Effects of Transcutaneous Electrical Nerve Stimulation and Body-Weight-Supported Treadmill Training on Motor Functions in Children with Spastic Cerebral Palsy

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CERTIFICATE OF ORIGINALITY

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DEDICATION

To my daughter, son and husband -
Jessye, Justin and Lawrence
whose love and smiles enrich my life,

and

to my late mentor, Dr. Sharyn Vanden Noven (1951 – 2005),
for her unconditioned love and unique talents
in showing how to live life to the fullest.

ABSTRACT

Transcutaneous electrical nerve stimulation (TENS) and body-weight-supported treadmill training (BWS-TT) have been separately proven to reduce spasticity and/or enhance gait functions in adults with neurological disorders. The extent to which a combination of such treatment approaches could reduce spasticity and facilitate gait performance in children with cerebral palsy (CP) has not been investigated. Since children are believed to have greater neuronal plasticity, we hypothesized that (1) TENS and/or TENS+BWS-TT would reduce spasticity more than placebo-TENS; and that (2) combining TENS with BWS-TT would further improve muscle function and walking performance than TENS alone in children with CP.

This study was a prospective, randomized, placebo-controlled clinical trial. Sixty-three children diagnosed with spastic CP were recruited from 6 special schools and 61 completed the study. Children with "mild", "moderate", or "severe" levels of ankle plantarflexor spasticity, as defined by the composite spasticity scale (CSS) score, were randomly allocated to 1 of 3 groups receiving TENS (n = 20), placebo-TENS (n = 21), or TENS+BWS-TT (n = 20). They were 6 to 15 years old, 32 were females and 29 males, 54 had spastic diplegia and 7 had spastic hemiplegia. All children received similar conventional therapy programs. In the TENS group, low-intensity TENS was applied via surface electrodes connected to a portable TENS stimulator to the skin overlying the common peroneal nerve. Continuous stimulation (0.125 msec square pulses, 100 Hz, intensity at 2 times the sensory threshold) was applied for 60 minutes, once a day, for 5 days a week for 3 weeks. In the placebo-TENS group, the same device and stimulation parameters as those in the TENS group were used with the circuit inside the device disconnected. In the TENS+BWS-TT group, TENS was

delivered for 60 minutes, followed by 20 to 30 minutes of BWS-TT according to the walking tolerance and progression of each child.

Outcome measurements included: (1) spasticity of the ankle plantarflexors assessed by CSS and stretch reflex as a function of maximum M response (SR/M), (2) muscle function assessed by maximum isometric voluntary contraction (MIVC) and EMG co-contraction ratios of ankle dorsiflexor and plantarflexor muscles, and (3) walking performance evaluated by walking speed and energy cost (physiological cost index, PCI) during a 6-minute walk test. These measurements were recorded *before* treatment (T_0), and *after* 1 week (T_1), 2 weeks (T_2), and 3 weeks of treatment (T_3), to examine the effects and time course of TENS, placebo-TENS and TENS+BWS-TT.

The results showed no significant differences among the groups before treatment. When compared with placebo-TENS, both TENS and TENS+BWS-TT produced a significant % decrease of CSS scores, respectively, after 3 and 2 weeks of treatment ($p < 0.006$). Interestingly, only TENS+BWS-TT but not TENS alone produced a significant % decrease of SR/M area ratio and of dorsiflexion co-contraction ratio, and a significant % increase of dorsiflexion torque after 3 weeks of treatment ($p < 0.006$). However, none of the interventions produced a significant change in plantarflexion torque or co-contraction ratio after 3 weeks of treatment. Despite no significant change of walking speed being noted among the groups, 3 weeks of TENS+BWS-TT produced a significant % decrease of PCI ($p < 0.006$). This may partly be explained by a significant % decrease of the heart rate change ($HR_{walk} - HR_{rest}$) after 3 weeks of TENS+BSW-TT.

In conclusion, both TENS and TENS+BWS-TT are feasible treatment protocols for children with spastic CP in the school setting. Both treatments significantly reduced clinical spasticity after being administered for only 2–3 weeks. However, voluntary contraction of ankle dorsiflexors, hyperactive SR of

plantarflexors and energy cost of walking were improved only when the 3 weeks TENS were combined with BWS-TT. These findings supported our hypothesis that combining TENS with specific locomotive training was needed to bring about functional gain.

This is the first randomized controlled trial which demonstrated that 15 sessions of combined TENS+BWS-TT treatment were superior to TENS alone in reducing spasticity and in enhancing voluntary muscle function and walking performance in children with spastic CP. This treatment strategy has the added benefits of being non-invasive, low cost, and without the side-effects often associated with drug intake or surgery such as dorsal rhizotomy. The extent to which 3 weeks of BWS-TT alone would bring significant improvement in muscle and mobility function requires further investigation.

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LIST OF ABBREVIATIONS

CP	:	Cerebral palsy
CNS	:	Central nervous system
AACPDM	:	American Academy for Cerebral Palsy and Developmental Medicine
GMFMS	:	Gross Motor Function Classification System
MIVC	:	Maximal voluntary isometric contraction
SR	:	Stretch reflex
CSS	:	Composite Spasticity Scale
EMG	:	Electromyography
MAS	:	Modified Ashworth Score
SDR	:	Selective dorsal rhizotomy
RCT	:	Randomized controlled trial
GMFM	:	Gross Motor Function Measure
PT	:	Physiotherapy
NDT	:	Neurodevelopmental treatment
TENS	:	Transcutaneous Electrical Nerve Stimulation
SCI	:	Spinal cord injury
TES	:	Threshold electrical stimulation
NMES	:	Neuromuscular electrical stimulation
BWS-TT	:	Body-weight-supported treadmill training
CPG	:	Central pattern generator
LTP	:	Long-term potentiation
FES	:	Functional electrical stimulation
T_0	:	Assessment before treatment
T_1, T_2, T_3	:	Assessment after 1, 2, and 3 weeks of treatment, respectively
ANOVA	:	Analysis of variance
TA	:	Tibialis anterior
msec	:	millisecond
mph	:	mile per hour
SR/M	:	Stretch reflex as a function of maximum M response
Nm	:	Newton meter
MΩ	:	megaohms

Hz	:	hertz
A/D	:	Analog to digital
S.D.	:	Standard deviation
PCI	:	Physiological cost index
HR_{rest}	:	Resting heart rate
HR_{walk}	:	Walking heart rate
Yrs	:	Years
Wt	:	Weight
Ht	:	Height
kg	:	kilogram
m	:	meter
BMI	:	Body-mass index
ATR	:	Achilles tendon reflex
%	:	Percent
Kg/m^2	:	kilogram per square meter
μV.s	:	micro-volt second
m/min	:	meter per minute
beats/m	:	beats per meter
mins/day	:	minutes per day

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CHAPTER 1

INTRODUCTION

1.1. Epidemiology of Cerebral Palsy

1.1.1. Definition of Cerebral Palsy

Cerebral Palsy (CP) is an umbrella term used to describe the clinical sequelae resulting from a non-progressive encephalopathy in an immature brain whose cause may be pre-, peri-, or postnatal (Bax 1964). CP is characterized by impairments of the neuromuscular, musculoskeletal, and sensory systems that are either the immediate results of the existing pathophysiology or are indirect consequences developed to compensate for the underlying abnormality. The signs often appear to be progressive because the abnormality affects a developing, albeit abnormal, central nervous system (CNS) that is attempting to interact with and influence other maturing systems. Although the hallmarks of CP are impaired posture and movement, CP is often complicated by mental retardation or learning disabilities (50 to 70%), speech and language disorders (65%), auditory impairments (25%), seizure disorders (25 to 35%), and visual disorders (25%) (Baroff 1991; Olney and Wright 2000). Social and family problems may occur secondary to the presence of the primary deficits of CP.

According to the American Academy for Cerebral Palsy and Developmental Medicine (AACPDM), CP can be divided by clinical types and the topographic distribution of movement impairment (Minear 1956). This classification system relies heavily on clinical judgment and experience. Based on the type of impairment, children are divided into the categories of spastic, dyskinesic, ataxic and hypotonic. The topographic distribution of abnormal tone, posture, or movement includes diplegia, hemiplegia, quadriplegia and double hemiplegia. Diplegic and hemiplgic CP are the subjects of interest in this study. Their characteristics are described in detail below. Children with diplegic CP have greater impairment of the lower body and legs than that of the arms, while children with hemiplegic CP have greater impairment of the arm and leg on one side of the body.

Accurate diagnosis of CP at a young age is important for economic, social, emotional, and medical reasons. However, similar insults to the developing brain of the fetus or newborn can produce strikingly different problems depending on the structure and physiology of the brain at the time of insult. In addition, developmental changes in the brain can lead to recovery from dysfunction, whereas ongoing maturation can uncover sensorimotor dysfunction that is not recognized until the infant develops movement against the force of gravity (Campbell and Wilhelm 1983; Hadders-Algra et al. 1997; Kahn-D'Angelo and Unanue 2000; Roth et al. 1994). As a result, the "diagnosis" of the child might change, because the child might present the disorders quite differently at various developmental and chronological stages and within the demands of various environments.

1.1.2. Incidence

CP is the second most common neuroimpairment in childhood, after mental retardation. Though formal statistics of the prevalence rate of CP are not compiled in Hong Kong, previous reports acknowledged that it affects about 2 in 1000 children in industrialized countries (Bottos et al. 1999; Howle 1999; Pharoah et al. 1998) and more than 1 million children under the age of 21 in the United States (Taub et al. 2004). This rate has not declined, due possibly to an increased survival rate of pre-term babies (Colver et al. 2000; Howle 1999). Spastic CP is the most common type of CP, and spastic diplegia is the most common type of spastic CP. Combined with spastic hemiplegia and quadriplegia, this group makes up to about 75% of all children with CP (Hagberg et al. 1989; Howle 1999). A local survey reported that the most common diagnostic type was spastic CP in Hong Kong (77%), with prematurity and asphyxia as the most quoted causes (Chan et al. 2005).

1.1.3. Disabilities

The designations *mild, moderate, severe* and *profound* are often applied to different types of CP to further define the extent of abilities and limitations in gross motor function. Children with *mild* disability are those who have sensorimotor impairments that lead to poorly coordinated and inefficient movement when compared with normal peers, but their functional limitations are found only in the most advanced age-appropriate gross motor skills. Children with *moderate* disability are those who have functional limitations such as changing postures, sitting, walking, hand use or speech. Their developmental milestones are behind those of non-disabled age peers, but with modification of the demand of the task or the environment, these children can participate in most age-appropriate activities. In contrast, the term *severe* is used to describe children whose disability restricts them from performing activities necessary to fulfill normal life roles, such as managing doors at school or carrying a book to class. These children are unable to be independent in their daily living skills because of a lack of balance; an inability to use their arms and hands for skilled movement; deficiencies in the ability to communicate, or a combination of these deficits. They are unable to participate in play or family activities independent from an adult. Children with *profound* disabilities are those who have no useful or purposeful motor ability. They cannot perform even the most basic motor functions and are unable to function independently of a caregiver. They are dependent on technology, mobility aids, and special equipment for all daily activities (Howle 1999).

Since children with CP experience a change in motor function with age and development, the Gross Motor Function Classification System (GMFCS) is a five-level, age-categorized system that places children with CP into categories of severity that represent clinically meaningful distinction in motor function (Palisano et al. 1997). In a study that examined 116 children in the 5 to 6 year age range, about 50%

and 97% of children with diplegia and hemiplegia, respectively, were classified as being at level I and level II on the GMFCS and were defined as having mild gross motor disabilities (Beckung and Hagberg 2000).

1.2. Spasticity, Motor Impairments, and Functional and Participation Levels of Children with Spastic CP

1.2.1. Spasticity

One prominent sensorimotor impairment of children with CP is spasticity. Over 75% of cases of CP have spasticity and it is conventionally considered to be a major cause of discomfort, gait abnormalities, and functional limitations (McLaughlin et al. 2002). There is a general consensus that no single measure of motor impairments is a fully adequate descriptor of the changes associated with spasticity. In the traditionally accepted view, spasticity has been defined as hyperactivity of the stretch reflex (SR) arc manifested by a velocity-dependent increase in tonic and phasic SR, sometimes accompanied by clonus (Lance 1980b). Changes in the biomechanical properties of the spastic muscle, however, also contribute to the manifestation of clinical spasticity (Lundy-Ekman 2002a). Due to the multiple manifestations of this neuroloigical disorder, recent investigators have favoured a barrage of measures to achieve a composite index of spasticity (Delwaide 1985; Dimitrijevic et al. 1983; Levin and Hui-Chan 1993b).

Clinically measured hypertonia is by itself only one manifestation of spasticity. Albeit subjective, clinical scales such as the Ashworth and Modified Ashworth Scales have been commonly used to assess the resistance to passive limb displacement as a measure of spasticity in children (Bohannon and Smith 1987). Other clinical measures used to assess spasticity include the excitability of tendon reflexes and the presence of clonus. Tendon reflexes, evoked by a rapid stretch of the tendon via a hand-held

reflex hammer, are employed clinically to assess excitability of the phasic SR and the result is expressed either qualitatively (i.e., 'sluggish' to 'brisk') or quantitatively via numerical rating scales. Clonus, a rhythmical (5 – 8 Hz) self-sustaining muscular contraction, is elicited by a sudden and maintained stretch of the affected muscle. It is thought to be due to a central mechanism leading to a self-sustaining oscillation in the SR pathway (Dimitrijevic et al. 1980; Rack et al. 1984). Clinically, clonus is quantified by numerical scales indicating its presence or absence and by the number of clonic beats elicited. Encompassing 3 clinical measures, namely tendon reflexes, clinically measured tone and clonus measures, the Composite Spasticity Scale (CSS) had been shown to be reproducible and better at describing ankle plantarflexor spasticity in adults with hemiplegia (Levin and Hui-Chan 1993b) and spinal cord injury (Goulet et al. 1996). Nevertheless, this scale has not yet been applied to the evaluation of children with CP.

To understand the pathophysiological mechanism underlying spasticity, objective neurophysiological measurements are frequently used. Measurements commonly used to provide quantitative indicators of alternations in segmental reflex pathways include H-reflex, SR, tendon jerk, and vibratory inhibition of monosynaptic SR (Ashby and Verrier 1976; Burke and Ashby 1972; Levin and Hui-Chan 1993b). For instance, analysis of SR could provide information about mono- and polysynaptic segmental and propriospinal pathways. Shortened SR latencies (Levin and Hui-Chan 1993b) and augmented SR magnitude (Burke and Lance 1973; Powers et al. 1989) have been reported in adults with hemiplegia. In contrast to studies on adults, very few studies on children quantify spasticity in an objective manner. Engsberg and co-workers measured spasticity using a KinCom dynamometer by passively stretching the ankle plantarflexors at different speeds to record the amount of resistive torque. Children with diplegic CP were found to have greater mean resistance to passive

movement/spasticity values of the ankle and knee (by 5 to 6 fold, respectively) than non-disabled children had (Engsberg et al. 2000; Ross et al. 2002). Compared with non-disabled peers, children with CP were also found to have earlier SR onset angle/threshold of their ankle plantarflexors (Brouwer et al. 1998). A similar result was observed by Jobin and Levin (2000) when the spastic elbow flexors of children with CP were analyzed.

1.2.2. Motor Impairments

CP is characterized by insufficient force generation by affected muscle groups, which is consistent with low levels of electromyographic (EMG) activity and decreased amount of force output (Berger et al. 1982). Using a hand-held dynamometer to measure the muscle strength of 15 diplegic CP, 15 hemiplegic CP and 16 age-matched controls, Wiley and Damiano (1998) demonstrated that the maximal isometric voluntary contraction (MIVC) of all the 8 lower limb muscles tested were weaker in both the diplegic and hemiplegic CP children than those of their age-matched peers. Furthermore, muscle weakness was more pronounced distally in the knee than in the hip. Similar observations were noted when muscles were tested isokineticaly. When tested at a slow speed of 10°/s, children with CP (n = 19) had significantly weaker hamstring and quadriceps strength than age-matched non-disabled children (n = 20) (Ross et al. 2001). Their weakness was also found to be more pronounced distally in the ankle than in the knee (Ross and Engsberg 2002).

Another distinguishing feature of sensorimotor deficits in children with spastic CP is the presence of an abnormal amount of co-contraction. Co-contraction normally occurs during movement requiring precision or made at high velocities against heavy loads (Bouisset and Lestienne 1974). In subjects with spasticity, however, an abnormal degree of co-contraction was often noted. Levin and Hui-Chan (1994)

recorded electromyography (EMG) of tibialis anterior and soleus muscles during isometric ankle plantarflexion in adults with hemiplgia, and expressed the co-contraction as the ratio of antagonist EMG area value to the total agonist plus antagonist EMG area values. They found that in these spastic adults, dorsiflexion co-contraction was substantially higher than that of age-matched normal adults and was associated with a significant reduction in the force production of the paretic dorsiflexors (r = -0.91). In a comparable study in children with CP, Brouwer et al. (1998) also noted abnormally high co-contraction ratios during plantarflexion and compromised plantarflexor force production. The relationship between EMG co-contraction and muscle strength in these children, however, has not been investigated.

1.2.3. Functional and Participation Levels

The functional and participation levels of children with CP are affected by the child's own specific impairment and by family and environmental factors (King et al. 1999). Based on the central registry of 5 Child Assessment Centers and networks of 2 parent organizations, Chan et al. (2005) conducted the first large-scale local survey to uncover the type of and interrelationship among impairments and functional and participation levels of young children with physical disabilities in Hong Kong. Among 181 parents who identified their children as having CP (mean age: 7 years 6 months), developmental problems were commonly reported: 48% were mentally retarded or had global developmental delay; 20% were non-verbal communicators and 63% had visual problems. Within this sample group, of the 77% diagnosed as having spastic CP, 60% and 39% were reported to need help with dressing and feeding, respectively. Only 28% of these children could dress or undress themselves alone or with minimal assistance. In terms of mobility, 64% of the spastic CP children were indoor walkers (42% independent, 22% assisted). The percentage dropped to 51%

(34% independent, 17% assisted) when they went outdoors and this was associated with an 11% increase in assisted wheelchair users. A high percentage (indoor, 70%; outdoor, 73%) of the independent walkers had normal intelligence. Seventy percent of the parents reported that they had difficulty going outdoors with their children because of problems with transportation (47%), poor access to buildings and railways or subway stations due to entry/exit problems (28%), and discrimination by others (23%). The major concerns of parents (70%) centered on the abilities of their children in self-care and mobility.

Relatively little has been published regarding the health and functional status of adults with CP. A Swedish survey conducted on 363 adults with CP (mean age: 36 years, range: 20 to 58 years) showed that 84% of the subjects reported problems with spasticity, and 64% of them could walk with or without walking aids (Andersson and Mattson 2001). One-quarter of the respondents who worked full-time were predominantly those with spastic hemiplegia and spastic diplegia. As many as 35% of the subjects reported decreased walking ability and 9% had stopped walking completely before 35 years of age. Many of the diplegic group claimed that their decreased walking ability occurred predominantly between 15 and 34 years of age, and the decrease was due to an increase in spasticity and balance problems coupled with deterioration of the condition and muscle strength. The reports by Chan et al. (2005) and Andersson and Mattson (2001) highlight the need to address spasticity and mobility in enhancing the participation level of people with CP.

1.3. Treatment of Spasticity and Gait Re-education

Many resources have been directed at the treatment of spasticity with the aim of improving function, such as walking. To manage spasticity, current treatment choices include oral medications, orthotics, orthopaedic surgical procedures, electrical

stimulation, intramuscular injection, intrathecal baclofen infusion, physiotherapy, and surgical intervention, such as selective dorsal rhizotomy. Procedures relevant to this study are presented below.

By blocking pre-synaptic release of the neurotransmitter acetylcholine at the neuromuscular junction, intramuscular injection of botulinum toxin-A has been shown to reduce spasticity (Modified Ashworth Score, MAS = -0.4 to -1.3) and to improve gross motor function (Albright et al. 1995; Love et al. 2000). A few studies reported that botulinum toxin-A injection into the gastrocnemius muscle of children with CP resulted in positive changes in several gait parameters, including improvements in the stance phase dorsiflexion range, step length, and other gait kinematics (Cosgrove et al. 1994; Thompson et al. 1998; Ubhi et al. 2000). This treatment approach was found to be at a moderately high cost (~HKD$12,000), but could delay the need for surgery by 3.7 years (Boyd et al. 2000b). Alternatively, intrathecal baclofen has been shown to reduce muscle tone in the upper extremities (mean MAS = - 0.41; Albright et al. 1995), lower extremities (mean MAS = -1.0; Gilmartin et al. 2000), and to improve the speed of movement and self-care skills in children with CP (Campbell et al. 1995). To allow continuous infusion of baclofen, an intrathecal catheter is typically placed at the level of T12 – L1 in the spine and connected to a pump placed in a subcutaneous pocket in the abdominal area. Older children, especially those with diplegia or spastic quadriplegia who are unable to walk, are considered to be ideal candidates for baclofen pump treatment (Von Kock et al. 2001). Despite its positive effect on spasticity, intrathecal baclofen pumps involve repeated clinical visits for clients to refill the pump and to adjust the desired level of infusion, high cost, extended hospitalization for initial screening procedures, and a high incidence of complications (Steinbok et al. 1995). Drawbacks associated with use of botulinum toxin-A injection,

on the other hand, are related to its short-lasting nature, variable effects, repeated painful injections and moderately high cost (Howle 1999).

In contrast to drug administration, surgical treatment by selective dorsal rhizotomy (SDR) could reduce spasticity permanently. Improvements in gait function, range of motion of lower limb joints, increased walking velocity and stride length were reported (Thomas et al. 1996 and 1997; Vaughan et al. 1991). Profound interest in this surgical technique boomed in the 1990's. Coincidently, 3 groups of investigators separately conducted randomized controlled trials (RCT) to compare the effects of SDR plus physiotherapy against physiotherapy (PT) alone using similar outcome measures (McLaughlin et al. 1998; Steinbok et al. 1997b; Wright et al. 1998). Subsequently, these investigators jointly conducted a meta-analysis of SDR using their original data (McLaughlin et al. 2002). Altogether, 82 children with CP under 8 years of age were analyzed. The majority of the candidates selected for SDR (n = 65) had diplegic CP, with GMFMCS level II or III disability. A significant reduction in the mean Modified Ashworth Scale score of -1.2 (range: -0.88 to -1.4) and an improvement in the mean GMFM score of +4.0 (range: 8% to 11.3%) were documented in children receiving SDR plus intensive physiotherapy for 9 to 12 months. The amount of nerve root that was cut was found to directly affect the degree of spasticity reduction and functional gains ($p < 0.01$). It was concluded that SDR plus physiotherapy was efficacious in reducing spasticity in children with spastic diplegia and that it had a small positive effect on gross motor function over physiotherapy alone. Nevertheless, concern was raised on whether or not an anticipated mean GMFM change score increment of a mere 4% above the amount of change with non-invasive care (i.e., PT alone) justified the time, effort, and risk involved (McLaughlin et al. 2002). Indeed, a previous report had shown that an average improvement of 6% in the GMFM score was observed in spastic CP children who mainly received

physiotherapy with no special interventions, such as orthopedic or neurological surgery, over a 6-month period (Russell et al. 1989). The general consensus is that SDR is most effective for children between 3 to 8 years of age, as children in this age range have academic and social demands that can accommodate intensive intervention (McLaughlin et al. 2002; Von Koch et al. 2001). Notwithstanding its affirmative effect on spasticity, the invasive nature, the possible complications and the high cost associated with SDR do not warrant it as a first choice of treatment for spasticity. Whether drugs or SDR were used, a key message from these RCT studies was that the weakness unmasked after removal/reduction of spasticity still requires a prolonged period of rehabilitation to regain function. Intensive rehabilitation programs focusing on anti-gravity muscle strengthening and functional training for 6 to 12 months were key to the success of SDR (McLaughlin et al. 2002).

Other than drugs and SDR, orthopedic surgical management is used on children with spastic diplegia with the goals to improve walking and to reduce the effects of spasticity at one or more joints in order to improve or maintain function and prevent secondary deformities. The procedures range from tenotomies, muscle lengthening, and muscle transplants to osteotomies, neurectomies, and fusion. Results of various procedures, however, are extremely variable (Howle 1999), and loss of manual muscle strength typically by one grade after these procedures has been reported (Bleck 1991).

1.4. Physiotherapeutic Management of Spasticity and Gait Re-education

Despite limited evidence-based support for its efficacy, physical therapy remains a cornerstone in the management of clients with spasticity and gait dysfunction (Goldstein 2001; Hur 1995; Mayston 2001; Richardson 2002). In addition to their importance in maximizing patient function, the success of other medical and

surgical interventions in the treatment of spasticity is highly dependent on a rehabilitation programme to optimize results. The key components of physiotherapeutic approaches include education of the clients and their carers, and the use of an "intervention cycle" involving accurate assessment, careful measurement, intervention and evaluation, accurate goal setting and a staged, stepwise approach of intervention. Specifically, physiotherapists provide range-of-motion exercises, strengthening regimes, and facilitatory/inhibitory exercise programs with positioning, as well as coordinating the use of casting and orthotic devices to maintain range of motion and to optimize biomechanics (Goldstein 2001; Helsel et al. 2001). When considering medical or surgical treatment of spasticity, input from the patient's physiotherapist is often requested to evaluate the patient's pre-treatment baseline status; to assist in the decision-making on the proposed intervention, such as on the optimal site for botulinum toxin injection or the selection of candidates for SDR; to establish and monitor treatment goals; and to assess the efficacy of the proposed intervention. Intensive post-treatment rehabilitation is often established as well (Palmer et al. 1988).

Historically, there have been different approaches in physiotherapy, such as Bobath therapy, neurodevelopmental treatment (NDT) and conductive education in the rehabilitation of children with CP. Siebes et al. (2002) evaluated 50 studies on therapeutic motor interventions for children with or at risk for CP between the period from 1999 to 2001. According to the level of evidence (Butler 1999; Butler and Darrah 2001; Sackett 1989), 27% of the reviewed studies could be classified as level I (i.e., RCT), while level II and III evidence was provided in 39% and 31%, respectively, of the studies examined. Often, the effectiveness and efficacy of therapeutic interventions for children with CP could not be determined owing to inadequate research design or methodological problems. The lack of positive results

and the deficiency in study design prevails for several reasons: CP is a highly heterogeneous condition; the growth and development of these children are very slow (Hur 1995); the condition is complicated by ongoing changes due to the process of growth and maturation; and there is a lack of instruments sensitive enough to detect small changes in motor ability (Fetters and Kluzik 1996). A greater constraint in recruiting children for research studies is another compounding factor. Several attempts have been made to use a better study design involving a control group. Yet, it is difficult to evaluate the effectiveness of any motor therapy approach for a host of reasons. Chief among these is that there are no specific treatments that are delivered in a standardized manner in clinical settings. In other words, there is no discrete "dosage" of care administered under specific, invariable procedures in conditions that are held constant. While the condition for a treatment could be standardized, the therapist's skill level and the specific needs of the child will vary. Therefore, the treatment skills for and the outcome of each child could vary accordingly (Giuliani 1991). A review by an expert panel from AACPDM concluded that except for immediate improvement in dynamic range of motion, there was no evidence that NDT changed abnormal motor responses, slowed or prevented contractures, or that it facilitated more normal motor development or functional motor activities (Butler et al. 2001). Similarly, the current literature does not provide sufficient guidelines to allow decision making regarding the use of conductive education in children with CP (Darrah et al. 2004). Since the bodies of evidence in many areas of developmental medicine are neither robust nor comprehensive enough to allow confident generalization to populations-at-large, the review reports by AACPDM serve to identify areas in which more meaningful research is needed. Current literature suggests that it is time for concerted efforts for other therapeutic approaches that have been proven to have improvement on motor functions in children with CP (Butler et al.

2001; Richardson 2002). These include task-orientated approaches, such as body-weight-supported treadmill training for gait re-education (Schindl et al. 2000), or constraint-induced movement therapy (Charles et al. 2006; Eliasson et al. 2005; Taub et al. 2004), dynamic systems concepts, as well as strength and endurance training (Damiano and Abel 1998; Darrah et al. 1997; Dodd et al. 2002).

1.5. Transcutaneous Electrical Nerve Stimulation (TENS)

1.5.1. Definition and Types of TENS

TENS has been used for pain relief for nearly 30 years. It involves the transcutaneous application of repetitive electrical stimulation via surface electrodes over either peripheral nerves, trigger points, acupuncture points or dermatomes related to the painful segment (Walsh 1977). Two types of TENS are commonly used in physiotherapy practice: conventional TENS and acupuncture-like TENS. Conventional TENS is applied at low intensity (2 to 3 times the sensory threshold) and high frequency (60 to 100 Hz), while acupuncture-like TENS is applied at high intensity (more than 3 times the sensory threshold) and low frequency (2 to 4 Hz). In an early study by Levin and Hui-Chan (1993a), the conduction velocities of the peripheral afferent fibers with both conventional and acupuncture-like TENS in 17 healthy subjects were examined. The authors found that these 2 types of TENS activated similar afferent fiber types, predominantly in the Aαβ range. Note that A-alpha fibers would include larger sensory fibers such as I_a and I_b fibers, respectively, from muscle spindles and tendon organs (Low and Reed 2000; Pechham 1999; Robinson and Snyder-Mackler 1995), as well as efferent motor fibers from the alpha motor neurons innervating the skeletal muscles.

1.5.2. TENS and Spasticity Management

Caution is required when comparing studies that examine the effect of electrical stimulation on sensorimotor function of clients, due to the variations of stimulation parameters and treatment periods employed among studies. In studies related to transcutaneous electrical stimulation delivered at the "sensory threshold" (i.e., stimulation without visible muscle contraction), the effects of TENS were mainly examined in adults with chronic stroke (Dewald et al. 1996; Levin and Chan 1989; Levin and Hui-Chan 1992; Potisk et al. 1995; Tekeoolu et al. 1998) and spinal cord injury (SCI; Bajd et al 1985; Goulet et al. 1996). The main findings from these studies with adult subjects were that repeated TENS treatment resulted in significant decrease in spasticity measured either clinically or in terms of SR latency and magnitude, or resistive torque to passive movement of the limb. Comparable, well-controlled studies in children with CP, however, are scarce (Dali et al. 2002; Maenpaa et al. 2004; Sommerfelt et al. 2001; Steinbok et al. 1997a), with none of them demonstrating similar effects on spasticity. The treatment effect of TENS on spasticity in children, especially in a randomized controlled trial, remains to be demonstrated.

In a study by Levin and Hui-Chan (1992) on adults with hemiparesis, 60 minutes of TENS at 5 times a week for 2 weeks was found to result in a significant decrease in clinical spasticity in the plantarflexors and an increase in the vibratory inhibition of the soleus H-reflex. These changes occurred with a substantial improvement in voluntary dorsiflexing force ranging from 5% to 820%, but not plantarflexing force. They were accompanied by a decrease in the EMG co-contraction ratios after a further week of stimulation. Potisk and colleagues (1995) also found that a 20-minute treatment of TENS to the sural nerve reduced calf hyperreflexia in patients with post-stroke hemiplegia, with the effects lasting up to 45

minutes. In a subsequent study by Tekeoolu et al. (1998), the effects of 40 sessions of daily 30- minute TENS on adults with hemiplegia were examined using the Barthel Index for Daily Living Activities and the Ashworth Scale. Thirty subjects each were assigned to placebo-TENS or TENS treatment, on top of a standard exercise program. Significant improvements were recorded in the TENS group in all parameters such as walking, stair climbing, transfer, feeding, hygiene, toileting or bathing as opposed to the placebo-TENS group, which showed improvement only in few of these daily living activities. Improvement in the total Barthel Index score, however, was statistically larger in the TENS group than that of the placebo-TENS group.

Interest in the area of CP and electrical stimulation continued to grow in the past decade because of its potential as a passive, non-invasive, home-based therapy, with reported gains in muscle strength and motor function. In a recent review by Kerr et al. (2004), the use of threshold electrical stimulation (TES; i.e., low-level sub-contraction electrical stimulus applied at home during sleep) on children with CP was examined. Pape et al. (1997), who first proposed its use in the early 1990's, suggested that TES increased blood flow during a time of trophic hormone secretion, which could result in increased muscle bulk. Three RCT on TES followed, with subject numbers ranging from 12 to 57, age ranging from 8 months to 15 years, and diagnoses ranging from hemiplegia to diplegia or quadriplegia (Dali et al. 2002; Sommerfelt et al. 2001; Steinbok et al. 1997a). Generally, lower limb muscles were stimulated and TES was given at home daily for 6 to 7 hours continuously during sleep. Two studies included clinical spasticity as an outcome measure, yet none of them reported change of spasticity after TES (Dali et al. 2002; Steinbok et al. 1997a). Only 1 of the 3 RCT TES studies demonstrated significant improvement in functional GMFM scores (Steinbok et al. 1997a). However, the participants in the study by Steinbok et al.

differed from those in the 2 other RCT studies in that the children had previously undergone SDR and had TES stimulation applied to a greater number of muscles.

Other than sensory stimulation, a number of studies employed neuromuscular electrical stimulation (NMES), an electrical current of sufficient intensity to elicit muscle contraction, in children with CP. Earlier, Carmick (1995) conducted a case study on children with CP and found that NMES applied during gait training with the same timing as the gastronemius on/off cycle (i.e., "on" during stance, "off" during the swing phase of a gait cycle) resulted in an improvement of muscle tone (measured clinically) and equinus gait during stimulation. Two RCTs NMES studies on children with CP subsequently showed significant improvements in the range of motion of the joint, muscle strength or gross motor function, but not spasticity (Hazlewood et al. 1994; Park et al. 2001). At this juncture, the scarcity of well-controlled trials makes it difficult to unequivocally support the use of electrical stimulation in the paediatric CP population.

1.5.3. Possible Mechanisms of TENS on Spasticity

Low threshold afferent conditioning has been found to modulate ongoing motorneuronal activity through segmental, propriospinal and/or supraspinal pathways. For example, a reduction in spasticity is reported to follow low-threshold afferent stimulation applied directly over antagonistic muscles (Alfieri 1982; Vodovnik et al. 1984), or remotely over the dorsal columns of the spinal cord (Cook and Weinstein 1973; Nashold and Friedman 1972). An improvement in spasticity and voluntary motor control may also be achieved by a decrease in afferent input, such as temporary nerve blocks with local anesthetic, or local cooling of the spastic muscle (Dimitrijevic and Nathan 1967; Knutsson 1970).

Several mechanisms have been proposed to explain these effects. Firstly, presynatpic inhibition could be involved, given the extensive convergence of descending pathways and of Ia, Ib and cutaneous afferents on common presynaptic inhibitory interneurons (Baldissera et al. 1981; Brink et al. 1984). In anaesthetized monkeys, dorsal column stimulation on spinothalamic tract neurons was reported to produce inhibitory effects, probably via a presynaptic inhibitory mechanism (Foreman et al. 1976). If presynaptic inhibition indeed is decreased in spasticity as suggested by Ashby and Verrier (1976), then enhancing low-threshold afferent input, as in dorsal column stimulation, may be one way of "switching on" presynaptic inhibitory mechanisms. The possibility of such a presynaptic inhibition mechanism was further supported by other studies. Levin and Hui-Chan (1993a) found that low intensity, high-frequency TENS activated predominately large diameters of afferent Aαβ nerve fibres, and repeated application of TENS enhanced vibratory inhibition of the H-reflex (Levin and Hui-Chan 1992). Since vibratory inhibition of the H-reflex has been attributed in part to presynaptic inhibition of Group I_a terminals (Burke et al. 1976; Gillies et al. 1969), it was suggested that repeated TENS applications increased vibratory inhibition of the H-reflex via an enhancement of presynaptic inhibition mechanism (Levin and Hui-Chan 1992).

Secondly, plastic changes in the CNS may account for some of the reported changes. In certain cases, repetitive electrical stimulation appeared to have a long-lasting effect on spasticity. For instance, dorsal column stimulation resulted in improvements that were developed slowly over time that might outlast the period of stimulation (Siegfried et al. 1978). Spasticity continued to decrease with repeated stimulation (10 minutes daily for 5 to 16 days) on muscles antagonistic to the spastic muscles (Alfieri 1982). In addition, the possibility of plastic changes in reflex pathways is reinforced by several findings of adaptive plasticity in the CNS. For

example, the vestibule-ocular reflex, once thought to be "hard-wired", can be modified following 2 to 3 weeks of altered vision conditions (Melvill Jones 1983). Finally, the time course of changes in motor function and spasticity following electrical stimulation are consistent with the time needed for development of sprouting in the CNS, thus inferring that the plastic mechanism may be implicated in mediating these changes (Hultborn and Malmsten 1983; Murray and Goldberger 1974).

Thirdly, TENS may reduce spasticity through triggering of the release of inhibitory neuromodulators. For example, TENS has been reported to release inhibitory neuromodulators or opiods in the cerebralspinal fluid and in the blood plasma of patients with pain and in those without pain (Almay et al. 1985; Salar et al. 1981). Thus, TENS may be acting via an augmentation of presynaptic inhibition, plastic changes, or the release of inhibitory neuromodulators in spasticity reduction.

1.6. Body-Weight-Supported Treadmill Training (BWS-TT) and Gait Re-education

1.6.1. Animal Studies

Animal models have provided a great deal of information about the development of locomotion. Recovery of locomotion after spinal cord transection was once considered to be largely dependent on the age of the animal at the time of the injury (Grillner 1973). In the early 1980's, Rossignol et al. (1986) and Barbeau et al. (1987) showed that in the absence of supraspinal input, cats spinalized (at the T13 level) as adults could recover a near normal locomotor pattern following an "interactive locomotor training" program. During this interactive locomotor training, the spinalized cats were supported by the tail and allowed to bear only the amount of weight such that they could walk with proper foot placement (with sole of the foot) on

a treadmill. Following a period of 1 to 3 months of training, the animals were capable of walking at different treadmill speeds, while completely supporting the weight of their hindquarters with proper foot placement. Moreover, the gait pattern was comparable in many aspects to that of an intact adult cat (Engberg and Lundberg 1969). Grillner (1985) suggested that these findings served as indirect evidence for the presence of a locomotor spinal central pattern generator (CPG). Such response to training has also added to the evidence on the capacity of the injured spinal cord for motor learning. The mechanisms for spinal cord learning, even in the absence of supraspinal control, are thought to include the effects of repeated segmental sensory inputs on lumbosacral motor neurons and interneurons during training, which could result in long-term potentiation (LTP; Grillner 1997). LTP has been shown to contribute to cortical representational plasticity during learning of skills after supraspinal injury. In addition, an increasing number of studies suggest the expanded effectiveness of residual corticospinal and afferent activity after stroke and SCI on spinal and cortical regulation of facilitation and recruitment (Davey et al. 1999; Jain et al. 1997). Furthermore, studies uncovered that hindlimb stepping in adult spinalized animals was improved by prolonged training on the treadmill, but became worse if these animals were merely standing for the same period of time (Edgerton et al. 1991; Lovely et al. 1986). Since these differences cannot be accounted for by changes in the skeletal muscular system, these results further supported the hypothesis that the isolated spinal cord is capable of learning (Edgerton et al. 1997; Hodgson et al. 1994). Taken together, evidence from these studies showed that interactive locomotor training is essential to the recovery of locomotion, at least in the adult spinalized cat model.

1.6.2. Clinical Studies of BWS-TT in Subjects with Neurological Impairments

Based on the above animal findings and clinical observation of inadequate weight bearing among neurologically impaired subjects, Barbeau and Blunt (1991) made the first leap from locomotor studies in spinal transected cats to the use of treadmills and partial weight support training in spastic paretic subjects. When human subjects with a profound, incomplete cervical or thoracic spinal cord injury were suspended in a harness and assisted to step on a moving treadmill belt, following a technique similar to the studies with cats, EMG activity can be elicited in lower extremity muscles that have little or no voluntary movement. Similar observations were noted by other investigators (Dobkin et al. 1995; Wernig and Müller 1991). Step-like EMG activity, without independent stepping, had also been elicited in subjects with a complete spinal cord injury during BWS-TT (Dietz et al. 1995; Dobkin et al. 1992, 1995). To examine the role of sensory information on efferent motor patterns, the level of loading, EMG patterns and kinematics of the lower limbs were examined during manually assisted or unassisted stepping with BWS-TT in subjects with SCI by Harkema et al. (1997). The modulation of lower limb EMG amplitude was found to be more closely associated with limb peak load than with muscle-tendon stretch or the velocity of the muscle-tendon stretch. It was therefore suggested that stretch reflexes were not the sole source of the phasic EMG activity in flexor and extensor muscles in the lower limbs. Instead, it appeared that the level of loading on the lower limbs provides cues that enable the human lumbosacral spinal cord to modulate efferent output in a manner that may facilitate the generation of stepping (Harkema et al. 1997).

The first large-scale clinical study of BWS-TT on SCI patients was reported by Wernig and Müller (1995). Eighty-nine incompletely paralyzed (44 chronic and 45 acute) para- and tetraplegics subjects underwent BWS-TT and were compared with 64

patients (24 chronic and 40 acute) treated conventionally. Patients in the BWS-TT group were trained daily for 3 to 20 weeks (median = 10.5 weeks) on a treadmill with BWS by a harness, and limb movements were encouraged through the assistance of the therapists as necessary. At the end of the training, improvements in locomotion were achieved in all 44 patients with chronic SCI, with 25 out of 33 chronic, non-ambulatory subjects regaining the ability to walk without external physical assistance (i.e., capable of walking with or without walking aids). In the group with acute SCI injury, 92% of treadmill-trained versus 50% of conventional-trained patients were able to walk without assistance after training. No difference in the recovery of voluntary muscle activity as elicited in a resting position, however, was noted between the treadmill- or conventional-trained groups. These results suggested that factors other than improvement in muscle strength might be the basis of the gain in walking abilities found after a period of BWS-TT.

An early study by Hesse et al. (1994) on patients with stroke reported that 9 hemiparetic adults who had required firm continuous support could reach independent walking after 25 sessions of BWS-TT. Hesse and coworkers (1995) further compared the effects of BWS-TT (phase A) with physiotherapy based on the Bobath concept (phase B) in 7 non-ambulatory hemiparetic subjects. A single case A-B-A study design was employed, with each treatment phase lasting for 3 weeks. BWS-TT was found to be more effective in terms of the restoration of gait ability (measured by the Functional Ambulation Category) and walking velocity (p values < 0.05) than with physiotherapy alone. A few years later, Visintin, Barbeau and colleagues (1998) reported the largest RCT to sort out the advantage of BWS in adults with stroke. In this study, 50 subjects were trained to walk with up to 40% of their body weight supported by a BWS system with an overhead harness (BWS group). The other 50 subjects were trained to walk bearing full weight on their lower extremities (no-BWS

group). After a 6-week training period, the BWS group scored significantly higher than the non-BWS group on functional balance, motor recovery, overground walking speed, and overground walking endurance (p values < 0.05). These results provided concrete evidence to support the use of this novel gait-training strategy to provide a dynamic and integrative approach for the treatment of gait dysfunction after stroke.

With a view to compare the effect of locomotor training using either BWS, functional electrical stimulation (FES), pharmacological approaches or a combination of these approaches, Barbeau et al. (1998) examined more than 20 clinical studies conducted by different research groups. The authors concluded that when these study results were combined and weighted by the number of subjects, there was a gradient of effects from small changes with the immediate application of FES or BWS to larger changes when locomotor training is combined with FES or BWS or pharmacological approaches. Even though the immediate effects of BWS or FES alone on walking function are minimal, these modalities can create a situation that facilitates locomotor training. For example, BWS allows acute stroke and SCI subjects to be trained even though they are not able to walk with full-weight-bearing on the treadmill or overground. Likewise, FES makes possible the initiation of lower limb movements, and thus locomotor training can take place. The combination of noradrenergic drugs and interactive locomotor training has proven thus far to be powerful in accelerating the recovery of locomotion in acute spinalized cats. Monoaminergic drugs have been shown to reduce signs and symptoms of spasticity and were associated with greater improvement in walking ability in subjects with SCI (Nance 1994; Rémy-Neris et al. 1998; Steward et al. 1991; Wainberg et al. 1990). The combined effects of monoaminergic drugs with a locomotor training program using BWS for 6 weeks (Fung et al. 1990) or FES for few months (Ladouceur et al. 1997) on patients with SCI has been shown to improve walking speed and locomotor ability,

respectively. These findings suggest that interactive locomotor training using BWS or FES may be a powerful approach to rehabilitation of walking after the patient has gained at least a minimal ability to take steps. The authors further speculated that pharmacological approaches may permit some subjects to regain some minimal ability to walk, thus enabling them to undergo locomotor training.

Several factors were postulated to influence the recovery of locomotion. The cause, extent, location of a CNS lesion, as well as the chronicity of the injury can have an impact on the potential and degree of plasticity or adaptability. In addition, the type, specificity, and duration of the intervention, as well as single versus combined treatment modalities can lead to different magnitudes of recovery (Barbeau et al. 1998).

Comparatively speaking, little has been published about the effects of BWS-TT on children with CP. Richards et al. (1997) endeavored to conduct the first feasibility study on 4 young spastic CP children (age range: 1.7 - 2.3 years) to examine the effect of a combination of conventional physical therapy and BWS-TT 4 times per week for 4 months. Bearing in mind the limitations of a small sample size and of proper research design, no significant changes were found in gait spatiotemporal parameters and the GMFM total score. The investigators concluded that intensive locomotor training was a feasible locomotion training program. However, the effects of BWS-TT on children remain unknown. One recent study by Schindl et al. (2000) reported promising results after BWS-TT in children. In this study, 6 non-ambulatory and 4 ambulatory school-age children with CP were recruited (mean age: 11.5 years, range: 6 - 18 years). Additional BWS-TT used 3 times a week, 25 minutes per sessions for 3 months was provided on top of the conventional therapy program in an outpatient setting to these children. The amount of BWS was set in such a way that the children were able to carry their body weight

sufficiently during the single-stance phase of each lower limb without knee collapse or excessive hip flexion and the support was reduced as soon as possible. At the completion of the training, significant improvements were found in GMFM scores in the standing section and walking section by 47% and 50%, respectively (p values < 0.05). Both non-ambulatory and ambulatory children demonstrated improvements in transfer and walking abilities to various extents. Although the study had not incorporated a comparison group, the preliminary results pointed to the potential benefits of using BWS-TT in children with CP. Even from an ethical point of view, these findings justify further studies to examine the effectiveness of BWS-TT using a well-controlled randomized design.

1.7. Rationale and Objective of the Present Study

1.7.1. Limitations of Previous Studies

Increasing amounts of evidence have demonstrated that novel neurorehabilitaiton approaches, such as TENS and BWS-TT, could offer promising results in spasticty reduction and enhancement of locomotion functions in adults with neurological dysfunction. The potential for these new treatment strategies to help children with spastic CP deserves our particular attention, due to the following reasons.

First, though an array of treatment options for spasticity is available, the variable effects, the moderate to high costs of drugs and surgery (such as SDR), and the invasive nature of surgery raise concerns on either approach being the best choice of treatment. Previous studies on adults have demonstrated the effect of TENS on spasticity, but this has not been demonstrated in studies on children. In fact, no study thus far has shown effects of any kind of electrical stimulation on spasticity in children with CP. A point to note is that the effect of TENS has been reported to be

comparable to that of anti-spastic drugs (Levin and Hui-Chan 1992). It will therefore be worthwhile to explore the use of TENS in children with spastic CP, since this treatment strategy has the added benefits of being non-invasive, low cost, and without the side effects often associated with drug intake (Howle 1999; Steinbok et al. 1995) or surgery (McLaughlin et al. 2002).

Second, evidence from 3 RCTs of SDR indicates that even when spasticity was reduced, the weakness unmasked thereafter still requires a prolonged period of rehabilitation to regain function (McLaughlin et al. 2002). Furthermore, the lack of correlation noted between spasticity and muscle strength (Engsberg et al. 2000, Ross and Engsberg 2002) calls for the need to consider spasticity and muscle weakness as relatively independent impairments in children with CP. Different treatment strategies may be needed to tackle these problems. BWS-TT has been shown to offer multiple benefits over isolated muscle strengthening, as it not only allows strengthening of lower limbs, but also enhances balance and coordination training in a functional context (i.e., walking). Ample evidence has demonstrated that BWS-TT can enhance locomotor recovery of adults after SCI or stroke (Barbeau et al. 1998). Limited studies thus far have examined the effects of such an interactive locomotor training regime in the paediatric population. The potential and efficacy of BWS-TT in children with spastic CP are yet to be investigated.

Third, previous animal studies and clinical trials suggested that combining BWS-TT with pharmacological intervention is a powerful approach in the rehabilitation of locomotion in adults with stroke or SCI. In some subjects, interactive locomotor training would not have been possible without pharmacological intervention (Barbeau et al. 1998). It thus seems appropriate to examine the combined effects of TENS and BWS-TT with the aim to determine if additional BWS-TT

implemented after TENS would allow better improvements in sensorimotor function in children with spastic CP.

Fourth, the phenomenon of spasticity is complex and probably multifactorial. One of the principal problems in understanding spasticity is that neither cat nor the primate findings should be generalized to humans due to inter-species differences. Furthermore, spasticity has been characterized in a number of ways, which range from polysynaptic reflexes to mechanical properties of muscles. The research on spasticity has mainly been conducted on the adult population, with recent investigators favouring a barrage of measures to achieve a composite index of spasticity. Nevertheless, comparable studies are lacking in children with CP.

Fifth, though many studies sought to quantify spasticity, co-contraction, muscle strength and walking performance objectively, thus far, no study has examined these issues concurrently in children with CP. Understanding the inter-relationship among various impairments and functions could allow better insights into the underlying mechanism affecting motor control in children with spastic CP. Furthermore, if we were to use these measurements to evaluate the effectiveness of a given intervention, the problem of reliability should first be addressed.

Available evidence reviewed in this chapter shows that TENS and BWS gait training have separately been shown to reduce spasticity and/or enhance motor functions in adults with spastic hemiparesis and SCI. We therefore hypothesize that these approaches would hold similar promise for children with CP. This hypothesis begs investigation, since children are believed to have even greater potential for recovery on account of the greater plasticity of their nervous systems. If the results from our study are positive, this treatment strategy could become a preferred choice for children with spastic CP, on account of its non-invasive nature, absence of the side-effects often associated with drug intake or surgery, and low cost. Note that the

treatments in the present thesis were implemented in a school setting while the children continued to attend classes in this study. This arrangement offers an added benefit to the children who want to undergo treatment without their studies being interrupted.

1.7.2. Statement of Hypotheses

The hypotheses of this study are that (1) TENS and/or TENS in combination with BWS-TT reduces spasticity more than placebo-TENS in children with CP; and that (2) combining TENS with BWS-TT further improves muscle function and walking performance than TENS alone in children with CP.

In the present thesis, TENS was given at low-intensity in a continuous mode (0.125 msec square pulses, 100 Hz, intensity at 2 times the sensory threshold) for 60 minutes, once a day, 5 days a week for 3 weeks to the skin overlying the common peroneal nerve of the more spastic leg of children with CP. In the placebo-TENS group, the same device and stimulation parameters as those in the TENS group were used with the circuit inside the device disconnected. In the TENS plus BWS-TT group, TENS was applied for 60 minutes, followed by 20 to 30 minutes of BWS-TT according to the walking tolerance and progression of each child.

1.7.3. Objectives of the Present Study

The objectives of this study are:

Objective 1: To quantify the status of spasticity, voluntary muscle contraction and walking gait performance, and the correlations among these variables in children with spastic CP.

Objective 2: To establish a reliable battery of tests, previously used to characterize spasticity and deficits in voluntary muscle contraction and walking performance in the adult population in children with CP.

Objective 3: To investigate the effects of TENS on spasticity and motor function in these children, by means of a comparison study with placebo-TENS.

Objective 4: To document the combined effects of TENS and BWS-TT gait training on spasticity and motor function in these children.

Chapter 2 describes the methodology of this study, including the study design, inclusion and exclusion criteria of subjects, protocols of treatment, methods of measurements, as well as the statistical methods used for data analysis. Chapter 3 reports the results of pilot studies that examined the reproducibility of the measurement protocols and characteristics of motor disorders in children with spastic CP. In Chapter 4, the relative effectiveness of adding TENS and/or TENS+BWS-TT on top of a conventional rehabilitation program in reducing spasticity and in improving voluntary muscle contraction in children with CP is reported. Chapter 5 examines the relative treatment effectiveness of adding (i) TENS, (ii) placebo-TENS, and (iii) TENS+BWS-TT on top of a conventional rehabilitation program in enhancing walking performance in children with spastic CP. Chapter 6 summarizes the findings of this study and presents the overall conclusions, limitations as well as significance of this study.

CHAPTER 2

METHODOLOGY

2.1 Summary

The objectives of the study are to (1) to quantify the status of spasticity, voluntary muscle contraction and walking performance of children with spastic cerebral palsy (CP); and (2) to determine whether TENS and/ or TENS+BWS-TT in addition to conventional therapy reduces spasticity and improved motor and ambulatory function in children with spastic CP. A randomized, placebo-controlled clinical trial was used to address these objectives as detailed below.

Subjects were school-aged children (6 – 15 years) with spastic CP, had moderate to severe spasticity over their calf muscles, and ambulated independently with or without walking aids for at least 6 minutes. The sample size and study power were calculated *a priori* using a power analysis of sample size (PASS). Informed consent from the children's parents was obtained. A total of 63 subjects recruited from special schools were stratified according to level of spasticity of the ankle plantarflexors and then randomly allocated into groups 1 to 3: TENS, placebo-TENS, and TENS+BWS-TT (body-weight-supported treadmill training).

All subjects continued to receive their conventional physiotherapy programs in their respective schools. The types, duration and frequency of the physiotherapy program for each child were recorded by his/her case therapist during the period of study. In the TENS group, low-intensity TENS was applied, via surface electrodes connected to a portable TENS stimulator, to the skin overlying the common peroneal nerve (L4-S2) posterior to the head of the fibula. Continuous stimulation (0.125 msec square pulses, 100 Hz, intensity at 2 times the sensory threshold) was applied for 60 minutes, once a day, and 5 days a week for 3 weeks. In the placebo-TENS group, the device and stimulation parameters were the same as those of the TENS group, except that the circuit in the device was disconnected. In the TENS+BWS-TT group, the same stimulation protocol as that of the TENS group was first delivered for 60

minutes, followed by 20 to 30 minutes of BWS-TT according to the walking tolerance and progression of each child.

Outcome measurements included: (1) spasticity of the ankle plantarflexors assessed by composite spasticity scale and stretch reflex, (2) muscle strength recorded by maximum isometric voluntary contraction and EMG co-contraction ratios of the ankle dorsiflexor and plantarflexor muscles, and (3) walking performance evaluated by the walking speed and energy cost during a 6-minute walk test. These measurements were recorded *before* treatment (T_0), and *after* 1 week (T_1), 2 weeks (T_2), and 3 weeks of treatment (T_3), to examine the effects and time course of TENS, placebo-TENS and TENS+BWS-TT.

Descriptive statistics were used to describe the characteristics of subjects in the 3 study groups. Repeated measure of analysis of variance (ANOVA) was chosen to compare outcome variables obtained *before* treatment (T_0), and *after* 1 week (T_1), 2 weeks (T_2), and 3 weeks of treatment (T_3). The between-subjects factor was the 3 groups, and the within-subjects factor was the 4 time intervals indicated. Pearson correlations were performed to determine possible relationships between some of the outcome measures. Before launching the main study, however, the reproducibility of all measurements protocols was evaluated and the status of spasticity, voluntary muscle contraction and walking performance of children with spastic CP are reported in Chapter 3.

2.2 Introduction

A randomized, placebo-controlled clinical trial design was used to address the objectives stated in Chapter 1 (section 1.7.3). This chapter describes the methodology and instrumentation used in the study. It describes the selection criteria of the subjects, the sample size calculation, the randomization procedures, and provides detail descriptions of each treatment protocol. In addition, description of the outcome measurements and procedures of data analysis are detailed below. In order to ensure that the outcome measurements used in the present study were repeatable, their reliabilities were examined and are reported in the subsequent chapter.

2.3 Subjects

2.3.1 Inclusion Criteria

Children with CP were recruited if they were:

(1) diagnosed with spastic diplegia or hemiplegia.

(2) aged 6- 15.

(3) suffered from mild to severe spasticity over their ankle plantarflexors.

(4) found to have a passive ankle dorsiflexion range to the neutral position of 0° and a passive plantarflexion range of 30°.

(5) able to follow instructions.

(6) able to ambulate with or without walking device for 6 minutes without manual assistance.

2.3.2 Exclusion Criteria

Children with CP were excluded if they were

(1) diagnosed as having other medical conditions such as mental retardation and seizures.

(2) known to have previous selective dorsal rhizotomy or excessive lengthening of the Tendo-Achilles.

(3) on antispasticity drugs.

Informed consent from their parents was obtained (Appendix 2.1). Recruited subjects were excluded *after* randomization if they could not tolerate the TENS/placebo-TENS stimulation or TENS+BWS-TT. Subjects were recruited from 5 special schools that provide service to children with physical disabilities in Hong Kong.

2.3.3 Sample Size and Study Power

The sample size was calculated using the PASS (version 6.0) statistical software package, based on the parameters reported in the previous study by Levin and Hui-Chan (1992). In their study, a significant reduction in clinical spasticity by 2.6, as measured by the composite spasticity score, was noted after 10 sessions of daily 1-hour TENS stimulation to adults with hemiparesis. Using this information, the effect size of TENS in reducing spasticity was calculated to be 0.96 (Appendix 2.2). Such an effect size is considered "strong" by Cohen (1988). Since there is no estimate available on the effect size of TENS+BWS-TT on spasticity, the sample size and power analysis were calculated based on a *t*-test instead of repeated measure ANOVA. Taking 5% alpha, 80% power, and a two-sided alternative test, the sample size needed for an effect size of 0.80 required a total of 63 subjects, with 21 subjects for each study group.

An extensive search on previous intervention studies conducted in children with CP revealed that the number of subjects was often much less than the intervention studies conducted on adults with neurological conditions. For instance, while the number of children with CP examined in assessment-type studies was up to

111 (Russell et al. 1989); for intervention studies, the number was much smaller (n = 38, Albright et al. 1995). Concrete examples from the literature indicated real limitations in recruitment of subjects in intervention studies conducted in children with CP. Indeed, after close consultation with school therapists, a realistic number of subjects for the study: was set at 63, with 21 subjects for each of the 3 study groups.

2.3.4 Randomization Procedures

Children consented to participate in this study were stratified according to their level of plantarflexor spasticity (using the composite spasticity scale, presented below) before being randomly allocated to 1 of the 3 treatment groups, TENS, placebo-TENS, TENS+BWS-TT, through drawing lots. All subjects received 5 sessions of treatment each week for 3 weeks, for a total of 15 treatments.

2.4 Treatment Protocol

2.4.1 Conventional Physiotherapy Program

Due to ethical reasons, subjects continued their conventional physiotherapy programs at their respective schools. The conventional physiotherapy programs across the 5 schools where the subjects were recruited included stretching exercises, positioning to prevent contractures, muscle strengthening, balance training, transfer and gait training. Case therapists of the subjects were invited to record the duration, frequency and the types of interventions implemented every week, to examine the homogeneity of this conventional program among the 3 study groups (Appendix 2.3).

2.4.2 Transcutaneous Electrical Nervous Stimulation (TENS)

The more spastic leg (as measured by the composite spasticity scale) of the diplegic CP children or the affected side of the hemiplegic CP children received

electrical stimulation in both TENS and placebo TENS groups. Staodyn® TENS – Maxima® III TENS portable stimulators (Figure 2.1) were used in both treatment groups. The stimulator was calibrated and delivered a high-frequency constant current of 100 Hz with single square pulses of 0.2 ms duration. Electrode locations were chosen following the protocol reported in a previous study (Levin and Hui-Chan 1992). Two rectangular rubber surface electrodes (4.6 cm x 4.6 cm) were attached to the skin with electric conductive gel and hypoallergenic tape. The positive electrode was applied to the skin overlying the common peroneal nerve (L4-S2) located just posterior to the head of the fibula, which supplies the muscle antagonistic (i.e. tibialis anterior, TA) to the spastic calf muscles. The negative electrode was applied over the middle of TA muscle belly (Figure 2.2). Correct positioning of the electrodes was confirmed by the subjects reporting a tingling sensation in the cutaneous distribution of the nerve along the anterior part of the leg and dorsum of the foot.

Figure. 2.1: TENS device used in this study (Staodyn® TENS – Maxima® III)

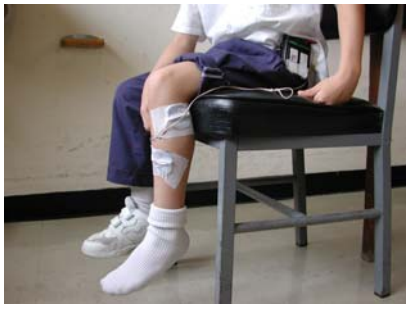


Figure.2.2: Location of the electrodes for TENS or placebo-TENS stimulation

The mean sensory threshold was determined as the average of 3 trials, during which the intensity of the stimulation was gradually increased to a level when the subject first reported a faint tingling sensation in the cutaneous distribution of the nerve. Continuous stimulation (0.125 msec square pulses, 100 Hz, intensity at 2 times

the sensory threshold) was applied for 60 minutes in each treatment session during class. Our pilot study showed that children could receive TENS stimulation while attending classes and that the stimulation threshold increased slightly after a few sessions of treatment. Therefore, the stimulation threshold and intensity were monitored during each treatment session and were adjusted upwards with time when needed.

2.4.3 Placebo-TENS

The same TENS machine, electrode placements, and treatment protocol (i.e., 60 minutes for each treatment session) were used to deliver placebo stimulation. The light indicator of the identical looking TENS stimulator was switched on without actual current output, as the electrical circuit inside the device has been disconnected manually. To eliminate subjects' suspicion, all subjects were informed prior to any stimulation that they might or might not feel any sensation associated with the stimulation.

2.4.4 TENS plus Body-Weight-Supported Treadmill Training (TENS+BWS-TT)

The same TENS stimulation protocol, as described in section 2.2.2, was delivered to each subject for 60 minutes in each treatment session during class. After TENS, subjects practiced walking on a treadmill in the Physiotherapy Department of the school, for 20 to 30 minutes, with rest intervals appropriate to their walking tolerance. The BWS-TT system includes a treadmill (model 600 HR) and a partial weight support system (model LiteGait I-150). The motor of the treadmill could operate at a very slow speed (minimum speed of 0.1 mph); with 0.1-mph increments to accommodate the slow walking speed of children with CP. The speed of the treadmill (range 0.6 – 1.5 mph) and the percentage of BWS (estimated range 10 –

40%) were selected to facilitate proper trunk and limb alignment and the transfer of weight to the lower limbs. The BWS system (LiteGait) has a monitor to reflect the amount of body weight supported (Figure 2.3), and those readings were recorded.

BiSym monitor to reflect the amount of body weight supported via the Y-yoke of the BSW-TT system

Figure 2.3: The body-weight-supported treadmill training system

2.5 Outcome Measurements

2.5.1 Measurement Battery and Assessment Schedule

Outcome measurements included: (1) spasticity of the ankle plantarflexors assessed by the composite spasticity scale and stretch reflex as a function of maximum M response (SR/M), (2) muscle strength recorded by maximum isometric voluntary contraction and EMG co-contraction ratios of the ankle dorsiflexor and plantarflexor muscles, and (3) walking performance evaluated by walking speed and energy cost during a 6-minute walk test. The time course and the effects of TENS, placebo-TENS and TENS+BWS-TT were examined *before* treatment (T_0), and *after* 1 week (T_1), 2 weeks (T_2), and 3 weeks of treatment (T_3). All assessments were performed by the author throughout the whole period of study. Reproducibility of all outcome measurements was assessed prior to the study and is presented in Chapter 3.

2.5.2 Measurement of Spasticity of the Ankle Plantarflexors

2.5.2.1 The Composite Spasticity Scale

With the subject lying supine and the knee stabilized at 60° of flexion, 3 clinical measures to assess spasticity were recorded: (a) Achilles tendon jerk was graded on a widely used 5-point scale, where '0' denoted 'no response' and '4' indicated 'maximally hyperactive response'. and (b) Resistance to full-range passive ankle dorsiflexion at a moderate speed was scored on a Modified Ashworth Scale (Bohannon and Smith 1987). Since this measurement closely represents the clinical manifestations of muscle tone, it was be doubly weighted. Thus a score of '0' indicated 'no resistance', and a score of '8' corresponded to 'maximally increased resistance'. (c) Finally, clonus was graded on a four-point scale, where '1' indicated 'clonus not elicited' and '4' represented 'sustained clonus'. The summation of the scoring of these 3 measurements provided a composite (albeit subjective) index of spasticity. Based on the previous study of Levin and Hui-Chan (1993b) and our clinical experience, composite spasticity scale (CSS) scores ranging from '0 to 9', '10 to 12' and '13 to 16' corresponded to 'mild', 'moderate' and 'severe' spasticity respectively. Detailed description of this scale is presented in Appendix 2.4.

2.5.2.2 Stretch Reflexes

2.5.2.2.1 Subject Position and Stretch Perturbations

Subjects remained in the same starting position (i.e. in supine lying) with the knee stabilized at 60° of flexion and the ankle fixed at 30º plantarflexion on a mechanical portable ankle stretching device (Figure 2.4). The mechanical ankle stretching device consisted of a footplate attached to a spring (spring constant = 10 Nm). The footplate could move the ankle from 30º of plantarflexion to the neutral ankle position at a velocity greater than 500º/sec, and the movement could be arrested

by a mechanical stopper. A load cell (Futek Reaction torque sensor, California, USA: Model JM-2, capacity: 500 in-lb, linearity -0.052%) and a variable resistor (TTelectronic wirewound rotary potentiometer, Hong Kong, China: Series ABW1: resistance 10 kΩ ± 10%l; linearity ± 2 %) were attached along the axis of rotation of the footplate to record torque and range of motion of the ankle, respectively. A thin sheet of a force-sensing resistor (heel sensor) was mounted on the footplate to detect if the foot remained in contact with the footplate during the stretch reflex test. Calibration of the variable resistor was performed to identify the voltage change when the ankle was moved through 30º range of motion. The load cell came with a calibration certificate that stated that 1 V equaled to 11.14 Nm.

The procedures for evoking stretch reflexes (SR) were as follows: The footplate and ankle were manually displaced to 30º of plantarflexion. The position was then kept in place by an electromagnet. Subjects were given the instruction, "Relax and do not intervene voluntarily". During this time, tibialis anterior (TA) and soleus electromyography (EMG) were monitored on-line, to ensure that there was no active muscle contraction. When the background EMG was sufficiently quiet, data collection started for at least 500 msec before the examiner released the electromagnet of the footplate to induce rapid ankle dorsiflexion of the subjects. This was done to guarantee that adequate baseline EMG was collected for subsequent data analysis. A total of 5 SR recordings were taken, with at least 30 sec of rest in between, to ensure full recovery of the excitability of the motor neuronal pool of the stretched muscles.

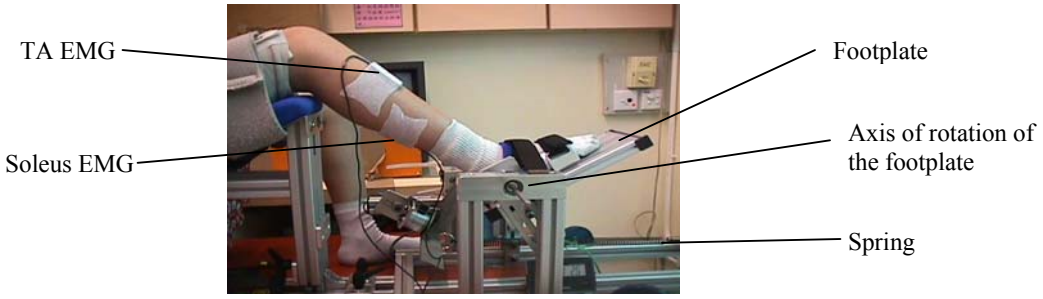


Figure 2.4: The mechanical portable ankle stretching device

2.5.2.2.2 Surface Electromyography of Ankle Muscles

Prior to applying the surface electrodes, the skin was shaved and cleaned carefully with rubbing alcohol to remove any grease and dead skin from the surface. Two bar-shaped surface active electrodes (B&L Engineering®,California, USA: Model BL-AE-WG) were placed over the TA and soleus muscles. Each active electrode had two stainless steel pads with an inter-electrode spacing of 1.4 inches and a ground reference electrode centered between the two sensing electrode pads. The electrode had a pre-amplifier to provide a gain of 330. The input impedance was greater than 100 megaohms (MΩ). The common mode rejection ratio was 95 db, and the bandwidth was 12 – 1000 Hz.

The electrodes were positioned using the anatomical references proposed by Levin and Hui-Chan (1993b). To record the TA EMG, the bar-shaped electrodes were orientated longitudinally along the middle of the muscle bulk. To record the soleus EMG, the bar-shaped electrodes were placed 2 cm distal to the intersection of the medial and lateral heads of the gastrocnemius and the Achilles tendon. The positions of the electrodes were outlined on the skin with a permanent marker at the end of each assessment session, and then monitored regularly to ensure that the array was re-applied accurately when re-assessing the subject on different days, to minimize variability due to different electrode locations.

2.5.2.2.3 Recording of Soleus Stretch Reflexes

During passive ankle dorsiflexion, a winDAD/Pro+ data acquisition software and a DataQ (DI-720-P) analog-to-digital acquisition card (12 bits) were used to capture the following signals into a notebook computer: (1) range of ankle dorsiflexion; (2) raw EMG signals of the TA being shortened; (3) raw EMG signals of the soleus being stretched; and (4) heel sensor (to ensure that the heel stayed in

contact with the footplate). All signals were sampled at a frequency of 2000 Hz per channel. Prior to data collection, the A/D data acquisition system was calibrated by feeding a known signal to an oscilloscope to calibrate the oscilloscope. Then, a function generator was used to feed a known signal to both the oscilloscope and the data acquisition system to calibrate the latter system by comparing the voltage display and the time marker between the two.

2.5.2.2.4 Recording of Soleus M-responses

Since EMG values can vary according to skin preparation and the electrode placements in the same subjects on different test days, the maximal M-response was recorded from the soleus muscle, and then used to normalize EMG amplitude and area values of the SR recorded from the same muscle. The maximal M–response ('M') is presumed to represent the total motorneuronal pool activated by a maximal electrical stimulus (Schiepatti 1987). Assuming that the recording conditions were constant, it would display strong intra-session stability. EMG area values of the SR were therefore expressed as ratios to those of the M-response recorded during the same session (i.e., SR area/M area x 100%). Such normalization procedures would allow the mean values across subjects and/or across sessions within the same subject to be compared (Levin and Hui-Chan 1993b).

The maximal M-response of the soleus muscle was collected in the following manner: one msec square-wave pulses were delivered via a Grass Stimulator (Model S88), at 0.1 Hz via a cathode (a 0.5 cm 3M Red Dot surface electrode) placed over the posterior tibial nerve in the popliteal fossa, and an anode (a 20 cm^2 tin plate covered with denim material soaked in saline solution) positioned superior to the patella for selective stimulation of the nerve trunk (Hugon 1973). The intensity of the stimulation was gradually increased so that maximal M-responses

were recorded by the EMG electrodes located over the soleus muscle. A total of 10 M-responses were collected for further data analysis.

2.5.2.2.5 Analysis of Stretch Reflexes and M-responses

SR and M-responses were analyzed following our previous protocol (Levin and Hui-Chan 1993b). Individual SR trials were analyzed off-line for EMG latency, EMG response duration and area using a customized LabView program (6*i* version). Test trials were screened qualitatively for inclusion in the data analysis to eliminate those in which the subject did not relax completely. Figure 2.5 shows a typical SR trial. The onset of displacement of the ankle was detected when the displacement surpassed 10 standard deviations (S.D.) of the baseline signals (i.e., about 2º of motion). EMG signals were first filtered at 500 Hz, then full-wave rectified. EMG latency was determined from the onset of ankle displacement to the time when the EMG signals exceeded 3 S.D. of the baseline value. The duration of the solues SR was calculated from the EMG onset (defined above) to the time when the EMG signals returned to 3 S.D. below the baseline. Also, SR areas were calculated by a computer algorhythm to determine the maximal integral of the EMG response over a window of 150 msec following its onset. These were expressed as percentages of the maximal M-response areas evoked in the same soleus muscle (i.e. SR/M area ratio).

The maximal M-response areas were computed off-line by rectifying and integrating the M wave within a window, determined from the EMG response onset to its offset (the point at which the trace exceeded, or returned, to 3 S.D. of the baseline). A typical trace of M-response is illustrated in Figure 2.6.

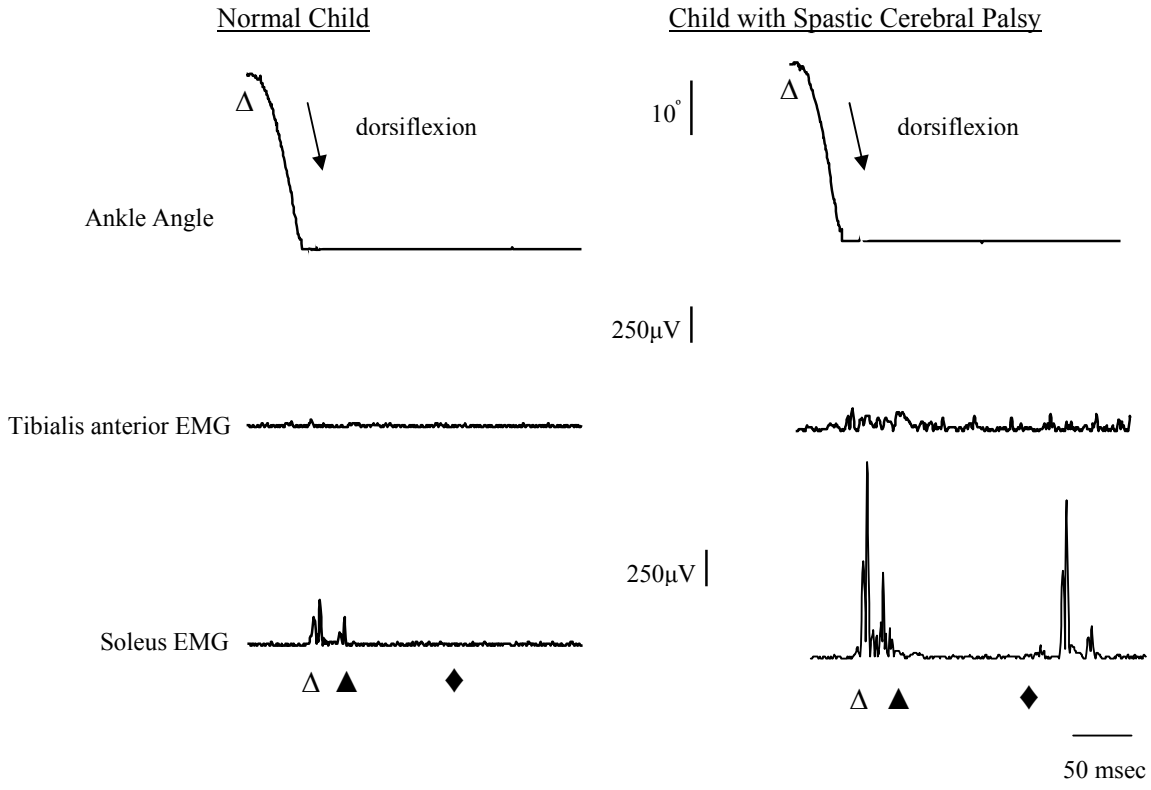


Figure 2.5: Typical stretch reflexes recorded in a normal child (left) and a child with spastic cerebral palsy (right). From top to bottom: angular displacement of the ankle (dorsiflexion indicated by downward deflection), tibialis anterior EMG, and soleus EMG. Soleus SR latencies were measured from the onset of the displacement (open triangle in the top trace) to the onset of EMG response (open triangle in lowest trace). Soleus SR duration was measured from the EMG onset (open triangle) to EMG offset (filled triangle) as shown in the lowest trace. SR areas were calculated by a computer algorhythm to determine the maximal integral of the EMG response over a window of 150 msec following its onset (filled diamond in the lowest trace).

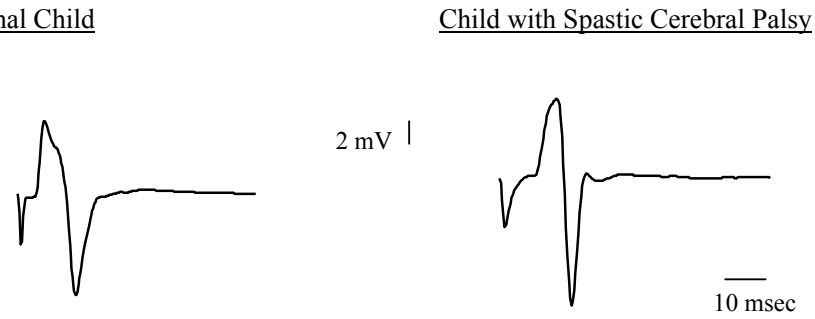


Figure 2.6: Typical maximal M-responses recorded in a normal child (left) and a child with spastic cerebral palsy (right).

2.5.3 Measurements of Maximum Isometric Voluntary Contractions and Agonist/Antagonist EMG Co-contraction Ratios of Ankle Dorsiflexors and Plantarflexors

With the footplate fixating the ankle at the same neutral position, subjects were asked to produce 5 seconds of maximal isometric voluntary contractions (MIVC) of their ankle dorsiflexors followed by their plantarflexors for 6 trials each, with about 1 second of rest between trials. Subjects were allowed 2 to 3 practice trials so that they learned to generate contractions with consistent force profiles in terms of the onset and the maximal force attained.

The load cell of the ankle device recorded the torque generated during MIVC of the ankle dorsiflexors and plantflexors. TA EMG and soleus EMG were recorded as described previously.

2.5.3.1 Analysis of MIVC and Agonist/Antagonist EMG Co-contraction Ratios

Individual MIVC trials were then analyzed off-line. They were screened qualitatively for inclusion in the data analysis to eliminate those trials in which the torque generated was inconsistent. Analysis of mean maximal torques and the corresponding mean agonist and antagonist EMG areas were calculated using the

Labview program (6*i* version). The EMG signals were first low-passed at 500 Hz and then full-wave rectified. Typical EMG (top two traces) and torque records (bottom trace) recorded during MIVC of dorsiflexors and plantarflexors of a normal child and a child with CP are shown in Figure 2.7. During ankle dorsiflexion, the mean maximal torque produced during a 500 msec window was calculated where the torque had reached a plateau. During the same time window, the mean EMG area values of the agonist (TA) and antagonist (soleus) EMG responses were calculated. During ankle plantarflexion, similar analysis was done to identify the mean maximal torque generated during MIVC of the plantarflexors and the corresponding mean areas values of TA and soleus EMG responses. A time window of 500 msec during peak torque was chosen for analysis, instead of the period of dynamic force production, because of the high variability of the force production profile in these subjects. In some children with CP, it was noted that the torque generated during ankle dorsi- and plantar-flexion could not be maintained for more than 1000 msec.

EMG co-contraction ratios were calculated from the mean agonist and antagonist EMG areas over the 500 msec window (Levin and Hui-Chan 1994). Individual EMG signals recorded on each test day were normalized by expressing the antagonist EMG area as a ratio of the total agonist plus antagonist EMG area values (see the formula below). Normalization was carried out because the area and amplitude values of raw EMG signals might have varied between subjects and across test sessions according to skin preparation and EMG electrode placements. As previously mentioned, such a procedure would allow comparisons of the data obtained on different test days for each subject, or between different subjects.

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

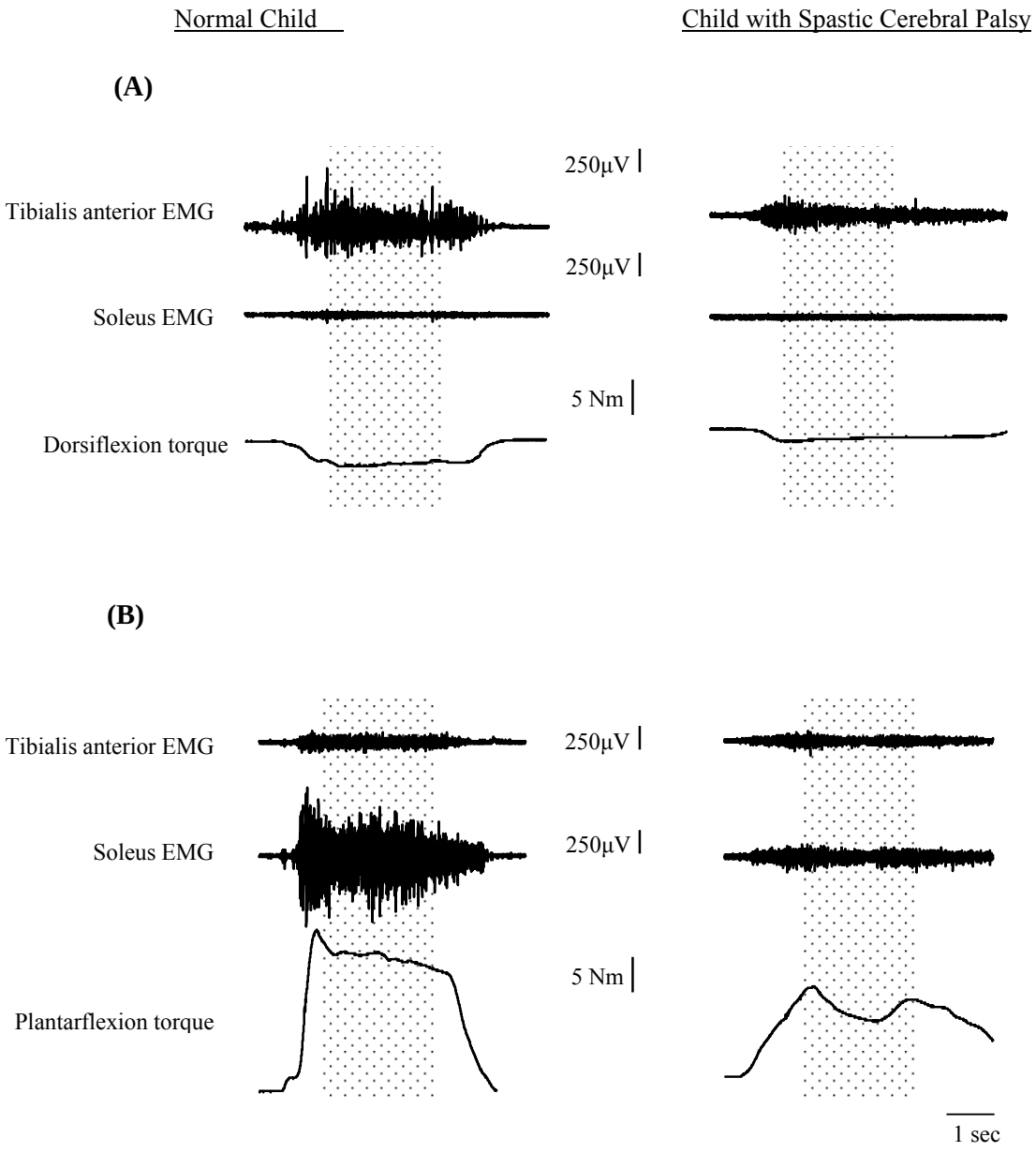


Figure 2.7: Typical raw tibialis anterior EMG (upper trace), soleus EMG (middle trace) and torque records (bottom trace) recorded during maximal isometric voluntary contraction (MIVC) of ankle (A) dorsiflexors and (B) plantarflexors in a normal child (left) and a child with spastic cerebral palsy (right). During MIVC, mean EMG and torque values were calculated over a 500 msec window when the force had reached a plateau (shaded areas).

2.5.4 Measurements of Walking Speed and Energy Cost – 6-Minute Walk Test

In a pilot test, it was observed that continuous walking for 6 minutes was perceived as a moderate to difficult task for the children recruited for the present study. Therefore, the 6-minute walk test was chosen to examine the energy cost of walking by measuring the physiological cost index (PCI; Bowen et al. 1998; Butler et al. 1984; Furukawa et al. 1998; Rose et al. 1990, 1991) and walking speed (Butler et al. 1984). The latter two indices were recorded in the following manner: a 10-meter walkway marked by plastic tapes at every 2 meters was selected within the premises of the special schools. After putting on the chest belt of a heart rate monitor system (Acumen) over the tip of their sternum and a telemetric stop watch over their wrist (Figures 2.8 and 2.9), subjects were asked to sit quietly for 5 minutes to record their resting heart rate (HR_{rest}). During this period of time, they were asked to rate their perceived general health status, and the procedures of the 6-minute walking test were explained. Subjects then walked with their usual walking aids and orthosis (if any) to and from the 10-meter walkway at their usual walking speed for 6 minutes. The heart rate recorded during their walk represented the walking heart rate (HR_{walk}). Because previous studies have shown that appropriate encouragements would enhance subject's performance (Guyatt et al. 1984), encouragements to continue to walk were given every 30 seconds by the author as "Keep going, you are doing well".

At the end of the 6-minute walk test, subjects were asked to rate the perceived exertion using the Borg Category Ratio scale – CR-10 (Borg 1982; Marinov et al. 2002) depicting fatigue (dyspnoea) from 'not at all' to 'maximal' by means of 10 grades. The heart rate monitor system was set to record the subject's heart rate every 10 seconds. The data collected were later downloaded to the computer. The distance covered every 2 minutes and the total distance walked were noted on the recording sheet (Appendix 2.5). Subjects then sat quietly until their heart rate returned to within

10% of their resting heart rate before they left the assessment room. Each child was allowed 1 practice session before actual data collection. During each assessment session, 1 trial of the 6-minute walk test was recorded.

Figure 2.8: The heart rate monitor system: chest belt and telemetric stopwatch.

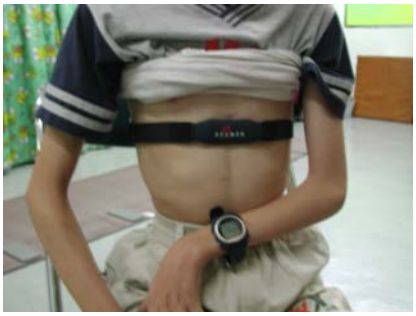


Figure 2.9: Subject wearing the chest belt and telemetric stop watch.

2.5.4.1 Analysis of Walking Speed and Physiological Cost Index

Walking speed was calculated as follows (Butler et al. 1984):

Walking speed = distance covered / time (Unit: meter/second).

Calculation of PCI was based on the method proposed by Rose et al. (1990):

$PCI = (HR_{walk} - HR_{rest}) / walking\ speed$ *(Unit: heart beats/meter).*

Note that walking speed, HR_{walk} and HR_{rest} were calculated using the average data in the last 2 minutes of the 6-minute walk test. This was because the heart rate became stabilized across all subjects between the fourth to sixth minutes of the walk. Hence, these recordings represented more accurately the energy cost of walking. A typical record of the heart rate profiles of this 6-minute walk test is presented in Figure 2.10.

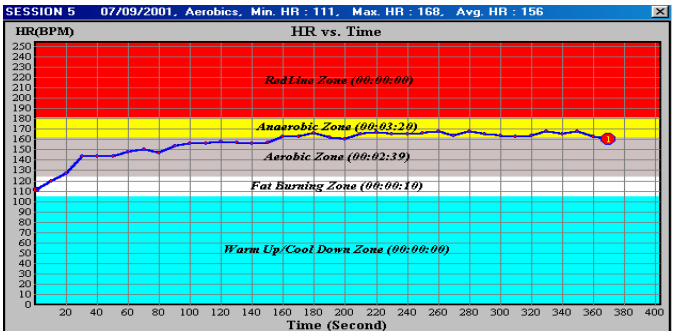


Figure 2.10: Typical record of the heart rate profile during the 6-minute walk test in a child with spastic cerebral palsy. (HR = heart rate; BPM = beats per minute)

2.6 Data Analysis

Baseline measurements of group characteristics, i.e., age, gender, weight and height, severity of spasticity, type of CP (diplegia or hemiplegia), and the types, duration and frequency of conventional physiotherapy among the 3 study groups were compared by one-way ANOVA.

To compare the effects before and after each treatment, the 3 batteries of measurements described above were analyzed using repeated analysis of variance (ANOVA) using SPSS (version 10.0). The design employed in this study had two factors. The between-subjects factor was the 3 groups (i.e., TENS, placebo-TENS, and TENS+BWS-TT). The within-subjects factors were the 4 assessment intervals (i.e., *before* treatment (T_0), and *after* 1 week (T_1), 2 weeks (T_2), and 3 weeks of treatment (T_3)). If there were some interactions in the results of the repeated ANOVA, multiple comparisons (post-hoc tests) with Bonferroni correction was used to compare the % changes in the outcome measures among the 3 treatment groups.

The baseline value for each outcome measurement was compared among the 3 groups to ascertain the homogeneity among the groups. That accomplished, and considering that the baselines values for each outcome measurement may vary

slightly among individuals, the data recorded after the treatment session (T_1 to T_3) were normalized with respect to their baseline values (T_0) for comparisons among the 3 treatment groups. That is, "percentage changes" in a given outcome measurement as a result of treatment were compared among groups. This was done by subtracting the results *after* treatment minus those *before* treatment (termed "baseline" values) divided by the baseline values and expressed as percentages. The significant level was set at 5% for all 2-tailed tests.

2.7 Ethical Considerations

Approval to recruit children in the 6 special schools for children with physical disabilities was sought from the Principal and/or the School Board prior to informed consent being obtained from children's parents. In some schools, special meetings were held to explain the study to the parents as a group or individually. The information sheet and consent form of the study are attached in Appendices 2.1a and 2.1b. Ethical approval was also obtained from the Ethical Committee of The Hong Kong Polytechnic University prior to the study.

CHAPTER 3

MOTOR DISORDERS IN SPASTIC CP:

SPASTICITY, VOLUNTARY MUSCLE CONTRACTION

AND WALKING PERFORMANCE

3.1 Summary

The abnormal reflex function and motor control in children with spasticity and their underlying pathophysiology are poorly understood. Comprehensive quantification of spasticity and motor function in the adult population has been reported, but comparable studies are scarce in children. In spite of this, measures of spasticity and voluntary motor function are often used to investigate the effects of therapeutic intervention in improving the motor function of children. Before launching our main study, which aims to examine the effects of TENS and/or TENS+BWS-TT in reducing spasticity and in enhancing muscle and ambulatory function in children with spastic cerebral palsy (CP), the characteristic, reproducibility and validity of all the measurement protocol for spasticity and motor function in these children were first examined and are reported in this chapter.

Specifically, the objectives of this pilot study were threefold: (1) to examine the reproducibility of clinical spasticity and stretch reflex (SR) measures, voluntary muscle contraction and walking performance in normal children and children with spastic CP in order to determine if they could be used to chart the effects of therapeutic treatment over time in the latter group of children; (2) to delineate possible differences of these measurements between normal and spastic children as one measure of validity; (3) to identify possible correlations among these measurements in the spastic children.

To address objectives 1 and 2, bilateral lower legs of 8 children with spastic CP and 9 age-matched normal children (aged 10.8 ± 2.8 years and 8.9 ± 2.4, respectively) were examined on 2 different days within a week. To achieve objective 3, data from 61 children with spastic CP (aged 10.7 ± 2.8 years) who participated in the main study were used for correlation analyses. Measurements included: (1)

spasticity of the ankle plantarflexors assessed by the composite spasticity scale and stretch reflex as a function of maximum M response (SR/M); (2) ankle muscle strength recorded by maximum isometric voluntary contraction (MIVC) and agonist/antagonist electromyography (EMG) co-contraction ratios of the ankle dorsiflexors and plantarflexors; and (3) walking performance evaluated by walking speed and energy cost during the 6-minute walk test.

Three main findings emerged. Firstly, high reliability of the clinical rating of spasticity (r = 0.97) and SR latency (r = 0.85) was found in the spastic group. Furthermore, high degree of inter-session consistency (r = 0.78 - 0.97) were also found in the SR/M area ratio, maximal dorsiflexion and plantarflexion torques, agonist EMG areas and co-contraction ratios during ankle dorsiflexion and plantarflexion, and walking speed and physiological cost index of the 6-minute walk test in both normal and spastic children.

Secondly, no significant differences in the measurements were noted between the left and right legs of either the normal or spastic children. However, the more spastic leg of the spastic children demonstrated significantly ($p < 0.05$) a larger soleus SR/M area ratio, smaller dorsiflexion and plantarflexion torques and smaller agonist EMG areas with larger co-contraction ratios during both voluntary dorsiflexion and plantarflexion than those of the dominant leg of normal children. In addition, the spastic children walked significantly ($p < 0.05$) slower with a higher physiological cost index than the normal children during the 6-minute walk.

Thirdly, spastic children who have larger SR/M area ratios were found to have larger plantarflexion co-contraction ratios (r = 0.28; p = 0.03), produced smaller plantarflexion torques (r = -0.48; p = 0.00) and dorsiflexion torques (r = -0.27; p = 0.04), and walked at slower speeds (r = -0.40; p = 0.01) and higher energy costs (r = 0.49; p = 0.00). Furthermore, a larger plantarflexion co-contraction ratio was found to

correlate with smaller plantarflexion torques (r = -0.47; p = 0.00). Those who produced smaller plantarflexion torques also produced smaller dorsiflexion torques (r = 0.48; p = 0.00). Subjects with smaller plantarflexion and dorsiflexion torques were found to walk at slower speeds (r = 0.36; p = 0.02 and r = 0.42; p = 0.01, respectively) and higher energy costs (r = -0.37; p = 0.01 and r = -0.43; p = 0.00, respectively). Furthermore, slower walking speeds were found to correlate with higher energy costs of walking (r = -0.74; p = 0.00).

Our results suggest that this battery of tests, previously used to characterize spasticity and deficits in voluntary muscle contraction and walking performance in the adult population, is a reliable and valid measure to characterize motor disorders in children with spastic CP. In addition, it could differentiate abnormal levels of spasticity, voluntary muscle contraction and walking performance in these children from those of normal children. Our results further demonstrated that motor impairment such as hyperactive SR and weakness of ankle dorsiflexors and plantarflexors are interrelated, and correlated with certain walking performance indices in such a way as to decrease the walking speed and increase the energy cost of walking in children with spastic CP. Our results highlight the role of SR on muscle function and walking performance in children with CP. The test battery we had designed, thus, could be used as a comprehensive evaluation tool for intervention studies on spasticity, motor deficits and walking performance in children with spastic CP.

3.2 Introduction

Motor disorders in children with CP may include spasticity and abnormal motor activity that could limit their daily activities such as walking. One of the most prominent clinical signs of spasticity is an exaggerated stretch reflex, or hyperreflexia. Mapping of stretch reflex (SR) changes may provide some insight into the pathophysiological mechanism underlying spasticity. For instance, soleus SR latencies were shorter and the SR/M area ratio, where M is the maximum muscle response evoked by transcutaneous electrical stimulation of the nerve, were augmented in adults with spasticity (Burke and Lance 1973, Powers et al. 1989, Levin and Hui-Chan 1993b). Moreover, impaired modulation of the SR has been proposed to contribute to impaired walking ability in adults with spasticity (Sinkjaer et al. 1996a). In contrast to studies on adults, studies on reflex excitability in children are scarce and have usually been performed under passive conditions. By displacing the ankle or elbow joint passively and examining the EMG activities of the stretched muscles, both Brouwer et al. (1998) and Jobin and Levin (2000) noted a lower SR threshold in ankle plantarflexors or elbow flexors, respectively, in children with spastic CP. Many researchers have come to realize that, in addition to reflex hyperexcitability, changes in the biomechanical properties of the muscle also contributed to the manifestation of clinical spasticity (Lundy-Ekman 2002a) and that no single measurement is an adequate descriptor of spasticity.

Clinically, spastic hypertonia has been defined as resistance to passive muscle stretch in a velocity-dependent manner (Lance 1980b). Albeit subjective, scales such as the Ashworth scale and the Modified Ashworth Scale are commonly used to measure spasticity owing to their clinical versatility. No correlation of the Ashworth scale with enhanced excitability of tendon tap reflexes (hyperreflexia), however, was demonstrated (Faist et al. 1994). Reliability of these 2 scales was good in the upper

extremities but less good in the lower extremities, especially in the ankle plantarflexors (Pandyan et al. 1999). In this regard, the Composite Spasticity Scale (CSS) has been shown to better describe plantarflexor spasticity (Levin and Hui-Chan 1993b, Goulet et al. 1996) and to correlate with the SR area ratio in adults with hemiplegia (Levin and Hui-Chan 1993b). Nevertheless, this scale has not yet been applied to evaluate children with CP.

In addition to spasticity, there is often muscle weakness in individuals with spasticity (Levin and Hui-Chan 1994). Strength assessment by maximal *isometric* voluntary contraction (MIVC) is a commonly used method (Bohannon et al. 1987; Canning et al. 1999; Damiano et al. 1995b; Levin and Hui-Chan 1994; Wiley and Damiano 1998), because some adults or children with spasticity do not have enough strength to move the lever arm of the strength testing device such as a isokinetic dynamometer (Damiano et al. 2000). Among the 8 lower limb muscles tested in children with CP, Wiley and Damiano (1998) found that the weakest muscles detected were the hip extensors, ankle dorsiflexors and plantaflexors, with strength values amounting to around 24%, 46% and 36%, respectively, of those of normal children.

Other than spasticity and muscle weakness, the presence of co-activation of the agonist and antagonist muscles has been frequently described in children with spastic CP (Brouwer et al. 1998). During MIVC of the dorsiflexors and plantarflexors, surface EMG activities of the tibialis anterior and soleus muscles have been used to calculate the co-contraction ratios of the ankle muscles to assess the extent of agonist-antagonist contraction (Canning et al. 1999; Levin and Hui-Chan 1994). In adults with hemiparesis, dorsiflexion co-contraction was substantially higher than in age-matched normal adults and was associated with a significant reduction in force production of the paretic dorsiflexors (r = -0.91, Levin and Hui-Chan 1994). In a comparable study, Brouwer et al. (1998) also noted compromised plantarflexor force production and

abnormally high co-contraction ratios during plantarflexion in children with CP, but the relationship between EMG co-contraction and muscle strength has not been reported.

Apart from recording motor impairments, such as spasticity, muscle strength and co-contraction, concurrent data collection on functional measures, such as walking, would allow one to gain a comprehensive understanding of a patient's motor disorders and to determine the most effective intervention. To examine walking performance, walking speed and energy cost of walking based on heart rate measurement, termed the "physiological cost index (PCI)", have been found to be clinically versatile and serve as good quantitative indicators of the level of physical handicap in children with CP (Bowen et al. 1998; Butler et al. 1984; Furkuawa et al. 1998; Rose et al. 1991). Although a 12-minute walk test was commonly used to examine walking speed and energy cost of walking in patients with various diseases, Butland and co-workers (1982) demonstrated that equivalent results can be obtained with a 6-minute walk test.

More studies have started to objectively quantify spasticity, co-contraction, muscle strength and walking performance and to examine their inter-relations, yet no study to date has examined these impairments concurrently in children with CP. Evaluation of changes in these impairments before and after a given treatment intervention could give us better insights into the underlying mechanism affecting the motor control of individuals with spasticity. If we were to use these measurements, however, data reproducibility becomes an important issue. To better understand the pathophysiology underlying the movement disorders in children with CP, the objectives of this study were threefold: (1) to quantify and examine the reproducibility of clinical spasticity and SR measures, maximal voluntary muscle contraction and co-contraction in the ankle muscles as well as walking performance in normal and

children with spastic CP; (2) to delineate possible differences of these measurements between the two study groups; and (3) to identify possible correlations among these measurements in the spastic children.

3.3 Subjects

Criteria for inclusion and exclusion of the children with spastic CP were the same as those outlined in section 2.3 of Chapter 2. Eight children with spastic CP (aged 10.8 ± 2.8 years; Table 3.1), recruited from a special school, and 9 age-matched normal children (aged 8.9 ± 2.4 years), recruited from a community center, were examined twice to evaluate repeatability and validity of the measurement protocol. Demographic data of these subjects are presented in Table 3.1. Data of 61 children with spastic CP (aged 10.7 ± 2.8 years; Table 3.2) who participated in the main study were used to analyze possible correlations among the measurements. The ethical committee of the Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, approved the study. Informed consent from parents of these children was obtained prior to the study.

3.4 Methods

To evaluate repeatability and validity of the measurement protocol and to delineate possible differences between the two groups of children, bilateral lower legs of the 8 spastic and 9 normal children were assessed twice within 1 week. For correlation analyses among the measurements, the more spastic legs of 61 spastic children who participated in the main study were examined once. Whenever possible, children with spastic CP were scheduled to be assessed at the same time of the day, to avoid unnecessary variability due to possible diurnal fluctuation of spasticity. Leg

Table 3.1: Demographic profile of the normal and spastic CP children

Subject	Age (yrs.)	Sex	Wt. (kg)	Ht. (m)	BMI	Leg	Diagnosis	ATR	Resis-tance	Clonus	CSS score	Degree of spasticity
Normal subjects												
1.	10	M	32.0	1.41	16.1							
2.	12.5	M	37.0	1.53	15.8							
3.	8.5	M	23.5	1.21	16.1							
4.	7	F	34.0	1.24	22.1							
5.	8	F	21.4	1.17	15.6							
6.	6	M	22.5	1.08	19.3							
7.	12	M	34.0	1.33	19.2							
8.	6	F	23.5	1.09	19.8							
9.	10	M	31.0	1.28	18.9							
Mean	8.9		28.8	1.26	18.1							
S.D.	2.4		6.0	0.2	2.3							
Spastic subjects												
1.	12	M	42.0	1.47	19.4	L	Diplegia	4	3	4	14	Severe
						R		4	2	4	12	Moderate
2.	11	F	36.0	1.38	18.9	L	Diplegia	4	2	2	10	Moderate
						R		3	2	2	9	Mild
3.	6	M	21.8	1.19	15.4	L	Diplegia	2	2	2	8	Mild
						R		3	3	3	12	Moderate
4.	13	M	30.0	1.47	13.9	L	Rt. Hemi.	-	-	-	-	-
						R		1	1.5	2	8	Mild
5.	14	M	47.0	1.63	17.7	L	Diplegia	0	2	2	6	Mild
						R		4	3	3	13	Severe
6.	9	M	26.4	1.08	22.6	L	Diplegia	4	3	4	14	Severe
						R		3	3	4	13	Severe
7.	8	F	24.0	1.26	15.1	L	Diplegia	2	2	2	8	Mild
						R		3	3	4	13	Severe
8.	13	F	33.2	1.53	14.2	L	Diplegia	3	2	3	10	Moderate
						R		2	1	2	6	Mild
Mean	10.8		32.6	1.38	17.2						10.4	
S.D.	2.8		8.8	0.2	3.1						2.8	

CSS = composite spasticity scale score
0 - 9: mild spasticity
10 - 12: moderate spasticity
13 - 16: severe spasticity

Wt. = weight
Ht. = height
ATR = Achilles tendon reflex
Resistance = as measured by the Modified Ashworth Scale
F, M = female, male
L, R = left, right
Hemi. = hemiplegia

Table 3.2: Demographic profile of the 61 spastic CP children who participated in the main study

	Mean	Standard deviation	Maximum	Minimum
Age (years)	10.7	2.8	15.0	6.0
Gender: M (%)	32 (52.5)			
F (%)	29 (47.5)			
Type of CP: Diplegia	54			
Hemiplegia	7 (4 Left, 3 Right)			
Side of leg treated: L (%)	31 (50.8)			
R (%)	30 (49.2)			
Weight (Kg)	32.4	9.7	62.0	18.0
Height (m)	1.4	0.2	1.6	1.0
BMI (Kg/m^2)	17.4	3.1	27.0	12.0
CSS score	11.2	2.0	14.0	7.0
SR/M area ratio (%)	71.2	53.5	216.0	10.0
MIVC: Dorsiflexion				
Mean maximal torque (Nm)	2.4	2.0	7.4	0.05
Co-contraction ratio (%)	25.07	16.5	89.0	9.0
MIVC: Plantar-flexion				
Mean maximal torque (Nm)	6.9	5.5	24.8	0.5
Co-contraction ratio (%)	44.3	13.8	72.0	17.0
Six-Minute Walk Test				
Walking speed (m/min)	39.2	16.5	66.0	4.0
PCI (beats/m)	1.8	1.5	8.0	0.5

BMI = body mass index
CSS = composite spasticity scale
SR/M area ratio = stretch reflex/ M-response area ratio
MIVC = maximal isometric voluntary contraction
PCI = physiological cost index

dominances of the normal subjects were noted by asking subjects which leg they used to kick a ball or to go up the stairs. The test battery consisted of 3 measures, all of which have been described in detail in Chapter 2 (Section 2.5). Briefly, they involved recording of: (1) clinical spasticity and SR of the ankle plantarflexors, (2) MIVC and agonist/antagonist EMG co-contraction ratios of the ankle dorsiflexor and plantarflexor muscles, and (3) walking performance during the 6-minute walk test.

3.5 Data Analysis

The variables analyzed included: CSS score, SR latency, duration, and area ratio, MIVC torques of ankle dorsiflexors and plantarflexors, agonist/antagonist EMG areas and co-contraction ratios, and walking speed and PCI during the 6-minute walk test. Detailed descriptions of these variables are given in Section 2.5 of Chapter 2.

Reproducibility of all measurements was evaluated by interclass correlation coefficients, a procedure that takes into account the proportion of the variance of an observation due to subject-to-subject variability (Fleiss 1986). Comparisons of measurements between the left and right legs of normal and spastic children were done using parametric paired *t*-tests; while comparisons between the more spastic legs of children with CP and the dominant legs of normal children was done using parametric independent paired *t*-tests. Note that log transformation was applied to the 'SR/M area ratio' due to the large heterogeneity of variance between the 2 study groups in these data, before performing the independent paired *t*-tests. Correlations among all measurements were done using Pearson's correlation statistics. A significant level of 0.05 was set for all two-tailed tests. All statistical procedures were performed with SPSS software (version 10.0).

3.6 Results

3.6.1 Reproducibility of the Measurement Protocol

No significant differences were noted on any measurement between the left and right legs of either the normal or spastic children (Appendces 3.1 to 3.3). Therefore, data reproducibility in each study group is reported only for the right leg in Table 3.3.

Stretch perturbations. The mean velocities of stretch perturbations delivered to the spastic and normal subjects were 556.9 ± 33.9 °/s and 549.4 ± 40.3 °/s, respectively and were not significantly different across groups or test days ($p > 0.05$).

Clinical spasticity and stretch reflex. A high degree of inter-session consistency (Table 3.3) was found in the clinical rating of spasticity ($r = 0.97$), SR latency ($r = 0.85$) and SR/M area ratio ($r = 0.97$), but not SR duration ($r = 0.56$) in the spastic children. In normal children, high day-to-day consistency was found only in the SR/M area ratio ($r = 0.91$), but not in SR latency and duration ($r = 0.47$ and 0.51, respectively).

Maximal isometric voluntary contraction. Table 3.3 shows that the mean values of maximal dorsiflexion and plantarflexion torques were highly reproducible in both spastic ($r = 0.94$ and 0.89, respectively) and normal children ($r = 0.96$ and 0.96, respectively). In spite of the well-known limitation in comparing "raw" EMG area recorded on different days (i.e. EMG signals not being normalized to a standard value such as maximum M response), "raw" agonist EMG area were reproducible during dorsiflexion ($r = 0.86$ and 0.94, respectively) and plantarflexion ($r = 0.79$ and 0.89, respectively) in both spastic and normal children, thus yielding a highly reproducible EMG co-contraction ratio during ankle dorsiflexion ($r = 0.94$ and 0.93, respectively) and plantarflexion ($r = 0.89$ and 0.78, respectively) in the spastic and normal groups.

Table 3.3: Reproducibility of measurements in the normal and spastic CP children on 2 different days

	Normal children (n = 9)			Spastic Children (n = 8)		
Measures	Day X	Day Y	r^a	Day X	Day Y	r^a
CSS score				10.8 (2.7) [b]	10.00 (3.0)	0.97
SR						
SR latency (msec)	53.1 (9.9)	55.0 (13.7)	0.47	50.6 (9.7)	49.3 (8.8)	0.85
SR duration (msec)	19.5 (7.5)	20.2 (6.7)	0.51	18.0 (4.9)	17.7 (7.2)	0.56
SR/M area ratio (%)	9.6 (6.1)	9.0 (6.2)	0.91	90.2 (72.2)	87.7 (86.6)	0.97
MIVC: Dorsiflexion						
Mean maximal torque (Nm)	11.4 (5.5)	10.7 (4.8)	0.96	2.8 (2.5)	3.2 (2.8)	0.94
Agonist EMG area (μV.s)	228.8 (128.8)	225.5 (141.3)	0.94	72.0 (43.7)	80.9 (51.3)	0.86
Antagonist EMG area (μV.s)	33.5 (10.3)	42.0 (8.3)	0.37	35.8 (26.2)	31.6 (16.4)	0.64
Co-contraction ratio (%)	13.9 (3.2)	13.9 (3.2)	0.93	29.5 (18.1)	27.4 (15.6)	0.94
MIVC: Plantarflexion						
Mean maximal torque (Nm)	28.8 (14.4)	29.7 (12.0)	0.96	6.3 (5.0)	5.5 (3.7)	0.89
Agonist EMG area (μV.s)	153.9 (73.7)	163.5 (80.7)	0.89	43.7 (21.6)	47.1 (21.6)	0.79
Antagonist EMG area (μV.s)	32.8 (7.7)	37.6 (4.3)	0.56	20.8 (5.8)	24.8 (11.7)	0.59
Co-contraction ratio (%)	18.9 (4.6)	20.8 (5.7)	0.78	34.0 (8.5)	34.3 (4.5)	0.89
Six-Minute Walk Test						
Walking speed (m/min)	70.2 (8.9)	69.8 (9.4)	0.90	43.9 (12.9)	45.4 (15.5)	0.94
HR_{rest} (beats/min)	79.2 (8.6)	78.5 (8.9)	0.87	102.7 (5.7)	102.4 (9.9)	0.87
HR_{walk} (beats/min)	101.2 (10.2)	100.3 (9.9)	0.91	158.9 (17.1)	157.0 (15.9)	0.83
PCI (beats/m)	0.47 (0.3)	0.46 (0.3)	0.89	1.38 (0.5)	1.36 (0.6)	0.93

CSS = composite spasticity scale
SR = stretch reflex
SR/M area ratio = stretch reflex/ M-response area ratio
MIVC = maximal isometric voluntary contraction
HR_{rest} = heart rate at rest
HR_{walk} = heart rate during walk
PCI = physiological cost index

r^a = interclass correlation coefficient
[b] = values are mean (S.D.)

Walking Performance. High reproducibility was noted in walking speed, HR_{rest}, HR_{walk}, and PCI during the 6-minute walk test in both spastic and normal groups, with *r* values ranging from 0.83 to 0.94 (Table 3.3).

3.6.2 Comparison of Left and Right Legs within Groups

Since the measurements were largely reproducible on the 2 test days, data of left and right legs of the normal and spastic children measured on the first assessment day (day X) are presented in Appendices 3.1 to 3.3. No significant difference ($p > 0.05$) between the left and right legs of either normal or spastic children was noted in all the measurements.

3.6.3 Comparison between Groups

Since no difference was found in all the measurements between the left and right legs of the normal children, comparisons between the more and less spastic leg based on the CSS score in each spastic child was justified and was done using paired *t*-tests. The more spastic leg was found to have significantly greater SR/M area ratio values and larger dorsiflexion co-contraction ratios than those of the less spastic leg ($p = 0.004$ and 0.02, respectively; Table 3.4). Because all normal subjects indicated that their right leg was the dominant one, data of the dominant (right) leg of the normal group were compared against the more spastic leg of the spastic group. Table 3.4 summarizes the results.

Clinical spasticity and stretch reflex. Table 3.4 shows that clinical spasticity score revealed moderate spasticity in the more spastic leg of the CP children, being 12.3 ± 1.7. Earlier examples of typical SR recorded in a normal and spastic child as shown in Figure 2.5 (Chapter 2) show that the SR/M area ratio of the more spastic

Table 3.4: Comparison of measurements between the two legs of spastic CP children, and between normal and spastic children

Measurement	Normal Children (n = 9)	Spastic Children (n = 8)		p^a	p^b
	Dominant (right) leg	More spastic leg	Less spastic leg		
CSS score		12.3 (1.7)[c]	8.9 (2.7)	0.07	
SR					
SR latency (msec)	53.1 (9.9)	46.5 (12.7)	53.7 (13.0)	0.07	0.25
SR duration (msec)	19.4 (7.5)	19.9 (6.1)	18.0 (4.6)	0.19	0.90
SR/M area ratio (%)	9.6 (6.1)	108.7 (72.6)	55.8 (28.3)	0.004*	0.00[lg*]
MIVC: Dorsiflexion					
Mean maximal torque (Nm)	11.4 (5.5)	2.2 (2.5)	3.2 (2.7)	0.43	0.01*
Agonist EMG area (μV.s)	228.8 (128.8)	71.0 (43.7)	79.5 (35.5)	0.38	0.006*
Antagonist EMG area (μV.s)	33.5 (10.3)	38.0 (26.1)	29.4 (24.0)	0.12	0.64
Co-contraction ratio (%)	13.9 (3.2)	35.0 (12.5)	26.8 (10.4)	0.02*	0.004*
MIVC: Plantarflexion					
Mean maximal torque (Nm)	28.8 (14.4)	7.3 (5.8)	8.5 (11.6)	0.74	0.02*
Agonist EMG area (μV.s)	153.9 (73.7)	46.0 (19.4)	42.0 (23.3)	0.69	0.002*
Antagonist EMG area (μV.s)	32.8 (7.7)	25.2 (10.4)	20.7 (6.7)	0.28	0.10
Co-contraction ratio (%)	18.9 (4.6)	35.8 (7.5)	34.8 (6.5)	0.78	0.000*
Six-minute Walk Test					
Walking speed (m/min)	70.2 (8.9)		43.9 (12.9)		0.04*
HR_{rest} (beats/min)	79.2 (8.6)		102.7 (5.7)		0.03*
HR_{walk} (beats/min)	101.2 (10.2)		158.9 (17.1)		0.02*
PCI (beats/m)	0.47 (0.3)		1.38 (0.5)		0.03*

CSS = composite spasticity scale
SR = stretch reflex
SR/M area ratio = stretch reflex/ M-response area ratio
MIVC = maximal isometric voluntary contraction
HR_{rest} = heart rate at rest
HR_{walk} = heart rate during walk
PCI = physiological cost index
p^a = paired *t* test between data of the more and less spastic legs of the spastic children
p^b = independent paired *t* test between the dominant (right) leg of normal children and the more spastic leg of spastic children
[c] values are mean (± S.D.)
* denote *p* value < 0.05
[lg] Log transformation applied before computing independent paired *t* test between normal and spastic children.

legs of the spastic children was significantly larger (108.7 ± 72.6%; Table 3.4) than that of the normal children (9.6 ± 6.1%; $p = 0.00$). SR latency tended to be shorter in the spastic children (46.5 ± 12.7 msec) than that of normal children (53.1 ± 9.9 msec), although it did not differ significantly. Similarly, SR duration was not significantly different between the two groups. Three of the spastic children had sustained clonus that was triggered by the stretch perturbation. The frequency of this stretch-evoked clonus was in the order of 3 to 5 Hz.

Maximal isometric voluntary contraction. Typical examples of torque and raw EMG recorded during MIVC of ankle dorsiflexion and plantarflexion were already presented in Figure 2.7 (Chapter 2). Table 3.4 shows that compared to normal children, the spastic children showed remarkable decreases in the amount of dorsiflexion and plantarflexion torques in both legs. The mean values of maximal torque were significantly smaller in the more spastic leg of the spastic children than in the dominant (right) leg of normal children. The values were, respectively, 2.2 ± 2.5 Nm and 11.4 ± 5.5 Nm for dorsiflexors ($p = 0.01$), and 7.3 ± 5.8 Nm and 28.8 ± 14.4 Nm for plantarflexors ($p = 0.02$). The more spastic leg of the spastic children also showed significant decreases in agonist EMG areas when compared to those of the dominant leg of normal children during both voluntary dorsiflexion (mean area = 71.0 ± 43.7 μV.s and 228.8 ± 128.8 μV.s, respectively; $p = 0.006$) and voluntary plantarflexion (46.0 ± 19.4 μV.s and 153.9 ± 73.7 μV.s, respectively; $p = 0.002$). In contrast, antagonist EMG areas did not differ significantly between the two groups during both dorsiflexion and plantarflexion. Consequently, co-contraction ratios were remarkably increased ($p = 0.004$) in the spastic children when compared to those of the normal children during dorsiflexion. They were 35.0 ± 12.5% and 13.9 ± 3.2%, respectively, which was an increase of 2.5 fold. Similarly, during plantarflexion, the spastic children had higher co-contraction ratios ($p = 0.000$) than those of the normal

children, being 35.8 ± 7.5% and 18.9 ± 4.6%, respectively, which was an increase of 1.9 fold.

Walking performance. A significantly slower walking speed was noted in the spastic children than in the normal children, being 43.9 ± 12.9 m/min and 70.2 ± 8.9 m/min, respectively (p = 0.04). Interestingly, the resting heart rate of the spastic children (102.7 ± 5.7 beats/min; Table 3.4) was significantly higher than that of the normal children (79.2 ± 8.6 beats/min; p = 0.03). During the 6-minute walk test, the walking heart rate of the spastic children (158.9 ± 17.1 beats/min) was up to 75.6% of their maximal heart rate (= 220 beats/min – age), which was significantly higher than that of the normal children (101.2 ± 10.2 beats/min, representing 47.9 % of their maximal heart rate; p = 0.02). The higher walking heart rate and lower walking speed explain why a higher PCI was noted in the spastic children (1.38 ± 0.5 beats/m; Table 3.4) than that of the normal children (0.47 ± 0.3 beats/m; p = 0.03).

3.6.4 Correlations among Measurements

Inter-correlations among all the reproducible measurements are shown in Table 3.5. Only those relationships that showed significant correlations are reported in Figure 3.1 (A to L). Spastic children who had more hyperactive plantarflexor SR (larger SR/M area ratio) were found to have larger plantarflexion co-contraction ratios (r = 0.28; p = 0.03; Figure 3.1A), produced smaller plantarflexion torque (r = -0.48; p = 0.00; Figure 3.1B) and dorsiflexion torque (r = -0.27; p = 0.04; Figure 3.1C), walked at slower speeds (r = -0.40; p = 0.01; Figure 3.1D) and at higher energy costs (r = 0.49; p = 0.00; Figure 3.1E). Furthermore, a larger plantarflexion co-contraction ratio was found to correlate with smaller plantarflexion torque (r = -0.47; p = 0.00; Figure 3.1F). Those who produced smaller plantarflexion torque also produced smaller dorsiflexion torque (r = 0.48; p = 0.00; Figure 3.1G). Spastic subjects who

Table 3.5: Correlation matrix among all the reproducible measurements, using the data of 61 CP children who participated in the main study

		SR			MIVC: Dorsiflexion		MIVC: Plantarflexion		Six-minute Walk Test	
	CSS score	Latency (msec)	Duration (msec)	SR/M area ratio (%)	Co-contraction ratio (%)	Mean maximal torque (Nm)	Co-contraction ratio (%)	Mean maximal torque (Nm)	Walking speed (m/min)	PCI (beats/m)
SR										
SR/M area ratio[lg]	0.06	0.07	0.09							
MIVC: Dorsiflexion										
Co-contraction ratio	0.18	0.23	0.38	-0.12						
Mean maximal torque	0.10	0.38	-0.05	-0.27*	0.06					
MIVC: Plantarflexion										
Co-contraction ratio	0.04	-0.04	0.44	0.28*	0.16	0.20				
Mean maximal torque	-0.01	0.17	0.48	-0.48*	0.07	0.48*	-0.47*			
Six-minute Walk Test										
Walking speed	0.24	-0.02	0.27	-0.40*	0.04	0.42*	-0.04	0.36*		
PCI	-0.01	0.11	0.35	0.49*	0.18	-0.43*	0.26	-0.37*	-0.74*	

SR = stretch reflex
SR/M area ratio = stretch reflex/M-response area ratio
MIVC = maximal isometric voluntary contraction
CSS = composite spasticity scale
PCI = physiological cost index
[lg] = log transformation applied before computing correlations
* = denote p values < 0.05, Pearson correlation coefficients

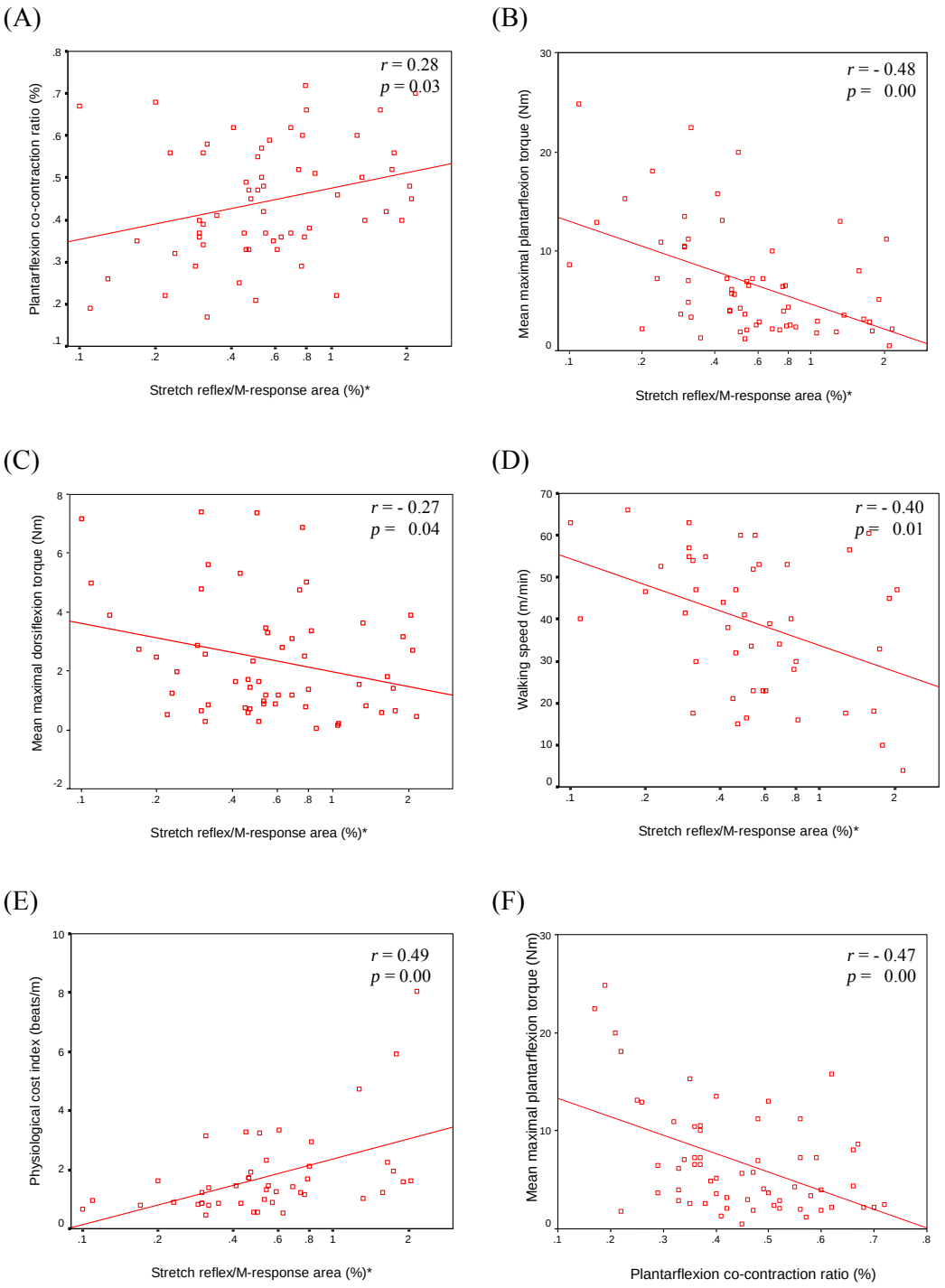


Figure 3.1: Significant correlations ($p < 0.05$) among the measurements: stretch reflex (SR/M response) area ratio with (A) plantarflexion co-contraction ratio, (B) mean maximal plantarflexion and (C) dorsiflexion torque, (D) walking speed, and (E) physiological cost index. Significant correlation between mean maximal plantarflexion torque with (F) plantarflexion co-contraction ratio.

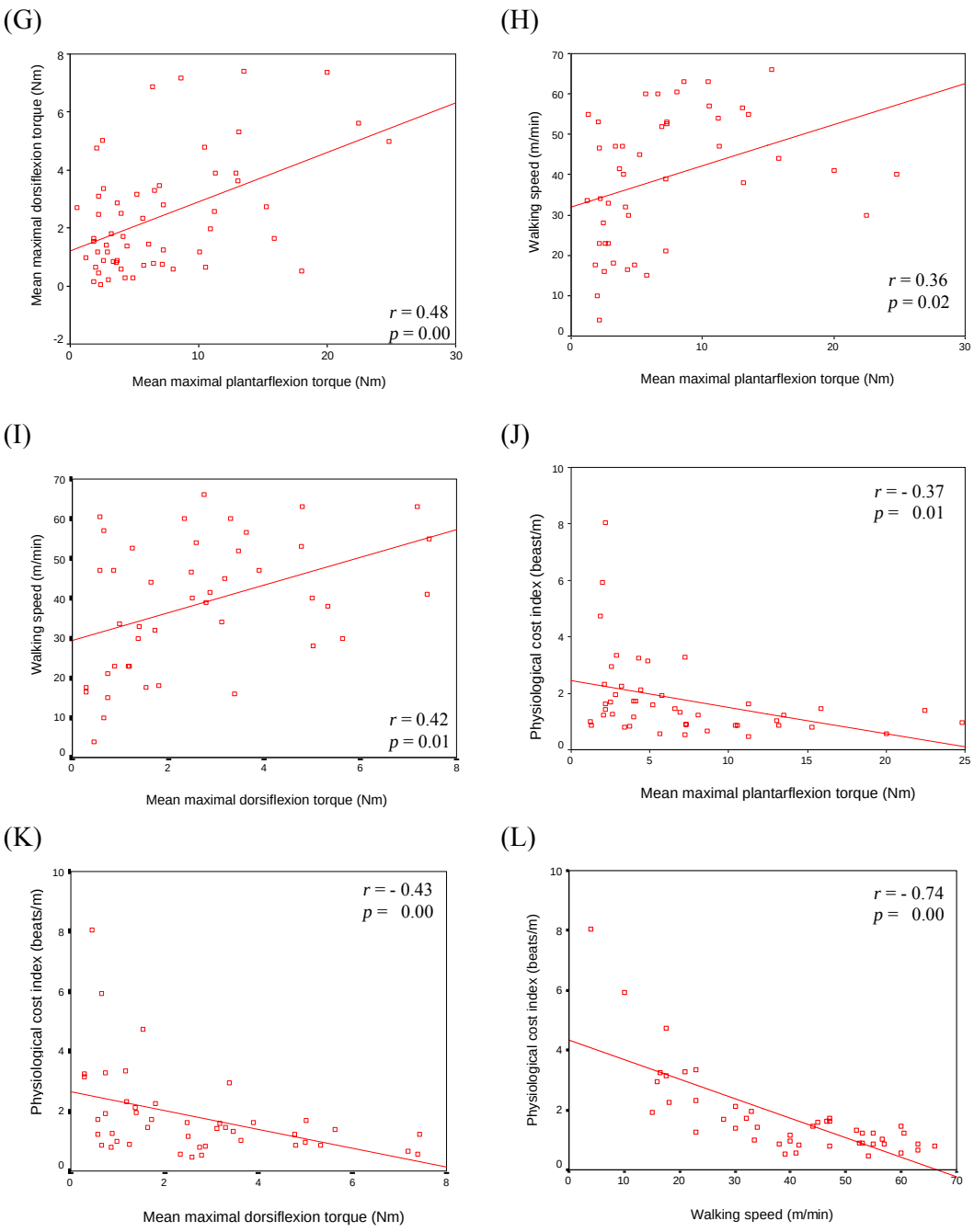


Figure 3.1: Significant correlations ($p < 0.05$) among the measurements: mean maximal plantarflexion torque with (G) mean maximal dorsiflexion torque, (H) walking speed, and (J) physiological cost index. Significant correlations between mean maximal dorsiflexion torque with (I) walking speed and (K) physiological cost index, and finally between (L) walking speed and physiological cost index.

produced lower plantarflexion and dorsiflexion torque were found to walk at slower speeds (r = 0.36; p = 0.02; Figure 3.1H and r = 0.42; p = 0.01; Figure 3.1I, respectively) and higher energy costs (r = -0.37; p = 0.01; Figure 3.1J and r = -0.43; p = 0.00; Figure 3.1K, respectively). Furthermore, a slower walking speed was found to correlate with a higher energy cost of walking (r = -0.74; p = 0.00; Figure 3.1L). No correlation between the SR/M area ratio and clinically measured spasticity was detected.

3.7 Discussion

3.7.1 Reproducibility of the Measurement Protocol

Similar to previous studies on spastic adults, measurements of clinical spasticity scores (Goulet et al. 1996; Levin and Hui Chan 1993b), SR/M areas (Levin and Hui Chan 1993b), MIVC dorsiflexion and plantarflexion torques and EMG cocontraction ratios during dorsiflexion (Levin and Hui Chan 1994) were highly consistent across test days in our normal and spastic children (Table 3.3).

Our experimental paradigm also showed highly reproducible measurements of walking speed and PCI in children with spastic CP. Unlike in our results, PCI was reported by Boyd et al. (1999) to be an unreliable measure, as opposed to an energy expenditure measurement based on oxygen uptake. Their conclusion was drawn based on comparing the measurements recorded in 5 children without disability over a 6 month period. The long test-retest period and, in particular, the small sample size in their study may account for the large variation of the PCI values measured on different test sessions. We are the first group who examined PCI with a large sample of children with CP.

The high reproducibility of most of our measurements may reflect the rigor of our experimental paradigm as well as the stability of the conditions of our patient

population. It also indicated that these measurements are reliable indicators of spasticity, voluntary muscle function and walking performance in children with spastic CP. Their stability warrants them as outcome measures in evaluating interventions directed at improving spasticity and motor function in children with CP. Indeed, some of these measurements have been shown to be sensitive enough to detect changes in clinical spasticity following 2 and 3 weeks of repetitive applications of transcutaneous electrical nerve stimulation in adults with spastic hemiparesis (Levin and Hui-Chan 1992) and to detect changes in PCI after 3 months of treadmill walking training in children with CP (Yu 2004). In addition, since this battery of tests has previously been used in adults with spasticity, adopting this battery of tests as outcome measures would further allow comparisons of the pathophysiological mechanisms underlying motor dysfunction between adults and children.

Other measurements such as SR duration did not display high reproducibility across different test days in both normal and spastic children, nor did SR latency in normal children (Table 3.3). This could probably be attributed to the slightly different degrees of resting motoneuronal excitability across different test days (Neilson 1972; Powers et al. 1988). To bring all the motorneurons to the same level of excitability, we could have required subjects to contract their soleus muscle to a pre-determined percentage of maximal voluntary force as Lee et al. (1987) did. However, this procedure would, in fact, preclude the possibility of measuring threshold changes. Also, SR occurred much less frequently and/or was smaller in amplitude in normal children than in spastic children, which rendered the detection of onset and offset of EMG signals difficult in normal children. This might explain the low reproducibility of SR latency ($p = 0.47$) and duration ($p = 0.51$) in them (Table 3.3).

With subjects' knee fixed approximately at 20° flexion, Brouwer et al. (1998) examined SR of the plantarflexors of children with spastic CP using a slower stretch

rate (mean 363.7 ± 14.2 °/s) and a larger stretch amplitude (from 60° plantarflexion to neutral ankle position) than those of our study. An SR onset angle at -32.4 ± 2.8° plantarflexion was noted in children with spastic CP, which was much earlier than that of normal children (at -4.0 ± 2.9° of plantarflexion). Previous study has shown that in normal children (n = 22, aged 3.9 to 13.6 years), the excitability of the spinal alpha motor neurons (stimulated by a tendon tape over the tendon Achilles) was strongly influenced by the position of the ankle joint, or the length of the soleus muscle (Lin et al. 1997). Jobin and Levin (2000) also viewed that the amplitude and pattern of EMG response depend on multiple parameters including stretch velocity and the position where SR was induced, as well as complex combination of central and peripheral influences. In our study, SR was recorded with subjects' knee stabilized at 60° flexion while the ankle was moved from 30° plantarflexion to the neutral ankle position. The difference in muscle length at which SR was induced between our study and that of Brouwer (1998) might explain why we were unable to detect the SR onset angle. A more likely explanation is that a supra-maximal stretch velocity was used in our study (mean 556.9 ± 33.9 °/s) versus that of the previous studies (Brouwer et al. 1998; Jobin and Levin 2000) in that the ankle displacement was completed before the stretch signals could be transmitted across the reflex loop. While the use of supra-maximal stretch velocity helped to ensure that the stretch stimulus activated the maximal SR amplitude, it would have precluded threshold changes in terms of either SR latency or onset angle being detected. Other alternate explanations for the lack of reproducibility could be due to the high inter-subject variability of our sample and the small sample size. Our results and these considerations suggest that inter-session changes in SR latency and duration should be interpreted with caution. All in all, the SR/M area ratio appeared to be a more stable

indicator of SR excitability in children with CP, as it showed a high correlation of 0.97 across the 2 testing sessions (Table 3.3).

It is well known that raw EMG signals recorded from different subjects on different test days are generally not reliable, as variations of recording conditions such as skin resistance and electrode placements cannot be fully avoided. Despite these limitations, efforts were made to duplicate EMG recording conditions in each testing session as closely as possible. Raw EMG area values recorded in the TA muscle were thus surprisingly reproducible during dorsiflexion but less so during plantarflexion. It could be argued that when EMG activities were maximal (i.e., TA acting as the agonist), their raw values could have more inter-session reliability (r = 0.86 and 0.94, respectively, for CP and normal children; Table 3.3) than when their activities were sub-maximal (i.e., TA acting as the antagonist, r = 0.59 and 0.56, respectively, for CP and normal children; Table 3.3). The lower reliability in recording raw soleus EMG area may be related to the lesser selectivity in recording muscle action potentials of the more deeply located soleus muscles than of the more superficially located TA muscles. To ensure greater consistency, normalization is deemed necessary as in the use of the EMG co-contraction ratio. Indeed, our findings verified that both dorsiflexion (r = 0.94 and 0.93, respectively; Table 3.3) and plantarflexion co-contraction ratios (r = 0.89 and 0.78, respectively; Table 3.3) were reliable measures in both spastic CP and normal children to allow data comparison among subjects and study groups.

3.7.2 Comparison of the Two Legs within Groups

We found no significant difference between the two legs on muscle strength and co-contraction ratios of the normal children. To our knowledge, no previous study has examined clinical spasticity, SR and voluntary muscle contractions of ankle

dorsiflexor and plantarflexor muscles concurrently as well as bilaterally in children with spastic CP. Our results showed no difference in ankle spasticity and ankle muscle strength between the two legs of spastic CP children. These results are in accordance with those of Ross and Engsberg (2002), who found no asymmetry in knee and ankle spasticity (as measured by KinCom dynamometer) and muscle strength between the two legs of children with spastic diplegia. Other studies that examined isometric muscle strength symmetry in children with diplegia or normal children using hand-held dynamometers (Wiley and Damiano 1998) and dynamometers (Buckon et al. 2002) or slow speed isokinetic tests (Ross and Engsberg 2002) also showed no significant differences in muscle strength between the two legs in both groups of children. Allthough no quantitative study on the co-contraction ratio between two legs is available for comparison in children, Buckon et al. (2002) attempted to examine the presence of co-contraction in normal and spastic children. In their study, visual inspection of the raw EMG signals was used to determine if there was simultaneous activation of agonist and antagonist muscles of bilateral elbow and knee flexors and extensors and ankle plantarflexors and dorsiflexors. Again, no significant difference in the co-contraction status was noted in these 6 muscle groups between the two legs of both groups.

3.7.3 Comparison between Groups

The significantly larger SR/M area ratio (p <0.05; Table 3.4) found in our spastic children with CP agreed with previous reports of enhanced SR excitability in adults with spastic hemiparesis (Levin and Hui-Chan 1993b). In contrast to previous reports on adults (Hale and Chan 1986; Levin and Hui-Chan 1993b), SR latency and duration were not different between our spastic and normal children. As discussed in section 3.7.1, the low reproducibility of SR duration (in both children groups) and SR

latency (in normal children) might have precluded valid comparisons between the groups.

Previous studies have reported that muscle strength in children with CP was significantly weaker than that of the normal children. Wiley and Damiano (1998) noted a significant weakness in voluntary isometric contraction (normalized to body weight) in 8 different lower-extremity muscle groups in children with spastic diplegia, whose ankle dorsiflexor and plantarflexor strengths were only 40% and 30%, respectively, of those of normal children. A slightly higher figure was reported by Buckon et al. (2002), who found dorsiflexor and plantarflexor torques to be 48% and 38%, respectively of those of normal children. Although the relationship between isometric and isokinetic muscle strength remains unclear, it has been proposed that both represent maximal voluntary contractions (Damiano et al. 2002). Studies comparing isokinetic leg muscle strength of children with spastic diplegia and age-matched controls have reported significantly lower peak torques, similar to the results of isometric strength studies. Tested at a speed of 10°/s on a dynamometer, the maximum torques generated by ankle dorsiflexors and plantarflexors in chidren with CP were only up to 56% and 40% of those of normal children (Ross and Engsberg 2002). Muscle weakness was more pronounced distally at the ankles compared with that of the knees (Ross and Engsberg 2002) or hips and knees (Wiley and Damiano 1998) in both isometric and isokinetic strength tests. Our findings are consistent with these previous reports in that spastic children had reduced ability in their ankle dorsiflexor and plantarflexor muscles to generate isometric torque. In fact, our spastic subjects were more affected in that their ankle dorsiflexor and plantarflexor MIVC torques were only 19% and 25%, respectively, of those of our normal children with similar BMI and gender distribution (Table 3.4).

Similar to previous reports on CP children (Brouwer et al. 1998) and hemiplegic adults with spastic ankles (Levin and Hui-Chan, 1994) which used the same data collection and analysis method as that of our study, the co-contraction ratios of ankle dorsiflexors and plantarflexors were significantly more pronounced in our spastic children than in those of the normal children. The reduction in MIVC torques could be attributed to the higher EMG co-contraction ratios during ankle dorsiflexion and plantarflexion in spastic children with CP (Table 3.4), which had also been previously reported in spastic subjects (Brouwer et al. 1998; Levin and Hui-Chan 1994). In fact, plantarflexion MIVC torque was found to be negatively correlated with plantarflexor co-contraction ratio in our subjects with CP (Figure 3.1F).

In accordance with previous reports (Boyd et al. 1999; Cameron and Drummond 1998; Rose et al. 1990), Table 3.4 shows that the walking speed of our subjects with CP was slower than that of normal children. Surprisingly, the resting heart rate of our spastic children was significantly higher than that of the normal children. To our knowledge, we are the first group to report this finding. Given that a linear relationship between heart rate and oxygen uptake over a wide range of walking speeds has been reported for normal children and children with CP (Rose et al. 1989), the higher resting heart rate noted in our spastic children may suggest that, even at rest, these children may have higher oxygen requirements than do their non-disabled peers in order to help maintain their upright sitting positions. In addition, a high walking heart rate exhibited in the spastic children, up to 75.6% of their maximum heart rate, indicates that even on level ground, the energy needs for walking in these children were higher than in their normal peers (Rose et al. 1990).

When walking at a mean speed of 45.3 m/min (range: 21.5 – 64.4 m/min), PCI values of normal children and children with CP were reported to be 0.41 beats/m and

1.46 beats/m, respectively (Rose et al. 1990). Similar to the findings of Rose et al. (1990), we found that our spastic subjects expended a higher energy costs for walking, being 1.38 beats/m. The higher PCI recorded in the spastic children than that of their normal peers indicates that a larger amount of energy was required to cover the same distance during the 6-minute walk test. Even though all children were allowed to walk at a comfortable speed, the energy cost of walking in the spastic children was higher than that in normal children (Table 3.4).

3.7.4 Correlations among Measurements

3.7.4.1 Clinical Spasticity and Stretch Reflex

Our results showed no correlation among clinically measured spasticity and SR parameters (i.e., latency, duration and area). Such a lack of correlation was consistent with previously reported findings of broad negative findings between reflex threshold or magnitude with clinically measured tone (Levin and Hui-Chan 1993b; Powers et al. 1988).

The lack of correlation between clinical spasticity and SR was not surprising. Electrophysiological testing, such as SR, addresses both reflex magnitude and threshold parameters. However, of the 3 clinical measurements of the Composite Spasticity Scale, none is particularly sensitive to threshold changes. Rather, they are more indicative of reflex magnitudes. In addition, the resistance to passive ankle dorsiflexion movement, as detected by the CSS, may be attributed to changes in muscle stiffness due to altered muscle properties with or without concurrent changes in SR magnitude and/ or threshold (Levin and Hui-Chan 1993b). Indeed, if spasticity could be attributed to a decrease in SR threshold, a more rigorous clinical measurement of this parameter must be designed. These results point to the need for a more sensitive clinical testing to be developed for children with spasticity.

In contrast to our findings on CP children, in participants with adult-onset spastic hemiparesis, a significant correlation between the level of clinically measured spasticity and SR threshold in the elbow flexors has been demonstrated (Levin and Feldman 1994; Levin et al. 2000). Using the same experimental paradigm, the same group of investigators, however, failed to find similar results in children with CP (Jobin and Levin 2000). Several explanations may have accounted for the difference in strength of the correlation observed in adult and pediatric participants with spasticity. Firstly, it has been suggested that, in younger children, the reflex or "neural" component of spasticity may predominate; whereas in older children, changes in muscle viscoelastic properties may contribute more to the increased resistance felt during passive limb displacement (Dietz 1999). Secondly, changes in the mechanical properties as well as non-contractile elements of the muscle have been shown to contribute to spastic muscle hypertonicity in the leg and elbow of adult stroke subjects (Dietz et al. 1981, 1991; Young and Mayer 1982). Indeed, more recent studies have demonstrated that muscle fiber compositions in children with CP were altered when compared to those of normal children (Rose and McGill 1998). For example, the spastic muscle of children with CP has been found to have increased fiber-size variations (Castle et al. 1979; Rose et al. 1994), type-1 (slow-twitch) fiber predominance (Rose et al. 1994; and Ito et al. 1996), and type-2 fiber atrophy in the gastrocnemius muscle (Ito et al. 1996). The impact of changes in mechanical factors on spasticity is likely to increase as the time from injury progresses. These factors may have had a lesser influence on the relation between clinical spasticity and SR in the adult participants cited by Levin and Feldman (1994) and Levin et al. (2000), as the mean time since injury of their adult participants to the time of their study (1.5 ± 1.3 years and 3.9 ± 1.9 years, respectively) was much shorter than that of our children (10.7 ± 2.8 years; Table 3.1). In addition, due to the large age range of our spastic

children, it is possible that different mechanisms may have contributed to an increase in variability of response and resulted in a lack of correlation between clinical spasticity and SR. Mechanism aside, our results are consistent with those of Jobin and Levin (2000) showing a lack of correlation among clinical spasticity and SR measures in children with CP. Results of our correlation study indicated that the severity of spasticity may not be fully described by either SR measurements or by clinical tone measure alone.

3.7.4.2 Stretch Reflex, Muscle Weakness and Co-contraction

The relationship between SR, muscle weakness and co-contraction in children with CP is controversial among clinicians and researchers. A major reason for the controversy is that, until recently, few studies examined these measures on children populations in a quantifiable manner. Compared with available studies on this issue, our results agreed with those of Brouwer et al. (1998). In their study, the spastic ankles of children with CP (assessed by SR threshold) were found to have reduced isometric plantarflexor strength and abnormally high plantarflexion co-contraction ratios between TA and soleus muscles. The authors made no comment on the relationship among SR, muscle strength and co-contraction of the spastic plantarflexor muscles. We are the first group to demonstrate that the soleus SR/M area ratio correlated positively with the plantarflexor co-contraction ratio (Figure 3.1A), but negatively with muscle strength of the plantarflexors (Figure 3.1B) and dorsiflexors (Figure 3.1C) during MIVC. The traditional belief that a spastic muscle with a hyperactive SR is a weak muscle is thus supported. Contrary to our findings, Ross and Engsberg (2002) reported no relationship between spasticity (measured as passive torque) and strength of the spastic plantarflexors in children with CP. Such differences would be accounted for by the different ways used to characterize

spasticity. In their study, spasticity was measured using a KinCom dynamometer that passively stretched the ankle plantarflexors at different speeds to record the amount of resistive torque. Areas within the torque-angle curve were used to calculate work values, and the slope of the linear regression between work values and stretch velocity was considered as a measure of spasticity. Unlike our study, EMG was not collected in their investigation. Thus, it was not clear whether the spastic plantarflexors has a hyperactive SR to the passive stretch applied in their study, thereby influencing the torque measured in addition to possible changes in the mechanical properties of the muscle. Thus, the relationship between SR and muscle strength cannot be inferred from their results. In adults with spastic hemiparesis, muscle hypertonia was found to be associated more with muscle-fibre contracture than with reflex hyperexcitability (Dietz 1999). Future study examining both SR and biomechanical properties of spastic muscles will be helpful to analyze the different components which contribute to hypertonia in children with spastic CP.

In fact, motor neurons supplying predominantly type-1 fiber postural muscles, such as soleus, are known to have a lower threshold for reflex activation than motor neurons supplying mixed fiber type, phasic muscle such as the gastrocnemius (Mendel et al. 1990). Therefore, the transformation towards predominantly type-1 fibers in spastic muscles may be accompanied by an increased sensitivity to stretch. The role of the peripheral nervous system in spasticity deserves further investigations.

While SR was found to be correlated with muscle weakness in our study, one could not infer that spasticity is the sole cause of the weakness. As illustrated from evidence from selective dorsal rhizotomy (SDR) studies (McLaughlin et al. 2002), surgical reduction of spasticity did not guarantee immediate return of muscle strength. Instead, prolonged intensive strengthening was required (6 to 9 months) to bring about improvements in muscle function (McLaughlin et al. 1998; Steinbok et al.

1997b; Wright et al. 1998). In examining spastic diplegia 1 year after SDR, when muscle strength values were normalized to account for the significant increases in height and weight, no significant increase or decrease in isometric muscle strength was evident (Buckon et al. 2002). On the contrary, increased hip adductor strength was noted in spastic diplegia 8 months post-rhizotomy (Engsberg et al. 2002). These results suggest that spasticity and weakness may be relatively separate features of children with chronic dysfunction of the central nervous system.

In accordance with previous studies (Levin and Hui-Chan 1994, Brouwer et al. 1998), during MIVC, spastic children who have larger plantarflexors co-contraction ratios (i.e., more TA contraction during voluntary plantarflexion) produced lower plantarflexor torque (r = -0.47; Figure 3.1F). It has been hypothesized that excessive antagonist (dorsiflexor) co-activation contributes to weakness in the spastic muscle (plantarflexor) by reducing the net force produced through reciprocal inhibition of the spastic agonist. Nevertheless, in a one-year follow-up study on CP children undergoing SDR, elimination of spasticity resulted in normalization of EMG co-contraction patterns without concurrent increase in the magnitude of isometric muscle force production of the knee muscles (Buckon et al. 2002). Such findings suggested that, in children with CP, factors affecting co-contraction and muscle strength could be multi-faceted.

Although the cause of weakness remains unclear, motor-units in the spastic muscles of adults with chronic stroke have been reported to have reduced firing rates, to be recruited at lower-force thresholds, to fire less rapidly, and to have failed to increase the firing rate appropriately with the strength of contraction (Jakobsson et al. 1992). These changes are thought to reduce the efficiency of the muscle contraction and thus lead to fatigue and weakness in adults with hemiparesis (Gemperline et al. 1995). Similar processes may have taken place in children with CP in that prolonged

lower-frequency firing rates may contribute to impaired ability to generate force. This was indeed shown by the significantly reduced agonist EMG areas during both dorsiflexion and plantarflexion (p = 0.006 and 0.002, respectively; Table 3.4) in our spastic subjects when compared with those of normal children. Indeed, changes in the size of muscle fibres and altered distribution of fiber types have been reported in children with CP (Ito et al. 1996). The variation in fibre area has found to correlate with the energy expenditure index and with prolongation of EMG activity during walking (r = 0.69, $p < 0.05$; Rose et al. 1994). The findings of these studies suggest that spasticity produces structural changes in the muscle that could result in metabolic inefficiency, fatigue, and altered muscle mechanical properties. In addition, all our diplegic subjects have been wearing a pair of rigid plastic ankle foot orthoses to prevent the development of plantarflexor contractures. The ankle-foot orthoses, however, may have also limited ankle movement during daily activities such as walking. Such an immobilizing effect might be another factor explaining the reduction of ankle dorsiflexion and plantarflexion torque in our spastic subjects. Results of our correlation study which demonstrated that hyperactive SR correlates positively with co-contraction but negatively with muscle strength highlight the need to revisit the role of SR in muscle function in children with CP.

3.7.4.3 Stretch Reflex, Muscle Weakness and Walking Performance

Our results concurred with that of Kramer and MacPhail (1994) who found a modest relationship between muscle strength and energy expenditure of walking (as measured by energy expenditure index). In their study, knee extensor strength was found to correlate negatively with walking efficiency (r = -0.44 to -0.50) as well as positively with gross motor ability (r = 0.57 to 0.69) in adolescents with CP. Our results also showed modest but significant positive correlations between ankle

plantarflexor and dorsiflexor torques and walking speed (r = 0.36 and 0.42, respectively, Figures 3.1H and 3.1I), and negatively with energy expenditure as measured by PCI (r = -0.37 and -0.43, respectively, Figures 3.1J and 3.1K).

Rose et al. (1994) showed that increased fiber-size variation and type-1 (slow-twitch) fiber predominance in spastic muscle of children with CP was related to energy expenditure during walking (r = 0.69, $p < 0.05$). As discussed earlier, changes in muscle properties may contribute to weakness. This might explain our findings of the correlation between muscle weakness of plantarflexors and dorsiflexors and slower walking speed (Figures 3.1H and 3.1I, respectively) and higher energy cost of walking (Figures 3.1J and 3.1K, respectively) in children with CP. This finding is in line with a recent study by Ng et al. (2005), in which a negative correlation was identified between plantarflexor strength and walking performance in adults with hemiplegia. In their study, subjects who have weakness of plantarflexors were found to have higher timed up and go scores (r = -0.86, p <0.01). A higher timed up and go score was noted to correlate negatively with walking speed (r = -0.90, $p < 0.01$) and walking endurance measured in terms of the distance covered in a 6-minute walk test. The author therefore postulated that plantarflexors are important in regulating gait speed to generate energy required to move the limbs forward during push-off phase of walking.

Lower limb muscle force and power production were inadequate during walking, and specific deficiency in the ankle plantarflexors and knee extensors have been reported by Olney et al. (1990). For instance, in children with mild hemiplegic CP, the plantarflexors generate one-half of the normal force during the push-off phase of gait (Olney et al. 1990). Normally, ankle plantaflexion during push-off represents the highest joint power generated during gait, and its absence may affect swing-phase motion of the hip and knee and reducing toe clearance (Meglan and Todd 1994). As a

major power generator for walking, reduction of spasticity using Botox injections has been shown to improve the power generated by the plantarflexors (Boyd et al. 2000a). This might explain why subjects with more hyperactive SR walked slower with a higher energy cost (Figures 3.1D and 3.1E). While clinicians have shifted their focus to muscle strengthening in children with spasticity with the view to improve their functional performance, results of our correlation study suggest that treatment focusing on both hyperactive SR and muscle weakness are important to help improve gait function in children with CP.

3.8 Conclusions

Our results show that the battery of tests, previously used to characterize spasticity and deficits in voluntary muscle contraction and walking performance in the adult population, is reliable and valid for measuring motor disorders in children with spastic CP. In addition, it could differentiate abnormal levels of spasticity, voluntary muscle contraction and walking performance in children with CP from those of normal children. Thus, the test battery we designed could be used as a comprehensive evaluation tool for intervention studies on spasticity, motor deficits and walking performance in the CP population. Results of our correlation analyses demonstrate that hyperactive SR, co-contraction and weakness of ankle dorsiflexors and plantarflexors were interrelated, and were further correlated with certain walking performance indices in such a way as to decrease the walking speed and increase the energy cost of walking in children with spastic CP. These findings point to the need to devise management strategies to tackle hyperactive SR and muscle weakness in these children in order to facilitate their walking performance.

CHAPTER 4

EFFECTS OF TENS AND BWS-TT ON SPASTICITY AND VOLUNTARY MUSCLE CONTRACTION IN CHILDREN WITH SPASTIC CP

4.1 Summary

The objectives of this study were to compare the relative treatment effectiveness of adding (i) TENS, (ii) placebo-TENS, and (iii) TENS+BWS-TT to conventional rehabilitation program in reducing spasticity and in enhancing voluntary muscle contraction in children with spastic CP.

The present study was a randomized, placebo-controlled clinical trial. The sample size was determined *a priori*. Sixty-three children diagnosed with spastic CP were recruited. Children recruited were stratified according to the level of ankle plantarflexor spasticity and then randomly allocated to 1 of 3 groups receiving TENS, placebo-TENS, or TENS+BWS-TT. One hour of TENS or placebo-TENS was administered once a day, 5 days a week for 3 weeks to the first 2 groups, while the TENS+BWS-TT group received an additional 20-30 min of gait training after TENS. Sixty-one children completed the study: 20 in the TENS group, 21 in the placebo-TENS group, and 20 in the TENS+BWS-TT group. Spasticity was measured by the composite spasticity scale (CSS) and stretch reflexes (SR) as a function of maximum M response (SR/M), while muscle function was measured by maximum isometric voluntary contraction (MIVC) and EMG co-contraction ratios of ankle dorsiflexor and plantarflexor muscles. These were recorded before treatment (T_0), and after 1 week (T_1), 2 weeks (T_2), and 3 weeks of treatment (T_3), to examine the effects and time course of TENS, placebo-TENS and TENS+BWS-TT.

When compared with baseline values within each group, our results showed that both TENS and TENS+BWS-TT, but not placebo-TENS produced a significant reduction in CSS score from 2 weeks of treatment onward ($p < 0.05$), and a significant reduction of the baseline SR/M area ratio, respectively after 3 and 1 week of treatment ($p < 0.05$). In terms of the voluntary ankle muscle contraction, only TENS+BWS-TT produced a significant increase in dorsiflexion torque and decrease in dorsiflexion co-

contraction ratio after 3 weeks of treatment ($p < 0.000$), but not TENS or placebo-TENS. No significant change was noted in any of the 3 treatment groups in either plantarflexion torque or co-contraction ratio after 3 weeks of treatment.

When compared with placebo-TENS, both TENS and TENS+BWS-TT produced a significant % decrease of CSS score, respectively after 3 and 2 weeks of treatment ($p < 0.006$). Interestingly, only TENS+BWS-TT but not TENS alone produced a significant % decrease of SR/M area ratio and of dorsiflexion co-contraction ratio, and a significant % increase of dorsiflexion torque after 3 weeks of treatment ($p < 0.006$). However, none of the interventions produced a significant change in plantarflexion torque or co-contraction ratio after 3 weeks of treatment.

In conclusion, both TENS and TENS+BWS-TT are feasible treatment protocols for children with spastic CP in the school setting. Both treatments significantly reduced clinical spasticity in these children after being administered for only 2 – 3 weeks. However, voluntary contraction of ankle dorsiflexors and hyperactive SR of plantarflexors were improved only when the 3 weeks of TENS were combined with BWS-TT. These results demonstrated that 15 sessions of combined TENS+BWS-TT were superior to TENS alone in reducing spasticity and in enhancing voluntary muscle function in children with spastic CP.

4.2 Introduction

Use of botox and intrathecal baclofen injection and selective dorsal rhizotomy (SDR) have been shown to be effective means to reduce spasticity and to improve gross motor functions in children with spastic CP (Albright et al. 1995; Love et al. 2000). However, the short-lasting, variable effects, repeated painful injections, and moderately high cost of botox injections (Howle 1999), and the invasive nature of SDR and the high cost involved are of concern. Furthermore, whether drugs or SDR was used to reduce spasticity, the muscle weakness unmasked thereafter still requires a prolonged period of rehabilitation (e.g., 6 to 12 months) to regain function. Animal model of spasticity had shown a lack of longitudinal growth of the spastic muscle relative to the bone, and a similar finding was demonstrated in young children with CP (Rang 1990). In addition, spastic muscles were found to undergo atrophy (Castle et al. 1979, Milner-Brown and Penn 1979). Thus, managing spasticity remains a key concern in the rehabilitation of children with CP.

Spasticity is the clinical manifestation of hyperactive SR and has been partly attributed to a defect in presynaptic inhibition of the stretch afferent fibers (Hale and Chan 1986a). In the 1990s, Hui-Chan and coworkers showed that low intensity transcutaneous electrical nerve stimulation (TENS) could be a non-invasive modality to reduce spasticity in clients with stroke. Specifically, in a controlled study on adults with spastic hemiparesis, it was found that both segmentally or heterosegmentally applied TENS caused an immediate increase in soleus H and SR latencies for up to 60 minutes post-stimulation (Hui-Chan and Levin 1993). Furthermore, in contrast to placebo stimulation, 15 sessions of daily TENS for 1 hour, applied to the skin overlying the peroneal nerve in patients with spastic hemiparesis significantly reduced their composite spasticity score in the lower leg (Levin and Hui-Chan 1992). These effects were comparable to those of anti-spastic drugs (i.e. Modified Ashworth Scale

= -0.4). Concomitant increase in vibratory inhibition of soleus H reflex, increase in ankle dorsiflexion force up to 820%, and reduction of the magnitudes of soleus SR and of the co-contraction ratio during dorsiflexion were also evident. Levin and Hui-Chan (1992) therefore suggested that the underlying mechanisms may be due partly to an enhancement in the presynaptic inhibition of the hyperactive stretch afferents innervating the spastic muscles, and partly to a possible "disinhibition" of descending voluntary commands to the non-spastic antagonist muscle. Subsequently, TENS has also been shown to reduce the excessive resistive torque, hyperactive stretch reflex and Achilles tendon reflex and clinical spasticity (measured by the Modified Ashworth Scale) in adults with hemiparesis and with spinal cord injury by other investigators (Potisk et al. 1995; Goulet et al. 1996). The possibility of TENS in reducing spasticity in children with neurological conditions deserves our particular attention.

Improving the strength of the lower limb muscles in children with CP had been shown to improve their walking ability and stride length (Damiano et al. 1995a; MacPhail and Kramer 1995). Gait training with body-weight-supported (BWS) is believed to assist clients who cannot cope with full-weight bearing, by providing them with a dynamic and task-specific approach to integrate their weight bearing, stepping and balance control during walking. Unloading 40% of body weight has been shown to improve trunk and knee alignment during walking in adults with hemiparesis (Visintin and Barbeau 1989). Furthermore, adults with stroke receiving up to 40% BWS gait training were found to score significantly higher than the no-BWS group in functional balance, motor recovery, over-ground walking speed and endurance (Visintin et al. 1998). The feasibility of BWS gait training for young children with CP was established (Richard et al. 1997) and a preliminary report of its effectiveness

has been published (Schindl et al. 2000). Nevertheless, concrete evidence for the effectiveness of its use is lacking.

Since TENS and BWS gait training has been shown to reduce spasticity and enhance motor functions in adults with spastic hemiparesis, we speculate that these approaches would hold great promises for children with CP. This proposition is particularly attractive, since children are believed to have even greater potential for recovery, due to the greater plasticity of their nervous system. On the other hand, one could argue that results from adult neurological populations could not be generalized to the paediatric group, since the neural control issues between adults and children could be very different (Howle 1991; Poon and Hui-Chan 2000).

In summary, reduction of spasticity and improvement of motor functions have been the key goals in managing children with spastic diplegia and hemiplegia. Although evidence of spasticity reduction by drugs or surgery exists, the treatment costs involved are high and there are often undesirable side-effects. Furthermore, surgery is invasive and it requires the children to discontinue with their schooling in order to receive treatment in the hospitals, in addition to possible long-term side-effects.

Therefore, this study aims to examine the potential benefits of two non-invasive rehabilitation approaches, specifically TENS alone or in combination with BWS gait training, both of which has been proven to either reduce spasticity and/or enhance gait functions in the adult neurological populations. If the results from our proposed study are positive, this low-cost, non-invasive treatment could become a preferred choice for children with spastic CP. Furthermore, implementing the study within the school schedule will be an added benefit to children who want to undergo treatment without their studies being interrupted. The objectives of this study were to compare the relative treatment effectiveness of adding (i) TENS, (ii) placebo-TENS,

and (iii) TENS+BWS-TT to conventional rehabilitation program in reducing spasticity and in improving voluntary muscle contraction in children with spastic CP.

4.3 Subjects

Criteria for inclusion and exclusion of children with spastic CP were the same as those outlined in Section 2.3 of Chapter 2. Sixty-three children were recruited from 6 special schools. The ethical committee of the Department of Rehabilitation Sciences, The Hong Kong Polytechnic University, approved the study. Informed consent from the parents of these children was obtained prior to the study.

4.4 Methods

Subjects were first stratified according to their level of plantarflexor spasticity measured with the composite spasticity scale (CSS) score before being randomly allocation to 1 of the 3 treatment groups by drawing lots: TENS, placebo-TENS and TENS+BWS-TT. The treatment protocol for each group was already detailed in Section 2.4 of Chapter 2. Briefly, in the TENS group, low-intensity TENS was applied, via surface electrodes connected to a portable TENS stimulator, to the skin overlying the common peroneal nerve (L4-S2) posterior to the head of the fibula. Continuous stimulation (0.125 msec square pulses, 100 Hz, intensity at 2 times the sensory threshold) was applied for 60 minutes, once a day, and 5 days a week for 3 weeks. In the placebo-TENS group, the device and stimulation parameters were the same as those in the TENS group, except that the circuit in the device was disconnected. In the TENS+BWS-TT group, the same stimulation protocol as that of the TENS group was first delivered for 60 minutes, followed by 20 to 30 minutes of BWS-TT according to the walking tolerance and progression of each child. Stimulation was applied only to the more spastic leg of diplegic CP subjects or to the

affected leg of hemiplegic CP subjects. All subjects continued to receive their conventional physiotherapy treatment in their respective schools while they received additional TENS, or placebo-TENS, or TENS+BWS-TT. The types, duration and frequency of physiotherapy program for each child were recorded by his/her case therapist during the period of study.

Outcome measurements included: (1) spasticity of the ankle plantarflexors assessed by CSS and SR as a function of maximum M response (SR/M), (2) muscle strength recorded by maximum isometric voluntary contraction (MIVC) and electromyography (EMG) co-contraction ratios of the ankle dorsiflexor and plantarflexor muscles (c.f. Section 2.5 of Chapter 2*)*. These measurements were recorded at baseline *before* treatment (T_0), and *after* 1 week (T_1), 2 weeks (T_2), and 3 weeks of treatment (T_3) to examine the effects of TENS, placebo-TENS and TENS+BWS-TT over time.

4.5 Data Analysis

Baseline measurements of group characteristics, i.e., age, gender, weight and height, type of CP (diplegia or hemiplegia), severity of spasticity, and the type, duration and frequency of conventional physiotherapy among the 3 study groups were compared by one-way ANOVA. To compare the effects before and after each treatment, the outcome measurements described before were analyzed using repeated analysis of variance (ANOVA). The design employed in this study had two factors. The between-subjects factor was the 3 groups (i.e., TENS, placebo-TENS, and TENS+BWS-TT). The within-subjects factors were the 4 assessment intervals (i.e., *before* treatment (T_0), and *after* 1 week (T_1), 2 weeks (T_2), and 3 weeks of treatment (T_3)). If there were some interactions in the results of the repeated ANOVA, one-way ANOVA followed by multiple comparisons (post-hoc tests) was used to compare the

treatment effects among the 3 groups. The significant level was set at 5%, with Bonferroni correction for multiple comparisons.

The baseline value for each outcome measurement was compared among the 3 groups to ascertain homogeneity among groups. That done, and considering that the baselines values for each outcome measurement might vary slightly among individuals, the data recorded after the treatment sessions (T_1 to T_3) were normalized with respect to their baseline values (T_0) for comparisons among groups. That is, 'percentage changes' in a given outcome measurement as a result of treatment were compared among groups. They were defined as the results *after* treatment minus those *before* treatment (termed "baseline" values) divided by the baseline values and expressed as percentages. All statistical procedures were performed with SPSS software (version 10.0).

4.6 Results

4.6.1 Demographic Data

The demographic characteristics of the subjects are shown in Table 4.1. Twenty-one children with spastic CP were recruited for each study group at the beginning of the study. However, 1 child in each of the TENS and TENS+BWS-TT groups dropped out from the treatment program, because 1 child was admitted to hospital and the other child did not want to continue with the assessment procedures, respectively. Sixty-one children completed the study: 20 in the TENS group, 21 in the placebo-TENS group, and 20 in the TENS+BWS-TT group.

Table 4.1 shows that the 3 study groups were similar in age, sex, weight, height and body-mass indices (p values > 0.05). In addition, the type, duration and frequency of conventional physiotherapy program were not different among groups (p

Table 4.1: Characteristics of the subjects in the 3 treatment groups

		TENS	Placebo-TENS	TENS+BWS-TT
Number of subjects		20	21	20
Age (years)		10.38 ± 2.5	10.43 ± 3.02	11.17 ± 3.07
Gender:	M (%)	9 (55)	10 (47.6)	13 (65)
	F (%)	11 (45)	11 (52.4)	7 (35)
Weight (Kg)		30.6 ± 8.7	30.4 ± 10.2	32.0 ± 10.3
Height (m)		1.3 ± 0.2	1.4 ± 0.1	1.4 ± 0.2
BMI (Kg/m^2)		16.8 ± 2.7	18.3 ± 3.5	17.1 ± 2.9
Type of CP:	Diplegia	18	18	18
	Hemiplegia	2 (1 left, 1 right)	3 (2 left, 1 right)	2 (1 left, 1 right)
Side of limb treated:	L (%)	12 (60)	10 (47.6)	9 (45)
	R (%)	8 (40)	11 (52.4)	11 (55)
Conventional PT program:	Type	Stretching, strengthening, positioning,, balance, standing, transfer and gait training exercises		
	Duration (mins/ day)	53.2 ± 19.6	56.0 ± 17.8	57.3 ± 14.9
	Frequency (times per week)	4.2 ± 0.6	4.0 ± 0.6	3.9 ± 0.5
CSS score		11.5 ± 2.1	10.8 ± 2.0	11.5 ± 2.0
SR/M area ratio (%)		63.2 ± 49.7	69.1 ± 58.8	81.5 ± 52.5
MIVC: Dorsiflexion				
Mean maximal torque (Nm)		2.3 ± 2.0	2.3 ± 2.2	2.6 ± 1.8
Co-contraction ratio (%)		24.2 ± 18.7	28.1 ± 18.2	22.7 ± 11.7
MIVC: Plantar-flexion				
Mean maximal torque (Nm)		8.2 ± 5.8	6.2 ± 6.2	6.3 ± 4.3
Co-contraction ratio (%)		42.3 ± 15.1	45.2 ± 14.0	45.5 ± 12.7

For this and subsequent tables, values are mean ± SD. TENS, placebo-TENS, TENS+BWS-TT denote the groups receiving transcutaneous electrical nervous stimulation, placebo-TENS, and TENS plus body-weight-supported treadmill training, respectively.

M/ F = male/ female
BMI = body mass index
CP = cerebral palsy
CSS = composite spasticity scale
PT = physiotherapy
SR/M area ratio = stretch reflex/M-response area ratio
MIVC = maximal isometric voluntary contraction

> 0.05). Being well matched at the baseline in their clinical ratings of spasticity, the mean CSS score did not differ among the study groups. On overage, subjects in each study group were rated as having a "moderate" degree of spasticity (Table 4.1). Also, no initial differences were noted in soleus SR area ratio, MIVC torque and co-contraction ratios during ankle dorsiflexion and plantarflexion among the 3 study groups ($p > 0.05$; Table 4.1).

4.6.2 Effect of the 3 Treatment Protocols on Spasticity and SR

Clinical Spasticity: The means, standard deviations, and percentage change of clinical spasticity score before and after 1, 2 and 3 weeks of TENS (stripped columns), or placebo-TENS (white columns), or TENS+BWS-TT (dotted columns) for each group are presented in Table 4.2, Figures 4.1 and 4.2. When compared with baseline values *within* each treatment group (Table 4.2 and Figure 4.1), both TENS and TENS+BWS-TT, but not placebo-TENS produced a significant reduction in the raw CSS score from 2 weeks of treatment onward (by -0.6 = 10.9 – 11.5, and -0.9 = 10.6 – 11.5; $p = 0.01$ and 0.000, respectively at T_2). Moreover, an additional week of TENS and TENS+BWS-TT treatment led to further reduction of the CSS score (by -1.6 and -2.3; $p = 0.000$ and 0.000, respectively at T_3). When compared with the placebo-TENS group, Figure 4.2 shows a significant % reduction of CSS score in the TENS+BWS-TT group after only 2 weeks of combined treatment (being -7.4%; $p = 0.001$; Table 4.2). However, 3 weeks of TENS treatment were required to produce a significant % reduction of CSS score (-13.9%; $p = 0.000$), at which time a further % reduction was observed in the combined TENS+BWS-TT treatment group (-19.7%; $p = 0.000$).

Stretch Reflex: The means, standard deviations, and percentage change of SR/M area ratio before and after 1, 2 and 3 weeks of TENS, or placebo-TENS, or

Table 4.2: Means, standard deviations, and percentage change of CSS score (in brackets) before and after 1, 2 and 3 weeks of treatment.

	TENS (n = 20)	Placebo-TENS (n = 21)	TENS+BWS-TT (n = 20)
T_0 (score)	11.5 ± 2.1	10.8 ± 2.0	11.5± 2.0
T_1 (score)	11.4 ± 2.0	10.5 ± 1.9	11.4 ± 1.8
$(T_1 – T_0) / T_0$ (%)	(- 0.9)	(-2.7)	(-0.9)
T_2 (score)	10.9 ± 1.8*	10.9 ± 2.1	10.6 ± 1.6*
$(T_2 – T_0) / T_0$ (%)	(-5.7)	(1.8)	(-7.4) $^{\#}$
T_3 (score)	9.9 ± 1.7*	10.5 ± 1.8	9.2 ± 1.5*
$(T_3 – T_0) / T_0$ (%)	(-13.9) $^{\#}$	(-2.7)	(-19.7) $^{\#}$

For this and subsequent tables and figures:
T_0 denotes before treatment; T_1, T_2 T_3 denotes after 1, 2 and 3 weeks of treatment, respectively.
Within group: * denote $p < 0.05$ when compared with baseline values (T_0).
Among groups $^{\#}$ denote $p < 0.006$ when compared with placebo-TENS group.

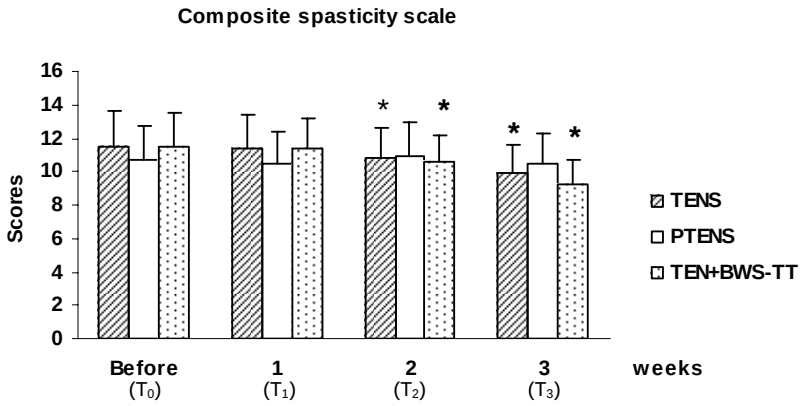


Figure 4.1: Means and standard deviations of CSS score over time. Note that TENS or TENS+BWS-TT, but not placebo-TENS, resulted in a significant within-group reduction in clinical spasticity from baseline values after 2 weeks of treatment, with further reduction after 3 weeks of treatment (* $p < 0.05$).

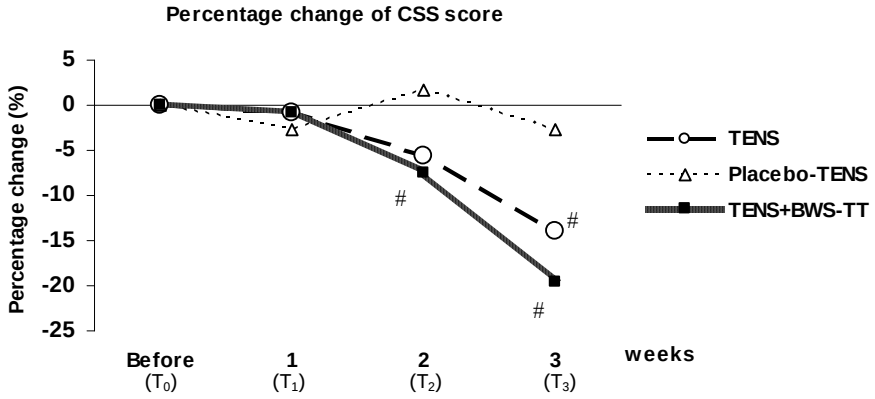


Figure 4.2: Mean percentage change of CSS score over time and among treatment groups. Note that TENS+BWS-TT reduced CSS score significantly after 2 or 3 weeks of treatment; while it required 3 weeks of TENS to reduce CSS score when compared to placebo-TENS ($^{\#}$ $p <$ 0.006).

Table 4.3: Means, standard deviations, and percentage change of SR/M area ratio (in brackets) before and after 1, 2 and 3 weeks of treatment.

	TENS (n = 20)	Placebo-TENS (n = 21)	TENS+BWS-TT (n = 20)
T_0 (%)	63.2 ± 49.7	69.1 ± 58.8	81.5± 52.5
T_1 (%)	55.4 ± 41.4	70.3 ± 64.2	59.8 ± 36.4*
$(T_1 – T_0) / T_0$ (%)	(- 12.9)	(-2.5)	(- 26.6)
T_2 (%)	51.7 ± 40.7	73.5 ± 61.8	61.8 ± 52.6*
$(T_2 – T_0) / T_0$ (%)	(-18.1)	(2.1)	(- 24.1)
T_3 (%)	49.8 ± 35.1*	75.6 ± 60.3	44.9 ± 24.8*
$(T_3 – T_0) / T_0$ (%)	(- 21.1)	(5.1)	(- 44.9)$^{\#}$

Within group: * denote $p < 0.05$ when compared with baseline values (T_0).
Among groups $^{\#}$ denote $p < 0.006$ when compared with placebo-TENS group.

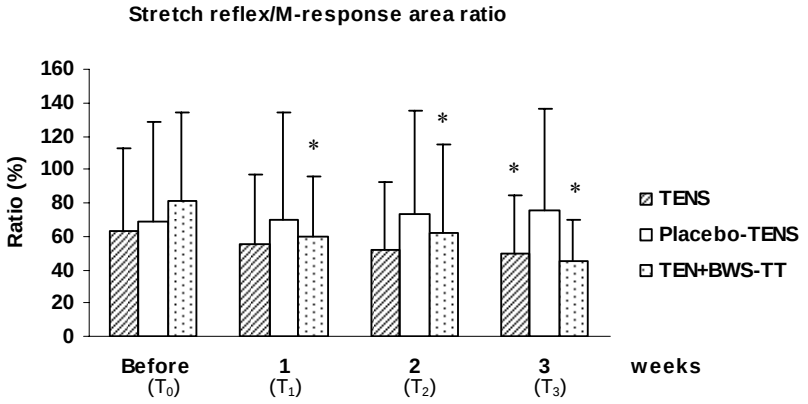


Figure 4.3: Means and standard deviations of SR/M area ratio over time. Note that TENS+BWS-TT resulted in a significant within-group reduction in SR/M area ratio from baseline values (* $p < 0.05$) after 1, or 2 and or 3 weeks of treatment; while TENS produced reduction of SR/M area ratio after 3 weeks of treatment.

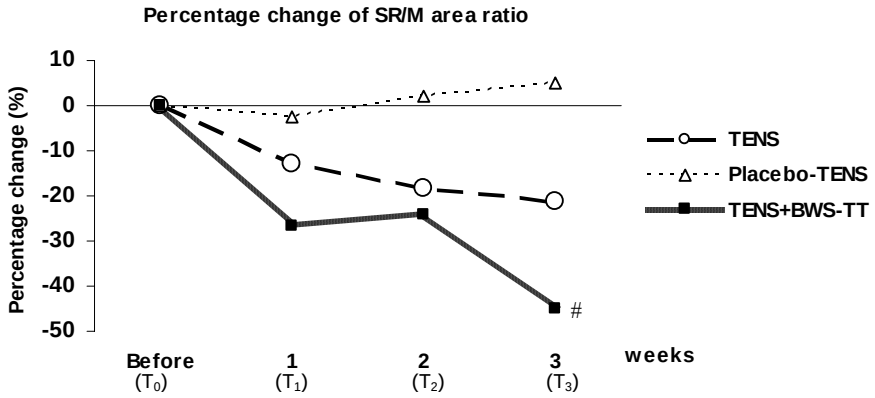


Figure 4.4: Mean percentage change of SR/M area ratio over time and among treatment groups. Note that only TENS+BWS-TT reduced SR/M area ratio significantly after 3 weeks of treatment when compared to placebo-TENS ($^{\#}$ $p < 0.006$).

TENS+BWS-TT are presented in Table 4.3 and Figures 4.3 and 4.4. When compared with the baseline values *within* each treatment group (Table 4.3 and Figure 4.3), the raw SR/M area ratio reduced significantly after only 1 week of TENS+BWS-TT (by -21.7%; $p = 0.019$), with a further reduction after 3 weeks of treatment (by -36.6%; $p = 0.000$). In contrast, it took 3 weeks of TENS to have a significant reduction in the SR/M area ratio (by -13.4%; $p = 0.039$), while the placebo-TENS group showed no significant change in SR/M area ratio during the 3-week treatment period. When compared with placebo-TENS, Figure 4.4 shows that only 3 weeks of TENS+BWS-TT produced a significant and marked % decrease of the normalized SR/M area ratio (by -44.9%; $p = 0.000$). Though 3 weeks of TENS produced a significant within-group reduction of the baseline SR/M area ratio (by -13.4%; $p = 0.039$), the % reduction of the normalized SR/M area ratio (-21.1%) did not reach significant difference from that of placebo-TENS.

4.6.3 Effect of the 3 Treatment Protocols on MIVC and Agonist/Antagonist EMG Co-contraction Ratios of Ankle Dorsiflexors and Plantarflexors

MIVC torque and co-contraction: The means, standard deviations, and percentage change of dorsiflexion torque and co-contraction ratio of the 3 treatment groups before and after 1 to 3 weeks of treatment are presented in Tables 4.4 to 4.5 and Figures 4.5 to 4.8. When compared with baseline values *within* each treatment group, only TENS+BWS-TT produced a significant increase in the raw dorsiflexion torque (by 0.5 Nm; $p = 0.024$, Table 4.4 and Figure 4.5) and a decrease in the raw dorsiflexion co-contraction ratio (by -8.4%; $p = 0.000$, Table 4.5 and Figure 4.7) after 3 weeks of treatment, but not TENS or placebo-TENS. In contrast, no significant change was noted in plantarflexion torque or co-contraction after 3 weeks of treatment in any of the 3 groups (Tables 4.6, 4.7, Figures 4.9 to 4.11, respectively in Appendix

Table 4.4: Means, standard deviations, and percentage change of MIVC dorsiflexion torque (in brackets) before and after 1, 2 and 3 weeks of treatment.

	TENS (n = 20)	Placebo-TENS (n = 21)	TENS+BWS-TT (n = 20)
T_0 (Nm)	2.29 ± 1.96	2.27 ± 2.22	2.61 ± 1.80
T_1 (Nm)	2.32 ± 1.74	2.21 ±2.11	2.98 ± 2.36
$(T_1 - T_0) / T_0$ (%)	(1.5)	(-6.1)	(8.1)
T_2 (Nm)	2.41 ± 1.78	2.14 ± 2.15	2.87 ± 2.02
$(T_2 - T_0) / T_0$ (%)	(5.5)	(-7.1)	(9.7)
T_3 (Nm)	2.42 ± 2.00	2.15 ± 2.11	3.11 ± 2.34*
$(T_3 - T_0) / T_0$ (%)	(5.9)	(-5.4)	(18.9) #

Within group: * denote $p < 0.05$ when compared with baseline values (T_0).
Among groups # denote $p < 0.006$ when compared with placebo-TENS group.

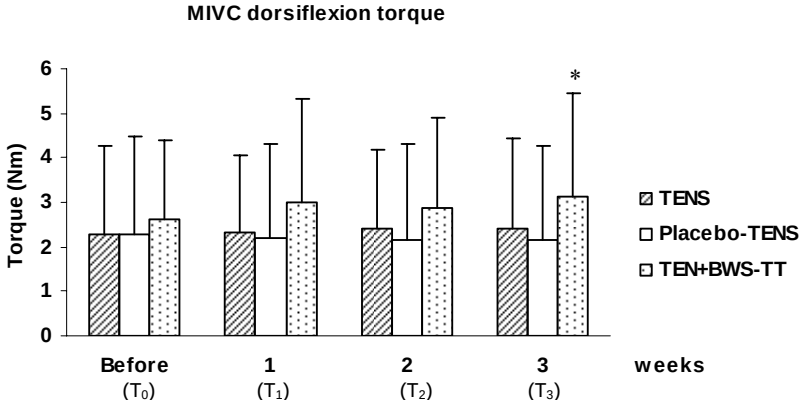


Figure 4.5: Means and standard deviations of MIVC dorsiflexion torque over time. Note that only TENS+BWS-TT resulted in a significant within-group increase in dorsiflexion torque from baseline value after 3 weeks of treatment (* $p < 0.05$).

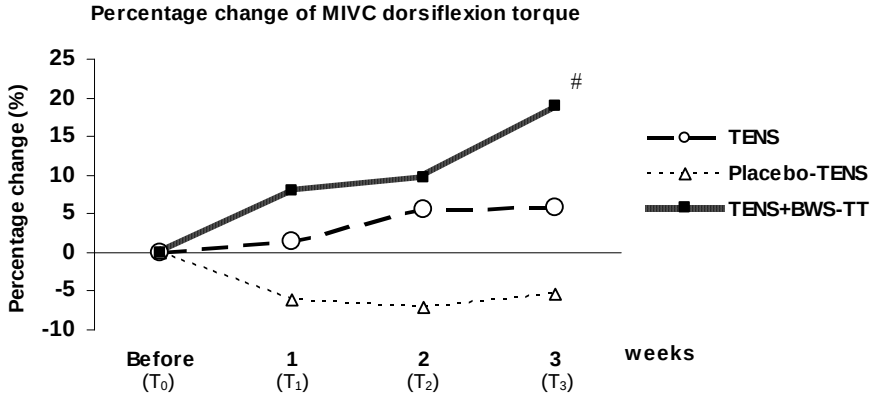


Figure 4.6: Mean percentage change of MIVC dorsiflexion torque over time and among treatment groups. Only 3 weeks of TENS+BWS-TT resulted in a significant improvement in dorsiflexion torque when compared to placebo-TENS (# $p < 0.006$).

Table 4.5: Means, standard deviations, and percentage change of dorsiflexion co-contraction ratio (in brackets) before and after 1, 2 and 3 weeks of treatment.

	TENS (n = 20)	Placebo-TENS (n = 21)	TENS+BWS-TT (n = 20)
T_0 (%)	24.16 ± 18.68	28.05 ± 18.20	22.72 ± 11.66
T_1 (%)	24.05 ± 20.72	28.65 ± 21.34	17.06 ± 12.04
$(T_1 – T_0) / T_0$ (%)	(-0.4)	(2.1)	(-29.1)
T_2 (%)	24.05 ± 23.92	27.15 ± 21.57	15.61 ± 9.72
$(T_2 – T_0) / T_0$ (%)	(-0.4)	(-3.2)	(-31.3)
T_3 (%)	20.37 ± 18.37	26.60 ± 20.36	14.28 ± 10.29*
$(T_3 – T_0) / T_0$ (%)	(-15.7)	(-5.2)	(-37.2) #

Within group: * denote $p < 0.05$ when compared with baseline values (T_0).
Among groups # denote $p < 0.006$ when compared with placebo-TENS group

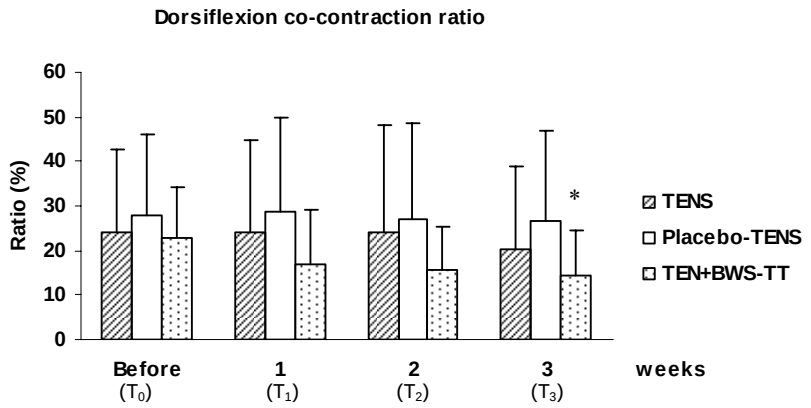


Figure 4.7: Means and standard deviations of dorsiflexion co-contraction ratio over time. Note that only TENS+BWS-TT resulted in a significant within-group decrease in dorsiflexion co-contraction ratio from baseline value after 3 weeks of treatment (*$p < 0.05$)

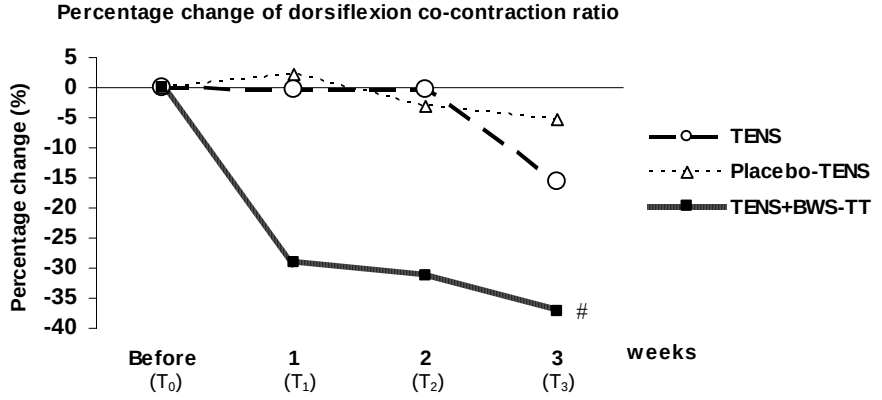


Figure 4.8: Mean percentage change of dorsiflexion co-contraction ratios over time and among treatment groups. Note that only TENS+BWS-TT reduced dorsiflexion co-contraction ratio significantly after 3 weeks of treatment when compared to placebo-TENS (# $p <$ 0.006).

4). When compared with placebo-TENS, only 3 weeks of combined TENS with BWS-TT resulted in a significant % increase of dorsiflexion torque (by 18.9%; p = 0.005, Figure 4.6) and a significant % decrease of dorsiflexion co-contraction ratio (by -37.2%; p = 0.003, Figure 4.8), but not TENS alone. In contrast, no significant % change in plantarflexion torque or co-contraction ratio during plantarflexion was noted after 3 weeks of treatment among the study groups (Figures 4.10 and 4.12 in Appendix 4).

4.7 Discussion

4.7.1 Effects of the 3 Treatment Protocols on Spasticity and SR

The present study showed that 3 weeks (15 sessions) of TENS significantly reduced plantarflexor spasticity and hyperactive SR in children with CP. Specifically, when compared with within-group baseline values, the mean raw CSS score and hyperactive SR (SR/M area ratio) were reduced (by -1.6 and -13.4%; Tables 4.2 and 4.3, respectively) after 3 weeks of TENS. Such changes were augmented when TENS was combined with BWS-TT in that more reduction in the raw CSS score and SR/M area ratio were noted (by -2.3 and -36.6%, respectively). In addition, reduction in the raw SR/M area ratio became evident only after 1 week of TENS+BWS-TT (-21.7%), with further reduction after 3 weeks of treatment (-36.6%). In contrast, 3 weeks of TENS was required to produce a reduction of baseline SR/M area ratio to a lesser extent (-13.4%). When compared with placebo-TENS, both TENS and TENS+BWS-TT produced significant % decrease of CSS score, respectively after 3 and 2 weeks of treatment (p < 0.006). After 3 weeks of treatment, a slightly higher % reduction of CSS score was observed in the TENS+BWS-TT group (-19.7%) than that of TENS group (-13.9%). In addition, only TENS+BWS-TT produced a significant % decrease of SR/M area ratio after 3 weeks of treatment (by a marked - 44.9%), but not TENS.

In summary, TENS+BWS-TT produced a larger % decrease of CSS score and an earlier and larger % reduction of SR/M area ratio than did TENS during the 3-week treatment period. These results suggest that the addition of BWS-TT to TENS may have augmented the effect TENS on spasticity and hyperactive SR. The extent to which BWS-TT alone could reduce spasiticty and hyperactive SR was not addressed in the present study. It is a topic deserving further investigation.

Our results agree with previous reports of therapeutic TENS interventions in spasticity of different origins. Briefly, Levin and Hui-Chan (1992) showed that 3 weeks of daily 60 minutes TENS but not placebo stimulation decreased clinical spasticity and SR magnitude (SR/M area ratio) in the spastic ankle plantarflexors of adults with hemiparesis. Tekeoolu et al. (1998) also found that 30 minutes of daily TENS for 8 weeks reduced clinical spasiticity (measured by the Ashworth Scale) in adults with hemiparesis. Moreover, reductions of SR torque and increase of mean threshold angle for the onset of passive torque were noted in 7 of 9 adults with hemiparesis after 10 minutes of surface electrical stimulation (Dewald et al. 1996). In 2 reports on adults with spinal cord injury, Bajd et al (1985) reported that 20 minutes of TENS applied segmentally over the L3/4 dermatome resulted in a marked decrease in knee extensor spasticity, as measured by a pendulum test in 3 of the 6 patients examined. Goulet et al (1996) also reported significant reduction of clinical spasticity scores (Achilles tendon reflex and modified the Ashworth test) after 30 minutes of TENS. Within the field of developmental medicine, smaller group studies and case reports prevailed, probably due to the greater constrains in recruiting children for research studies and other reasons (c.f. Chapter 4.1). Kerr et al. (2004) showed that, thus far, only 4 non-randomized-controlled-trials (RCT) on therapeutic electrical stimulation (TES) exist but none of them examined spasticity as their outcome measure (Beck 1997; Maenpaa et al. 2004; Pape et al. 1990 & 1993). To our

understanding, this RCT study was first of its kind that documented significant reduction of spasticity after 3 weeks of TENS in children with CP.

Among the TES studies on children, most authors employed similar stimulation parameters: frequencies were generally in the range of 30 to 45 Hz; pulse durations ranged from 100 to 300 μs; intensity was set just above the sensory threshold when subjects felt an initial tickling sensation around the stimulation electrode; and stimulation was applied directly over the spastic agonist or muscle antagonistic to the spastic muscle. Treatment duration lasted for a minimum of 30 hours per week for 6 to 17 months. Compared with our study and previous adult studies of TENS (Hui-Chan and Levin 1993; Levin and Hui-Chan 1992; Potisk et al. 1995; Tekeoolu et al. 1998), which had demonstrated positive effects on spasticity reduction, different stimulation protocols from those of TES were employed. In the TENS studies, stimulation at a higher stimulation frequency (100 Hz), with longer pulse width (0.2 to 0.3 ms), higher intensity, shorter treatment duration (20 minutes to 1 hour) per session and shorter treatment periods (3-8 weeks) than those of TES studies were employed. The stimulation intensity was either adjusted to a level just below the threshold of a visible muscle contraction (Potisk et al. 1995), or at bearable pain level (Tekeoolu et al. 1998), or at twice the sensory threshold so that subjects reported a tingling sensation in the cutaneous distribution of the nerve being stimulated (Goulet et al. 1996; Hui-Chan and Levin 1993a; Levin and Hui-Chan 1992). In particular, all these studies had the stimulation electrodes placed over the muscle antagonistic to the spastic muscle. Taken together, the difference in electrode placement and stimulation parameters may account for our findings being different from those of TES in term of spasticity reduction in children with CP, and that different mechanism could be associated with the 2 different treatment approaches.

The time course of spasticity reduction is another point to note. As opposed to adult studies discussed previously, 3 instead of 2 weeks of TENS were required before significant reduction in spasticity and hyperactive SR were detected in our spastic children. The exact time course of the improvement of spasticity cannot be judged based on the few studies to-date. It has been suggested that there may be a critical duration for disinhibition or restitution of function following multimodal stimulation (Walsh and Cummins 1976). The critical time period, however, is unknown. Since no previous studies on children have documented a change in spasticity after electrical stimulation, comparison could only be made with those of adult reports. Few studies have examined short-term effect of TENS on spasticity. In adults with hemiparesis, Levin and Chan (1989) reported that a single 45 minutes of TENS applied to the ipsilateral leg or the contralateral wrist delayed H and SR latencies without decreasing the magnitude of the reflex activity. These authors therefore suggested that increases in SR thresholds, as reflected by prolonged reflex latencies, may be the first changes observed following a brief intervention to reduce spasticity. However, for a noticeable therapeutic effect, a reduction in reflex magnitude would also be expected. Twenty minutes of surface electrical stimulation (at 20 Hz frequency) over the spastic upper elbow biceps has also been reported to reduce the passive torque in response to stretch (elbow extension) in 7 of 9 adults with hemiparesis (Dewald et al. 1996). In subjects with spinal cord injury, knee extensors spasticity (as assessed by the pendulum test) was decreased in 50% of the subjects after 20 minutes of TENS (Lehmann et al. 1989); and clinical spasticity (Achilles tendon reflex and Modified Ashworth Test) was reduced after 30 minutes of TENS (Goulet et al. 1996).

In 2 studies that examined the cumulative effective of TENS, Levin and Hui-Chan (1992) noted that 2 weeks of daily 60 minutes TENS were necessary to decrease

clinical spasticity and increase vibratory inhibition of the H-reflex. Reduction of SR/M area ratio, however, was evident with another week of TENS. Tekeoolu et al. (1998) also reported reduction of clinical spasticity (Ashworth Scale) after 40 sessions of daily 30 minutes TENS over 8 weeks. Since they recorded the outcome measure before and after the 8-week intervention, it was unknown if there was change/ reduction of clinical spasticity after 3 weeks of intervention as Levin and Hui-Chan (1992) found.

The differences in age, chronicity and the nature of spasticity and movement disorders between children with spastic CP and adults with chronic hemiparesis could be other factors that contributed to the differences in the treatment outcome. The chronicity of spasticity and motor dysfunction could be much longer in children with CP, as the damage to their CNS occurred during the perinatal period (i.e., the period before, during, or shortly after birth). Damage to the immature supraspinal structures was believed to lead to a secondary disorder of a developing spinal cord in children (Myklebust et al. 1982). Indeed, data from non-human animal studies indicate that dissimilar neuronal mechanisms may underlie the motor deficits seen following perinatal and adult-onset brain damage (Carlson 1984; Goldman et al. 1978; Leonard et al. 1987). In children with CP, abnormal patterns of reciprocal excitation, reciprocal innervations, and changes in agonist control have been reported. Myklebust et al. (1982) reported reciprocal excitation of the TA muscle in response to a soleus muscle stretch, which suggests a functionally disordered spinal circuitary in children with CP. Kundi et al. (1989) reported that children with CP had abnormal somatosensory evoked potentials (SEPs) before dorsal rhizotomy. After dorsal rhizotomy, H-reflexes and dorsal cord potentials from SEPs were depressed, but the SEPs recorded over the cortex did not change. These investigators concluded that the somatosensory disorder was in the spinal cord below the cervical level. These observations and another report

by Brouwer and Ashby (1989) provided additional evidence for the hypothesis that CP may be a disorder of the spinal circuitry as well as a disorder of the brain. Taken together, the problem of movement control in children with CP could be different from that of adult-onset brain damage. In addition, human response to brain damage was postulated to be dependent on the stage of development of both damaged and surviving pathways at the time that the damage occurs. Partially damaged pathways may sprout (Bernstein and Stelzner 1983; Kalil 1979), whereas undamaged pathways may retain projections normally lost during development if damage occurs prior to a critical period (Goldman et al. 1978; Leonard et al. 1987). The neural substrate subserving hyperreflexia and spasticity in children with CP and those with adult-onset hemiparesis is, therefore, likely to be quite different (Leonard 1994).

In this study, TENS and/or TENS+BWS-TT applied to diplegic and hemiplegic school age children (age range: 6 to 15 years) could reduce clinical spasticity (CSS score by -13.9% and -19.7%, respectively) after just 3 weeks of treatment when compared with placebo-TENS. The results supported our hypothesis, as stated in the Section 1.7.2 of Chapter 1 that TENS and/or TENS+BWS-TT hold promise for children with CP in terms of spasticity management.

4.7.2 Effects of the 3 Treatment Protocols on Muscle Function

In our spastic children, 3 weeks of TENS led to a significant within-group reduction of clinical spasticiy and hyperactive SR (Tables 4.2, 4.3 and Figures 4.1, 4.3) but not improvement in muscle function (Tables 4.4, 4.5 and Figures 4.5, 4.7) when compared with their own baseline values. In contrast, improvements in both clinical spasticity, hyperactive SR, as well as muscle function were noted in the TENS+BWS-TT group after 3 weeks of treatment. When compared with placebo-TENS, only the combined use of TENS and BWS-TT, but not TENS alone, was able to bring about

improvements in hyperactive SR and muscle function, in terms of % increase of dorsiflexion torque (by 18.9%; Table 4.4 and Figure 4.6) and % decrease of dorsiflexion co-contraction ratio (by -37.2%; Table 4.5 and Figure 4.8).

In the study by Levin and Hui-Chan (1992) on adults with hemiparesis, repeated daily 60 minutes of TENS over 2 weeks resulted in a significant decrease in clinical spasticity in the plantarflexors and an increase of vibratory inhibition of the soleus H-reflex. These changes occurred with a substantial improvement in voluntary dorsiflexing force ranging from 5% to 820%, but not plantarflexing force, concomitant with a decrease in the EMG co-contraction ratios after a further week of daily stimulation. In a subsequent study by Tekeoolu et al. (1998), the effect of 40 sessions of daily 30 minutes TENS on adults with hemiplegia was examined using the Barthel Index for Daily Living Activities and the Ashworth Scale. Thirty subjects each was assigned to receive placebo-TENS or TENS treatment on top of a standard exercise program. In the TENS group, reduction of clinical spasticity occurred with significant improvements in all parameters such as feeding, transfer, hygiene, toileting, bathing, walking or stair climbing as opposed to the placebo-TENS group, which have improvement in only a few of these activities of daily living. Improvement in the total Barthel Index score was also statistically larger in the TENS group than that of placebo-TENS group.

Conflicting results about the effects of repeated electrical stimulation on motor function of children with CP existed. Disregarding the level of evidence or study design types, of the 6 studies applying TES on the lower limb muscles, 2 reported statistically significant improvements in gross motor function (Pape et al. 1993; Steinbok et al. 1997a), 2 reported no statistically significant effects (Sommerfelt et al. 2001; Dali et al. 2002), and the remaining 2 case reports described improvements in active movement or daily function (Beck 1997; Pape et al. 1990). One report applying

TES to upper extremities of children with CP reported improvement in active elbow and wrist movement (Maenpaa et al. 2004). Specifically, among the 3 RCTs of TES, both Sommerfelt et al. (2001) and Dail et al. (2002) found no effects of TES on motor function after 1 year of treatment, but only Steinbok et al. (1997a) found significant changes in the GMFM score after TES . It is noteworthy that participants in the study by Steinbok et al. (1997a) differed significantly from those of the other TES studies, in that subjects recruited were spastic diplegics who had previously undergone SDR. In addition, more muscles were stimulated in their study. As discussed in the last section, SDR has been shown to reduced spasticity immediately post-operation, such as H-reflexes (Cahan et al. 1987; 1988) and resulted in increased range of movement in joints. Improvements in strength and in the ability to control and coordinate movement patterns, however, were gained slowly over a prolonged period of time (9 to 12 months) with rehabilitation (Giuliani 1991). Thus, the improvement in motor functions in the study by Steinbok et al. (1997a) may not have resulted purely from TES treatment alone, but could be due to the effects of maturation and/ or increased capability for movement after SDR.

The lack of improvement in muscle function after repeated TENS in our spastic children may be related to the chronicity and the different nature of their spasticity than with that of adults. Unlike adults with hemiparesis or spinal cord injury who have had normal experiences in motor control and movement before their neurological insult, experience in normal movement is lacking in children with CP. Often, they activate muscles in abnormal sequences and patterns, and use compensatory movement for function (Giuliani 1991). Our results showed that combined use of TENS with BWS-TT was needed to bring about motor improvement in terms of % decrease of dorsiflexion co-contraction ratio and % increase of dorsiflexion torque.

Direct comparison on changes in spasticity and muscle function after TENS or TENS+BWS-TT with those of children receiving SDR plus physiotherapy (McLaughlin et al. 2002) is not feasible, owing to the difference in the outcome measures employed. Worth noting is that results of this study support our hypothesis that TENS would reduce spasticity significantly more than placebo-TENS and that combining TENS with BWS-TT would further improve muscle function in children with CP. These findings are consistent with the observation in children with CP after SDR in that removal of primary impairment, such as spasticity, does not result in immediate return of motor function. However, the addition of only 3 weeks of task-related training such as BWS-TT to TENS was effective in bringing about significant improvements in reflex and voluntary muscle function. The mechanisms associated with spasticity and voluntary movement control might be interactive. Though botulinum toxin-A injections has been proven to reduce spasticity and improve gross motor functions, its short-lasting nature, need for repeated injections and high cost are of concern. Use of intrathecal baclofen for spasticity management on the other hand has a limited body of evidence for its use (Butler and Campbell 2000). The challenge to rehabilitation of children with CP therefore lies very much in identifying specific characteristics of motor control that contribute to movement dysfunction to help develop customized treatment that could improve function. Mechanisms aside, the positive results from this study will stimulate further studies on the effect of electrical stimulation in enhancing sensorimotor function of children with CP.

Many of the previous studies examining the effect of electrical stimulation on children would have been benefited from the use of valid and reliable outcome measures. As reported in Chapter 3 (Section 3.6), the outcome measures used in this study were highly reproducible. This main study further shows that these outcome measures have the sensitivity to detect changes of sensorimotor function after only 3

weeks of therapeutic intervention. These results confirm that the battery of tests we designed could be used as a comprehensive evaluation tool to examine intervention studies on spasticity and muscle function in children with CP.

4.7.3 Possible Mechanism of Repeated TENS on Spasticity and Muscle Function

Although repeated electrical stimulation has been used to improve sensorimotor recovery in adults with hemiplegia or children with CP over the last decade, the mechanisms mediating these effects are still unclear.

The TENS parameters used in our present study (low-intensity, high frequency) have been shown to activate mainly larger diameter afferent fibers. Examining the conduction velocities of the peripheral fibres of 17 healthy subjects, Levin and Hui-Chan (1993a) found that conventional TENS activated predominantly lager-diameter nerve fibers in the A-α-β range. Accordingly, by using the same mode of electrical stimulation (0.2 msec square pulse, 100 Hz, 2 times sensory threshold) in the present study, we expected that there would be activation of large diameter nerve fibers. It should be note that A-alpha fibers would include larger sensory fibers such as I_a and I_b fibers, respectively, from muscle spindles and tendon organs (Low and Reed 2000; Pechham 1999; Robinson and Snyder-Mackler 1995), as well as those innervating the skeletal muscles (i.e., the alpha motor neurons).

The study by Levin and Hui-Chan (1992) showed that repeated high frequency TENS enhanced vibratory inhibition of the H-reflex. Since vibratory inhibition of the H-reflex has been attributed in part to presynpatic inhibition of Group I_a terminals (Burke et al. 1976; Gillies et al. 1969), it is possible that repeated TENS applications increased vibratory inhibition of the H-reflex via an enhancement of presynaptic inhibition, which has been thought to be suppressed in adults with spastic hemiplegia

(Ashby and Verrier 1976). Levin and Hui-Chan (1992) further suggested that the improvement in paretic muscle strength could be due to the disinhibition of descending voluntary commands to the motor neurons of the paretic muscles. They suggested that hyperactive segmental activity from the spastic muscle (i.e., ankle plantarflexors) could effectively "mask" or override any descending excitation of the paretic agonist motorneuronal, by producing excessive reciprocal I_a inhibition. Repetitive TENS stimulation increased presynaptic inhibition of the hyperactive SR in the spastic muscle, concomitant with a reduction of the EMG co-contraction ratio. Indeed, reduced hyperactive SR was noted in our spastic children after 3 weeks of repeated TENS and/or TENS+BSW-TT, and increased dorsiflexor toque was evident in the TENS+BWS-TT group.

From an anatomical point of view, TENS may effect plastic changes of the brain. Intracellular recordings of cortical neurons in primates, as well as neuroimaging and neurophysiological studies in humans have demonstrated that cortical representation areas ("cortical maps") can be modified by sensory stimulation (Johansson 2000). The latter could be triggered by TENS, as evidenced by the vibratory sensation that it produced. Johansson et al. (1993) and Magnusson et al. (1994) postulated that sensory stimulation might enhance the functional plasticity of the brain. Indeed, cutaneous signals are reported to have an excitatory influence on cortical motor neurons and, in their absence, a stronger motor command is required (c.f. Lundy-Ekman 2002b). It is possible that a stronger motor command could be achieved by increasing the sensory input via TENS to compensate for the reduced corticomotorneural activities in patients who have damaged cortical neuronal function. In a review paper, Buonomano and Merzenich (1998) noted that similar natural stimulation of skin surface resulted in an expansion of its cortical representation. In other words, increasing afferent input by repeated electrical stimulation might

contribute to the so-called Hebbian plasticity (also called "associative plasticity"). Hebbian plasticity, based on the temporal correlations of inputs, is thought to play an important role in both cortical development and cortical reorganization in the adult brain. Thus, repeated input to the cortex from the same stimulated skin location would be integrated into a larger receptive field. Each small sector of skin is then an effective source of competitive input for the Hebbian network, and receptive fields therefore shrink in size as the zones of representation of the engaged skin surface grow in size (Buonomano and Merzenich 1998).

4.7.4 Possible Mechanism of Additional BWS-TT on Spasticity and Muscle Function

In the study by Levin and Hui-Chan (1994) on chronic hemiplegic adults (29.0 ± 21.2 months post-stroke) who had moderate degrees of clinical spasticity (CSS score = 11.5 ± 2.7), maximal dorsiflexing force and the amount of EMG co-contraction were found to be significantly and negatively related to clinical spasticity of the ankle plantarflexor. Spasticity has been attributed to hyperactivity and abnormal organization in mono- and poly-synaptic reflex pathways (Lance 1980a; Nichols 1989). Among other factors, it may result from a lowering of SR thresholds in spastic muscles (Feldman 1986; Powers et al. 1988). Indeed, H and SR latencies, which may reflect thresholds, are decreased in spasticity, while SR magnitudes (H/M ratios and SR/M area ratio) are enhanced (Ashby and Verrier 1976; Hale and Chan 1986b). Despite the obvious hyperactivity in SR observed in the spastic subjects, no correlation among SR latency and magnitude and clinical spasticity was noted in the studies on adults with hemiparesis (Hale and Chan 1986b; Levin and Chan 1989). Likewise in our study, we found no correlation between SR/M area ratio with clinical spasticity in spastic CP children. However, as reported in Chapter 3 (Section 3.7.4),

larger SR/M area ratios were found to correlate with smaller MIVC dorsiflexion torques (r = -0.40; p = 0.01), suggesting that an amelioration of hyperactive soleus SR (SR/M area ratio) could be manifested with larger MIVC torque production in the antagonist. A reduction of dorsiflexion EMG co-contraction ratio accompanying the increase in dorsifexion torque in the TENS+BWS-TT group would imply that there was less contraction of the antagonistic plantarflexors during dorsiflexion.

The combined use of BWS-TT with TENS in our study resulted in a greater % reduction of CSS score and SR/M area ratio than that of TENS alone after 3 weeks of treatment. Perhaps a closer analysis of CSS and SR may provide some insights into the mechanism behind such findings. Electrophysiological testing, such as SR, allows the recording of both reflex magnitude and threshold parameters. However, of the 3 components of the CSS, none is particularly sensitive to threshold changes. Rather, they are more indicative of reflex magnitude. In addition, the resistance to passive ankle dorsiflexion, as detected by one component of the CSS, could be attributed to changes in muscle stiffness due to altered muscle properties, with or without concurrent changes in SR magnitude and/or threshold (Levin and Hui-Chan 1993b). In subjects who received additional BWS-TT, it was observed that most subjects had difficulty unloading their legs to bring about the swing phase. As such, more time was spent in the stance phase of walking. Their weight-bearing limb was often brought backward into extension by the movement of the belt of the treadmill system. This would resemble repetitive stretching of the soft tissues at the back of the ankle (i.e., Tendo-Achilles and tricep surae muscles) during certain period of BWS-TT. In an early study by Sinkjaer et al. (1996a) in patients with spastic multiple sclerosis, non-reflexive passive torque was found to contribute substantially to spasticity and to impaired walking ability. It is possible that repetitive stretching of soft tissues at the back of ankle during BWS-TT led to a decrease of muscle stiffness of the

plantarflexors, thus allowing dorsiflexion to occur more readily. This might explain why a greater % reduction of CSS score and an improvement in motor function (i.e., % increase of dorsiflexion torque and % decrease of EMG cocontraction) was observed only after 3 weeks of TENS+BWS-TT, but not TENS alone.

It remains unclear why an earlier and greater % reduction of SR/M area ratio was observed in subjects receiving additional BWS-TT than in the TENS group. In a review, Zehr and Stein (1999) draw on numerous studies to examine the role of various reflexes (e.g., cutaneous reflex, SR, etc) during locomotion. In normal subjects, Akazawa et al. (1982) observed that stretch and H-reflexes were deeply modulated throughout the step cycle, such that they were larger during stance and smaller during the swing phase of walking. Studies on animals and humans proved that modulation of SR occurs and acts to stabilize limb trajectory (Berger et al. 1984; Dietz et al. 1987), and assists force production during stance (Sinkjaer et al. 1996b; Yang et al. 1991). It is likely that different classes of reflexes act together in an integrative manner to control and finely regulate the step cycle. While reflexes may function usefully during normal locomotion, after neurotrauma or in disease, however, they no longer function well during normal locomotion (Sinkjaer et al. 1995a, 1995b). For instance, the modulation function of SR was found to be impaired in patients with neurological diseases (Sinkjaer et al. 1996a). However, Zehr and Stein (1999) suggested that reflexes still have the potential to be clinically exploited in gait rehabilitation. Although SR was not recorded during locomotion in this study, the greater reduction of the SR/M area ratio after additional BWS-TT may imply possible influence of BWS-TT on SR. We suggest that this would provide an interesting area for further investigation.

For decades, because of the complications of spasticity and motor control, muscle strength has rarely been quantified in children with CP. The compelling

clinical evidence from RCT studies on SDR (McLaughlin et al. 1998; Steinbok et al. 1997b; Wright et al. 1998), which showed that reduction of spasticity did not restore normal motor control but instead uncovered profound underlying weakness of the spastic muscles, sparkled renewed interest in strength assessment and training in children with CP. Buckon et al. (2002) and Wiley and Damiano (1998) both showed that lower limb muscles in children with CP were indeed weaker than those of age-matched peers, with strength values amounting to around 24 to 48% of those of normal children. In fact, our spastic subjects were more affected in that their ankle dorsiflexor and plantarflexor MIVC torques were only 19% and 25%, respectively, of those of the normal children in our study who had similar BMI and gender distribution (c.f. Table 3.4 in Chapter 3). Progressive interest in search of effective strengthening protocols in CP children has grown. Subsequently, reports consistently showed that muscle strengthening could increase the ability of children with CP to produce force without concomitant change in spasticity or deleterious effect (Andersson et al. 2003; MacPhail and Kramer 1995; Ross et al. 2001). In a series of studies examining the relationship between muscle strength and spasticity (measured as resistance to passive muscle stretch), Engsberg and Ross (2000), and Ross and Engsberg (2002) revealed that no relationship existed between the two, either within the same muscle group, or in opposing muscle groups of the knee and ankle in children with CP. Moreover, they reported that not all the subjects they tested had spasticity; however, muscle weakness was a consistent finding. The investigators therefore suggested that spasticity might not be the primary cause of atypical movement patterns observed in individuals with CP. Collectively, this evidence calls for the need to consider spasiticity and muscle weakness as relatively independent impairments in children with CP and therefore, different treatment strategies may be required to tackle them.

In this regard, the use of BWS gait training on a treadmill would allow multi-lower limb muscle strengthening in a functional context. Providing BWS by symmetrically unloading both lower limbs creates an environment that discourages the use of compensatory strategies and facilitates new motor behavior to emerge when compared with gait training with walking aids. In a study examining the effect of BWS on normal human locomotion, unloading 70% of body weight resulted in decreases in the percentage of stance, the percentage of total-limb support time, and maximum hip and knee flexor swing angles. Other adaptations to BWS included reduced mean burst EMG amplitude in the muscles required for weight acceptance (i.e., errator spinae and gluteus medius muscles), and push-off (i.e., medial gastronemius), and increased EMG burst amplitude in the tibialis anterior muscle during swing (Finch et al. 1991). With the use of the BWS system, unloading of the limbs at the toe-off phase could facilitate the activation of flexor muscles to bring about leg swing. This is particularly important in subjects who are unable to control the unloading of their own limbs. Alternatively, gradual strengthening of extensor muscles during stance becomes possible as the amount of body weight support is decreased. Therefore, an interactive BWS gait training strategy would allow children lacking in muscle control to develop the strength and coordination required to walk (Finch et al. 1991). In addition, limited dorsiflexion has been reported to be related to the passive restraints of the plantarflexor rather than to active restraints produced by plantarflexor spasticity (Guiliani et al. 1991). If repeated stretching of the back of the ankle happened during BWS-TT and led to decrease of plantarflexor stiffness, dorsiflexion would occur more readily. This may explain why the combined use of BWS-TT with TENS but not TENS alone was able to bring about improvements in muscle function (i.e., % increase of dorsiflexion torque and % decrease of EMG co-contraction ratio) in the present study sample.

With all these considerations, one should be mindful that additional treatment time on BWS-TT was offered to children in the TENS+BWS-TT group than those assigned to the TENS alone group. As such, the improvements in reflex and voluntary muscle function observed after 3 weeks of TEN+BWS-TT, but not TENS, might be attributed to an increase in total treatment time rather than to the specific treatment effect offered by BWS-TT. Ideally, it would be desirable to add another group receiving BWS-TT alone to the research design, in order to delineate the specific effects of BWS gait training. However, in view of the very stringent inclusion and exclusion criteria used in the study, subject recruitment would be a problem if more groups were added. These latter considerations will form the subject of a further investigation.

4.8 Conclusions

The present study has shown that repeated TENS treatment (60 minutes daily treatment for 3 weeks) or TENS in combination with BWS-TT reduced clinical spasticity in children with spastic CP when compared with those receiving placebo-TENS. The findings support the use of TENS+BWS-TT rather than TENS alone in children with CP, as the combined treatment produced larger % decrease of clinical spasiticty and an earlier and larger % reduction of hyperactive SR (SR/M area ratio). Such changes were accompanied by a significant % increase of dorsiflexion torque and % decrease of EMG co-contraction which were not found when TENS was given alone. The study thus provides evidence for combining TENS with task-specific gait training to enable children with CP to have more optimal improvements in reflex and voluntary muscle function. These results serve to stimulate further research to examine the use of electrical stimulation and innovative motor training strategies in the paediatric CP population.

CHAPTER 5

EFFECTS OF TENS AND BWS-TT ON WALKING PERFORMANCE IN CHILDREN WITH SPASTIC CP

5.1 Summary

The objectives of this study were to compare the relative treatment effectiveness of adding (i) TENS, (ii) placebo-TENS, and (iii) TENS+BWS-TT to conventional rehabilitation program in enhancing walking performance in children with spastic CP.

The present study was a randomized, placebo-controlled clinical trial. The sample size was determined *a priori*. Sixty-three children diagnosed with spastic CP were recruited. Children recruited were stratified according to the level of ankle plantarflexor spasticity and then randomly allocated to 1 of 3 groups receiving TENS, placebo-TENS, or TENS+BWS-TT. One hour of TENS or placebo-TENS was administered once a day, 5 days a week for 3 weeks to the first 2 groups, while the TENS+BWS-TT group received an additional 20-30 min of gait training after TENS. Sixty-one children completed the study: 20 in the TENS group, 21 in the placebo-TENS group, and 20 in the TENS+BWS-TT group. Walking performance was evaluated by walking speed and energy cost (physiological cost index, PCI) during a 6-minute walk test. These were recorded before treatment (T_0), and after 1 week (T_1), 2 weeks (T_2), and 3 weeks of treatment (T_3), to examine the effects and time course of TENS, placebo-TENS and TENS+BWS-TT.

When compared with the baseline values within each group, no significant change of walking speed was noted in any of the 3 treatment groups after 3 weeks of treatment ($p > 0.05$). However, only 3 weeks of TENS+BWS-TT produced a significant within-group reduction in PCI ($p < 0.05$), but not 3 weeks of TENS or placebo-TENS alone.

When compared with placebo-TENS, despite no significant change of walking speed being noted among-groups, 3 weeks of TENS+BWS-TT produced a significant

% decrease of PCI ($p < 0.006$). This may partly be explained by a significant % decrease of the heart rate change ($HR_{walk} - HR_{rest}$) after 3 weeks of TENS+BSW-TT.

In conclusion, 15 sessions of TENS combined with BWS-TT to provide specific locomotive training were needed to bring about a reduction in the physiological cost of walking in children with spastic CP, rather than TENS or placebo-TENS alone. The extent to which 3 weeks of BWS-TT alone would bring significant improvement in mobility function requires further investigation.

5.2 Introduction

Improving or maintaining walking ability is often a prime concern to parents who have children with spastic diplegic or hemiplegic CP. Although the majority of these children may eventually be able to ambulate, the acquisition of skills is often delayed and differs qualitatively from normal pediatric gait (Damiano et al. 1995a). The energy expenditure for walking in children with CP was reported to be almost three-fold compared with that of healthy children (Uninithan et al. 1996). Consequently, children with CP often complain of fatigue after walking for a short distance.

Kramer and MacPhail (1994) first reported a positive relationship among knee extensor strength, walking efficiency (Energy Expenditure Index) and gross motor ability (Gross Motor Function Measure) in adolescents with CP. Subsequently, 2 review reports confirmed that progressive muscle strengthening could warrant improvement in muscle performances in individuals with CP (Darrah et al. 1997; Dodd et al. 2002). However, among these studies, only 3 studies reported functional gains in term of improved stride length (Damiano et al. 1995a) or gross motor function after the resistance-training program in adolescents (McPhail et al. 1995) and children with CP (Damiano and Abel 1998). More recently, Andersson et al. (2003) reported that 10 weeks of multiple lower limb muscle strength training could lead to improvement in muscle strength, walking speed and timed-up-and-go scores in adults with CP. A moderate to good correlation was noted between muscle strength and gross motor function measures (r = 0.56 - 0.70, p = 0.02-0.002), but the correlation between muscle strength and walking speed varied from only fair to good (r = 0.25 - 0.66; p = 0.3 - 0.04).

While more studies have begun to examine the relationship between muscle strength and functional performance, the effect of spasticity and muscle co-contraction on functional performance in children with CP seems to have received less attention. In a case report, reduction of spasticity through the intrathecal baclofen bump in a 13-year-old boy, who had been on a carefully calculated diet and fed by gastrostomy, was reported to lead to marked weight gain (Hemingay et al. 2001). The author therefore cautioned that in children with severe disability, reduction of spasticity may have side effects that alter a child's energy requirement. In another study examining the oxygen cost of walking in children with CP, co-contraction of the thigh and lower leg muscles were found to correlate with submaximal energy cost of walking in children with CP, but not in the age-matched control children. Specifically, thigh and lower leg muscle co-contraction was noted to account for 51.4% and 42.8% respectively, of the variability in oxygen uptake for children with CP (Uninithan et al. 1996). While a certain amount of co-contraction was thought to be beneficial for joint stability during walking and was associated with a certain oxygen cost (Sutherland et al. 1980), excessive cocontraction in children with CP, however, was found to induce high energy cost for walking (Uninithan et al. 1996).

In an effort to improve walking function in children with CP, therapists usually emphasize tone-inhibiting maneuvers, balance training and gait-preparatory tasks such as standing and weight-shifting. Contemporary motor control research seeks to enhance movement on several different levels of the CNS with the assumption that different sub-systems contribute to the development of motor control. The task-orientated model of motor control assumes that control of movement is organized around goal-directed, functional behaviors rather than on muscles or movement patterns (Horak 1991). "The one who wants to learn walking has to walk" (Carr and Sherpherd 1998). In this regard, body-weight-supported treadmill training

(BWS-TT) has been proven to be effective in restoring some of the gait functions in adults with hemiplegia (Hesse et al. 1994 and 1995; Vistintin et al. 1998) and SCI (Dietz et al. 1995; Wernig and Müller 1991 and 1995). An earlier pilot study by Richard et al. (1997) has proven that BWS-TT was a feasible treatment for young children with CP. Schindl et al. (2000) further showed that additional BWS-TT 3 times a week, 25 minutes per sessions for 3 months resulted in improvements in GMFM standing section and walking section scores (p values < 0.05). Nevertheless, concrete evidence for the efficiency of its use in a well-controlled randomized manner, is still lacking.

As reported in Chapter 4, previous reports had shown positive effects of TENS on spasticity reduction in adults with hemiparesis (Levin and Hui-Chan 1992) or SCI (Potisk et al. 1995; Goulet et al.1996). In addition, evidence from SDR studies verified that prolonged intensive muscle strengthening was necessary to warrant functional gains in children with CP after surgical removal of spasticity (McLaughlin et al. 2002). It thus seems appropriate to apply the concepts of possible reduction of spasticity by TENS, and enhancement of locomotion capabilities by BWS-TT with the aim to improve ambulatory capabilities of children with CP. In Chapter 4, the relative effectiveness of adding TENS and/or TENS+BWS-TT to conventional rehabilitation program in reducing spasticity and in improving voluntary muscle contraction in children with CP are reported. The objectives of this study were to compare the relative treatment effectiveness of adding (i) TENS, (ii) placebo-TENS, and (iii) TENS+BWS-TT to conventional rehabilitation program in enhancing walking performance in children with spastic CP.

5.3 Subjects

See 4.3 for details.

5.4 Methods

See 4.4 for details.

5.5 Data Analysis

See 4.5 for details.

5.6 Results

5.6.1 Demographic Data

The demographic data is reported in Chapter 4 (see Section 4.6.1 for details).

5.6.2 Effect of the 3 Treatment Protocols on Walking Performance

Walking speed, PCI and heart rate: The means, standard deviations, and percentage change of walking speed, PCI, heart rate change, resting heart rate, walking heart rate change during the 6-minute walk test before and after 1, 2 and 3 weeks of TENS, or placebo-TENS, or TENS+BWS-TT for each study group are presented in Table 5.1 to 5.5 and Figures 5.1 to 5.10. When compared with the baseline values *within* each treatment group, no significant change of walking speed was noted after 3 weeks of treatment in any of the 3 treatment groups (Table 5.1, Figures 5.1 and 5.2 in Appendix 5). Only 3 weeks of TENS+BWS-TT treatment resulted in a significant decrease in raw PCI value (by -0.34 beats/m; $p = 0.04$, Table 5.2 and Figure 5.3) concomitant with a decrease in heart rate change (by -15.73 beats/min; $p = 0.000$, Table 5.3 and Figure 5.5), but not TENS or placebo-TENS. When compared with placebo-TENS, despite there being no significant change of walking speed among the groups (Figure 5.2, see Appendix 5), 3 weeks of TENS+BWS-TT produced a significant % decrease of PCI from 1.70 ± 1.09 beats/m to 1.36 ± 0.81 beats/m i.e., by -25.1% ($p = 0.001$; Table 5.2 and Figure 5.4). This

Table 5.2: Means, standard deviations, and percentage change of PCI before and after 1, 2 and 3 weeks of treatment.

	TENS (n = 20)	Placebo-TENS (n = 21)	TENS+BWS-TT (n = 20)
T_0 (beats/m)	1.72 ± 1.4	1.91 ± 1.86	1.70 ± 1.09
T_1 (beats/m)	1.73 ± 1.30	1.97 ± 1.96	1.43 ± 1.02
$(T_1 - T_0) / T_0$ (%)	(0.76)	(3.14)	(-4.66)
T_2 (beats/m)	1.69 ± 1.33	2.03 ± 1.95	1.45 ± 0.85
$(T_2 - T_0) / T_0$ (%)	(-1.26)	(5.87)	(-16.69)
T_3 (beats/m)	1.69 ± 1.38	1.99 ± 1.94	1.36 ± 0.81*
$(T_3 - T_0) / T_0$ (%)	(-1.75)	(4.05)	(-25.13)[#]

Within group: * denote $p < 0.05$ when compared with baseline values (T_0).
Among groups [#] denote $p < 0.006$ when compared with placebo-TENS group.

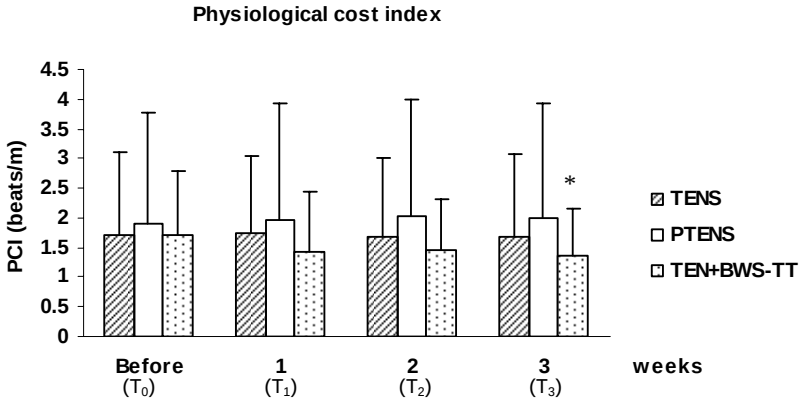


Figure 5.3: Means and standard deviations of PCI over time. Note that only TENS+BWS-TT resulted in a significant within-group reduction in PCI from baseline value after 3 weeks of treatment (* $p < 0.05$).

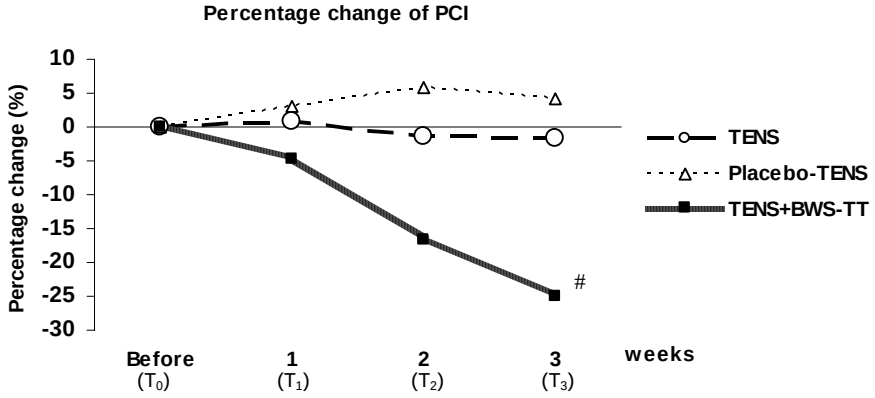


Figure 5.4: Mean percentage change of PCI over time and among treatment groups. Note that only TENS+BWS-TT resulted in significant % reduction of PCI after 3 weeks of treatment when compared with that of placebo-TENS ([#] $p < 0.006$).

Table 5.3: Means, standard deviations, and percentage change of heart rate change (HR_{walk} - HR_{rest}) before and after 1, 2 and 3 weeks of treatment.

	TENS (n = 20)	Placebo-TENS (n = 21)	TENS+BWS-TT (n = 20)
T_0 (beats/min)	58.02 ± 16.45	48.16 ± 15.93	59.06 ± 18.01
T_1 (%)	59.24 ± 15.55	45.73 ± 14.14	53.87 ± 19.82
$(T_1 - T_0) / T_0$ (%)	(2.10)	(-5.03)	(-8.79)
T_2 (beats/min)	56.31 ± 11.10	49.78 ± 17.15	50.67 ± 17.56
$(T_2 - T_0) / T_0$ (%)	(-2.95)	(3.35)	(-14.20)
T_3 (%)	56.83 ± 13.06	45.82 ± 13.52	43.33 ± 14.60*
$(T_3 - T_0) / T_0$ (%)	(-2.83)	(-4.85)	(-26.63) #

Within group: * denote $p < 0.05$ when compared with baseline values (T_0).
Among groups # denote $p < 0.006$ when compared with placebo-TENS group.

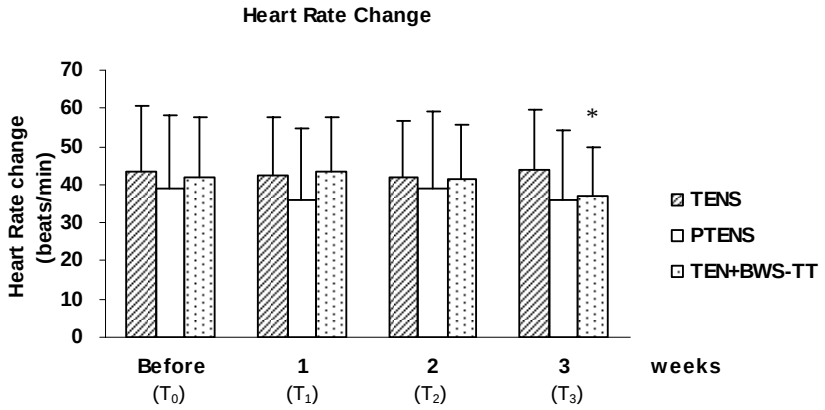


Figure 5.5: Means and standard deviations of heart rate change over time. Note that only TENS+BWS-TT resulted in a significant within-group reduction in heart rate change from baseline value after 3 weeks of treatment (* $p < 0.05$).

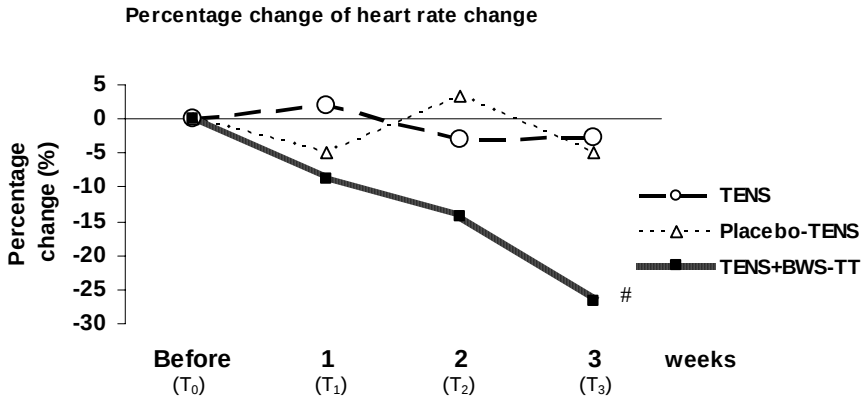


Figure 5.6: Mean percentage change of heart rate change over time and among treatment groups. Note that only TENS+BWS-TT reduced heart rate change significantly after 3 weeks of treatment (# $p < 0.006$).

Table 5.5: Means, standard deviations, and percentage change of walking heart rate before and after 1, 2 and 3 weeks of treatment.

	TENS (n = 20)	Placebo-TENS (n = 21)	TENS+BWS-TT (n = 20)
T_0 (beats/min)	149.89 ± 13.74	147.70 ± 14.57	153.88 ± 21.11
T_1 (beats/min) $(T_1 - T_0) / T_0$ (%)	147.87 ± 18.30 (-1.35)	139.98 ± 12.14 (-5.23)	144.83 ± 22.23 (-5.88)
T_2 (beats/min) $(T_2 - T_0) / T_0$ (%)	147.58 ± 13.08 (-1.54)	142.03 ± 15.73 (-3.84)	142.61 ± 19.06 (-7.32)
T_3 (beats/min) $(T_3 - T_0) / T_0$ (%)	151.21 ± 18.27 (0.88)	140.33 ± 14.91 (-4.99)	135.25 ± 18.52* (-12.11)$^{\#}$

Within group: * denote $p < 0.05$ when compared with baseline values (T_0).
Among groups $^{\#}$ denote $p < 0.006$ when compared with placebo-TENS group

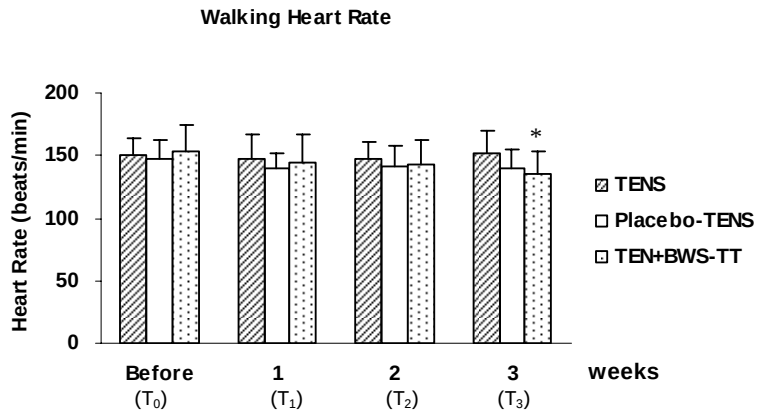


Figure 5.9: Means and standard deviations of walking heart rate over time. Note that only TENS+BWS-TT resulted in a significant within-group reduction in walking heart rate from baseline value after 3 weeks of treatment (* $p < 0.05$).

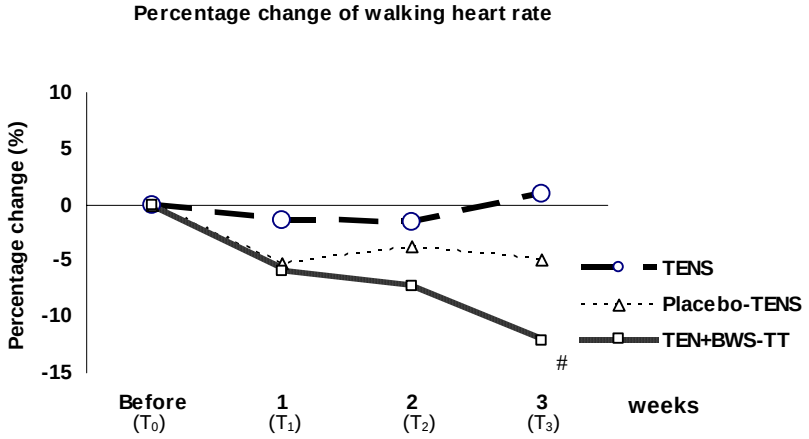


Figure 5.10: Mean percentage change of walking heart rate over time and among treatment groups. Note that only TENS+BWS-TT resulted in a significant % decrease in walking heart after 3 weeks of treatment ($^{\#}p < 0.006$).

may partly be explained by a significant % decrease of heart rate change (HR_{walk} - HR_{rest}; being -26.6%, p = 0.003; Table 5.3 and Figure 5.6) after 3 weeks of TENS+BWS-TT. Note that the resting heart rate remained similar in each group at all assessment intervals (Table 5.4, Figures 5.7 and 5.8 in Appendix 5), but the walking heart rate changed from 153.88 ± 21.11 beats/min to 135.25 ± 18.52 beats/min (i.e., by -12.11%; p = 0.005; Table 5.5 and Figure 5.10) after 3 weeks of TENS+BWS-TT.

5.7 Discussion

5.7.1 Effect of the 3 Treatment Protocols on Walking Performance

In our spastic children, only 3 weeks of TENS+BWS-TT led to significant decrease of raw PCI value and heart rate change when compared with baseline values, but not TENS or placebo-TENS. No significant change in walking speed, however, was noted in any of the 3 groups after 3 weeks of treatment. When compared with placebo-TENS, only TEN+BWS-TT resulted in improvement in walking performance in terms of % decrease of PCI (-25.1%; Table 5.2 and Figure 5.4) and % decrease of heart rate change (-26.6%; Table 5.3 and Figure 5.6), but not TENS.

Improvement in functional performance had been reported after 40 sessions of TENS in adults with stroke in the study by Tekeoolu et al. (1998). In their study, significant improvements in terms of feeding, transfer, toileting, bathing, walking or climbing ability were noted in different subjects and thus gave rise to a statistically larger total Barthel Index score in the TENS group than that of placebo-TENS group. It should, however, be noted that TENS or placebo-TENS was delivered to subjects on top a standard exercise program. Also, improvement in a few daily activity items was noted in the placebo-TENS group. Thus, the extent of improvement in a particular functional performance, such as walking, could not be readily identified from the study by Tekeoolu et al. Moreover, the improvement in functional

performance may not have resulted purely from administering TENS alone, but could be due to the combined effects of TENS plus exercise. Similarly, repeated and prolonged application of therapeutic electrical stimulation (TES) on children with CP post-rhizotomy was reported to result in significant improvement in Gross Motor Function Measures scores (Steinbok et al. 1997a), However, since the children who participated in that study had surgical removal of spasticity prior to TES treatment, the pure effect of electrical stimulation on functional performance remains unknown (c.f. Chapter 4, Section 4.7.2.)

Our results agree with previous reports of enhanced walking performance in adults with SCI or stroke after receiving BWS-TT training. In a large scale study involving 89 incompletely paralyzed para- and tetraplegics, Wernig, Müller and co-workers (1995) demonstrated that 3 to 20 weeks (median = 10.5 weeks) of BWS-TT enhanced locomotion ability of all 44 adults with chronic SCI. Out of 33 of these non-ambulatory chronic subjects regained ability to walk without external assistance. In the group with acute SCI injury, 92% of treadmill-trained versus 50% of conventional-trained patients were able to walk without assistance post training. Preliminary reports of positive results of BWS-TT on adults with stroke were published by Hesse and co-workers (1994 and 1995). The advantage of BWS was subsequently proven by Visintin, Barbeau and colleagues in 1998. In their study, 100 adults with chronic stroke were recruited. After a 6-week training period, the BWS group (n = 50) scored significantly higher than the no-BWS group (n = 50) for functional balance, motor recovery, overground walking speed and overground walking endurance (p values < 0.05). Our results echo with these findings in that intensive BWS-TT could enhance walking performance in children with spastic CP in terms of walking endurance. Comparisons of the present findings with those of previous adult studies would be difficult, since the cause, extent, location of a CNS

lesion, as well as the chronicity of the injury can have an impact on the potential and degree of plasticity or adaptability. Also, different type, specificity, and duration of intervention of BWS-TT were employed across these studies which could lead to different magnitudes of recovery (Barbeau et al. 1998).

As uncovered by our findings in Chapter 4, the combined use of TENS with BWS-TT was needed to bring about reduction in spasticity as well as improvement in voluntary muscle contraction. In this study, when compared to placebo-TENS, although 3 weeks of TENS+BWS-TT did not result in an increase in walking speed (Table 5.1, see Appendix 5), it did significantly reduce the energy expenditure as measured by PCI during the 6-minute walk test (Table 5.2 and Figure 5.4), but not TENS. Such a finding further suggests that task-specific locomotion training is a valuable therapeutic approach to bring about improvement in walking performance in these children.

A number of studies during the last decade have consistently reported improved muscle strength but not motor function after a strengthening program in children with spastic CP. In 2 reviews that examined the pure effect of a progressive resistance exercise program for subjects with CP (e.g., without the confounding effects of post-surgery or aerobic conditioning), Darrah et al. (1997) and Dodd et al. (2002) reported that only 1 out of 10 studies used a randomized, controlled-trial design (McCubbin et al. 1985), and most studies had outcome measures targeted primarily at the impairment level (e.g., strength, range of motion, spasticity etc). Among them, 3 non-RCT studies reported functional gains in terms of improved stride length (Damiano et al. 1995a) or GMFM scores (McPhail and Kramer 1995; Damiano and Abel 1998) after the resistance-training program. A recent home-based strength-training RCT conducted by Dodd et al. (2003), likewise, denoted trends in improvement in GMFM scores and muscle strength in children with CP. Since

improvement in functional independency is often the major goal for the child and family, it is imperative that changes in muscle strength be related to functional outcome. It could be argued that even a standardized outcome measure such as the GMFM does not evaluate function in the context of day-to-day activities. GMFM could capture a greater range of functional gait-related activities; however, it is thought to be particularly sensitive to motor performance in supported and slow walkers (Drouin et al. 1996). In the study by Drouin et al. (1996), it was noted that walking velocity correlated linearly (r = 0.91) with the GMFM sections D (standing) and E (walking) which include gait-related activities, indicating that walking velocity is a parameter capable of reflecting functional locomotor behavior in children with CP. However, the correlation between GMFM section E (walking) and walking speed became lower in children who walked without support (r = 0.35) than those who walked with support (r = 0.69). These results suggest that the GMFM section E score becomes less discriminant at walking speed above 45 cm/s (27 m/min). Indeed, the choice of a parameter for gait assessment will depend on which aspect of gait is to be assessed and the functional locomotion behavior of subjects. Among various gait measures, energy expenditure is thought to be dependent on balance, cardiovascular fitness, and the strength and co-ordination of other muscle groups, in particular, the ankle plantarflexors and hip extensors (Olney et al. 1990). Increasing severity of functional involvement of children with CP has reported to increase the energy cost of walking (Johnston et al. 2004). In our spastic subjects, the mean walking speed in the 3 study groups was above 36 m/min by the end of the 3-week treatment period. As a result, it would be inappropriate to use GMFM as an outcome measure. Instead, walking speed and energy expenditure would be more sensitive to reflect changes in functional locomotion behavior of our spastic subjects. Indeed, energy expenditure was lowered in children receiving 3 weeks of TENS+BWS-TT in our study.

As discussed in Chapter 3, compared to age-matched normal children, our spastic subjects walked significantly slower with a higher resting heart rate as well as walking heart rate, thus giving rise to a higher PCI (c.f. Chapter 3, Section 3.6.3). Age and severity of disability has been reported as major factors influencing walking speed in children with disabilities. In general, walking speed increases as the child matures. In a group of young child with CP (aged 4.2 ± 2.2 years), the mean walking speed recorded in independent walkers and supported walkers CP were 57 m/min and 13.8 m/min, respectively (Drouin et al. 1996). Based on these figures, during the 3-week treatment period, our spastic subjects would be considered as "supported walkers", as their walking speeds remained within the range of 36.14 m/min to 43.48 m/min (Table 5.1 in Appendix 5). This was indeed the case, as all many of our subjects did utilize assistive devices for outdoor ambulation.

The lack of improvement in walking speed after 3 weeks of TENS+BWS-TT in our study was not unexpected. Conflicting results on changes in walking speed after a strengthening program exist. While Damiano and Abel (1998) found a significant increase in walking speed after strength-training, MacPhail and Kramer (1995) reported the opposite. In contrast to MacPhail and Kramer's program, which involved strengthening of quadriceps and hamstrings regardless of each individual's assessment, Damiano and Abel targeted training at each participant's weakest lower limb muscle. Their finding suggests that strength-training programs that are tailored to individual needs may result in better functional outcomes than do less individualized programs. As well, strengthening of only 1 to 2 muscle groups may have been insufficient to influence energy expenditure during walking (Dodd et al. 2002). Direct comparison of walking speed of our sample of spastic children with that of previous studies examining effects of strengthening program (Damiano and Abel

1998; MacPhail and Kramer 1995), hence, is not feasible, due to the difference in the age range of children included among these studies.

Thus far, none of the previous studies examining the effect of strengthening exercises on children with CP reported changes in walking efficiency as measured by the Energy Expenditure Index (Damiano and Abel 1998; Darrah et al. 1999; MacPhail and Kramer 1995). Recently, Andersson et al. (2003) demonstrated improvements in muscle strength, GMFM scores (standing and walking sections) and functional ability in terms of walking speed and the time-up-and-go scores after 10 weeks of multiple lower-limb strengthening for 1 hour twice a week in adults with CP (mean age 31, range 23 – 44 years) when compared with the control group. The progressive training program in this study consisted of 10 exercises with emphasis on the lower extremities and was followed by a stretching program for 15 minutes. Often, individuals with CP experience deterioration in motor capacities after reaching adulthood, either due to lack of interest, or time in continuing an exercise/activity program. It is encouraging to learn that it is possible to restore motor capacities in adults with CP. However, it is unclear if such a comprehensive lower extremity strengthening program involving multiple muscle groups could be applied to children with CP, as it is well known that the attention span of younger children is often short-lived. To our understanding, our study was the first RCT that showed combining TENS with task-specific locomotion training improved muscle strength as well as walking performance in terms of energy expenditure.

No previous study showed improvement in walking endurance after a strengthening program in children with CP, but walking speed and endurance has been shown to be increased in adults with stroke receiving a 6-week BWS-TT program (Visintin et al. 1998). In our study, after 3 weeks of TENS+BWS-TT, a significant reduction of mean PCI value from a mean value of 1.70 beats/m to 1.36

beats/m was noted, while walking speed remained similar. Although the energy expenditure for walking in our spastic children remains to be higher than that of normal children (0.4 beats/m, Rose et al. 1990) at the end of 3 weeks of TENS+BWS-TT, these results indicate that at the same level of exertion (walking speed), the energy expenditure of walking was lowered. Indeed, a number of parents reported that in the second and third weeks of TENS+BWS-TT, they noticed better walking performance in their children. Some parents described that their children "got tired less readily", "did not lean as much on my hand when we went outdoors", and "walked for longer distance before needing a rest". Parents were excited to observe an effect on their child's walking ability within such as short period of treatment, and some asked if they could continue with the treatment program. To better understanding the impact of this combined treatment strategy on the "Participation Level" of children with CP, however, future study incorporating measures on participation level is essential. In this regard, measures such as the Pediatric Evaluation of Disability Inventory or Gross Motor Function Classification System would worth considering.

5.7.2 Possible Mechanism of Additional BWS-TT on Walking Performance

In keeping with the motor learning principle of task specificity, practicing resistance exercise in a more functional position – e.g., walking on a treadmill - may have a greater transfer to overground gait performance than isolated joint exercise or strengthening program alone (Giuliani 1992). The use of BWS-TT not only allows strengthening of lower limbs, but also enhances balance and coordination training in a functional context (i.e., walking). In addition, providing a load appropriate to the level of exercise for each individual, e.g., through the body-weight-supported system, creates an environment that facilitates development of a better gait pattern and

discourages the use of compensatory gait strategies. Previously, unloading 70% of body weight through BWS system in normal healthy adults had been found to alleviate the loading imposed on muscles required for weight acceptance (i.e., errator spinae and gluteus medius muscles) during stance phase and push off (i.e., medial gastronemius). Consequently, better gait patterns could emerge, such as more EMG burst of the tibialis anterior muscle to prepare for leg swinging (Finch et al. 1991). In another study on spastic paretic adults, 40% of BWS had resulted in more appropriate EMG timing of lower limb muscles in relation to the gait cycle, straighter trunk and knee alignment, increased single limb support time, decreased total support time and increased maximum comfortable walking speed during treadmill walking (Visintin and Barbeau 1989). Decreasing the double-leg support time implies that subjects were more able to transfer their weight from one leg to another with greater ease, requiring less support from both legs during the loading phases. Indeed, our results showed that the significant % reduction of dorsiflexion co-contraction and % increase of dorsiflexion torque occurs only after 3 weeks of TENS+BWS-TT, but not TENS alone. Such improvement in muscle function may be resulted from the decrease in loading on the lower extremities through the BWS system. BWS gait training allows dynamic and task-specific training that integrates 3 essential components of walking, which are: weight bearing, balance and stepping. Practicing walking over the treadmill has an added effect in that it simulates repetitive and rhythmic stepping (Visintin et al. 1998). In our experience, treadmill walking indeed could force the child to continue walking practice without frequent rests, which are common when the same child walks freely overground.

Though our results provide evidence that BWS-TT offers multiple benefits over isolated muscle strengthening, one cannot assume the similarities of BWS-TT to overground walking. There appear to be different postural demands, sources of

resistance to limb movement, sources of sensory stimuli during limb movement, and directions of external forces interacting with internal segment and muscle forces among overground walking and treadmill locomotion (Giuliani 1992). Training patients a task in one context (e.g., treadmill walking) does not necessarily transfer to another context (e.g. overground walking). Therapists should therefore consider BWS-TT as a condition to facilitate acquisition of walking ability. Continued effort to structure variable practice is important, such as varying the speed and effort during treadmill walking, so as to increase the capability of patients to carry this improved ambulatory capacity to overground walking, as well as to cope with novel situations.

As discussed in Chapter 4, SR is modulated during locomotion. It acts to stabilize limb trajectory (Berger et al. 1984; Dietz et al. 1987) and assists in force production during stance (Sinkjaer et al. 1996b; Yang et al. 1991). Although SR was measured under static conditions in our study, the greater reduction of the SR/M area ratio after additional BWS-TT may imply possible influence of BWS-TT on SR. In addition, a reduction of dorsiflexion EMG co-contraction ratio accompanying the increase in dorsifexion torque in the TENS+BWS-TT group may imply that there was less contraction of the antagonistic plantarflexors during dorsiflexion. If reflex activities were lowered, a normal pattern of modulation may be able to emerge (Barbeau and Fung 1992). The better expression of motor function in children receiving TENS+BWS-TT could therefore be due, in part, to a reduction of SR hyperactivity.

Apart from specificity of practice, BWS-TT also allows cardiovascular training. Treadmill training has been used commonly to promote cardiovascular fitness in various populations. In a preliminary study, Macko et al. (1997) investigated the effects of treadmill aerobic-exercise training in 9 ambulatory, chronic stroke patients. Their study showed that 6 months of 40 minutes per week walking at 50% to

60% of heart rate reserve produced substantial and progressive reductions in the energy expenditure and cardiovascular demands of the subjects. Improvement in cardiovascular fitness was evident in our spastic subjects after 3 weeks of TENS+BWS-TT, as shown by a significantly decrease of walking heart rate during the 6-minute walk test. Decreases in walking heart rate consequently allow these spastic children to carry on ambulation for a prolonged period of time and thus to increase their walking endurance.

The use of BWS-TT in humans stems from locomotion studies in spinal transected cats. Evidence for a central pattern generator (CPG) has been derived from studies in a variety of vertebrates, including adult cats and marmosets that have undergone thoracic cord transection and lumbosacral afferent denervation (Fedirchuk et al. 1998). These preparations have been found to produce rhythmic flexor and extensor motor output called fictive locomotion. Adult cats who underwent a complete spinal cord transection at a low thoracic level, but had their segmental afferents intact, were trained to walk on a moving treadmill belt (Barbeau and Rossignol 1987; Deleon et al. 1998; Lovely et al. 1986). Locomotor recovery on the treadmill was noted, and has served as indirect evidence for a locomotor neural circuitry, akin to a CPG, within the lumbosacral motor pools. Barbeau and colleagues first introduced this BWS-TT concept into humans, and it was found that the lower limb muscles of subjects with profound, incomplete cervical or thoracic spinal cord injury can be excited and produced EMG activities (Barbeau and Blunt 1991; Wernig and Müller 1991; Dobkin et al. 1995). It was believed that such response arise from the spinal locomotor pools in response to an ensemble of sensory inputs provided during a step cycle (Harkema et al. 1997). In a review on the neurophysiology of BSW-TT (Dobkin 1999), the mechanisms for spinal cord learning, even in the

absence of supraspinal connectively, are thought to be likely to include the effects of repeated segmental sensory inputs into lumbosacral motor neurons and interneurons during practice that leads to long-term potentiation (LTP). Use-dependent sensorimotor learning mechanisms, including LTP, have been shown to contribute to cortical representational plasticity during skills learning after a supraspinal injury. In addition, a growing number of studies point to the expanded effectiveness of residual corticospinal and afferent activity after stroke and SCI on spinal and cortical regulation of facilitation and recruitment (Davey et al. 1999; Jain et al. 1997). For instance, in subjects with stroke and incomplete SCI, sensory inputs from the hip and feet during step training with BWS-TT are appreciated by the locomotor region of the cord (Pearson 1998; Nielsen et al. 1997; Van Wezel et al. 1997), and to a varying degree can be appreciated by the efferent copy system of the cerebellum (Jueptner et al. 1998) and higher motor centers (Muir and Steeves 1997). Such inputs would likely expand cortical and subcortical movement representations for locomotion, much as training and recovery accompanied by changes in the size and involvement of sensorimotor networks after a focal cerebral injury caused by a stroke (Liepert et al. 1998; Nudo and Miliken 1996; Weiller et al. 1993). Therefore, it stands to reason that behavioral gains might follow a strategy that optimize residual sensorimotor integration for walking after stroke, SCI, and other neurological disease, such as CP, that impair lower limb and truncal function.

As discussed in Chapter 4, muscle weakness is only one type of impairment in children with CP. Consequently, a combined therapeutic approach that concurrently addresses other impairments, such as spasticity and lack of coordination among various body parts, should hold greater promise than a strengthening program alone. This study provided evidence that the combined use of TENS and BWS-TT to address

balance, coordination and strength needed for walking after reduction of spasticity is an effective means to enhance locomotion ability of children with CP.

5.8 Conclusions

Our findings showed that 15 sessions of combining TENS with BWS-TT could reduce the physiological cost of walking in CP children. This treatment strategy has the added benefits of being non-invasive, low cost, and without the side-effects often associated with drug intake or surgery such as dorsal rhizotomy. The results of our study lay the ground for further research to identify the best treatment protocol, in terms of multiple sites of TENS, treadmill speed, training frequency and facilitation techniques in enhancing locomotive function in children and adults with neurological deficits. The extent to which 3 weeks of BWS-TT alone would bring significant improvement in mobility function requires further investigation.

CHAPTER 6

SUMMARY AND CONCLUSIONS

6.1 Rationale of the Study

Managing spasticity and improving motor function are two key concerns in the rehabilitation of children with cerebral palsy (CP). Although anti-spastic drugs and selective dorsal rhizotomy (SDR) have been shown to reduce spasticity and improve gross motor functions in children with CP (Albright et al. 1995; Love et al. 2000), the variable effects, the moderate to high cost of drugs and surgery, and the invasive nature of surgery raise concerns for either approach being the best choice of treatment. Furthermore, whether drugs or SDR were used to reduce spasticity, the weakness unmasked thereafter still requires a prolonged period of rehabilitation (e.g. 6 to 12 months) to regain function (McLaughlin et al. 2002). Previous studies on adult spastic patients showed that repeated TENS treatment resulted in significant decrease in spasticity. Levin and Hui-Chan (1992) first showed that 15 sessions of low intensity transcutaneous electrical nerve stimulation (TENS), applied for 1 hour per session to adults with spastic hemiparesis, significantly reduced their spasticity and increased their ankle dorsiflexion force. A further study showed that TENS applied either segmentally or hetero-segmentally reduced the spasticity in clients with stroke (Hui-Chan and Levin 1993). A point to note was that the effect of TENS was comparable to that of anti-spastic drugs. Subsequent studies have also shown that TENS reduced the excessive resistive torque, or hyperactive stretch reflex and Achilles tendon reflex in adults with hemiparesis and spinal cord injury (Goulet et al. 1996, Potisk et al. 1995). Comparable, well-controlled studies in children with CP, however, are scarce with none of them demonstrating similar effects on spasticity (Dali et al. 2002, Maenpaa et al. 2004, Sommerfelt et al. 2001, Steinbok et al. 1997a). The possibility for TENS to reduce spasticity in children with neurological conditions deserves our particular attention.

Evidence from SDR (McLaughlin et al. 2002) and reports of the lack of correlation between spasticity and muscle strength (Engsberg et al. 2000, Ross and Engsberg 2002) in individual with CP call for the need to consider spasiticity and muscle weakness as relatively independent impairments in children with CP. Therefore, different treatment strategies may be required to tackle them. In this regard, the use of BWS during gait training on a treadmill would allow multi-lower limb muscle strengthening in a functional context. Clients with stroke receiving 40% of body-weight-supported treadmill training (BWS-TT, n = 50) were found to score significantly higher than the no-BWS group (n = 50) in functional balance, motor recovery, over-ground walking speed and endurance (Visintin et al. 1998). The feasibility of BWS gait training for young children with CP had also been established (Richard et al. 1997). Schindl et al. (2000) further showed that additional BWS-TT for 3 times a week, 25 minutes per sessions for 3 months resulted in improvements in GMFM standing section and walking section scores (p values < 0.05). Nevertheless, concrete evidence for the efficacy of its usage is lacking. Since TENS and BWS gait training have separately been shown to reduce spasticity and enhance motor functions in adults with spastic hemiparesis, we hypothesized that these approaches would hold similar promises for children with CP. This hypothesis begs investigation, since children are believed to have even greater potentials for recovery on account of the greater plasticity of their nervous system.

6.2 Study Design

The present study was a randomized, placebo-controlled clinical trial. The hypotheses were that TENS or TENS+BWS-TT would reduce spasticity more than placebo-TENS and that combining TENS with BWS treadmill training would further

improve muscle function and walking performance in children with CP than TENS alone.

The sample size was calculated using PASS (version 6.0). Based on the study by Levin and Hui-Chan (1992) that examined the effect of TENS on spasticity, the sample size needed for an effect size of 0.80 required a total of 63 subjects, with 21 subjects for each study group. Sixty-three children diagnosed with spastic CP, aged 6 – 15 years old were recruited from 6 special schools and 61 completed the study. After obtaining informed consent from their parents, children with "mild", "moderate", or "severe" levels of ankle plantarflexor spasticity, as defined by the composite spasticity scale (CSS) scores, were then randomly allocated to 1 of 3 groups receiving TENS, placebo-TENS, or TENS+BWS-TT.

All children continued to receive conventional physiotherapy in their respective schools. In the TENS group, low-intensity TENS was applied, via surface electrodes connected to a portable TENS stimulator, to the skin overlying the common peroneal nerve (L4-S2) posterior to the head of fibula. Continuous stimulation (0.125 msec square pulses, 100 Hz, intensity at 2 times the sensory threshold) was applied for 60 minutes, once a day, 5 days a week for 3 weeks. In the placebo-TENS group, the device and stimulation parameters were the same as those in the TENS group, except that the circuit in the device was disconnected. In the TENS+BWS-TT group, the same stimulation protocol as that of the TENS group was first delivered for 60 minutes, followed by 20 to 30 minutes of BWS-TT according to the walking tolerance and progression of each child. Stimulation was applied to the more spastic leg of diplegic CP or to the affected leg of hemiplegic CP.

Outcome measurements included spasticity of the ankle plantarflexors assessed by Composite Spasticity Scale (CSS) and stretch reflex (SR) as a function of maximum M response (SR/M), muscle function in terms of maximum isometric

voluntary contraction (MIVC) and EMG co-contraction ratios of the ankle dorsiflexor and plantarflexor muscles, and walking performance in terms of walking speed and energy cost (physiological cost index, PCI) during a 6-minute walk test. These measurements were recorded at baseline *before* treatment (T_0), and *after* 1 week (T_1), 2 weeks (T_2), and 3 weeks of treatment (T_3), to examine the effects of TENS, placebo-TENS and TENS+BWS-TT over time. Before launching the main study, the characteristics and reproducibility of the measurement protocol for spasticity and motor function in normal and spastic CP children were examined in the 2 pilot studies as summarized below.

6.3 Pilot Studies

6.3.1 Pilot Study I: Reproducibility of the Measurement Protocols

Eight children with spastic CP and 9 age-matched normal children (aged 10.8 ± 2.8 years and 8.9 ± 2.4, respectively) participated in this study. The outcome measures were recorded in both legs on 2 different days within a week by the same examiner as described above.

The results showed high test-retest reliability of the clinical rating of spasticity (r = 0.97) and SR latency (r = 0.85) in the spastic children. Furthermore, a high degree of inter-session consistency (r = 0.78 to 0.97) was also found in the SR/M area ratio, maximal ankle dorsiflexion and plantarflexion torques, agonist EMG areas and co-contraction ratios during dorsiflexion and plantarflexion, and walking speed and PCI of the 6-minute walk test in both normal and spastic children. The high reproducibility of these measurements indicated that they are reliable indicators of spasticity, voluntary muscle function and walking performance in children with spastic CP, and warrant their use as outcome measurements in evaluating intervention directed at improving spasticity and motor function in these children.

6.3.2 Pilot Study II: Motor Disorders in Children with Spastic CP

To delineate possible differences of the outcome measurements between normal and spastic children as one measure of validity, data on 8 children with spastic CP and 9 age-matched normal children who participated in pilot study I were compared. To identify possible correlations among these measurements in the spastic children, 61 children with spastic CP (aged 10.7 ± 2.8 years) who participated in the main study were used for correlation analyses.

The results showed that the more spastic leg of spastic children demonstrated significantly ($p < 0.05$) larger soleus SR/M area ratios, smaller dorsiflexion and plantarflexion torques, and smaller agonist EMG areas with larger co-contraction ratios during both voluntary dorsiflexion and plantarflexion than those of the dominant leg of normal children. In addition, the spastic children walked significantly ($p < 0.05$) slower with a higher physiological cost index than the normal children during the 6-minute walk test.

In the spastic children, those who had larger SR/M area ratios were found to have larger plantarflexion co-contraction ratios ($r = 0.28$; $p = 0.03$), produced smaller plantarflexion torques ($r = -0.48$; $p = 0.00$) and dorsiflexion torques ($r = -0.27$; $p = 0.04$), and walked at slower speeds ($r = -0.40$; $p = 0.01$) and higher energy costs ($r = 0.49$; $p = 0.00$). Furthermore, a larger plantarflexion co-contraction ratio was found to correlate with smaller plantarflexion torques ($r = -0.47$; $p = 0.00$). Those who produced smaller plantarflexion torques also produced smaller dorsiflexion torques ($r = 0.48$; $p = 0.00$). Subjects with smaller plantarflexion and dorsiflexion torques were found to walk at slower speeds ($r = 0.36$; $p = 0.02$ and $r = 0.42$; $p = 0.01$, respectively) and higher energy costs ($r = -0.37$; $p = 0.01$ and $r = -0.43$; $p = 0.00$, respectively). Furthermore, slower walking speeds were found to correlate with higher energy costs of walking ($r = -0.74$; $p = 0.00$).

6.3.3 Conclusions from the Pilot Studies

The results from these pilot studies demonstrated that this battery of tests, previously used to characterize spasticity and deficits in voluntary muscle contraction and walking performance in the adult population, is a reliable and valid measure to characterize motor disorders in children with spastic CP. In addition, it could differentiate abnormal levels of spasticity, voluntary muscle contraction and walking performance in these children from those of normal children. Thus, the test battery we had designed could be used as a comprehensive evaluation tool for intervention studies on spasticity, motor deficits and walking performance in the CP population.

To our understanding, this was the fist study which demonstrated that motor impairments, such as hyperactive SR and weakness of ankle dorsiflexors and plantarflexors, are interrelated and correlated with certain walking performance indices in such a way as to decrease the walking speed and increase the energy cost of walking in children with spastic CP. While clinicians have shifted their focus to strengthening exercises in children with spasticity with the view to improve their function, the significant negative relationship observed in our study between hyperactive SR and walking performance suggests that treatment focusing on both muscle weakness and spasticity may be more effective to help improve motor function in children with CP.

6.4 Effects of TENS and BWS-TT on Spasticity and Voluntary Muscle Contraction in Children with Spastic CP

Sixty-three children diagnosed with spastic CP were recruited. Children recruited were stratified according to the level of ankle plantarflexor spasticity and then randomly allocated to 1 of 3 groups receiving TENS, placebo-TENS, or TENS+BWS-TT after obtaining informed consent from their parents. Sixty-one

children completed the 3 weeks of treatment within their school settings, where they continued to receive conventional rehabilitation programs. Among them, 20 were assigned to the TENS group, 21 to the placebo-TENS group, and 20 to the TENS+BWS-TT group. They were 6 to 15 years old (10.7 ± 2.8 years), 32 were females and 29 were males, 54 had spastic diplegia and 7 had spastic hemiplegia. All children received similar conventional rehabilitation programs. The treatment protocols and outcome measurements were described briefly above (Section 6.2), and in detail in Sections 2.4 and 2.5 of Chapter 2, respectively.

The results showed that the mean CSS score did not differ among groups at baseline. On overage, subjects in each study group were rated as having "moderate" degree of spasticity. In addition, no differences in baseline values were noted in SR/M areas, EMG co-contraction ratios and MIVC torques during ankle dorsiflexion and plantarflexion, as well as in walking speed and in PCI among the 3 study groups ($p >$ 0.05). Hence, any change in the baseline values could be attributed to the intervention given.

Since within-group differences are less meaningful than among-group differences, only the latter are highlighted below to avoid confusion. The results demonstrated that there was negligible % change of CSS score in the placebo-TENS group over the 3-weeks treatment period. When compared with placebo-TENS, a significant % reduction of CSS score was noted in the TENS+BWS-TT group after only 2 weeks of combined treatment (-7.4%; p = 0.001). In contrast, it required 3 weeks of TENS to produce a significant % reduction of CSS score (-13.9%; p = 0.000), at which time a further % reduction (-19.7%, p = 0.000) was observed in the combined treatment group. With respect to hyperactive SR, only 3 weeks of TENS+BWS-TT produced a significant and marked % reduction of SR/M area ratio (-44.9%; p = 0.000). In contrast, 3 weeks of TENS produced a significant within-group

reduction of baseline SR/M area ratio, but the % reduction did not reach significant difference from that of placebo-TENS. With regard to muscle function, significant differences were found only between the TENS+BWS-TT and placebo-TENS groups. Briefly, 3 weeks of combined TENS with BWS-TT but not TENS alone resulted in a significant % increase of dorsiflexion torque (by 18.9%; $p = 0.005$) and a significant % decrease of dorsiflexion co-contraction ratio (by -37.2%; $p = 0.003$) when compared with placebo-TENS. However, none of the interventions produced significant % change of plantarflexion torque or co-contraction ratio after 3 weeks of treatment.

To our understanding, this RCT study was first of its kind that documented significant reduction in spasticity after 3 weeks of TENS in children with CP. The difference in electrode placement and stimulation parameters may account for our findings being different from that of previous studies that examined effects of electrical stimulation, such as therapeutic electrical stimulation, on spasticity. As opposed to adult study (Levin and Hui-Chan 1992), 3 instead of 2 weeks of TENS were required before significant reduction in spasticity and hyperactive SR were detected, while no significant improvement in muscle function was noted in our spastic children. The differences in age, chronicity and the nature of spasticity and movement disorders between children with spastic CP and adults with chronic hemiparesis could be factors contributed to the differences in the treatment outcome.

The TENS parameters used in our present study (low-intensity, high frequency) have been shown to activate mainly larger diameter fibers in the A-α-β range (Levin and Hui-Chan 1993a). Taken together the findings of Levin and Hui-Chan (1992) in adults with chronic stroke and those of our study in children with CP, repetitive stimulation of large diameter afferents via TENS over a prolonged period of time (weeks) could lead to a reduction in spasticity, and in adults with chronic stroke an

improvement in voluntary ankle dorsiflexion as well. Several mechanisms may explain these effects. In an earlier study by Hale and Chan (1986a) on adults with chronic stroke, 2 weeks of TENS were found to enhance the vibratory inhibition of the H-reflex. This finding pointed to the possible involvement of an enhanced presynaptic inhibitory mechanism in mediating the reduction of hyperactive soleus SR, thus contributing to the reduction of the EMG co-contraction ratio during ankle dorsiflexion. These mechanisms probably serve to "disinhibit" or "unmask" the descending excitatory pathway to dorsiflexor motor neurons (Levin and Hui-Chan 1992). Indeed, reduced hyperactive SR was noted in our spastic children after 3 weeks of repeated TENS and/or TENS+BWS-TT, and increased dorsiflexion torque was evident in the TENS+BWS-TT group. Alternatively, cutaneous signals have been reported to have an excitatory influence on cortical motor neurons and, in their absence, a stronger motor command is required (c.f. Lundy-Ekman 2002b). It is possible that a stronger motor command could be achieved by increasing the sensory input via TENS to compensate for the reduced corticomotorneural activities in subjects who have damaged cortical neuronal function.

In subjects who received additional BWS-TT, it was observed that most subjects had their weight-bearing legs brought backward into extension by the movement of the belt of the treadmill system. This would resemble repetitive stretching of the soft tissues at the back of the ankle during certain period of BWS-TT. A previous study had shown that non-reflexive passive torque contributed substantially to spasticity and to impaired walking ability in patients with spastic multiple sclerosis (Sinkjaer et al. 1996a). It is possible that repetitive stretching of soft tissues at the back of ankle during BWS-TT led to a decrease of muscle stiffness of the plantarflexors, thus allowing dorsiflexion to occur more readily. These results might explain why a greater % reduction of CSS score and improvement in motor

function (i.e., % increase of dorsiflexion torque and % decrease of EMG co-contraction) were observed only after 3 weeks of TENS+BWS-TT, but not TENS. Although SR was not recorded during locomotion in this study, the greater reduction of SR/M area ratio after additional BWS-TT may imply possible influence of BWS-TT on SR. This would be an interesting area for further investigation.

The conclusion from this study is that, when compared with children who received placebo electrical simulation plus a conventional rehabilitation program, 15 sessions of 60 minutes daily TENS or TENS in combination with BWS-TT reduced clinical spasticity in children with spastic CP. The findings further support the use of TENS+BWS-TT rather than TENS alone in children with CP, as the combined treatment produced a larger % decrease of clinical spasticity, an earlier and larger % reduction of hyperactive SR, concomitant with significant % increase of dorsiflexion torque and % decrease of EMG co-contraction during dorsiflexion. The study thus provides evidence for combining TENS with task-specific gait training to enable children with CP to have more optimal improvements in reflex and voluntary muscle function, and serve to stimulate further research to examine the use of electrical stimulation and innovative motor training strategies in the paediatric CP population.

6.5 Effects of TENS and BWS-TT on Walking Performance in Children with Spastic CP

Although the majority of children with spastic diplegia or hemiplegia may eventually be able to ambulate, the energy expenditure for walking in children with CP was reported to be almost three-fold compared with that of healthy children (Uninithan et al. 1996). Consequently, these children often complain of fatigue after walking a short distance. In the last experiment, the relative effectiveness of adding TENS and/or TENS+BWS-TT to conventional rehabilitation program in enhancing

walking performance in children with CP was examined. The same study sample and study designed as those reported in Sections 6.4 and Section 6.2, respectively, were employed in this study.

The results showed no significant change of walking speed among the groups. Nevertheless, 3 weeks of TENS+BWS-TT produced a significant % decrease of PCI value (-25.1%; p = 0.001) when compared with placebo-TENS. This may partly be explained by a significant % decrease of heart rate change (HR_{walk} - HR_{rest}; being -26.6%, p = 0.003) during the 6-minute walk test. Such a decrease in the heart rate change was resulted from a significant % decrease of the walking heart rate (-12.11%; p = 0.005) after 3 weeks of combined treatment, while the resting heart rate remained similar in each study group at all assessment intervals.

The exclusive effect of electrical stimulation on walking performance remains unknown in either adults or children with neurological dysfunction. Our results demonstrated that task-specific locomotion training is a valuable therapeutic approach to bring about improvement in walking performance in children with spastic CP. A lower PCI value after 3 weeks of TENS+BWS-TT indicates that at the same level of exertion (walking speed), these children expended less energy for walking. Coincidently, subjective reports from parents also described improved walking performance in that their children "got tired less readily" and "walked for longer distance before needing a rest".

A possible mechanism for the effect of additional BWS-TT on walking performance is that BWS-TT was designed in accordance with the motor learning principle of task specificity. The BWS system not only permits decreased loading on the lower extremities, it also allows dynamic and task specific training that integrates 3 essential components of walking, which are weight bearing, balance and stepping. In addition, practicing walking over the treadmill has an added effect in that it

simulates repetitive and rhythmic stepping. Furthermore, treadmill training promotes cardiovascular fitness, as evident by a significant decrease in the walking heart rate during the 6-minute walk test after 3 weeks of combined TENS with BWS-TT. Both basic (Fedirchuk et al. 1998) and clinical studies (Barbeau and Blunt 1991) have suggested that a locomotor neural circuitry, called the central pattern generator (CPG), within the lumbosacral motor pools may exist. BWS-TT may facilitate spinal cord learning through repeated segmental sensory inputs into lumbosacral motor neurons and interneurons during practice that lead to long-term potentiation (Dobkin 1999). A growing number of studies point to the expanded effectiveness of residual corticospinal and afferent activity after stroke and spinal cord injury on spinal and cortical regulation of facilitation and recruitment (Davey et al. 1999; Jain et al. 1997). Such inputs would likely expand cortical and subcortical movement representations for locomotion (Nudo and Miliken 1996).

The conclusion from this study is that 15 sessions of combined TENS with BWS-TT could reduce the physiological cost of walking in CP children, but not TENS alone. This treatment strategy has the added benefits of being non-invasive, low cost, and without the side-effects often associated with drug intake or surgery such as dorsal rhizotomy. The results of our study lay the ground for further research to identify the best treatment protocol, in terms of multiple sites of TENS, treadmill speed, training frequency and facilitation techniques in enhancing locomotive function in children and adults with neurological deficits. The extent to which 3 weeks of BWS-TT alone would bring significant improvement in mobility function requires further investigation.

6.6 Limitations

The study was not a true double-blind design. The investigator knew to which group each child had been assigned, as a result of implementing the treatments. It should be noted, however, that except for the CSS score, all the outcome measurements are objective measurements recorded by instrumented machines and a computer, which are blinded to the purpose of the study.

Second, the research design included one placebo-control group to determine if TENS could reduce spasticity and improve motor functions more than possible placebo effects plus spontaneous recovery/regression. Comparing the effects of TENS versus TENS+ BWS gait training helped to delineate if additional gait training, giving during the period of spasticity reduction after TENS, would further enhance motor function. As such, the improvements in reflex and voluntary muscle function observed after 3 weeks of TEN+BWS-TT, but not TENS, might be attributed to an increase in the total treatment time rather than to the specific treatment effect offered by BWS-TT. Ideally, it would be desirable to add another group receiving BWS-TT alone to the research design, in order to delineate the specific effects of BWS gait training. However, in view of the very stringent inclusion and exclusion criteria used in the study, subject recruitment would be a problem if more groups were added. These latter considerations will form the subject of a further investigation.

Thirdly, progressive improvement in all outcome measures was noted with each additional week of treatment on either TENS or TENS+BWS-TT. It would therefore be useful to have continued the treatment for an additional 1 to 2 weeks to exploit if longer treatment duration could have further improvements in various aspects of motor functions of these children.

Fourthly, it will be interesting to have follow-up assessments at 1-week or 2-week interval and/or 3 to 6 months after treatment to determine whether there will be short-term or prolonged effects of treatment and how long those effects will be.

In addition, single site TENS stimulation was employed in this study. It is unclear if multi-site stimulation, in particular, TENS stimulation on bilateral limbs of children with diplegic CP would enhanced the effects of treatment. Positive results of this study point to support such a treatment approach.

Besides, the effect of treatment on motor functions of children with diplegic CP or hemiplegic CP was not delineated in this study. It would be useful to include a larger group of children with hemiplegic CP in future to reveal the effect of treatment on this particular population of children.

Lastly, although there was significant improvement in PCI after 3-weeks of combined TENS+BWS-TT, the extent of such a change in walking endurance on the "Participation" level of our children sample was unknown. Future study employing measures on participation level is recommended. All in all, positive findings of this study will serve to stimulate future studies on possible carry-over effects.

6.7 Significance of the Study

The present study provides a scientific understanding in addition to delineating the effectiveness of adding TENS and/or BWS-TT to conventional rehabilitation programs for children with spastic CP.

First, to our understanding, this was the fist study which demonstrated that motor impairment such as hyperactive SR and weakness of ankle dorsiflexors and plantarflexors are interrelated and correlated with certain walking performance indices in such a way as to decrease the walking speed and increase the energy cost of walking in children with spastic CP. With the view to improve their function, these

findings suggest that treatments focusing on both muscle weakness and spasticity may be more effective to help improve motor function in children with CP.

Second, the battery of tests, previously used to characterize spasticity and deficits in voluntary muscle contraction and walking performance in the adult population, can be used reliably and can differentiate abnormal levels of spasticity, voluntary muscle contraction and walking performance in children with CP from those of normal children. Thus, the test battery we designed can be used as a comprehensive evaluation tool for intervention studies on spasticity, motor deficits and walking performance in the CP population. Moreover, adopting this battery of tests as outcome measures would further allow comparisons of the pathophysiological mechanism underlying motor dysfunction between adults and children.

Third, to our knowledge, this is first large scale study that implemented TENS or combined TENS with BWS-TT to children with spastic CP, using a randomized study design with placebo control. Our results demonstrated that both treatments are feasible treatment protocols for use in the school settings. This RCT study was first of its kind that documented significant reduction of spasticity after 3 weeks of TENS in children with CP.

Fourth, no study so far has examined the relative effectiveness between TENS and TENS+BWS-TT in reducing spasticity and in enhancing muscle function and walking performance in children with spastic CP. The results demonstrated that 15 sessions of combined TENS with BWS-TT were more superior than TENS alone in this regard. It confirms that task-specific locomotion training is a valuable therapeutic approach to bring about functional gains in these children. This combined treatment strategy could become a preferred choice of treatment, on account of its non-invasive nature, low cost and absence of the side-effects often associated with drug intake or surgery such as dorsal rhizotomy.

REFERENCES

References

Akazawa K., Aldridge J.W., Steeves J.D., Stein R.B. (1982) Modulation of stretch reflexes during locomotion in the mesencephalic cat. *Journal of Physiology*, 329:553-567.

Albright A.L., Barry M.J., Fasick M.P., Janosky J. (1995). Effects of continuous intrathecal baclofen infusion and selective posterior rhizotomy on upper extremity spasticity. *Pediatric Neurosurgery*, 23:82-85.

Alfieri V. (1982). Electrical treatment of spasticity. *Scandinavian Journal of Rehabilitation Medicine*, 14:177-182.

Almay B.G.L, Johansson F., von Knorring L., Sakurada T., Terenius L. (1985). Long-term high frequency transcutaneous electrical nerve stimulation (hi-TENS) in chronic pain: Clinical response and effects on CSF-endorphins, mono-amine metabolites, substance P-like immunoreactivity (SPL1) and pain measures. *Psychosomatic Research*, 29:247-257.

Andersson C., Grooten W., Hellsten M., Kaping K., Mattsson E. (2003). Adults with cerebral palsy: walking ability after progressive strength training. *Developmental Medicine and Child Neurology,* 45:220-228.

Andersson C., Mattson E. (2001). Adults with cerebral palsy: a survey describing problems, needs, and resources, with special emphasis on locomotion. *Developmental Medicine and Child Neurology,* 43:76-82.

Ashby P., Verrier M. (1976). Neurophysiologic changes in hemiplegia. *Neurology,* 26:1145-1151.

Bajd T., Gregoric M., Volovnik L., Benko H. (1985). Electrical stimulation in treating spasticity resulting from spinal cord injury. *Archives of Physical Medicine and Rehabilitation*, 66:515-517.

Baldissera F., Hultborn H., Illert M. (1981). Integration in spinal neuronal systems. In: Brooks V.B. (eds), *Handbook of Physiology. Section 1: Motor Control* (509-595). Bethesda: American Physiology Society.

Barbeau H., Blunt R. (1991). A novel interactive locomotor approach using body weight support to retrain gait in spastic paretic subjects. In: Werning A. (ed.), *Plasticity of Motorneuronal Connections* (461-474). Amsterdam: Elsevier.

Barbeau H., Fung J. (1992). New experimental approaches in the treatment of spastic gait disorders. In: Forssberg H, Hirschfeld H. (eds.), *Movement Disorders in Children* (36:234-246). Basel, Karger: Medical Sport Science.

Barbeau H., Norman K., Fung J., Visintin M., Ladouceur M. (1998). Does neurorehabilitation play a role in the recovery of walking in neurological populations? In: Neuronal Mechanisms for Generating Locomotor Activity, (860:377-392). *Annals of the New York Academy of Sciences.*

Barbeau H., Rossignol S. (1987). Recovery of locomotion after chronic spinalization in the adult cat. *Brain Research*, 412:84-95.

Baroff G.S. (1991). *Developmental Disabilities.* Psychosocial Aspects: Texus Pro-Ed.

Bax M.C. (1964). Terminology and classification of cerebral palsy. *Developmental Medicine and Child Neurology,* 6:295-296.

Beck S. (1997). Use of sensory level of electrical stimulation in the physical therapy management of a child with cerebral palsy. *Pediatric Physical Therapy,* 9:137-138.

Beckung E., Hagberg G. (2000). Correlation between ICICH handicap code and gross motor function classification system in children with cerebral palsy. *Developmental Medicine and Child Neurology*, 42:669-673.

Berger W., Dietz V., Quintern J. (1984). Corrective reactions to stumbling in man: Neuronal co-ordination of bilateral leg muscle activity during gait. *Journal of Physiology*, 357:109-125.

Berger W., Quintern J., Dietz V. (1982). Pathophysiology of gait in children with cerebral palsy. *Electroencephalography and Clinical Neurophysiology,* 53:538-548.

Bernstein D.R., Stelzner D.J. (1983). Plasticity of the corticospinal tract following midthoracic spinal injury in the postnatal rat. *Journal of Comparative Neurology*, 221:382-400.

Bleck E.E. (1991). Spastic hemiplegia. In: *Orthopaedic Management in Cerebral Palsy,* (240-257). Cambridge University Press

Bohannon R.W., Larkin P.A., Smith M.B., Horton M.G. (1987). Relationship between static muscle strength deficits and spasticity in stroke patients with hemiparesis. *Physical Therapy,* 67:1068-1071.

Bohannon R.W., Smith M.B. (1987). Inter-rater reliability of a modified ashworth scale of muscle spasticity. *Physical Therapy,* 67:206-207.

Borg G.A.V. (1982). Psychophysical bases of perceived exertion. *Medicine and Science in Sports and Exercise*, 14:377-381.

Bottos M., Garnato T., Allibrio G., Gioachin C., Puato M.L. (1999). Prevalence of cerebral palsy in north-east Italy from 1965 to 1989. *Developmental Medicine and Child Neurology*, 41:26-39.

Bouisset S., Lestienne F. (1974). The organization of a simple voluntary movement as analysed from its kinematic properties. *Brain Research*, 71:451-458.

Bowen T.R., Lennon N., Castango P., Millrt F., Richards J. (1998) Variability of energy-consumption measures in children with cerebral palsy. *Journal of Pediatric Orthopedics*, 18:738-742.

Boyd R., Fatone S. Rodda J., Olesch C., Starr R., Cullis E., Gallargher D., Carlin J.B., Nattrass G.R., Graham K. (1999). High- and low-technology measurements of energy expenditure in clinical gait analysis? *Developmental Medicine and Child Neurology*, 41:676-682.

Boyd R., Roland S., Wolfe R., Kerr H. (2000a). Biomechanical transformation of the gastro-soleus muscle with botulinum toxin-A in children with cerebral palsy. *Developmental Medicine and Child Neurology*, 42:32-41.

Boyd R.N., Houltran J., Noble I., Flett P., Corry I., Graham H.K. (2000b). An economic evaluation of the use of Botulinum toxin A in the conservative management of equines in children with cerebral palsy. (Abstract). *Developmental Medicine and Child Neurology,* 83:7.

Brink E., Jankowska E., Scoog B. (1984). Convergence onto interneurons subserving primary afferent depolarization of group I afferents. *Journal of Neurophysiology*, 51:432-449.

Brouwer B., Ashby P. (1989). Corticospinal projections: Do they differ in patients with cerebral palsy? (Abstract) *Developmental Medicine and Child Neurology (Supplementary)*, 59:22.

Brouwer B., Wheeldon R.K., Allum J. (1998). Reflex excitability and isometric force production in cerebral palsy: the effect of serial casting. *Developmental Medicine and Child Neurology,* 40:168-175.

Buckon C.E., Thomas S.S., Harris G.E., Piatt J.H., Aiona M.D., Sussman M.D. (2002). Objective measurement of muscle strength in children with spastic diplegia after selective dorsal rhizotomy. *Archives Physical Medicine Rehabilitation,* 83:454-460.

Buonomano D.V., Merzenich M.M. (1998). Cortical plasticity: from synapses to maps. *Annual Reviews of Neuroscience*, 21:149-186

Burke D., Ashby P. (1972). Are spinal "presynaptic" inhibitory mechanisms suppressed in spasticity? *Journal of Neurological Science,* 15:321-326.

Burke D, Lance JW. (1973). Studies of the reflex effects of primary and secondary spindle endings in spasticity. In: Desmedt J.E., Karger J.E. (eds.), *New Developments in Electromyography and Clinical Neurophysiology* (vol. 3:475-495). Basel.

Burke D. Hagbarth K.E., Lofstedt L., Wallin B.G., (1976). The response of human muscle spindle ending to vibration of non-contracting muscles. *Journal of Physiology (London)*, 261:673-693.

Butland R.J.A., Pang J., Gross E.R. (1982). Two-, six-, and twelve-minute walking tests in respiratory disease. *British medical Journal*, 284:1607-1608.

Butler C., Campbell S. (2000). Evidence of the effects of intrathecal baclofen for spastic and dystonic cerebral palsy. (Report approved by: AACPDM Treatment Outcomes Committee Review Panel: Adam R., Abel M., Chambers H., Goldstein M.,

Leach J., Darrah J., Msall M., Edgar E., McLaughlin J., Damiano D., Stott N.S., Samson-Fang L., Logan L., Albright L., Armstrong R., O'Donnell M.). *Developmental Medicine and Child Neurology*, 42:634-645.

Butler C., Chambers H., Goldstein M., Harris S., Leach J., Campbell S., Adams R., Darrah J. (1999). Evaluating research in developmental disabilities: A conceptual framework for reviewing treatment outcomes. *Developmental Medicine and Child Neurology*, 41:55-59.

Butler C., Darrah J. (2001). Effects of neurodevelopmental treatment (NDT) for cerebral palsy: an AACPDM evidence report. (Report approved by: AACPDM Treatment Outcomes Committee Review Panel: Richard A., Chambers H., Abel M., Damiano D., Edgar T., Msall M., Samson-Fang L., Stott N.S., Law M., Leach J., Goldstein M., O'Donnell M., McLaughlin J.). *Developmental Medicine and Child Neurology*, 43:778-790.

Butler P., Engelbrecht M., Major R.E., Tait J.H., Stallard J., Patrick J.H. (1984). Physiological cost index of walking for normal children and its use as an indication of physical handicap. *Developmental Medicine and Child Neurology*, 26(5):607-612.

Cahan L.D., Beeler L., McPherson D. (1988). Clinical electrophysiologic and kinesilologic studies of selective dorsal rhizotomy. (Abstract). *Developmental Medicine and Child Neurology*, 57:4-5.

Cahan L.D., Kundi M.S., McPerson D. (1987). Electrophysiologic studies in selective dorsal rhizotomy for spastiicty in children with cerebral palsy. *Applied Neurophysiology*, 50:459-462.

Cameron M.E., Drummond S.J. (1998). Measurements to quantify improvement following serial casting program for equines deformity in children with cerebral palsy. *New Zealand Journal of Physiotherapy*, April, 28-32.

Campbell S., Wilhelm I. (1983). Development of infants at risk for central nervous system dysfunction: Progress report. In Slaton D.S., Wilson J.M. (eds.), *Caring for special babies.* Chapel Hill, University of North Carolina at Chapel Hill: Division of Physical Therapy.

Campbell S.K., Almeida G.L., Penn R.D., Corcos D.M. (1995). The effects of intrathecally administered baclofen on function in patients with spasticity. *Physical Therapy*, 75:352-362.

Canning C.G., Ada L., O`Dwyer N. (1999). Slowness to develop force contributes to weakness after stroke. *Archives of Physical Medicine and Rehabilitation*, 80:66-70.

Carlson M. (1984). Development of tactile discrimination capacity in Macaca Mulatta II: effects of partial removal of primary somatic sensory cortex (SmI) in infants and juveniles. *Brain Research*, 16:83-101.

Carmick J. (1995). Managing equines in children with cerebral palsy: electrical stimulation to strengthen the triceps surae muscle. *Developmental Medicine and Child Neurology*, 37:965-975.

Carr J., Shepherd R. (1998). Neurological rehabilitation. Oxford: Butterworth and Heinemann.

Castle M.E., Reyman T.A., Schneider M. (1972). Pathology of spastic muscle in cerebral palsy. *Clinical Orthopedics,* 142:223-233.

Chan H.S.S., Lau P.H.B., Fong K.H., Poon D., Lam C.C.C. (2005). Neuroimpairment, activity limitation, and participation restriction among children with cerebral palsy in Hong Kong. *Hong Kong Medical Journal,* 11:342-350.

Charles J.R., Wolf S.L., Schneider J.A., Gordon A.M. (2006). Efficacy of a child-friendly form of constraint-induced movement therapy in hemiplegic cerebral palsy: a randomized control trial. *Developmental Medicine and Child Neurology*, 48:635-642.

Cohen J (1988). Statistical power analysis for the behavioural sciences. Hillsdale: Erlbaum Associates, Inc.

Colver A.F., Gibson M., Heys E.H., Jarvis S.N., Mackie P.C., Richmond S. (2000). Increasing rates of cerebral palsy across the severity spectrum in north-east Englasn 1964-1993. *Archives of Disease in Childhood, Fetal and Neonatal Edition (London)*, 83:F7-12.

Cook A.W., Weinstein S. (1973). Chronic DCS in multiple sclerosis. *New York State Journal of Medicine*, 73:2868-2872.

Cosgrove A.P., Corry I.S., Graham H.K. (1994). Botulinum toxin in the management of the lower limb in cerebral palsy. *Developmental Medicine and Child Neurology*, 36:386-396.

Dali C., Hansen F.J., Pedersen S.A., Skov L., Hilden J., Bjornskov I., Strandberg C., Christensen J., Haugsted U., Herbst G., Lyskjaer U. (2002). Threshold electrical stimulation (TES) in ambulant children with CP: a randomized double-blind placebo-controlled clinical trial. *Developmental Medicine and Child Neurology,* 44:364-369.

Damiano D.L., Abel M.F. (1998). Functional outcomes of strength training in spastic cerebral palsy. *Archives of Physical Medicine and Rehabilitation*, 79: 119-125.

Damiano D.L., Dodd K., Taylor N.F. (2002). Should we be testing and training muscle strength in cerebral palsy? *Developmental Medicine and Child Neurology*, 44:68-72.

Damiano D.L., Kelly L.E., Vaughn C.L. (1995a). Effect of quadriceps femoris muscle strengthening on crouch gait in children with spastic diplegia. *Physical Therapy*, 75:658-671.

Damiano D.L., Martellotta T.L., Quinlivan J.M., Abel M.F. (2000). Deficits in eccentric versus concentric torque in children with spastic cerebral palsy. *Medicine and Science in Sports and Exercise*, 117-122.

Damiano D.L., Vaughan C.L., Abel M.F. (1995b). Muscle response to heavy resistance exercise in children with spastic cerebral palsy. *Developmental Medicine and Child Neurology,* 37:731-739.

Darrah J., Fan J.S.W., Chen L.C., Nunweiler J., Watkins B. (1997). Review of the effects of progressive resisted muscle strengthening in children with cerebral palsy: a clinical consensus exercise. *Pediatric Physical Therapy,* 9:12-17.

Darrah J., Watkin B., Chen L., Bonin C. (2004). Conductive education intervention for children with cerebral palsy: An AACPDM evidence report. *Developmental Medicine and Child Neurology,* 46:187-203.

Darrah J., Wessel J., Nearingburg P., O'Connor M. (1999). Evaluation of a community fitness program for adolescents with cerebral palsy. *Pediatric Physical Therapy,* 11:18-23.

Davey N., Smith H., Savic G., Maskill D., Ellaway P., Frankel H. (1999). Comparison of input-output patterns in the corticospinal system of normal subjects and incomplete spinal cord injured patients. *Experimental Brain Research*, 127:382-390.

DeLeon R., Hodgson J., Roy R., Edgerton V. (1998). Locomotor capacity attributable to step training versus spontaneous recovery after spinalization in adult cats. *Journal of Neurophysiology*, 79:1329-1340.

Delwaide P.J. (1985). Electrophysiological testing of spastic patients: its potential usefulness and limitations. In: Delwaide P.J., Young R.R. (eds.), *Restorative Neurology: Clinical Neurophysiology in Spasticity* (1:185-204). Amsterderm: Elsevier.

Dewald J.P., Given J.D., Rymer W.Z. (1996). Long-lasting reductions of spasticity induced by skin electrical stimulation. *IEEE Transactions on Rehabilitation Engineering,* 4(4):231-242.

Dietz V. (1999). Supraspinal pathways and the development of muscle-tone dysregulation. *Developmental Medicine and Child Neurology*, 41:708-715.

Dietz V., Colombo D., Jensen L., Baumgartner L. (1995). Locomotor capacity of spinal cord paraplegic patients. *Annals of Neurology,* 37:574-582.

Dietz V., Quintern J., Berger W. (1981). Electrophysiological studies of gait in spasticity and rigidity. Evidence that altered mechanical properties of muscle contribute to hypertonia. *Brain*, 104:431-449.

Dietz V., Quintern J., Sillem M. (1987). Stumbling reactions in man: significance of proprioceptive and pre-programmed mechanisms. *Journal of Physiology*, 386:149-163.

Dietz V., Trippel M., Berger W. (1991). Reflex activity and muscle tone during elbow movements in patients with spastic paresis. *Annals of Neurology*, 30:767-779.

Dimitrijevic M.R., Faganel J., Lehmkuhl D., Sherwood A. (1983). Motor control in man after partial or complete spinal cord injury. In: Desmedt J.E. (ed.), *Motor Control Mechanisms in Health and Disease* (915-926). New York: Raven Press.

Dimitrijevic M.R., Nathan P.W. (1967). Studies of spasticity in man. I: Some features of spasticity. *Brain*, 90:1-30.

Dimitrijevic M.R., Nathan P.W., Sherwood A.M. (1980). Clonus: The role of central mechanisms. *Journal of Neurology, Neurosurgery and Psychiatry,* 43:321-332.

Dobkin B., Edgerton V., Fowler E., Hodgson J. (1992). Training induces rhythmic locomotor EMG patterns in subjects with complete SCI. *Neurology*, 42(Suppl 3):207-208.

Dobkin B., Harkema S., Requejo P., Edgerton V. (1995). Modulation of locomotor-like EMG activity in subjects with complete and incomplete chronic spinal cord injury. *Journal of Neurological Rehabilitation*, 9:183-190.

Dobkin B.H. (1999). An overview of treadmill locomotor training with partial body weight support: A neurophysiologically sound approach whose time has come for randomized clinical trials. *Neurorehabilitation and Neural Repair*, 13:157-165.

Dodd K.J., Tayler N.F., Graham H.K. (2003). A randomized clinical trial of strength training in young people with cerebral palsy. *Developmental Medicine and Child Neurology,* 45:652-657.

Dodd K.J., Taylor N.F., Damiano D.L. (2002). A systematic review of the effectiveness of strength-training programs for people with cerebral palsy. *Archives of Physical Medicine and Rehabilitation*, 83:1157-1164.

Drouin L.M., Malouin F., Richard C.L., Marcoux S. (1996). Correlation between the gross motor function measures scores and gait spatiotemporal measures in children with neurological impairments. *Developmental Medicine and Child Neurology,* 38:1007-1019.

Edgerton V., Roy R., DeLeon R., Tillakaratne N., Hodgson J. (1997). Does motor learning occur in the spinal cord. *Neuroscientist*, 3:287-294.

Edgerton V.R., De Guzman C.P., Gregor R.J., Roy R.R., Hodgson J.A., Lovely R.G. (1991). Trainability of the spinal cord to generate hindlimb stepping patterns in adult spinalized cats. In: Shimamura M., Grillner S., Edgerton V.R. (eds), *Neurobiological Basis of Human Locomotion* (411-423). Tokyo: Japan Scientific Society .

Eliasson A.C., Krumlinde-Sundholm L., Shaw K., Wang C. (2005). Effects of constraint-induced movement therapy in young children with hemiplegic cerebral palsy: an adapted model. *Developmental Medicine and Child Neurology,* 47:266-275.

Engberg I., Lundberg A. (1969). An electromyographic analysis of muscular activity in the hindlimb of the cat during unrestrained locomotion. *Acta Physiologica Scandinavica,* 75:614-630.

Engsberg J.R., Ross S.A., Olree K.S., Park T.S. (2000). Ankle spasticity and strength in children with spastic diplegic cerebral palsy. *Developmental Medicine and Child Neurology,* 42:42-47.

Engsberg J.R., Ross S.A., Wagner J.M., Park T.S. (2002). Changes in hip spasticity and strength following selective dorsal rhizotomy and physical therapy for spastic cerebral palsy. *Developmental Medicine and Child Neurology,* 44:220-226.

Faist M., Mazevet D., Dietz V., Pierrot-Deseilligny E. (1994). A quantitative assessment of presynaptic inhibition of Ia afferents in spastics: Differences in hemiplegics and paraplegics. *Brain,* 117:1449-1155.

Fedirchuk B., Nielson J., Petersen N., Hultborn H. (1998). Pharmacologically evoked fictive motor patterns in the acutely spinalized marmoset monkey. *Experimental Brain Research*, 122:351-361.

Felman A.G. (1986). Once more on the equilibrium-point hypothesis (λ model) for motor control. *Journal of Motor Behavior*, 18:17-54.

Fetters L., Kluzik J. (1996). The effects of neurodevelopmental treatment versus practice on the reaching of children with spastic cerebral palsy. *Physical Therapy,* 76:346-358.

Finch L., Barbeau H., Arsenault B. (1991). Influence of body weight on normal human gait: development of a gait retraining strategy. *Physical Therapy*, 71:842-856.

Fleiss J.L. (1986). The design and analysis of clinical experiments. New: York.Wiley

Foreman R.D., Beall J.E., Applebaum A.E., Cloutier J.D., Willis W.D. (1976). Effects of dorsal column stimulation on primate spinothalamic tract neurons. *Journal of Neurophysiology,* 39:534-545.

Fung J., Stewart J.E., Barbeau H. (1990). The combined effects of clonidine and cyproheptadine with interactive training on the modulation of locomotion in spinal cord injured subjects. *Journal of Neurological Sciences*, 100:85-93.

Furukawa A., Nil E., Iwatsuki H., Nishiyama M., Uchida A. (1998). Factors of influence on the walking ability of children with spastic cerebral palsy. *Journal of Physical Therapy Science*, 10:1-5.

Gemperline J.J., Allen S., Walk D., Rymer W.Z. (1995). Characteristics of motor unit discharge in subjects with hemiparesis. *Muscle and Nerve*, 18:1101-1114.

Gilles J.D., Lance J.W., Neilson P.D., Tassinari C.A. (1969). Presynaptic inhibition of the monosynaptic reflex by vibration. *Journal of Physiology (London)*, 205:329-339.

Gilmartin R., Bruce D., Storrs B.B., Abbott R., Krach L., Ward J., Bloom K., Brooks W.H., Johnson D.L., Madsen J.R., Mclaughlin J.F., Nadell J. (2000). Intrathecal baclofen for management of spastic cerebral palsy: multicenter trial. *Journal of Child Neurology,* 15:71-77.

Giuliani C.A. (1991). Dorsal rhizotomy for children with cerebral palsy: Support for concepts of motor control. *Physical Therapy*, 71:248-259.

Giuliani C.A. (1992). Commentary to "Use of an intensive task-orientated gait training program in a series of patients with acute cerebrovascular accidents." *Physical Therapy*, 72:781-793.

Goldman P.S., Galkin T.W. (1978). Prenatal removal of frontal association cortex in the fetal rhesus moneky: anatomical and functional consequences in postnatal life. *Brain Research*, 152:451-485.

Goldstein E.M. (2001). Spasticity management: an overview. *Journal of Child Neurology,* 16:16-23.

Goulet C., Arsenault B., Bourbonnais D., Laramee M.T., Lepage Y. (1996). Effects of transcutaneous electrical nerve stimulation on H-reflex and spinal spasticity. *Scandinavian Journal of Rehabilitation Medicine,* 28:169-176.

Grillner S. (1973). Locomotion in the spinal cat. In: Stein R.B., Pearson K.G., Smith R.S., Bedford J.B. (eds), *Control of Posture and Locomotion*. (515-535). New York: Plenum.

Grillner S. (1985). Neurobiological bases for rhythmic motor acts in vertebrates. *Science*, 228:143-149.

Grillner S. (1997). Ion channels and locomotion. *Science*, 278:1087-1088.

Guyatt G.H., Pugsley S.O. Sullivan M.J., Thompson P.J., Berman L.B., Jones N.L., Fallen E.L., Taylor D.Y. (1984). Effect of encouragement on walking test performance. *Thorax*, 39:818-822.

Hadders-Algra M., Klip-Vanden Nieuwendijk A., Martinjn A., van Eyhern L.A. (1997). Assessment of general movements: Towards a better understanding of a sensitive method to evaluate brain function in young infants. *Developmental Medicine and Child Neurology*, 39:88-98.

Hagberg B., Hagberg G., Loow I., vonWendt L. (1989). The changing panorama of cerebral palsy in Sweden. V. The birth year period 1979-82. *Acta Paediatrica Scandinavica*, 78:283-290.

Hale J.L., Chan C.W.Y. (1986a). Possible enhancement of presynaptic inhibitory mechanisms following nine days of TENS in hemiplegic patients. *Proceedings of the International Union of Physiological Sciences,* XVI:256.

Hale J.L., Chan C.W.Y. (1986b) The acute effects of conventional TENS in the management of spasticity. *Physiotherapy Canada*, (Suppl. 5):38.

Harkema S.J., Hurley S.L., Patel U.K., Requejo P.S., Dobkin B.H., Edgerton V.R. (1997). Human lumbosacral spinal cord interprets loading during stepping. *Journal of Neurophysiology*, 77:791-811.

Hazlewood M.E., Brown J.K., Rowe P.J., Salter P.M. (1994). The use of therapeutic electrical stimulation in the treatment of hemiplegic cerebral palsy. *Developmental Medicine and Child Neurology,* 36:661-673.

Helsel P., McGee J., Graveline C. (2001). Physical management of spasticity. *Journal of Child Neurology,* 16:24-30.

Hemingway C., McGrogan J., Freeman J.M. (2001) Energy requirements of spasticity. *Developmental Medicine and Child Neurology,* 43:277-278.

Hesse S., Bertelt C., Jahnke M., Baake P., Mauritz K. (1995). Treadmill training with partial weight body weight compaed with physiotherapy in nonambulatory hemiparetic patients. *Stroke,* 26:976-981.

Hesse S., Bertelt C., Schaffrin A., Malezic M., Mauritz K.H. (1994). Restoration of gait in nonambulatory hemiparetic patients by treadmill training with partial body weight support. *Archives of Physical Medicine and Rehabilitation*, 75:1087-1093.

Hodgson J., Roy R.R., De Leon R., Dobkin B., Edgerton V.R. (1994). Can the mammalian lumbar spinal cord learna motor task? *Medicine and Science in Sports and Exercise*, 26:1491-1497.

Horak F.B. (1991). Assumptions underlying motor control for neurologic rehabilitation. In: Lister M.J. (ed.), *Contemporary Management of Motor Control Problems.* (11-27). Alexandria, Virginia: Proceedings of the II Step Conference, Foundation of Physical Therapy.

Howle J.M.W. (1999). Cerebral Palsy. In Campbell S (ed), *Decision Making in Pediatric Neurologic Physical Therap*y (23-83). New York: Churchill Livingstone.

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

Hui-Chan., Levin M.F. (1993). Stretch reflex latencies in spastic hemiparetic subjects are prolonged after transcutaneous electrical nerve stimulation. *Canadian Journal of Neuroloigcal Sciences*, 20:97-106.

Hultborn H., Malmsten J. (1983). Changes in segmental reflexes following chronic spinal cord hemisections in the cat I: Increase monosynaptic and polysynaptic ventral root discharges. *Acta Physiologica Scandinavica*, 119:405-422.

Hur J.J. (1995). Review of research on therapeutic interventions for children with cerebral palsy. *Acta Neurologica Scandinavica,* 91:423-432.

Ito J., Araki A., TAnka H., Tasaki T., Cho K., Yamazaki R. (1996). Muscle histopathology in spastic cerebral palsy. *Brain and Development*, 18:299-303.

Jain N., Catania K., Kaas J. (1997). Deactivation and reactivation of somatosensory cortex after dorsal spinal cord injury. *Nature*, 386:495-498.

Jakobsson K., Grimby L., Edstrom L. (1992). Motorneuron activity and muscle fibre type composition in hemiparesis. *Scandinavian Journal of Rehabilitation Medicine*, 24:115-119.

Jobin A., Levin M. (2000). Regulation of stretch reflex threshold in elbow flexors in children with cerebral palsy: a new measure of spasticity. *Developmental Medicine and Child Neurology* 42:531-540.

Johansson B.B. (2000). Brain plasticity and stroke rehabilitation. *Stroke*, 31:223-230.

Johansson K., Lindgren I., Widner H., Wiklund I., Johansson B.B. (1993). Can sensory stimulation improve functional outcome in stroke patients. *Neurology*, 43:2189-2192.

Johnston T.E., Moore S.E., Quinn L.T., Smith B.T. (2004). Energy cost of walking in children with cerebral palsy: relation to the gross motor function classification system. *Developmental Medicine and Child Neurology,* 46:34-38.

Jueptner M., Weiller C. (1998). A review of differences between basal ganglia and cerebellar control of movements as revealed by functional imaging studies. *Brain*, 121:1437-1449.

Kahn-D'Angelo L., Unanue R.A. (2000). The Special Care Nursery. In: Campbell S.K., Vander Linden D.W., Palisano R.J. (eds), *Physical Therapy for Children* (840-880). 2nd ed. Philadelphia: W.B. Saunders.

Kalil K. (1979). Regrowth of severed axons in the neonatal central nervous system: establishment of normal connections. *Science*, 205:1158-1161.

Kerr C., McDowell B., McDonough S. (2004). Electrical stimulation in cerebral palsy: a review of effects on strength and motor function. *Developmental Medicine and Child Neurology*, 46:205-213.

King G., Law M., King S. (1999). The participation of children with physical disabilities. Ontario: *CanChild Centre for Childhood Disability Research*.

Knutsson E. (1970). Muscle activation patterns of gait in spastic hemiparesis, paraparesis and cerebral palsy. In: Fugl-Meyer A. (ed), Stroke with Hemiplegia. *Scandinavian Journal of Rehabilitation,* Suppl. 7:47-52.

Kramer J.F., MacPhail H.E.A. (1994). Relationships among measures of walking efficiency, gross motor ability, and isokinetic strength in adolescents with cerebral palsy. *Pediatric Physical Therapy,* 6:3-8.

Kundi M.S., Cahan L.D., Starr A. (1989). Somatosensory evoked potentials in cerebral palsy after partial dorsal root rhizotomy. *Archives of Neurology*, 46:524-529

Ladouceur M., Pépin A., Norman K.E., Barbeau H. (1997). Recovery of walking after spinal cord injury. *Advances in Neurology*, 72:249-225.
Lance J.W. (1980a). The control of the muscle tone, reflexes and movement. *Neurology,* 30:1303-1313.

Lance J.W. (1980b). Symposium synopsis. In: Feldman RC, Young RR, Koella KP, (eds), *Spasticity: Disordered Motor Control* (485-494). Chicago, IL: Year Book Medical Publishers.

Lee W.A., Boughton A., Rymer W.Z. (1987). Absence of stretch reflex gain enhancement in voluntarily activated spastic muscle. *Experimental Neurology*, 98:317-335.

Lehmann J.F., Price R., de Lateur B., Hinderer S., Traynor C. (1989). Spasticity: quantitative measurements as a basis for assessing effectiveness of therapeutic intervention. *Archives of Physical Medicine and Rehabilitation*, 70:6-15.

Leonard C. (1994) Motor behavior and neural changes following perinatal and adult-onset brain damage: implications for therapeutic interventions. *Physical Therapy*, 74:753-767.

Leonard C.T., Goldberger M.E. (1987). Consequences of damage to the sensorimotor cortex in neonatal and adult cats, II: maintainance of exuberant projections. *Developmental Brain Research*, 32:15-30.

Levin M.F., Chan C.W.Y. (1989). Stretch reflex latency changes following repetitive reciprocal and hetero-segmental stimulation in spastic hemiplegic subjects. *Society of Neuroscience Abstract,* 15:916.

Levin M.F., Feldman A.G. (1994). The role of stretch reflex threshold regulation in normal and impaired motor control. *Brain Research*, 657:23-30.

Levin M.F., Hui-Chan C. (1992). Relief of hemiparetic spasticity by TENS is associated with improvement in reflex and voluntary motor functions. *Electroencephalography and clinical Neurophysiology,* 85:131-142.

Levin M.F., Hui-Chan C.W.Y. (1993a). Conventional and acupuncture-like transcutaneous electrical stimulation excite similar afferent fibers. *Archives of Physical Medicine and Rehabilitation*, 74:54-60.

Levin M.F., Hui-Chan C. (1993b). Are H and stretch reflexes in hemiparesis reproducible and correlated with spasticity? *Journal of Neurology,* 240:63-71.

Levin M.F., Hui-Chan C. (1994). Ankle spasticity is inversely correlated with antagonist voluntary contraction in hemiparetic subjects. *Electromyography and Clinical Neurophysiology*, 334:415-425.

Levin M.F., Selles R.W., Verheul M.H.G., Meijer O.G. (2000). Deficits in the coordination of agonist and antagonist muscles in stroke patients: implications for normal motor control. *Brain Research*, 853:352-369.

Lin J.P., Brown J.K., Walsh E.G. (1997). Soleus muscle length, stretch reflex excitability, and the contractile properties of muscle in children and adults: a study of the functional joint angle. *Developmental Medicine and Child Neurology* 39:469-480.

Love S., Valentine J., Chauvel P., Price C. (2000). The effect of botulinum toxin on the functional ability of the child with spastic hemiplegia: a randomized controlled trial. (Abstract). *Developmental Medicine and Child Neurology,* Suppl. 83(42):27.

Lovely R.G., Gregor R.J., Roy R.R., Edgerton V.R. (1986). Effects of training on the recovery of full-weight bearing stepping in the adult spinal cats. *Experimental Neurology*, 92:421-435.

Low J., Reed A. (2000). *Electrotherapy explained: principles and practices* (53-140, 3rd ed). Oxford: Butterworth.

Lundy-Ekman L. (2002a). Motor system: motor neurons. In: Lundy-Ekman L. (ed), *Neuroscience: Fundamentals for Rehabilitation* (170-212). 2nd ed. Philadelphia, PA: W.B. Saunders Company.

Lundy-Ekman L. (2002b). Somatosensory System; Somatosensensation Clinical Applications. In: Lundy-Edman L. (ed.), *Neuroscience: Fundamentals for Rehabilitation*. (99-119, 123-137). 2nd ed. Philadelphia, PA: W.B. Saunders Company.

Macko R.F., DeSouza C.A., Tretter L.D. (1997). Treadmill aerobic exercise training reduces the energy expenditure and cardiovascular demands of hemiparetic gait in chronic stroke patients: A preliminary report. *Stroke*, 28:326-330.

MacPhail H.E.A., Kramer J.F. (1995). Effect of isokinetic strength training on functional ability and walking efficiency in adolescents with cerebral palsy. *Developmental Medicine and Child Neurology*, 37:763-775.

Maenpaa H., Jaakkola R., Sandstrom M., Airi T., Wendt L.V. (2004). Electrostimulation at sensory threshold level improves function of the upper extremities in children with cerebral palsy: A pilot study. *Developmental Medicine and Child Neurology*, 46:84-90.

Magnusson M., Johansson K., Johansson B.B. (1994). Sensory stimulation promotes normalization of postural control after stroke. *Stroke*, 25:1176-1180.

Marinov B., Kostianev S., Turnovska T. (2002). Ventilatory efficiency and rate of perceived exertion in obese and non-obese children performing standardized exercise. *Clinical Physiology and Functional Imaging*, 22:254-260.

Mayston M.J. (2001). People with cerebral palsy: Effects of and perspectives for therapy. *Neural Plasticity*, 8:31-69.

McCubbin J.A., Shasby G.B. (1985). Effects of isokinetic exercise on adolescents with cerebral palsy. *Adapted Physical Activity Quarterly,* 56-64.

McLaughlin J., Bjornson K.F., Astley S.J., Graubert C., Hays R.M., Roberts T.S., Price R., Temkin N. (1998). Selective dorsal rhizotomy: Efficacy and safety in an investigator-masked randomized clinical trial. *Developmental Medicine and Child Neurology*, 40:220-232.

McLaughlin J, Bjornson K, Temkin N, Steinbok P., Wright V., Reiner A., Roberts T., Drake J., O'Donnell M., Rosenbaum P., Barber J., Ferrel A.(2002). Selective dorsal rhizotomy: Meta-anlaysis of three randomized clinical trials. *Developmental Medicine and Child Neurology*, 44:17-25.

Meglan D., Todd F. (1994). Kinetics of human locomotion. In: Rose J., Gamble J.G. (eds.), *Human Walking*. (94). 2nd ed. Baltimore: William and Wilkins.

Melvill Jones G. (1983). Auto-adaptive control of central plasticity: Observations and speculations. In: Basar E., Flohr H., Hakan H., Mandell A.J. (eds), *Synergetics of the Brain* (122-138). Berlin: Springer.

Mendel L.M., Collins W.F., Korber R.H. (1990). How are Ia synapses distributed on spinal motorneurons to permit orderly recruitment. In: Binder M.D., Mendell Z.M., (eds.), *The Segmental Motor System* (309-311). New York: Oxford University Press.

Milner-Brown H.S., Penn R. (1979). Pathophysiological mechanisms in cerebral palsy. *Journal of Neurology, Neurosurgery Psychiatry*, 42:606-618.

Minear W.I. (1956). A classification of cerebral palsy. *Pediatrics*, 18:841-844.

Muir G., Steeves J. (1997). Sensorimotor stimulation to improve locomotor recovery after spinal cord injury. *Trends in Neuroscience*, 20:72-77.

Murray M., Goldberger M.E. (1974). Restitution of function and collateral sprouting in the cat spinal cord: The partially hemisected animal. *Journal of Comparative Neurology*, 158:19-36.

Myklebust B.M., Gottleib G.L., Penn D. (1982). Developmental abnormalities of the spinal cord in cerebral palsy: reciprocal excitation of antagonistic muscles as a differentiating feature in spasticity. *Annals of Neurology*, 12:367-374.

Nance P.W. (1994). A comparison of clonidine, cyproheptadine and baclofen in spastic spinal cord injured patients. *Journal of American Paraplegia Society*, 17:150-156.

Nashold B.S., Friedman H. (1972). Dorsal column stimulation for control of pain: Preliminary report on 30 patients. *Journal of Neurosurgery*, 36:590-597.

Neilson P.D. (1972). Interaction between voluntary contraction and tonic stretch reflex transmission in normal and spastic patients. *Journal of Neurology, Neurosurgery, and Psychiatry*, 35:853-860.

Ng S.S., Hui-Chan C.W. (2005). The timed up and go test: its reliability and association with lower-limb impairments and locomotor capacities in people with chronic stroke. *Archives Physical Medicine and Rehabilitation*, 86:2138-2143.

Nichols T.R. (1989). Coordination of muscular action in cat hindlimb by proprioceptive spinal pathways. In: T.S. Park, L.H. Philips and W.J. Peacock (eds.), *Neurosurgery*: *State of the Art Reviews* (303-314). Philadelphia, PA: Hanley and Belfus.

Nielsen J., Petersen N., Fedirchuk B. (1997). Evidence suggesting a transcortical pathway from cutaneous foot afferents to tabialis anterior motorneurons in man. *Journal of Physiology*, 501:473-484.

Nudo R., Milliken G. (1996). Reorganization of movement representations in primary motor cortex following focal ischemic infarcts in adult squirrel monkeys. *Journal of Neurophysiology,* 75:2144-2149.

Olney S.J., MacPhail H.E.A., Hedden D.M., Boyce W. (1990). Work and power in hemiplegic cerebral palsy gait. *Physical Therapy,* 70:431-438.

Olney S.J., Wright M.J. (2000). Cerebral Palsy. In Campbell S.K., Vander Linden D.W., Palisano R.J. (eds), *Physical Therapy for Children* (533-570). 2nd ed. Philadelphia, PA: W.B. Saunders.

Palisano R., Rosenbaum P., Walter S., Russell D., Wood E., Galuppi B. (1997). Development and reliability of a system to classify gross motor function in children with cerebral palsy. *Developmental Medicine and Child Neurology*, 39:214-223.

Palmer F.B., Shapiro B.K., Wachtel R.C. (1988). The effects of physical therapy on cerebral palsy. *New England Journal of Medicine*, 318:803-808.

Pandyan A.D., Johnson G.R., Price C.I.M., Curless R.H., Barnes M.P., Rodgers H. (1999). A review of the properties and limitations of the ashworth and modified ashworth scales as measures of spasticity. *Clinical Rehabilitation,* 13:373-383.

Pape K.E. (1997). Therapeutic electrical stimulation (TES) for the treatment of disuse muscle atrophy in cerebral palsy. *Pediatric Physical Therapy*, 9:110-112.

Pape K.E., Kirsch S.E., Bugaresti J.M. (1990). New therapies in spastic cerebral palsy. *Contemporary Pediatric,* 3:6-13.

Pape K.E., Kirsch S.E., Galil A., Boulton J.E., White M.A., Chipman M. (1993). Neuromuscular approach to the motor deficits of cerebral palsy. *Journal of Pediatric Orthopaedics,* 13:628-633.

Park E.S., Park C.I., Lee H.J., Choy Y.S. (2001). The effects of electrical stimulation on the trunk control in young children with spastic dipelgic cerebral palsy. *Journal of Korean Medical Science,* 16:347-350.

Pearson K., Misiaszek J., Fouad K. (1998). Enhancement and resetting of locomotor activity by muscle afferents. *Annals of New York Academy of Sciences*, 860:203-215.

Pechham P.H. (1999). Principles of electrical stimulation. *Topics in Spinal Cord Injury Rehabilitation*, 5:1-5.

Pharoah P.O.D., Cooke T., Johnson M.A., King R., Mutch L. (1998). Epidemiology of cerebral palsy in England and Scotland, 1984-9. *Archives of Disease in Childhood, Fetal and Neonatal Edition (London)*, 79:F21-25.

Poon D.M.Y., Hui-Chan C.W.Y. (2000). Quantitative measurement of spasticity in children with spastic cerebral palsy. *Pediatric Physical Therapy,* 12(4):206

Potisk K.P., Gregoric M., Vodovnik L. (1995). Effects of transcutaneous electrical nerve stimulation (TENS) on spasticity in patients with hemiplegia. *Scandinavian Journal of Rehabilitation Medicine*, 27:169-174.

Powers R.K., Marder-Meyer J., Rymer W.Z. (1988). Quantitative relations between hypertonia and stretch reflex threshold in spastic hemiparesis. *Annals of Neurology*, 23:115-124.

Powers R.K., Campbell D.L., Rymer WZ. (1989) Stretch reflex dynamics in spastic elbow flexor muscles. *Annals of Neurology,* 25:32-42.

Rack P.M.H., Ross H.F., Thilmann A.F. (1984). The ankle stretch reflexes in normal and spastic subjects: The response to sinusoidal movement. *Brain*, 107:637-654.

Rang M. (1990). *Cerebral palsy.* In: Morrissey R.T. Lovell & Winter J.B. (eds). Paediatric Orthopaedics. (465-506). 3rd ed. Philadephia: Lippincott & Co.

Rémy-Neris O., Denys D., Barbeau D., Bussle D., Bussle B. (1998). Effects of intrathecal clonidine on spinal reflexes, locomotion and bladder function in incomplete paraplegic subjects. *Electroencephalography and Clinical Neurophysiology*, 106:30.

Richard CL, Malouin F, Dumas F, Dumas F, Sylvie M., Celine L., Lepage C., Caroline M. (1997). Early and intensive treadmill locomotor training for young children with cerebral palsy: a feasibility study. *Pediatric Physical Therapy,* 9:158-165.

Richardson D. (2002). Physical therapy in spasticity. *European Journal of Neurology,* (Suppl 1)9:17-22.

Robinson A.J., Synder-Mackler L. (1995). *Clinical Electrophysiology: Electrotherapy and Electrophysiological Testing*. (83-119). 2nd ed. Baltimore: Williams & Wilkins.

Rose J., Gamble J.G., Burgos A., Medeiros J., Haskell W.L. (1990). Energy expenditure index of walking for normal children and for children with cerebral palsy. *Developmental Medicine and Child Neurology*, 32:333-340.

Rose J., Gamble J.G., Lee J., Lee R., Haskell W.L. (1991). The energy expenditure index: A method to quantitate and compare walking energy expenditure for children and adolescents. *Journal of Pediatric Orthopaedics*, 11:571-578.

Rose J., Gamble J.G., Medeiros J.M., Burgos A., Haskell W.L. (1989). Energy cost of walking in normal children and in those with cerebral palsy: Comparison of heart rate and oxygen uptake. *Journal of Pediatric Orthopaedics*, 9:276-279.

Rose J., Haskell W.L., Gamble J.G., Hamilton R.L., Brown D.A., Rinsky L.A. (1994). Muscle pathology and clinical measures of disability in children with cerebral palsy. *Journal of Orthopaedic Research*, 12:758-768.

Ross J., McGill K. (1998). The motor unit in cerebral palsy. *Developmental Medicine and Child Neurology*, 40:270-277.
Ross S.A., Engsberg J.R. (2002). Relation between spasticity and strength in individuals with spastic diplegic cerebral palsy. *Developmental Medicine and Child Neurology*, 44:148-157.

Ross S.A., Engsberg J.R., Olree K.S., Park T.S. (2001). Quadriceps and hamstring strength changes as a function of selective dorsal rhizotomy and rehabilitation. *Pediatric Physical Therapy,* 13:2-9.

Rossignol S., Barbeau H., Julien C. (1986). Locomotion of the adult chronic spinal cat and its modifications by monoaminergic agonists and antagonists. In: Goldberger M.E., Gorio A., Murray M. (eds), *Development and Plasticity of the Mammalian Spinal Cord* (323-345). Padova: Liviana Press Fidia Research Series.

Roth S.C., Baudin J., Pezzani-Goldsmith M. (1994). Relationship between neurodevelopmental status of very preterm infants at one and eight years. *Developmental Medicine and Child Neurology*, 36:1049-1062.

Russell D.J., Rosenbaum P.L., Cadman D.T., Gowland C., Hardy S., Jarvis S. (1989). The gross motor function measure: A means to evaluate the effects of physical therapy. *Developmental Medicine and Child Neurology*, 31:341-352.

Sackett D.L. (1989). Rules of evidence and clinical recommendations on the use of antithrombotic agents. *Chest*, 95:2S-4S.

Salar G., Job I., Mingrine S., Bosio A., Trabucchi M. (1981). Effect of transcutaneous electrotherapy on CSF β-endorphin content in patients without pain problems. *Pain*, 10:169-172.

Schiepatti M. (1987). The Hoffmann reflex: A means of assessing spinal reflex excitability and its descending control in man. *Progress in Neurobiology*, 28:345-376.

Schindl M.R., Forstner C., Helmut K., Hesse S. (2000). Treadmill training with partial weight support in nonambulatory patients with cerebral palsy. *Archives of Physical Medicine and Rehabilitation*, 81:301-306.

Siebes R.C., Wijnroks L., Vermeer A. (2002). Qualitative analysis of therapeutic motor intervention programmes for children with cerebral palsy: An update. *Developmental Medicine and Child Neurology*, 44:593-603.

Siegfried J., Krainick J.U., Hass H., Adorjani C., Meyer M., Thoden U. (1978). Electrical spinal cord stimulation for spastic movement disorders. *Applied Neurophysiology*, 41:134-141.

Sinkjaer T., Anderson B.A., Nielson J.F. (1996a). Impaired stretch reflex and joint torque modulation during spastic gait in multiple sclerosis patients. *Journal of Neurology*, 243:566-574.

Sinkjaer T., Jacob B.A., Birgit L. (1996b). Soleus stretch reflex modulation during gait in man. *Journal of Neurophysiology*, 76:1112-1120.

Sinkjaer T., Nielsen J, Toft E. (1995a). Mechanical and electromyographic analysis of reciprocal inhibition at the human ankle joint. *Journal of Neurophysiology*, 74:849-855.

Sinkjaer T., Toft E., Hansen H.J. (1995b). H-reflex modulation during gait in multiple sclerosis patients with spasticity. *Acta Neurologica Scandinavica*, 91:239-246.

Sommerfelt K., Markestad T., Berg K., Saetesdal I. (2001). Therapeutic electrical stimulation in cerebral palsy: A randomized, controlled, crossover trial. *Developmental Medicine and Child Neurology*, 43:609-613.

Steinbok P., Daneshvar H., Evans D., Kestle J.R. (1995). Cost analysis of continuous intrathecal baclofen versus selective functional posterior rhizotomy in the treatment of spastic quadriplegia associated with cerebral palsy. *Pediatric Neurology,* 22:225-264.

Steinbok P., Reiner A.M., Beauchamp R., Armstrong R.W., Cochrane D.D., Kestle J. (1997b). A randomized clinical trial to compare selective posterior rhizotomy plus physiotherapy with physiotherapy alone in children with spastic diplegic cerebral palsy. *Developmental Medicine and Child Neurology*, 39:178-184.

Steinbok P., Reiner A., Kestle J.R.W. (1997a). Therapeutic electrical stimulation following selective posterior rhizotomy in children with spastic diplegic cerebral palsy: A randomized clinical trial. *Developmental Medicine and Child Neurology*, 39:515-520.

Steward J.E., Barbeau H., Guuthier S. (1991). Modulation of locomotor patterns and spatcitiy with clonidine in spinal cord injured patients. *Canadian Journal of Neurological Sciences*, 18:321-332.

Sutherland D.H., Olshen R., Cooper L., Woo S. (1980). The development of mature gait. *Journal of Bone and Joint surgery,* 62A:336-353.

Taub E., Ramey S.L. DeLuca S., Echols K. (2004). Efficacy of constraint-induced movement therapy for children with cerebral palsy with asymmetric motor impairment. *Pediatrics*, 113:305-312.

Thomas S., Aiona M.D., Buckon C.E. (1997). Does gait continue to improve two years following selective dorsal rhiztomy? *Journal of Pediatric Orthopedic,* 17:387-387-391.

Thomas S., Aiona M.D., Pierce R., Piatt J.H. (1996). Gait changes in children with spastic diplegia after selective dorsal rhizotomy. *Journal of Pediatric Orthopedics,* 16:747-752.

Thompson N.S., Baker R.J., Cosgrove A.P. (1998). Musculoskeletal modeling in determining the effects of botulinum toxin on the hamstrings of patients with crouch gait. *Developmental Medicine and Child Neurology*, 40:622-625.

Tekeoolu Y., Adak B., Goksoy T. (1998). Effect of transcutaneous electrical nerve stimulation (TENS) on barthel activities of daily living (ADL) index score following stroke. *Clinical Rehabilitation*, 12:277-280.

Ubhi T., Bhakta B.B., Ives H.L., Allgar V., Roussounis S.H. (2000). Randomised double blind placebo controlled trial of the effect of botulinum toxin on walking in cerebral palsy. *Archives of Disease in Childhood,* 83:481-487.

Unnithan V.B., Dowling J.J., Frost G., Bar-O O. (1996) Role of cocontraction in the O_2 cost of walking in children with cerebral palsy. *Medicine and Science in Sports and Exercise*, 28(12):1498-1504.

Van Wezel B., Ottenhoff F., Duysens J. (1997). Dynamic control of location-specific information in tactile cutaneous reflexes from the foot during human walking. *Journal of Neuroscience*, 17:3804-3814.

Vaughan C.L., Berman B., Peacock W.J. (1991). Cerebral palsy and rhizotomy. A 3-year follow-up evaluation with gait analysis. *Journal of Neurosurgery,* 74:178-84.

Visintin M., Barbeau H., Korner-Bitensky N., Mayo N.E. (1998). A new approach to retrain gait in stroke patients through body weight supoprt and treadmill stimulation. *Stroke,* 29:1122-1128.

Vistintin M., Barbeau H. (1989). The effects of body weight support on the locomotor pattern of spastic paretic patients. *Canadian Journal of Neurology,* 16:315-325

Vodovnik L., Bowman B.R., Hufford P. (1984). Effects of electrical stimulation on spinal spasticity. *Scandinavian Journal of Rehabilitation Medicine*, 16:29-34.

Von Koch C.S., Park T.S., Steinbok P., Smyth M., Peacock W.J. (2001). Selective posterior rhizotomy and intrathecal baclofen for the treatment of spasticity. *Pediatric Neurosurgery*, 35:57-65.

Wainberg M.H., Barbeau H., Gauthier S. (1990). The effects of cyproheptadine on locomotion and on spasticity in patients with spinal cord injuries. *Journal of Neurology, Neurosurgery and Psychiatry,* 53:754-763.

Walsh D.M. (1997). *TENS: Clinical Applications and Related Theory.* New York: Churchill Livingstone.

Walsh R.N., Cummins R.A. (1976). Neural responses to therapeutic sensory environments In: R.N. Walsh R.N., Greenough W.T. (eds.), *Environments as Therapy for Brain Dysfunction* (171-200). New York: Plenum.

Weiller C., Ramsay S., Wise R., Frackowiak R. (1993). Individual patterns of functional reorganization in the human cerebral cortex after capsular infarction. *Annals of Neurology*, 33:181-189.

Wernig A., Müller S. (1991). Improvement of walking in spinal cord injured persons after treadmill training. In: Wernig A., (ed.), *Plasticity of Motorneuronal Connections* (475-485). Amsterdam: Elsevier.

Wernig A., Müller S., Nanassy A., Cagol E. (1995). Laufband thearpy based on"Rules of Spinal Locomotion" is effective in spinal cord injured persons. *European Journal of Neuroscience*, 7:823-829.

Wiley M.E., Damiano D.L. (1998). Lower-extremity strength profiles in spastic cerebral palsy. *Developmental Medicine and Child Neurology,* 40:100-107.

Wright F.V., Sheil E.M., Drake J.M., Wedge J.H., Naumann S. (1998). Evaluation of selective dorsal rhizotomy for the reduction of spasticity in cerebral palsy: A randomized controlled trial. *Developmental Medicine and Child Neurology*, 40:239-247.

Yang J.F., Stein R.B., James K.B. (1991). Contribution of peripheral afferents to the activation of the soleus muscle during walking in humans. *Experimental Brain Research*, 87:679-687.

Young J.L., Mayer R.F. (1982). Physiological alterations of motor units in hemiplegia. *Journal of Neurological Sciences*, 54:410-412.

Yu C.M. (2004). *An exploratory study of the effect of body weight support treadmill training for children with cerebral palsy*. Un-published master's thesis. The Hong Kong Polytechnic University, Hong Kong.

Zehr E.P., Stein R.B. (1999). What functions do reflexes serve during human locomotion? *Progress in Neurobiology*, 58:185-205.

APPENDICES

Appendix 2.1a: The Informed Consent Form (English version)

The Hong Kong Polytechnic University
Department of Rehabilitation Sciences

Informed Consent Form

Project Title: Effects of Transcutaneous Electrical Nerve Stimulation (TENS) and Body-Weight-Support Treadmill Training (BWS-TT) on Motor Functions in Children with Spastic Cerebral Palsy (CP)

Investigators: Ms. Poon Mei Ying, Professor W.Y. Hui-Chan

Objective of the Study:

To investigate the effect of TENS and BWS-TT in ehancing motor function in children with spastic cerebral palsy.

Design of the Study:

Children consented to participate in the study will be randomly assigned to one of the following treatment group:

1. TENS
2. Placebo-TENS
3. TENS plus BWS-TT

TENS and BWS-TT have been separately proven to reduce spasticity and/or enhance gait functions in adults with neurological disorders. Since children are believed to have greater neuronal plasticity, we hypothesized these two treatment approaches will hold promise in children with spastic CP. Our pilot study showed that children could receive TENS stimulation while attending classes. Each treatment session will last for about 1 hour per day, 5 days per week for 3 weeks. All treatment will be implemented by a qualified physiotherapist (Miss Poon Mei Ying). If your child is involved in the TENS treatment group, he/she will receive high frequency low intensity TENS for 60 minutes during class (Figure 1). If your child is involved in placebo-TENS treatment, he/she will receive no stimulation. Children joining the TENS+BWS-TT treatment group will received 60 minutes TENS during class, followed by 20 to 30 minutes of BWS-TT which will be conducted during recess, lunch period or physiotherapy session (Figure 2).

To evaluate effects of treatment, measurements including spasticity, voluntary muscle contraction and walking performances will be charted before, and after 1, 2 and 3 weeks of treatment (Figure 3). Each assessment session will last for about 30 to 45 minutes and it will be scheduled during recess, lunch or after school period. Please be reassured that the electrical stimulation and testing procedures have been well used and approved as safe with negligible side effects, both clinically and experimentally. Ethical approval was also obtained from the Ethical Committee of The Hong Kong Polytechnic University prior to the study and from the Principal and/or the school Board. Participation of your child is strictly voluntary and the school holds no responsibility for any incident related to the conduct of this study.

Potential Risks:

While receiving the electrical stimulation, children may report a tingling sensation in the cutaneous distribution of the nerve along the anterior part of the leg and dorsum of the foot. The stimulation normally bears no harm.

Benefits and Risks:

The major benefit from participating in this study is that you may have the opportunity to know the level of spasticity and motor function of your child. The results may be beneficial for planning an innovative treatment program in enhancing motor function of children with CP.

Confidentiality:

Any personal information obtained through this study will be kept confidential and your child will not be identified by any communication related to this study.

Enquiries:

Any questions about this study will be answered by Miss Poon Mei Ying who can be reached at the Department of Rehabilitation Sciences, The Hong Kong Polytechnic University located at Hum Hong, Kowloon or by phone at 2766-6746. You may also contact Ms. Michelle Leung by telephone at 2766-5397.

Declaration:

I, _____ (parent of _____) understand that participation of my child in this study is strictly voluntary and my child may withdraw at any time during the course of the study with no penalty. I have been told that this study has been approved by the Ethics Committee of the Hong Kong Polytechnic University and the Principal and/ Board of the school. In addition, any personal information obtained from me/ my child through this study will be kept confidential and my child will not be identified in any communication related to this study. I am entitled to keep a copy of this consent form for future reference. I understand the explanation of this research study and give consent of my child to participate in the study.

Signature of parent: _____ Date: _____

Signature of witness: _____ Date: _____

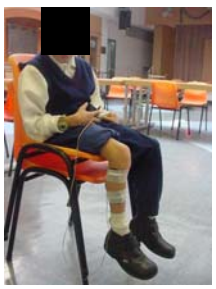


Figure 1: Application of TENS/ placebo-TENS

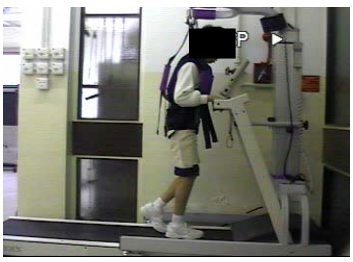


Figure 2: BWS-TT

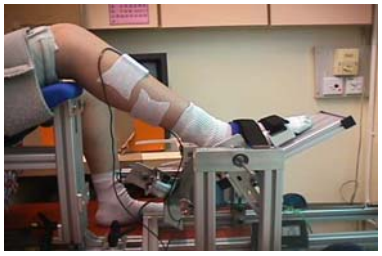


Figure 3: Evaluation of spasticity

Appendix 2.1b: The Informed Consent Form (Chinese version)

香港理工大學康復治療學系
參與研究同意書

致 貴家長：

本人任教於香港理工大學康復治療科學系物理治療學部 o 現誠邀 貴子/女參與一項研究計劃，其詳情如下：

研究項目: 透皮神經電刺激及步行運動對大腦麻脾兒童活動功能的療效

研究員: 潘美英小姐，許陳雲影教授

研究目的

此項研究目的為掌握透皮神經電刺激及步行運動對減輕大腦麻脾兒童痙攣的徵狀及提高活動功能的療效 o

研究過程

若經閣下同意， 貴子/女將被隨機編擬接受以下其中之一種治療程序：

(1) 透皮神經電刺激，或
(2) 對照刺激，或
(3) 透皮神經電刺激及步行運動

此項治療每天需時約一小時 o 你的小孩將接受總共十五次治療 o 物理治療師(潘美英小姐)將安放兩個細小的電墊(長及闊各約一吋)於你的小孩子的一邊小腿上(見圖一) o 透皮神經電刺激已證實可減輕老人中風所引起的痙攣徵狀 o 其於以往研究報告，小孩的神經系統之可吊塑性，一般比成年人為高 o 故此我們相信，此治療對減輕大腦麻脾兒童痙攣的徵狀及提高活動功能也會有一定的療效 o 初部研究，已知此治療可在孩子上課其間使用而不影響課堂之進行，因此不會影響孩子之學習進度 o 接受透皮神經電刺激及步行運動(即第三種治療程序)之小孩子將在電刺激後小息時間或午飯後進行約二十分鐘至半小時之步行運動 (見圖二) o

另外，為了解治療成效,幾項測試(包括痙攣程度及步行方法，見圖三)將於第一節治療前及後*、第五、第十、及第十五節後進行。每次測試為時約半小時，並會安排在小息或午飯後進行 o 另外, 透皮神經電刺激，或對照刺激之電量極低 o 這些治療程序均十分安全，及已通過香港理工大學康復治療學系之道德委員會之審批 o 另外，此研究之目的及過程，亦已向香港痙攣協會，學校校長及物理治療師報告。唯 貴子/女之參與，是純基於自願性 o 此研究與香港痙攣協會並無特別關係 o
(註: *第一節治療後之測試為時約一小時)

因研究而可能導致的危險與不適

你的孩子在接受透皮神經電刺激或對照刺激的過程中，被電刺激的部位可能有輕微跳動的感覺，這是無害的 o

參與研究的益處

你的孩子參與此項研究，除了接受透皮神經電刺激或對照刺激或/及步行運動治療以外，將不會獲得任何實際利益 o

參與者的私隱權

你的孩子的所有個人資料均會保密 o 若然將來研究的數據需要刊登於醫學之文獻或作教學用途，你的孩子的名子或身份亦不會刊登 o

查詢辨法

若閣下如有任何關於此項研究的疑問，可致電潘美英小姐查詢(電話:2766-　　，可留言；或手提電話：9727-　　)，以得到滿意的回覆 o 本人亦同時可獲得一份同意書副本，以作參考 o

有關拒絕或終止參與研究

你的孩子參與此項研究乃屬自願牲質，因此閣下或你的孩子可於任何時候查詢, 拒絕或終止參與研究 o 而且無論在任何情況下，你的孩子將不會受到處罰 o

研究員聲明

潘美英小姐已向參與此研究之孩童的家長解釋清楚此項研究的目的，程序，益處或可能發生的危險 o

_____　　_____

研究員　　日期

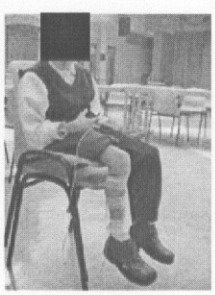
本人_____(_____ 小孩之家長)已經閱畢及明白此同意書，及證實潘美英小姐已向本人解釋清楚此項研究的目的，程序，益處，或可能發生的危險 o 最後本人聲明我的孩子參與此項研究乃屬自願牲質，並可隨時退出此項研究而不受任何處罰 o 本人亦明白，此研究與香港痙攣協會並無特別關係 o

_____　　_____

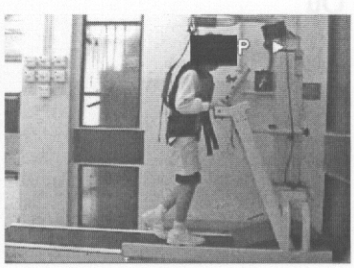
孩子家長　　日期

_____　　_____

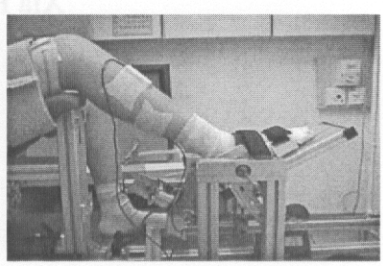
見証人　　日期



圖一: 透皮神經電刺激的電墊安放於小孩子的一邊小腿上



圖二: 步行運動



圖三: 痙攣程度測試

Appendix 2.2: Calculation of Sample Size and Study Power

Based on the study by Levin and Hui-Chan (1992), the mean and standard deviations of composite spasticity score before (control) and 2 weeks after TENS or placebo stimulation were presented in Table 2.2.1. Note that TENS but not placebo stimulation resulted in a significant improvement in clinical spasticity (p <0.05)*:

Table 2.2.1: Mean and S.D. of Composite Spasticity Scale score before and after 10 sessions of daily TENS or placebo-TENS stimulation for 1 hour

	Pre-TENS (Mean ± S.D.)	Post-TENS (Mean ± S.D.)
TENS group (n=11)	11.8 ± 2.5	9.2 ± 2.4*
Placebo-TENS group (n=6)	11.2 ± 2.9	11.8 ± 2.6

Power analysis for *t*-test is based on the effect size index, *d*, which expresses the difference between the two sample means in standard deviations. For independent sample *t*-test,

$$d = \frac{\overline{X}_1 - \overline{X}_2}{s}$$

$\overline{X}_1$ and $\overline{X}_2$ are the group means, and s is their common standard deviation. Assuming equality of variance, s can be the standard deviation from either group, or it can be their arithmetic average. In this case,

$$s = \frac{2.9 + 2.5}{2} = 2.7$$

$$\text{thus,} \quad d = \frac{11.8 - 9.2}{2.7} = 0.96$$

.

Appendix 2.3: Therapist-generated List of Therapeutic Tasks used in Individuals with Cerebral Palsy

Physiotherapist _____ Therapist code _____ Date _____
Subject _____ Subject code _____ Type of CP _____

Date (Period):

Treatment Program	Task (in sequence)	Amount of time spent (freq/ week)	No. of repetitions (if applicable)	Subject's level of movement	PT's role
Individual session/wk					
Flexistand or Standing session/wk					
Daily stretch					
Morning exercise (20 minutes)					
Small group session/wk (2 or more students)					
Task series session/wk					
Social class session/wk					
Others					

Remarks:
- Each treatment program lasted for 35 minutes per session (except morning exercises)
- Task (in sequence): Please list the task of the subject during the treatment program session. If there is more than one task, list them in sequence and specify the amount of time spent…. etc. clearly

Subject's Exercise Level
1 Subject moves independently
2 Subject moves under supervision, with cues (verbal, tactile) or with feedback signals
3 Subject moves with manual guidance
4 Subject is largely dependent on others to move

Physiotherapist (PT's) Role
0 Therapist assigns another person to assist, as needed
1 Therapist monitors from a distance
2 Therapist provides cues (verbal, tactile) or gives instruction
3 Therapist provides manual guidance (may include verbal input)
4 Therapist produces the movements (passive movements or reflex activity)

Appendix 2.4: The Composite Spasticity Scale (Levin and Hui-Chan 1993b)

The Composite Spasticity Scale consists of 3 clinical measures. The measurements were taken while subjects were comfortably seated and the knee supported at 60° of flexion.

Clinical Spasticity Score = A + 2B + C

where A = Achilles tendon jerk
B = Modified Ashworth Scale (Bohannon and Smith 1987)
C = Ankle clonus

Achilles Tendon Jerk:

0 = No tendon jerk elicited
1 = Minimal response (hypoactive tendon jerk)
2 = Normal response
3 = Moderately hyperactive response
4 = Maximally hyperactive response

Modified Ashworth Scale (Bohannon and Smith 1987)

0 = No increase in tone
1 = Slight increase in tone, manifested by a catch & release, or by minimal resistance at the end of range of motion
1+ = Slight increase in tone, manifested by a catch, followed by minimal resistance throughout less than half of the range of motion
2 = More marked increase in tone throughout most of the range of motion, but affected parts are easily moved
3 = Considerable increase in tone, passive movement is difficult
4 = Affected parts is rigid in flexion or extension

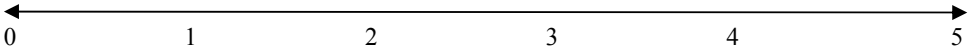
Ankle Clonus:

1 = No clonus elicited
2 = 1 - 2 beats of clonus (if it is close to 2 beats, marked as grade 2)
3 = More than 2 beates of clonus, unstanined (less than 10 beats)
4 = Sustained clonus

Appendix 2.5: Recording Sheet of the 6-Minute Walk Test

Subject/code:	_____	Age/Sex:	_____
Diagnosis:	_____	Center/class:	_____
Date:	_____	Wt(kg)/Ht (m):	_____
Amb. status:	Independent	Assistive device:	1 cane/ 2 canes/ 1 crutch 2 crutches/ rollator/ k-walker
Session:	Practice/ day 1/ day 2		

- Attach HR monitor
- Start timer, record resting heart rate (HR_{rest}), average: _____(beats/min)
- General health status: Today, how do you rate your health?



0	1	2	3	4	5
Very poor	Poor	Fair/average	Good	Very good	Excellent

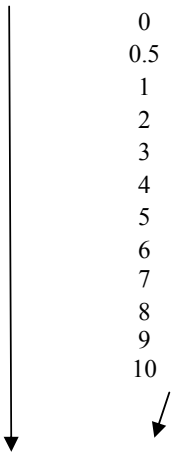
- Explain test procedure, give instruction
- At the 5th minute, "stop", "stop + hold" to store data
- Subject at start of 10-meter walkway, start timer, record walking heart rate (HR_{walk})
- Give verbal encouragement every 30 sec as "Keep going, you're doing well"

	2 minutes	4 minutes	6 minutes
Distance covered			
HR (beats/min)			

Peak heart rate during the walk: _____ (Make sure not exceeding 170 beats/min)

- At the 6th minute, "stop", "stop + hold" to store data
- Rate of perceived exertion (Borg Category Ratio scale – CR-10): _____(Borg 1982)

Rate of Perceived exertion (自我辛苦評估指數)



0	Not at all	完全不吃力
0.5	Very, very weak	非常非常輕微
1	Very weak	非常輕微
2	Weak	輕微
3	Moderate	一般
4	Somewhat strong	一點兒吃力
5	Strong	吃力
6	---------	---------
7	Very Strong	非常吃力
8	---------	---------
9	---------	---------
10	Very very strong	非常非常吃力
	Maximal	極限

- Subject seated, record recovery heart rate
- Monitor heart rate until it returns to within 10% of resting heart rate

Appendix 3.1: Profiles of clinical spasticity and stretch reflex measures of the left and right legs in normal and spastic CP children

			Stretch Reflex					
No. of subjects	Composite Spasticiy Score		Onset latency (msec)		Duration (msec)		SR/M area ratio (%)	
Leg	Left	Right	Left	Right	Left	Right	Left	Right
Normal subjects (n = 9)								
1.			49.6	52.5	32.2	26.0	11.2	13.0
2.			60.5	69.6	12.0	16.5	2.5	5.8
3.			64.8	60.0	19.0	18.9	8.9	13.4
4.			46.8	47.5	12.1	11.7	7.8	5.8
5.			51.7	64.9	20.0	11.9	6.9	4.0
6.			42.8	49.3	24.7	20.0	7.5	18.4
7.			48.5	39.3	21.3	32.1	5.4	6.2
8.			44.6	44.8	28.9	26.8	13.8	17.6
9.			49.5	50.0	14.5	11.1	2.4	2.2
Mean			51.0	53.1	20.5	19.5	7.4	9.6
S.D.			7.2	9.9	7.1	7.5	3.7	6.1
Spastic subjects (n = 8)								
1.	14	12	58.4	59.0	16.8	15.0	155.5	57.3
2.	10	9	29.7	53.0	28.7	18.6	42.5	48.7
3.	8	12	46.2	44.3	19.4	18.4	25.0	53.3
4.	-	8	73.1	66.0	13.8	13.3	20.9	38.7
5.	6	13	69.5	50.5	25.6	26.7	82.0	249.0
6.	14	13	32.7	34.1	18.1	16.8	130.4	103.3
7.	8	13	49.1	52.5	12.1	12.2	69.7	132.0
8.	10	6	37.9	45.8	24.8	23.1	68.1	39.5
Mean	10.0	10.8	49.6	50.6	19.9	18.0	74.3	90.2
S.D.	3.1	2.7	16.3	9.6	5.9	4.9	43.4	72.2

SR/M area ratio = stretch reflex/ M-response area ratio

All variables showed no significant difference between the left and right legs of either normal or spastic children, $p > 0.05$.

Appendix 3.2: Profiles of maximal isometric voluntary contractions during dorsiflexion of the left and right legs in normal and spastic CP children

	MIVC: Dorsiflexion							
No. of subjects	Agonist EMG area (μV.s)		Antagonist EMG area (μV.s)		Co-contraction ratio (%)		Mean maximal torque (Nm)	
Leg	Left	Right	Left	Right	Left	Right	Left	Right
Normal subjects (n = 9)								
1.	170.3	168.7	28.5	36.1	14.4	17.6	12.4	12.8
2.	207.0	169.6	38.1	30.2	15.5	15.1	18.0	18.9
3.	126.4	145.5	19.2	21.7	13.2	13.0	11.2	10.7
4.	291.9	167.2	28.5	29.4	8.9	15.0	5.2	5.6
5.	152.7	92.2	19.1	15.4	11.1	14.3	10.2	10.0
6.	178.5	212.5	29.4	38.4	14.1	15.3	6.3	6.3
7.	242.6	447.8	44.6	47.2	15.5	9.5	17.7	20.0
8.	143.7	208.5	22.0	43.2	13.3	17.2	6.8	5.0
9.	416.0	447.0	47.7	39.9	10.3	8.2	11.0	13.5
Mean	214.4	228.8	30.8	33.5	12.9	13.9	11.0	11.4
S.D.	91.7	128.8	10.5	10.3	2.3	3.2	4.6	5.5
Spastic subjects (n = 8)								
1.	131.5	107.3	46.1	39.4	26.0	26.9	8.1	5.1
2.	130.7	143.2	30.0	18.6	18.7	11.5	1.0	7.7
3.	32.7	55.0	12.3	45.3	27.3	45.2	0.4	2.8
4.	53.6	0.0	13.1	0.0	19.7	0.0	5.6	0.0
5.	77.6	54.1	28.1	19.1	26.6	26.1	2.4	2.4
6.	74.8	71.7	48.7	26.6	39.4	27.0	0.8	0.4
7.	52.6	47.4	17.0	52.3	24.5	52.5	1.3	1.1
8.	74.7	97.5	89.7	85.6	54.6	46.8	1.6	3.1
Mean	78.5	72.0	35.6	35.8	29.6	29.5	2.6	2.8
S.D.	35.8	43.7	25.9	26.2	11.9	18.1	2.7	2.5

MIVC = maximal isometric voluntary contraction

All variables showed no significant difference between the left and right legs of either normal or spastic children, $p > 0.05$.

Appendix 3.3: Profiles of maximal isometric voluntary contractions during plantarflexion of the left and right legs in normal and spastic CP children

	MIVC plantarflexion							
No. of subjects	Agonist EMG area (μV.s)		Antagonist EMG area (μV.s)		Co-contraction ratio (%)		Mean maximal torque (Nm)	
Leg	Left	Right	Left	Right	Left	Right	Left	Right
Normal subjects (n = 9)								
1.	114.8	136.4	31.6	35.3	21.6	20.5	26.8	31.7
2.	104.4	124.4	24.3	31.7	18.9	20.3	26.3	37.4
3.	112.3	81.5	20.1	26.3	15.2	24.4	17.5	16.5
4.	119.5	109.2	31.8	28.5	21.0	20.7	11.2	11.2
5.	91.5	105.1	28.5	20.7	23.8	16.5	24.9	23.6
6.	144.3	121.4	41.4	42.0	22.3	25.7	27.7	25.7
7.	246.3	233.5	64.3	39.7	20.7	14.5	47.6	51.6
8.	110.0	160.6	27.8	28.2	20.2	14.9	16.9	14.4
9.	276.7	312.6	40.3	43.4	12.7	12.2	46.6	47.6
Mean	146.6	153.9	34.4	32.8	19.6	18.9	27.3	28.8
S.D.	67.0	73.7	13.1	7.7	3.5	4.6	12.5	14.4
Spastic subjects (n = 8)								
1.	45.6	39.3	36.3	26.1	44.3	39.9	5.3	5.7
2.	62.8	37.5	39.8	25.4	38.8	40.4	20.0	16.9
3.	21.9	66.7	11.6	28.6	34.6	30.0	1.0	7.6
4.	70.0	26.6	30.3	13.2	30.2	33.2	34.1	9.4
5.	31.4	22.2	18.2	17.7	36.6	44.4	2.9	2.9
6.	29.4	29.6	20.4	19.3	40.9	39.5	2.1	1.0
7.	21.3	42.5	12.1	13.3	36.3	23.8	2.3	2.9
8.	72.3	85.3	32.0	22.7	30.7	21.0	7.9	3.8
Mean	44.3	43.7	25.1	20.8	36.6	34.0	9.4	6.3
S.D.	21.4	21.6	10.9	5.8	4.8	8.5	11.6	5.0

MIVC = maximal isometric voluntary contraction

All variables showed no significant difference between the left and right legs of either normal or spastic children, $p > 0.05$.

Appendix 4: Results of MIVC plantarflexion torque and co-contraction before and after 1, 2, 3 weeks of treatment

Table 4.6: Mean and standard deviations, and percentage change of MIVC plantarflexion torque before and after 1, 2 and 3 weeks of treatment.

	TENS (n = 20)	Placebo-TENS (n = 21)	TENS+BWS-TT (n = 20)
T_0 (Nm)	8.12 ± 5.82	6.21 ± 6.17	6.28 ± 4.32
T_1 (Nm)	8.12 ± 6.12	6.24 ± 6.19	7.00 ± 4.55
$(T_1 – T_0) / T_0$ (%)	(0.07)	(0.48)	(11.58)
T_2 (Nm)	8.93 ± 6.80	6.67 ± 6.74	7.31 ± 5.07
$(T_2 – T_0) / T_0$ (%)	(9.93)	(7.40)	(16.52)
T_3 (Nm)	8.35 ±7.08	6.97 ± 6.81	7.25 ± 4.65
$(T_3 – T_0) / T_0$ (%)	(2.91)	(6.96)	(9.69)

Within group: * denote $p < 0.05$ when compared with baseline values (T_0).
Among groups # denote $p < 0.006$ when compared with placebo-TENS group.

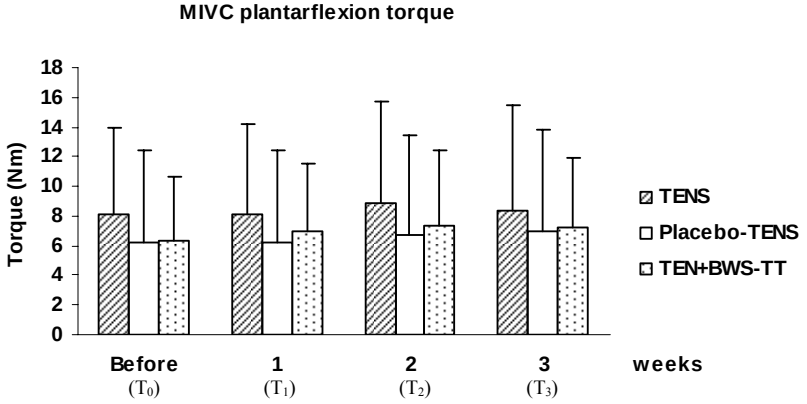


Figure 4.9: Mean and standard deviations of MIVC plantarflexion torque over time. No significant change from baseline values was noted in any of the 3 treatment groups after 3 weeks of treatment. .

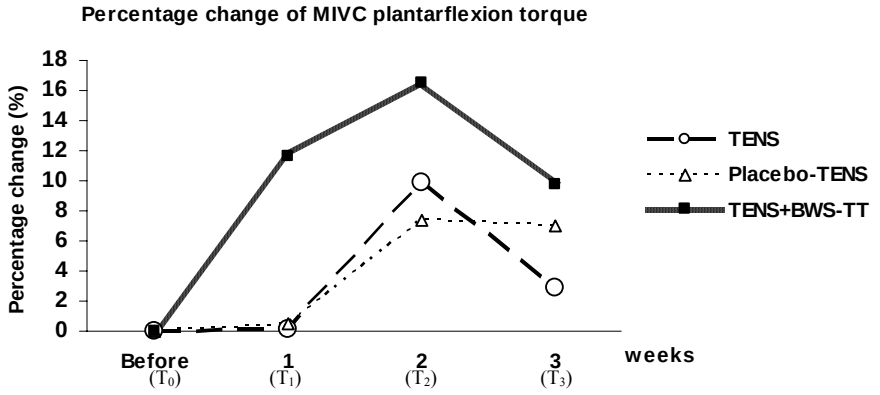


Figure 4.10: Mean percentage change of MIVC plantarflexion torque over time and among treatment groups. No significant change in values was noted in either TENS or TENS+BWS-TT group after 3 weeks of treatment when compared to placebo-TENS.

Table 4.7 Mean and standard deviations, and percentage change of plantarflexion co-contraction ratio before and after 1, 2 and 3 weeks of treatment.

	TENS (n = 20)	Placebo-TENS (n = 21)	TENS+BWS-TT (n = 20)
T_0 (%)	42.25 ± 15.06	45.19 ± 13.99	45.45 ± 12.73
T_1 (%)	39.40 ± 18.22	45.19 ± 13.27	41.60 ± 11.16
$(T_1 - T_0) / T_0$ (%)	(-6.75)	(0.00	(-2.97)
T_2 (%)	38.40 ± 18.22	43.14 ± 14.55	44.10 ± 16.32
$(T_2 - T_0) / T_0$ (%)	(-9.11)	(-4.53)	(-12.76)
T_3 (%)	41.05 ± 14.73	42.14 ± 14.11	41.80 ± 12.69
$(T_3 - T_0) / T_0$ (%)	(-2.84)	(-6.74)	(-8.03)

Within group: * denote $p < 0.05$ when compared with baseline values (T_0).
Among groups: # denote $p < 0.006$ when compared with placebo-TENS group.

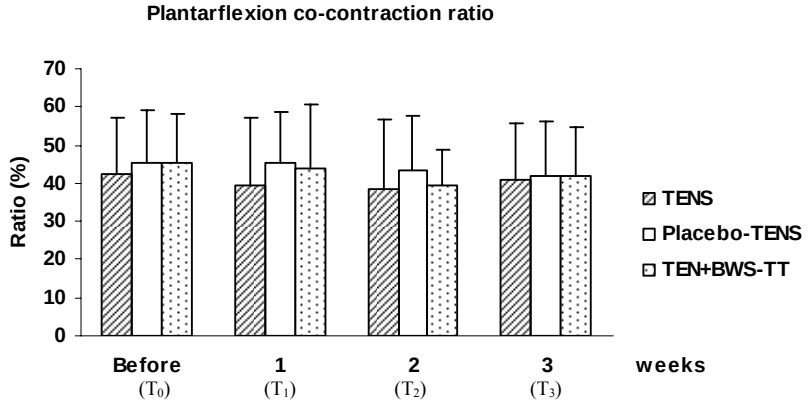


Figure 4.11: Mean and standard deviations of plantarflexion co-contraction ratios over time. No significant change from baseline values was noted in any of the 3 treatment groups after 3 weeks of treatment.

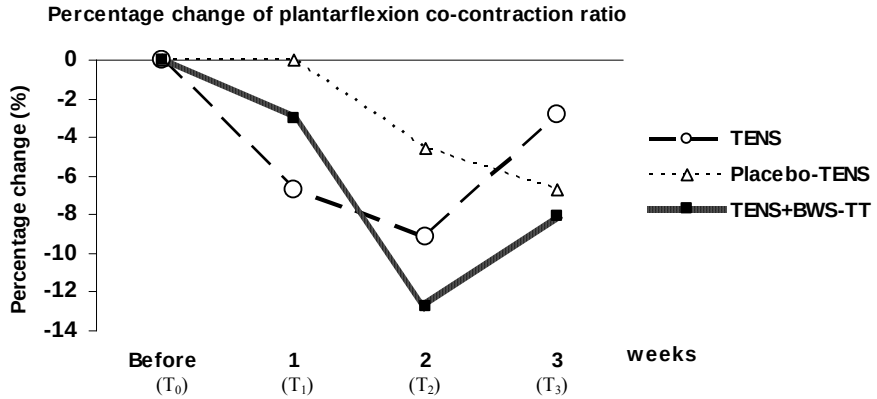


Figure 4.12: Mean percentage change of plantarflexion co-contraction ratio over time and among treatment groups. No significant change in values was noted in either TENS or TENS+BWS-TT groups after 3 weeks of treatment when compared to placebo-TENS.

Appendix 5: Results of walking speed and resting heart rate before and after 1, 2, 3 weeks of treatment

Table 5.1: Mean, standard deviations, and percentage change of walking speed before and after 1, 2 and 3 weeks of treatment.

	TENS (n = 20)	Placebo-TENS (n = 21)	TENS+BWS-TT (n = 20)
T_0 (m/min)	43.48 ± 17.21	38.89 ± 19.32	41.81 ± 15.68
T_1 (m/min)	42.25 ± 15.36	36.09 ± 18.39	43.43 ± 14.38
$(T_1 – T_0) / T_0$ (%)	(-2.84)	(-7.20)	(3.89)
T_2 (m/min)	41.95 ± 14.70	38.97 ± 19.99	41.17 ± 14.33
$(T_2 – T_0) / T_0$ (%)	(-3.53)	(0.20)	(-1.53)
T_3 (m/min)	43.69 ± 15.84	36.14 ± 18.21	37.09 ± 12.77
$(T_3 – T_0) / T_0$ (%)	(0.48)	(-7.06)	(-11.29)

Within group: * denote $p < 0.05$ when compared with baseline values (T_0).
Among groups # denote $p < 0.006$ when compared with placebo-TENS group.

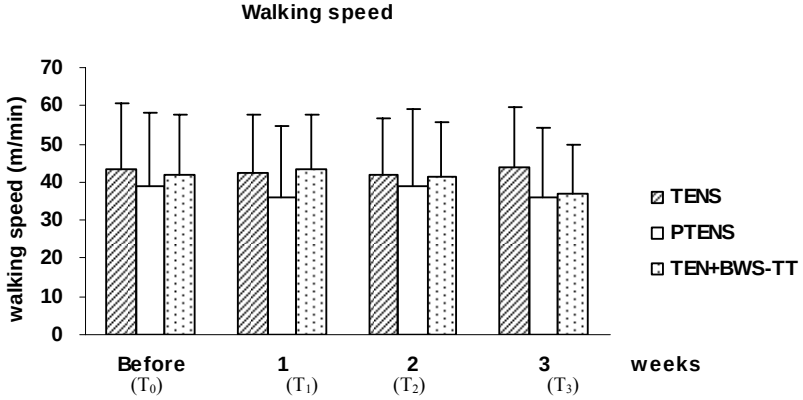


Figure 5.1: Mean and standard deviations of walking speed change over time and among treatment groups. No significant change from baseline values was noted in any of the 3 treatment protocols after 3 weeks of treatment.

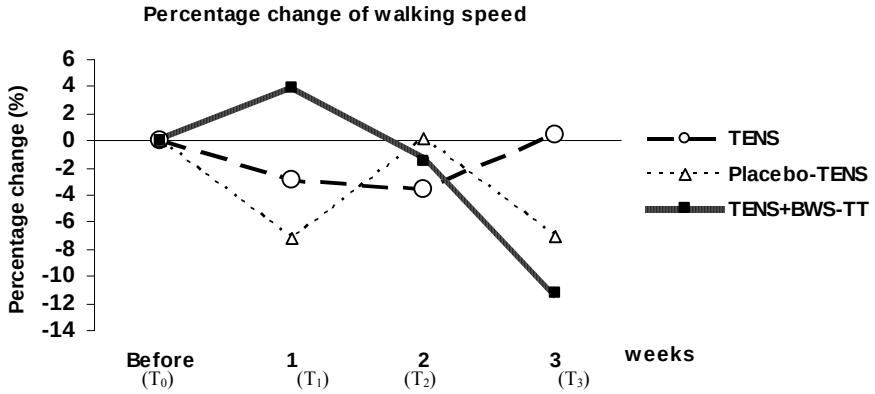


Figure 5.2: Mean percentage change of walking speed over time and among treatment groups. No significant change in values was noted in either TENS or TENS+BWS-TT groups after 3 weeks of treatment when compared to that of placebo-TENS group.

Table 5.4: Mean, standard deviations, and percentage change of resting heart rate before and after 1, 2 and 3 weeks of treatment.

	TENS (n = 20)	Placebo-TENS (n = 21)	TENS+BWS-TT (n = 20)
T_0 (beats/min)	91.8 ± 10.44	99.55 ± 9.03	94.82 ± 11.5
T_1 (beats/min)	88.63 ± 13.85	94.24 ± 8.77	90.96 ± 11.41
$(T_1 - T_0) / T_0$ (%)	(-3.53)	(-5.33)	(-4.07)
T_2 (beats/min)	91.27 ± 13.98	92.25 ± 8.47	91.51 ± 11.1
$(T_2 - T_0) / T_0$ (%)	(-0.65)	(-7.33)	(-3.49)
T_3 (beats/min)	94.81 ± 14.44	94.51 ± 11.66	91.91 ± 13.58
$(T_3 - T_0) / T_0$ (%)	(3.20)	(-5.06)	(-3.07)

Within group: * denote $p < 0.05$ when compared with baseline values (T_0).
Among groups # denote $p < 0.006$ when compared with placebo-TENS group.

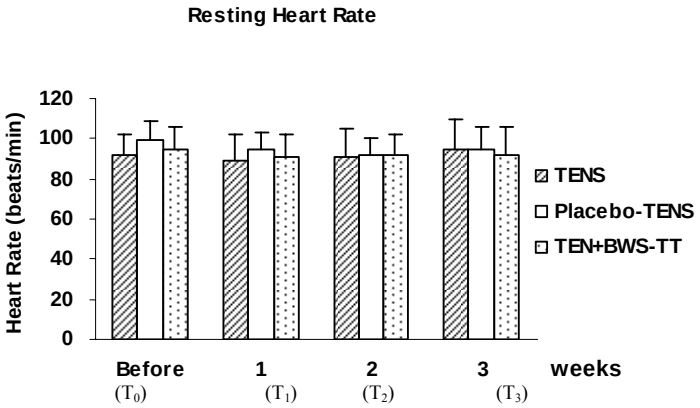


Figure 5.7: Mean and standard deviations of resting heart rate over time and among treatment groups. No significant change from baseline values was noted in any of the 3 treatment protocols after 3 weeks of treatment.

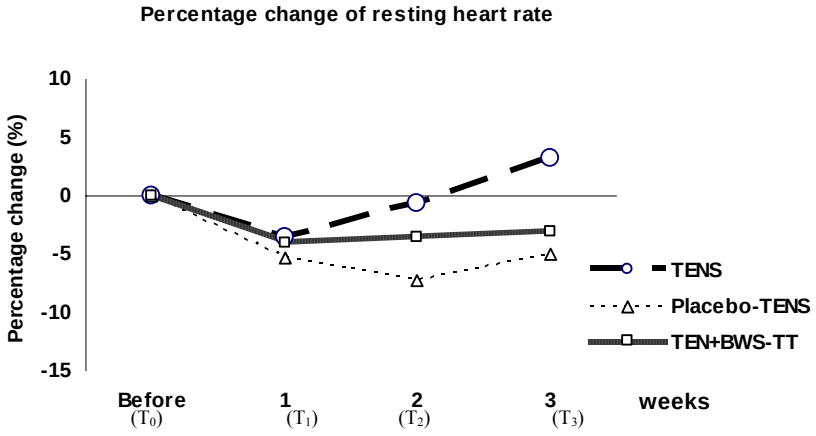


Figure 5.8: Mean percentage change of resting heart rate over time and among treatment groups. No significant change in values was noted in either TENS or TENS+BWS-TT groups after 3 weeks of treatment when compared to that of placebo-TENS group.