). The groups were:

Group 1: TENS alone (60 min)

Group 2: placebo-TENS (60 min) plus (TRT) (60 min)

Group 3: TENS (60 min) + TRT (60 min)

Group 4: control with no active treatment

The treatment in Groups 1, 2 and 3 was conducted by a physiotherapist. A doctor blinded to the treatment received by the patients conducted the assessments.

4.2.2 Subjects

A total of 623 subjects were screened. Five hundred and nineteen subjects were excluded because of being < 12 months after a stroke, scoring < 8 in AMT, and having major orthopaedic or chronic pain conditions. One hundred and four subjects fulfilled

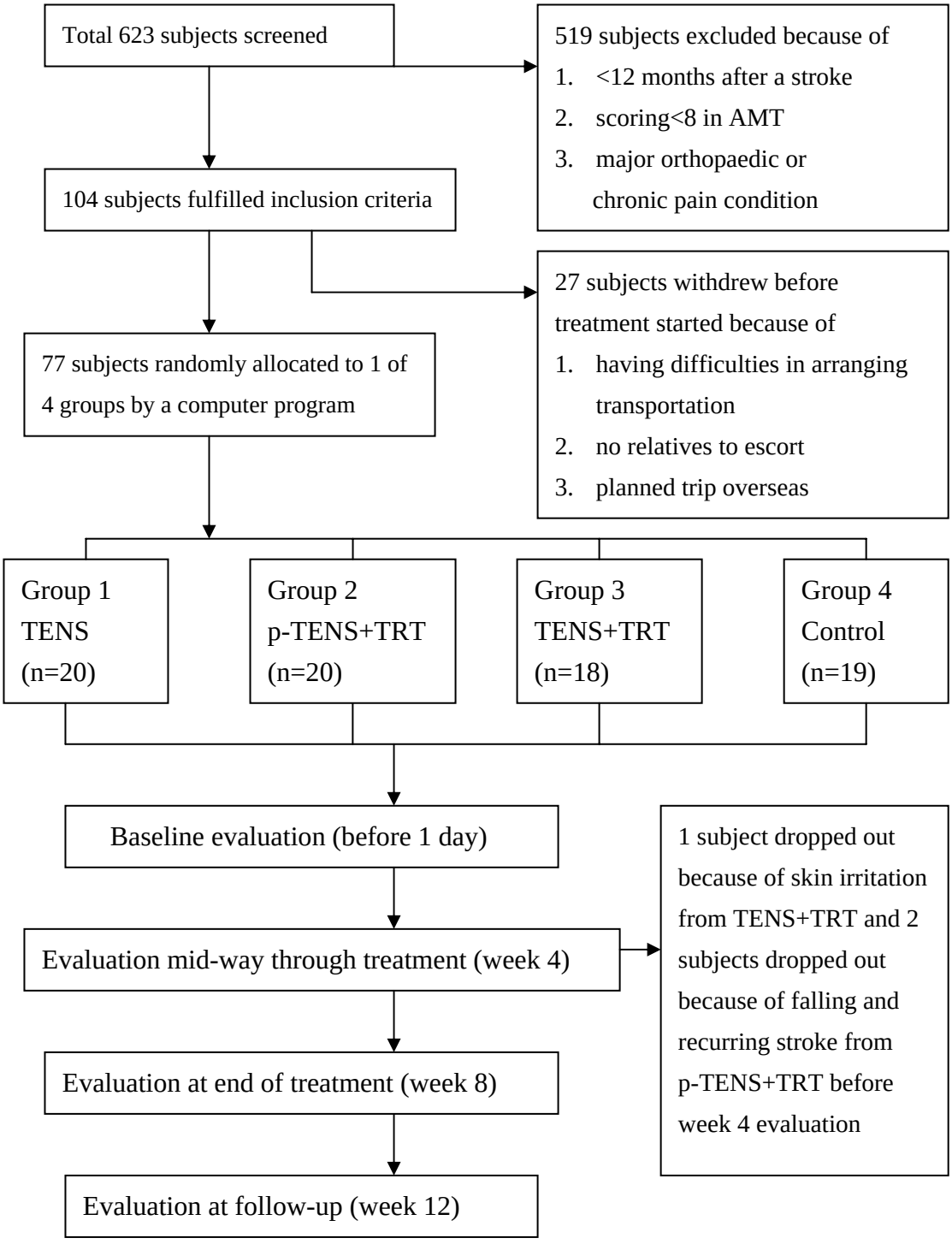


Fig. 4.1 Flow chart of subject recruitment and time schedule of treatment and assessment.

the inclusion criteria, but 27 subjects withdrew before treatment started because they had either difficulties arranging transportation, or no relatives to escort them, or overseas trips. Seventy-seven subjects with hemiplegia participated in this study (Table 4.1). The mean age of the subjects was 59.4±7.5 years, and the mean duration post-stroke was 48.2±33.5 months. The study protocol was approved by The Hong Kong Polytechnic University before the subjects were recruited. After giving their informed consent, the subjects were randomly assigned to 1 of the 4 groups: TENS (n=20), placebo-TENS + TRT (n=20), TENS + TRT (n=18), and the control group without active treatment (n=19) (Fig. 4.1). Three patients dropped out because of falling, stroke recurrence or irritation in response to TENS.

Relevant demographic characteristics of the subjects are presented in Table 4.1. There were no significant differences among the groups in baseline measurements of the study variables recorded before the experiment. Therefore, any significant changes after treatment should be due to the intervention received by the particular group.

4.2.3 Interventions

The TENS and TRT treatment protocols have been described in Chapter 2 (sections 2.2.5-2.2.6) and will not be reiterated here.

4.2.4 Outcome measurements

The following outcome measures were recorded in the paretic arm: (1) the Composite Spasticity Index (CSI), (2) the maximum isometric voluntary contraction (MIVC) force of elbow flexors and extensors and of hand grip, (3) the reaction time for wrist flexion and extension, and (4) the WMFT functional ability and time scores.

Assessments were carried out before treatment on day 1 (the baseline assessment), at week 4 (mid-way through treatment), and at week 8 at the end of the 8 weeks of treatment, and 4 weeks after treatment ended (the follow-up assessment).

4.2.5 Statistics

The CSI scores, MIVC forces, reaction times and WMFT functional ability and time scores were analyzed using repeated measures analysis of variance (ANOVA) to compare the main effects. The between-subjects factors were the 4 subjects groups: TENS, p-TENS + TRT, TENS + TRT, and control with no active treatment. The within-subjects factors were the 4 assessment intervals: pre-treatment, week 4, week 8 and follow-up. If significant differences were found, post-hoc test (Bonferroni) was used to compare treatment effects among the 4 groups. To obtain the between group differences at each assessment interval, one-way ANOVA was used to compare the results among each assessment interval, followed by post hoc test (Bonferroni). Because force production is related to a subject's body mass index (BMI) as a confounding factor, co-variance analysis was applied to analyze the elbow flexion and extension and hand grip force data. The study was carried out over a 12-week period, so some patients dropped out. To take this into consideration, analysis of the outcomes was based on the intention-to-treat approach, which included all the patients who had received at least one assessment in addition to the baseline data. Within the intention-to-treat approach, the last observation carried forward model was used. The significance level was set at 5%.

Table 4.1 Characteristics of the subjects for each group

	TENS	p-TENS+TRT	TENS+TRT	Control
Number of subjects	20	20	18	19
Number of dropouts	0	2	1	0
Age (years)	58.4±8.0	57.8±8.5	61.2±5.9	60.4±7.4
Gender: M	14	14	13	12
F	6	6	5	7
Weight (kg)	68.2±12.1	68.9±11.5	70.4±12.3	71.1±11.6
Height (m)	1.7± 0.2	1.7± 0.3	1.7± 0.1	1.7± 0.1
BMI (kg/m^2)	24.1± 5.5	25.3± 6.1	26.3± 4.6	26.2±3.7
Paretic arm: Left	8	10	11	12
Right	12	10	7	7
Type of stroke: Ischemic	14	12	11	16
Hemorrhagic	6	8	7	3
Duration post-stroke (months)	49.8±26.2	45.5±30.1	54.8±43.2	42.9±34.7
CSI (score)	7.2±1.8	7.2±1.7	7.1±1.8	7.3±1.7
Fugl-Meyer (score)	34.8±15.4	36.1±10.6	39.7±12.7	33.3±12.1
WMFT : Functional ability (score)	2.9±0.9	2.8±0.9	2.9±0.9	2.8±0.9
Time (s)	43.7±37.6	31.2±26.1	26.9±30.1	32.6±33.4

Values are mean ± SD. No statistically significant difference was found among the groups before treatment.

4.3 Results

4.3.1 Muscle tone

Table 4.2 presents the mean CSI scores and the percentage changes relative to the baseline score for the 4 group at the different assessment intervals. There were no

significant differences in the CSI scores among the 4 groups at any assessment interval, nor in the percentage change relative to the score at week 0.

Table 4.2 Comparison of the mean score and % change in the CSI among the 4 groups

	TENS	p-TENS+TRT	TENS+TRT	Control
Week 0 (score)	7.2± 1.8	7.2± 1.7	7.1± 1.8	7.3± 1.7
Week 4 (score)	6.9± 1.4	7.0± 1.2	6.7± 1.2	7.3± 1.7
Week 4-Week 0/Week 0 (%)	-1.4± 6.4	-2.1±12.5	-7.1±11.0	-1.6± 7.5
Week 8 (score)	7.1± 1.8	6.9± 1.9	6.9± 1.8	7.4± 1.9
Week 8-Week 0/Week 0 (%)	-1.1±16.7	-6.9±10.0	-5.7±15.8	-1.6±15.5
Week 12 (score)	6.9± 1.7	7.1± 2.2	7.0± 1.6	7.2± 2.1
Week 12-Week 0/Week 0 (%)	-1.1±15.5	-3.3±12.1	-4.1±16.6	-0.6±14.1

Values are mean ± SD. CSI denotes the Composite Spasticity Index. No statistically significant difference was found among the 4 groups at any time interval.

4.3.2 MIVC force of elbow flexors and extensors and of paretic hand grip

Tables 4.3 and 4.4 present the mean values of the MIVC force of elbow flexor and extensor force and of hand grip recorded at weeks 0, 4, 8 and 12 on the affected side, and the percentage changes compared with week 0. No significant difference among the groups was found in terms of either the force or their percentage change.

Table 4.3 Comparison of maximum isometric voluntary elbow flexion and extension force among the 4 groups

	TENS	p-TENS+TRT	TENS+TRT	Control
Elbow flexion				
Week 0 (N)	142.2±73.8	149.2±78.0	149.3±77.0	129.9±73.7
Week 4 (N)	147.0±79.4	152.9±69.6	137.1±71.2	117.7±70.3
Week4-Week0/Week 0(%)	6.0±30.1	11.6±35.5	-1.0±34.2	-6.8±29.4
Week 8 (N)	157.9±71.0	138.5±72.7	150.5±74.5	123.8±71.5
Week8-Week0/Week 0(%)	22.7±45.1	-2.3±31.2	9.6±38.5	-1.7±32.0
Week 12 (N)	156.1±67.2	153.0±69.1	143.8±79.4	130.2±76.4
Week12-Week0/Week 0(%)	21.5±43.5	15.1±45.7	-3.4±28.5	3.6±32.1
Elbow Extension				
Week 0 (N)	82.7±56.0	104.6±67.1	101.9±72.8	77.4±47.9
Week 4 (N)	97.4±60.0	103.3±50.6	93.2±53.2	75.2±41.5
Week4-Week0/Week 0(%)	43.7±84.4	26.9±87.6	27.0±85.3	11.7±50.0
Week 8 (N)	100.3± 73.4	97.1±52.3	98.4±58.2	80.7±54.5
Week8-Week0/Week 0(%)	57.4±170.3	8.8 ±59.4	14.3±54.7	12.3±60.2
Week 12 (N)	94.1±59.1	89.0±60.4	101.8± 55.5	76.0±50.2
Week 12-Week 0/Week 0(%)	45.9±96.1	-2.9±58.8	48.5±137.6	6.5±64.3

Values are mean ± SD. No statistically significant difference was found among the 4 groups at any time interval.

Table 4.4 Comparison of maximum voluntary grip force in the affected hand among the 4 groups

	TENS	p-TENS+TRT	TENS+TRT	Control
Week 0 (N)	127.2±97.1	124.2±72.4	132.2±74.6	126.4±104.6
Week 4 (N)	128.5±99.0	125.3±60.3	147.6±95.0	125.3±98.0
Week 4-Week 0/Week 0 (%)	11.6±55.3	14.3±49.1	38.5±113.7	20.1±62.4
Week 8 (N)	120.9±99.0	132.0±60.1	143.6±79.1	133.8±111.5
Week 8-Week 0/Week 0 (%)	9.6±45.2	24.2±54.6	15.1±38.1	17.7±65.0
Week 12 (N)	129.8±102.8	129.9±102.8	155.3±83.7	135.5±98.8
Week 12-Week0/Week 0 (%)	8.2±25.1	18.6±44.8	37.2±71.3	79.9±261.0

Values are mean ± SD. No statistically significant difference was found among the 4 groups at any time interval.

4.3.3 Reaction time for wrist flexion and extension in the paretic arm

Table 4.5 presents the mean values and percentage changes in reaction time for wrist flexion and extension in the paretic arm of the 4 groups at weeks 0, 4, 8 and 12. Figure 4.2 presents the percentage changes graphically. Baseline wrist flexion and extension RTs were comparable among the 4 groups (F=1.286, *P*=0.286; F=1.376, *P*=0.257 respectively). Repeated-measures ANOVA showed significant effects of groups (F=4.611, *P*=0.005) and no significant effects of time (F=0.435, *P*=0.615) and groups by time interaction (F=1.209, *P*=0.309) in percentage change of wrist flexion RT. It showed that percentage decrease of wrist flexion RT was greater in p-TENS+TRT and TENS+TRT group than that in control group (*P*=0.039, *P*=0.022 respectively). The results obtained for each assessment interval tested by means of one-way ANOVA followed by post hoc tests showed that, by week 8, the TENS+TRT

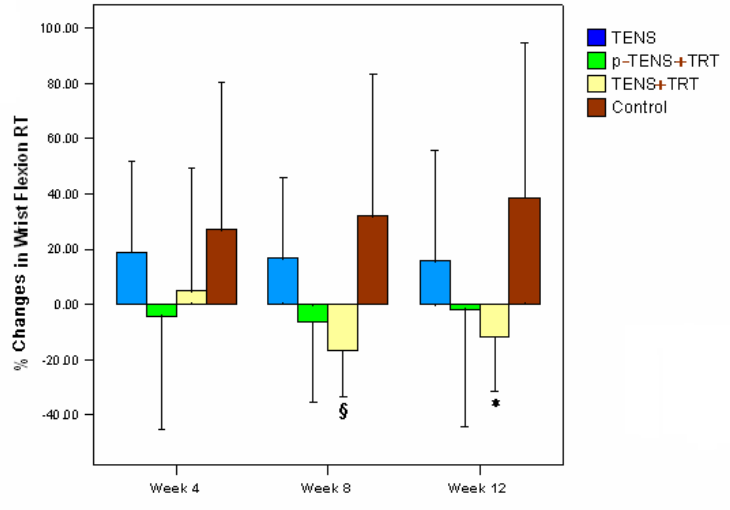
group had significantly greater percentage decrease in wrist flexion RT than

Table 4.5 Comparison of wrist flexion and extension reaction time among the 4 groups

	TENS	p-TENS+TRT	TENS+TRT	Control
Wrist flexion				
Week 0 (ms)	440.7±158.3	399.8±129.6	422.2±215.9	343.4±140.9
Week 4 (ms)	503.8±168.5	354.5±126.8	404.5±202.1	387.0±123.1
Week 4-Week 0/Week 0(%)	18.3±31.0	-5.1±38.8	5.1±44.1	23.5±51.4
Week 8 (ms)	517.6±183.4	349.7±74.5	336.5±175.9	401.2±147.8
Week 8-Week 0/Week 0(%)	22.5±42.2	-6.4±27.3	-16.8±16.5 §	26.5±51.7
Week 12 (ms)	495.9±195.9	355.1±78.3	379.8±274.0	417.4±172.6
Week 12-Week 0/Week 0(%)	17.7±42.6	-2.1±39.9	-11.6±20.1*	31.1±58.0
Wrist extension				
Week 0 (ms)	422.1±168.9	357.1±130.6	401.2±233.0	322.0±121.7
Week 4 (ms)	454.1±167.7	315.4±98.7	365.3±170.5	345.3±114.5
Week 4-Week 0/Week 0(%)	13.8±37.8	-5.2±28.7	-1.9±35.6	13.7±35.8
Week 8 (ms)	474.1±168.3	292.9±86.6	354.0±223.9	344.3±122.5
Week 8-Week 0/Week 0(%)	19.3±40.3	-12.1±26.8#	-7.5±25.6	12.6±39.4
Week 12 (ms)	515.0±271.2	311.8±101.8	356.5±245.8	367.3±152.5
Week 12-Week 0/Week 0(%)	26.5±57.3	-8.0±24.9	-11.5±18.7#	18.7±44.7

Values are mean ± SD. * denotes significant difference (P<0.05) when compared with the control group. # denotes significant difference (P<0.05) when compared with the TENS group. § denotes significant difference (P<0.05) when compared with the TENS group and control group.

(A)



(B)

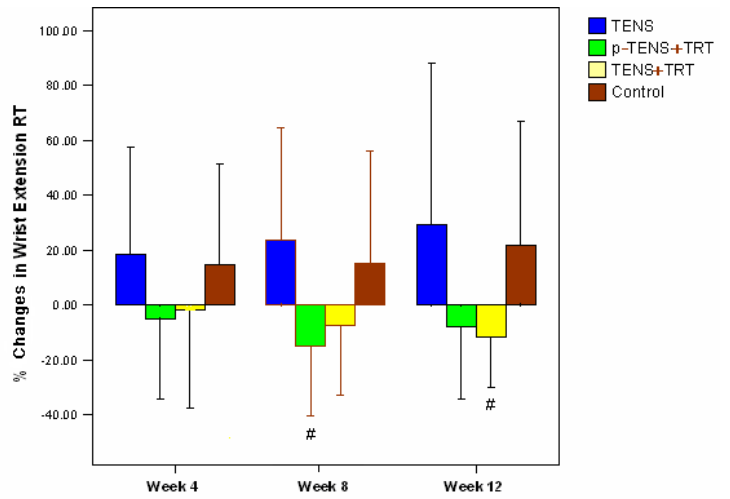


Fig. 4.2 Percentage change in the reaction time for (A) wrist flexion and (B) extension at weeks 4, 8 and 12 among the 4 groups.

Values are mean ± SD. * denotes significant difference (P<0.05) when compared with the control group. # denotes significant difference (P<0.05) when compared with the TENS group. §denotes significant difference (P<0.05) when compared with the TENS group and control group.

either the TENS group (P=0.013) or the control group (P=0.006), but the p-TENS+TRT group only differed from the control group at a marginal level (P=0.052). Four weeks after treatment ended at week 12, the TENS+TRT group maintained the

significantly greater percentage decrease in their wrist flexion RTs than the control group (P=0.023). (Table 4.5, Fig 4.2).

Similar results were obtained for wrist extension reaction times as shown in Fig. 4.2. Repeated-measures ANOVA showed significant effects of groups in percentage decrease of wrist extension RT (F=5.163, P=0.003), and no significant effects of time (F=0.261, P=0.757) and groups by time interaction (F=0.573, P=0.751). It showed that the percentage decrease of wrist extension RT was greater in p-TENS+TRT and TENS+TRT group than that in TENS group (P=0.014, P=0.030 respectively). The results obtained for each assessment interval by means of one-way ANOVA followed by post hoc test showed that the p-TENS+TRT group had significantly better percentage decrease than the TENS group (P=0.031) at week 8. At week 12, the p-TENS+TRT group only showed a tendency towards greater percentage decrease than the TENS group (P=0.056). However, the TENS+TRT group again maintained the greater percentage decrease in wrist extension RT When compared with the group receiving TENS alone (P=0.033).

4.3.4 Upper limb motor function

Table 4.6 and Fig. 4.3 present the mean values and percentage changes in the WMFT functional ability and time score for the 4 patient groups.

Baseline WMFT functional ability and time scores were comparable among 4 groups (F=0.449, P=0.719; F=0.961, P=0.416 respectively). Repeated-measures ANOVA showed significant effects of time (F=11.758, P<0.001) and groups by time interaction (F=2.345, P=0.036), but not groups (F=1.862, P=0.143) and groups by time interaction (F=2.345, P=0.036) in the percentage changes of WMFT functional ability. It also showed significant effects of time (F=11.979, P<0.001), but not groups (F=0.282, P=0.042) and groups by time interaction (F=2.122, P=0.057) in the percentage change

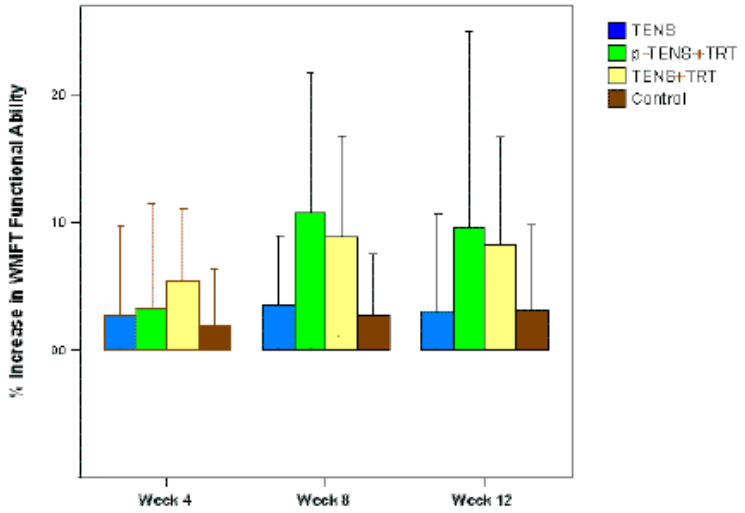
of WMFT time scores. Only at week 8 did the p-TENS+TRT group and the TENS+TRT group show a significant percentage decrease in their WMFT time scores when compared with the control group (P=0.029, P=0.014 respectively), (Table 4.6, Fig. 4.3).

Table 4.6 Comparison of WMFT functional ability and time scores among the 4 groups

	TENS	p-TENS+TRT	TENS+TRT	Control
Functional ability				
Week 0 (score)	2.9±0.9	2.9±0.9	2.9±0.9	2.8±0.9
Week 4 (score)	3.0±0.8	2.9±0.8	3.1±0.8	2.8±0.8
Week 4-Week 0/Week 0(%)	3.4±6.5	2.9±7.9	5.4±5.7	1.8±4.3
Week 8 (score)	3.2±0.9	3.1±0.9	3.2±0.9	3.0±0.9
Week 8-Week 0/Week 0(%)	4.4±6.9	9.7±10.8	8.9±7.8	2.9±4.8
Week 12 (score)	2.7±1.1	2.7±1.1	2.7±1.1	2.6±1.1
Week 12-Week 0/Week 0(%)	3.9±8.6	8.6±14.8	8.2±8.4	3.2±6.5
Time				
Week 0 (s)	43.7±37.6	31.2±26.1	26.9±30.1	32.6±33.4
Week 4 (s)	40.6±36.0	28.5±25.1	22.0±25.4	28.7±30.0
Week 4-Week 0/Week 0(%)	-10.7±16.3	-10.6±17.5	-16.1±18.2	-8.1±15.2
Week 8 (s)	39.7±36.5	24.0±24.0	19.1±24.8	29.7±30.9
Week 8-Week 0/Week 0(%)	-18.8±20.2	-26.1±19.7*	-28.0±17.1*	-8.6±10.7
Week 12 (s)	39.9±35.3	25.6±25.4	20.7±24.7	29.6±32.3
Week 12-Week 0/Week 0(%)	-17.4±19.9	-22.3±21.7	-23.0±24.2	-13.3±17.9

Values are mean ± SD. * denotes a significant difference at the 5% level when compared with the control group.

(A)



(B)

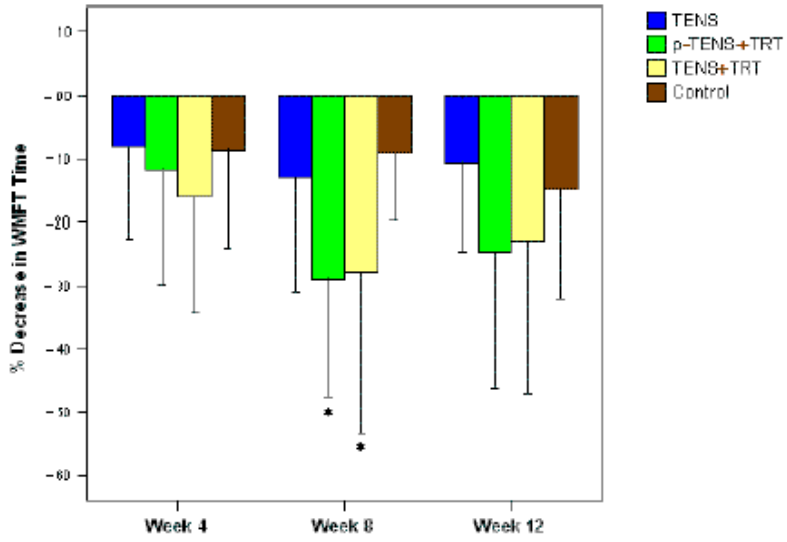


Fig. 4.3 Percentage change in WMFT (A) functional ability (B) and time score

* denotes a significant difference at the 5% level when compared with control group.

4.4 Discussion

4.4.1 Effects on muscle tone

The results show a lack of significant changes in the CSI scores at every assessment interval. Electrical stimulation and/or task-related training were not able

to decrease spasticity as measured by the CSI score in the upper limbs of stroke survivors. The effect of electrical stimulation on spasticity has been investigated for a long time. Levine et al. (1952) showed that stimulating a muscle antagonistic to the spastic muscle resulted in relaxation of the spastic muscle. TENS can produce a significant reduction in upper extremity spasticity and a significant increase in elbow extension torque after 4 weeks (Kim 1994). Low levels of cutaneous electrical stimulation over the biceps muscle have produced significant reductions in reflex torque in the triceps for at least 30 minutes in hemiparetic stroke survivors (Dewald et al.1996). Functional electrical stimulation with an implanted peroneal nerve stimulator for 6 months can reduce tonic activity in both the tibialis anterior and triceps surae muscles in stroke survivors (Stefanovska et al. 1988). TENS applied over the peroneal nerve has resulted in decreased plantarflexor spasticity and greater dorsiflexor force production in stroke patients (Levin & Hui-Chan 1992, Ng & Hui-Chan 2007). But in the present study, electrical stimulation and/or task-related training failed to decrease spasticity significantly. The reason may be that most of the subjects had only mild spasticity with a baseline CSI score of 7.1 to 7.3 when compared to that of 11.8 to 12.2 in the study by Ng and Hui-Chan (2007), so any reduction might not have been evident.

4.4.2 Effects on muscle strength

Though the TRT program included some strength training, it was not the main objective of the training protocol. Therefore, the results showed no significant change in MIVC force for elbow flexion or extension or for hand grip. Morris et al. (2004) have reviewed 3 randomized, controlled trials and 5 pre-post trials of progressive resistance strength training lasting from 4 weeks to 12 weeks following stroke. They found that progressive resistance strength training increased muscle strength in most of the studies, but it is not yet clear how strength training may promote the performance of

specific functional activities or more participation in the society. As for effects of electrical stimulation on muscle strength in the affected hand post-stroke, a 2-hour period of median nerve stimulation has been shown to produce an increase in pinch strength, and it is correlated with stimulus intensity (Conforto et al. 2002). The stimulation duration and location in this study were different from those of Conforto's group with the TENS duration being half of that study, which could explain the different results between the 2 studies.

4.4.3 Effects on reaction time

The wrist flexion and extension RT decreased more in the 2 exercise groups than in the group receiving TENS without exercise or in the control group. Other studies have also found no significant change in reaction time after weight training, proprioceptive neuromuscular facilitation without resistance, and proprioceptive neuromuscular facilitation with maximum resistance in normal subjects (Surburg 1979). However, Kauranen et al. (1998) found that reaction times in the ULs of normal subjects decreased after 10 weeks of resistance strength training. They proposed that the subjects were able to recruit more type IIa and IIb motor units, which are fast-twitch muscle fibers during rapid movements. Another study showed that virtual reality training and computer-based biofeedback training decreased reaction times in elderly subjects (Bisson et al. 2007). After stroke, Cauraugh and Kim (2002) showed that simple reaction time in the affected hand was significantly reduced after bilateral movement training or unilateral movement training plus EMG-triggered stimulation compared with a control group that received no movement assistance. Our results are similar to their findings by using TRT with or without TENS.

Reaction time includes premotor reaction time related to stimulus perception and decision (the central component), and motor reaction time related to the musculature

(its peripheral component) (Schmidat & Timothy 2005, Fig. 2.6). In a simple reaction time paradigm, sensory input has been found to reach the brain areas for motor processing (Kansaku et al. 2004). Electrical stimulation (Alary et al. 1998, Spiegel et al. 1999, Weiller et al. 1996) and exercise (Jang et al. 2004, Johansen-Berg et al. 2002) has both been shown to induce plastic changes in brain areas including the sensory input and motor output regions. This helps explain how wrist flexion or extension RT might be reduced after a period of TENS+TRT in our study. In addition, the strength training component of our TRT programme may recruit more type IIa and IIb motor units. This could affect motor RT and contribute to the reduction in total reaction time. In this study, only the TENS+TRT group showed significantly greater percentage decrease of wrist flexion RT than that of the control group, and wrist extension RT than that of the TENS group by week 12 (Table 4.5, Fig 4.2). The exact mechanisms need to be further investigated. However, the presence of carry over effect after treatment ended suggests plastic changes in the brain being developed in a functionally related manner.

4.4.4 Effects on upper limb motor function

It was only at week 8 that the p-TENS+TRT group and the TENS+TRT group show a significant percentage decrease in their WMFT time score when compared with the control group (Table 4.6, Fig. 4.3). These results suggested that significant improvement in motor function requires an optimal period of task-related training with or without TENS.

Some studies have shown that patients with chronic stroke (>12 months) can achieve significant motor improvement after they underwent prolonged constraint-induced movement therapy (Page et a. 2004) or repetitive bilateral arm training with auditory cues (Whitall et al. 2000). Gentile (2000) pointed out that task-related training (TRT) must be designed to provide useful control strategies for solving stroke

survivors' motor problems. Winstein et al. (2004) showed that TRT was more effective for this purpose than other conventional therapiese. Langhammer and Stanghelle (2000) noted that physiotherapy treatment using motor relearning methods such as task-oriented training is preferable to the Bobath approach in the rehabilitation of acute stroke. The beneficial training effects of task-related practice for subacute stroke survivors have been verified by Duncan et al. (2003). More affected patients seemed to benefit most from TRT (Thielman et al. 2004). In the present study, the 2 task-related training groups made the best progress in improving the speed of their motor functional performance. Similar results have been found in the lower limbs of patients with chronic stroke (Ng & Hui-Chan, 2007). Conforto et al. (2007) also showed that functional improvement of UL after training was greater than the improvement obtained immediately after electrical stimulation in patient with stroke.

While task-oriented arm training has been shown to induce functional brain reorganization (Jang et al. 2004, Johansen-Berg et al. 2002, Nelles et al. 2001), peripherally applied electrical stimulation has also been demonstrated to have a direct effect on cortical (Golaszewski et al. 1999, Han et al.2003) and subcortical brain centres (Spiegel et al. 1999). For example, prolonged stimulation of afferent nerves in humans has been found to increase the excitability of the motor cortex and the size of cortical muscle maps (Mckay et al. 2002, Ridding et al. 2000). These findings showed that electrical stimulation may have an important role in stimulating cortical sensory areas to allow for improved motor function.

Indeed, 2-hour period of median nerve stimulation has been shown to induce an increase in pinch strength, and the improvement was found to be correlated with stimulus intensity (Conforto et al. 2002). After 5 weeks of a home-based, self-administered program of functional electrical stimulation, patients with stroke demonstrated significant improvements in UL movement performance as measured by

the Jebsen-Taylor and 'box and blocks' tests (Alon et al. 2003). Following 18 weeks of home-based (mainly sensory) electrical stimulation and neuromuscular electrical stimulation of the upper limb, a patient with chronic stroke was reported to show significant improvement in motor function by Sullivan & Hedman (2004). Electrical stimulation for two hours has also been shown to improve the performance of Jebsen-Taylor Hand Function Test after stroke (Wu et al. 2006). However, the results of our study did not demonstrate any significant difference in motor performance between the TENS group and the control group. One reason may be that the treatment duration and location of our TENS protocol stimulation were different from those of the other studies. Even though similar treatment duration and intensity has been found to decrease the spasticity of LL and to increase the walking velocity in patients with chronic stroke (Ng & Hui-Chan 2007), in view of the more severely affected UL as a result of CVA of the middle cerebral artery (Nowak et al. 2007), these parameters might to be increased to achieve effective treatment of the affected ULs.

The effected of combining electrical stimulation with exercise training has also been investigated in recent years. McDonnell et al. (2007) found that electrical afferent stimulation (1 hour) plus task-specific training (1 hour) 3 times a week for 3 weeks led to greater improvements in grip-lift task performance than sham stimulation plus task-specific training. Stimulating the ulnar and median nerves for 2 hours combined with task-specific training was more effective than stimulation alternating every 15 minutes between the median and ulnar nerves, and more effective than sham stimulation plus take-specific training (Celnik et al. 2007).

The present study showed that at the end of the 8-week treatment period, there was no significant difference whether subjects undergoing TRT received real TENS or only p-TENS, though both groups generally progressed better than the TENS and/or the control group in terms of percentage decrease in wrist flexion or extension RT (Table

4.5, Fig. 4.2) and of WMFT time score (Table 4.6, Fig. 4.3b). One reason may be that the treatment and assessment protocols were different from those of previous studies (Celnik et al. 2007, McDonnell et al. 2007). Another reason could be that placebo effect might not be eliminated entirely because patients with chronic conditions respond better to placebo treatment than those with acute conditions (Bourne 1971). Since our 4 groups of patients had suffered a stroke some 42.9 to 54.8 months ago (Table 4.1), they could be more susceptible to placebo effects than the patients with less chronic stroke in some of the studies mentioned before. Furthermore, placebo effect was found to be highly correlated with the relationship between doctors and patients (Spiegel & Harring 2008).

Some studies have investigated the "summation effect" of electrical stimulation on voluntary movement. The effects of functional electrical stimulation on motor cortex excitability could be enhanced by an agonistic voluntary effort, or decreased by an antagonistic voluntary drive (Khaslavasksia & Sinkjaer 2005). Therefore, a combination of afferent electrical stimulation and motor voluntary effort may have a summation effect (Khaslavasksia & Sinkjaer 2005). The summation may result from the fact that a voluntary contraction could reduce intracortical inhibitory interneuron excitability and facilitate the activity of motor neurons in the cortex (Ridding et al.1995). Furthermore, Ridding & Rothwell (1999) suggested that the afferent input resulting from peripheral nerve stimulation could decrease intracortical inhibition as well. Thus, both movement and stimulation-induced afferent input could lead to disinhibition. Decreased intracotical inhibition is able to unmask pre-existing excitatory connections in the brain and reorganize cortical maps (Jacobs & Donoghue 1991). Another possible summation mechanism may be that the afferent stimulation (Ridding et al. 2000) and motor training (Hauptmann et al. 1997) increased the motor cortex excitability of the same involved muscle. If so, both afferent stimulation and motor

training could lead to plastic changes in the brain. This is the basis for treating stroke patients with electrical stimulation combined with task-related training. For stroke patients, repetitive movements with electrical stimulation can be effective in producing increased ipsilateral primary sensory cortical activity (Kimberley et al. 2004). Electrical stimulation of the arm has been shown to enhance exercise training effects to produce use-dependent plastic changes in the brain, but motor training alone with no electrical stimulation failed to generate use-dependent plasticity (Sawaki et al. 2006). According to these previous studies, movements with accompanying electrical stimulation can elicit obvious use-dependent plastic changes in the brain, and this may be the most effective treatment protocol for stroke survivors. Indeed, our finding showed that at follow-up 4 weeks after treatment ended, only the TENS+TRT group presented a significantly greater percentage decrease in wrist flexion RT when compared with the control group, and in wrist extension RT when compared with the TENS group (Table 4.5, Fig. 4.2).

4.5 Conclusion

In general, there were no significant differences in CSI results or MIVC force among the 4 groups. The 2 training groups (p-TENS+TRT and TENS+TRT) showed significant decreases in their wrist flexion or extension reaction times, and in their WMFT timing scores after 8 weeks of treatment. Interestingly, only in the TENS+TRT group the percentage decrease of wrist flexion RT compared with the control group and of wrist extension RT compared with the TENS group could be maintained to follow-up at week 12. The results suggest that 8 weeks of a combined TENS+TRT program produced faster RT and faster functional performance of the UL in patients with chronic stroke, with the former improvement showing persistent effect when compared with either TENS alone or no active treatment.

CHAPTER 5

SUMMARY AND CONCLUSIONS

5.1 Introduction

Stroke is an upper motor neuron syndrome with positive and negative features. The positive features are muscle overactivity, either excessive muscle contraction or some sort of inappropriate muscle activity such as spasticity or clonus, increased tendon reflexes and abnormal muscle co-contraction. The negative features include muscle weakness, loss of dexterity. Though some studies have investigated characteristics of these abnormalities, their relationships have not been explored (Boissy et al.1997, 1998, 2000). Such studies have dealt with only small samples, which limits the applicability of their findings.

Previous studies have shown that transcutaneous electrical nerve stimulation can alleviate ankle spasticity in patients with chronic stroke (Levin and Hui-Chan 1993). It turns out that electrical sensory stimulation can elicit sensory and motor cortical reorganization (Golazewski et al. 2004, Kaelin-Lang et al. 2002, Wu et al. 2005) and may influence functional recovery in patients with stroke (Conforto et al. 2002, Wu et al. 2006). Other studies have shown that task-related training is more effective than other conventional therapies such as the Bobath approach for patients with acute stroke (Langhammer and Stanghelle 2000, Winstein et al. 2004) and chronic stroke (Thielman et al. 2004).

A few studies have explored the combined effect of electrical stimulation and training with stroke patients. When TENS was combined with task-related training, it was found to be more effective than TENS alone in improving patients' lower limb muscle strength and walking velocity (Ng and Hui-Chan 2007). Following somatosensory stimulation and motor training, patients with stroke improved their motor performance significantly more than control subjects (Conforto et al. 2007). In another study, patients with stroke showed significantly greater improvements in grip-lift performance after combined afferent stimulation and task-specific training

conducted 3 times a week for 3 weeks than after sham stimulation (McDonnell et al. 2007). But this study did not find a statistically significant difference between the groups in terms of Action Research Arm Test results or using the Fugl-Meyer assessment. These results suggest that combining TENS with TRT for the upper limb may promote greater recovery in motor performance than either treatment alone in patients with chronic stroke. However, some of the studies used the same training protocol to assess the patients (Celnik et al. 2007, Conforto et al. 2007). Thus, learning effect cannot be excluded when using the same tool to assess the treatment effect. As for the study by McDonnell et al.(2007), the location of electrical stimulation was on the first dorsal interosseous and abductor pollicis, muscles with were in involved with the grip-lift task. But in clinical assessment such as the Action Reach Arm Test and Fugl-Meyer Assessment, no significant difference was found to be between the 2 groups. Furthermore, this study did not include a pure electrical stimulation group, thus the effect of pure electrical stimulation could not be determined.

Therefore, this study was designed to compare the treatment effects among 4 groups (TENS, p-TENS+TRT, TENS+TRT and control group). Patients with stroke received a training protocol in this study which was different from the assessment protocol to exclude the learning effect. We also carry out more sensitive clinical assessment scale i.e. WMFT functional ability and time scores, and other quantitative measures such as force and RT to obtain more comprehensive results. The main aim of this research was to compare the effectiveness of a program combining TENS with task-related training in promoting motor recovery in the upper extremity of patients after stroke with either TENS or p-TENS+TRT treatment or no treatment (control).

5.2 Methodology

In **study 1**, 98 patients with stroke and 20 healthy normal subjects meeting a set of inclusion-exclusion criteria were recruited. Six sets of variables were measured in the non-affected side and affected side of patients and the dominant side of normal subjects: (1) Abnormal muscle tone by Composite Spasticity Index (CSI) and associated reaction by Associated Reaction Rating Score (ARRS), (2) EMG and force of maximum isometric voluntary contraction (MIVC) of elbow flexors and extensors, and maximum isometric voluntary contraction of hand grip, (3) IEMG of the affected biceps and triceps during maximum voluntary hand grip as a measure of associated reaction, (4) reaction time (RT) of wrist extension and flexion, (5) Fugl-Meyer assessment, and (6) Wolf Motor Function Test (WMFT).

A number of statistical methods in the Statistical Package for Social Sciences (SPSS) version 14.0 were utilized to analyze the results. To test the reproducibility of measurement protocols, the mean score of each outcome measure between days were analyzed. Correlations among relevant measurements were examined by computing Pearson correlation coefficients or Spearmman correlation coefficients, depending on whether the data tested displayed normal distribution or non-normal distribution, respectively.

In **study 2**, a double-blind, randomized, placebo-controlled design was carried out. Seventy-seven patients with stroke meeting carefully selected inclusion-exclusion criteria were recruited. The sample size, as calculated by using “Java applets for power and sample size” software, was actually 64. In anticipation of drop-out, 77 patients were examined. All subjects were randomly allocated to 4 groups: (1) TENS, (2) placebo-TENS plus task-related training (TRT), (1) TENS +TRT, and (4) control without active treatment. Patients received treatment daily, at 5 days a week, for 8 weeks. The following 4 outcome measures of study 2 included: (1) Composite

Spasticity Index, (2) MIVC of elbow flexors and extensors, and maximum hand grip force, (3) reaction time of paretic wrist flexion and extension, and (4) Wolf Motor Function Test.

Outcome measurements of CSI, MIVC of elbow flexors and extensors, maximum hand grip strength, RT of wrist flexion and extension, and WMFT functional ability and time scores were analyzed with repeated measure of variance (ANOVA) to compare the main effects. The between-subject factor was the 4 subjects groups. The within-subject factor was the 4 assessment intervals. One-way ANOVA followed by multiple comparisons (post-hoc tests) was used to compare treatment effects among the 4 groups. Taking into consideration, patients' drop-out factor, the intention-to-treat (ITT) analysis was conducted. The significant level was set at 5%.

5.3 Main findings

5.3.1 Reproducibility of the measurement protocols

In the clinical CSI, ARRS and WFMT tests, the ICCs were very high, with 0.978 for CSI, 0.912 for ARRS, and 0.987 for functional ability and 0.872 for time score of the WFMT, and *P* values <0.001 for all. The quantitative variables including MIVC force, IEMG and RTs showed relatively high ICCs ranging from 0.802 to 0.928. The ICCs for MIVC of the elbow extensors and flexors and for hand grip force ranged from 0.804 to 0.863. The ICCs for the IEMG ranged from 0.802 to 0.928. The reaction time for wrist flexion and extension in patients with stroke ranged from 0.863 to 0.883. These results all had *P* values <0.001.

5.3.2 Motor impairments of the upper limbs following stroke and inter-relationship among motor parameters

The results showed that the affected UL in patients with stroke produced significantly smaller force during MIVC of elbow flexors, extensors and hand grip than those of their non-affected UL in patients with stroke and of normal subjects (P<0.01). There were no significant differences in the co-contraction ratio of maximum isometric voluntary (MIV) elbow flexion and extension among the affected and unaffected sides of the stroke survivors, and the normal subjects. When the stroke survivors performed a maximum grip using their non-paretic hand, associated reaction was manifested as elbow flexion (62.2 %), elbow extension (27.6%), or no elbow movement (11.2 %) in the paretic arm. Reaction time (RT) in wrist flexion and extension in the stroke survivors' affected hands were significantly longer than that in the normal subjects and their unaffected hands (P<0.01 for both).

Statistically significant correlations were found between MIVC force recorded during elbow flexion in the affected arm and ARRS (negatively; ρ=-0.321, P=0.001), and WMFT functional ability (ρ=0.380, P<0.001) and time score (negatively; ρ=-0.389, P<0.001). MIVC force recorded during elbow extension in the affected arm was found to produce similar results. It correlated with ARRS (negatively; ρ=-0.291, P=0.004), and with WMFT functional ability (ρ=0.277, P=0.006) and time score (negatively; ρ=-0.403, P=0.002). Maximum voluntary contraction (MVC) force recorded during hand grip in the affected arm correlated moderately with CSI (negatively; ρ= -0.425, P<0.001), ARRS (ρ=-0.430, P<0.001), and with WMFT functional ability (ρ=0.658, P<0.001) and time score (negatively; ρ=-0.630, P<0.001).

There were no significant associations between the co-contraction ratios during MIV elbow flexion and the CSI, ARRS, and WMFT results. However, the co-contraction ratio during MIV elbow extension correlated moderately but significantly with CSI (ρ=0.227, P<0.05), ARRS (ρ=0.377, P<0.001), and with the

WMFT functional ability score (negatively; ρ=-0.358, P<0.00), and time score (ρ=0.360, P<0.001).

Moderate but statistically significant correlations were also found between the paretic biceps IEMG recorded as an index of associated reaction during non-paretic hand grip and CSI (ρ= 0.418, P<0.001), ARRS (ρ=0.557, P<0.001), and with WMFT functional ability (negatively; ρ=-0.561, P<0.001) and time score (ρ=0.559, P<0.001). Although the paretic triceps IEMG recorded as an index of associated reaction during non-paretic hand grip correlated marginally with CSI (ρ=0.199, P=0.05); like the biceps IEMG, it correlated moderately with ARRS (ρ=0.371, P=0.001), and with WMFT functional ability (negatively; ρ=-0.378, P<0.001) and time score (ρ=0.403, P<0.001).

The wrist flexion RT correlated moderately with CSI (ρ=0.412, P<0.001) and ARRS (ρ=0.341, P<0.001), and with WMFT functional ability (negatively; ρ=-0.531, P<0.001) and time score (ρ=0.504, P<0.001). Similarly the wrist extension RT correlated moderately with CSI (ρ=0.429, P<0.001), ARRS (ρ=0.374, P<0.001), and with WMFT functional ability (ρ=-0.531, P<0.001) and time score (ρ=0.486, P<0.001).

5.3.3 Effects of TENS and task-related training in promoting upper limb motor function after stroke

No significant differences were found in all the outcome measures at baseline, indicating homogeneity among the 4 subjects groups. Furthermore, there were no significant differences in the CSI and MIVC force in elbow flexion and extension and hand grip among the 4 groups at any assessment interval. However, Significant differences between groups were found in time domains. After 8 weeks of treatment, the TENS+TRT group showed a significantly greater percentage decrease in the

reaction time of wrist flexion (-16.8%) when compared with the TENS group (22.5%, $P<0.05$) and control group (26.5%, $P<0.05$). The p-TENS+TRT group presented a significantly greater percentage decrease in the reaction time of wrist extension (-12.1%) when compared with TENS group (19.3%, $P<0.05\%$). At follow-up 4 weeks after treatment ended, only the TENS+TRT group presented a significantly greater percentage decrease in wrist flexion RT (-11.6%) when compared with the control group (31.1%, $P<0.05$), and of wrist extension RT (-11.5%) when compared with the TENS group (26.5%, $P<0.05$). With regard to WMFT, the 2 groups receiving TRT (i.e. p-TENS+TRT and TENS+TRT) showed a significant percentage decrease of the WMFT time when compared with the control group after 8 weeks of treatment.

5.4 The significance of these results

In **study 1**, the characteristics of motor impairments of upper limb following stroke were examined using 98 hemiparetic subjects. The MIVC of elbow flexion /extension and hand grip, co-contraction ratios of elbow flexors /extensors, associated reaction in the elbow muscles during non-paretic hand grip, and wrist flexion and extension reaction times were measured. The results showed that the affected UL in patients with stroke produced significantly smaller force during MIVC of elbow flexors, extensors and hand grip than those of their non-affected UL in patients with stroke and of normal subjects. Reaction time (RT) in wrist flexion and extension in the stroke survivors' affected hands were significantly longer than that in the normal subjects and their unaffected hands. These results were similar to some previous studies.

Although some previous studies have investigated these quantitative variables in patients with stroke, the correlations among them and clinical evaluations of ARRS, CSI and WMFT have not been documented. This study delineated these relationships using a relatively large patient sample. The results should contribute to a better

understanding of the characteristics of motor impairments of the upper limb and the relationships among these quantitative and clinical variables following stroke.

In **Study 2,** the findings did not support the assumption that improvement in function after stroke is mainly spontaneous recovery (Dombovy and Bachy-Rita 1988). they demonstrated that, although no significant differences were found in the CSI results or MIVC force among the 4 groups, the 2 TRT groups showed significant percentage decreases in their reaction times and in their WMFT time scores after 8 weeks of treatment with or without TENS. Furthermore, in the TENS+TRT group, the percentage decrease of wrist flexion RT compared with the control group and of wrist extension RT compared with the TENS group could be carried over to 4 weeks after the 8-week treatment ended. In patients with chronic stroke, the combined TENS+TRT appear to be better approach over the other treatment programs because of the persistent benefits outlasting the treatment period.

5.5 The limitations of this study

This study did not cover all the categories of stroke due to the subject selection criteria. For instance, patients with lesions at the brain stem or cerebellum were excluded. Similarly, subjects younger than 45 or older than 75 were excluded. This is a common shortcoming of randomized controlled trials using age limits. In addition, this study was not a true double blind trial. The two exercise groups (p-TENS+TRT, TENS+TRT) were aware of the exercise aspect of the intervention, so not all patients were fully blinded to the nature of their treatment. Better motivation in these two groups may have affected the results. The two exercise groups showed similar improvements in week 8, so placebo effects might not be excluded completely as a potential cause. Where possible, pure task-related training group without TENS should be included in future research. Furthermore, due to the limited time frame of a

PhD project, outcome measures were directed at motor and functional performance and sensory abnormalities were not measured.

5.6 Direction for future studies

Because of the limitation of patients sample and duration of a PhD project, the present study is not flawless. Future studies should address some of the limitations of the present study. (1) Adding a pure TRT group would shed light on possible placebo effect of TENS. (2) Because TENS excites afferent pathways projecting to the sensory cortex (Conforto et al. 2007), its effects on sensory abnormalities will also be examined. (3) Since the effect of TENS had been shown to be related to stimulus intensity, and to be more effective than sham stimulation plus TRT (Celnik et al. 2007), we will apply longer and more intensive TENS to achieve more clear out results. (4) Finally, the mechanisms underlying the improvements obtained by TENS+TRT will be explored by using fMRI, EEG and TMS.

Appendix I

The Informed Consent Form (English Version)

The Hong Kong Polytechnic University

Department of Rehabilitation Sciences

Project entitled: Treatment of upper limb paresis by transcutaneous electrical nerve stimulation and task-related training during chronic stroke

Investigators: Dr. Bi Sheng, Professor Christina W.Y. Hui-Chan.

Purpose

To investigate the effectiveness of a novel rehabilitation program combining transcutaneous electrical nerve stimulation (TENS) with task-related training to promote motor recovery in the upper limb of patients with chronic stroke.

Methods

All subjects will be randomly assigned to 5 groups receiving: (1) transcutaneous electrical nerve stimulation (TENS) alone or (2) with task-related training or (3) placebo stimulation plus task-related training, and (4) control with no active treatment. Real or placebo TENS and task-related training for the upper limb will be administered for 60 minutes each, 5 days a week for 8 weeks.

In any group, you will be assessed for possible improvement of upper limb functions on 4 occasions before treatment, after 4 and 8 weeks of treatment, and at 4 weeks after treatment ended. You will be required to come to the laboratory in the Department of Rehabilitation Sciences of The Hong Kong Polytechnic University for approximately two hours on each occasion. Measurements will include level of spasticity of the upper limb, maximal isometric voluntary contraction of the elbow flexors and extensors,

reaction time of wrist flexion and extension, grip force and the Wolf Motor Function Test for the upper limb.

Benefits and Risks

The major benefit from participating in this study is that you may have the opportunity to know your own level of spasticity, upper limb muscle strength and functional abilities. The additional benefit is that there may be improvement in these measures if the treatment you have received is proven to be beneficial.

The electrical stimulation and testing procedures have been found to be safe and have negligible side effects both clinically and experimentally. Some subjects may feel tired from the assessment. Therefore, rest will be given between assessment procedures. A few subjects may have very mild skin irritation from the conducting gel where the electrodes for the electrical stimulation are applied. This will be cured with anti-irritation cream in one to two days.

Confidentiality

Your participation in this research study is strictly voluntary, and you may withdraw at any time without penalty. The Department of Rehabilitation Sciences of The Hong Kong Polytechnic University has approved this study. The results of this study will provide information about the reproducibility of the measurement protocol and the effectiveness of the rehabilitation program in improving upper limb functions. Any personal information obtained by us through this study will be kept confidential and you will not be identified in any communication concerning this study.

Enquiries

Questions about this study will be answered by Dr. Bi Sheng and/or Professor Christina Hui-Chan who can be reached at the Department of Rehabilitation Sciences, The Hong Kong Polytechnic University located at Hung Hom, Kowloon, or by telephone at 2766-6723.

Informed Consent

I, _____, have been explained the details of this study. I voluntarily consent to participate in this study. I understand that I can withdraw from this study at any time without giving reasons, and my withdrawal will not lead to any punishment or prejudice against me. I am aware of any potential risk in joining this study. I also understand that my personal information will not be disclosed to people who are not related to this study and my name or photograph will not appear on any publications resulted from this study without my consent.

I can contact the chief investigator, Dr. Bi Sheng at 2766-6723 or Professor Christina Hui-Chan at telephone 2766-6703 for any questions about this study. If I have complaints related to the investigators, I can contact Ms. Michelle Leung, secretary of the Departmental Research Committee, at 2766-5397. I know I will be given a signed copy of this consent form.

Signature (subject): _____

Date: _____

Signature (Witness): _____

Date: _____

Informed Consent Form (Chinese Version)

香港理工大學康復治療學系

中風康復治療研究病人參加研究同意書

項目名稱:　經皮神經電流刺激及任務相關性訓練治療晚期中風病人上肢功能障礙。

研究目的:　採用經皮神經電流刺激及任務相關性訓練治療晚期中風病人上肢運動功能障礙，檢驗這種新的治療方法的傚果。

負責人:　畢勝博士研究生，許陳雲影教授

研究方法:　所有參與此項研究之中風病人將隨機分成五組，分別接受: (1) 高量經皮神經電流刺激治療；(2) 高量經皮神經電流刺激治療及上肢任務相關性訓練；(4)微量經皮神經電流刺激治療及上肢任務相關性訓練; (4)對炤組不接受任何治療。每次電療及運動時間均為一小時，即每次治療共須兩小時。整個研究及治療將持續八個星期。

所有參與人士治療期間，須定時到香港理工大學康復治療學系之研究實驗室，接受共 4 次，每次為時約兩小時之有關上肢功能恢復的檢查，時間為：治療開始前一天，治療 4 週，治療 8 週，以及治療結束后 4 週。內容包括量度參與人士之上肢痙攣、上肢肌肉力量及活動功能等數據。

若能參與此研究，內容包括量度參與人士之上肢痙攣、上肢肌肉力量及活動功能等狀況外，並能提供重要數據，幫助研究家居康復治療對晚期中風病人下肢功能恢復的影響。整個檢查及治療過程十分安全，唯期間小部份參與人士可能會感到

少許疲倦，參與人士可按需要於測試期間作中段休息。亦有小部份參與人士可能會於神經肌肉電流刺激的電極擺放處有輕微的皮膚過敏反應，只須在患處塗上抗敏的藥膏，二至三天便能自行痊癒。是項研究並已獲得香港理工大學的安全審批。

所有參與人士均屬自願性質，並於療程中段可隨時退出此項研究。所有個人資料均絕對保密。

參與人士若對是項研究如有任何疑問，可致電康復治療學系博士研究生畢勝 (電話：2766 6723) 及許陳雲影教授 (電話：2766 6704) 查詢。若對研究人員有任何投訴，本人可聯絡康復治療科學系研究委員會秘書梁小姐 (電話：2766 5397) 。

中風康復治療研究病人參加研究同意書

本人_____ (香港身份證號碼: _____)

現聲明自願參加此中風康復治療之研究項目。本人明白是項研究的目的及程序，並證明負責人已將是次項目解釋清楚。本人也明白在此項研究中，所有個人資料會絕對保密，本人並可以隨時退出此項研究，而不會受到任何處罰。本人亦明白此項研究的一切有關風險。

簽名: _____

見證人簽名: _____

日期: _____

本人 _____ 現聲明，本人已把是項研究的目的、程序、好處及風險，向上列有關人士解釋清楚

研究負責人簽署: _____

日期: _____

Appendix Ⅱ Abbreviated Mental Test (Chinese Version**;** Sze et al. 2000)

簡易智力測試

1． 妳今年幾歲 ？（＋/－ 5 歲）	0	1
2． 現在是什么時間 ？（約幾點種，上午、下午，夜晚）	0	1
3． 在測試最后，請復述 “ 上海街 42 號 ”	0	1
4． 今年是 200 幾年（＋/－年）（或今年是什么生肖年）	0	1
7． 妳幾時生日 ？（ 月 日 ）	0	1
8. 中鞦節是幾月幾日？	0	1
9. 現任香港特首是誰或現任中國領導人是誰？	0	1
10 試由 20 到數至 1。	0	1

8-10-分	妳的認知能力正常
4－7 分	妳的認知能力痲痲
0－3 分	妳的認知能力好差

Appendix III COMPOSITE SPASTICITY INDEX (Kim 1994, Levin and Feldman 1994)

==========

EVALUATION

TENDON JERK (BICEPS)

0 No response
1 Normal response
2 Mildly hyperactive response
3 Moderately hyperactive response
4 Maximally hyperactive response

RESISTANCE TO FULL RANGE PASSIVE JOINT DISPLACEMENT (e.g., elbow extension)

* performed at moderate speed (> 100 deg/s)

0 No resistance (hypotonic)
2 Normal resistance
4 Mildly increased resistance
6 Moderately increased resistance
8 Maximally increased resistance

CLONUS (wrist)

1 Clonus not elicited
2 1 – 3 beats of clonus elicited
3 3 – 10 beats of clonus elicited
4 Sustained clonus

==========

COMPOSITE SPASTICITY SCORE _____ / 16

Appendix IV **Associated Reaction Rating Score** (Macfarlane et al. 2002)

Patient ……..... Rater…….…… Date ……..

A) Excursion and duration of associated reaction

0) No involuntary movement/excursion of the limb.

1) Excursion of the limb occurs on effort and disappears when effort ceases.

2) Excursion of the limb occurs on effort, may be variable through the task and remains present for some time after the task has been completed. Residual posturing may be evident.

3) Static 'stereotypical posturing'. Limb reaction remains essentially present and unchanging throughout task.

B) Number of joints in the affected upper limb involved in associated reaction

0) No involuntary movement of joints during task

1) Limb reaction confined to 1–2 joints.

2) Limb reaction involves 3–4 joints.

3) All joints of the limb involved + trunk.

C) Release of associated reaction

1) No limb reaction. Release not required.

2) Initial position is regained through the subject's conscious control or with the assistance of gravity alone.

3) Subject needs to use unaffected hand in order to return affected limb towards starting position.

4) Subject needs to use unaffected hand in order to return affected limb towards starting position but limb immediately returns to stereotypical posture when handling ceases. Or limb is unable to be released.

D) Affect of upper limb associated reaction on functional task (sit-to-stand, stand to sit).

0) No limb reaction. Task unaffected.

1) Limb reaction present but does not interfere with task.

2) Obvious interference with task, but able to complete task.

3) Significantly affects ability to complete task *or* task not completed.

MODAL SCORE = …… 0 = None, 1 = Mild, 2 = Moderate, 3 = Severe

Most frequently occurring. If scores are equally distributed between 2 levels, score the higher (most severe).

TOTAL SCORE = …….

Appendix V **Fugl-Meyer assessment** (Fugl-Meyer et al. 1975)

	SHOULDER/	ELBOW/	FOREARM	
Reflex-activity	Flexors	0	1	2
	Extensors	0	1	2
Shoulder	Retraction	0	1	2
	Elevation	0	1	2
	Abduction	0	1	2
	Outwards rotation	0	1	2
Elbow	Flexion	0	1	2
Forearm	Supination	0	1	2
Shoulder	Add-/inw.rotatio	0	1	2
Elbow	Extension	0	1	2
Forearm	Pronation	0	1	2
Hand to lumbar spine		0	1	2
Shoulder	Flexion	0	1	2
Elbow 90	Pro-/Supination	0	1	2
Shoulder	Abduction 0-90	0	1	2
	Flexion90-180	0	1	2
Elbow 0	Pro-/Supination	0	1	2
Norma reflex-activity		0	1	2
		WRIST		
Elbow 90	Wrist-stability	0	1	2
Elbow 90	Wrist-flexion/extension	0	1	2
Elbow 0	Wrist-stability	0	1	2
Elbow 0	Wrist flexion/extension	0	1	2
Circumduction		0	1	2
		HAND		
Fingers	Massflexion	0	1	2
Fingers	Massextension	0	1	2
Grasp a	grip	0	1	2
Grasp b	paper	0	1	2
Grasp c	pencil	0	1	2
Grasp d	cylinder	0	1	2
Grasp e	ball	0	1	2
	COORDINATION/	SPEED		
Tremor		0	1	2
Dysmetria		0	1	2
Time		0	1	2

Appendix VI WOLF MOTOR FUNCTION TEST (Wolf 1989)

Task	Time(s)	Functional Ability	Comment
1. Forearm to table (side)		0 1 2 3 4 5	
2. Forearm to box (side)		0 1 2 3 4 5	
3. Extend elbow (side)		0 1 2 3 4 5	
4. Extend elbow (weight)		0 1 2 3 4 5	
5. Hand to table (front)		0 1 2 3 4 5	
6. Hand to box (front)		0 1 2 3 4 5	
7. Weight to box	_____lbs.		
8. Reach and retrieve		0 1 2 3 4 5	
9. Lift can		0 1 2 3 4 5	
10. Lift pencil		0 1 2 3 4 5	
11. Lift paper clip		0 1 2 3 4 5	
12. Stack checkers		0 1 2 3 4 5	
13. Flip cards		0 1 2 3 4 5	
14. Grip strength	_____kgs.		
15. Turn key in lock		0 1 2 3 4 5	
16. Fold towel		0 1 2 3 4 5	
17. Lift basket		0 1 2 3 4 5	

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