#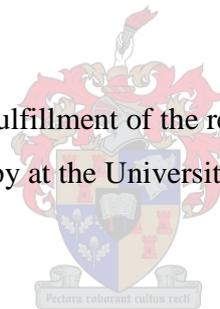 THE IMPACT OF FUNCTIONAL ELECTRICAL STIMULATION TO THE LOWER LEG AFTER A SINGLE BOTULINUM TOXIN INJECTION IN CHILDREN WITH A SPASTIC EQUINUS GAIT DUE TO CEREBRAL PALSY

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March 2008

DECLARATION

By submitting this thesis electronically, I declare that the entirety of the work contained therein is my own, original work, that I am the owner of the copyright thereof (unless to the extent explicitly otherwise stated) and that I have not previously in its entirety or in part submitted it for obtaining any qualification.

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ABSTRACT

Cerebral palsy (CP) is a common neurological condition seen in children which results in childhood disability. Damage to the developing brain results in abnormal muscle tone and decreased force generation, which leads to loss of independent function. Previous studies investigating interventions targeting the typical equinus gait pattern seen in spastic CP have reported inconclusive and widespread outcomes.

Objectives

The objectives of the study were to determine (1) the effect of functional electrical stimulation (FES) after a single botulinum toxin injection into the triceps surae muscle as a functional orthosis on various gait parameters and economy of movement; (2) caregivers' perceptions of the impact of the intervention on their child's function and participation, and (3) optimal timing intervals for introducing FES after a botulinum toxin injection.

Method

Single-subject research with a multiple baseline approach was conducted on five ambulant subjects (average age 5.1 years, SD=1.4) in the Cape Metropole with a dynamic equinus gait due to hemiplegic CP. Two-dimensional gait analysis, isometric dynamometry, Energy Expenditure Index (EEI), and a caregiver questionnaire were used to gather data on walking speed, ankle angles at initial contact of gait, isometric plantar- and dorsiflexior muscle strength, energy expenditure during gait, as well as caregiver perception on participation changes. Statistical analysis was conducted by means of ANOVA tests and graphic data illustrations.

Results

A statistically significant pre- to post intervention (FES after botulinum toxin) change was found for plantarflexor muscle strength. This effect was partially maintained over the withdrawal phase. Caregivers felt the intervention to have a positive influence on their children's walking speeds, as well as on age-appropriate function and participation. Self-selected walking speed, dorsiflexor muscle strength, and ankle angles at initial contact did not change significantly. A 32-day interval between between botulinum toxin and the FES programme resulted in the most pronounced improvements in terms of walking speed, EEI scores, and plantarflexor muscle strength.

Conclusion

FES to the lower limb, 32 days after botulinum toxin into the triceps surae, applied for 30 minutes per day, five times a week over a total of four weeks, seemed to improve selected gait parameters as well as caregiver perception of impact on function and activities of daily living. However, further research is needed.

ABSTRAK

Serebrale verlamming (SV) is 'n algemene neurologiese toestand in kinders wat tot ongeskiktheid lei. Skade van die ontwikkelende brein veroorsaak abnormale spiertonus en 'n vermindering in kragvoortbrenging, wat 'n verlies aan onafhanklike funksionering tot gevolg het. Vorige studies wat intervensies nagevors het om die tipiese toonloopgang in spastiese SV aan te spreek, het onbesliste en wydverspreide uitkomste getoon.

Doel

Die doel van die studie was om die effek van funksionele elektriese stimulasie (FES) na afloop van 'n enkele botulinum toksien inspuiting in die triseps surae spier (1) as 'n funsionele loophulpmiddel op verskeie loopparameters en energieverbruik met beweging te bepaal, sowel as om (2) die versorgers se indruk rakende die impak van die intervensie op hulle kinders se funksionering en deelname asook (3) om die beste tydsinterval vir die begin van FES na 'n botulinum toksien inspuiting te bepaal.

Metodologie

Enkel-deelnemer navorsing met 'n veelvoudige basislyn benadering is op vyf ambulante deelnemers met 'n dinamiese toonlooppatroon as gevolg van SV (gemiddelde ouderdom: 5.1 jaar, SD=1.4) in die Kaapse Metropool onderneem. Twee-dimensionele loopanalises, isometriese kragmetings, "Energy Expenditure Index" (EEI), en 'n versorger vraelys is gebruik om data oor loopspoed, enkelhoeke tydens eerste kontak van loop, isometriese plantar- en dorsifleksor spierkrag, energieverbruik tydens loop, sowel as die versorger se indruk rakende veranderinge in alledagse deelname te versamel. Statistiese analise is uitgevoer deur middel van "ANOVA" toetse en grafiese data-illustrasies.

Resultate

'n Statisties beduidende verskil in terme van plantarfleksor spierkrag is getoon. Hierdie uitkoms is gedeeltelik volgehou oor die twee-maande onttrekkingsfase. Versorgers het gevoel dat die intervensie (FES na botulinum toksien) 'n positiewe uitwerking op hulle kinders se loopspoed sowel as op ouderdomstoepaslike funksie en deelname gehad het. Loopspoed, dorsifleksor spierkrag, en enkelhoeke by eerste kontak van loop het nie beduidende veranderinge getoon nie. 'n Interval van 32 dae tussen die botulinum toksien inspuiting en die begin van die FES program het die mees uitgesproke effekte in terme van loopspoed, EEI, en plantarfleksor spierkrag getoon.

Gevolgtrekking

FES tot die onderbeen, 32 dae na 'n botulinum toksien inspuiting in die triseps surae spier, vir 30 minute per dag, vyf keer 'n week oor 'n total van vier opeenvolgende weke, blyk om geselekteerde loopparameters sowel as die versorger se indruk van die intervensie se impak op funksionering en deelname te verbeter. Verdere navorsing word benodig.

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CHAPTER 1

INTRODUCTION

Cerebral palsy (CP) is a common neurological condition seen in children following an early insult to the brain and which results in childhood disability. Normal development is affected and the impact on functional independence and social interaction can be severe. Due to the varying clinical presentations seen in children with CP, decision-making regarding therapy and management of these children is often difficult. Ongoing research seeking more appropriate and continuous rehabilitation for this population is thus required.

1.1 Definition and clinical presentation

CP is defined as a group of non-progressive movement and posture disorders caused by a lesion to the developing brain (Rosenbaum et al., 2007). Spasticity is one of the key impairments in these children, affecting approximately two thirds of this population (Delgado and Albright, 2003). In the lower limb, spasticity typically causes an equinus gait pattern and children with CP thus present with a decreased active ankle range of motion (ROM) and a lack of heel strike at initial contact (Bleck, 1987; Gage, 1991).

Traditionally, spasticity has been viewed as the main movement disorder in children with CP, and strength training has thus been avoided for fear of exacerbating the already high muscle tone (Alfieri, 1982). More recent literature has, however, shown that muscle weakness is an integral part of the clinical presentation of CP (Olney et al., 1990; Brown et al., 1991; Wiley and Damiano, 1998), and the contribution of both weakness and spasticity towards the clinical presentation of CP is thus a topic of debate in current literature.

Spasticity and muscle weakness result in a lack of mobility and independent functioning in CP (Brunstrom, 2001), and contribute to the higher energy expenditure during gait in this population (Rose et al., 1990). The resultant sedentary lifestyle can result in a high prevalence of associated orthopaedic and nutritional complications, including scoliosis, obesity, osteoporosis, hip fractures, and contractures.

1.2 Management

All of the above-mentioned characteristics of CP can interact to present a broad spectrum of individual clinical presentations. However, a common feature in children with CP is a decline in mobility and functional independence. Secondary complications are common (Campbell, 1996), and children with CP thus present with a combination of motor, social, and cognitive dysfunctions (Rosenbaum et al., 2007). The management of children with CP is thus not uniform and each child should be individually assessed and managed on his or her own merits within the constraints of his or her environment (Campbell, 1996). Treatment should encompass an ongoing multi-disciplinary approach, with the general aims of optimising each individual's functional capacity and preventing secondary complications.

1.2.1 Medical management

The medical management of children with CP can take on either a conservative or a surgical approach. Conservative treatment options are generally aimed at reducing abnormally high muscle tone, and include oral pharmacotherapy such as anti-spasmodics and muscle relaxants, as well as intrathecal Baclofen pumps, botulinum toxin, or phenol injections. Typical spastic muscles, such as the gastrocnemius, hamstrings, and hip adductor muscles, as well as the thenar muscle group and the biceps brachii muscle, have all been injected with varying effect (Goldstein, 2001; Jefferson, 2004).

Spasticity can also be addressed by means of a selective posterior rhizotomy, during which branches of the posterior nerve root are cut (Peacock et al., 1991). Other treatment

options include the surgical lengthening of shortened muscles (one of the complications that occur as a result of spasticity and / or prolonged inactivity). Typical lower limb contractures occur in the hamstring and gastrocnemius muscles, and lengthening may be considered to improve hip, knee and ankle ROM as well as function (Bleck, 1987).

1.2.2. Nutritional management

The combination of varying degrees of physical, social, behavioural, and intellectual impairments prevalent in CP commonly result in a sedentary lifestyle and concomitant obesity (Brunstrom, 2001). These severely hamper independent and / or assisted mobility, and it is thus imperative that a qualified dietician monitors the nutritional intake of the CP child.

1.2.3 Therapeutic management

Due to the wide variety of clinical presentations within the diagnosis of CP, no clearly defined rehabilitation protocol exists. Treatment outcomes are determined on an individual basis, and are influenced by social, functional, emotional, and intellectual factors (Stanger and Oresic, 2003). The therapy team is thus comprised of professionals addressing each child's specific impairments. A speech therapist may be included in order to address speech, hearing, and / or language problems, whereas an occupational therapist will often work in conjunction with a physiotherapist in order to optimise functional independence and quality of life.

1.2.3.1 Physiotherapy

Other than assistance by means of issuing external assistive devices (frequently in conjunction with an occupational therapist), the physiotherapist plays an integral part in the continuous management of the individual with CP. The therapist aims to identify specific missing components in the movement patterns of the individual, and addresses these by means of targeted treatment programmes.

One approach used for this purpose is neurodevelopmental therapy (NDT), which was developed by Karl and Bertha Bobath in the 1940's with the aim to improve postural control and to promote normal motor development (The Bobath Centre, 2007). Normal movement patterns are encouraged by therapeutic facilitation of functional activities (Campbell, 1996), while active participation in the activity is encouraged.

Since then, the physiological understanding of muscle tone and spasticity has evolved, and adjuncts to therapy such as splinting and orthoses have contributed significantly towards the management of CP. Therapists also aim to set measurable treatment outcomes and to make goals more specific to the individual patient, as well as more task-orientated (Mayston, 2002). The principles of striving towards normal muscle tone and improved active function have, however, remained constant.

Other treatment approaches include the Voijta concept (which makes use of reflexology to improve postural control) (De Groot et al., 2000), the Phelps method (characterised by passive movements performed by the therapist), as well as the Peto method (during which all activity is to be initiated by the child and which integrates education and rehabilitation goals) (Campbell, 1996).

Other management options emphasise the orthopaedic components of CP. One of these is constraint-induced therapy, which involves restraining the unaffected arm to promote functional use of the affected arm and is based on the motor learning model of neurodevelopment (Shumway-Cook and Woollacott, 1995). Furthermore, specific stretching programmes may also be implemented, which aim to maintain and improve ROM in the affected limbs. However, evidence regarding the efficacy of this intervention on increases in ROM, reduction of spasticity, and improvement of walking efficiency, is limited (Pin et al., 2006). In addition to stretching, strengthening programmes address muscle weakness and imbalances (Damiano et al., 1995; Dodd et al., 2003).

Although spasticity has historically been regarded as the main contributing factor influencing the motor presentation in CP, many researchers including Olney et al. (1990),

Brown et al. (1991), and Wiley and Damiano (1998) have reported on extensive muscle weakness in this population, especially in the hip extensor and ankle dorsi- and plantarflexors. There is increasing evidence that strengthening programmes can address specific missing components and thus form a vital component of the physiotherapy treatment of CP. This has been achieved by progressive resistance training (Damiano et al., 1995; Dodd et al., 2003; Unger et al., 2006), body weight supported treadmill training (Schindl et al., 2000), isokinetic exercise (Fowler et al., 2001), and / or neuromuscular electrical stimulation (Carmick, 1995; Comeaux et al., 1997). Not only has improved muscle strength been shown to correlate with increased levels of functional skills (Kramer and MacPhail, 1994) and thus reduced dependence on caregivers and assistive devices, but it also results in improved cardio-respiratory endurance.

However, many previous studies conducted in the CP population were either case reports or single-subject research studies, and deductions as to the effect of interventions on the greater CP population must be made with care. Physiotherapists in current clinical practice are thus faced with the problem of conflicting evidence concerning a wide variety of treatment techniques, as well as a lack of empirical evidence regarding the efficacy of treatment approaches such as strengthening modalities (including electrical stimulation therapy) in the CP population as a whole.

CHAPTER 2

LITERATURE REVIEW

As the clinical picture of cerebral palsy (CP) is so multi-dimensional, it is imperative to obtain a holistic overview of this condition and its impact on the individual's level of function and participation. An immense amount of information regarding the definitions of CP, its classifications, impact on function, and treatment options is available. An on-line literature search was thus conducted on the MEDLINE (Pubmed), CINAHL, PsychInfo, ScienceDirect, Pedro, Journals@Ovid, and Cochrane databases in order to obtain comprehensive information regarding CP and its management options. Further information was sourced through pearling and library hand searches.

2.1 Definition of CP

CP was first recognised and described by Little in 1862, and was initially referred to as "cerebral paresis" (Bleck, 1987) occurring due to prematurity and associated complications (Stanley, 1984). Since then, this definition has undergone continuous revision to include and adapt to the most recent evidence in the neurodevelopmental field. Currently, CP is defined as a group of non-progressive movement and posture disorders caused by a lesion to the developing brain. These are often accompanied by any combination of sensory, cognitive, communicative, behavioural, and / or perceptive impairments, as well as seizure disorders (Rosenbaum et al., 2007).

This definition for CP spans a great variety of clinical presentations, and many classification systems have been implemented since the first categorisation by Freud in 1892 (Ingram, 1984). The most common modern grouping, however, follows type of motor disorder and abnormal motor function, and renders the following sub-groups: spastic (severe or moderate), athetoid (including chorea-athetosis, pure athetosis, or

presenting with tonic spasms), ataxic (pure or with spasticity), hypotonic, and mixed presentations (Nelson and Ellenberg, 1978; Rosenbaum et al., 2007).

2.2 Etiology

Causes for the development of CP can be grouped into three categories according to period of onset: prenatal, perinatal, and postnatal causes.

2.2.1 Prenatal

Although certain causative factors can be linked to the development of CP (e.g. the development of congenital ataxia due to the genetic transmission of an autosomal recessive trait), these are in the minority (Bleck, 1987). Environmental factors known to produce teratogens and potentially result in CP include iodine deficiencies (resulting in cretinism), fetal alcohol syndrome, rubella and cytomegalovirus infections, intrauterine toxoplasmosis, and smoking during pregnancy (Bleck, 1987). Rhesus-incompatibility, metabolic disturbances (including diabetes), radiation, and cerebral bleeding due to pharmacological agents (e.g. aspirin) are further potential causes of prenatally acquired CP (Burger, 2003).

2.2.2 Perinatal (during or within seven days of delivery)

The relationship between prematurity and CP has been studied extensively, although it is unclear whether the damage to the central nervous system is due to the adverse effect of prematurity on neuronal development, or due to the risk for the development of an intracerebral haemorrhage with premature delivery. In both instances, the risk for the development of CP further increases if ventilation is required (Bleck, 1987).

Furthermore, a birth weight of less than 800 grams has been linked to a 40% chance of severe impairment, whereas a birth weight of between 1000 and 1500 grams reduces this risk to between ten and 18% (Burger, 2003). Hagberg et al. (1975) have also shown a

positive link between low birth weight and CP, especially in perinatally acquired CP. Perinatal obstetrical problems such as prolonged labour, breech births, a prolapsed umbilical cord, as well as birth trauma can result in neonatal asphyxia and may result in CP (Stanley, 1984; Bleck, 1987). In South Africa, Arens et al. (1978) and Arens and Molteno (1989) have shown cerebral infections (including bacterial meningitis) to be a cause of CP, with it being the cause of 50% of CP in white children, compared to the cause of 66% in coloured children (Arens et al., 1978). No other population group formed part of the study sample in this case. The researchers also reported that head trauma (especially due to motor-vehicle accidents), cerebrovascular accidents after severe gastroenteritis, as well as kernicterus were risk factors in the South African population (Arens et al., 1978; Arens and Molteno, 1989).

2.2.3 Postnatal

Postnatal infections (including neonatal meningitis) are the most common cause for CP developing after birth, resulting in 60% of cases (Bleck, 1987; Burger, 2003). Stanley (1984) reported that the majority of infections resulting in CP are caused by gram-negative organisms. Head injuries account for 20% of postnatally acquired CP, while near drowning, asphyxia, cardiac arrest, cerebrovascular accidents, and tumours are further identified causes (Stanley, 1984; Bleck, 1987; Burger, 2003).

2.3 Incidence and prevalence

When discussing this topic, a distinction must be made between high-risk babies (e.g. prematurely born infants, babies born with a low birth weight, and infants exposed to infection due to poor birth environments) and low-risk (e.g. term) babies. Due to different potential risk factors, the incidence and prevalence rates may differ in these two groups.

2.3.1 Incidence

It is difficult to clearly establish the incidence of CP at birth, as motor dysfunctions are frequently only noted when normal developmental progress dictates increases in independent functions such as sitting and walking (Mair, 1961). Although few epidemiological studies have been conducted in South Africa, Cooper and Sandler (1997) have reported that 10% of high-risk babies born with very low birth weights (below 1500g) surviving to the age of 18 months in a rural community in South Africa developed CP. This is similar to incidence rates in very low birth weight infants reported by other researchers, including studies conducted in developed countries (Cooke, 1990; Veen et al., 1991; Robertson et al., 1994). Odding et al. (2006) report that newborns weighing less than 2500g now make up half the CP population in Europe, while Himmelmann et al. (2005) have shown an incidence of 1.9 per 1000 live births over the period of 1995-1998 in Sweden. The highest percentage (77 per 1000 children) in this instance occurred in infants born before a gestational age of 28 weeks. In a South African study on infants weighing more than 2500g at birth, Arens et al. (1978) reported a higher incidence of especially perinatally acquired CP in the coloured population, particularly due to perinatal asphyxia.

2.3.2 Prevalence

Mair (1961) has stated that the most accurate assessment regarding prevalence in CP can be made in children of school-going age. Mair (1961) found the prevalence of CP in this population to be 2.4 per 1000, which coincides with figures from later studies for Sweden (Hagberg et al., 1975) as well as Ireland, Denmark, England, Iceland, Western Australia, and the United States of America (Paneth and Kiely, 1984). Odding et al. (2006) have reported that the prevalence of CP in Europe has risen from about 1.5 per 1000 live births in the 1960's to about 2.5 in thirty years. Although the researchers did not discuss potential reasons for this increase, it is possible that higher survival rates due to improved medical care could potentially have resulted in an increased prevalence of CP. A higher

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prevalence rate of 10 per 1000 was reported by Couper (2002) for a rural community in South Africa, while Arens and Molteno (1989) found the highest prevalence in the coloured South African population group (2.86%), compared to 2.21% in white and 2.11% in black children between the ages of five and nine years. As the quality of health care can be expected to have been higher in Europe than in rural South Africa at this time, it is not surprising that a higher prevalence in CP was recorded in the latter area.

2.4 Presentation

Individuals with CP can present with any of a wide variety of motor, sensory, cognitive, as well as behavioural impairments, which in turn combine to result in differing clinical presentations of CP. These impairments will now be discussed individually, followed by a discussion of their implications on function and participation.

2.4.1 Impairments

Children with CP can present with a wide variety of impairments, which combine to result in a multitude of individual clinical presentations.

2.4.1.1 Spasticity

Spasticity is one of the key motor dysfunctions in children with CP, affecting approximately two thirds of this population. It is defined as the resistance to passive muscle stretching and occurs in conjunction with upper motor neuron lesions (Delgado and Albright, 2003). It is thus commonly present in combination with "negative" signs such as weakness and decreased endurance and co-ordination, as well as with "positive signs". These include "clasp-knife" type spasticity, clonus, increased tendon reflexes, the persistence of primitive reflexes, and co-activation of muscles (Mayer, 1997; Goldstein 2001; Delgado and Albright, 2003). In CP, these signs are the result of a loss of inhibitory modulating influences on muscle spindle activity on the level of the spinal reflex arc (Goldstein, 2001).

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In a normal muscle, a contraction is initiated by efferent impulses traveling along the peripheral nerve causing the release of acetylcholine at the neuromuscular junction. This neurotransmitter then binds to appropriate receptors on the post-synaptic cell membrane, increasing its sodium permeability, and thus initiating an action potential in the sarcolemma (depolarisation of the nerve) (Gamble, 1988; Rose and McGill, 1998). The muscle thus contracts, and feedback regarding its activity is generated in the muscle spindles and Golgi tendon organs. This feedback is then relayed to the dorsal root ganglia in the spinal cord via afferent neurons, where interneurons complete the loop to the motorneurons (Skinner, 1992; Mayer, 1997; Goldstein, 2001).

Resting muscle tone is thus determined by the integration of excitatory and inhibitory influences at the level of the alpha motorneuron in the spinal cord. In the case of CP, however, this interaction is disrupted due to a loss of supraspinal control (inhibition), resulting in an abnormally high resting muscle tone (Skinner, 1992). Antigravity muscles are generally most affected by this phenomenon (Mayer, 1997). Spasticity is velocity-dependent and is also influenced by emotional changes, body position, and levels of discomfort (e.g. muscle tone increases in the presence of pain, anxiety, and increased physical exertion). Movements generally occur in stereotypical mass synergy patterns (Mayer, 1997). Spastic muscles do not grow at the same pace as adjoining structures, which could potentially lead to fixed deformities, decreases in joint range of motion (ROM), and progressive hip dislocations. The treatment of these is complex, and may necessitate corrective surgery (Bleck, 1987).

2.4.1.2 Muscle weakness

Traditionally, spasticity has been viewed as the main movement disorder in children with CP, and strength training has thus been avoided for fear of exacerbating the already high muscle tone (Alfieri, 1982). More recently, however, Wiley and Damiano (1998) have shown significant weakness of all muscles of the affected side in hemiplegic CP in comparison with age-matched controls, and bilateral weakness in diplegic CP. The researchers found that the weakest muscles were the hip extensors and ankle dorsi- and

plantarflexors. Brown et al. (1991) have also reported on significant muscle weakness in the hip, knee, and ankle musculature of the affected leg of hemiplegic CP. Olney et al. (1990) have found that the plantarflexors of CP children produce approximately one third of the total work of the affected limb, compared to two thirds in typically developing children. The findings of Stackhouse et al. (2005) are similar. In this study, the researchers examined maximal voluntary isometric muscle force as well as muscle activation patterns in children with spastic CP. Force production in the triceps surae muscle group was 73% of that of a control group, while muscle activation ratios were 49% lower in CP children. In addition, increased co-activation of the tibialis anterior muscle was noted during voluntary triceps surae contractions. However, subjects in the study by Stackhouse et al. (2005) were not required to present with an ankle dorsiflexion (DF) ROM beyond a neutral position. The lack of full DF ROM could thus have influenced the measurement results.

Normally, all muscle fibres at birth represent slow-twitch properties (type I, non-fatiguable fibres) and develop into fast-twitch (type II, fatiguable) fibres within the first five weeks of life. Certain muscles then retain these characteristics, while others revert to the initial slow-twitch properties (Wolpaw and Carp, 2006). In normal muscle tissue, subsequent fibre size per muscle is relatively constant, and type I and type II fibres are similar in size. Fibre type distribution varies amongst different muscles, with the soleus and tibialis anterior muscles normally exhibiting a predominantly type I composition (Castle et al., 1979).

In cross-innervation studies, however, Buller et al. (1960) have shown that a muscle's contractile properties are influenced by the characteristics of the particular innervating motorneuron, and are prone to change if the electrophysical properties of the neural system change. Additionally, Buller et al. (1960) have shown that damage to the central nervous system inhibits the reacquisition of slow-twitch properties in certain muscles, while the initial development of slow- into fast-twitch fibre type is not affected. It would thus be expected that the muscles of children with CP exhibit a predominance of type II muscle fibres, with concomitant type I deficiency. The findings of Castle et al. (1979)

concur with this hypothesis, as the researchers have shown varying degrees of type I fibre atrophy with concomitant type II fibre hypertrophy in spastic gastrocnemius, biceps femoris, soleus, a well as tibialis anterior and posterior muscles.

Although Ito et al. (1996) have shown type I fibre atrophy in spastic muscles, the presence of these muscle fibres was still predominant over type II fibres. The researchers postulate that perinatal cerebral damage and the associated loss of supraspinal impulse inhibition may interfere with the maturation of undifferentiated type IIC muscle fibres into type I, IIA and IIB fibres, resulting in an abnormal type I fibre predominance. As this fibre type distribution reflects that of a stabilising muscle, it is thus not surprising that muscles which are expected to exhibit phasic qualities (e.g. the gastrocnemius muscle) now display tonic muscle characteristics.

Where severe muscle atrophy was present, an increased amount of peri- and endomysial connective tissue and interstitial adipose tissue was also found (Castle et al., 1979). In the case of the soleus and tibialis anterior and posterior muscles, the researchers state that joint fixation, loss of anterior horn cells, or a loss of inhibitory influences on these cells could be responsible for type I fibre atrophy. These fibres have a lower stimulation threshold than type II fibres, and are thus continually recruited due to the loss of higher modulatory inhibiting influences. They could thus have undergone initial hypertrophy, followed by exhaustion and atrophy (Castle et al., 1979). The associated hypertrophy of type II fibres could be explained by the compensatory increase in workload on these muscle fibres in order to maintain the contractile capabilities of the muscle.

In addition, Gemperline et al. (1995) have shown that the motor units of spastic muscles are recruited at lower thresholds and fire less rapidly than normal muscle tissue. Firing rates are also not increased in response to an increase in contractile muscle strength, as is the case in a normal motor unit. This fact, together with a mismatch of firing rates and mechanical muscle properties, may result in reliance on an increase in recruitment ratio to increase contractile muscle force, which may lead to weakness and fatigue (Bigland-

Ritchie et al., 1983; Gemperline et al., 1995). Spasticity also causes corresponding weakness of the antagonist muscle by reciprocal inhibition (Johnson et al., 2002).

2.4.1.3 Associated impairments

Although spasticity and weakness play integral roles in the physical abilities of children with CP, a host of associated conditions may also be present. Intellectual impairment occurs in up to two thirds of children with CP, with the diagnosis of quadriplegia being associated with the most severe intellectual deficits (Crothers and Payne, 1959). Seizure disorders (including epilepsy) are present in approximately one third of CP children (Illingworth, 1958), and frequently become evident before the age of two years (Mitchell, 1961). Although different types of seizure disorders may be present, generalised convulsions are most common.

Visual and visual-motor deficits also occur (Ghasia et al., 2008). Visual deficits differ in children who have mild versus severe CP. In mild cases, children present with sensorimotor deficits resembling those of neurologically normal children with strabismus and amblyopia, whereas children with higher levels of impairment have more severe deficits such as high myopia, absence of binocular fusion, dyskinetic strabismus, severe gaze dysfunction, and optic neuropathy or cerebral visual impairment. Douglas (1961) found severe ophthalmologic defects to be linked to severe mental and physical impairments. Mowat (1961) has found a 23% incidence of deafness associated with CP, which the researcher believes to be linked to the severity of physical and intellectual impairments. CP of perinatal origin is thought to result in selective high-frequency deafness. In terms of somato-sensory impairments, stereognosis and two-point discrimination of the hands are deficient in 44-51% of all children with CP, while proprioceptive dysfunctions and chronic pain may also occur (Yekutiel et al., 1994).

Dental features common in children with CP include marginal or hypertrophic gingivitis, owing to facial muscle paralysis and a resultant defective chewing mechanism (Munro,

1961). The researcher also found a higher incidence of tongue thrusting and malocclusion, as well as delayed dental development (prevalence of 60%).

The combination of the defects discussed above can result in a range of speech and learning problems, as well as various behavioural disorders. Social and emotional disorders such as depression are also common (Nelson and Ellenberg, 1978; Brunstrom, 2001).

2.4.2 Functional implications

As ambulation is a vital prerequisite for social independence, the impact of the above mentioned impairments on gait will now be discussed.

2.4.2.1 Gait development in CP

Berger et al. (1984) have electrophysiologically observed four stages in the gait development of typically developing children, and have discussed their results in comparison with typical gait patterns observed in CP. In typically developing children younger than one year of age, supported stepping movements can be induced by a moving treadmill. Unsupported walking is achieved in children aged one to two years, although their gait pattern is unsteady and irregular. During this time, EMG analysis shows the tibialis anterior muscle to be active throughout the gait cycle. Increased muscle activity is observed during the swing phase, although this is ineffective in causing ankle DF. Initial contact is thus made with the ball of the foot during walking.

Between the ages of two and five years, gait becomes smoother, which is due to the start of reciprocal muscle activation of the calf musculature at this time. The gastrocnemius muscle is strongest at age four to five years, with EMG values doubling those of the tibialis anterior muscle. Heel strike at initial contact is thus more constant. The gait pattern and EMG readings of children older than five years do not differ significantly from those of adults.

Through EMG studies, Dietz et al. (1981) have shown that the gastrocnemius muscle remains active throughout the stance phase of gait under normal circumstances, controlling the anterior movement of the tibia on the foot (Perry et al., 1974). Sutherland et al. (1980) further state that the calf musculature serves to minimise the vertical translation of the body's center of gravity at this time by minimising the leg length difference and thus the energy expenditure during gait. Push-off is thus a mechanical process caused by the anterior movement of the tibia over the foot (Perry et al., 1974). This correlates with the EMG analysis of Dietz et al. (1981), who found decreased gastrocnemius EMG activity levels at the start of plantarflexion (PF) at terminal stance. At this time, tibialis anterior muscle activity begins, and persists until the beginning of the following stance phase. Berger et al. (1984) hypothesise that with normal gait maturation, the large reflex potentials seen in the gastrocnemius muscle at the beginning of stance become integrated into maturing muscle activity, resulting in an increase in strength. As the tibialis anterior muscle is not influenced by reflex activity, its strength remains constant over the development phases (Berger et al., 1984).

In spastic muscles, however, EMG readings of the tibialis anterior muscle are significantly higher during stance, with reduced gastrocnemius co-activation during stance and large reflex EMG potentials at the beginning of this phase (Dietz et al., 1981; Berger et al., 1984). This phenomenon eliminates the "roll-off" pattern at terminal stance, thus causing a vertical rise in the body's center of gravity, and a concomitant increase in energy expenditure during gait (Bleck, 1987).

Despite the stronger tibialis anterior muscle, no active ankle DF occurs during the swing phase of gait, which is comparable to the gait pattern of a typically developing one year old child (Berger et al., 1984). Dietz et al. (1981) proposed that the mechanical properties of the calf musculature are responsible for this phenomenon in that the contractile properties of the slow-twitch muscle fibres show an increased resistance to stretch, as it would occur with ankle DF during swing.

2.4.2.2 Gait patterns in CP

The impact of muscle weakness is evident during the gait of children with CP. Under normal circumstances, an increase in motor unit firing rate is seen in the stance and swing phases in order to accomplish adequate push-off and subsequent toe clearance (Winters et al., 1987). As explained above, however, this does not occur in the case of spastic CP, resulting in an equinus gait pattern.

Although not all children with CP can be expected to walk, Brown et al. (1991) report that children with hemiplegic CP should be able to ambulate either independently or with the assistance of walking aids. Bleck (1987) states that ambulation usually occurs between the ages of 18 and 21 months. Independent or assisted walking should also be accomplished by children with diplegic CP (Steinwender et al., 2001). Typical patterns for hemiplegic and diplegic gait are as follows.

Hemiplegic gait

One third of all CP children present with hemiplegia (Brown, 1984). Their gait pattern is characterised by a longer double support phase, and a significantly longer swing phase with lower peak swing velocities in the affected leg due to weak hip flexors and the presence of spasticity around the hip (Brown et al., 1991). Speed of movement is also significantly limited at the ankle and toes. Cadence is higher than in age-matched controls, and step lengths are significantly reduced as a result of a loss of forward propulsion by the calf muscles and a lack of adequate knee extension at terminal swing (Brown et al., 1991). Circumduction of the hip is thus the result, with a lack of heel strike at initial contact. Foot contact is made with either the lateral border of the foot or the toes, followed by either a toe-heel pattern, or a persistent equinus gait.

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Diplegic gait

Steinwender et al. (2001) have shown that children with diplegic CP display a slow walking speed (especially in the presence of a crouch gait pattern) together with a high cadence and short stride length. Reduced power output levels at the ankle were recorded in children with diplegic CP compared to typically developing children. The researchers speculate that this finding could result in increased power output levels in the hip extensors of the contralateral limb during the double stance and the first half of the subsequent single stance phases as a compensating mechanism. In addition, the researchers found that diplegic children presented with higher levels of internal hip rotation during the initial part of stance, resulting in pseudo hip adduction

2.4.2.3 Energy expenditure during gait

Both weakness and spasticity contribute to the higher energy expenditure during gait in children with CP compared to age-matched controls (Rose et al., 1990). Atrophy of type I (slow-twitch) muscle fibres with concomitant type II (fast-twitch) fibre hypertrophy would be expected to result in poor muscle endurance and thus higher energy consumption rates during gait. In addition, the mechanical properties of the spastic calf musculature results in an abnormally high vertical displacement of the body's centre of gravity during gait, which increases the energy consumption during walking (Bleck, 1987).

Energy efficiency during gait is defined as the amount of energy utilised per unit of distance covered (Brehm et al., 2007). In their study comparing energy expenditure index (EEI) measurements based on heart rate and oxygen uptake in CP as well as in typically developing children, Rose et al. (1990) found that EEI levels decreased with increasing walking speeds up to a point of maximum energy efficiency during gait (applicable to both typically developing and CP children), after which a further increase in speeds resulted in a concomitant increase in EEI scores. However, the mean economical walking

speed (speed associated with the lowest EEI value) was more than three times higher in CP children than in typically developing subjects, and occurred at slower walking speeds.

In a study investigating the relationships between walking efficiency, gross motor abilities, and isokinetic muscle strength in adolescents with CP, Kramer and MacPhail (1994) found that there was a positive correlation between these three outcome variables. Correlation ratios between muscle strength and motor abilities were significantly higher for concentric than eccentric muscle work, from which the researchers deduced that impaired concentric muscle action may be the cause of limited functional capacities.

Furthermore, Kramer and MacPhail (1994) have shown that EEI measurements for their subjects (adolescents with CP) were 48% higher than those of non-disabled adolescent subjects in Rose et al. (1985), despite similar walking speeds. Kramer and MacPhail (1994) supposed that adolescents with CP had learned to walk at higher walking speeds to keep up with the physical abilities of their able-bodied peers at the expense of energy economy during gait.

In their study to assess the reproducibility of gross (resting plus net) versus net (gross minus resting) energy consumption during gait, Brehm et al. (2007) have shown that gross energy consumption measurements provide a more sensitive method of examining energy efficiency during gait in CP children. As exercise participation as well as food consumption varied between subjects prior to testing in this study, resting heart rate vales differed, and thus influenced net energy consumption scores. Although previous researchers have suggested the use of net energy consumption as a more reliable method of assessing walking efficiency during gait (Baker et al., 2001), Brehm et al. (2007) have shown this not be a reliable option.

2.4.2.4 Implications for independence and participation

All of the above-mentioned characteristics of CP can interact to present various spectra of individual clinical presentations. However, a common feature in all children with CP is a

decrease in mobility and functional independence. This, in turn, leads to a host of secondary musculoskeletal problems, including hip dislocations and fractures, scoliosis, heart disease, obesity, osteopaenia, and osteoporosis, (Bleck, 1987; Brunstrom, 2001). Depending on their severity, these complications can necessitate intensive and expensive management (including orthopaedic surgery). These musculoskeletal impairments can result in reduced capabilities for independent mobility and self-care, which may negatively impact on social interaction and the individual's participation in his or her own environment (e.g. schooling or access to public areas). Together with possible cognitive impairments, this decrease in participation may result in emotional and behavioural problems such as loss of self-worth and depression (Brunstrom, 2001).

The management of children with CP should thus encompass a multi-disciplinary approach, with the overall aim of maximising each individual's functional and participation capacities in the most cost-effective manner possible.

2.5 Outcome measures

Although spasticity is such a common feature in CP, a user-friendly objective measurement tool or scale for its assessment has yet to be developed (Delgado and Albright, 2003). One of the most widely used grading scales in the clinical setting is the Ashworth scale. However, it does not differentiate between spasticity, rigidity, and dystonia, and can thus not be used for objective grading of spasticity alone. A further commonly implemented measurement tool is the Tardieu scale, which assesses the amount of resistance to a passive stretching after a "spastic catch" has occurred. Unfortunately, this scale has not been validated for use in neither the paediatric nor the adult population, and results should thus be analysed with care (Delgado and Albright, 2003). Additional assessment tools include EMG recordings and deep tendon reflex testing, but are not frequently used due to the high costs involved (Skinner, 1992; Engsberg et al., 1996).

In terms of assessing muscle strength, isokinetic dynamometry is generally regarded as the gold standard. Although it has been proven to be a reliable measuring tool, it is costly and is thus not readily accessible in clinical practice. In comparison to isokinetic dynamometry, Roy and Doherty (2004) have shown that a hand-held dynamometer exhibits high test-retest reliability for the knee extensors. Even though isometric strength values are dependent on tester experience and strength as well as motivation and personal effort on the part of the subject, it has proven to be a cost-effective means of objectively scoring muscle strength. In their study to determine the reliability of a hand-held dynamometer for assessing lower limb muscle strength in dipegic CP children, Crompton and Galea (2007) have shown good reliability for intra- session measurements for most of the lower limb muscles, and acceptable inter-session reliability for the hip and knee flexors and extensors in supine, as well as the ankle dorsiflexors with stabilisation. The ankle plantarflexors revealed poor reliability. The researchers predominantly attribute this finding to a lack of limb stabilisation during testing, and suggest that muscle strength testing should be conducted separately for each muscle group in both limbs. Changes in measurements should also be interpreted relative to body weight.

Another form of assessing muscle strength is by manual testing (e.g. using the Oxford scale). In this instance, the tester's perception of normal strength values strongly influences the scoring process, which is rendered more difficult by natural variation in muscle strength in terms of sex, age, gender, and general fitness levels.

An outcome measure frequently used to evaluate energy expenditure during gait is the EEI, which is indicative of the amount of energy required to walk a specified distance. This value has historically been calculated by assessing oxygen uptake with walking, but has not been widely used due to the lack of the necessary equipment in the clinical setting as well as its expense and unwieldiness (Rose et al., 1989). In this comparison study by Rose et al. (1989), however, the researchers have shown calculations based on heart rate to be a valid and clinically more convenient method to determine energy costs of walking in children with CP. The formula for calculating EEI is as follows:

$$EEI \ (HR) = \frac{\text{Final heart rate} - \text{resting heart rate}}{\text{Walking speed}}$$

$$= \text{beats / metre}$$

2.6 Management

In terms of predicting a diagnosis of CP, Cooper and Sandler (1997) have shown a diagnosis of periventricular leukomalacia / porencephaly on a cranial ultrasound (performed during the initial hospital stay) to be the best predictor for CP later in life, which correlates with similar findings of previous researchers (Pidcock et al., 1990; Pinto-Martin et al., 1995). More recently, however, Einspieler and Prechtl (2005) have shown that the absence of general movements within the first four months after birth have a strong positive predictive value for the diagnosis of CP in later life. Either way, predictions regarding a probable diagnosis of CP can now be made early on in an infant's life, which allows close monitoring as well as appropriate interventions to be introduced. This would be expected to lead to an improved prognosis and potentially higher levels of individual function and participation.

As previously discussed, CP encompasses a very broad spectrum of clinical pictures, and thus no recipe-like approach to its management exists. Accessibility to health care services, the level of the relevant health care practitioner's experience, financial constraints, as well as social support structures all influence decision-making regarding management and ongoing rehabilitation. Each individual case thus needs to be assessed on its own merits, and decisions regarding intervention and management made accordingly. The following options, however, are available to the multi-disciplinary team in this regard.

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2.6.1 Medical management of impairments

The medical management of CP can take on either a conservative or a surgical approach.

2.6.1.1 Oral medication

Most forms of pharmacological treatment are aimed at reducing spasticity. Oral pharmacotherapy is appropriate where a generalised decrease in muscle tone is required. These medications act by inhibiting excitatory or by potentiating inhibitory neurotransmitters at spinal cord level (Gracies et al., 1997). Common drugs used for this purpose are baclofen and diazepam. However, these chemical compounds are not selective in their action, and may result in sedation due to central neurotransmitter changes (Goldstein, 2001).

2.6.1.2 Chemodenervation

Chemodenervation is achieved by phenol or botulinum toxin injections (Goldstein, 2001). Both target focal muscle spasticity, as the compounds are injected into the motor point of the hypertonic muscle. Phenol causes the denaturation of protein compounds, thus inducing axonal necrosis, and consequently disrupting efferent signals emitted by the spinal cord's anterior horn cells (Gracies et al., 1997). However, side effects of this method of treatment include pain and dysthesia, which are the results of the necrosis of sensory axons in peripheral nerves. Nausea and lethargy can occur due to systemic absorption of the drug, and the potential for skin necrosis at the injection site exists (Gracies et al., 1997).

A second form of chemodenervation therapy exists in the form of botulinum toxin injections. This toxin is a product of the gram-negative anaerobic bacterium *Clostridium botulinum* (Davis and Barnes, 2000). Seven serotypes have previously been identified, of which only type A is commercially available.

Botulinum toxin type A

This compound was first approved for the treatment of strabismus, blepharospams, and seventh cranial nerve disorders (Scott, 1989). Since then, its use has been expanded to include treatment of primary hyperhidrosis of the axillae, spasticity in paediatric CP, spasmodic torticollis, and facial dystonias (Cosgrove et al., 1994; Botox® South Africa: package insert).

Botulinum toxin type A (Allergan®) is a schedule four drug, and is a neuroprotein consisting of a heavy chain (molecular weight of about 100 000 Da), and a light chain with a molecular weight of about 50 000 Da (Aoki and Guyer, 2001). These chains are bound by a disulphide bond, which must be nicked by proteases in order to become active. When cleaved, the heavy chain binds to cholinergic nerve terminals at the neuromuscular junction, while the light chain is transported into the nerve terminal itself by endocytosis. This portion of the toxin then blocks the pre-synaptic release of acetylcholine via exocytosis, thus weakening the contractile force of the muscle (Davis and Barnes, 2000). Clinical effect is usually seen between 24 to 72 hours after administration, but can be evident immediately (Brin, 1997). All seven serotypes of botulinum toxin act via this mechanism, but exhibit different duration times, potencies, and target different intracellular proteins (Aoki and Guyer, 2001). Initial recovery of muscle action occurs through non-collateral neuronal sprouting from the unmyelinated terminal axon just proximal to the motor endplate (Brin, 1997), whereas later recovery is due to the return of normal neurotransmitter transport across the pre-synaptic membrane with a concomitant regression of neurons (Aoki and Guyer, 2001).

The most common adverse effects of botulinum toxin include localised pain and bruising, as well as an incidence of viral and ear infections, which usually occur within a few days after injection and are transient (Brin, 1997; Botox® South Africa: package insert). A 17% incidence of side-effects has been reported. Contra-indications for the use of botulinum toxin are known hypersensitivity to botulinum toxin type A or its constituents,

inflammation or infection at the proposed injection site, and / or the use of aminoglycoside antibiotics.

Impact of botulinum toxin on gait

Focal reduction in muscle tone is frequently combined with strengthening of the antagonist muscle during therapy (Goldstein, 2001). Although the effect of the toxin wears off after three to six months (Cosgrove et al., 1994; Koman et al., 2001), the aim of this combined treatment approach is to integrate improved movement patterns on a central basis in order to achieve functional gains that last longer than the action of the chemical compound (Russman et al., 1997; Koman et al., 2001).

Baker et al. (2002) administered a single botulinum toxin injection with a dosage of either ten, 20, or 30 units / kg to subjects with diplegic CP. The researchers found a continuous increase in Gross Motor Functional Measure (GMFM) scores, even after a period of 16 weeks, at which time the action of the toxin would have been expected to wane. The researchers have shown that the dynamic component of gait (the difference between active and passive muscle lengths) was significantly improved after botulinum toxin injections in children with diplegic CP, with the greatest change evident after four weeks. Although improvements were maintained for four months, passive ankle ROM remained unchanged. Cosgrove et al. (1994) also reported on improved ambulatory status in half their subjects for up to six months after the injection in spastic hemiplegic, diplegic, as well as quadriplegic subjects.

In their randomised and placebo-controlled study, Ubhi et al. (2000) found a similar significant increase in active ankle ROM and concomitant frequency of heel strike at initial contact after six and 12 weeks after a single botulinum toxin injection. GMFM scores increased as well, while passive ankle ROM and energy efficiency during gait did not change. Similar results were reported by Koman et al. (2001), who administered repeated botulinum toxin injections to paediatric CP subjects. In their study assessing the dynamic component of spasticity in the gastrocnemius muscle after repeated botulinum

toxin injections, Eames et al. (1999) have found a strong correlation between the magnitude of the spasticity and the duration of the response, especially in hemiplegic children.

2.6.1.3 Orthopaedic surgery

Surgery is indicated in children who present with structural changes to the limbs and / or trunk that are or may become disabling (Bleck, 1987). In ambulant children, this usually involves surgical interventions to the lower limb to improve function, whereas wheelchair-bound children will benefit from procedures aiding individual or assisted transfers. The clinical presentation and needs of each child must be assessed on an individual basis, and the choice for surgical procedures made accordingly. Possible procedures include a hamstring or achilles tendon lengthening, iliopsoas recession, adductor longus and gracilis myotomy, and / or a neurectomy of the anterior branch of the obturator muscle (Bleck, 1987).

2.6.1.4 Selective dorsal rhizotomy

This technique is appropriate for children with lower limb spasticity. The motor and sensory nerve roots are separated, and muscle activity of the lower leg is recorded with manual stimulation of the sensory nerve rootlets (Peacock et al., 1991). The rootlets with the most abnormal sensory feedback to the spinal motorneuron pool are thus identified, and the respective sensory rootlets are cut at spinal level. A permanent reduction in lower limb spasticity is thus achieved. This technique is most commonly performed in children with spastic diplegia who are able to walk with or without assistive devices (Peacock et al., 1991).

2.6.1.5 Intrathecal baclofen

In the presence of severe generalised spasticity, baclofen can be administered into the subarachnoid space around the lumbar spinal cord via an implanted pump (Goldstein,

2001). This method of administration achieves levels of baclofen that far exceed those obtained by oral administration, and minimises adverse effects of the presence of high levels of this drug in the brain. GABA-mediated reduction of spasticity is potentiated by this approach.

2.6.2 Therapeutic management

The therapeutic team consists of the occupational and speech and language therapists, the dietician, as well as the physiotherapist. Occupational and physiotherapy are considered to be the cornerstones of the management of children with CP, and are used in conjunction with medical treatment modalities to maximise functional improvements. Occupational and physiotherapists will often work together to issue assistive devices, orthoses and walking aids, as well as to adapt seating systems tailored to each individual's home and school environment. It is generally believed that the best treatment outcomes are achieved with early intervention (Bleck, 1987; Campbell, 1996), in order to minimise the impact of secondary orthopaedic complications and to benefit from advantage of neural plasticity in young children.

2.6.2.1 Physiotherapy

The overall goal of physiotherapy treatment is the improvement of motor components such as ROM, muscle strength, selective muscle control, motor planning skills, co-ordination, and flexibility. The physiotherapist has a range of treatment modalities at his or her disposal, depending on the individual presentation of each patient.

Neurodevelopmental therapy (NDT)

Karl and Bertha Bobath were the founders of NDT in the 1940's, and this approach to rehabilitation still forms the cornerstone of the treatment of CP to date. The Bobaths' philosophy was that normal movement could only take place against a background of normal postural tone. Movement patterns following the normal stages of motor

development thus need to be facilitated, in an attempt to normalise postural control against gravity (Bleck, 1987; The Bobath Centre, 2007). Normal sensory-motor feedback is supplied by eliciting normal movement patterns (facilitation of automatic reactions), which results in reduced synaptic resistance to these normal motor patterns. The aim is for the child to eventually adopt these movement patterns on a voluntary basis.

Other neurodevelopmental approaches include the Voijta concept, which advocates the use of reflexology to improve postural control, and the Dorman-Delacato method, during which the child is subjected to a rigid therapy regimen involving passive movements or patterning performed by a variety of individuals in the child's home environment (De Groot et al., 2000). Further approaches include the Phelps method, during which the therapist performs passive movements, as well as the Peto method, which stipulates that all forms of therapy need to be administered by a single individual (the conductor) and which integrates rehabilitation with educational goals. All activity needs to be initiated by the child, instead of passively awaiting input from a therapist (Campbell, 1996).

Although NDT treatment approaches require involved therapy over a long period of time, they are now frequently combined with treatment programmes that focus on short- or medium-term goals (and that are often impairment-orientated), such as stretching and strengthening programmes to improve joint ROM or to strengthen specific muscles. These will now be discussed in more detail.

Casting, orthotics, and walking aids

External assistive devices are used to improve and / or maximise joint ROM, as well as to improve joint biomechanics and prevent secondary complications. Functional capacities can be optimised, and subsequent dependence on others diminished. Examples of frequently prescribed assistive devices include ankle-foot orthoses, splints of various natures, and CP chairs. Walking aids include walking frames and crutches, and are prescribed on an individual basis after careful assessment of the individual's physical needs. Occupational and physiotherapists frequently work in conjunction for this purpose.

Stretching programmes

Passive stretching of specific muscles is thought to help to improve muscle length and thus available ROM at the necessary joints in order to maximise function and participation, although Pin et al. (2006) have shown that evidence regarding increases in ROM, improved walking efficiency, as well as reductions in spasticity is lacking.

Strengthening programmes

As discussed above, weakness forms an integral part of the clinical presentation of CP. Historically, therapists have avoided strengthening programmes due to a fear of increasing the tone in already spastic muscles (Alfieri, 1982), and because children with CP were thought to lack selective muscle control to perform weight training (Damiano et al., 1995).

These assumptions were not based on research findings, and more recent research has in fact pointed out the importance of specific strengthening exercises for functional rehabilitation (Olney et al., 1990; Wiley and Damiano, 1998; Stackhouse et al., 2005). Damiano et al. (1995) hypothesise that strengthening programmes addressing muscle imbalances around a joint are more beneficial than performing surgery on a weak muscle, which only serves to reduce its contractile capabilities even further. The researchers have shown that children with spastic CP are indeed able to isolate muscle contractions in order to perform weight training over a period of six weeks, and have shown an increase in quadriceps muscle strength to normal levels (Damiano et al., 1995). An increase in antagonistic muscle activity was not found. The researchers suggested that future strengthening programmes should be conducted in a functional manner in order to improve carry-over of strengthening benefits to functional and participation levels.

Similarly, Dodd et al. (2003) and McBurney et al. (2003) targeted the ankle plantarflexors as well as the knee and hip extensors in a home-based six-week long isotonic exercise programme, with positive results for all three muscle groups. These

improvements coincided with a trend towards increased GMFM scores in terms of walking, running, and jumping, although these did not reach statistical significance (Dodd et al., 2003). Benefits were maintained for three months after termination of the exercise programme, which the researchers believed to be due to the resultant improved levels of activity, which in itself could be responsible for further muscle conditioning and strengthening (Dodd et al., 2003; McBurney et al., 2003). McBurney et al. (2003) also provided anecdotal reports on improvements in function and participation, but did not substantiate these with objective data.

Unger et al. (2006) also reported on a significantly improved degree of crouch gait in children with spastic CP who had undergone a school-based eight-week strength training programme. As in McBurney et al. (2003), functional improvements were made by the subjects, although changes on an impairment level (walking speed, cadence, stride length) were not significant.

Functional electrical stimulation (FES)

One modality gaining popularity in addressing both spasticity and weakness in CP is FES. It is characterised by the stimulation of intact peripheral nerves in order to activate their target muscles in a functional manner (Odstock Medical FES, 2006). By applying electrical stimulation to the agonist, muscle strengthening is brought about by increasing motor unit recruitment as well as by increasing contractile proteins, with resultant muscle hypertrophy (Reed, 1997). In addition, electrical stimulation applied to the antagonist can cause a decrease in tone in the agonist (Liberson, 1965) by the process of reciprocal inhibition (Apkarian and Naumann, 1991).

These two concepts represent different approaches to spasticity, as they promote the stimulation of both the agonist and antagonist muscle groups. As a result, recent studies on FES in the CP population have targeted spastic muscles and their antagonists to various degrees, using a wide spectrum of outcome measures to assess the effect of the intervention (Carmick, 1993; Van der Linden et al., 2003).

2.6.2.2 Multi-disciplinary approach: FES in combination with botulinum toxin

Several studies have advocated a multi-disciplinary approach to the management of children with CP (Wiley and Damiano, 1998; Dodd et al., 2003; Postans and Granat, 2005). Although extensive investigations into the separate effects of FES and botulinum toxin have been conducted (as discussed above), very few studies have combined these two modalities.

In their studies administering FES to the ankle dorsiflexors after botulinum toxin injections to the triceps surae muscle group, Johnson et al. (2002) and Johnson et al. (2004) have shown a statistically significant decrease in energy expenditure, an increased median walking speed, and greater stability during gait in adults after a stroke. When applying FES after a botulinum toxin injection in the upper limb, Hesse et al. (1998) have shown that muscle tone as assessed by means of the Modified Ashworth Scale was significantly reduced. Upper limb position at rest also improved markedly, and a resultant improvement in functional activities was noted. In contrast, short-term electrical stimulation to the lower leg has also been shown to augment the physiological effect of the toxin in adults (Hesse et al. 1995; Frasson et al., 2005).

In the paediatric population, Detrembleur et al. (2002) were unable to show significant improvements in active ankle ROM or gait variables following botulinum toxin combined with FES to the lower leg.

This range of results for the combined use of botulinum toxin and FES in the treatment of spasticity could potentially be due to the fact that different populations were used (adults versus children), and because a neurological diagnosis can cover a broad spectrum of impairments and varies considerably in terms of clinical presentation (Nelson and Ellenberg, 1978). No literature was found regarding optimal timing intervals for the introduction of FES after botulinum toxin.

2.7 Impact of varying clinical presentations of CP on research

Since the clinical presentations of CP vary so immensely, research methodologies need to be adapted to suit this population.

2.7.1 Outcome measures

Any variety of clinical presentations (as discussed above) could occur in children with CP. However, motor, behavioural, cognitive, and sensory deficits should not be considered as separate entities. The World Health Organisation advocates the International Classification of Impairment, Function, and Participation (ICF) (2001) as a holistic approach to understanding and classifying disability. Under this banner, the impact of specific impairments is placed into an integrated functional context, and outcome measures are aimed at assessing changes in individual participation levels.

Nelson and Ellenberg (1978) have stated that a neurological diagnosis can cover a broad spectrum of impairments and varies considerably in terms of clinical presentation. Within a specific diagnosis, for example, mobility and functional capability vary immensely. Treatment outcomes should thus be set on an individual basis, and cannot always be standardised across patient groups (Martin and Epstein, 1976; Stanger and Oresic, 2003).

Improvement (or deterioration) in an individual's participation levels in daily activities is difficult to assess by means of an objective scale or tool, as is reflected in the wide variety of outcome measures addressing a range of impairments and functional deficits which have thus far been implemented in the CP population. Treatment is tailored according to individual needs, and therefore standardised outcome measures are not always applicable tools to assess treatment efficacy on function and participation. For that reason, previously used outcome measures were mainly aimed at evaluating treatment outcomes on an impairment level, including measurements of step length, passive and active ankle ROM, frequency of heel strike during gait, and muscle strength (Carmick,

1993 and 1995; Hazlewood et al., 1994; Comeaux et al., 1997; Bertoti et al., 1997; Van der Linden et al., 2003; Durham et al., 2004).

On a functional level, gait parameters and posture as well as energy expenditure during gait have been examined, while anecdotal comments on functional changes have addressed participation. Tools such as two- or three-dimensional gait analysis are frequently used for this purpose, as well as pedograph and physiological cost index (PCI) data. Manual muscle testing and EMG analysis also form part of the list of assessment tools available to researchers. However, a vast amount of research reports on outcomes by means of anecdotal comments regarding changes on participation level (Carmick 1993 and 1995; Bertoti et al., 1997; Van der Linden et al., 2003).

2.7.2 Study designs

Given that such a wide variety of clinical presentations exist in CP, it is difficult to conduct structured research by matching subjects in a randomised controlled trial. In order to compensate for the great variability of clinical presentations amongst subjects, Martin and Epstein (1976) and Gonnella (1989) have advocated the use of more single-subject research (N=1) in the CP population. In this design, each subject acts as his own control (Tervo et al., 2003). Gonnella (1989) and Tervo et al. (2003) have further supported the implementation of single-subject research in the CP population, as this study design places the focus on recognisable individual change that is relevant on a clinical level. Replicating the study in as many subjects as possible augments the external validity of research results (Gonnella, 1989). The majority of previous research in the CP population has thus been conducted as case studies and single-subject research (Carmick, 1993 and 1995; Bertoti et al., 1997; Durham et al., 2004).

Due to the lack of evidence and the diverging approaches concerning the use of FES in the paediatric population, a systematic review was conducted on this topic with the aim to synthesise and analyse available data. This is presented in the following chapter.

CHAPTER 3

SYSTEMATIC REVIEW – FUNCTIONAL ELECTRICAL STIMULATION (FES)

As discussed in previous chapters, the leg musculature of children with cerebral palsy (CP) is affected by spasticity as well as by marked weakness. The ankle dorsiflexors (antagonist) and plantarflexors (agonist) as well as the hip extensors are affected and could thus benefit from strengthening (Wiley and Damiano, 1998). Although initial studies advocated the strengthening of non-spastic muscles only for fear of exacerbating existing spasticity (Alfieri, 1982), more recent evidence suggests that strengthening of spastic muscles can result in significant functional improvements (Dodd et al., 2003). Both weakness and spasticity contribute to the higher energy expenditure during gait in children with CP compared with age-matched controls (Rose et al., 1990). This in turn could lead to decreased levels of participation, and secondary complications due to a more sedentary lifestyle (Brunstrom, 2001).

One modality gaining popularity in addressing weakness or loss of force generating ability around the ankle in CP is FES. It can be distinguished from neuromuscular electrical stimulation (NMES) in that NMES is aimed at muscle strengthening and / or spasticity reduction and is not always applied functionally (Bührs, 2007). NMES is applied at a higher intensity than FES, and the timing of the stimulation is set according to muscle fatigue (Bührs, 2007). In comparison, FES is aimed at augmenting function, and thus only requires intensity settings allowing for the required action to take place.

By applying NMES to the agonist, muscle strengthening is brought about by increasing motor unit recruitment as well as by increasing contractile proteins, with resultant muscle hypertrophy (Reed, 1997). In addition, electrical stimulation applied to the antagonist can cause a decrease in tone in the agonist (Liberson, 1965) by the process of reciprocal

inhibition (Akarian and Naumann, 1991). These differing concepts suggest that stimulation to both the agonist and antagonist muscle groups can be effective.

Recent studies on FES in CP have targeted various muscle groups, including the tibialis anterior (Carmick, 1993; Bertoti et al., 1997; Comeaux et al., 1997; Durham et al., 2004; Pierce et al., 2004) and triceps surae muscles (Carmick, 1993; Bertoti et al., 1997; Comeaux et al., 1997; Pierce et al., 2004) as well as the gluteals (Bertoti et al., 1997), quadriceps (Bertoti et al., 1997) and hamstring muscles (Carmick, 1993). These studies used a wide spectrum of outcome measures and reported on varying findings regarding muscle strength and spatiotemporal gait parameter improvements, functional gains, and carry-over effects.

Stimulation can be administered by either surface (S-FES) or percutaneous (P-FES) stimulation. With S-FES, electrodes are placed on the skin, whereas they are implanted into the target muscle for P-FES (Orlin et al., 2005). In a comparison study, P-FES was perceived to be significantly more comfortable for patients (Chae and Hart, 1998) and resulted in more marked increases in active ankle dorsiflexion (DF) angles during gait (Pierce et al., 2004), possibly because P-FES bypassed cutaneous receptors, allowing for a stronger muscle contraction. P-FES, however, is a costly procedure (Chae and Hart, 1998) and may thus not be readily available to therapists and patients. For that reason, S-FES remains the preferred mode of stimulation in the clinical setting.

Current available evidence on electrical stimulation highlights uncertainty regarding the choice of target muscle(s) in the presence of spasticity (Liberson, 1965; Apkarian and Naumann, 1991; Reed, 1997). The objective of this review was thus to systematically assess and synthesise the existing evidence regarding the use of FES in children with CP when applied to the lower limb. Key aspects included the assessment of the effect of FES on kinematic and spatiotemporal gait parameters as well as on activities of daily living. The stimulation protocols and target muscles used for this purpose were also examined.

3.1 Review Method

The following inclusion and exclusion criteria were applied to select studies for this review.

3.1.1 Inclusion criteria

Intervention studies published in English were considered for inclusion in the review if they reported on primary data. All publications from the date of inception of the relevant database until December 2006 were included. Within each study, the stimulation had to have been applied to any lower leg muscle(s) during a functional activity by either S-FES or P-FES as a treatment program, and subjects had to have been under the age of 18 years with a diagnosis of CP. As the reviewers wanted to assess the evidence on carry-over effects into a functional setting, the stimulation device was required to be removed or switched off at the time of testing.

3.1.2 Exclusion criteria

Articles were excluded if the full-text articles were not available in South Africa. Studies were also excluded if subjects presented with any additional neurological conditions or a combination of movement disorders (e.g. spasticity with ataxia), or if they had undergone orthopaedic surgery to the affected leg within six months prior to the start of the intervention.

3.1.3 Search strategy (Figure 1)

The primary reviewer conducted a comprehensive search, repeated four times between October and December 2006. Internet databases accessible via the Stellenbosch University library service - CINAHL, Pubmed, Journals@Ovid, ScienceDirect: Medicine

and Dentistry and Neurosciences, PEDro, ProQuest: Medical Library and Science Journals, PsycInfo – were searched**.** A wide variety of key words were used in order to accommodate for the different indexing terms of each database (refer to Appendix 1). MeSH terminology and truncation was used as appropriate for each individual database. A hand search was also conducted by perusing the reference lists of the Poster and Platform Presentations for the 2004 and 2005 Combined Sections Meeting of *Pediatric Physical Therapy*, as well as the references cited during the South African Neurodevelopmental Theory Association Congress of 2005. In addition, pearling was done on all relevant articles to source additional literature.

3.1.4 Quality of evidence

Each study was critically appraised by two independent reviewers using the Critical Review Form for Quantitative Studies developed by the McMaster University Occupational Therapy Evidence-Based Practice Research Group (Law et al., 1998). It contains 15 questions of equal weight, all to be answered by yes (allocated one point), no (allocated zero points), or not discussed (allocated zero points). The secondary reviewer was blinded to each article's author and publication source, as this could have influenced the scoring process.

3.1.5 Data processing

All articles included in the review were summarised on an Excel spreadsheet in terms of authors, date, research design, sample size, outcome measures and measurement instruments used, stimulated muscles, critical appraisal score, and level of evidence (Sackett, 1996) (Table 1). The reviewers intended to conduct a meta-analysis of collated data if at least three studies had used homogeneous outcome measures and if data for these was available. As this was impossible, outcomes will thus be discussed narratively.

Database searched	Strategy 1			Strategy 2		
	Hits	Accepted after reading title/ abstract (including duplicates)	Duplicates	Hits	Accepted after reading title/ abstract	Duplicates
Pubmed	55	9		22	9 (all in strategy 1)	9
CINAHL	44	14	5	0	0	0
PEDro	1	1	0	0	0	0
PsycINFO	16	1	1	0	0	0
Cochrane	6	0	0	0	0	
Journals@Ovid	123	7	2	77	8 (all in strategy 1)	8
ProQuest (Medical Library + Science Journals)	29	6	6	0	0	0
ScienceDirect	577	9	4	389	12 (all in strategy 1)	12
Total	851	47	18	488	29 (all in strategy 1)	29
Total after exclusion of duplicates (strategy 1 and 2): 29						
Hand search	Hits: 2; Duplicates: 2					

Figure 1. Search process

Pearling	Hits: 8; Duplicates: 0
Total after reading titles/ abstracts (strategy 1 and 2)	37

Exclusion after reading articles

Strategy 1: n=24   Strategy 2: N/A   Pearling: n=8
(all duplicates)

Included in review (n=5)
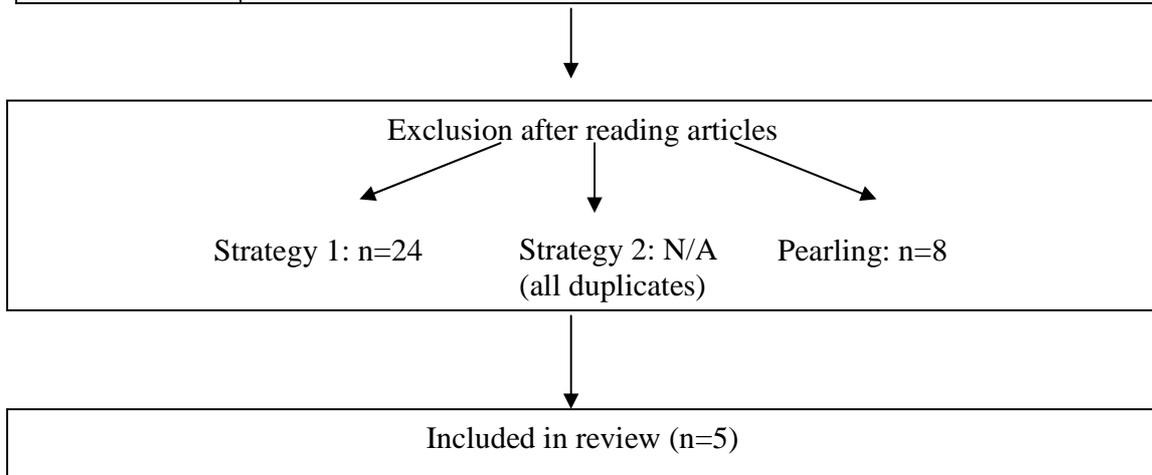
Figure 1. Search process (continued)

Table 1. Methodological details

Authors	Design	Sample size	Outcome measures
Carmick (1993)	Case studies	3	Heel strike incidence; frequency of falling; foot position; active ankle ROM; step length; walking speed; functional abilities; muscle strength; energy efficiency during gait
Durham et al. (2004)	ABA	10	Walking speed; frequency of heel strike; step length; stance time; double stance; swing time
Comeaux et al. (1997)	Cross-over design	14	DF angle at initial contact
Bertoti et al. (1997)	Case reports	2	Walking speed; hip ROM; functional abilities; step width and length; balance; use of orthoses
Pierce et al. (2004)	Case reports	2	DF angles during gait; isometric muscle force; muscle force during gait; ankle work during gait; walking speed; cadence; step length walking speed; cadence; step length

DF=dorsiflexion; ROM=range of motion

Table 1. Methodological details (continued)

Measurement instruments	Muscles stimulated	Critical appraisal score	Sackett's level of evidence
PCI; pedographs; video analysis; observation	TA; TA/GA; GA; Hamstrings	7/15	4
Questionnaire; video analysis	TA	8/15	2C
Video analysis	TA/GA; GA	12/15	2C
Pedographs; EMG analysis	Gluteals; TA; GA; Quadriceps	8/15	4
3-D gait analysis (video data and ground reaction force data); isokinetic dynamometry	TA; GA/TA; GA	8/15	4

PCI=physiological cost index; TA=tibialis anterior muscle; GA=gastrocnemius muscle

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3.2 Results

Primary and secondary searching was conducted and the researchers are confident that the majority of evidence regarding the use of FES in the CP population was located, as 66% of articles found were duplicated at least once.

3.2.1 Description of studies

There was full agreement between the two reviewers regarding the final inclusion of articles for the review, and final scores were awarded by discussion. Studies were excluded due to subjects being older than 18 years, stimulation not being applied functionally, stimulation not being used as a treatment programme, stimulation devices not being removed or switched off at the time of outcome testing, and articles not being available in South Africa.

Of the studies included in this review, three articles were case reports (Carmick, 1993; Bertoti et al., 1997; Pierce et al., 2004), while Durham et al. made use of a single-subject research design and Comeaux et al. (1997) used a cross-over design (Table 1). In terms of Sackett's (1996) hierarchy of evidence, two articles ranked as evidence level 2C (Comeaux et al., 1997; Durham et al., 2004), while the other three studies ranked as level 4 (Carmick, 1993; Bertoti et al., 1997; Pierce et al., 2004).

3.2.2 Methodological quality

Although it was initially decided that articles scoring below 8/15 (i.e. below 50%) would be excluded from the review, the low number of articles scoring above this cut-off point necessitated the inclusion of an article scoring 7/15 as well. The average score was 8.8/15 (SD=1.9), ranging from 7/15 (Carmick, 1993) to 12/15 (Comeaux et al., 1997) (Table 1). All studies clearly stated the purpose of their respective research and conducted a thorough review of the relevant literature. Although three of the five articles were case

studies, the reviewers deemed this design appropriate, owing to the variability of the clinical presentation of CP.

None of the studies reported on the reliability of their outcome measures, and only Comeaux et al. (1997) referred to the validity of the outcome measures used. Carmick (1993) did not describe the intervention in sufficient detail, and no researchers reported on potential contamination of results by concomitant therapeutic treatment. Four articles (Carmick, 1993; Bertoti et al., 1997; Comeaux et al., 1997; Durham et al., 2004) reported on the clinical and / or statistical significance of their results, although Bertoti et al. (1997) did not implement appropriate analysis methods to support their statements, and the link between the results and subsequent conclusions was unclear in a study by Carmick (1993).

3.2.3 Subjects

One study (Carmick, 1993) failed to adequately describe the sample in sufficient detail. None of the reviewed studies provided information on where the subjects had been recruited from or motivated their choice of sample size. The average age of the subjects was 8.0 years (range: 1.6 – 15 years), with a median of four subjects per sample. Subjects with hemiplegia accounted for 53.9% of the study participants, 41.2% presented with diplegia, and subjects with quadriplegia and ataxia each accounted for 2.9% of the sample.

3.2.4 Intervention

The target muscle(s) as well as stimulation protocols and dosages implemented in the reviewed studies will now be discussed.

3.2.4.1 Muscles stimulated

Different studies applied S-FES to the tibialis anterior (Carmick, 1993; Durham et al., 2004), gastrocnemius (Carmick, 1993; Comeaux et al., 1997), tibialis anterior and gastrocnemius alternatingly (Carmick, 1993; Comeaux et al., 1997), and hamstring muscles (Carmick, 1993). P-FES was applied to the gluteals and quadriceps (Bertoti et al., 1997), as well as the gastrocnemius (Bertoti et al., 1997; Pierce et al., 2004) and the tibialis anterior (Bertoti et al., 1997; Pierce et al., 2004) muscles. Pierce et al. (2004) also applied stimulation to the gastrocnemius and tibialis anterior muscles alternatingly (Table 1).

Comeaux et al. (1997) included a four-week withdrawal phase in their research design, while Durham et al. (2004) allowed 12 weeks after completion of the intervention before re-assessment. Carmick (1993) commented on the carry-over effect at differing periods of time during the respective case studies (ranging from two days to one year post intervention). Pierce et al. (2004) and Bertoti et al. (1997) were the only researchers not to include a withdrawal phase in the research design, and assessed the dependent variables immediately after each of the stimulation phases.

3.2.4.2 Stimulation dosage and parameters

The stimulation parameters as well as the length of exposure to the intervention varied between studies, with the latter ranging from one week (Pierce et al., 2004) to approximately nine months (Carmick, 1993) (Table 2). No details regarding stimulation parameters were provided by Carmick (1993).

Table 2. Stimulation dosage and parameters

	Minutes per day	Days per week	Weeks	Frequency (Hz)	Intensity (mA)	On:off (s)	Pulse width (micro-seconds)	Ramp (s)
Comeaux et al. (1997)	15	3	8	32	N.S.	15:15	100	0.5
Bertoti et al. (1997)	15	5	28 and 40	N.S.	20	1:2.5	1-200	N.S.
Pierce et al. (2004)	45 mins twice a day	7	1 week per intervention	50 (except for tibialis anterior stimulation in subject B: 20)	20		200	N.S.
Durham et al. (2004)	N.S.	N.S.	12 weeks per phase	40	15-100		3-350	0-4

N.S. = not specified

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3.2.5 Outcome measures

A wide variety of outcome measures were used to assess the efficacy of FES on impairment, functional, and participation levels (Table 3). However, in keeping with the aim of this review, only outcome measures that were used in at least three of the reviewed studies and that relate to gait will be discussed at this point. Additionally, most studies reported on functional and / or participation changes in an anecdotal manner, which renders the discussion of these outcomes difficult in a group context.

3.2.5.1 Functional changes

Walking speed

The effect of stimulation will be discussed in terms of the different target muscles. When the tibialis anterior and the gastrocnemius muscle were stimulated reciprocally, an increase in walking speed was recorded after the intervention (increase of 3.9m/min and 3.5m/min in two subjects) (Carmick, 1993) while Bertoti et al (1997) showed no change in walking speed after 28 and 40 weeks of treatment in two subjects. When the tibialis anterior muscle was stimulated alone (Pierce et al., 2004), an increase of 0.01m/s (normalized for height) was recorded by Durham et al. (2004).

After a treatment period of one week using during which the tibialis anterior and gastrocnemius muscles were stimulated reciprocally, Pierce et al. (2004) recorded slower walking speeds with the stimulating device on compared to off (average difference of 2.7m/min). When only the tibialis anterior muscle was stimulated, subjects showed a slightly faster walking speed with the device switched on compared to with the device switched off (difference of 3.4m/min). This was the only study which stimulated the triceps surae alone, and recorded a 1.12m/min faster walking speed in one subject with the stimulation device switched on, while a second subject showed a slower speed with

the device switched on (1.8m/min) difference. This study's stimulation was applied for one week per target muscle group and examined the immediate effect of the stimulation on walking speed.

Step length

This outcome measure was investigated by four of the five studies (Carmick, 1993; Bertoti et al., 1997; Durham et al., 2004; Pierce et al., 2004). Durham et al. (2004) found no difference in step length in the affected leg after three months of tibialis anterior muscle stimulation, which contrasted with the 7.7cm increase in step length recorded in Bertoti et al. (1997). When the tibialis anterior and gastrocnemius muscles were stimulated reciprocally, a decrease of 3.9cm was recorded in one subject, compared to a 1.0cm increase in another (Carmick, 1993).

In all the three studies assessing step length and walking speed, one of the two variables always remained unchanged. Only Bertoti et al. (1997) evaluated cadence, and found that a decrease in cadence accompanied a greater step length to produce an unchanged walking speed in two six year-old subjects. A lack of raw data prevented the reviewer from conducting cadence calculations from Pierce et al.'s study (2004), while both walking speed and step length (and thus cadence) remained unchanged in Durham et al. (2004).

3.2.5.2 Changes in activities of daily living and participation

Functional improvements were only reported on anecdotally and ranged from a longer distance that a subject was able to gallop (Carmick, 1993) to increased participation in

Table 3. Data extraction framework

Demographics	Intervention	Independent variables		
		Impairment level	**Functional level**	**Participation level**
Average age of subjects	P-FES / S-FES	Number of heel strikes at initial contact	Walking speed	Functional independence/ activities of daily living
Diagnosis (type of CP)	Length of intervention programme	Passive ankle ROM	Step width and length	
Sample size	Follow-up assessment	Muscle strength	Stance time	
	Stimulated muscles	Foot position	Double stance time	
	Stimulation parameters	Hip ROM and position	Swing time	
	Outcome measures used	Active ankle DF angles during gait	Cadence	
		Isometric muscle force	Posture	
		Muscle force during gait	Use of orthoses	
		Ankle work during gait	Posture	
			Balance	

P-FES=percutaneous FES; S-FES=surface FES; ROM=range of motion; DF=dorsiflexion

age-appropriate sporting activities, a decreased frequency of falling (Carmick, 1993; Bertoti et al., 1997), and less need for external assistance during walking (Carmick, 1993; Bertoti et al., 1997).

3.3 Discussion

The findings of this review seem to suggest that FES applied to the lower limb in children with CP has a positive effect on gait and function. However, given the wide variety of intervention protocols and outcome measures used in the reviewed articles, analysis of the outcomes was difficult.

3.3.1 Methodological quality

Three of the five articles included in the review were case reports. Validity and reliability of outcome measures were poorly reported on, and study samples were generally not well described. The average score of 8.8/15 points reflects a general lack of structured research in this field. As the CP population is very diverse and physical presentations range greatly amongst individuals (Stanger and Oresic, 2003), it is difficult to conduct research with a high measure of external validity. If sampling were to conform to a strict set of criteria, the generalisability of the outcomes would be low. Consequently, single-subject research designs (Martin and Epstein, 1976) or within-subject designs are recommended as more appropriate for this population. The advantage of the within-subject design is that the same subjects can be used repeatedly, with a washout period between intervention phases (Schuster and Powers, 2005). This design allows the use of fewer subjects, and has a higher statistical power than if subjects are only used once (Schuster and Powers, 2005). Single- or within-subjects are suggested for future research in order to facilitate clinical decision-making regarding the choice and timing of interventions for specific clinical presentations.

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3.3.2 Subjects

According to Bleck (1987) and Campbell (1996), early physiotherapy intervention delivers the most promising outcomes, as movement patterns are not yet as fixed and secondary deformities not as prevalent. The average age of subjects in this review was 8.0 years, which falls into the age bracket deemed suitable for early intervention (Bleck, 1987; Campbell, 1996). The present review, however, revealed mixed outcomes in terms of age. A 6.7 year-old subject in Carmick (1993) showed an increase of 13.9m/min after receiving stimulation therapy, whereas a subject of similar age showed no change in terms of walking speed in another study (Bertoti et al., 1997). Subjects of around ten years of age showed lesser improvements in terms of walking speed (Carmick, 1993; Pierce et al., 2004). The greatest effect size was recorded in the 6.7-year old subject (Carmick, 1993), which seems to suggest that younger subjects respond more favourably to stimulation treatment. However, the lengths of the stimulation protocols varied significantly across these studies, and could account for different treatment effects.

Younger subjects tended to present with an increased step length after intervention (Bertoti et al., 1997), whereas older subjects (Durham et al., 2004) showed no change in this outcome variable. As children with diplegic CP generally rely on increases in cadence to increase their walking speed with a less pronounced increase in step length (Abel and Damiano, 1996), data of at least two of these parameters are necessary to deduce clinical efficacy of FES. A change in walking speed, cadence, or step length following an intervention needs to be quantified in terms of the concomitant changes in the other variables in order to provide clinically relevant data. In addition, improvements in all or some of these variables may occur at the cost of energy economy during gait (Abel and Damiano, 1996). It is thus important to report on changes in spatiotemporal gait parameters in conjunction with gait economy measures, as improvements in some of these gait parameters may lose their clinical relevance when viewed in conjunction with energy economy during gait.

3.3.3 Intervention

Although studies stimulating the same target muscle(s) differed from each other in terms of stimulation parameters and subject demographics, grouping the results according to target muscle allows some interpretation of optimal treatment approaches. Stimulation of the tibialis anterior muscle seems to have limited success (Durham et al., 2004) and carry–over effect (Carmick, 1993), or could even result in a deterioration of the gait pattern (Carmick, 1993). A higher incidence of heel strike with a greater carry-over effect was evident when the tibialis anterior muscle was stimulated alternatingly with the plantarflexors (Carmick, 1993; Comeaux et al., 1997; Pierce et al., 2004). Similar improvements were also found when the triceps surae muscle group was stimulated alone (Carmick, 1993). Increased active DF range of motion, a higher incidence of heel strike at initial contact, and greater functional independence maintained for one year after the end of the intervention program have been reported with this application protocol (Carmick, 1993). Future research specifically regarding different stimulation parameters is needed in order to allow conclusive deductions on optimal treatment protocols to be made.

Although the main aim of FES is to facilitate function rather than to increase individual muscle strength, strengthening may have occurred due to repetitive activity in muscles that were previously inactive or weak. FES may thus contribute to some strengthening and result in subsequent increases in ROM as secondary effects, thereby contributing to the carry-over effects reported by Carmick (1993).

Wiley and Damiano (1998) have shown that both the dorsi- and plantarflexors are weak in CP, and thus both need strengthening. Targeting only one of these muscles can thus create a muscle imbalance, which could account for some of the deterioration in gait reported by Carmick (1993). Furthermore, the dorsiflexors are stronger than their antagonists in CP (Dietz et al., 1981; Wiley and Damiano, 1998). Stimulation of this

muscle group alone would thus have further strengthened the "stronger" of the two muscles without addressing the weak plantarflexors.

In comparison, stimulating the plantarflexors alone showed positive outcomes (Carmick, 1993; Pierce et al., 2004). As the triceps surae complex plays a vital role in stabilising the knee and ankle during gait as well as to decelerate the anterior movement of the tibia on the foot during stance (Sutherland et al., 1980), stimulation of this muscle group alone could account for the positive intervention results recorded by Carmick (1993) and Pierce et al. (2004). Olney et al. (1990) have also shown that the positive work done by the plantarflexors during gait in CP is a third less than in typically developing subjects, and positive intervention outcomes with triceps surae stimulation alone could thus also be attributed to improved work output by this muscle group. Only one study targeted the hamstring muscle alone (Carmick, 1993), which immediately resulted in improved gait as well as functional capabilities (including galloping, riding a bicycle, and balancing), maintained for four weeks following the intervention. More rigorous research investigating proximal muscle strength needs to be conducted in order to confirm these findings.

In contrast to what has previously been a hesitancy to stimulate spastic muscles, the functional improvements reported on in the reviewed studies seem to suggest that FES does not increase spasticity. Although FES is not aimed at improving muscle strength, it can be expected to cause at least some strength gains due to changes in muscle composition, as well as due to improvements in neural drive (a point made by Bührs, 2007), subsequent improvements in motor learning, and thus resulting in functional gains. As most of the results discussed above were obtained during case studies (Carmick, 1993; Bertoti et al., 1997; Pierce et al., 2004) and thus have low levels of evidence, extrapolations to the greater CP population should not be made without support from further research.

3.3.4 Stimulation parameters

Comeaux et al. (1997) and Bertoti et al. (1997) applied electrical stimulation during gait and gait subtasks by means of FES and NMES, respectively. However, the outcomes used in these studies were not assessed separately after FES and NMES, but were assessed at the end of the entire stimulation programme. It is thus not possible to attribute the effects of the intervention to either NMES or FES, as both were used. Future studies should thus clearly distinguish between FES and NMES and base their choice of intervention on the required aim of the intervention - functional improvement versus muscle strengthening versus spasticity reduction. Outcomes should also be assessed separately for these two intervention modes.

As a guideline, frequencies of around 30Hz are used during FES to elicit a smooth contraction (De Vahl, 1992), as a balance between muscle fatigue and an effectively maintained contraction occurs in this range. These settings were generally used in the reviewed studies (Table 2). De Vahl (1992) further states that most stimulation devices accommodate a pulse width range of 0.2 – 0.4 microseconds, and the settings of all reviewed studies fall into this range. It is interesting to note that both Bertoti et al. (1997) and Pierce et al. (2004) made use of an unusually low amplitude of 20mA. The higher the amplitude, the more nerve fibers are recruited, and thus a more effective muscle contraction is achieved (Reed, 1997). Although these researchers reported similar functional (Bertoti et al., 1997) and kinematic (Bertoti et al., 1997; Pierce et al., 2004) improvements as other studies, they implemented P-FES, which could account for comparable treatment effects to those of other studies, while using lower intensity settings.

3.3.5 Outcome measures

Although an extensive number of outcome measures were implemented by the reviewed studies, they were mostly aimed at assessing changes in impairment and function (Table 3). Improvements in activities of daily living were assessed anecdotally, which rendered structural analysis of data impossible. As impairment-orientated improvements cannot be assumed to effect functional gains (Van der Linden et al., 2003), future investigations should incorporate participation targeted outcome measures (World Health Organisation, 2001).

One of the difficulties of research in a heterogeneous population such as CP is the significantly different clinical presentations between subjects, which render objective comparisons of participation levels between subjects inappropriate. In order to compensate for this situation, single- or within-subject research designs during which change is assessed on an individual basis have been suggested as a more appropriate approach in the CP population (Martin and Epstein, 1976). Although this design has a low level of evidence, the translation of available evidence into clinical practice becomes more relevant.

3.4 Conclusion and implications for research

This review has revealed that a wide variety of FES application methods and stimulation protocols exist. Although treatment results were often not assessed in a standardised manner, available evidence seems to suggest that FES application to either the triceps surae complex alone or in conjunction with the tibialis anterior muscle is favourable. Due to the lack of evidence regarding the effects of proximal muscle stimulation, further studies need to be conducted in order to substantiate available data. Most studies showed a low level of evidence and also did not clearly distinguish FES from NMES. Future research needs to ensure that the mode of application (FES or NMES) coincides with the

aims of the intervention in order to provide results attributable to that intervention. Additionally, the majority of outcome measures in the reviewed studies were impairment focused. Future studies thus need to strive towards assessing the impact of their intervention on a more holistic level.

CHAPTER 4

METHODOLOGY

Following the literature review, it is apparent that very few studies have previously been conducted to determine the efficacy of functional electrical stimulation (FES) to the lower leg after botulinum toxin into the triceps surae muscle in the cerebral palsy (CP) population. The current study therefore aims to address the following question:

4.1. Research question

What are the short- and medium-term effects of FES applied to the gastrocnemius and tibialis anterior muscles after a botulinum toxin injection into the triceps surae muscle in children aged four to six years with spastic hemiplegia due to CP?

4.2 Objectives

The objectives of the study were to:
   a) determine the effect of FES after a single botulinum toxin injection on:
      i.   the average dorsiflexion (DF) angle at initial contact during gait
      ii.   self-selected walking speed
      iii. strength of the ankle dorsi- and plantarflexors
      iv.   energy expenditure during gait
   b) determine the caregivers' perceptions of the impact of the intervention on their children's walking, function, and participation
   c) determine optimal timing intervals for introducing FES after a botulinum toxin injection

4.3 Hypotheses

H_0   FES to the lower leg after botulinum toxin into the triceps surae muscle has no effect on energy expenditure during gait, self-selected walking speed, ankle dorsi- and / or plantarflexor strength, the average ankle DF angle at initial contact, or subjective caregiver assessments of gait and function in children with spastic hemiplegic CP.

H_1   FES after botulinum toxin will influence the average ankle DF angle at initial contact during gait.

H_2   FES after botulinum toxin will influence energy expenditure during gait.

H_3   FES after botulinum toxin will influence the strength of the ankle dorsi- and plantarflexors.

H_4   FES after botulinum toxin will influence self-selected walking speed.

H_5   FES after botulinum toxin will influence caregivers' subjective gait assessments.

4.4 Research design

Experimental research in the form of a single-subject (N=1) design with a multiple-baseline approach across subjects was conducted (Figure 2). Data was collected in four phases in an ABCA pattern, where phase A represents no intervention, phase B represents the time period immediately following the botulinum toxin injection, and phase C represents the FES phase.

Population: four to six year old children with
hemiplegic CP with a spastic equinus gait pattern

Pilot trial (N=8): to standardise the procedure
and to determine intra-subject variability for
the following outcome measures (tested in each
session):
- Isometric muscle strength
  (dynamometry)
- Energy expenditure during gait
  (Energy Expenditure Index)
- Ankle DF angles at initial contact (2-
  D gait analysis)
- Walking speed (2-D gait analysis)

Main study sampling (N=5)

Baseline testing: same outcome measures as during the pilot trial, repeated three
times over a one week period (measurement sessions 1 – 3):
- Isometric muscle strength (dynamometry)
- Energy expenditure during gait (Energy Expenditure Index)
- Ankle DF angles at initial contact (2-D gait analysis)
- Walking speed (2-D gait analysis)

Botulinum toxin injection

Measurement session 4 (same four outcome measures used at baseline)

| Intervention protocol 1 (n=1) | Intervention protocol 2 (n=1) | Intervention protocol 3 (n=1) | Intervention protocol 4 (n=1) | Intervention protocol 5 (n=1) |

3 days

7 days

14 days

32 days

35 days

Measurement session 5 and start
of FES (same four outcome measures used
at baseline plus self-compiled questionnaire)

Figure 2: Study design

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┌─────────────────────────────────────────────────────────────────────┐
│                         FES for four weeks                          │
└─────────────────────────────────────────────────────────────────────┘
                                    │
                                    ▼
┌─────────────────────────────────────────────────────────────────────┐
│   Measurement session 6 (same four outcome measures used at baseline plus self- │
│                      compiled questionnaire)                        │
└─────────────────────────────────────────────────────────────────────┘
                                    │
                                    ▼
┌─────────────────────────────────────────────────────────────────────┐
│                    60 day withdrawal period (no FES)                │
└─────────────────────────────────────────────────────────────────────┘
                                    │
                                    ▼
┌─────────────────────────────────────────────────────────────────────┐
│   Measurement session 7 (same four outcome measures used at baseline plus self- │
│                      compiled questionnaire)                        │
└─────────────────────────────────────────────────────────────────────┘
                                    │
                                    ▼
┌─────────────────────────────────────────────────────────────────────┐
│                  Data processing and statistical analysis           │
└─────────────────────────────────────────────────────────────────────┘
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Figure 2: Study design (continued)

4.5 Population

Although children with both hemiplegic and diplegic spastic CP can be expected to walk, their gait patterns display different characteristics and are thus difficult to compare (Brown et al., 1991; Steinwender et al., 2001). Since one third of all patients with CP present with hemiplegia (Brown, 1984), the target population of this study has been limited to children with hemiplegia who exhibit a spastic equinus during gait. Children between the ages of four and six years were considered for inclusion in the study, as the gait pattern of this group is consistent (Berger et al., 1984).

4.6 Sampling

The databases of the Paediatric Departments of the Tygerberg and Red Cross Children's Hospitals were searched for potential subjects in the greater Cape Town area. Furthermore, children were referred by the physiotherapy departments of Tygerberg

Hospital as well as Eros and Paarl Schools (schools for children with special needs situated in the Cape Metropole) for assessments for inclusion into the study.

4.6.1 Inclusion criteria

For inclusion into the study, subjects needed to:

- present with a definitive diagnosis of hemiplegia with spastic equinus due to CP (diagnosed by a paediatrician with experience in CP)
- be eligible for a botulinum toxin injection, as decided by a multi-disciplinary team (paediatrician, orthopaedic surgeon, and physiotherapist)
- be between four and six years old
- be ambulant with or without assistive devices and / or orthoses
- have full passive range of motion (ROM) of the knee and ankle of the affected leg
- reside in the greater Cape Town area
- speak and understand either English, Afrikaans, or Xhosa
- have a caregiver that speaks either English, Afrikaans, or Xhosa
- be able to understand basic instructions
- have supplied assent for participation
- have written caregiver consent.

4.6.2 Exclusion criteria

Subjects were excluded from the study if:

- they presented with any additional neurological problems
- they had previously received chemodenervation therapy of any kind
- they had undergone achilles tendon lengthening or other orthopaedic surgery to the affected lower limb within the past 24 months
- they had received previous FES treatment

- they were unable to attend all specified measurement and / or intervention sessions.

4.7 Pilot trial

In order to establish the stability of the CP condition in terms of self-selected walking speed, ankle dorsi- and plantarflexor muscle strength, energy expenditure during gait and ankle angles at initial contact during gait over a period of four weeks, a pilot trial was conducted. It included both subjects with a diagnosis of spastic hemiplegic CP (N=5) as well as typically developing children (N=3). The latter group was included in the pilot trial to establish the measurement variance in typically developing children over four weeks. Variations in the dependent variables needed to be taken into consideration during effect size calculations in the main study (i.e. changes in measurements in the main study needed to exceed the degree of variability found in the pilot trial in order to be considered significant). The data of the pilot trial also helped to establish the number and spread of baseline measurements for the main study, and served to refine the measurement procedures.

Selective sampling for the subjects with CP (subjects one to five) was conducted at Eros School as well as at Red Cross Children's Hospital, and included subjects based on the inclusion criteria described above. Subjects six to eight (typically developing children) were family members of the primary researcher as well as children from colleagues. No intervention was administered to any of the subjects, as the study was aimed at assessing the stability of the condition over time, as well as at refining the measurement procedure. Written explanations of the study with all necessary information (available in English and Afrikaans; refer to Appendix 2) were given to the caregivers of the subjects selected for participation, with an explanation that their children would not receive the intervention. Caregivers were then asked to sign an informed consent form in the language of their choice (refer to Appendix 3), and verbal assent for participation was obtained from the subjects. Subjects participating in the pilot trial were tested by the same measurement procedure as intended for the main study. Measurements were taken over a period of four

weeks on days one, three, five, seven, 15, and 28. Subjects one to four were assessed at Eros School, whereas data for subject five were collected at Red Cross Children's Hospital. For the typically developing children, data were collected in a location convenient for both the caregivers and the researcher, ensuring that there was sufficient space for the ten metre walkway as well as for the set distance of three metres between the subject and the camera. If applicable, subjects were allowed to continue with their regular physiotherapy sessions (excluding the use of any electrical stimulation therapy), as this situation was to be mirrored by the circumstances of the subjects in the main study.

4.7.1 Outcome measures

The following outcomes were assessed in the pilot trial:

- Average ankle DF angle at initial contact during gait
- Self-selected walking speed
- Energy expenditure during gait
- Isometric muscle strength of the ankle dorsi- and plantarflexors of the affected leg

4.7.2 Instrumentation

In order to measure the outcomes described above, the following instruments were used.

4.7.2.1 Sony PC 10 Digital Video Camera

A Sony PC 10 Digital Video Camera was used to take video recordings of the subjects' gait. These recordings were stored on compact discs, and were used to measure ankle DF angles at initial contact by two-dimensional gait analysis.

4.7.2.2 Image Tool V 3.0 (University of Texas Health Science Centre, San Antonio, Texas)

Image Tool V3.0 is computer software that can be used to measure joint kinematics from freeze-frame digital images and was used to determine ankle DF angles at initial contact during gait in this study.

4.7.2.3 TIMEX® heart rate monitor

A TIMEX® Bodylink monitor was used to determine the heart rate of the subjects before and after each of the walking tests. These readings were necessary to calculate the Energy Expenditure Index.

4.7.2.4 Energy Expenditure Index (EEI)

The EEI is indicative of the amount of energy required to walk a specified distance. Rose et al. (1989) and Rose et al. (1990) concluded that, compared to calculations based on oxygen consumption, scoring EEI based on heart rate is a reliable and a clinically convenient method to determine the energy cost of walking in children with CP. In the present study, EEI scores were used to strengthen and verify the subjective feedback provided by the caregivers, and to provide objective data of energy expenditure during walking. The formula for calculating EEI is as follows (Rose et al., 1990):

$$\text{EEI (HR)} = \frac{\text{Final heart rate} - \text{resting heart rate (b/min)}}{\text{Walking speed (m/min)}}$$

$$= \text{beats / metre}$$

4.7.2.5 Stopwatch

A "Sport Timer" stopwatch was used to measure the time it took each subject to complete the walking test. These values were needed to calculate the subject's self-selected walking speed for each test.

4.7.2.6 Hand-held dynamometer

A hand-held dynamometer (Myometer, calibrated and adapted for the use on the lower limb by an independent mechanical engineer in September 2006) was used to test the isometric strength of the ankle dorsi- and plantarflexors. Hand-held dynamometry has been shown to be a reliable and valid way to objectively measure the strength of lower limb muscles (Roy and Doherty, 2004). It correlates well with isokinetic strength testing, and is portable and user-friendly (Roy and Doherty, 2004).

4.7.3 Data collection procedure

The measurement procedure will now be described for each of the individual outcome measures. All data was collected by the principal researcher and was recorded on a data capture sheet (refer to Appendix 4).

4.7.3.1 Walking speed

The protocol followed was based on the one described by Burridge et al. (1997), which the authors have shown to be reliable and to correlate well with other gait measures. A level ten-metre walkway was marked with tape at floor level. Two metres were allocated before the start and two metres after the finish line to allow for acceleration at the beginning and deceleration at the end of the walk, respectively. Blue removable skin markers were placed on the subject's fibula head, lateral malleolus, and fifth metatarsal head. The TIMEX® Bodylink heart rate monitor was fastened to the subject's chest with a chest strap. It was necessary for a trained assistant to walk alongside the subject, as the

wristwatch calculating the heart rate needed to be within one metre from the chest strap. Although the presence of the assistant could have affected the subject's self-selected walking speed, it was impossible to attach the wristwatch to the subject's own arm, as this proved to be a significant distracting factor.

The subject was then asked to walk from the start to the end of the walkway at his or her own pace and instructed to walk normally past the finish line. This walking test was repeated three times, with a 30 second rest period between consecutive walks during which the subject sat down and quietly looked at a children's story book. Although walking aids (as used by each subject on a day-to-day basis) would have been permitted during testing, none of the subjects made use of any lower limb assistive devices. Orthoses were not to be worn during testing, as these could have influenced the active ROM available at the ankle joint. Digital video recordings of all three walking tests at a set distance of three meters from the subject (lateral view) were taken at the same time.

A stopwatch was used to measure the time taken to cover the distance from the instant at which the subject crossed the start line to the instant he or she crossed the finish line. The walking speed for each of the three walks, expressed in metres per second, was then calculated and recorded on the data sheet.

4.7.3.2. EEI

Before and after each of the three walks, the subject's heart rate (in beats per minute) was read off the heart rate monitor by the trained assistant. Heart rate values were needed to calculate the EEI scores for each walk, which were recorded on the data sheet. For the purpose of EEI calculations, walking speeds were converted to metres per minute.

4.7.3.3 Isometric muscle strength testing

After the third walk, the subject was given a five minute rest period before isometric muscle strength was tested. Roy and Doherty (2004) stated that the lower limbs need to

be warmed up yet rested to allow maximal force production. The subject was asked to lie supine with his or her legs extended. This position allows maximal stabilisation of the ankle, and optimal positioning of the dynamometer (Wiley and Damiano, 1998). The researcher placed the hand-held dynamometer over the dorsal aspect of the foot, with a foam layer between the force pad and the foot to provide comfort and skin protection. The researcher stabilised the ankle joint and held the dynamometer still, while the subject exerted a maximal DF force against it. The subject was instructed to gradually increase the force of the contraction, and not to contract the muscle explosively. (S)he was asked to hold the contraction for five seconds, as maximum force is usually reached during this period (Roy and Doherty, 2004). Verbal encouragement was provided throughout. The maximum value of force production during these five seconds was then recorded on the data sheet (Wiley and Damiano, 1998).

Isometric strength measurements for the dorsiflexors were taken with the ankle in the neutral position and in ten degrees of DF, while measurements for the plantarflexors were taken in neutral and in ten degrees of plantarflexion (PF). All measurements were taken three times, and the maximum value for each ankle position was recorded. A rest period of 30 seconds was included between measurement repetitions in order to minimise the effect of muscle fatigue and reciprocal inhibition on the strength readings. The order of muscle strength testing remained the same at all times because of the effect of reciprocal inhibition after a maximal voluntary muscle contraction (Kramer and MacPhail, 1994). Taking measurements in different ankle positions means that results are more representative of muscle strength through full ROM, as opposed to isometric measurements in a single position. In addition, the strength values for the dorsiflexors with the ankle in neutral as well as in ten degrees of DF were averaged, as this provides a more holistic impression of muscle strength through range. Similarly, average strength values were calculated for the two testing positions for the plantarflexors.

4.7.3.4 Ankle DF angle at initial contact of gait

After all the measurements had been taken, the digital video images were loaded onto a personal computer, and stored on compact discs. The researcher then used Image Tool V3.0 on freeze-frame images of initial contact to measure the ankle DF angles using the markers on the head of the fibula, the lateral malleolus, and the head of the fifth metatarsal as reference points. The average DF angles (obtuse angles) at all instances of initial contact were then measured per walk for each subject, and the average value per walk recorded on the data sheet.

Figure 3: Example of instance of initial contact used for ankle angle measurements (main study subject)

4.8 Difficulties experienced during the pilot trial

- Some of the freeze-frame images obtained from the video footage were out of focus, which rendered angle measurements difficult. This was particularly obvious in the images of subject five, as the required three metres distance

between the video camera and the subject were unavailable due to severe space limitations. A high zoom power thus had to be implemented to capture images of the lower leg. In addition, a parallax error resulted in angle measurements not being admissible for analysis.

- Instances of initial contact were not always within the frame captured by the video, resulting in the forced discarding of those particular instances of initial contact.

- The start and finish markers on the walkway were often unclear, as they did not contrast well enough with the underlying floor colour.

- Subjects frequently interrupted walks by turning around or speeding up to a run. This was often due to external distracting factors such as other children entering the testing venue.

- Angle measurements were further made difficult by the use of blue skin markers. As most subjects had darkly pigmented skin, these markers were not always easily visible and angle measurements could thus have been inaccurate.

- The lighting in the testing area was not always optimal, which further obscured measurements.

- It was not always possible to test the subjects at the same time every day.

- Although attempts were made to remind subjects and their caregivers of the data collection dates (telephonic and vis-à-vis reminders), none of the subjects attended all six data collection sessions. The reasons for this were illness, forgotten appointments, and transport difficulties due to a taxi strike. Repeated measures analysis of variance (ANOVA) tests were thus performed for each dependent variable for the baseline sessions (measurement sessions one to three) and the last measurement session for all subjects in order to examine the changes over time.

4.9 Pilot trial results

The results obtained in the pilot trial will be discussed in terms of each of the dependent variables, as they influenced the spread of the baseline measures of the main study. A

change in measurement value was accepted to be significant if the relevant p-value was less or equal to 0.05.

4.9.1 Walking speed

When comparing data from the first three measurement sessions, the measures were fairly constant in the CP subjects, and did not vary significantly over the time period of one week (decrease of 0.5m/s between measurement session one and three) (p=0.69).

4.9.2 Isometric plantarflexor muscle strength in a neutral ankle position

Measurements for this outcome measure showed a greater variance than the strength data for the dorsiflexors. The average initial strength value for subjects with CP was 13.0N. Although measures varied for all CP subjects over the first three measurement sessions (baseline), this variance did not reach statistical significance (p=0.71). The greatest variance was recorded in subject one, who showed a difference of 6.7N between measurement sessions one and three. Again, the difference between the average of the first three measures and the last measurement session showed that data variability (increase of 1.6N) was not statistically significant (p=0.17). Strength measurements increased by 0.9N over the first three measures in typically developing children, which was not statistically significant (p=0.90). However, between the average of the first three and the last measurement sessions, a significant increase of 3.3N was recorded (p=0.00).

4.9.3 Isometric plantarflexor muscle strength in ten degrees of ankle PF

Over the first three measures for subjects with CP, an increase of 2.4N (p=0.06) was recorded. Measurement values between the first three and the last session showed a significant increase in isometric muscle strength of 1.7N (p=0.01). Strength increases exceeding 1.7N will thus be accepted as resulting from the intervention in the main study.

In comparison, typically developing children showed a significant increase in strength measurements of 0.7N over the period of baseline measurements (p=0.05), and a strength decrease of 0.2N over the entire four week period (p=0.83).

4.9.4 Average plantarflexor muscle strength (average of isometric plantarflexor strength in neutral and in ten degrees of ankle PF)

The subjects with CP showed a strength increase of 3.4N over the one-week baseline period (p=0.21) while the typically developing subjects showed a 4.8N increase (p=0.45). Between the average of the first three (baseline) and the last measurement session, however, the subjects with CP showed a statistically significant increase in measurement values of 2.3N (p=0.02), while the typically developing subjects showed a 1.6N increase over the same time period (p=0.43). Increases exceeding the 2.3N change will thus be accepted as resulting from the intervention in the main study.

On average, walking speed and plantarflexor strength measurements were higher during the second measurement session of the pilot trial than during the first and third sessions. This could have been due to the fact that the subjects (despite repeated reminders to complete the walks at their normal pace) were now acquainted with the measurement procedure. This hypothesis is supported in view of the fact that later measurements (as from session three onwards) were more in line with data from the first session – the subjects would have settled and calmed down during testing, providing a more accurate reflection of their gait patterns and muscle strengths.

4.9.5 Isometric dorsiflexor muscle strength in a neutral ankle position

One subject with CP had no active DF at all. Across the first three measurement sessions of the remaining four CP subjects, a significant decrease of 1.4N was recorded (p=0.01). However, data variability was not statistically significant when values from the baseline

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(average of measurement sessions one to three) and the sixth sessions were analysed for all participating subjects with CP (increase of 0.3N) (p=0.58). Similarly, there was no statistically significant variance in isometric dorsiflexor strength in typically developing children over the same time interval (increase of 0.9N) (p=0.13).

4.9.6 Isometric dorsiflexor muscle strength in ten degrees of ankle DF

CP subjects were much weaker in this position and only two of the subjects were able to actively maintain the required position for strength measurements to be taken. Both subjects showed no statistical significance in terms of measurement variability during the baseline period (p=0.76) or between baseline and the last measurement session (p=0.14) (overall strength increase of 0.6N). Similarly, there was no statistically significant variance in strength measurements in typically developing children over the same time interval (increase of 0.9N) (p=0.07).

4.9.7 Average dorsiflexor muscle strength (average of isometric dorsiflexor strength in neutral and in ten degrees of ankle DF)

No statistically significant change was calculated for average dorsiflexor strength for the baseline period in neither the CP subjects (decrease of 1.4N between measurement sessions one and three) (p=0.57), nor in the typically developing subjects (increase of 0.8N) (p=0.39). Similar results were found over a period of four weeks for the six measures in the CP subjects (increase of 1.0N) (p=0.17) and in typically developing subjects (increase of 1.3N) (p=0.16).

4.9.8 Ankle angles at initial contact during gait

Ankle angle measurements increased by 8.9 degrees over the baseline period for the CP subjects (p=0.23), while the typically developing subjects showed a decrease of 1.5 degrees over the same time period (p=0.58). Measurements from the CP subjects showed an overall decrease of 0.3 degrees from a baseline value of 125.4 degrees to the last

measurement session, which does not represent a statistically significant change (p=0.33). Similarly, the 0.2 degree increase in ankle angles at initial contact over four weeks was not statistically significant for the typically developing subjects (p=0.91).

Furthermore, a registered physiotherapist who was unaffiliated with the study was asked to conduct DF angle measurements on a random selection of ten pictures of initial contact. This was done in order to ensure inter-rata reliability and to subsequently establish reliability of the measurement results. Inter-rata reliability testing revealed an average difference of 1.05 degrees difference between the researcher and the independent physiotherapist, with a standard deviation of 1.19 degrees. The intraclass correlation co-efficient (ICC) was 0.98, which indicates a high degree of correlation between the principal researcher and the independent physiotherapist. Allowing for a measurement error of 1.05 degrees, a difference between sessions exceeding this value will be accepted as resulting from the intervention in the main study.

4.9.9 Energy efficiency during gait (EEI)

Unfortunately, the measurement protocol was difficult to follow as the young group of subjects in the present study could not sit still for long enough to allow their heart rates to return to resting rates between walks. Subjects thus presented with elevated heart rates at the start of the trials, which stabilised during the walks. This resulted in negative EEI values being calculated, which implies that data for this outcome measure was found to be unreliable.

4.9.10 Conclusion

Three measures for each of the above outcomes were deemed appropriate to serve as reliable and stable baseline measures for the main study, as variability over the period of one week stabilised and the average of these three measures did not differ significantly from further measures. Three measurement sessions were therefore also selected as baseline measures for the EEI outcome. Data variability for this measure was reassessed

using these three baseline measures of the main study and analysis adapted accordingly. Previous researchers have also collected data over three data collection points per phase of single-subject research (Durham et al., 2004), although the phases in this instance were 12 weeks long. In the present study, measurements recorded during the first three sessions were thus taken to be an accurate reflection of baseline data variability, and baseline measurements in the main study were to be taken on three days spread evenly over one week.

4.10 Adaptations to the measurement protocol for the main study

- The set distance of three metres between the video camera and the subject was strictly maintained at all times. Measurements took place in a gymnasium, which provided sufficient space for measurements to be taken according to the procedure described previously.
- The testing venue was closed off to everyone except the subjects, their caregivers, and the principal researcher. This minimised distractions from intervening with measurement procedures.
- All the lights were switched on in the testing venues in order to produce clear video footage for analysis.
- The video camera was mounted on a tripod at a set height of 81cm, which in turn was secured on to a rolling wooden platform (nine centimetres above the ground). This ensured that the smoothest possible video footage was captured.
- The start and finish lines of the walkway were marked with brightly coloured rulers.
- White skin markers with central holes replaced the blue ones for angle measurements. The holes ensured that ankle angle measurements were as accurate as possible.
- Subjects were required to sit down at the end of each walk and look at a children's story book for one minute before the commencement of the successive walk. This ensured a more stable resting heart rate at the start of the consecutive walk, and thus permitted more accurate EEI scores to be calculated.

- If possible, measurements were taken at the same time of day for each measurement session in order to standardise the level of physical activity prior to testing as much as possible. EEI scores based on heart rate were thus more accurate than those obtained in the pilot trial.

- The zoom power on all video footage was set to include the lower leg of the subject in the frame only, and stayed constant over all measurement sessions.

- The lack of statistically significant measurement variance over four weeks in the pilot trial's CP subjects (other than for isometric plantarflexor muscle strength in ten degrees of ankle PF and average plantarflexor strength) indicates relative stability of the dependent variables over time. Although significant data variance occurred over the baseline period for dorsiflexor strength, the change in average dorsiflexor strength value for the same time period was not significant. Baseline measurements for the main study were thus taken on three separate days spread out evenly over one week in order to ensure a realistic representation of data before the administration of the botulinum toxin.

4.11 Main study

After the completion of the pilot trial and the necessary amendments to the measurement protocol, data collection for the main study commenced.

4.11.1 Sampling

Potential subjects for inclusion into the main study were obtained from the database of the Tygerberg Children's Hospital as well as from Paarl School. A multi-disciplinary team (comprised of the principal researcher, an orthopaedic surgeon, and paediatric consultants at Tygerberg Children's Hospital) selected subjects based on the inclusion and exclusion criteria as previously described. The first five children who met these criteria were approached to participate in the main study. Caregiver written informed consent in the language of their choice was sought (refer to Appendix 3) as well as the child's willingness to participate.

Although it had been initially decided to exclude children below the age of four years, the small number of potential subjects between the ages of four and six years adhering to all inclusion criteria necessitated the inclusion of younger children as well. The final age bracket of subjects thus included in the main study was three to six year old children.

4.11.2 Data collection procedure

The principal researcher randomly allocated each subject to one of the five different treatment protocols (Figure 2) by drawing numbers out of a hat. These time intervals were based on findings from the literature concerning the optimum effects of botulinum toxin (Botox® South Africa: package insert), as well as the carry-over effects of FES applied to the tibialis anterior and the gastrocnemius muscles on active ankle ROM (Carmick, 1993; Comeaux et al., 1997). As no literature was found regarding optimal timing intervals for the introduction of FES after botulinum toxin, the time frame for the multiple-baseline approach used in this study falls into the time period deemed most effective for treatment interventions following botulinum toxin (Brin, 1997; Botox® South Africa: package insert). Although Carmick (1995) and Comeaux et al. (1997) have shown the effects of FES to outlast the intervention by at least three months, time constraints in the main study prevented the withdrawal phase to exceed two months. Subjects were to continue with activities (including regular physiotherapy treatment) as per usual during the entire study.

Three baseline measurements were taken, spread out over a period of one week. On the day after the third measurement, an orthopaedic surgeon administered botulinum toxin under general anesthesia (refer to Appendix 5) at Tygerberg Hospital. On the same day as the injection, the principal researcher collected data during measurement session four (four to five hours after the injection, immediately after discharge from hospital). Subjects were required to wear an ankle-foot orthosis after the injection (other than when the FES device was applied to the leg) in order to prevent contractures from occurring.

Measurement session five took place on the day of the start of the FES programme, i.e. between three and 35 days after the botulinum toxin injection (Figure 2). At this time, the researcher demonstrated the use of the stimulation device to all subjects and their caregivers, and gave instructions for home use.

Four weeks after the start of the FES programme, data for measurement session six were collected. At that point, FES was withdrawn and the subjects were required to return the stimulation device to the principal researcher. A seventh measurement session took place two months later to determine medium-term carry-over effects. As during the pilot trial, all data were recorded on a data capture sheet (refer to Appendix 4).

4.11.2.1 Perception of Gait and Function Questionnaire

Assessments of the caregivers' perception of the intervention's impact on their children's function and participation were deemed more valuable than assessments from the subjects themselves, as the young age of the subjects rendered it unlikely that they would be able to give reliable answers. No standardised questionnaire that sought to determine caregiver perception of change in their child's gait and function could be found. It was thus necessary to design a new questionnaire. The questionnaire consists of three questions relating to fatigue during gait, walking speed, and participation in daily activities (refer to Appendix 6). Caregivers were asked to answer the three questions at the start of the FES programme (i.e. during measurement session five), again at the end of the FES phase (during measurement session six), and again after the withdrawal phase (during measurement session seven). In addition, an opportunity was given to the caregivers during the last measurement session to explain and quantify their answers. The questionnaire was limited to three questions, as the researcher merely wanted to supplement the data obtained from the objective measurements, and did not need to obtain extensive qualitative data.

As all of the objective outcome measures included in this study were aimed at the World Health Organisation's impairment and function levels, the subjective questionnaire was

included in order to gather qualitative information regarding participation changes resulting from the intervention. Van der Linden et al. (2003) have shown that a change in impairment-level outcome measures does not always correlate with participation gains, and the inclusion of the subjective questionnaire thus allowed a more holistic assessment of the intervention's effect in the present study.

Although it was a newly developed questionnaire, it was impossible to pilot it during the pilot trial, as some of the questions refer to the FES programme implemented in the main study. As none of the children participating in the pilot trial received stimulation therapy, administering this questionnaire to the caregivers would have served no purpose.

4.12 Intervention

FES was applied to the tibialis anterior and the gastrocnemius muscles by means of the Odstock Two Channel Stimulator (O2CHS II). For the purpose of this study, three identical stimulating units were provided by the manufacturer. The O2CHS II (O2CHSPI V3.0) was designed at the Department of Medical Physics and Biomedical Engineering, Salisbury District Hospital, Salisbury, United Kingdom, in order to assist patients with neurological impairments to walk. If used to stimulate DF, it allows foot clearance during the swing phase of gait, which in turn decreases the effort of walking and results in a concomitant reduction of spasticity in the gastrocnemius muscle (Taylor, 2002).

The O2CHS II is a two-channel stimulator, powered by a nine-volt battery. It permits the selection of either asymmetrical or symmetrical biphasic output. In this study, the former mode was selected to allow for maximum power output. A single force sensitive foot-switch, placed in the ipsilateral shoe of the subject, was synchronised to trigger emission of two channels. The optimal position for the foot switch in the shoe was determined by the individual's pattern of weight-bearing.

Channel one was used to stimulate the tibialis anterior muscle. Emission was set to start when pressure was removed from the weight-bearing part of the foot. The output was set

to last until initial contact, and thus adapted to the subject's walking speed (adaptive timing mode). The maximum permissible output (time control) was set as just longer than the normal swing period, and is variable between 0.5 and six seconds. An added period of stimulation (between zero and 1.5 seconds) was added after initial contact, preventing foot slap by stimulating eccentric control by the tibialis anterior muscle (extension time). This ensures a more normal gait pattern (a point made by Taylor, 2002). The final settings for each subject were determined on an individual basis.

The rising and falling edge ramp controls represent the times required for the output to reach its maximum level, and return to zero afterwards, respectively (both are variable between zero and four seconds). This avoids a stretch reflex from being elicited, and is more comfortable for the subject. Again, these were set on an individual basis.

The second channel was used to stimulate the gastrocnemius muscle. The configurations were the same as for channel one, except that emission was set to start at initial contact. A delay of zero to two seconds between channels one and two were set to allow for weight transfer during gait. Refer to Figure 4 for the stimulation algorithm.
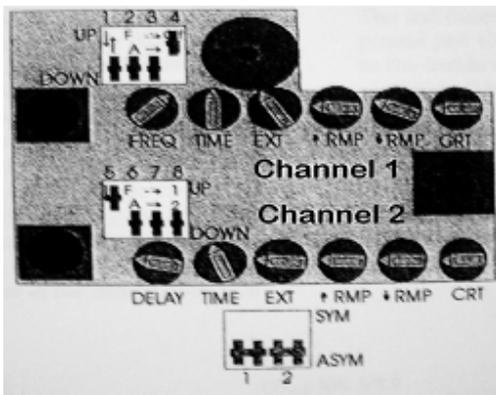
Figure 4: Algorithm for stimulator settings

As a starting point, the following settings were used for both channels:

- Rising edge ramp control: 0.3 seconds
- Falling edge ramp control: 0.2 seconds
- Time control: 3 seconds
- Extension: 0.3 seconds
- Current control: 20 mA
- Timing mode: adaptive timing

This algorithm follows the one being used in the Department of Medical Physics and Biomedical Engineering, Salisbury District Hospital, Salisbury, United Kingdom.

These settings were used to determine the most effective electrode positions. Pals Plus self-adhesive electrodes were implemented. During electrode application, the knee was positioned in full extension to limit skin movement over the underlying bony structures. To maximise conduction, the skin of the application area was washed with warm water before use. The active electrode of channel one was placed over the common peroneal nerve, with the top edge of the electrode in line with the top of the fibula head. The inactive electrode was positioned five centimeters infero-medially to the active electrode, over the tibialis anterior motor point. If an ineffective contraction was produced, the positions of the active electrode were adjusted accordingly. The electrodes of channel two were placed over the medial and lateral heads of the gastrocnemius muscle. The electrodes needed to be positioned correctly, as this allows a lower output current to be used for the same physiological effect. This makes for greater comfort during use. Stimulation (on the front panel of the device) was then increased to produce the desired movements.

After the botulinum toxin injection and the relevant pre-FES phase, the principal researcher demonstrated the use of the O2CHS II to the subject and the caregiver, and gave instructions for home use. The researcher set the device according to the

individual's needs. Potential discomfort occurring from the use of the stimulator was discussed with the relevant caregivers (refer to Appendix 2). Caregivers were thus only required to apply the electrodes, connect the leads, and switch the device on. A user manual was also provided for their reference. The researcher marked the skin areas where the electrodes were to be placed with a marker to ensure proper positioning with each application. The subject was then required to practice walking at home with the device on for 30 minutes per day, five times a week, for four consecutive weeks (total of 20 sessions). Caregivers were instructed to retrace the outlines for the electrode positions with each application in order to ensure their proper positioning during subsequent use. The subject was asked to continue with his or her regular physiotherapy sessions, which were not permitted to include any form of electrical stimulation. The researcher called the caregiver on a weekly basis to enquire about any problems with the use of the stimulation device, and to encourage compliance with the prescribed protocol (refer to Appendix 7). In addition, the researcher was telephonically available at all times to address any queries or problems, and to conduct home visits (if necessary) to address problems and encourage compliance with the prescribed programme.

4.13 Statistical analysis

An independent statistician from the Centre for Statistical Consultation at the University of Stellenbosch conducted the data analysis of the pilot trial as well as the main study. For the pilot trial, data for each outcome measure for each subject were graphed to illustrate change in values over time. Repeated measures analysis of variance (ANOVA) tests were also conducted on each dependent variable, in order to determine the change over time. Subjects with a diagnosis of CP were included in the data analysis if they had been present during the first and last measurement sessions.

Data of the main study were analysed in the same manner. In addition, Tukey HSD tests were used to investigate the statistical significance in data variance between each of the individual measurement sessions. Data were also graphed (illustrating the minimum and

maximum values for the relevant outcome measure) in order to show measurement trends over time. Qualitative data obtained in the questionnaire was to be discussed narratively.

4.14 Ethical considerations

The following ethical aspects were addressed during the course of this study:

- The study was registered with the Research and Ethics Committee from the Faculty of Health Sciences, Stellenbosch University (reference number N06/05/083).
- Consent was obtained from the Department of Education for testing to be conducted at Eros and Paarl Schools (refer to Appendix 8).
- Consent was obtained from the Medical Superintendent from the Red Cross Children's Hospital for testing to be conducted at the hospital (refer to Appendix 9).
- Written informed consent for participation and video recording were obtained from the caregivers of the subjects (refer to Appendix 3).
- Participation in the study was entirely voluntary.
- Subjects were allowed to withdraw from the study at any time, without their future medical treatment and / or therapy being influenced in any way.
- All personal details of the subjects were kept confidential at all times, and their identities were concealed during all forms of data collection, analysis, and presentation.
- Subjects were to continue with any therapy sessions as per usual. No form of electrical stimulation was permitted to be included in these treatments.
- There is no conclusive evidence to suggest an optimal time period after botulinum toxin injection before the introduction of FES – no subject thus received treatment of an inferior quality than another.
- FES was administered by a registered physiotherapist (the principal researcher), trained in the application of the two-channel stimulator.

- Each subject's caregiver was present during testing to reduce anxiety and to increase co-operation.

- The orthopaedic surgeon who injected the subjects with the botulinum toxin was available for medical attention to the subjects as required.

- No financial benefits were paid to the subjects, although all transport costs incurred due to participation were fully refunded.

- The results were made available to all subjects and their caregivers on request, as well as to the Paediatric Departments at the Tygerberg and Red Cross Children's Hospitals. Decisions for further management rested with the subjects' caregivers, therapists, and paediatricians.

- All video recordings and freeze-frame images will be destroyed upon completion of the study and submission of a thesis for MSc degree purposes.

CHAPTER 5

RESULTS

A description of the study sample will precede the results of the main study, which will be described according to each of the dependent variables in line with the objectives set for this study. As during the pilot trial, a change in measurement values was accepted to be significant if the relevant p-value was less or equal to 0.05.

5.1 Subject characteristics

All subjects participating in the main study presented with spastic hemiplegia due to cerebral palsy (CP), and were between the ages of three and six years (Table 4).

All subjects co-operated well during baseline testing and the botulinum toxin injection. However, subject one developed a skin reaction at the botulinum injection sites shortly after the procedure, and could thus not continue with the stimulation protocol until eight days after the intended start of the programme, during which time the subject was treated with antibiotics. The principal researcher subsequently conducted a home visit in order to again demonstrate the correct positioning of the electrodes to the caregiver and to ensure proper implementation of the stimulation device. The research design was thus adapted (Figure 5).

Although subjects were required to wear an ankle-foot orthosis after the botulinum toxin injection (apart from the times of FES use), compliance in all subjects was poor.

Table 4: Subject characteristics

Subject	Age at start of study	Gender	Affected Limb	Frequency of physiotherapy treatment	Use of lower limb orthoses	Use of other assistive devices
1	6 years 4 months	M	Left	None	None	None
2	3 years 4 months	M	Right	Alternate weeks	None	None
3	6 years 4 months	F	Left	Twice weekly	None	None
4	3 years 11 months	M	Right	Once a week	None	None
5	5 years 7 months	F	Left	Once a month	None	None
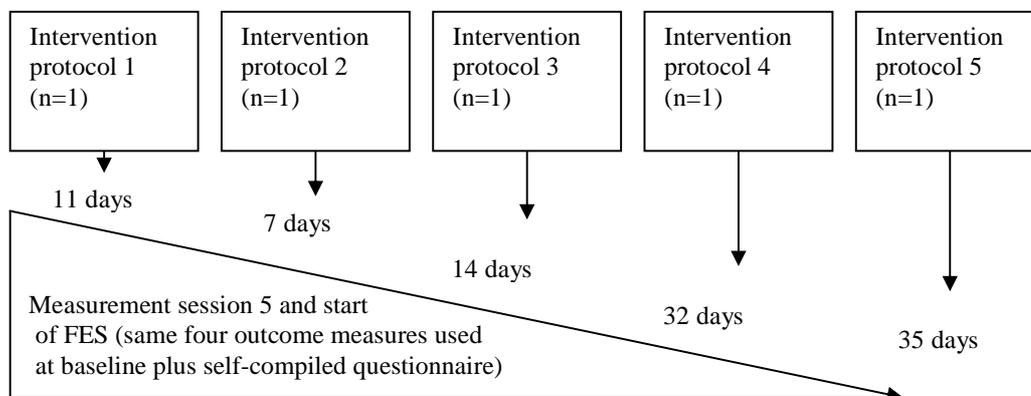
Figure 5. Amended intervention protocol

Furthermore, subjects two and five subsequently refused to co-operate with the stimulator being applied to their lower leg. Subject two tolerated a sub-maximal stimulation intensity (intensity setting of one, instead of a required setting of at least four), but refused to walk with the electrodes attached to the leg. Subject five refused to allow the electrodes to be applied to the leg at all. Administration of the required stimulation during gait was thus impossible for these two subjects, even after repeated attempts and extensive reassurance (from both the relevant caregiver and the principal researcher). This included attempts to start the stimulation at very low intensity levels with the aim to later increase it to an acceptable level. Although five subjects participated in the main study, the researcher was thus able to compare subjects two and five (who did not receive the FES intervention) with the remaining three subjects (who did receive the FES). For this purpose, subjects two and five were grouped into a non-FES group, whereas subjects one, three, and four made up the FES group. Data analysis was thus conducted per subject as well as for the two groups.

Caregivers were telephonically reminded of the data collection dates three days prior to the respective day, which resulted in a 100% attendance rate. All caregivers were literate in either English or Afrikaans, and there was thus no need for translations of any documents into another language. Although all caregivers were asked to record the dates and times of FES use at home, only one caregiver complied with this instruction. However, these diary entries were incomplete and only provided details on 11 of the 20 practice sessions. All caregivers attested to using the stimulation device for the entire 20 sessions, as prescribed.

5.2 Walking speed

Most subjects showed consistency in terms of self-selected walking speed over the baseline phase (Figure 6). When walking speed was measured immediately after the botulinum toxin injection (during measurement session four), subjects two, three, four, and five showed decreases in walking speeds compared to before. Although subject one's walking speed had increased by 0.14m/s at this point, this difference was not significant

(p=0.78). Between the injection and the commencement of the FES programme, subjects three, four, and five showed slight decreases in walking speeds, whereas increases were recorded for the other two subjects.

When comparing walking speeds immediately before and after the stimulation programme in the FES group, subject four showed the largest increase of 0.07m/s, but this was not maintained post intervention. Subject one's average walking speed did not change during the FES phase, while subject three's average speed showed a decrease of 0.18m/s. Both subject one and three showed an increase in walking speed during the withdrawal phase. Although subject two did not receive any FES, he showed an increase in walking speed of 0.27m/s (p=0.01) between measurement session four and five, whereas subject five's walking speed had remained constant.
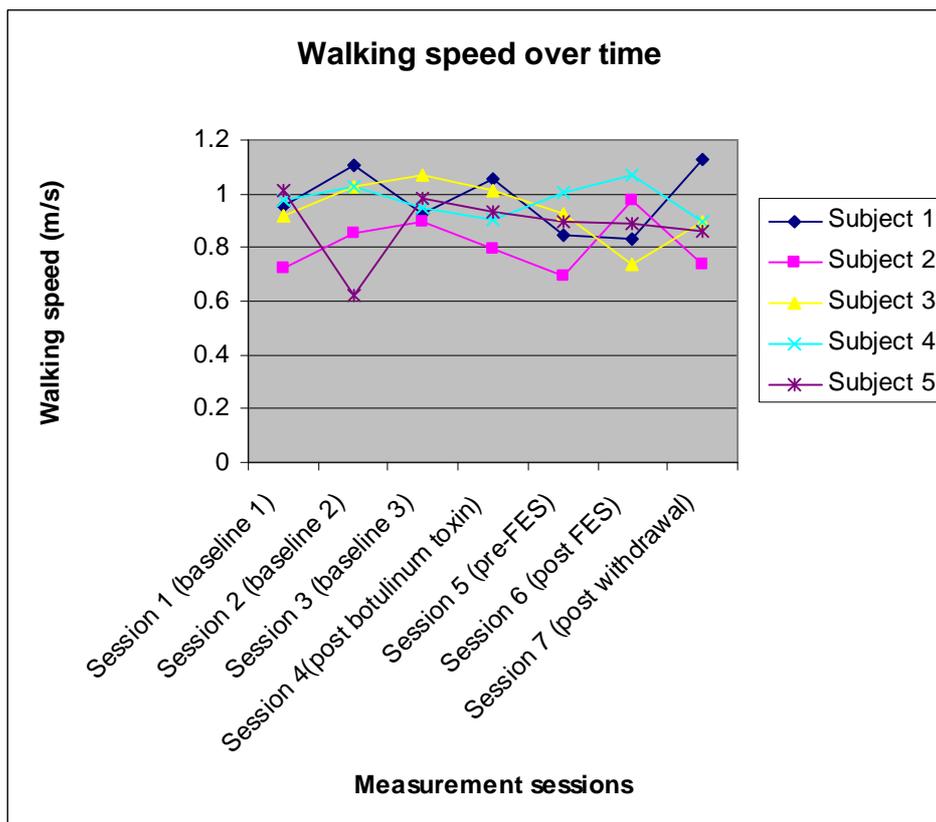
Figure 6: Walking speed over time per subject (m/s)

The average walking speed of the subjects in the FES group (0.96m/s; SD=0.02) was significantly higher than that of the non-FES group (0.85m/s; SD=0.02) (p=0.04). A repeated measures ANOVA test revealed no significant change in walking speed between baseline and the last measurement session in either group (p=0.37), although subjects in the FES group showed a 0.02m/s decrease between baseline and the last measurement session, compared to the 0.05m/s decrease in the non-FES group.

Analysis by means of a Tukey HSD test (which provides data on statistical significance for a given variable between individual measurement sessions) showed that the average walking speeds for the baseline measurements were not statistically different to the average walking speeds measured immediately following the botulinum toxin injection (p=0.10). In addition, neither the difference in average walking speeds between baseline data and the start of stimulation programme, nor the difference between the beginning and the end of the stimulation programme were statistically significant (Figure 7).
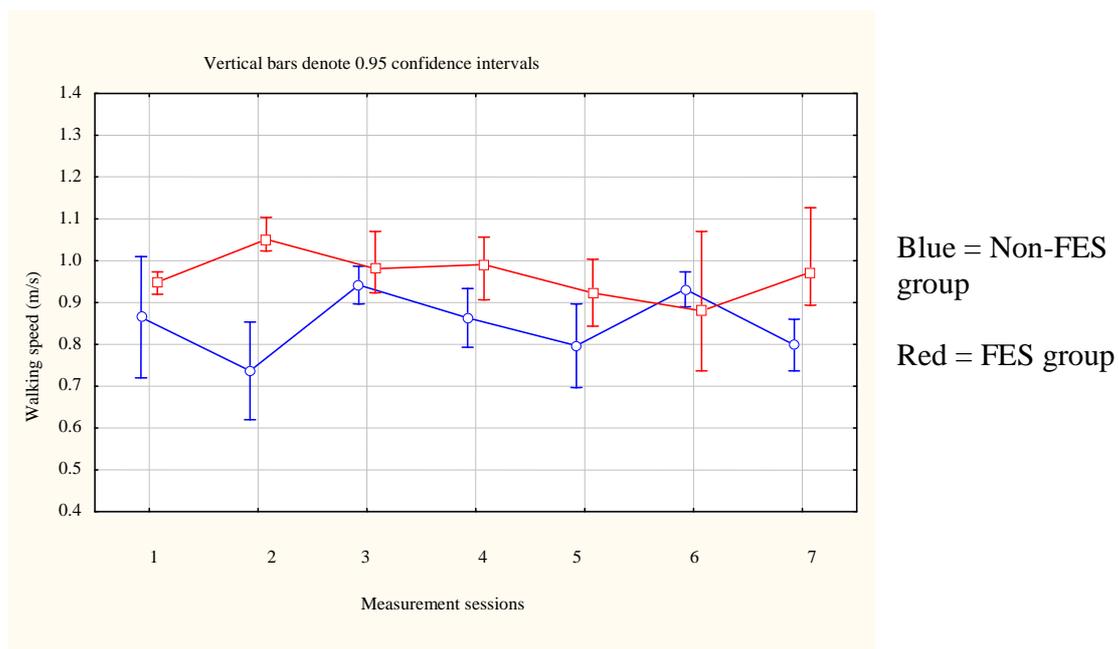
Figure 7: Average walking speeds for the FES and non-FES groups over time

5.3 Energy Efficiency Index (EEI)

Despite considerable attempts to allow the subjects' heart rates to return to resting values between individual trials, the principal researcher had considerable difficulty adhering to the intended measurement protocol for this outcome measure, as subjects did not always follow instructions to sit down between repeated tests. If the heart rate prior to a walking test was higher than afterwards, an EEI score of 0 was assigned to the relevant test. Refer to Table 5 for individual measurements per subject.

As can be seen from this table, baseline measurements varied greatly among all subjects. Increases in EEI scores can be seen between baseline values and the measurement immediately following the botulinum toxin injection in subject five, while measurements remained stable in subjects one and four, and decreased in the remaining two subjects.

At the start of the FES programme, subjects two and four showed an increase in EEI scores compared to before, while the energy consumption during gait of subject one and five had decreased during this time, and subject three's scores had remained constant. After the completion of the prescribed intervention, subjects one and three (in the FES group) displayed an increase in EEI scores, compared to decreases in the other three subjects. Subjects three and four were able to reduce their energy expenditure during the two-month withdrawal phase, while the other three subjects showed increases during this time period. Refer to Figure 8 for an illustration of individual measurement variance.

In a comparison between the FES and the non-FES groups, subjects in the latter group showed an average EEI of 0.17b/m (SD=0.19), while the three subjects in the FES group displayed a higher EEI of 0.22b/m (SD=0.19). Repeated measures ANOVA tests did not show this difference between the FES and the non-FES group to be statistically significant (p=0.56). There was also no significant change found between baseline and the last measurement session within each of the groups (p=0.94).

Table 5: Average EEI scores per subject (b/m)

		FES group			Non-FES group	
		Subject 1	Subject 3	Subject 4	Subject 2	Subject 5
Baseline sessions	**Session 1**	0.23	0.26	0.03	0.08	0.18
	Session 2	0.22	0.15	0.14	0.04	0.06
	Session 3	0.08	0.07	0.11	0.09	0.06
	Average	0.17	0.16	0.09	0.07	0.10
Post botulinum toxin	**Session 4**	0.20	0.04	0.11	0.02	0.74
Pre-FES	**Session 5**	0	0.03	0.55	0.41	0.20
Post FES	**Session 6**	0.09	0.41	0.40	0	0.09
Post Withdrawal	**Session 7**	0.26	0.10	0.16	0.18	0.18
	Overall Average	0.16	0.15	0.34	0.12	0.22
	SD	0.07	0.14	0.36	0.14	0.24
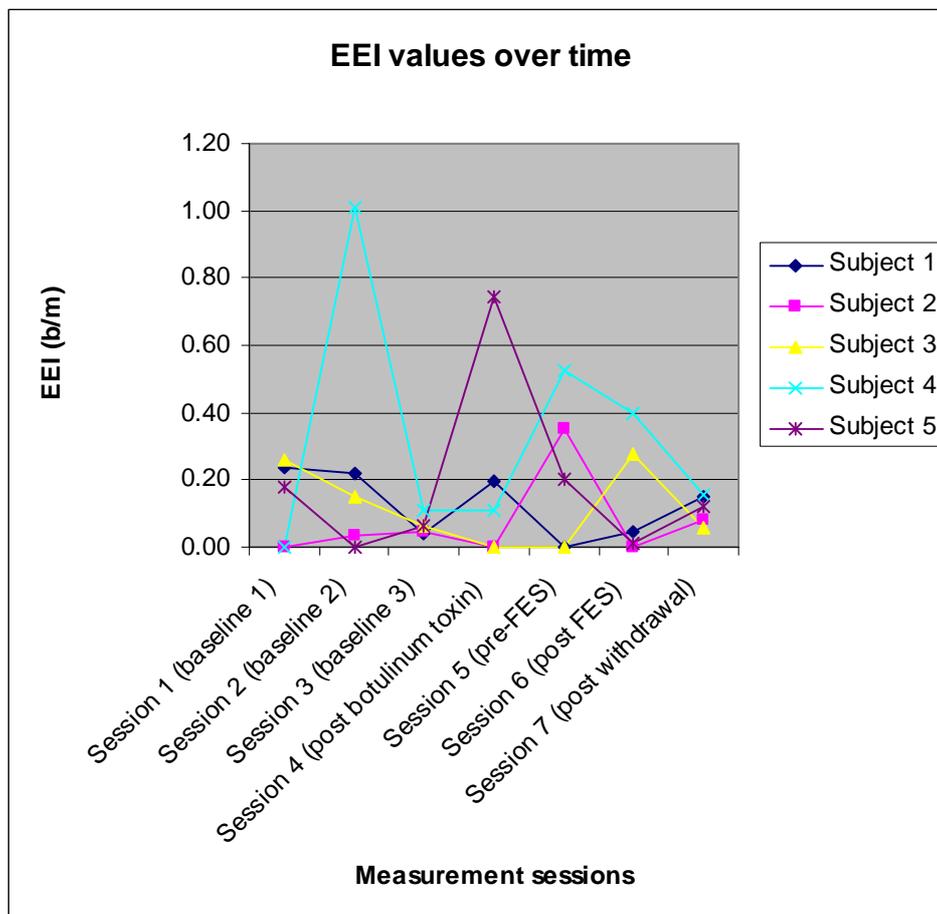
Figure 8: Individual EEI scores over time

5.4 Isometric dorsiflexor muscle strength in a neutral ankle position

A wide range of measurements was recorded in most subjects (Table 6). Between the botulinum toxin injection and the start of the intervention programme, strength values decreased in subjects one and three (FES group), remained unchanged in subjects two and four, and increased in subject five. Of the subjects receiving the prescribed intervention, subject three showed the largest effect size (strength increase of 0.7N) during the FES programme, followed by subject one (increase of 0.4N). Isometric dorsiflexor muscle strength in neutral did not change for subject four. For the two subjects that did not receive the FES intervention as intended, a strength increase of 0.5N was recorded in subject two, while a decrease was observed in subject five.

Table 6: Isometric dorsiflexor muscle strength (N) in a neutral ankle position

		FES group			Non-FES group	
		Subject 1	Subject 3	Subject 4	Subject 2	Subject 5
Baseline sessions	Session 1	0.5	1.8	0.8	0.5	4.5
	Session 2	1.0	1.7	0.5	0.8	1.1
	Session 3	1.4	0.7	1.1	0	1.1
	Average	1.0	1.4	0.8	0.4	2.2
Post botulinum toxin	Session 4	0.7	0.9	0	0	1.1
Pre-FES	Session 5	0.1	0.5	0	0	1.7
Post FES	Session 6	0.5	1.2	0	0.5	1.1
Post withdrawal	Session 7	0.1	0	0	0	0
	Overall Average	0.61	0.95	0.34	0.26	2.09
	SD	0.47	0.65	0.46	0.34	2.87

Between the baseline and the last measurement session, subjects in the FES group showed a 1.0N decrease (p=0.03), compared to the non-FES group's 1.3N decrease (p=0.42) (Figure 9).
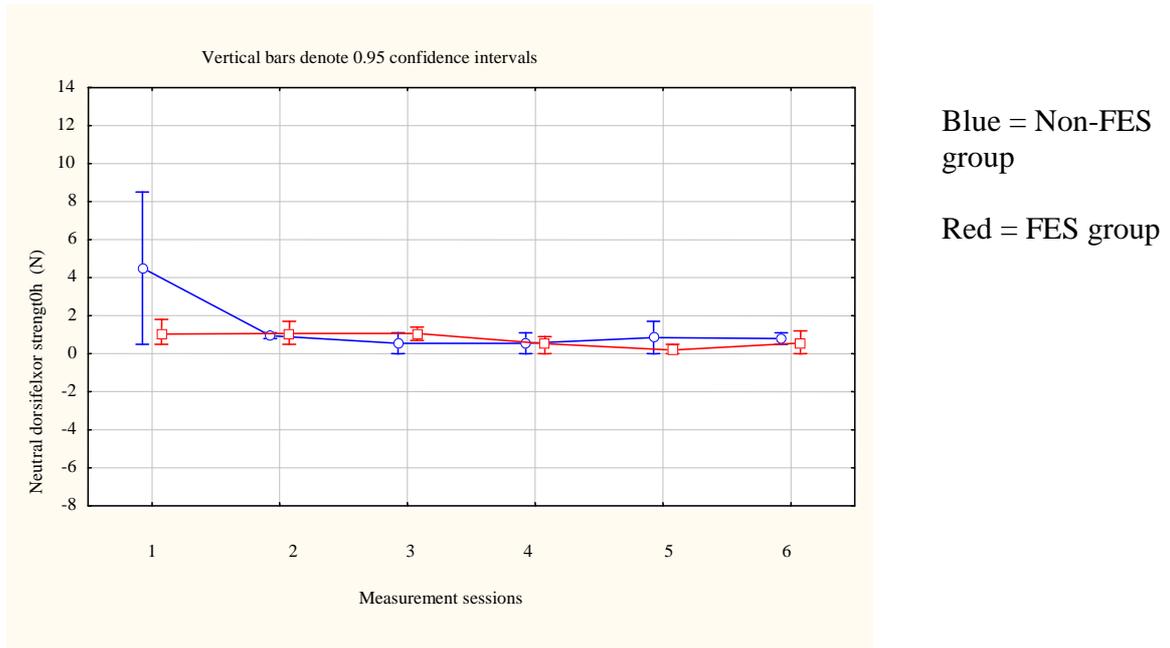
Figure 9: Average isometric dorsiflexor strength in neutral over time in the FES and non-FES groups

5.5 Isometric dorsiflexor muscle strength in ten degrees of ankle DF

Only one subject per group was able to maintain the required ten degrees of DF for testing, and in both instances the subject could only maintain this position for the first measurement session. Subject one (FES group) showed a maximum strength value of 0.04N during the first test of measurement session one, but was unable to maintain the required position for further testing. Similarly, subject five (non-FES group) showed a maximum isometric muscle strength of 2.5N during measurement session one, but was unable to maintain this position during subsequent sessions.

5.6 Average dorsiflexor muscle strength values

Data was stable for this outcome measure over the baseline period for the main study (p=0.28). Data variance between baseline and the last measurement session was also not statistically significant for neither the FES group (p=0.08) nor for the non-FES group (p=0.10).

5.7 Isometric plantarflexor muscle strength in a neutral ankle position

Subjects in the main study showed an average increase of 2.6N over the baseline period. Between the botulinum toxin injection and the commencement of the FES phase, subjects one to four showed decreases in isometric muscle strength, while subject five showed an increase. Refer to Table 7 for individual isometric strength with the ankle in a neutral position.

In a pre- and post-intervention comparison for the FES group, the largest strength increase was measured in subject four (increase of 2.0N during the intervention phase). Subject one showed a lesser increase of 1.7N during this time, while subject three showed a decrease of 1.5N during the same time period. Both subjects in the non-FES group also showed muscle strength improvements of 2.0N at this time, even though they had not received the intervention as prescribed.

The difference between strength values in the FES and the non-FES groups was not statistically significant (p=0.07) (Figure 10). However, when the change in pre- to post-intervention measurements for all five subjects was analysed, a statistically significant difference was calculated (p=0.05). Analysis by means of separate Tukey HSD tests for the FES and the non-FES groups did not reveal any significant difference in data between any of the measurement sessions for either of the two groups.

Table 7: Isometric plantarflexor strength of main study subjects in a neutral ankle position

		FES-group			Non-FES group	
		Subject 1	**Subject 3**	**Subject 4**	**Subject 2**	**Subject 5**
Baseline sessions	**Session 1**	13.7	19.4	9.8	6.8	8.5
	Session 2	9.8	14.4	16.2	6.5	7.4
	Session 3	14.0	18.9	13.6	14.0	10.8
	Average	12.5	17.6	13.2	9.1	8.9
Post botulinum toxin	**Session 4**	14.2	19.1	16.1	8.5	7.5
Pre-FES	**Session 5**	12.3	16.4	10.0	8.1	9.5
Post FES	**Session 6**	14.0	14.9	12.0	10.1	11.5
Post withdrawal	**Session 7**	14.5	15.3	12.9	13.6	12.6
	Overall Average	13.2	16.9	12.9	9.7	9.7
	SD	1.7	2.2	2.6	3.1	2.0
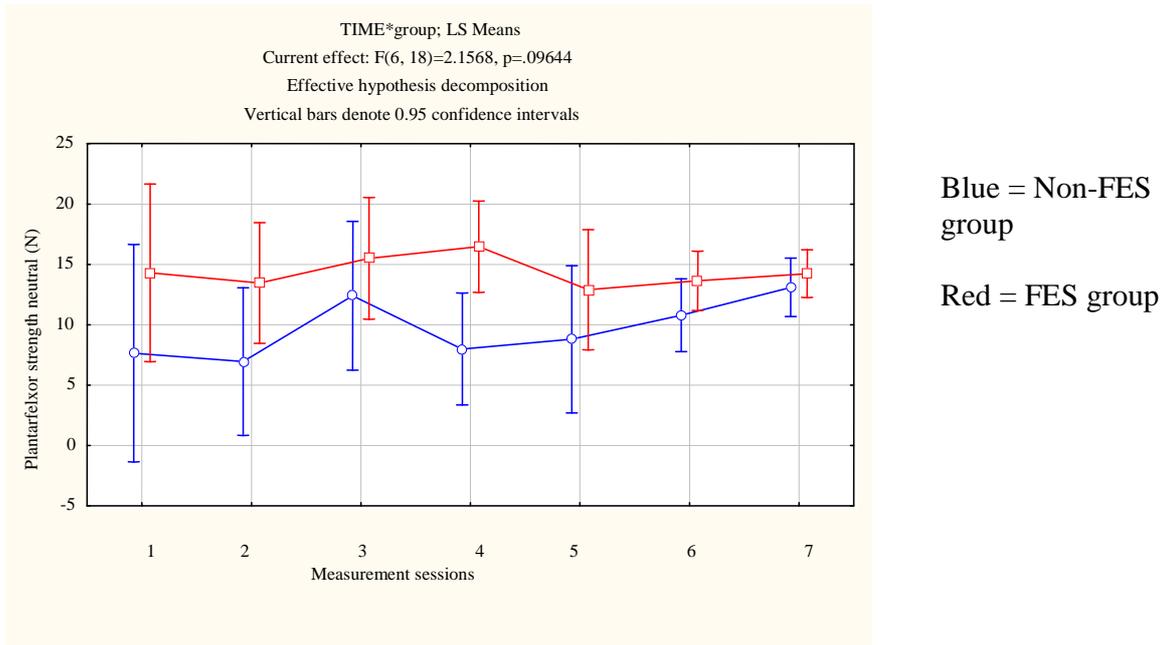
Figure 10: Average isometric plantarflexor strength (FES and non-FES groups) in a neutral ankle position over time

5.8 Isometric plantarflexor muscle strength in ten degrees of ankle PF

Baseline values did not vary significantly (p=0.21) for all subjects. All subjects showed a decrease in muscle strength between the botulinum toxin injection and the start of the FES phase, which was most pronounced in subject four (decrease of 7.8N). Refer to Table 8 for individual measurements per subject.

During the stimulation phase, all three subjects of the FES group showed an increase in isometric plantarflexor strength in ten degrees of ankle PF (p=0.04). The largest effect size was achieved in subject four with an increase of 3.6N, compared to 2.7 and 2.8N increases for subjects one and three, respectively. Subjects one and three were able to maintain these improvements for two months after the intervention had ended, although a decrease in plantarflexor muscle strength was measured for this time period in subject four (decrease of 4.1N) (p=0.16) (Table 8).

Table 8: Individual isometric muscle strength (N) in ten degrees of ankle PF

		FES group			Non-FES group	
		Subject 1	Subject 3	Subject 4	Subject 2	Subject 5
Baseline sessions	Session 1	11.1	9.6	7.5	4.6	5.3
	Session 2	8.6	13.6	11.1	4.0	5.2
	Session 3	9.1	14.5	10.7	4.5	7.1
	Average	9.6	12.6	9.8	4.4	5.9
Post botulinum toxin	Session 4	9.1	18.3	13.8	4.6	5.1
Pre-FES	Session 5	7.5	11.3	6.0	3.2	4.6
Post FES	Session 6	10.2	13.1	9.6	4.3	5.6
Post withdrawal	Session 7	11.3	13.5	5.5	4.9	4.7
	Overall Average	9.6	13.4	9.2	4.3	5.4
	SD	1.4	2.7	3.0	0.6	0.9

Although subjects in the non-FES group also showed an increase in isometric muscle strength over the time period of the intended stimulation phase, this change was smaller than in the FES group subjects. Subject two showed a further strength increase during the withdrawal phase, while subject five's isometric plantarflexor strength decreased during this time interval.

When the FES group is compared with the non-FES group as a whole, a repeated measures ANOVA test showed no significant measurement variance over time for either

group, but did reveal a significant difference between the two groups (p=0.05). Refer to Figure 11 for a graph illustrating the measurement trends for the FES and the non-FES groups.
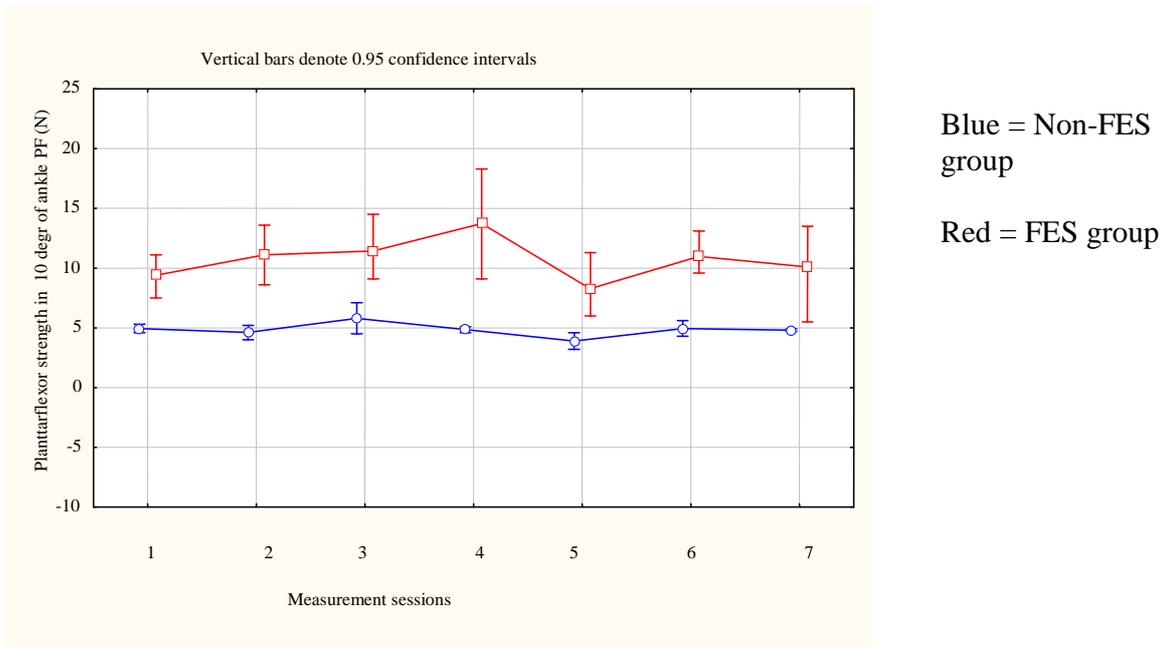
Figure 11: Average plantarflexor strength measurements in ten degrees of ankle PF over time (FES and non-FES group)

5.9 Average plantarflexor muscle strength

Subjects participating in the main study showed a trend towards statistical significance over the baseline period (p=0.06), while neither the FES nor the non-FES groups showed significant data variance between baseline and the last measurement session (decrease of 0.5N for the FES group, p=0.08; decrease of 1.0N for the non-FES group, p=0.20).

5.10 Ankle angles at initial contact during gait

When initial contact angles immediately after the botulinum toxin injection and the commencement of the stimulation programme are compared in the FES group, subjects one and three did not show much change with a 0.3 degree increase and a 0.2 degree decrease, respectively. In contrast, subjects in the non-FES group (subjects two and five) showed an increase in ankle angles, while subject four showed a small decrease in measurements (Table 9).

Table 9. Ankle DF angles at initial contact during gait (degrees)

		FES group			Non-FES group	
		Subject 1	Subject 3`	Subject 4	Subject 2	Subject 5
Baseline sessions	**Session 1**	131.3	146.2	123.9	140.1	134.7
	Session 2	130.1	128.7	118.9	131.6	136.4
	Session 3	130.3	131.0	139.4	137.0	135.0
	Average	130.6	135.3	127.4	136.2	135.4
Post botulinum toxin	**Session 4**	129.4	135.2	128.8	143.2	128.9
Pre-FES	**Session 5**	129.7	135.0	125.9	145.4	133.3
Post FES	**Session 6**	129.4	137.3	125.5	127.9	127.6
Post withdrawal	**Session 7**	133.8	140.6	134.3	141.6	125.5
	Overall Average	130.6	136.3	128.1	138.1	131.6
	SD	1.6	5.9	6.8	6.4	4.2

Subjects one and four (in the FES group) showed small decreases in average ankle angles at initial contact of gait after the stimulation programme (decrease of 0.3 degrees in

subject one, and 0.4 degrees in subject four). Subject three, however, showed an increase of 2.3 degrees over this time interval. When the same outcome measure was assessed after a two-month withdrawal phase, average DF angles at initial contact had increased again in all three FES group subjects, with the largest effect size measured in subject four (increase of 8.8 degrees). In the non-FES group, subject two showed a decrease in ankle angles at initial contact during the intended stimulation period, although this was not maintained over the withdrawal phase. In contrast, subject five displayed a mild decrease in ankle angles, maintained until the end of the study period.

Repeated measures ANOVA tests, however, revealed no statistical significance between the FES and the non-FES groups (p=0.12) (Figure 12), and also no statistically significant change between baseline and the last measurement session for the individual subjects (p=0.24) (Figure 13).

Blue = Non-FES group
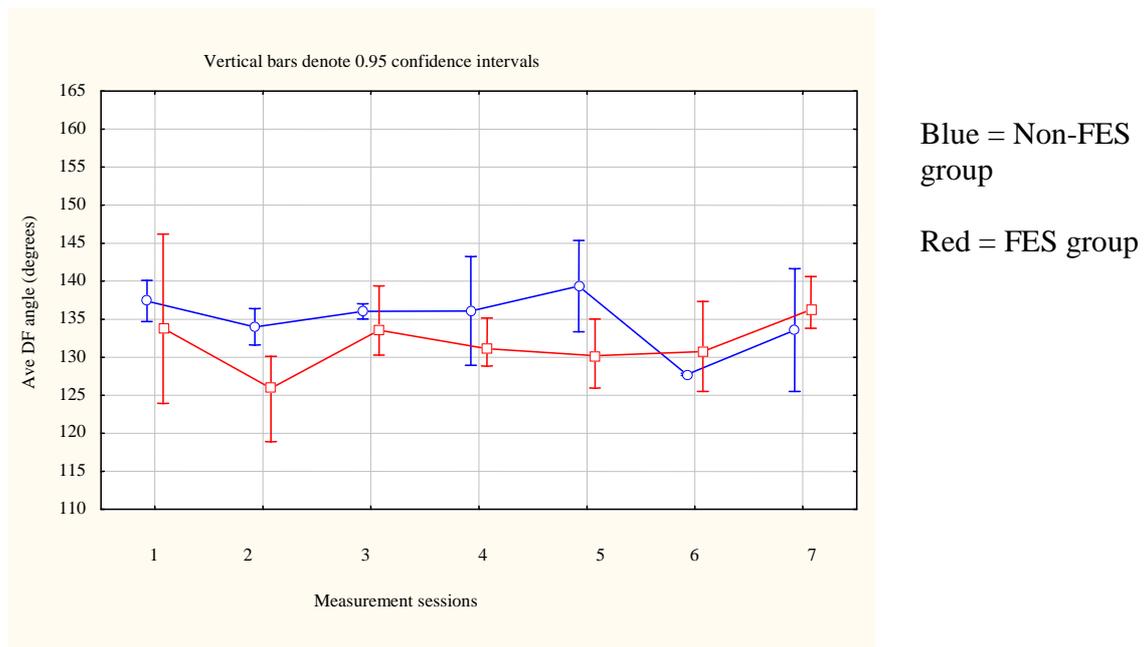
Red = FES group

Figure 12: Average ankle DF angles at initial contact during gait in the FES and non-FES groups over time
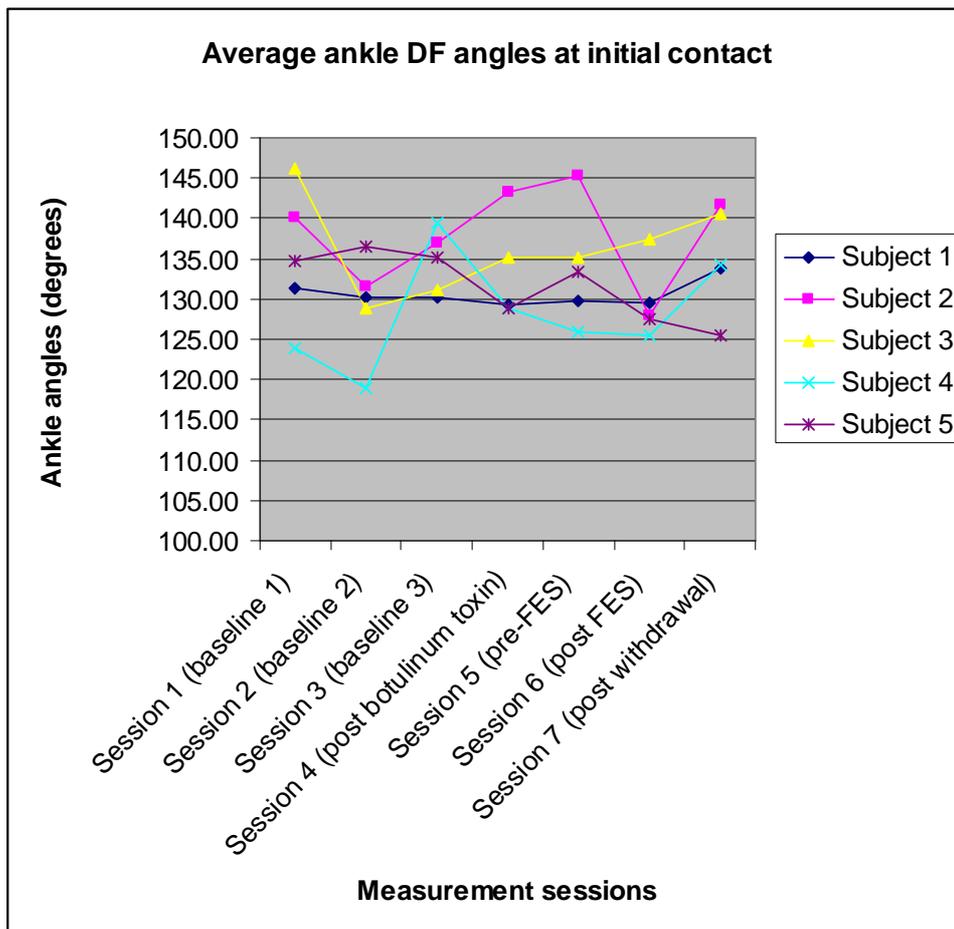
Figure 13: Average DF angles at initial contact during gait per subject

5.11 Subjective feedback from caregivers – questionnaire

All caregivers completed the questionnaire at the required times. According to their caregivers, all subjects had improved in terms of walking and functional abilities during the course of the study, with no clear difference between the FES and the non-FES group. Four out of five caregivers felt that their child tired less after the botulinum toxin injection, and all five felt their child was able to walk faster and could participate to a greater extent in age-appropriate activities of daily living at this time. When asked to answer the same questions at the end of the FES phase, three out of five caregivers replied that the administration of the stimulation device allowed their child to walk

without fatiguing as rapidly as before (these were three caregivers who had affirmatively answered the same question previously). The caregiver of subject two (non-FES group) felt that there was no difference in fatigue after the FES application phase compared to before. Again, all caregivers felt that their child could walk faster and participate to a greater extent in daily activities

After the two-month withdrawal phase, three caregivers replied that their children walked with less fatigue than immediately after the stimulation phase (two of them had answered yes to this question immediately following the intervention), and three out of five felt that their child could walk faster (one caregiver had previously answered no to this question). All caregivers felt that participation in daily activities had improved. Although caregivers were given the opportunity to explain and quantify their answers at this stage, none expressed the need to do so.

5.12 Summary

This study has shown significant pre- to post-intervention strength increases in the plantarflexor muscles with the ankle in a neutral position as well as in ten degrees of PF, with some subjects maintaining these improvements for two months after the intervention had been removed. However, the fact that two subjects did not receive the intervention as intended would have adversely affected the significance of the findings. Althought the subjects in the non-FES group also showed strength gains with the ankle in ten degrees of PF, the change was smaller than in the FES group. Caregivers felt the intervention to have a positive influence on their child's walking speed, as well as on age-appropriate function and participation. Dorsiflexor muscle strength with the ankle in a neutral position increased after FES to the lower leg in some subjects, although these improvements were not maintained after the withdrawal phase in any subject (FES and non-FES groups). No definite correlation was noted between the application of FES to the lower leg after a single botulinum toxin injection and changes in self-selected walking speed. Energy expenditure during gait increased after the intervention in some subjects, although the researcher had difficulty adhering to the intended measurement protocol.

FES after botulinum toxin did not seem to significantly influence ankle angles at initial contact during gait. Although subjects in the FES group showed no significant change in angle measurements, while subjects who had not received the stimulation showed smaller ankle angles at initial contact during gait after the intended intervention phase (which represents a greater degree of toe walking). A detailed discussion of these results will follow in the next chapter.

CHAPTER 6

DISCUSSION

It was hypothesised that electrical stimulation (FES) to the tibialis anterior and gastrocnemius muscles of children with an equinus gait pattern due to cerebral palsy (CP) can augment the effects of a single botulinum toxin injection into the calf musculature. The results of this study have shown that FES can increase isometric plantarflexor muscle strength and that isometric dorsiflexor strength may also increase following FES, although subjects in the non-FES group also showed improvements. Subjects in this study however, despite improvements in muscle strength, did not demonstrate changes in self-selected walking speeds. Similarly, the dorsiflexion (DF) angle at initial contact remained unchanged. Caregivers of the participating subjects, however, felt the intervention to have a positive influence on their child's walking speed, as well as on age-appropriate function and participation.

The effect of FES after botulinum toxin on each of the dependent variables as well as the significance of the study sample and the implemented research design will now be discussed in more detail.

6.1 Subject characteristics

Subjects participating in the main study were children with spastic hemiplegia due to CP, and were between the ages of three and six years old. The gender ratio in the present study mirrored those of previous studies addressing the paediatric population (Detrembleur et al., 2002; Baker et al., 2002). Although it was initially decided to exclude subjects under the age of four years in order to obtain a sample with as homogenous a gait pattern as possible, a shortage of potential subjects above the age of four years necessitated the inclusion of younger subjects as well. Berger et al. (1984) stated that the gait pattern of children with spastic CP is comparable to that of a typically developing

one-year old child in terms of muscle activation patterns as well as active ankle DF during the swing phase of gait. Although the subjects participating in the main study differed in terms of age, their gait patterns could thus be expected to display similar characteristics.

As mentioned in the previous chapter, subject one developed a skin reaction at the botulinum toxin injection sites, and could thus only commence with the FES programme eight days after the intended start. He was thus unable to follow the prescribed intervention plan, and experienced an 11 day interval between the injection and the start of the FES intervention. The impact of this change in protocol will be discussed per outcome measure below.

Due to the adverse reaction of two of the subjects to the stimulating device, it became possible to group the subjects into a FES and a non-FES group. This provided the researchers with a control group (i.e. subjects who had received the botulinum toxin but not the electrical stimulation). The results from this study will thus be discussed in terms of the significant change per subject, as well as in terms of the FES group compared to the non-FES group. Although the researchers would have preferred to continue recruiting patients until a sample of five subjects adhering to the prescribed intervention protocol was obtained, financial and logistical constraints made this impossible.

6.2 Walking speed

This outcome measure will be discussed in terms of the variability recorded in the pilot trial and the main study, followed by a discussion of the main study results.

6.2.1 Variability of walking speed

The highest average walking speed was recorded in the CP subjects participating the pilot trial, followed by the typically developing subjects in the pilot trial, the FES group of the main study, and lastly by the non-FES group of the main study. It is interesting to note

that the average walking speeds in the pilot trial were higher for those subjects with a diagnosis of spastic CP than for the typically developing subjects. These results contrast those of Abel and Damiano (1996) as well as those of Ho et al. (2006), who have investigated the effects of FES on stride length and frequency in CP over a distance of 12 meters five stride lengths, respectively, and have found higher average walking speeds in typically developing children than their CP counterparts.

6.2.2 Effect of FES after botulinum toxin on walking speed

Baseline measurements did not vary significantly for the main study subjects, and all subsequent measurement variance was thus attributed to the intervention. The decrease in walking speed between the third baseline measurement and the measurement immediately after the botulinum toxin injection seen in most subjects was to be expected, as the toxin blocks the pre-synaptic release of acetylcholine, and thus weakens the contractile force of the muscle (Davis and Barnes, 2000). However, the effects of the toxin can take up to 72 hours to take effect (Brin, 1997), which could explain the slight increase in walking speed recorded in subject one immediately after the injection procedure (i.e. the toxin may not have taken full effect at this time). Although the decreases in walking speeds in the remainder of the subjects were not statistically significant, the fact that four of the five subjects showed slower walking speed measured immediately after the botulinum toxin injection compared to during the baseline measurements, is clinically significant. It could be assumed that an even greater reduction in walking speeds could have been measured if measurement session four had taken place a day or two later, as this would have provided sufficient time for the chemodenervation to take full effect.

Between the botulinum toxin injection and the commencement of the FES programme, subjects three, four, and five showed slight decreases in walking speed, whereas increases were recorded for the other two subjects. Measurement five for subjects one and two took place very soon after the botulinum toxin injection (11 and seven days, respectively), and it could thus be assumed that the toxin had not reached its full potency at the start of the

FES programme. It is thus conceivable that self-selected walking speed would not have decreased at this time. Subject five, on the other hand, experienced a 35-day interval between the injection and the start of the FES programme. The botulinum toxin could be expected to have resulted in maximal spasticity reduction (exposing underlying muscle weakness), with a resulting decrease in self-selected walking speeds at this point.

When comparing walking speeds immediately before and after the stimulation programme, subjects two and four showed the largest increases in walking speed, while the other subjects either showed a decrease, or no change. In this context, it is interesting to note that subject two showed the largest increase in walking speed during this time interval, even though he did not receive the FES as prescribed.

Although subject four had shown an increase in walking speed during the FES programme, he was unable to maintain these improvements during the withdrawal phase. One possible explanation is the length of the prescribed treatment programme. Subjects were supposed to use the stimulator for a total of 20 sessions, spread out over four weeks. This was a significantly shorter time interval compared to the length of exposure in Johnson et al. (2002), who have shown increases in mean walking speeds after combining FES treatment to the tibialis anterior and gastrocnemius muscles with botulinum toxin in adults. The intervention phase in Johnson et al. (2002) spanned 12 weeks, although specific individual treatment times were not specified. Other researchers have implemented strength training programmes for between six and ten weeks (McCubbin and Shasby, 1985; Darrah et al., 1999), although they were targeted at adolescents with CP, and did not use electrical stimulation as a strengthening modality. In contrast, Hesse et al. (1995) have shown an increase in mean walking speed maintained for four weeks after combining FES treatment to the tibialis anterior and gastrocnemius muscles with botulinum toxin in children during an intensive three-day treatment programme. The researchers applied the stimulation devices six times a day for three consecutive days after the injection, with each session lasting 30 minutes. It is thus feasible that the intervention of the present study did not reach sufficient intensity levels in order to facilitate adequate muscle strengthening to significantly improve walking speed.

In a study that applied FES to the triceps surae complex in children, Ho et al. (2006) implemented comparable treatment times to the ones used in the present study (15 treatment sessions, with each sessions lasting between 20 and 30 minutes). Although Ho et al. (2006) found that the intervention increased the impulse generation during the push-off phase of gait, these results did not translate into greater stride lengths or faster walking speeds. Similar to the researchers of the present study, Ho et al. (2006) hypothesised that a longer intervention period would be needed for these changes to take effect.

An interesting finding of the present study is that the subject who showed the largest increase in terms of plantarflexor muscle strength both with the ankle in a neutral as well as in a plantarflexed position during the FES period (subject four), also showed the largest increase in self-selected walking speed. Interestingly, no change in dorsiflexor muscle strength occurred in this subject. The other two subjects in the FES group showed smaller effect sizes in terms of plantarflexor strength increases, accompanied by small increases in dorsiflexor muscle strength and no increases in walking speed. The results from this study thus correlate with the findings of Kramer and MacPhail (1994), which have shown that improvements in muscle strength may positively influence functional abilities in CP. Although Kramer and MacPhail (1994) targeted the knee flexors and extensors, available evidence seems to suggest that strengthening the lower limb may have a positive influence on self-selected walking speed in CP.

When average ages are correlated with average walking speeds for all groups with CP subjects (i.e. including CP subjects participating in the pilot trial), however, it becomes evident that the higher the age, the faster the walking speed. This could be assumed to occur due to increased lower limb muscle strength and advanced gait maturation in older children, as detailed in Berger et al. (1984). However, the small sample size used in this study prevents the results from being generalisable to the CP population as a whole without support from further research.

6.3 Energy efficiency index (EEI)

As with walking speed, a discussion of the main study's EEI data will be preceded by a discussion regarding the variability of this outcome measure in the pilot trial and main study populations.

6.3.1 Data variability

EEI is an indication of the energy economy of gait, and has been shown to be inversely proportional to walking speed in adolescents with CP (Kramer and MacPhail, 1994). Rose et al. (1990) have proven EEI calculations based on heart rate to be a convenient yet reliable method of calculating energy efficiency during gait in the clinical setting. Unfortunately, the researchers had difficulty in following the data collection procedure as previously described. Reasons for this were uncontrolled levels of activity prior to the measurement sessions and uncooperative subjects running around between measurement repetitions. Resting heart rates were thus frequently higher than those after the walking trials, resulting in a negative EEI score.

On average, subjects with a diagnosis of CP (in the pilot trial as well as both main study groups) had higher EEI scores than the typically developing subjects. The highest average EEI scores were calculated in the FES group of the main study, who also showed the highest average walking speeds. Rose et al. (1990) stated that the mean economical EEI in CP is more than three times higher than that of typically developing children. The findings of the present study seem to correlate with the results of Rose et al. (1990), as higher walking speeds accompanied higher EEI scores.

One reason for the higher EEI scores in CP subjects compared to typically developing children is the abnormal muscle activation pattern seen in CP. In the presence of spasticity, EMG activity in the tibialis anterior muscle is markedly elevated during stance phase and is accompanied by reduced co-activation of the gastrocnemius muscle, following large reflex potentials in the calf musculature at the start of the stance phase

(Dietz et al., 1981; Berger et al., 1984). This phenomenon eliminates the "roll-off" pattern at terminal stance, thus causing a vertical rise in the body's center of gravity, and a concomitant increase in energy expenditure during gait (Bleck, 1987). The higher average EEI of CP subjects compared to typically developing children is thus understandable, as the latter group did not present with spasticity and / or abnormal muscle activation patterns.

6.3.2 Energy efficiency during gait after FES and botulinum toxin

In the main study, baseline measurements varied greatly among all subjects. The largest effect size (increase) in EEI scores can be seen between baseline values and measurements immediately following the botulinum toxin injection in subject five, compared to a decrease over the same time period in subject three. The other subjects' EEI scores remained fairly constant. However, none of these changes recorded reached statistical significance. The results of subject five in the present study are similar to the findings of Ubhi et al. (2000), who have found minimal increases in Physiological Cost Index (PCI) scores after a single botulinum toxin injection in children with diplegic and hemiplegic CP. Although Ubhi et al. (2000) do not offer an explanation for their results, the induced muscle weakness in the lower leg could be expected to result in greater energy expenditure during gait. Furthermore, increases in heart rate following a procedure under general anesthesia can be expected in the paediatric population, as tachycardia was induced in theatre in the present study in order to prevent other cardiac complications (personal communication: Du Toit, 2007). However, as all subjects in the present study received different anesthetics, no comment regarding the impact of the specific drug on heart rate (and thus EEI scores) during measurement session four, taken four to five hours after the injection, can be made.

After the completion of the prescribed FES intervention, changes in EEI scores varied across the present study's FES and non-FES groups. This is an unexpected finding, as the FES was intended as a functional orthosis for the muscles of the lower leg, and was thus intended to reduce the amount of energy required during gait. These findings do not

correlate with the results of Johnson et al. (2004), who have applied FES daily for 16 weeks after a single botulinum toxin injection into the gastrocnemius muscle of adult stroke patients. Johnson et al. (2004) recorded a significant downward trend in PCI scores over the intervention period. However, the population group differed from that of the present study, and the intervention was applied for a significantly longer period of time. Similarly, Burridge et al. (1997) have also shown significant reductions in PCI scores in stroke patients after ten hour-long sessions of FES distributed over one month, administered by a trained physiotherapist. Again, however, the population differed from the one used in the present study, and comparisons between the results of the present study with the findings of Johnson et al. (2004) and Burridge et al. (1997) are difficult. In addition, all subjects participating in the present study showed an EEI score of 0 during at least one trial during the data collection period, due to higher heart rates before compared to after the walking tests. In the case of subjects one and two, this resulted in an average EEI score of 0 for one measurement session. The results from this study are thus unreliable and need to be interpreted with care, as the intended measurement procedure could not be adhered to at all times, and results can thus not be accepted to be generalisable to the CP population as a whole.

During the stimulation programme, scores for the FES group stayed relatively constant, compared to the average decrease of 0.26b/m in the non-FES group. Although none of these changes are statistically significant, it is interesting that it is the group that did not receive the stimulation that showed the improved energy efficiency after the intervention. Again, the lack of reliable EEI data (i.e. having to assign a score of 0 during some of the walking tests) prevents any deductions from being made in this regard.

6.4 Isometric dorsiflexor and plantarflexor muscle strength

In the present study, FES was applied to both the agonist (gastrocnemius muscle) and the antagonist (tibialis anterior muscle) for 30 minutes a day, five times a week, for four consecutive weeks. Although the main aim of FES is functional improvement rather than individual muscle strengthening as such, it results in repetitive activity in muscles that

were previously inactive and / or weak. FES should thus contribute to some strengthening and subsequent increases in range of motion (ROM) as secondary effects, although these results are sub-maximal (compared to those achieved with neuromuscular electrical stimulation).

The strength data in this study was not normalised for weight, as not all subject's body weights were available at the times of each measurement session, and were not documented in the medical records. Although correcting data for weight would have rendered strength data to be more comparable between subjects (McArdle et al., 1996), uncorrected data can still provide valuable information in terms of individual measurement change over time.

6.4.1 Data variability

Changes in data will be discussed separately for the ankle dorsi- and plantarflexors.

6.4.1.1 Dorsiflexor muscle strength

Although significant measurement variance for the dorsiflexors with the ankle in a neutral position over the baseline period was recorded in the CP subjects of the pilot trial, subsequent measurements remained stable. In terms of dorsiflexor strength with the ankle in a dorsiflexion position, data were stable over the baseline period as well as between baseline and the last measurement sessions. Similarly, average dorsiflexor strength values (averaged over the two testing positions) showed no significant changes in the pilot trial.

When comparing isometric dorsiflexor muscle strengths in a neutral versus a dorsiflexed ankle position, all subjects in the pilot trial measured lower strength values in the latter position. This difference can be attributed to the fact that the tibialis anterior muscle is in a biomechanically shortened position with the ankle in DF, thus limiting the amount of force it is able to exert (Marsh et al., 1991).

6.4.1.2 Plantarflexor muscle strength

Initial strength values with the ankle in a neutral position in the main study (average of 9.7N in the non-FES group; average of 14.3N in the FES group) were comparable to those of the CP subjects in the pilot trial (average of 13.0N). Subjects in the main study subsequently showed an average increase of 2.6N over the baseline period, which correlates with the increase over the same time period recorded in the subjects with CP participating in the pilot trial (2.7N). In addition, the average strength values were lower in the main study (0.6N in the FES group; 1.2N in the non-FES group) compared to the pilot trial (7.3N).

Isometric plantarflexor muscle strength in ten degrees of ankle PF tended towards a significant increase over the baseline period in the pilot trial. In contrast, subjects in the main study showed stable data in terms of this outcome measure (p=0.21). Subjects participating in the main study showed a decrease in muscle strength between the botulinum toxin injection and the start of the FES programme. Subsequent strength gains were recorded for the subjects in the FES group during the stimulation phase, which remained during the withdrawal phase.

In terms of average plantarflexor muscle strength between baseline and the last measurement session (averaged over the two testing positions), subjects with CP in the pilot trial showed a statistically significant increase in average plantarflexor strength (2.3N; p=0.02), while subjects participating in the main study did not show a significant change. A possible explanation is provided by Frasson et al. (2005). The researchers of this study have found that low-frequency nerve stimulation to the extensor digitorum brevis muscle improves the neuromuscular blockade induced by the botulinum toxin in spastic muscles. Reduction in muscle tone (and thus exposed muscle weakness) would be augmented by the combination of FES and botulinum toxin. Although not all subjects in the present study received the FES as intended, the results found by Frasson et al. (2005)

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could explain the significant strength increase in the pilot trial compared to the unchanged data of the main study.

6.4.2 Effect of FES after botulinum toxin on isometric dorsiflexor strength

Although Reed (1997) has shown that electrical stimulation applied to the agonist can improve muscle strength by increasing motor unit recruitment as well as by increasing contractile proteins with resultant muscle hypertrophy, stimulation in this instance was not applied functionally. Conversely, it has been shown that FES applied to the antagonist can cause a decrease in tone in the agonist muscle (Liberson, 1965) by the process of reciprocal inhibition (Apkarian and Naumann, 1991). The results from the present study support these findings, as strength improvements in both the dorsiflexors as well as the plantarflexors were recorded after the intervention.

Between the botulinum toxin injection and the start of the FES programme in the present study, strength recordings decreased in two subjects, while an increase was noted in subject five. The reduction in muscle strength after botulinum toxin is due to the blocking of the pre-synaptic release of acetylcholine, thus weakening the contractile force of the muscle (Davis and Barnes, 2000). It is possible that the long intermission period for subject five between the injection and the start of the FES programme allowed for the weakened calf musculature to become accustomed to the altered neural input and to develop compensatory mechanisms (including axonal sprouting). This subject received no regular physiotherapy, and the increase in isometric strength could thus not have resulted from conventional treatment.

Of the subjects receiving the prescribed FES intervention, subject three showed the largest effect size during the FES programme, followed by subject one. The change in measurements during this time period in both these subjects exceeded the data variability recorded in the pilot trial, and can thus be attributed to the intervention. The subjects experienced intervals of 11 and 14 days between the botulinum toxin injection and the

start of the FES programme, respectively, and can thus be expected to present with similar results. Although improved dorsiflexor muscle strength could be thought to improve active DF ROM during the swing phase of gait and thus result in greater frequencies of heel strike at initial contact, the results from the present study do not support this theory. The greatest increase in dorsiflexor muscle strength was recorded in subject three, who displayed greater ankle angles at initial contact of gait (i.e. a greater extent of toe walking). In contrast, subjects who showed less marked degrees of strength gains showed concomitant smaller ankle angles at initial contact (i.e. a lesser extent of toe walking). The findings of this study thus support the statement of Van der Linden et al. (2003), who found that impairment-orientated gains do not always translate into functional improvements.

Strength measurements after the two-month withdrawal phase showed that all subjects had decreased isometric dorsiflexor strength readings compared to immediately after the FES phase, with a concomitant increase in ankle angles at initial contact (i.e. a greater extent of toe walking). Although the changes for this outcome measure did not reach statistical significance, this study illustrates that FES can improve isometric dorsiflexor strength readings with the ankle in a neutral position, although a longer intervention period may be needed in order for the gains to last beyond the intervention phase.

This hypothesis is further supported by strength data comparisons between baseline measurements with measurements from the last measurement session. Significant decreases were recorded in the FES (p=0.03), but not in the non-FES groups (p=0.42). These findings seem to suggest that FES after a single botulinum toxin injection can improve isometric dorsiflexor muscle strength, even though strengthening is not a primary aim of this mode of electrical stimulation.

The low isometric dorsiflexor muscle strength with the ankle in a neutral position in the main study compared to the pilot trial data can be explained by the fact that although all main study subjects presented with the required full passive DF ROM, considerable effort was needed by the researcher to overcome the resistance of the calf musculature at the

end of passive DF range. This was due to either increased tone in the gastrocnemius muscle, and / or increased mechanical resistance due to physiological muscle shortening. Ito et al. (1996) have shown that the spastic gastrocnemius muscle displays a type I muscle fibre atrophy accompanied by type II fibre hypertrophy, although type I fibres predominate in the muscle's composition. These findings account for the increased stiffness of the calf musculature, as the slow-twitch fibres pose an increased resistance to stretch, as would occur during active or passive DF. The resting position of the ankle would thus have been in varying degrees of PF, which places the calf musculature in a more advantageous position for the initiation of muscle activity, which only exacerbates the problem of muscle stiffness and dorsiflexor weakness. These factors would thus have made active DF difficult for the subjects, and it can be hypothesised that the weak dorsiflexors were unable to overcome the resistance offered by the triceps surae complex.

Only one subject per group was able to maintain the required ankle position for dorsiflexor strength readings to be taken in ten degrees of ankle DF. Mechanical resistance combined with increased muscle tone in the triceps surae together with dorsiflexor muscle weakness prevented most subjects from attaining ten degrees of DF actively. Due to the lack of strength data for the ankle in a position of DF, average dorsiflexor strength values (averaged over the two testing positions) did not show significant variance during the main study.

Although previous studies have assessed the effect of FES on gait of both children and adults, no studies were found that assessed isometric muscle strength after applying FES to both the tibialis anterior and gastrocnemius muscles in this population. Carnstam et al. (1977) recorded an increase in dorsiflexor EMG recordings after merely ten minutes of peroneal nerve stimulation, with a carry-over effect of 35 minutes. However, the subjects were adults with hemiparesis mostly due to multiple sclerosis, and did not use the stimulator while walking.

6.4.3 Effect of FES after botulinum toxin on isometric plantarflexor muscle strength

In a pre- and post-intervention comparison, the largest strength increase with the ankle in a neutral position was measured in subject four, followed by subjects one and three. These results suggest that an interval of one month between botulinum toxin and FES is optimal for strength gains to occur, although some improvements can be seen with shorter intervals as well. All these improvements were maintained during the withdrawal phase. However, the subjects in the non-FES group also showed strength increases of 2.0N over this time interval. These results thus seem to suggest that FES after botulinum toxin is not superior to botulinum toxin injections alone. The results from this study correlate with the findings of Detrembleur et al. (2002), who have shown that combining botulinum toxin with electrical stimulation to the triceps surae complex is not superior compared to botulinum toxin alone in terms of improving Physical Rating Scores, ankle position at initial contact of gait, or spasticity as measured on the Modified Ashworth Scale. No studies investigating the influence of botulinum toxin alone on plantarflexor muscle strength could be found.

When strength measurements before and after the intervention phase (measurement sessions five and six) are compared, the non-FES group presented with an increase of 2.0N, compared to the FES group's 0.7N increase. Although the change over the intervention phase is only significant if data for all five subjects are analysed collectively, the fact that the smaller increase was recorded in the FES group, in spite of the fact that these subjects received the stimulation modality as prescribed, was unexpected. As previously discussed, however, Frasson et al. (2005) have shown electrical stimulation to augment the effects of botulinum toxin. These results could explain the smaller plantarflexor strength increases in the present study's FES group compared to the non-FES group.

With the ankle in ten degrees of ankle PF, the greatest strength increase during the stimulation phase was recorded in subject four, followed by subjects one and three. Subjects one and three were able to maintain these improvements for two months after the intervention had ended. Subjects in the non-FES group also showed an increase in plantarflexor muscle strength in ten degrees of ankle PF over the stimulation phase, although the change was not as marked as in the other three subjects and may be attributable to a learning effect.

Isometric muscle strengths for all subjects (FES and non-FES groups) were significantly higher for the plantarflexors than the dorsiflexors. This is likely due to the fact that the effect of spasticity would have elevated the scores of the plantarflexor strength readings, especially since the measurements were taken in supine with the legs extended in accordance with the measurement protocol outlined by Wiley and Damiano (1998). The researchers thus suggest repeating the measurements in an adapted testing position for future studies (e.g. placing a small bench underneath the subjects' lower legs, so that the hips and knees form 90 degree angles). Although this position places the gastrocnemius muscle in a shortened position, spasticity is less likely to confound results. Data from both testing positions can then be analysed to provide a better representation of isometric muscle strength.

6.5 DF ankle angles at initial contact during gait

The method of ankle angle measurements with the relevant reference points used in this study is explained in a previous chapter. As the lateral malleolus, the head of the fifth metatarsal, and the head of the fibula were used as bony markers, it has to be appreciated that the DF angle will nearly always be larger than 90 degrees. Ankle angles at initial contact are thus not expected to reach 90 degrees. In line with this fact, changes in ankle angles at initial contact will be discussed on an individual basis.

6.5.1 Data variability

During the pilot trial, no statistically significant changes in average ankle angles at initial contact were recorded. However, an increase of 6.1 degrees from 127.2 degrees was noted in the typically developing subjects between measurement sessions three and five. This coincided with an increased walking speed of 0.2m/s, compared to an increase of only 0.09m/s in the subjects with CP. Typically developing subjects thus increased their walking speed to a greater extent than the CP children, together with a greater extent of toe walking than before. Although a learning effect had thus occurred in both groups, the motor dysfunctions of the CP subjects probably prevented them from increasing their walking speeds to the same extent as the typically developing subjects.

Compared to average ankle angles at initial contact during gait in the pilot trial (127.1 degrees), both groups in the main study showed larger average angles (134.9 degrees in the non-FES group, and 131.7 degrees in the FES group). As in the pilot trial, baseline measures varied significantly in most subjects participating in the main study. Subjects participating in the pilot trial showed a decrease of 4.5 degrees in ankle angles at initial contact (i.e. lesser degrees of toe walking) during the period which correlated with the FES phase of the main study. However, no statistically significant change was recorded in either of these trials.

6.5.2 Effect of FES after botulinum toxin on DF angles at initial contact during gait

In the FES group, subjects one and four showed lesser degrees of toe walking after the stimulation programme. In contrast, subject three showed a marked increase in ankle angles at initial contact over this time interval (i.e. a greater extent of toe walking). When the same outcome measure was assessed after a two-month withdrawal phase, all three subjects' average DF angles during gait had increased with the largest effect size

measured in subject four (increase of 8.8 degrees). All three subjects who had received the FES as prescribed thus reverted to toe walking after the two-month withdrawal phase.

Comeaux et al. (1997) have shown that FES to either the gastrocnemius and tibialis anterior muscles (alternated) or FES to the gastrocnemius muscle alone can significantly improve ankle DF angles during gait. In this instance, subjects received daily stimulation for 15 minutes over four weeks, which was not restricted to gait. The researchers have shown an average improvement of four degrees in active ankle ROM during gait with both treatment approaches, maintained for a period of four weeks. The case reports of Carmick (1993 and 1995) also seem to suggest an improved ankle ROM during gait after FES (to either the tibialis anterior muscle alone, the gastrocnemius muscle alone, or the two combined). In contrast, no significant change in ankle angles was observed in the present study. This could be attributed to the shorter total treatment time compared to the previously mentioned studies (Carmick 1993 and 1995; Comeaux et al., 1997).

Although no significant changes in DF angles at initial contact were recorded in the present study, it was noted that the frequency of heel strike across the ten-metre walkway had improved after the stimulation phase in the FES group subjects (this was not an outcome measure used in the present study). This could be explained by changes in knee excursion during gait (i.e. increased knee extension during terminal swing). As the gastrocnemius muscle is a two-jointed muscle, stiffness (either mechanical or due to hypertonicity) in the calf musculature would result in reduced knee extension during gait. Subjects would thus have had to compensate for the resultant shortened leg length by means of toe walking. Both the botulinum toxin injection as well as the FES would be expected to have increased the dynamic length of the triceps surae muscle, resulting in a greater ROM at the knee. This would have resulted in an increased potential for heel strike during gait, even though the actual DF angles would not necessarily need to have changed dramatically. As neither knee angles nor leg length were measured during this study, this hypothesis remains speculative at this stage, and future studies should thus include analyses of both these outcome measures in order to validate this theory.

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6.6 Subjective feedback from the caregivers

Most caregivers reported that their child fell less, participated more in activities of daily living, and fatigued less rapidly after the administration of the botulinum toxin injection, the FES phase, as well as after the withdrawal phase. Although most of these answers did not correlate with objective measurements regarding walking speed, energy expenditure during gait, or isometric muscle strength, data on knee angle ROM during gait (and concomitant ankle ankles at initial contact) could have assisted to substantiate the subjective data.

It could be argued that it is the subjective impression of change that matters most – if the subjects and their caregivers do not feel that the intervention has changed their function and participation in daily activities, it is unlikely that they will continue implementing the intervention at home, and it has to be debated whether it is worth conducting the intervention at all. In the present study, participation in activities of daily living reportedly improved throughout the course of the study, which is indicative of the positive holistic effect of the intervention. Significant strength changes were recorded for the ankle plantarflexors, which may have contributed towards the subjective impression of improvements in function and participation reported by the subjects' caregivers. These findings support the results of Kramer and MacPhail (1994), which have shown that improvements in muscle strength may be associated with improved functional abilities and gait economy. Even though very few statistically significant changes were measured in the impairment-orientated dependent variables in the present study, a perceived carry-over effect into functional activities seems to have occurred.

6.7 Research methodology

Although the single-subject research design has previously been shown to be appropriate for the use in the CP population (Martin and Epstein, 1976; Gonnella, 1989), it has limitations.

6.7.1 Sampling method

In the present study, subjects were recruited by means of selective sampling. Sampling bias in the form of a popularity bias (subjects in all groups were recruited from limited sources) could have resulted in the inclusion of a non-representative sample. The sample sizes for the pilot trial as well as for the main study were small, and results cannot be readily assumed to apply to the entire CP population. Ideally, the researchers would have liked to duplicate the intervention for the main study (i.e. having two subjects per intervention protocol), but financial and time constraints prevented this from being feasible. Due to the small number of subjects participating in the study, the results can only be taken as trends, and cannot be extrapolated to the CP population as a whole without substantiation from further research.

6.7.2 Botulinum toxin administration

The botulinum toxin injection was administered by a trained orthopaedic surgeon. Previous studies in the CP population have made use of a general sedative combined with a local sedative or analgesic (Ubhi et al., 2000; Koman et al., 2001; Baker et al., 2002) or general anesthesia (Cosgrove et al., 1994), or have even administered the toxin without any form of analgesic or sedative (Koman et al., 1993). However, the principal researcher and the orthopaedic surgeon of the present study felt that administering the injection under local anesthesia was thought to be too traumatic for the subjects, and could

potentially have reduced subject co-operation during the subsequent FES programme and / or during the measurement sessions. The botulinum toxin in the present study was thus administered under general anesthesia in theatre. Measurement session four in the present study was conducted four to five hours following the botulinum toxin injection, which could have negatively influenced the results (subjects could have still been drowsy at the time of testing, or could have presented with elevated heart rates due to the anesthetic). However, the researchers wanted to minimise the number of necessary trips for the subjects and their caregivers to the testing venues, which necessitated measurement four being scheduled on the same day as the injecting procedure.

6.7.3 Measurement procedure

All data in the main study were collected by the principal researcher. Although this could have resulted in a potential measurement bias, considerable effort was implemented to standardise the measurement procedure as much as possible - verbal input during isometric muscle testing as well as during video gait analysis was standardised, data collection occurred at the same time of day for each measurement session, the same trained assistant was used for heart rate readings for each subject, measurements took place in the same location for each session, and reliability testing was conducted on samples of ankle angles during gait.

6.7.4 Outcome measures

In this study, a range of outcome measures was implemented in order to assess potential changes on the ICF's impairment as well as function and participation levels. A potential bias was thus avoided by evaluating the effect of the intervention in as holistic a manner as possible.

Although FES is not primarily intended to increase muscle strength, the repeated use of muscles that were previously weak or inactive during a functional task should result in improved muscle strength on a cellular level, as well as in improved neural drive. Impairment-focused outcome measures thus included isometric muscle strength, as well as DF ankle angles at initial contact of gait. Functional changes were assessed by means of measurements of walking speed and energy expenditure during gait, while participation changes were addressed by means of a questionnaire administered to the caregivers. Previous researchers (Van der Linden et al., 2003) have shown that improvements on an impairment level do not necessarily result in changes in either function or participation. This statement was supported by the findings of the present study, as impairment, function and participation improvements only correlated in one subject in the main study (subject four).

6.7.5 Multiple baseline research design

Experimental research in the form of a single-subject design with a multiple-baseline approach across subjects was conducted. Gonnella (1989) and Tervo et al. (2003) have supported the application of single-subject research in the CP population, as this study design places the focus on recognisable individual change that is relevant on a clinical level.

In the present study, all subjects received a single botulinum toxin injection into the gastrocnemius muscle after three baseline measurements, after which the subjects were randomly allocated to different intervention protocols. As FES was the intervention modality implemented in this study, measurement changes between sessions five and six (pre- and post intervention) were taken as representative of the intervention's outcome.

When the dependent variables are discussed according to the different baselines in the subjects receiving both the FES and the botulinum toxin, the greatest effect size seems to

have occurred in subject four, who had a 32-day interval between the botulinum toxin injection and the commencement of the FES phase. At the end of the intervention, this subject's walking speed had increased, while his energy expenditure during gait had decreased. Isometric plantarflexor muscle strength in both neutral and ten degrees of ankle PF had increased. Ankle DF angles at initial contact during gait had decreased slightly (indicating a lesser degree of toe walking), while isometric dorsiflexor muscle strength had remained unchanged in both measurement positions. His caregiver had also reported on improved participation in daily activities.

It is interesting to note that a functional improvement (increased walking speed) was recorded with strength improvements occurring in the ankle plantarflexors, but not the dorsiflexors. It can thus be deduced that the gastrocnemius muscle plays a vital role in gait as well as activities of daily living involving the lower limbs. The results from the present study's subject four support the statement made by Olney et al. (1990) that strength improvements in the triceps surae muscle group could be assumed to result in improved work output ratios around the ankle, resulting in lower levels of energy expenditure during gait.

After the two-month withdrawal phase, subject four in the present study presented with increased EEI scores compared to immediately after the intervention, and had also lost a significant amount of plantarflexor muscle strength in ten degrees of PF. Walking speed had also decreased during this interval, while neutral plantarflexor strength had remained fairly stable. This finding supports the positive correlation between impairment and function discussed above, as the loss of gastrocnemius muscle strength in this instance coincided with a certain reduction in functional capabilities. Although the intervention as administered to subject four thus seems to have favourable outcomes, longer exposure to the intervention may be necessary in order to effect longer lasting improvements such as found by other researchers (Carmick 1993 and 1995).

Although subject one in the present study also showed impairment-focused improvements (increased active ankle DF angles at initial contact during gait, stronger plantarflexor muscles in both testing positions, as well as stronger dorsiflexors with the ankle in a neutral position), no functional changes occurred (walking speed did not change over the course of the intervention, and EEI scores increased minimally during this time). Impairment and function orientated outcome measures also did not correlate in the results of subject three. The results of this study thus seem to suggest that a period of approximately one month between botulinum toxin and the commencement of FES to the lower leg may result in impairment as well as functional and / or participation changes. After such a time interval, the chemodenervating effect of botulinum toxin would have resulted in maximal spasticity reduction, and the tachycardia induced by the general anesthetic would have subsided. As only plantarflexor muscle strength changes in both testing positions reached statistical significance, however, these results merely represent trends at this point and need to be confirmed by future studies.

Interestingly, subject four was one of the youngest subjects participating in the main study (aged 3 years 11 months at the onset of the study), which confirms Bleck's (1987) and Campbell's (1996) statement that early intervention achieves optimum results. However, understanding and co-operation can be a problem in the treatment of young children with FES. The researchers of the present study suggest that subjects eligible for receiving FES treatment after a botulinum toxin injection be tested - stimulation should be applied to the lower leg before the botulinum toxin is administered. If the subject tolerates the device, this combined form of treatment is appropriate.

Throughout the main study, caregiver compliance in terms of documenting the dates and times of stimulator use was poor. Although all caregivers attested to using the FES device as prescribed, the researchers had no objective control over the administration of the intervention, and the stimulation could thus not have been implemented as initially planned. However, utilising FES as a home-based programme necessitated reliance of the

researchers on the caregivers. In order to maximise compliance to the prescribed FES programme, the principal researcher called the caregivers on a weekly basis.

A further limitation of this study was the single application of the intervention. The researchers would have liked to repeat the intervention (FES) after the initial withdrawal period in order to obtain more statistically sound results, time and financial constraints prevented this.

The present study has provided insight into the impact of FES applied to the lower leg after a single botulinum toxin injection into the triceps surae muscle. In order to confirm the results found in this study and to further investigate aspects needing clarification (e.g. proximal versus distal leg muscle stimulation), suggestions for future research will be made in the following chapter.

CHAPTER 7

CONCLUSION AND RECOMMENDATIONS

It was hypothesised that functional electrical stimulation (FES) to the tibialis anterior and gastrocnemius muscles of children with an equinus gait pattern due to cerebral palsy (CP) can augment the effects of a single botulinum toxin injection into the calf musculature. The effect of FES on isometric plantarflexor and dorsiflexor muscle strength, self-selected walking speed, energy expenditure during walking, and on initial contact during gait had varying outcomes. The results of this study have shown that FES can increase isometric plantarflexor muscle strength. However, despite improvements in muscle strength, subjects in this study did not demonstrate changes in self-selected walking speeds. Similarly, the dorsiflexion (DF) angle at initial contact remained unchanged. However, caregivers of the participating subjects felt the intervention to have a positive influence on their children's walking speeds, as well as on age-appropriate function and participation. Furthermore, a 32-day interval between the botulinum toxin injection and the start of the stimulation programme seems to have the greatest effect on most of the above variables.

In this study, the principal researcher attempted to collect data in as structured a manner as possible, with the aim of providing clinically relevant information. Certain shortcomings, however, were experienced and must be taken into consideration in data analysis, and need to be addressed in future studies.

Although the diversity of clinical presentations of children with a diagnosis of CP render an N=1 research design appropriate for this population, the researchers recommend that future studies apply the intervention to more than one subject per protocol. This will permit more reliable deductions to be made in terms of general applicability of the results.

The researchers in this study took measurements on set days following the start of each subject's FES programme. This meant that subjects were not all tested on the same days after the injection procedure (i.e. at the same time), which renders comparisons for outcomes over time following the botulinum toxin difficult. Although the present study aimed at assessing change per subject on an individual basis, future studies should schedule the measurement sessions for all subjects on the same days, regardless of the individual time frames for the start of the intervention. This will permit more reliable descriptions of change over time, and therefore accurate comparisons of results between subjects.

With regards to the FES intervention, more research into different FES protocols (e.g. proximal versus distal muscle stimulation) as well as stimulation dosages and parameters as well as their effect on specific outcomes needs to be conducted, in order to provide clinicians with feasible guidelines for implementing FES in clinical practice. In addition, perhaps neuromuscular electrical stimulation (NMES) should be applied in a controlled environment such as a school or during physiotherapy sessions in order to adequately strengthen weak muscles, prior to introducing FES as a home-programme. This would present a feasible cost-effective long-term management option for children with CP, as individual therapy sessions are costly and having to bring a child into a formal treatment establishment on a regular basis is not a practical solution for a third-world country such as South Africa, in which resources are already limited and cost-effective treatment options need to be found. Following NMES, a FES programme should commence in a formal institution (either a school or hospital) in order to instruct the caregivers on the application of the stimulation device and to ensure that the subject's response to the intervention is appropriate, and then to expand the programme for home use (following an intensive training programme for the relevant caregiver).

Furthermore, a clear differentiation between FES and neuromuscular electrical stimulation (NMES) needs to be made. Although FES is a subgroup of NMES, it is intended for functional augmentation with muscle strengthening occurring as a secondary

effect, and thus requires different stimulation settings and parameters than NMES. The choice of the type of electrical stimulation needs to be based on the aim of the intervention – pure muscle strengthening and / or reduction of spasticity (for which NMES would be used), or improvement in function (requiring FES). Unfortunately, much of the research that has been conducted to date does not clearly distinguish between these two forms of electrical stimulation, and little can thus be said about the effect of FES on various outcome measures.

Along the same lines, outcome measures need to correlate with the aim of the research as well as with the type of electrical stimulation implemented. They should include assessments of the intervention's impact on impairment as well as on function and participation levels, as evidence in this study as well as in previous research has shown that changes on one level cannot always be assumed to correlate with changes on another level.

One of the outcome measures implemented in the present study must be discussed at this point. As previously mentioned, the researchers experienced difficulties with energy expenditure index (EEI) measurements in the pilot trial as well as in the main study (to a lesser degree). This experience raises the question whether EEI measurements are a reliable outcome measure in such a young population as used in this study. Although EEI scores have been extensively used in previous studies, few researchers have commented on levels of physical activity prior to testing, or on the control of subjects during repeated measurements. For this reason, the researchers propose incorporating a practice session for all outcome measures a few days prior to the first measurement session, as this would allow subjects to become accustomed to all the measurement procedures, without excitement adversely influencing data. Although excluding uncooperative subjects from future studies could result in more reliable EEI data for the CP population, children with CP frequently present with varying forms of cognitive impairments (Crothers and Payne, 1959). Excluding subjects based on behavioural and / or cognitive impairments thus limits the external validity of the results. In an attempt to supplement data from EEI

measurements, the researchers in the present study included a caregiver subjective assessment of function and participation. One of the questions referred to the subjects' participation levels during daily activities, which are at least in part related to energy consumption. Future studies thus need to be conducted in order to assess the reliability of EEI scores in a young CP population.

Furthermore, future studies should strive to assess the impact of FES after botulinum toxin on lower leg muscle strength as objectively as possible, in order to supply clinicians with reliable information in terms of optimal FES treatment protocols. This will allow physiotherapists in clinical situations to provide their patients with the best possible evidence –based treatment. The researchers also suggest that muscle strength recordings should be conducted in more than one joint position in future studies, as the present study has shown considerable data variability for some muscles. Interpretation of results based on single measurements may thus provide a false impression of strength, and a truer reflection of muscle strength through range of motion will be obtained by using average values across more than one testing position.

REFERENCE LIST

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

Abel MF and Damiano DL (1996). Strategies for increasing walking speed in diplegic cerebral palsy, *Journal of Pediatric Orthopedics,* 16:753-758

Aoki KR and Guyer B (2001). Botulinum toxin type A and other botulinum toxin serotypes: a comparative review on biochemical and pharmacological actions, *European Journal of Neurology,* 8(Suppl):21-29

Arens LJ, Molteno CD, Marshall SR, Robertson WI, Rabkin J (1978). Cerebral palsy in Cape Town: a comparative 12-year retrospective study, *South African Medical Journal,* 53:319-324

Arens LJ and Molteno CD (1989). A comparative study of postnatally-acquired cerebral palsy in Cape Town, *Developmental Medicine and Child Neurology,* 31:246-254

Apkarian JA and Naumann S (1991). Stretch reflex inhibition using electrical stimulation in normal subjects and subjects with spasticity, *Journal of Biomedical Engineering,* 13:67-73

Baker R, Hausch A, McDowell B (2001). Reducing the variability of oxygen consumption measurements, *Gait and Posture,* 13:202-209

Baker R, Jasinski M, Maciag-Tymecka I, Michalowska-Mrozek J, Bonikowski M, Carr L, MacLean J, Lin J-P, Lynch B, Theologis T, Wendorff J, Eunson P, Cosgrove, A (2002). Botulinum toxin treatment of spasticity in diplegic cerebral palsy: a randomized, double-blind, placebo-controlled dose-ranging study, *Developmental Medicine and Child Neurology,* 44:666-675

Berger W, Altenmueller E, Dietz V (1984). Normal and impaired development of children's gait, *Human Neurobiology,* 3:163-170

Bertoti DB, Stanger M, Betz RR, Akers J, Maynahon M, Mulvahey MJ (1997). Percutaneous intramuscular functional electrical stimulation as an intervention choice for children with cerebral palsy, *Pediatric Physical Therapy,* 9:123-127

Bigland-Ritchie B, Johansson R, Lippold OCJ, Woods JJ (1983). Contractile speed and EMG changes during fatigue of sustained maximal voluntary contractions, *Journal of Neurophysiology,* 50:313-324

Bleck EE (1987). *Orthopaedic Management in Cerebral Palsy, 2nd Edition,* Philadelphia: JB Lippincott Company

Botox® South Africa: package insert (last updated 04/11/2005)

Brehm M-A, Becher J, Harlaar J (2007). Reproducibility evaluation of gross and net walking efficiency in children with cerebral palsy, *Developmental Medicine and Child Neurology,* 49:45-48

Brin MF (1997). Botulinum toxin: chemistry, pharmacology, toxicity, and immunology, *Muscle and Nerve,* 6(Suppl):S146-S161

Brown JK (1984). Hemiplegic cerebral palsy, In *Textbook of Paediatrics* (Ed Forfar JO and Arneil G)*,* Edinburgh: Churchill Livingstone

Brown JK, Rodda J, Walsh EG, Wright GW (1991). Neurophysiology of lower-limb function in hemiplegic children, *Developmental Medicine and Child Neurology,* 33:1037-1047

Brunstrom JE (2001). Clinical considerations in cerebral palsy and spasticity, *Journal of Child Neurology,* 16:10-15

Bührs D. *FES.* E-mail to A.Seifart (online). 16 September 2007. Available email: deonbuhrs@worldonline.co.za

Buller AJ, Eccles JC, Eccles RM (1960). Interactions between motoneurones and muscles in respect of the characteristic speeds of their responses, *Journal of Physiology,* 150:417-439

Burger M (2003). *Pediatric Neurology.* Unpublished class notes (Paediatric Neurology 473). University of Stellenbosch

Burridge JH, Taylor PN, Hagan SA, Wood DE, Swain ID (1997). The effects of common peroneal nerve stimulation on the effort and speed of walking: a randomised controlled trial with chronic hemiplegic patients, *Clinical Rehabilitation,* 22:201-211

Campbell SK (1996). Quantifying the effects of intervention for movement disorders resulting from cerebral palsy, *Journal of Child Neurology,* 11:S61-S70

Carmick J (1993). Clinical use of neuromuscular electrical stimulation for children with cerebral palsy, part 1: lower extremity, *Physical Therapy,* 73:505-513

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

Carnstam B, Larsson L-E, Prevec TS (1977). Improvement of gait following functional electrical stimulation, *Scandinavian Journal of Rehabilitation and Medicine,* 9:7-13

Castle ME, Reyman TA, Schneider M (1979). Pathology of spastic muscle in cerebral palsy, *Clinical Orthopaedics and Related Research,* 49:223-233

Chae J and Hart R (1998). Comparison of discomfort associated with surface and percutaneous intramuscular electrical stimulation for persons with chronic hemiplegia, *American Journal of Physical Medicine and Rehabilitation,* 77:516-522

Comeaux PA, Patterson ND, Rubin MO, Meiner R (1997). Effect of neuromuscular electrical stimulation during gait in children with cerebral palsy, *Pediatric Physical Therapy,* 9:103-109

Cooke RWI (1990). Cerebral palsy in very low birthweight infants, *Archives of Disease in Childhood,* 65:201-206

Cooper PA and Sandler DL (1997). Outcome of very low birth weight infants at 12 to 18 months of age in Soweto, South Africa*, Pediatrics,* 99:537-552

Cosgrove AP, Corry IS, Graham HK (1994). Botulinum toxin in the management of the lower limb in cerebral palsy, *Developmental Medicine and Child Neurology,* 36:386-396

Couper J (2002). Prevalence of childhood disability in rural KwaZulu-Natal, *South African Medical Journal,* 92:549-552

Crompton J and Galea MP (2007). Hand-held dynamometry for muscle strength measurement in children with cerebral palsy, *Developmental Medicine and Child Neurology,* 49:106-111

Crothers B and Payne RS (1959). *The Natural History of Cerebral Palsy,* Cambridge, Mass.: Harvard University Press

Damiano DL, Vaughan CL, Abel MF (1995). Muscle response to heavy resistance exercise in children with spastic cerebral palsy, *Developmental Medicine and Child Neurology,* 37:731-739

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

Davis EC and Barnes MP (2000). Botulinum toxin and spasticity, *Journal of Neurology, Neurosurgery, and Psychiatry,* 69:143-147

De Groot L, Appelman M, Zeillemaker A, Van der Putten A (2000). Oefenmethoden in de kinderfysiotherapie, In *Kinderfysiotherapie* (Ed van Empelen R, Nijhuis-van der Sanden R, Hartman A), pp.171-204, Maarssen: Elsevier Gezondheidszorg

Delgado MR and Albright AL (2003). Movement disorders in children: definitions, classifications, and grading systems, *Journal of Child Neurology,* 18:S1-S8

De Vahl J (1992). Neuromucular Electrical Stimulation in Rehabilitation, In *Electrotherapy in Rehabilitation* (Ed Gersh M)*,* pp. 218-268, Philadelphia: Davies Company

Ghasia F, Brunstrom J, Gordon M, Tychsen L (2008). Frequency and severity of visual sensory and motor deficits in children with cerebral palsy: gross motor function classification scale, *Investigative Opthalmology and Visual Science,* 49:572-580

Detrembleur C, Lejeune TM, Renders A, Van den Bergh PY (2002). Botulinum toxin and short-term electrical stimulation in the treatment of equinus in cerebral palsy, *Movement Disorders,* 17:162-169

Dietz V, Quintern J, Berger W (1981). Electrophysiological studies of gait in spasticity and rigidity, *Brain,* 104:431-449

Dodd KJ, Taylor NF, Graham HK (2003). A randomised clinical trial of strength training in young people with cerebral palsy, *Developmental Medicine and Child Neurology,* 45:652-657

Douglas AA (1961). Opthalmological aspects. In *Cerebral Palsy in Childhood and Adolescence* (Ed Hendersen JL), pp. 197-241, Edinburgh: E.&S.Livingstone

Durham S, Eve L, Stevens C, Ewins D (2004). Effect of functional electrical stimulation on asymmetries in gait of children with hemiplegic cerebral palsy, *Physiotherapy,* 90:82-90

Du Toit J (2007). Personal telephone call. 10 November, Table View

Eames NWA, Baker R, Hill N, Graham K, Taylor T, Cosgrove A (1999). The effect of botulinum toxin A on gastrocnemius length: magnitude and duration of response, *Developmental Medicine and Child Neurology,* 41:226-232

Einspieler C and Prechtl HF (2005). Prechtl's assessment of general movements: a diagnostic tool for the functional assessment of the young nervous system, *Mental Retardation and Developmental Disabilities Research Reviews,* 11:61-67

Engsberg JR, Olree KS, Ross SA, Park TS (1996). Quantitative clinical measure of spasticity in children with cerebral palsy, *Archives of Physical Medicine and Rehabilitation,* 77:594-599

Fowler EG, Ho TW, Nwigwe AI, Dorey FJ (2001). The effect of quadriceps femoris muscle strengthening exercises on spastiicity in children with cerebral palsy, *Physical Therapy,* 81:1215-1223

Frasson E, Priori A, Ruzzante B, Diodone G, Bertolasi L (2005). Nerve stimulation boosts botulinum toxin action in spasticity, *Movement Disorders,* 20:624-629

Gage JR (1991). *Gait Analysis in Cerebral Palsy, 2ⁿᵈ Edition,* New York: Cambridge University Press

Gamble JG (1988). Nerve and Muscle. In *The Musculoskeletal System: Physiological Basis,* pp.116-137, New York: Raven Press

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

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

Gonnella C (1989). Single subject experimental paradigm as a clinical decision tool, *Physical Therapy,* 69:601-609

Gracies J-M, Nance P, Elovic E, McGuire J, Simpson DM (1997). Traditional pharmacological treatments for spasticity part I: local treatments, *Muscle and Nerve,* 6(Suppl):6:S61-S91

Hagberg B, Hagberg G, Olow I (1975). The changing panorama of cerebral palsy in Sweden 1954 – 1970, *Acta Pediatrica Scandinavia,* 64:187-200

Hazlewood ME, Brown JK, Rowe PJ, Salter PM (1994). The use of electrical stimulation in the treatment of hemiplegic cerebral palsy, *Developmental Medicine and Child Neurology,* 36:661-673

Hesse S, Jahnke MT, Luecke D, Mauritz KH (1995). Short-term electrical stimulation enhances the effectiveness of botulinum toxin in the treatment of lower limb spasticity in hemiparetic patients, *Neuroscience Letters,* 201:37-40

Hesse S, Reiter F, Konrad M, Jahnke MT (1998). Botulinum toxin type A and short-term electrical stimulation in the treatment of upper limb flexor spasticity after stroke: a randomised, double-blind, placebo-controlled trial, *Clinical Rehabilitation,*12:381-388

Himmelmann K, Hagberg G, Beckung E, Hagberg B, Uvebrant P (2005). The changing panorama of cerebral palsy in Sweden. IX. Prevalence and origin in the birth-year period 1995-1998, *Acta Pediatrica,* 94:287-294

Ho C-L, Holt KG, Saltzman E, Wagenaar RC (2006). Functional electrical stimulation changes dynamic resources in children with spastic cerebral palsy, *Physical Therapy,* 86:987-1000

Illingworth RS (1958). *Recent Advances in Cerebral Palsy, 1st Edition,* London: Churchill

Ingram TTS (1984). A historical review of the definition and classification of the cerebral palsies, In *The Epidemiology of the Cerebral Palsies. Clinics in Developmental Medicine No 87* (Ed Stanley F and Alberman E), pp.35-45, London: S.I.M.P with Blackwell Scientific; Philadelphia: Lippincott

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

Jefferson RJ (2004). Botulinum toxin in the management of cerebral palsy, *Developmental Medicine and Child Neurology,* 46:491-499

Johnson CA, Burridge JH, Strike PW, Wood DE, Swain ID (2004). The effect of the combined use of botulinum toxin type A and functional electrical stimulation in the treatment of spastic drop foot after stroke: a preliminary investigation, *Archives of Physical Medicine and Rehabilitation,* 86:902-909

Johnson CA, Wood DE, Swain ID, Tromans AM, Strike P, Burridge JH (2002). A pilot study to investigate the combined use of botulinum neurotoxin type A and functional electrical stimulation, with physiotherapy, in the treatment of spastic dropped foot in subacute stroke, *Artificial Organs,* 26:263-266

Koman LA, Mooney JF, Smith B, Goodman A, Mulvaney T (1993). Management of cerebral palsy with botulinum-A toxin: preliminary investigation, *Journal of Pediatric Orthopaedics,* 13:489-495

Koman LA, Brashear A, Rosenfeld S, Chambers H, Russman B, Rang M, Root L, Ferrari E, Garcia de Yebenes Prous J, Smith BP, Turkel C, Walcott JM, Molloy PT (2001). Botulinum toxin type A in the treatment of equinus foot deformity in cerebral palsy: a multicenter, open-label clinical trial, *Pediatrics,* 108:1062-1071

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

Law M, Stewart D, Pollock N, Letts L, Bosch J, Westmorland M (1998). Critical review form – quantitative studies. McMaster University Occupational Therapy Evidence-Based Practice Research Group

Liberson WT (1965). Experiment concerning reciprocal inhibition of antagonists elicited by electrical stimulation of agonists in a normal individual, *American Journal of Physical Medicine,* 44:306-308

Mair A (1961). Incidence, prevalence and social class. In *Cerebral Palsy in Childhood and Adolescence* (Ed Hendersen JL)*,* pp.15-21, Edinburgh: E.&S.Livingstone

Marsh E, Sale D, McComas AJ, Quinlain J (1981). Influence of joint position on ankle dorsiflexion in humans, *Journal of Applied Physiology,* 51:160-167

Martin JE and Epstein LH (1976). Evaluating treatment effectiveness in cerebral palsy, *Physical Therapy,* 56:286-294

Mayer NH (1997), Clinicophysiological concepts of spasticity and motor dysfunction in adults with an upper motorneuron lesion, *Muscle and Nerve,* 6(Suppl):S1-S10

Mayston M (2002). Setting the scene, In *Neurological Physiotherapy, 2nd Edition* (Ed Edwards S), Churchill Livingstone

McArdle WD, Katch FI, Katch VL (1996). Muscular strength: training muscles to become stronger, In *Exercise Physiology: Energy, Nutrition and Human Performance, 4th Edition,* Baltimore: Williams and Wilkins

McBurney H, Taylor NF, Dodd KJ, Graham HK (2003). A qualitative analysis of the benefits of strength training for young people with cerebral palsy, *Developmental Medicine and Child Neurology,* 45:658-663

McCubbin JA and Shasby GB (1995). Effects of isokinetic exercise on adolescents with cerebral palsy, *Adapted Physical Activity Quarterly,* 2:56-64

Mitchell RG (1961). In *Cerebral Palsy in Childhood and Adolescence* (Ed Hendersen JL), pp.142-194. Edinburgh: E&S Livingstone

Mowat J (1961). Ear, nose and throat disorders: deafness, In *Cerebral Palsy in Childhood and Adolescence* (Ed Hendersen JL)*,* Edinburgh: E.&S. Livingstone

Munro D (1961). Dental features, In *Cerebral Palsy in Childhood and Adolescence* (Ed Hendersen JL)*,* Edinburgh: E.&S. Livingstone

Nelson KB and Ellenberg JH (1978). Epidemiology of cerebral palsy, *Advances in Neurology,* 19:421-435

Odding E, Roebroeck ME, Stam HJ (2006). The epidemiology of cerebral palsy: incidence, impairments and risk factors, *Disability and Rehabilitation,* 28:183-191

Odstock Medical Functional Electrical Stimulation Web site (2006). Available at: www.odstockmedical.com/FES.htm. Accessed April 20, 2007

Olney SJ, MacPhail HEA, Hedden DM, Boyce WF (1990). Work and power in hemiplegic cerebral palsy gait, *Physical Therapy,* 70:431-438

Orlin MN, Pierce SR, Stackhouse BT, Johnston T, Shewokis PA, McCarthy JJ (2005). Immediate effect of percutaneous intramuscular stimulation during gait in children with cerebral palsy: a feasibility study, *Developmental Medicine and Child Neurology,* 47:684-690

Paneth N and Kiely J (1984). The frequency of cerebral palsy: a review of population studies in industrialised nations since 1950, In *The Epidemiology of the Cerebral Palsies. Clinics in Developmental Medicine No 8.* (Ed Stanley F and Alberman E), pp.46-56, Philadelphia: Lippincott

Peacock WJ, Staudt LA, Nuwer MR (1991). A neurosurgical approach to spasticity: selective posterior rhizotomy, In *Neurosurgery Update II: Vascular, Spinal, Pediatric, and Functional Neurosurgery* (Ed Wilkins RW, Rengachary SS), pp.403-407, New York: McGraw Hill

Perry JP, Hoffer MM, Giovan P, Antonelli D, Greenberg R (1974). Gait analysis of the triceps surae in cerebral palsy, *Journal of Bone and Joint Surgery,* 56-A:511-520

Pidcock FS, Graziani LJ, Stanley C, Mitchell DG, Merton D (1990). Neurosonographic features of periventricular echodensities associated with cerebral palsy in preterm infants, *Journal of Pediatrics*, 116:417-422

Pierce SR, Orlin MN, Lauer RT, Johnston TE, Smith BE, McCarthy JJ (2004). Comparison of percutaneous and surface electrical stimulation during gait in a child with hemiplegic cerebral palsy, *American Journal of Physical Medicine and Rehabilitation,* 83:798-805

Pin T, Dyke P, Chan M (2006). The effectiveness of passive stretching in children with cerebral palsy, *Developmental Medicine and Child Neurology,* 48:855-862

Pinto-Martin JA, Riolo S, Cnaan A, Holzman C, Susser MW, Paneth N (1995). Cranial ultrasound prediction of disabling and nondisabling cerebral palsy at age two in a low birth weight population, *Pediatrics*, 95:249-254

Postans NJ and Granat MH (2005). Effect of functional electrical stimulation, applied during walking, on gait in spastic cerebral palsy, *Developmental Medicine and Child Neurology,* 47:46-52

Reed B (1997). The physiology of neuromuscular electrical stimulation, *Pediatric Physical Therapy,* 9:96-102

Robertson C, Sauve RS, Christianson HE (1994). Province-based study of neurologic disability among survivors weighing 500 through 1249 grams at birth, *Pediatrics,* 93:636-640

Rose J, Medeiros JM, Parker R (1985). Energy cost index as an estimate of energy expenditure of cerebral-palsied children during assisted ambulation, *Developmental Medicine and Child Neurology,* 27:485-490

Rose J, Gamble JG, Medeiros J, Burgos A, Haskell WL (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, Gamble GJ, Burgos A, Medeiros J, Haskell WL (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 and McGill KC (1998). The motor unit in cerebral palsy, *Developmental Medicine and Child Neurology,* 40:270-277

Rosenbaum P, Paneth N, Goldstein M, Bax M (2007). A report: the definition and classification of cerebral palsy, April 2006, *Developmental Medicine and Child Neurology*, 49:8-14

Roy MAG and Doherty TJ (2004). Reliability of hand-held dynamometry in assessment of knee extensor strength after hip fracture, *American Journal of Physical Medicine and Rehabilitation,* 83:813-818

Russman BS, Tilton A, Gomley ME Jr (1997). Cerebral palsy: a rational approach to a treatment protocol, and the role of botulinum toxin in treatment, *Muscle and Nerve,* 6(Suppl):S181-193

Sackett DL (1996). Evidence based medicine: what it is and what it isn't, *British Medical Journal,* 312:71-72

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

Schuster DP, Powers WJ (2005). Experimental study designs, In *Translational and Experimental Clinical Research* (Eds Schuster DP, Powers WJ)*,* pp.88-90, Lippincott William and Wilkins

Scott A (1989). Clostridial toxins as therapeutic agents, In *Botulinum Neurotoxin and Tetanus Toxin* (Ed Simpson L), San Diego, CA: Academic Press

Shumway-Cook and Woollacott (1995). *Motor Control: Theory and Practical Applications,* pp.3-21, Philadelphia: Lippincott Williams and Wilkins

Skinner SR (1992). Direct Measurement of Spasticity, In *The Diplegic Child* (Ed Sussman MD), pp.31-44, Rosemont IL: American Academy of Orthopedic Surgeons

Stackhouse SK, Binder-Macleod SA, Lee SCK (2005). Voluntary muscle activation, contractile properties, and fatiguability in children with and without cerebral palsy, *Muscle and Nerve,* 31:594-601

Stanley F (1984). Perinatal risk factors in the cerebral palsies, In *The Epidemiology of the Cerebral Palsies. Clinics in Developmental Medicine No 87* (Ed Stanley F and Alberman E), pp.98-113, London: S.I.M.P with Blackwell Scientific, Philadelphia: Lippincott

Stanger M and Oresic S (2003). Rehabilitation approaches for children with cerebral palsy: overview, *Journal of Child Neurology,* 18:S79-S88

Steinwender G, Saraph V, Zwick EB, Steinwender C, Linhart W (2001). Hip locomotion mechanisms in cerebral palsy crouch gait, *Gait and Posture,* 13:78-85

Sutherland DH, Cooper L, Daniel D (1980). The role of the ankle plantar flexors in normal walking, *The Journal of Bone and Joint Surgery,* 62-A :354-363

Taylor P (2002). *The Odstock 2 Channel Stimulator (O2CHSII) User Instruction Manual,* Course notes: Functional Electrical Stimulation, Cape Town

Tervo RC, Estrem TL, Bryson-Brockmann W, Symons FJ (2003). Single-case experimental designs: applications in developmental-behavioral pediatrics, *Developmental and Behavioral Pediatrics,* 24:438-448

The Bobath Centre [Online] (2007). Available at: www.bobath.org.uk. Accessed November 5, 2007

Ubhi T, Bhakta BB, Ives HL, Allgar V, Roussounis SH (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

Unger M, Faure M, Frieg A (2006). Strength training in adolescent learners with cerebral palsy: a randomized controlled trial, *Clinical Rehabilitation,* 20:469-477

Van der Linden ML, Hazlewood ME, Aitchinson AM, Hillman SJ, Robb JE (2003). Electrical stimulation of gluteus maximus in children with cerebral palsy: effects on gait characteristics and muscle strength, *Developmental Medicine and Child Neurology,* 45:385-390

Veen S, Ens-Dokkum MH, Schreuder AM, Verloove-Vanhorick SP, Brand R, Ruys JH (1991). Impairments, disabilities and handicaps of very preterm and very-low-birthweight infants at five years of age, *Lancet,* 338:33-36

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

Winters TF, Gage JR, Hicks R (1987). Gait patterns in spastic hemiplegia in children and young adults, *Journal of Bone and Joint Surgery,* 69-A:437-441

Wolpaw JR and Carp JS (2006). Plasticity from muscle to brain, *Progress in Neurobiology,* 78:233-263

World Health Organisation. International Classification of Functioning, Disability, and Health (2001). Short Version. Geneva

Yekutiel M, Jariwala M, Stretch P (1994). Sensory deficit in the hands of children with cerebral palsy: a new look at assessment and prevalence, *Developmental Medicine and Child Neurology,* 36:619-624

APPENDIX 1

Search strategies implemented

Strategy 1:   cerebral palsy AND electrical stimulation OR electric stimulation OR electric stimulation therapy OR surface stimulation OR percutaneous stimulation

Strategy 2:   strategy 1 AND gait OR lower limb OR leg OR gastrocnemius OR tibialis anterior OR triceps surae OR gluteus OR hamstrings OR quadriceps OR energy economy OR energy expenditure

APPENDIX 2

Participant information sheet

Title of the project: What are the short- and medium-term effects of functional electrical stimulation (FES) following a botox injection into the calf muscle in children aged four to six years with spastic hemiplegia due to cerebral palsy (CP)?

Reference number: N06/05/083

Principal investigator: Anja Seifart

Address: University of Stellenbosch
Faculty of Health Sciences, Tygerberg Medical Campus,
Department of Physiotherapy

You and your child are being invited to take part in a research project. Please read the information in this letter, and feel free to ask the study staff about anything that is unclear to you. Participation is entirely voluntary, and your child's future medical treatment will not be negatively influenced if you decide not to take part. If you do agree to participate, you are free to withdraw from the study at any time without your child's future medical treatment being influenced whatsoever.

This study has been approved by the Committee for Human Research at the University of Stellenbosch, and will be conducted according to the South African Guidelines for Good Clinical Practice and the Medical Research Council (MRC) Ethical Guidelines for Research.

What is the study about?

The aim of this study is to determine the most effective treatment protocol for FES after botox injection in children with spastic hemiplegic CP in order to maximise their ability to function. Five children will be given a device that will electrically stimulate the muscles of the lower leg to contract. The stimulation is not painful, and feels like tingling or slight pins and needles. Your child will continue with his / her normal physiotherapy treatment as before.

What do you need to do?

- Your child will be expected to attend the following sessions:
  a) three measurement sessions at either Tygerberg or Paarl School before the botox injection

  b) botox injection and measurement session immediately afterwards (on the same day) at Tygerberg Hospital

  c) one measurement session at either Tygerberg Hospital or Paarl School before the start of the strengthening (FES) programme

  d) one measurement session after the strengthening programme

  e) one measurement session at the end of the study

- All your travel expenses will be refunded.
- A qualified physiotherapist will visit teach you how to use the device, and answer any questions you may have. If necessary, a home visit will be arranged to address any queries. Your child will need to practice walking with the device on at home for 30 minutes per day, five times a week, for four weeks in a row.
- Your child will be videotaped during all assessments, and the recordings will be stored on CD's. The strength of your child's leg will also be tested at the same time. Only the legs will need to be uncovered. After four weeks of using the stimulation device at home, you will need to return it. Your child will, however,

be assessed for a last time two months later, to see what the medium-term effect of the treatment was.

Why have you been invited to take part?

Your child has tight calf muscles and has been selected for botox injections by his / her doctor. This study hopes that FES will further improve the ankle movements during walking. This will help to determine what the best treatment option is for the condition that your child has.

Will you benefit from taking part?

You will not get to keep the machine, but the improvements that take place have been shown to stay for up to four months. Your child could thus participate more normally in his / her activities. Once the best treatment option has been identified, more children with the same condition as your child can be treated more effectively than before. You will not be paid to take part in this study.

Are there any risks?

No side effects have previously been reported due to the treatment with electrical stimulation.

Will my child remain anonymous?

None of your child's personal details will be made public to anyone other than the study staff, and will not be published in any form. The data of your child will be stored and presented in an anonymous and confidential way. All images and video recordings will be destroyed after completion of the study.

What happens if I have any questions?

You are welcome to address any questions to Anja Seifart on 082 747 6909 at any time. You are also welcome to contact the Committee for Human Research of the University of Stellenbosch on (021) 938 9207 if you have any questions or complaints that have not been answered by the study staff.

What happens afterwards?

If you wish, you will be sent the results of the study as soon as they become available. You will then be advised as to what the best treatment options for your child is, which you will need to discuss with your child's physiotherapist and doctor.

Inligtingsblad vir studiedeelname

<u>Titel van die navorsingsprojek:</u> Wat is die kort- en medium-termyn effek van funksionele elektriese stimulasie (FES) na 'n botox inspuiting tot die kuit in kinders tussen vier en ses jaar oud met spastiese hemiplegie as gevolg van serebrale verlamming?

<u>Verwysingsnommer:</u> N06/05/083

<u>Hoofnavorser:</u> Anja Seifart

<u>Adres:</u> Universiteit van Stellenbosch

Fakulteit Gesondheidswetenskappe, Tygerberg

Mediese Kampus

Departement Fisioterapie

U en u kind word hiermee uitgenooi om deel te neem aan 'n navorsingstudie. Lees asb hierdie inligting, en rig u vrae aan die studie personeel. Deelname aan die studie is heeltemal vrywillig, en u kind se toekomstige mediese behandeling sal geensins nadelig beïnvloed word as u besluit om die uitnodiging nie te aanvaar nie. U mag ter alle tye u kind van die studie onttrek, sonder dat u kind se toekomstige mediese behandeling benadeel sal word.

Hierdie studie is goedgekeur deur die Universiteit van Stellenbosch se Menslike Navorsingskomitee, en sal uitgevoer word volgens die etiese riglyne en beginsels van die Internasionale Verklaring van Helsinki en die Etiese Riglyne vir Navorsing van die Mediese Navorsingsraad (MNR).

Waaroor gaan die studie?

Die doel van die studie is om die mees effektiewe behandelingsprotokol vir FES na botox in kinders met spastiese serebrale verlamming te bepaal, sodat hulle hulle maksimale funksionele vlak kan bereik. Vyf kinders sal elkeen 'n toestel gegee word wat die spiere van die kuit elektries sal stimuleer om saam te trek. Die stimulasie is nie pynlik nie, en voel soos prikkels of ligte naelde en spelde. U kind sal met sy gewone fisioterapie aangaan soos voorheen.

Wat moet u doen?

- U kind sal die volgende sessies moet bywoon:
  a) drie metingsessies by die Tygerberg Kinderhospitaal of by Paarl Skool voor die dag van die inspuiting

  b) botox inspuiting en een metingsessie onmiddelik daarna (op dieselfde dag) by Tygerberg Hospitaal

  c) een metingsessie by Tygerberg Kinderhospitaal of Paarl Skool voor die begin van FES

  d) een metingsessie aan die einde van die stimulasie program

  e) een metingsessie aan die einde van die studie

- Al u reisonkonstes sal vergoed word.
- 'n Gekwalifiseerde fisioterapeut sal vir u en u kind leer hoe om die stimulasie toestel te gebruik en sal al u vrae beantwoord. Indien nodig, sal 'n tuisbesoek gereël word om enige probleme uit te klaar. U kind sal gevra word om vir 30 minute elke dag, vyf dae 'n week, vir vier opeenvolgende weke by die huis met die toestel te oefen om te loop.
- U kind sal tydens elke metingsessie met 'n videokamera afgeneem word. Die opnames sal op kompakskywe gestoor word. Die krag van u kind se beenspiere sal ook tydens hierdie sessies getoets word. Slegs die bene sal vir hierdie prosedures ontbloot word.

- Na vier weke sal u die stimulasietoestel moet teruggee. U kind sal egter na 'n verdere twee maande 'n laaste metingsessie ondergaan, om te bepaal wat die medium-termyn uitwerking van die behandeling was.

Hoekom is u uitgenooi om deel te neem?

U kind het stywe kuitspiere en is deur sy dokter gekies om botox te ontvang. Die navorser hoop dat FES verder die looppatroon van u kind sal verbeter. Dit sal help om die beste behandelingsprotokol te bepaal vir die toestand wat u kind het.

Sal u daarby baat om deel te neem?

U sal nie die stimulasie toestel kan hou nie, maar die verbeteringe wat tydens die vier weke van gebruik plaasvind, is bewys om tot vier maande lank te bly. U kind sal dus moontlik op 'n meer normale vlak in alledaagse aktiwiteite kan deelneem. Sodra die beste behandelingsprotokol vir kinders met serebrale verlamming bepaal is, sal meer kinders met dieselfde toestand meer doeltreffend as tevore behandel kan word. U sal nie finansiële vergoeding ontvang deur deel te neem aan die studie nie.

Is daar enige risiko's?

Geen newe-effekte is tot dusver as gevolg van behandeling met elektriese stimulasie aangemeld nie.

Sal my kind anoniem bly?

U kind se persoonlike besonderhede sal aan niemand anders as die navorsingspersoneel bekend gemaak word nie. Dit sal ook in geen vorm gepubliseer word nie. Die data van u kind se meetings sal op 'n anonieme en vertroulike manier gestoor en oorgedra word. Al die video opnames en beeldmateriaal sal na die einde van die studie vernietig word.

Wat gebeur as ek vrae het?

U is welkom om u vrae ter enige tyd aan Anja Seifart (082 747 6909) te rig. U is ook welkom om die Menslike Navorsingskomitee by (021) 938 9207 te skakel as u enige vrae het wat nie tot u bevrediging deur die navorsingspersoneel beantwoord is nie. U sal 'n afskrif van hierdie inligting ontvang.

Wat gebeur na die studie?

As u wil, sal u die uitslae van die studie ontvang sodra dit bekend gemaak word. U sal dan aangeraai word wat die beste behandelingsopsies vir u kind is. Hierdie inligting en hoe u daarop gaan reageer, sal u dan met u kind se fisioterapeut en dokter moet bespreek.

APPENDIX 3

Declaration of consent

I,………………………., hereby agree for my child………………………………..to take part in the study entitled "What are the short- and medium-term effects of FES following a botox injection to the calf in children aged four to six years with spastic hemiplegia due to cerebral palsy?"

I declare that:

- I have read or had read to me this information and consent form and it is written in a language I am comfortable to use.
- I have had a chance to ask any questions, and they were answered to my satisfaction.
- Participation is entirely voluntary, and I have not been pressured into taking part.
- I may withdraw my child from the study at any time without his / her future medical treatment being influenced whatsoever.
- My child may be asked to leave the study before it has finished if the study doctor or researcher feels it is in my child's best interests, or if my child does not follow the study plan as agreed to.

Signed at………………………….on……………………………………

……………………………………   …………………………….
Signature of parent or legal guardian   Signature of witness

Verklaring van toestemming

Ek,…………………………., gee hiermee toestemming vir my kind

…………………………..om deel te neem aan die studie met die titel "Wat is die kort- en medium-termyn effek van FES na 'n botox inspuiting tot die kuit in kinders tussen vier en ses jaar oud met spastiese hemiplegie as gevolg van serebrale verlamming?"

Ek verklaar dat:

- Ek die inligting en verklaringsvorm gelees het / dat iemand dit vir my gelees het, en dat dit in 'n taal is wat ek goed verstaan en waarmee ek gemaklik is.
- Ek 'n geleentheid gehad het om vrae te vra, en dat hulle tot my bevrediging beantwoord is.
- Deelname aan die studie heeltemal vrywillig is, en dat ek nie tot deelname gedwing is nie.
- Ek my kind ter enige tyd van die studie mag onttrek, sonder dat sy toekomstige mediese behandeling nadelig beïnvloed sal word.
- My kind gevra mag word om aan die projek te onttrek voordat dit afgehandel is indien die studiedokter of navorser van oordeel is dat dit in sy / haar beste belang is, of indien my kind nie die ooreengekome studieplan volg nie.

Geteken ter………………………….op……………………………………

…………………………………   …………………………………..
Handtekening van ouer of voog   Handtekening van ooggetuie

APPENDIX 4

Data sheet

Name of child: …………………………………………………………

Gender: …………………………………………………………

Age: …………… **DOB:** ………………………………………

Affected leg: …………………………………………………………

Assistive devices: ……………………………………………………

Name of parent / legal guardian: ……………………………………

Contact nr: ……………………………………………………………

Address: ………………………………………………………………

Tested at: ……………………………………………………………

Details of child's physiotherapist:

Name:………………………………………………………….

Contact number:……………………………………………….

Location of practice:…………...…………………………...

Frequency of treatment:……………………………………….

		Session1 Date	Session2 Date	Session3 Date	Session4 Date	Session5 Date	Session6 Date	Session7 Date
Time for 10m walk (s)	**Walk 1**							
	Walk 2							
	Walk 3							
Self-selected walking speed (m/s)	**Walk 1**							
	Walk 2							
	Walk 3							
	Average							
Average DF angle at initial contact	**Walk 1**							
	Walk 2							
	Walk 3							
	Average							
Heart rate (b/min)	**Before walk 1**							
	After walk 1							
	Before walk 2							
	After walk 2							
	Before walk 3							
	After walk 3							

EEI (b/min)	**Walk 1**						
	Walk 2						
	Walk 3						
	Average						
Isom DF strength (N)	**Neutr** 10^0 **DF**						
	Neutr 10^0 **DF**						
	Neutr 10^0 **DF**						
	Max neutr **Max DF**						
Ave DF strength (N)							
Isom PF strength (N)	**Neutr** 10^0 **PF**						

	Neutr **10^0 PF**							
	Neutr **10^0 PF**							
	Max neutr **Max PF**							
Ave PF strength (N)								

APPENDIX 5

Botulinum toxin type A (Allergan®; Registration number 27/30.4/0164)

Botulinum toxin type A (Allergan®) is a schedule four drug, and is a purified form of a Clostridium botulinum culture. It is indicated for use in children older than two years with spastic equinus due to CP. It presents as a vacuum-dried powder, which needs to be reconstituted with sterile normal saline before injection. The reconstituted product should be used within four hours, during which time it needs to be stored in a refrigerator. Any remaining solution should be discarded, as it contains no preservative. A trained professional is required to administer the toxin (Botox® South Africa: package insert).

Contra-indications for the use of botulinum toxin are:
- Known hypersensitivity to botulinum toxin type A or its constituents
- Inflammation or infection at the proposed injection site

Caution should be exercised if subjects are taking aminoglycoside antibiotics, as these may potentiate the effect of the toxin. The recommended dosage of four units per kilogram weight for patients with hemiplegic CP should not be exceeded, as this may result in the formation of antibodies. It is advised to have resuscitation equipment available during injection (Botox® South Africa: package insert). Localised pain and bruising have previously been reported after injection in CP, as well as an incidence of viral and ear infections. Less common side effects include general and local weakness, knee and ankle pain, leg pain, falling, myalgia, cramps, urinary incontinence, sleepiness and lethargy, gait deviations, rash, malaise, paraesthesia, and pyrexia. These effects usually occur within a few days after injection (Botox® South Africa: package insert). A 17% incidence of side effects has been reported.

The recommended volume per injection site for spastic CP is 0,1 – 0,5 ml. The table below states dilution specifications (100 units botulinum toxin per vial). A sterile 26ml gauge / 0.16mm needle should be used to inject the medial and lateral heads of the gastrocnemius muscle on the hemiplegic side, following the dosaging guidelines stated above.

Table: Dilution specifications

Diluent to be used (sterile normal saline)	Resulting dose (in units per 0,1 ml)
0.5 ml	20.0 U
1.0 ml	10.0 U
2.0 ml	5.0 U
2.5 ml	4.0 U
4.0 ml	2.5 U
8.0 ml	1.25 U

The symptoms of over-dosing with botulinum toxin (botulism) include ptosis, diplopia, dysphagia, speech impairments, cranial nerve symptoms, generalised weakness, or respiratory muscle paresis. Subjects presenting with these symptoms require medical supervision with symptomatic treatment.

APPENDIX 6

Self-compiled questionnaire

Section A (to be completed at the start of the FES phase)

Compared to before the injection:

a. does your child now get less tired when walking?	Yes	No
b. can (s)he now walk faster (without falling)?	Yes	No
c. can (s)he participate more in daily activities (e.g. playing with other children)?	Yes	No

Section B (to be completed at the end of FES treatment phase)

Compared to after the injection, but before the start of the stimulation programme:

d. does your child now get less tired when walking?	Yes	No
e. can (s)he now walk faster (without falling)?	Yes	No
f. can (s)he participate more in daily activities (e.g. playing with other children)?	Yes	No

Section C (to be completed at the end of the withdrawal phase)

Compared to immediately after the FES programme:

d. does your child now get less tired when walking?	Yes	No
e. can (s)he now walk faster (without falling)?	Yes	No
f. can (s)he participate more in daily activities (e.g. playing with other children)?	Yes	No

Self-opgestelde vraelys

Afdeling A (moet voltooi word aan die begin van die FES program)

In vergelyking met voor die inspuiting:

a. raak u kind nou minder moeg met loop?	Ja	Nee
b. kan hy vinniger loop (sonder om te val)?	Ja	Nee
c. kan hy nou meer in alledaagse aktiwtiteite deelneem (b.v. met ander kinders speel)?	Ja	Nee

Afdeling B (moet na afloop van die FES fase voltooi word)

In vergelyking met na die inspuiting, maar voor die begin van FES:

a. raak u kind nou minder moeg met loop?	Ja	Nee
b. kan hy vinniger loop (sonder om te val)?	Ja	Nee
c. kan hy nou meer in alledaagse aktiwtiteite deelneem (b.v. met ander kinders speel)?	Ja	Nee

Afdeling C (moet aan die einde van die studie voltooi word)

In vergelyking met onmiddelik na die FES program:

a. raak u kind nou minder moeg met loop?	Ja	Nee
b. kan hy vinniger loop (sonder om te val)?	Ja	Nee
c. kan hy nou meer in alledaagse aktiwtiteite deelneem (b.v. met ander kinders speel)?	Ja	Nee

APPENDIX 7

Protocol for telephone calls to caregivers

Good day, this is Anja Seifart speaking.

1. I am phoning in connection with the FES study that your child is participating in.
2. Are you or your child experiencing any problems with the stimulation programme?
3. If so, what are they?
4. Does your child practice walking with the device on for 30 minutes a day, four times a week?
5. If you experience any problems at a later stage, you are welcome to contact me on 082 747 6909.

Thank you for your time. Goodbye

APPENDIX 8

CONSENT LETTERS FROM THE WESTERN CAPE EDUCATION DEPARTMENT

Navrae	
Enquiries	**Dr RS Cornelissen**
IMibuzo	

Telefoon	
Telephone	(021) 467-2286
IFoni	

Faks	
Fax	(021) 425-7445
IFeksi	

Verwysing	
Reference	20060828-0035
ISalathiso	

Wes-Kaap Onderwysdepartement

Western Cape Education Department

ISebe leMfundo leNtshona Koloni

Miss Anja Seifart
203 Villa Della Fonte
24 Arum Road
BLOUBERGSTRAND
7441

Dear Miss A. Seifart

RESEARCH PROPOSAL: AN INVESTIGATION INTO THE EFFECTS OF FUNCTIONAL ELECTRICAL STIMULATION ON GAIT IN CEREBRAL PALSY CHILDREN.

Your application to conduct the above-mentioned research in schools in the Western Cape has been approved subject to the following conditions:

1. Principals, educators and learners are under no obligation to assist you in your investigation.
2. Principals, educators, learners and schools should not be identifiable in any way from the results of the investigation.
3. You make all the arrangements concerning your investigation.
4. The programmes of educators are not to be interrupted.
5. The Study is to be conducted from **28th August 2006 to 01st October 2006**.
6. No research can be conducted during the fourth term as schools are preparing and finalizing syllabi for examinations (October to December 2006).
7. Should you wish to extend the period of your survey, please contact Dr R. Cornelissen at the contact numbers above quoting the reference number.
8. A photocopy of this letter is submitted to the Principal where the intended research is to be conducted.
9. Your research will be limited to the following schools: **Eros and Paarl**.
10. A brief summary of the content, findings and recommendations is provided to the Director: Education Research.
11. The Department receives a copy of the completed report/dissertation/thesis addressed to:
    The Director: Education Research
    Western Cape Education Department
    Private Bag X9114
    CAPE TOWN
    8000

We wish you success in your research.

Kind regards.

Signed: Ronald S. Cornelissen
for: **HEAD: EDUCATION**
DATE: 28th August 2006

MELD ASSEBLIEF VERWYSINGSNOMMERS IN ALLE KORRESPONDENSIE / PLEASE QUOTE REFERENCE NUMBERS IN ALL CORRESPONDENCE / NCEDA UBHALE IINOMBOLO ZESALATHISO KUYO YONKE IMBALELWANO

GRAND CENTRAL TOWERS, LAER-PARLEMENTSTRAAT, PRIVAATSAK X9114, KAAPSTAD 8000
GRAND CENTRAL TOWERS, LOWER PARLIAMENT STREET, PRIVATE BAG X9114, CAPE TOWN 8000

WEB:

INBELSENTRUM /CALL CENTRE
INDIENSNEMING- EN SALARISNAVRAE/EMPLOYMENT AND SALARY QUERIES ☎0861 92 33 22
VEILIGE SKOLE/SAFE SCHOOLS ☎ 0800 45 46 47

Navrae
Enquiries   **Dr RS Cornelissen**
IMibuzo

Telefoon
Telephone   **(021) 467-2286**
IFoni

Faks
Fax   **(021) 425-7445**
IFeksi

Verwysing
Reference   **20060828-0035**
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Wes-Kaap Onderwysdepartement

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Miss Anja Seifart
203 Villa Della Fonte
24 Arum Road
BLOUBERGSTRAND
7441

Dear Miss A. Seifart

RESEARCH PROPOSAL: AN INVESTIGATION INTO THE EFFECTS OF FUNCTIONAL ELECTRICAL STIMULATION ON GAIT IN CEREBRAL PALSY CHILDREN.

Your application to conduct the above-mentioned research in schools in the Western Cape has been approved subject to the following conditions:

1.   Principals, educators and learners are under no obligation to assist you in your investigation.
2.   Principals, educators, learners and schools should not be identifiable in any way from the results of the investigation.
3.   You make all the arrangements concerning your investigation.
4.   The programmes of educators are not to be interrupted.
5.   The Study is to be conducted from **19th February 2007 to 21st September 2007**.
6.   No research can be conducted during the fourth term as schools are preparing and finalizing syllabi for examinations (October to December 2006).
7.   Should you wish to extend the period of your survey, please contact Dr R. Cornelissen at the contact numbers above quoting the reference number.
8.   A photocopy of this letter is submitted to the Principal where the intended research is to be conducted.
9.   Your research will be limited to the following school: **Paarl School**.
10. A brief summary of the content, findings and recommendations is provided to the Director: Education Research.
11. The Department receives a copy of the completed report/dissertation/thesis addressed to:
        The Director: Education Research
        Western Cape Education Department
        Private Bag X9114
        CAPE TOWN
        8000
We wish you success in your research.

Kind regards.

Signed: Ronald S. Cornelissen
for: **HEAD: EDUCATION**
DATE: 16th **February 2007**

MELD ASSEBLIEF VERWYSINGSNOMMERS IN ALLE KORRESPONDENSIE / PLEASE QUOTE REFERENCE NUMBERS IN ALL CORRESPONDENCE / NCEDA UBHALE IINOMBOLO ZESALATHISO KUYO YONKE IMBALELWANO

GRAND CENTRAL TOWERS, LAER-PARLEMENTSTRAAT, PRIVAATSAK X9114, KAAPSTAD 8000
GRAND CENTRAL TOWERS, LOWER PARLIAMENT STREET, PRIVATE BAG X9114, CAPE TOWN 8000

WEB:

INBELSENTRUM /CALL CENTRE
INDIENSNEMING- EN SALARISNAVRAE/EMPLOYMENT AND SALARY QUERIES ☎0861 92 33 22
VEILIGE SKOLE/SAFE SCHOOLS ☎ 0800 45 46 47

APPENDIX 9

CONSENT LETTERS FROM THE RED CROSS
CHILDREN'S HOSPITAL

Verwysing
Reference   **RESEARCH**
Isalathiso

Navrae
Enquiries   Dr. K.R. Ramiah
Imibuzo

Telefoon
Telephone   [021] 658-5383
Ifax   (021) 658-5166

Departement van Gesondheid
Department of Health
iSebe lezeMpilo

5 September 2006

Anja Seifart
Dept. of Physiotherapy
University of Stellenbosch
Tygerberg Campus

Dear A Seifart,

Research Project: **"An Investigation into the short and medium term effects of functional electrical stimulation after Botulinum Toxin Injection in children aged four to six years with Spastic Gait due to Hemiplegic Cerebral Palsy"**

Project number: **N06/05/083**

Thank you for your study protocol and request to conduct this study at RCCH. Permission is granted for you to access patient's between the ages of 4 & 6 in the CP clinic and Physiotherapy at RCCH – initially for your pilot (5 patients) and then for the actual study (10 patients), on condition that the Head of Physiotherapy approved your request.

Your study will be from September 2006 to February 2007 at RCCH in the Physiotherapy department. Please discuss details of this study with Asha Parbhoo who also needs to approve from a Physio perspective, what you intend to do in relation to patients here.

This study will need approval and support from Asha Parbhoo.

Yours sincerely,

Dr K R Ramiah
Chief Operations Officer

cc   Asha Parbhoo
        C.J. Van Tonder (US)

(Send a letter .... to Anja Seifart)

Dear Anja
I have read through your proposal and been in discussion with the
medical superintendent. Everything seems to be in order . You may
proceed with your study as required.
I wish you all the best with your forthcoming studies
Regards
Asha

Asha Parbhoo
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