DISSERTATIONES KINESIOLOGIAE UNIVERSITATIS TARTUENSIS
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NEUROMUSCULAR FUNCTION IN CHILDREN WITH SPASTIC DIPLEGIC CEREBRAL PALSY

KARIN TAMMIK

TARTU UNIVERSITY
PRESS

Institute of Exercise Biology and Physiotherapy, University of Tartu, Tartu, Estonia

Dissertation is accepted for the commencement of the degree of Doctor of Philosophy in Exercise and Sport Sciences (Kinesiology and Biomechanics) on December 14, 2007 by the Council of the Faculty of Exercise and Sport Sciences, University of Tartu.

Supervisor: Mati Pääsuke, PhD, professor
Co-supervisor: Vahur Ööpik, PhD, professor

Opponents: Helga Hirschfeld, Ph.D., Associate Professor, Department of Neurobiology, Care Science and Society, Division of Physiotherapy, Karolinska Institutet, Stockholm, Sweden
Anu Sööt, M.D, Ph.D., Children's Clinic, Tartu University Hospital, Tartu, Estonia

Commencement: room of the Council of the University of Tartu, 18 Ülikooli Street, Tartu on December 14, 2007 at 2 p.m.

Publication of this dissertation is granted by the University of Tartu

ISSN 1406–1058
ISBN 978–9949–11–775–8 (trükis)
ISBN 978–9949–11–776–5 (PDF)

Tartu Ülikooli Kirjastus
www.tyk.ee
Tellimus nr 502

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LIST OF ORIGINAL PUBLICATIONS

The thesis is based on the following original papers, which will be referred to in the text by Roman numerals (I–III):

I. Tammik K, Ereline J, Gapeyeva H, Pääsuke M. Leg extensor muscle strength during bilateral and unilateral contraction in children with cerebral palsy and without disabilities. Biology of Sport, 2004, 21 (2): 159–169.

II. Tammik K, Matlep M, Ereline J, Gapeyeva H, Pääsuke M. Muscle contractile properties in children with spastic diplegia. Brain and Development, 2007, 29 (9): 553–558.

III. Tammik K, Matlep M, Ereline J, Gapeyeva H, Pääsuke M. Quadriceps femoris muscle voluntary force production and relaxation capacity in children with spastic diplegic cerebral palsy. Pediatric Exercise Science (accepted for publication 2007)

ABBREVIATIONS

BI	−	bilateral index
BLD	−	bilateral strength deficit
BM	−	body mass
BMI	−	body mass index
CP	−	cerebral palsy
CT	−	contraction time
EMG	−	electromyography, electromyogram
HRT	−	half-relaxation time
KE	−	knee extensor
LAT_C	−	latency of contraction
LAT_R	−	latency of relaxation
LE	−	leg extensor
MU	−	motor unit
MVC	−	maximal voluntary contraction
PAP	−	postactivation potentiation
Pf	−	peak force
PF	−	plantarflexor
RFD	−	maximal rate of force development
RFD_{50}	−	rate of isometric force development at the level of 50% of MVC
RR	−	maximal rate of relaxation
VA	−	voluntary activation

1. INTRODUCTION

Cerebral palsy (CP) is the most common physical disability in childhood which results from a non-progressive injury to the developing central nervous system. Children with CP have many neurological disorders of which motor dysfunction is the most remarkable. This impairment includes: (1) increased muscle tone, (2) impaired muscle control and (3) decreased muscle strength. The primary culprit of motor dysfunction has been debatable for a long time. Muscle strength is a reflection of motor control and evidence now strongly supports that increased muscle strength results in better performance. Muscle function in children with CP has been intensively studied during the last decade. The available data reveals muscle weakness in this population in comparison with children without disabilities. It is evident that muscle weakness has an impact on motor performance and that an increase in muscle strength could improve motor performance. Consequently, understanding the causes of muscle weakness is important for prescribing an appropriate rehabilitation programme.

Many investigators have reported a reduction in isometric maximal voluntary contraction (MCV) force induced by a simultaneous bilateral contraction as compared to the sum of MVC force of separately performed unilateral contractions. This phenomenon is designated as bilateral strength deficit (BLD). There is not enough information available about BLD in children with spastic diplegic CP. The degree of voluntary activation (VA) is rarely taken into consideration when assessing maximal isometric force in children with CP. VA refers to the level of neural drive to muscle during MVC.

In children with CP, little attention has been paid to the capacity for rapid voluntary force production and relaxation, which is an important indicator of neuromuscular performance and movement control.

Motor disabilities in CP are not only caused by primary impairment of the central nervous system, but also by secondary deterioration in muscle contractile properties resulting from muscle fibre atrophy. Electrical stimulation techniques have been used to assess contractile properties of skeletal muscles in healthy humans and in patients with different neuromuscular dysfunctions. Very few studies have examined muscle contractile properties in children with spastic CP. However, the assessment of muscle contractile properties in the resting position and the postactivation potentiation (PAP) condition can provide additional information about the pathophysiological process in skeletal muscles in CP and about the adaptability of neuromuscular function to reduced muscle activity. The PAP, defined as an increase in twitch contraction force after a brief conditioning isometric MVC, has been well documented in humans. To the best of our knowledge, no prior studies of the capacity for twitch PAP in skeletal muscles have been conducted in children with CP. Understanding muscle contractile properties and the capacity for PAP in children with CP may also have clinical rehabilitation significance for designing programmes based on neuromuscular electrical stimulation.

The main goal of the present study was to identify the peculiarities of the electrically and voluntary evoked force-generation capacity and of the relaxation characteristics of the extensor muscles of lower extremities in children with spastic diplegic CP.

2. REVIEW OF LITERATURE

2.1. Definition, epidemiology and causes of cerebral palsy

The exact definition of the term "cerebral palsy" has been a topic of debate for more than 150 years and discussions about how different manifestations of CP can be best definied continue to the present day. According to the International Workshop on Definition and Classification of Cerebral Palsy, CP is defined in terms of motor features and effects on the function as follows: CP describes a group of disorders of the development of movement and posture, causing activity limitation, that are attributed to non-progressive disturbances that occurred in the developing fetal or infant brain (Bax *et al*., 2005).

In the Baltic countries, the following definition is used: CP is an impairment of movement and posture resulting from a non-progressive defect or lesion (of mainly hypoxic-ischemic origin) of the brain during the ante- or intranatal period. The motor impairment is expressed by spastic syndromes, disorders of coordination and balance, dyskinetic or dystonic movements or their combinations, and is often accompanied by speech and cognitive disorders, and/or epilepsy (Talvik *et al*., 1987). This definition refers to the main pathogenetical pathways, leading to the formation of a brain injury, underlying CP, and aims to narrow the criteria for the term "immature brain"; it also attempts to concretize the time of the stroke and includes associated neurodevelopmental and other problems of co-morbidity.

CP is not an etiologic diagnosis but a clinical descriptive term. Ideally, the diagnosis should be comprised of the etiology (often unknown), a central nervous system lesion (if suitable neuroimaging is available), identification of associated impairments (often occurring at a later age), description of the movement disorder, and the functional status (Jarvis *et al*., 2003; Blair and Watson, 2005; Johnston *et al*., 2002). In conclusion, according to the current international consensus, CP has remained a description defined by clinical observation rather than a diagnosis informative about etiology, pathology or prognosis (Carlsson *et al*., 2003; Ashwal *et al*., 2004; Bax *et al*., 2005).

As a diagnosis, the term "cerebral palsy" itself does not address the broader issues of neurodevelopmental dysfunction (Carr, 2005). However, the most striking dysfunction is motor impairment and it is included as the main component in any definition of CP. CP is a complex neurodevelopmental condition (Blair and Love, 2005). Its co-morbidities include sensory, perceptual and cognitive impairment, communication disorders, behavioural challenges and epilepsy, all being less important than motor disabilities in terms of the quality of life (Rosenbaum, 2003).–

CP is the most common physical disability in childhood (Stanley *et al*., 2000; Rosenbaum, 2003). CP results from a non-progressive injury to the developing

central nervous system and is the most common cause of physical disability in children with an incidence of 1.5 to 2.5 cases per 1000 live births (Ingram, 1984; Lenski *et al*., 2001; Mutch *et al*., 1992; Granata *et al*., 2000; Tammassen and Curzon, 2003). Many forms of CP have been defined, of which, spastic diplegia and hemiplegia are the most prevalent (Krägeloch-Mann *et al*., 1993; Hagberg and Hagberg 1994; Aicardi and Bax, 1998; Bache *et al*., 2003). The term "diplegia" refers to weakness and movement incordination involving the lower limbs more than the arms. People with spastic diplegia typically walk slowly and have difficulty in perfoming activities such as walking up and down steps or running (Dodd *et al*., 2003)

The frequency of CP increases with a decreasing gestational age (Albertsson and Karlberg, 1994), affecting approximately 7.0–7.3% of survivors with a birth weight lower than 1500 g (Volpe, 1994; Krägeloh-Mann, 2004; Platt *et al*., 2007). It has been documented that the rate of CP is more than 70 times higher in the very low birth weight infants compared with those weighing 2500 g or more at birth (Cummins *et al*., 1993). Half of CP cases arise in neonates with a normal birth weight, for which the best available predictor for CP is neonatal encephalopathy (Nelson, 2002).

The overall rate of prevalence of CP in the representative sample of the child population of Tartu City and county area was 5.9 per 1000 live births, including mild cases. The prevalence of moderate to severe cases was 2.3 per 1000 live births, thus being comparable with the data from developed countries (Stelmach, 2006).

A recent analysis of, explained that the incidence of CP was 30% higher in males than in females (Olsen *et al*., 1998; Jarvis *et al*., 2005, Tioseco *et al*., 2006; Zhu *et al*., 2006). Studies have also showed that the likelihood of more severe CP was greater at the extremes of birth weight (O'Shea, 2002; Badawi *et al*., 2005), with the risk of severe CP increased almost fourfold for male infants with birth weights at the 97th centile and 16 times higher for male infants at the 3rd centile. The male to female ratio of the child population of Tartu City and county was 1.4:1 (Stelmach, 2006).

The cause of CP in the majority of affected individuals is unclear (Ferriero, 1999). Research on the pathogenesis of CP continues to yield new information about the mechanisms through which factors such as extreme prematurity, infection, sex and hypoxia-ischemia damage the developing brain (Barkovich and Truwit, 1990; Dammon and Leviton, 1997; Badawi *et al*., 1998; Johnston *et al*., 2001; Stanley *et al*., 2001; Blair and Stanley, 2002; Penneth *et al*., 2003; Shevell *et al*., 2003; Nelson and Lynch, 2004). The vulnerability of different brain structures and types of disability associated with CP are strongly influenced by the gestational age at which development is disturbed (Albertsson-Wikland and Karlberg, 1994; Ferreiro, 2004; Johnson *et al*., 2001, 2002; Krägeloch-Mann, 2004). Better insight into these mechanisms could lead to strategies to protect the brain and reduce the incidence of CP and related

disorders (Mutch *et al*., 1992). It has been found that the main risk factors that could cause CP are prematurity, intrauterine growth restriction, intrauterine or postpartum infection, multiple pregnancy, low apgar score, hypoxic-ischemic encephalopathy and aborning or postpartum trauma (Badawi *et al*., 1989, 2005; Thornberg *et al*., 1995; Levene *et al*., 1986; Johnston *et al*., 2001; Moster *et al*., 2001; Milsom *et al*., 2002; Cowan *et al*., 2003; Cans *et al*., 2004; Topp *et al*., 2004).

CP is a chronic central nervous system disorder for which neither cure exists, nor is one seen in near future (Nelson, 2003). Therefore all current treatments, i.e. surgery, therapy, or medications, aim to alleviate such peripheral effects on the musculoskeletal system as muscle tightness, spasticity and weakness (Reimers, 1990; Abel *et al*., 1999; Ross and Park, 1999; Boyd and Hays, 2001; Willy, 2006). Training programmes and continuous therapy can help to live a productive life in persons with CP (Hutton *et al*., 1994; Furlong *et al*., 2005; Morris *et al*., 2005; Varni *et al*., 2005).

2.2. Motor dysfunction in cerebral palsy

Children with CP have many neurological deficits leading to dysfunction and difficulties in daily activities (Belanger *et al*., 1985; Evans and Alberman, 1985; Diez and Berger, 1995; Dabney *et al*., 1997; Palisano *et al*., 1997; Ketelaar *et al*., 1998; Himmelmann, 2006; Grage, 2004, Shevell and Bodensteiner, 2004). These impairments include neuromuscular and musculo-skeletal problems such as: (1) increased muscle tone or a velocity-dependent resistance to passive muscle stretch in synergistic muscle groups; (2) a selective loss of motor control; (3) deficient postural reactions; (4) a relative imbalance of muscle forces across the joints (Bleck, 1975; Ohtsuki, 1983; Vandervoort *et al*., 1984; Schmidt, 1988; Schantz *et al*., 1989; Ferbert *et al*., 1992; Kramer and MacPhail, 1994; Damiano *et al*., 1995; Palisano *et al*., 1997; Engsberg *et al*., 1999, 2000; Ross *et al*., 2001; Bartlett and Palisano, 2002; Abel *et al*., 2003; Elder *et al*., 2003; Grahm and Selber, 2003; Stackhouse *et al*., 2005; Himmelmann, 2006; Vooreman *et al*., 2007).

Spasticity and decreased muscle strength (weakness) are two major impairments associated with individuals with CP (Knutsson, 1985; Peacock and Staud, 1991; Engsberg *et al*., 1996; Nordmark *et al*., 2001; Goh *et al*., 2006; Engsberg *et al*,. 2007; Ross, Engsberg, 2007). The relation between these impairments is a question that has remained unanswered and is controversial among clinicians and researchers (Palisano *et al*., 2000; Beckung and Hagberg 2002; Rosenbaum, 2002). A major reason for the controversy is that until resently, measurements of spasticity and muscle strength were not typically quantified in individuals with CP (Rab, 1992; Delp, 2003).

An equally important motor symptom of CP is deficient sensomotor control (Nashner *et al*., 1983; Forssberg, 1999, 2003). It has been shown that children with CP more frequently first activated a muscle other than the intended prime mover as compared to children without disabilities, especially when the prime mover was a distal muscle (Ikeda *et al*., 1998). For a long time neuromuscular activation in CP has been assessed to clarify the mechanisms underling the motor deficit and identify the factors that contribute to movement and gait disorders (Krägeloh-Mann *et al*., 1995; Ross and Engberg, 2000). Weakness and imbalance of muscle strength have been identified in children with CP (Bohannon, 1989; Ayalon *et al*., 2000), but these findings have not been quantified precisely and the etiologies of weakness and imbalance of muscle strength are still poorly understood (Forssberg, 2003).

For decades, rehabilitation of persons with an upper motor neurone lesion was dominated by the assumption that spasticity was the primary culprit in producing the observed motor dysfunction (Castle *et al*., 1979; Damiano *et al*., 1995). A collary to this assumption was that the emergence and development of voluntary motor coordination was suppressed by the spasticity and would improve if this factor was eliminated or reduced. Muscle weakness, although clinically recognized, was likewise considered a consequence of the spastic restraint and was not thought to play a primary role in producing the motor deficit (Damiano *et al*., 2000).

Muscle strength, which is an essential component of normal motor control, has been shown repeatedly to be deficient in CP (Damiano and Abel, 1998; Engsberg *et al*., 1998; Wiley and Damiano, 1999; Damiano *et al*., 2000; Beckung and Hagberg 2002). Muscle strength is directly related to functional performance (Kramer and Mac Pheil, 1994). It has been shown that ambulatory children who were stronger tended to walk faster, required less ambulatory assistance, and had a higher capacity to increase their walking speed and also had higher scores of the Gross Motor Function Measure (Johnson *et al*., 1997; Damiano and Abel, 1998; Dodd *et al*., 2003; Johnston *et al*., 2004; Rodda *et al*., 2004; Chen and Woollacott, 2007; Stackhouse *et al*., 2007).

Conventional clinical wisdom in physical therapy argued against the use of muscle strength testing and training in children with CP for a long time (Rosenbaum *et al*., 2002). It was suggested that a strong, near maximal effort, would exacerbate spasticity and that the impaired selective control in CP essentially prohibited performance of strengthening activities (Palisano *et al*., 2000). However, this conception is still debateable despite the lack of evidence to suggest that strengthening is determinal in the presence of spasticity. There is evidence that strength training but not ordinary motor practice can markedly increase the measured muscle strength and motor performance (Lee *et al*., 2007). This points to weakness as a major factor in CP and argues for validity of muscle strength testing in CP (McCubbin and Shashy, 1985; Bohannon, 1989; Tweedy, 1995; Ayalon *et al*., 2000). Leg muscle strength has been shown to be

significantly related to a freely selected walking velocity and to Gross Motor Function Measure scores (Damiano *et al*., 1995; Damiano and Abel, 1996, 1998; Tervo *et al*., 2002). Darrah and colleagues (1997) found that muscle strengthening programmes not only improved muscle strength but also significantly enhanced the perceived physical appearance in children with CP.

While the clinicians feared that exerting the maximal effort could exacerbate spasticity, this has not been verified empirically (Ross and Engsberg, 2002). In a single case study, Horvat (1987) found the increased range of motion in a spastic muscle after strengthening its antagonists, which did not support the suspicion of the increasing muscle tightness resulting from strengthening. Another study showed that the quadriceps femoris muscle strength increased more than 50% with no significant change in the hamstring muscle strength after the strengthening programme in children with CP (Damiano *et al*., 1995).

In fact, research findings are accumulating which indicate that children with CP are indeed weak (Slominski, 1984; Wiley and Damiano 1999), that muscle strength is directly related to motor function (Tweedy, 1995; Abel 1998) and that strengthening programmes can result in functional improvements (Styer-Acevedo, 1999). Documented positive outcomes from increasing muscle strength include the increasing stride length and decreased crouch during the gait, greater energy efficiency when walking and higher Gross Motor Function Measurement scores (Horvat, 1987; Holland, 1990; Gage, 1991).

2.3. Muscle weakness in children with cerebral palsy

Numerous previous studies have demonstrated that muscle weakness is a sole culprit in producing motor dysfunction in CP (Van der Berg-Emons, 1986; Peacock and Staudt, 1991; Damiano and Abel, 1998). In addition, trans-formation of the muscle fibres and abnormal dynamic muscle activation patterns, such as excessive co-contraction and diminished agonist force, may play an important role in the development of muscle weakness in children with CP (Dietz and Berger, 1995; Ito *et al*., 1996; Cowan *et al*., 1998; Ikeda and Abel, 1998; Wiley and Damiano, 1999; Martini *et al*., 2002).

Muscle co-contraction can be defined as the simultaneous activation of agonist and antagonist muscle groups crossing the same joint and acting in the same plane (Olney, 1985). Co-contraction, another aspect of motor behaviour, is recognized as a common motor control strategy when stability or improved motor accuracy is needed (Van Roon *et al*., 2005). However, knowledge is lacking about the distinction between normal and excessive co-contraction, such as might hamper a variety of movements and/or tension generation in children with CP (Damiano, 1993).

Co-activation has been described in the antagonistic muscles in children with CP and a suggestion has been made that muscle strength is reduced as a

function of coactivation (Zimmermann and Bilaniuk, 2006). Ikeda *et al*. (1998) studied proximal leg extensor (LE) muscles and found that children with CP had knee extensor (KE) muscle weakness due to antagonist muscle activity. Elder *et al*. (2003) found that ankle dorsiflexion isometric torque was reduced per unit of the muscle cross-sectional area secondary to the dorsiflexor/plantar-flexor coactivity. An increased co-contraction has been shown qualitatively during the gait in children with CP (Berger *et al*., 1982). Recently, Unnithan and colleagues (1995) showed a direct relationship between greater co-contraction magnitudes, scaled to individual electromyography (EMG) maximal values of the muscles of lower extremities during either gait or during testing of the isometric MVC force in children with CP. Quantification of the contraction during knee flexion and extension isometric MVCs revealed that the children with CP had significantly higher co-contraction ratio than normal children during knee extension but not during knee flexion (Ikeda *et al*., 1998).

It has been suggested, that the increased agonist restraint (co-contraction) may also possibly explain the pervasive weakness documented in spastic CP (Wiley and Damiano, 1999). Leonard *et al*. (1991) have suggested that the reciprocal inhibition of antagonistic motor neurons via the corticospinal control of the Ia inhibitory interneuron is not properly functioning in children with CP. Part of the increased coactivation in the above-mentioned studies may also be due to the impaired cortical control of the spinal interneurons involved in segmental reflex control.

It is shown that the neuromuscular activation and motor unit (MU) firing characteristics, such as firing rate, recruitment and short term synchronisation could cause weakness and loss of dexterity typically seen in children with CP (Belanger and McComas 1989; Kernell, 1990; Rose *et al*., 1994; Frontera *et al*., 1997; Gerrits *et al*., 2001).

Muscle force is highly dependent on the degree of MU activation, which is influenced by the development of the central nervous system (Gamperline *et al*., 1995; Pääsuke *et al*., 2000, 2003). A lowered force production in CP has been attributed to incomplete MU recruitment (Macefield *et al*., 1996). The force generated by a muscle contraction is determined by the MUs firing rates, which is decreased in CP (Harrisson, 1971). The reduced force-generation capacity of skeletal muscles in CP could be partly attributable to a reduced ability to recruit higher threshold (fast) MUs or to drive lower threshold (slow) MUs to the higher firing rates (Rose and McGill, 1998). The inability to produce high firing rates could be responsible for the structural abnormalities including type I (slow-twitch) muscle fibre predominance and fibre size variability (Rose *et al*., 1994). Gibbs *et al*. (1999) found that children with CP also exhibited a reduced short-term synchronization of the MUs in the anterior tibial muscle. The reduction of synchronization is thought to reflect a disorder of a direct cortico-motoneural connection, which would be consistent with a reduction in strength.

Another source of CP related weakness may lie within the morphology of single muscle fibres or a whole muscle (Rose *et al*., 1994; Harridge *et al*., 1996; Ito *et al*., 1996). The most common findings are the increased incidence of muscle fibre atrophy, increased intramuscular fat and connective tissue in the most involved muscle groups (Rose *et al*., 1994; Ito *et al*., 1996; Booth *et al*., 2001; Marbini *et al*., 2002). An increased percent of type I muscle fibres (Jacobsson *et al*., 1992; Rose *et al*., 1994; Dietz and Berger 1995; Ito *et al*., 1996) has been demonstrated in CP. Histological and histochemical studies have also shown some mild myopathic changes in muscles and atrophy of type I and type II (fast twitch) muscle fibres in children with CP (Rose, 1994). Ito *et al*. (1996) reported a selective atrophy of type II muscle fibres during development in CP. Moreover, during growth there is a progressive fibrosis and the number of sarcomeres does not increase as rapidly as in children without CP. An abnormal variation in the size of muscle fibres and in myosin heavy chain expression (Rose, 1994) and an abnormal distribution of acetylcholine receptors relative to acetylcholinesterase at the neuromuscular junction (Wiley and Damiano, 1999) have been found in children with spastic CP.

It has been suggested that muscle cells in patients with spastisity are shorter and stiffer than normal muscle cells (Friden and Lieber, 2003). Elder *et al*. (2003) demonsterated that muscle weakness in PF muscles in subjects with CP is based partly on the reduced muscle cross-section area and an inability to produce muscle torque levels commensurate with the cross-sectional area. Also we could conclude that these peripheral factors can reduce muscle force-generation capacity in children with CP.

In conclusion, the analysis of literature reveals that although CP is defined as a non-progressive disorder, muscle function often becomes progressively more compromised in CP due to spasticity and often positive features of the upper motor neuron syndrome as well as muscle weakness, loss of selective motor control and balance deficits as negative features. These impairments lead to reduced mobility and difficulties in perfoming everiday functional activities and cause diminished quality of life. There is much research which showes that muscle weakness in CP is caused by primary impairment but it could depend on secondary deterioration too. However, little attention has been paid to the evaluation of the capacity of rapid voluntary force production and relaxation, and the VA of the skeletal muscles of lower extremities in children with spastic diplegic CP. Only few studies have examined twitch contractile properties of the skeletal muscles in children with spastic CP. We believe that the knowledge about these neuromuscular function characteristics have significance in understanding the mechanisms underlying muscle weakness in children with spastic diplegic CP.

3. OBJECTIVES OF THE STUDY

The main purpose of the present study was to identify the peculiarities of the electrically and voluntarily evoked force-generation capacity and the relaxation characteristics of the extensor muscles of lower extremities in children with spastic diplegic CP.

The specific objectives were:

(1) To evaluate the isometric MVC force of the KE and plantarflexor (PF) muscles, and LE muscles in association with BLD (Papers I–III).

(2) To assess the electrically evoked isometric twitch contractile characteristics of the PF muscles (Paper II).

(3) To investigate the voluntary activation of the KE muscles (Paper III).

(4) To assess the capacity for rapid isometric voluntary force production and relaxation of the KE muscles (Paper III).

4. MATERIALS AND METHODS

4.1. Subjects

Twenty-five children with spastic diplegic CP aged 6–12 years and 25 age- and gender-matched children without disabilities as controls participated in this study. Table 1 demonstrates the division of the subjects and their mean age anthropometric characteristics in different studies.

Table 1. Anthropometric characteristics of the subjects (mean±SE).

Papers	n	Age (yrs)	Height (cm)	BM (kg)	BMI ($kg \cdot m^{-2}$)
Paper I					
Children with spastic diplegic CP	13	6.4±0.2	119.0±1.8	21.4±0.5	15.4±0.3
Children without disabilities	13	6.3±0.3	121.1±1.2	23.6±1.1	16.0±0.6
Paper II					
Children with spastic diplegic CP	12	11.2±0.2	136.8±2.2	33.0±3.3	17.4±1.2
Children without disabilities	12	11.2±0.2	138.9±2.2	33.7±2.9	17.3±1.0
Paper III					
Children with spastic diplegic CP	12	11.2±0.2	136.8±2.2	33.0±3.3	17.4±1.2
Children without disabilities	12	11.2±0.2	138.9±2.2	33.7±2.9	17.3±1.0

CP = cerebral palsy;
BM = body mass;
BMI = body mass index.

The study was carried out in part of Easten and Southern Estonia and this region belongs to the catchment area of the Children's Clinic of Tartu University Hospital. The criteria for contingent selection were: (1) diagnosis of spastic diplegia; (2) presence of spasticity with a rating of 2 or 3 on the Modified Ashworth Scale (Bohannon and Smith, 1987); (3) no fixed contractures of the lower extremities; (4) severity of disorders corresponding mainly to level II on the Gross Motor Function Classification System (Palisano *et al.*, 1997), (5) ability to ambulate at least 10 m without stopping; (6) no impairment of a visual, somatosensory, hearing or vestibular function – ability to follow instructions; (7) prepubertal stages of children assessed by Tanner scale (1962) – to eliminate the influence of changes that accompany puberty and may affect the outcome of parameters. All children (CP and controls) and parents and guardians were informed of the purpose and experimental methods and gave a written and verbal consent to be participants. The study was approved by the University Ethics Committee.

4.2. Study design

The present study was carried out from 1999 to 2004. All measurements were performed at the Laboratory of Kinesiology and Biomechanics, University of Tartu.

Recordings were made from the LE, PF and KE muscles that are important in posture and movement and are involved in many everyday activities.

Subjects were given instructions 24 to 48 hours before data collection, and the testing of isometric muscle force production and electrical stimulation procedures were demonstrated. This was followed by practice sessions to familiarize the subjects with the procedures. The subject's dominant leg was determined based on a kicking preference.

On reporting to the laboratory, the subject sat resting for about 25 min before commencing the experiment. The rest period minimized any potentiation effect from walking to the laboratory.

In Paper I, the differences in the isometric MVC force of the LE muscles during unilateral and bilateral contractions, and BLD were compared between groups of 6-years-old children with spastic diplegic CP (8 girls and 5 boys) and age- and gender-matched children without disabilities (8 girls and 5 boys).

In Paper II, isometric MVC force and electrically evoked isometric twitch contraction characteristics, and the capacity for PAP of the PF muscles were compared in 11–12-years-old children with spastic diplegic CP (6 girls and 6 boys) and age- and gender-matched children without disabilities (6 girls and 6 boys).

In Paper III, the difference in rapid voluntary force production and relaxation capacity of the KE muscles was compared in 11–12-years-old children with spastic diplegic CP (6 girls and 6 boys) and age- and gender-matched children without disabilities (6 girls and 6 boys).

4.3. Methods

4.3.1. Measurement of the leg extensor muscles

Apparatus

The subjects were seated on a specially designed dynamometric chair in a horizontal frame with knee and hip angles equal to 110° and 120°, respectively (Raudsepp and Pääsuke, 1995) (Fig. 1). The body position of the subjects was secured by two Velcro belts placed over the chest and hip. The feet were placed on a footplate mounted on a steel bar held in ball-bearings on the frame. The isometric force production of the LE muscles was recorded by a standard strain-gauge transducer (1778 DST-2, Russia) connected with a footplate. Signals from the strain-gauge transducer were linear from 0 to 15000 N. The force signals were sampled at a frequency of 1 kHz and stored in a hard disk of a computer using software WsportLab (Urania, Estonia). Acceptable reliability of the isometric MVC force of the LE muscles during bilateral and unilateral contractions in children using this dynamometer was demonstrated (Tammik *et al*., 2004). Test-retest correlations with a 1-week interval between measurements in this study was r=0.86–0.92 in 6-year-old boys and r=0.82–0.89 in age-matched girls.

Experimental protocol

Isometric MVC force of the LE muscles was measured during unilateral and bilateral contractions (leg press exercise). During testing the subjects were instructed to push the footplate as forcefully as possible for approximately 3 s in three cases: (1) unilateral contraction of the right leg; (2) unilateral contraction of the left leg and (3) bilateral contraction. Three maximal attempts were recorded for each case and the best result was taken for further analysis. Strong verbal encouragement and visual online feedback were used to motivate the subjects. A rest period of 2 min was allowed between the trials. During unilateral exertions, the contralateral leg was allowed to rest. The BI was calculated by the formula (Howard and Enoka, 1991):

$$BI\ (\%) = 100\ [BL\ /(UL_R + UL_L)] - 100,$$

where BL is isometric MVC force during bilateral contraction, UL_R and UL_L are isometric MVC forces during right and left leg unilateral contractions, respectively. A negative BI indicated a BLD, while a positive BI indicated a bilateral facilitation.

Twenty-four to fourty-eight hours before data collection the subjects were given instructions and the strength testing procedures were demonstrated. This was followed by a practice session to familiarize the subjects with the procedures. Durin testing, subjects began with the bilateral contractions, followed by the unilateral contractions presented randomly. The same researcher with long-

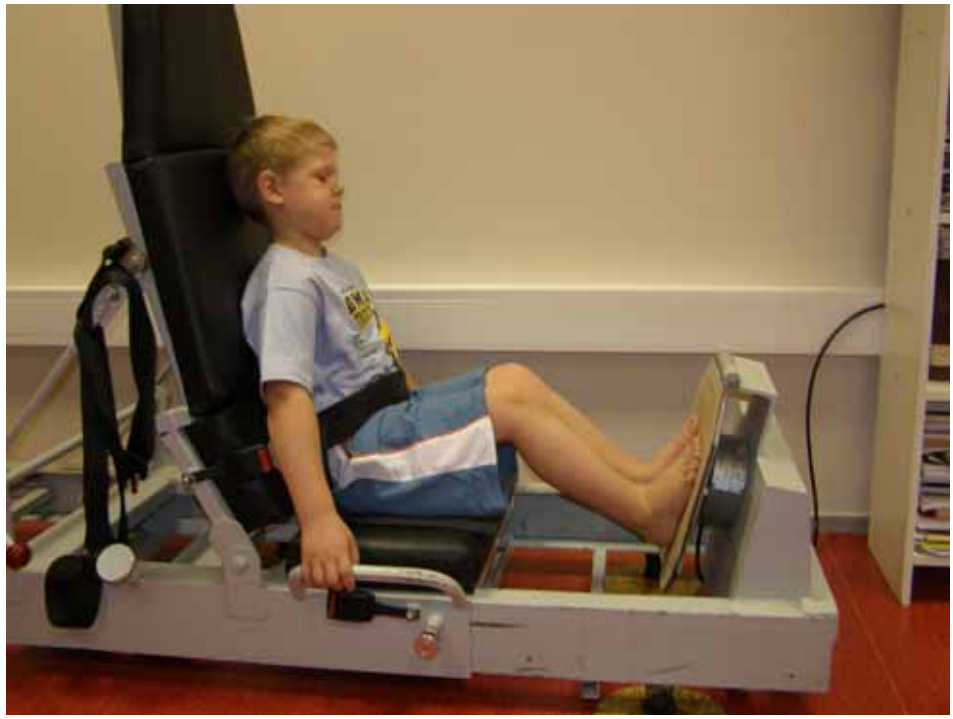

Figure 1. Experimental setup for the measurement of isometric MVC force of the leg extensor muscles.

term experience in this kind of testing procedure tested all subjects between 11 am and 3 pm.

4.3.2. Measurement of the plantarflexor muscles

Apparatus
During the experiment, the subjects were seated in a custom-made dynamometer with the dominant leg (usually the right leg) flexed 90° at the knee and ankle angles, and mounted inside a metal frame (Pääsuke *et al*., 2000) (Fig. 2). The foot was strapped to an aluminium footplate. The inclination of the foot could be altered by rotating the footplate about an axis that corresponded to that of the ankle joint, i.e. the medial malleolus. The knee cap and front side of the thigh were held down by an adjustable pad. Torques acting on the footplate was sensed by a standard strain-gauge transducer connected with the foot plate by a rigid bar. The electrical signals from the strain-gauge transducers were amplified and displayed with a special amplifier. The system was linear from 10 to 1600 N. The point of application of force to the footplate was located on the articulation regions between the metatarsus and ossa digitorum pedis. The force signals were sampled at a frequency of 1 kHz and stored on a hard disk for further analysis.

Electrical stimulation
To determine the twitch contraction characteristics of the PF muscles, the posterior tibial nerve was stimulated through a pair of 2 mm-thick self-adhesive surface electrodes (Medicompex SA, Ecublens, Switzerland). Prior to attaching the stimulating electrodes, electrode gel was applied to the contact surface, and the underlying skin was prepared by shaving, sanding and rubbing with isopropyl alcohol. The cathode (5 × 5 cm) was placed over the tibial nerve in popliteal fossa and an anode (5 × 10 cm) was placed 2–3 cm proximally to the patella (Fig. 2). Supramaximal square wave pulses of 1-ms duration were delivered from an isolated voltage stimulator Medicor MG-440 (Budapest, Hungary). The evoked compound action potential (M-wave) of the soleus muscle was recorded using bipolar (20 mm interelectrode distance) EMG electrodes (Beckman miniature skin electrodes). The electrodes were placed longitudinally on the belly of the soleus muscle after the skin was cleaned using alcohol swabs and abraded lightly with fine sand paper. As a reference electrode, self-adhesive surface electrodes (Medicompex SA, 5 × 10 cm) was placed over the proximal part of the triceps surae muscle between the stimulating and recording electrodes. The EMG signals were amplified and displayed using a standard Medicor MG – 440 (Budapest, Hungary) preamplifier with frequency band ranging from 1 Hz to 1 kHz. These signals were sampled at 1 kHz.

Experimental protocol

The subjects were given instructions 24 to 48 hours before data collection, and the testing of the isometric MVC force of the PF muscles and electrical stimulation procedures were demonstrated. This was followed by practice sessions to familiarize the subjects with the procedures. The subject's dominant leg was determined based on a kicking preference.

On reporting to the laboratory, the subject sat resting for about 25 min before the dominant leg was placed in the apparatus. The rest period minimized any potentiation effect from walking to the laboratory. A maximal isometric twitch contraction at rest was elicited by delivering a series of single stimuli of increasing intensity until a plateau of M-wave amplitude was obtained. During the twitch contraction recording the stimulus intensity varied from approximately 25 V to supramaximal in increments of 30–50% (130–150 V). Firstly, three maximal isometric twitches of the PF muscles were elicited. Two minutes after the last resting twitch was recorded, the subjects were instructed to make a 5-s conditioning MVC and then to relax. The postactivation twitch contraction was elicited within 2 s after the onset of relaxation. Two minutes after the postactivation twitch contraction was recorded, the subjects performed three isometric MVCs of the PF muscles. The joint position was the same as for the previous twitch contraction measurements. The subjects were instructed to push the foot plate as forcefully as possible for 2–3 s. Strong verbal encouragement and visual feedback were used to motivate the subjects. The greatest force of the three maximal efforts was taken as the isometric MVC force. Two-minute rest periods were allowed between trials. The skin temperature of the tested muscle group was continuously monitored and maintained at 35ºC with an infrared lamp.

The following characteristics of the resting isometric twitch contraction were calculated (Fig. 3): peak force (Pf) – the highest value of isometric force production; contraction time (CT) – the time to twitch maximal force; half-relaxation time (HRT) – the time of half of the decline in twitch maximal force, maximal rate of force development (RFD) – the first derivate of the development of force (dF/dt) and maximal rate of relaxation (RR) as the first derivate of the decline of force (-dF/dt). The percentage increase in the post-activation twitch Pf in relation to the resting twitch was taken as an indicator of the capacity for PAP. The resting twitch Pf was expressed as a ratio to the MVC force (Pf:MVC). The MVC force was calculated in relation to BM of the subjects (MVC:BM).

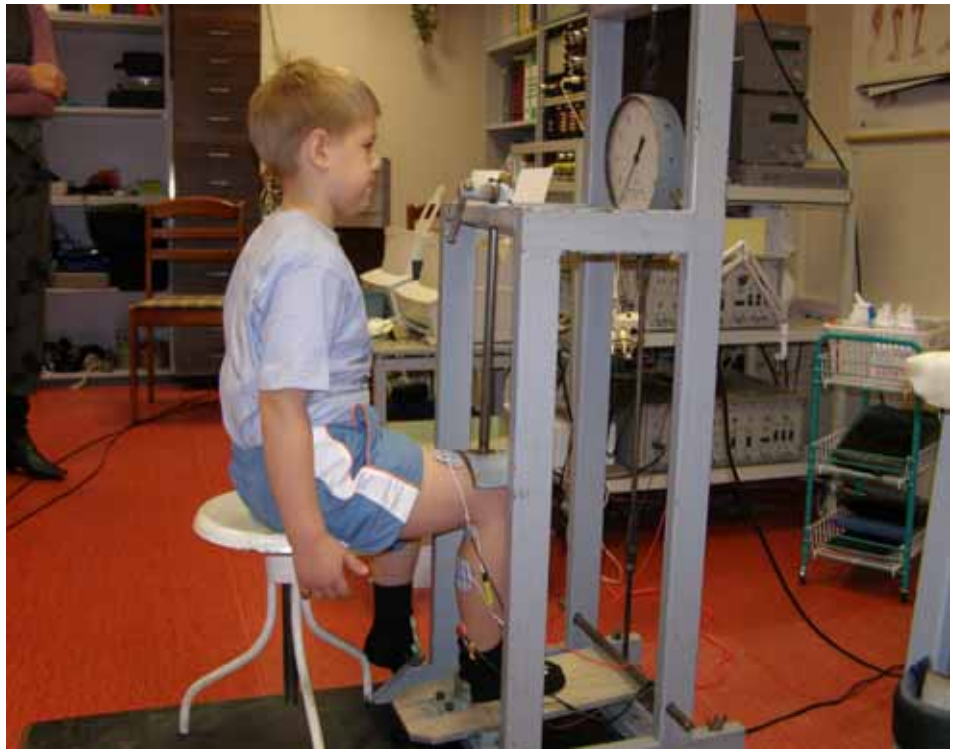

Figure 2. Experimental setup for the measurement of isometric MVC force and electrically evoked twitch contraction characteristics of the plantarflexor muscles**.**

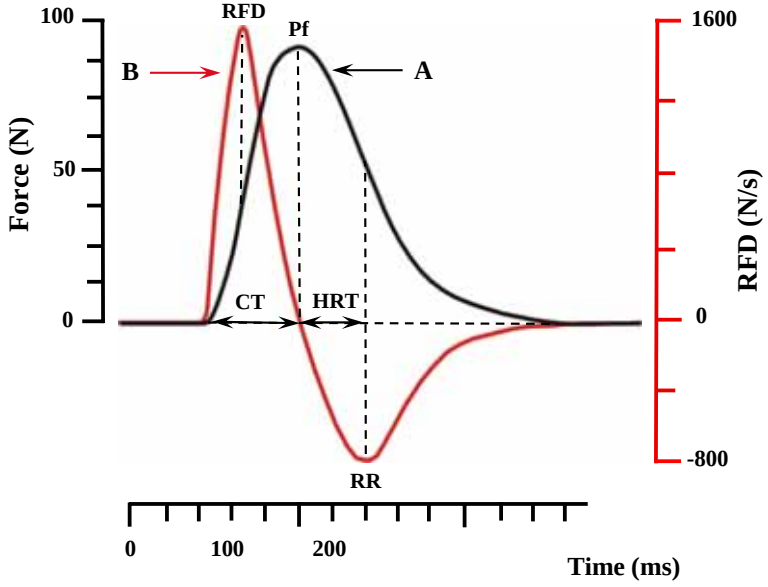

Figure 3. Isometric twitch force-time curve (A) and first derivate (B). Pf – peak force; CT – contraction time; HRT – half-relaxation time; RFD – maximal rate of force development (dF/dt); RR – maximal rate of relaxation (-dF/dt).

4.3.3. Measurement of the knee extensor muscles

Apparatus

During measurement the subjects sat in a custom-made dynamometric chair with the knee and hip angles equal to 90° and 110°, respectively (Fig. 4). The body position of the subjects was secured by three Velcro belts placed over the chest, hip and thigh. The unilateral knee extension force was recorded by a chair-fixed standard strain-gauge transducer (DST 1778 (Russia) connected with the plate by a rigid bar. The strain-gauge transducer pad was placed approximately 3 cm above the apex of the lateral malleolus on the anterior side of the leg. Signals from the strain gauge transducer were linear from 0 to 2500 N. The force signals were sampled at the frequency of 1 kHz and stored on a hard disk of computer using software WSportLab (Urania, Estonia).

Experimental protocol

During the testing of isometric MVC force of the KE muscles, the subject was asked to exert knee extension against the pad of the strain-gauge system as forcefully as possible. The maximal contraction effort was held for approximately 3 s. Three maximal trials were recorded and the best result was taken for further analysis. Strong verbal encouragement and visual online feedback were used to motivate the subject. A rest period of 2 min was allowed between the trials. The isometric MVC force relative to the BM (MVC:BM) was calculated.

During testing the isometric force–time and relaxation-time characteristics of the KE muscles the subject was instructed to react to the visual stimuli (lighting of the signal lamp, placed 1.5 m from the subject) as quickly and forcefully as possible by extending the leg against a cuff fixed to a strain gauge system, to maintain the maximal effort as long as the signal was on (2 s) and to relax the muscles quickly after the disappearance of the signal. Three trials were carried out and the trial with higher isometric MVC force was used for further analysis. A rest period of 2 min was allowed between the attempts. The following characteristics were calculated: latency of contraction (LAT_C) – the time delay between the visual signal and the onset of muscle force production; rate of isometric force development at the level of 50% of MVC (RFD_{50}) – the first derivate of force development (dF/dt) at the level of 50% of MVC; latency of relaxation (LAT_R) – the time delay between the visual signal stopping and the onset of a quick decline in force production during relaxation; and HRT – the time of half of the decline in force during relaxation.

During the testing of the VA of the KE muscles, the transcutaneous electrical stimulation with supramaximal square wave pulses of 1 ms duration was applied using an isolated voltage stimulator (Medicor MG-440, Hungary) and two self-adhesive surface electrodes (5 × 10 cm, Medicompex SA, Ecublens, Switzerland) were placed transversely on the proximal (cathode) and distal (anode) third of the anterior thigh (Fig. 4). Skin preparation for each electrode

included shaving and light abrasion of the skin followed by cleaning with isopropyl alcohol. The VA of the KE muscles was estimated by the twitch interpolated technique (Knight and Kamen, 2001). Subjects were asked to reach their maximal force level in approximately 3 s and to maintain it after the supramaximal stimulus was delivered until they were told to relax. The total duration of this contraction was approximately 5 s. Visual feedback was provided by the display of strain a gauge amplifier. In fully activated KE muscles no additional force is generated by the muscles as a result of superimposed electrical twitches. If the VA of the KE muscles is reduced, additional force can be generated by superimposed twitches (Norregaard *et al*., 1997). This indicates additional activity from MUs not fully activated at the time of stimulus. The intensity for supramaximal stimuli was assessed during familiarization session and corresponded to 10% of the above level required to evoke a resting maximal twitch contraction (Morton *et al*., 2005). Three trials were performed with the interval of 2 min and the trial with the greatest pre-stimulus voluntary force was taken for further analysis. The VA of the KE muscles was calculated from force-time curve by the formula:

$$VA = (F_V : F_{ES}) \cdot 100[\%],$$

where F_V is the voluntary isometric force produced immediately prior to the electrical stimulus and F_{ES} is the peak force produced by the electrical stimulus superimposed on the voluntary effort. VA $\geq$ 95% was used as an operational definition of full activation of the KE muscles (Norregaad *et al*., 1997; Morton *et al*., 2005).

Subjects were given instructions 24 to 48 hours before data collection, and the testing of isometric MVC force, force-time and relaxation-time characteristics of the KE muscles and electrical stimulation procedures were demonstrated. This was followed by a practice session to familiarize the subjects with the procedures. The subject's dominant leg was determined based on a kicking preference. During testing, the recording of isometric MVC force of the KE muscles followed with the assessment of the isometric force-time and relaxation-time characteristics. After a 5 minutes resting period the VA of the KE muscles was recorded. The same researcher with long-term experience in this kind of testing procedure tested all subjects between 11 am and 3 pm.

4.4. Statistical evaluation of the data

Standard statistical methods were used to calculate the means and standard errors of the mean (±SE). One-way analysis of variance (ANOVA) followed by Tukey (Paper I) and Scheffe (Paper II and III) *post hoc* comparisons were used to test for differences between groups of children, whereas Tukey (Paper I) *post hoc* comparisons were used to test for differences between the legs. In Paper I,

Figure 4. Experimental setup for the measurement of isometric MVC force–time and relaxation-time characteristics, and voluntary activation of the knee extensor muscles.

Pearson's linear correlations were calculated to observe the relationship between the measured characteristics. In Paper III, main differences in three primary measures (MVC force, RFD_{50} and VA) between two measured groups of children were tested for statistical signification (alpha=0.05).

5. RESULTS

5.1. Isometric MVC force of the leg muscles

Isometric MVC force during unilateral contraction of the KE, PF and LE muscles was significantly lower in children with spastic diplegic CP compared with controls (Table 2 and Fig. 5, see Papers I–III). Children with spastic diplegic CP had a significantly lower MVC:BM ratio of the KE and PF muscles of the dominant leg (Fig. 6, see Papers II and III) compared with controls. The Isometric MVC force of the LE muscles during bilateral contraction was significantly lower in children with spastic diplegic CP compared with controls (Table 2, see Paper I). As shown in Table 2, the marked negative BI, i.e. BLD of the LE muscles was observed in children with spastic diplegic CP and controls. However, the BI did not differ significantly (p>0.05) between the groups.

Table 2. Isometric MVC force of the leg extensor muscles during UL and BL contractions (mean±SE).

Variables	Children with spastic diplegic CP (n=13)	Children without disabilities (n=13)
MVC force during BL contraction (N)	394.2±31.0***	620.2±36.5
MVC force during UL contraction of right leg (N)	287.5±26.7**	409.6±26.1
MVC force during UL contraction of left leg (N)	250.4±16.3***	396.7±23.9
BI (%)	–25.4±5.5	–22.0±3.5

CP = cerebral palsy;
BL = bilateral;
UL = unilateral;
BI = bilateral index
** p<0.01, *** p<0.001 compared with children without disabilities.

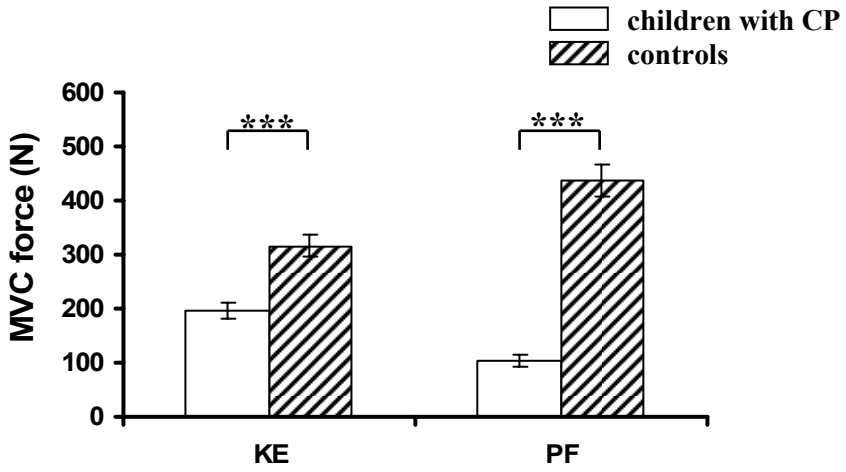

Figure 5. Mean (±SE) isometric maximal voluntary contraction (MVC) force of the knee extensor (KE) and plantarflexor (PF) muscles of the dominant leg in children with spastic diplegic cerebral palsy (CP) and controls. *** $p<0.001$.

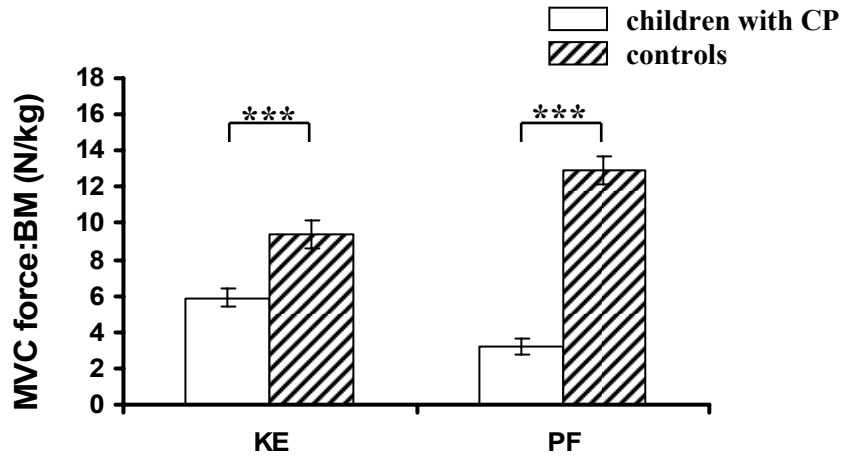

Figure 6. Mean (±SE) isometric maximal voluntary contraction (MVC) force relative to the body mass (BM) of the knee extensor (KE) and plantarflexor (PF) muscles of the dominant leg in children with spastic diplegic cerebral palsy (CP) and controls. *** $p<0.001$.

5.2. Force-generation characteristics of electrically evoked isometric twitch of the plantarflexor muscles

5.2.1. Twitch peak force

As shown in Fig. 7A (see Paper II), the children with spastic diplegic CP produced a significatly lower electrically evoked twitch Pf of the PF muscles in resting state as compared with control group. They had also significatly greater resting twitch Pf expressed as a ratio to the MVC force (Pf:MVC) (Fig. 7B).

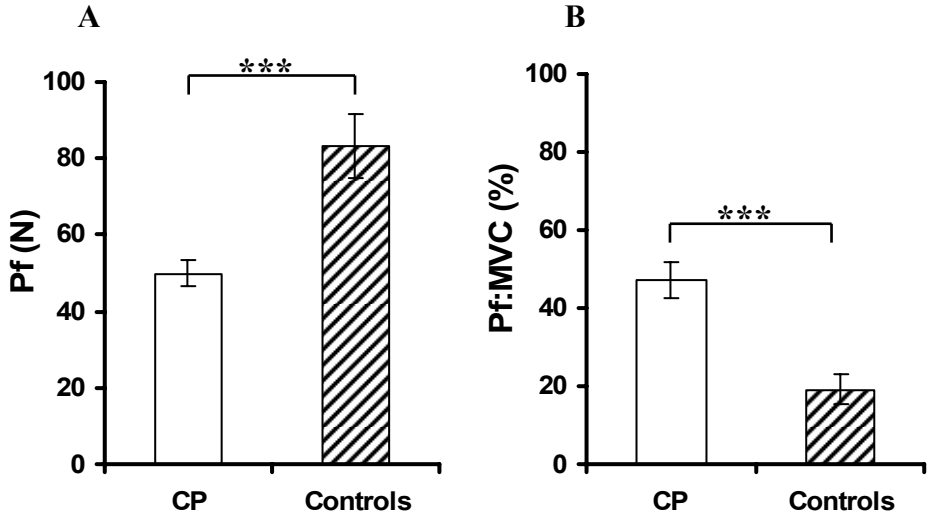

Figure 7. Mean (±SE) twitch contraction peak force (Pf) (A) and twitch contraction Pf relative to maximal voluntary contraction force (Pf:MVC) (B) of the plantarflexor muscles in children with spastic diplegic cerebral palsy (CP) and controls. *** $p<0.001$.

5.2.2. Postactivation potentation

The PAP of electrically evoked twitch contraction force of the PF muscles after a 5-s conditioning MVC was significantly lower in children with spastic diplegic CP compared with control group (Fig. 8, see Paper II).

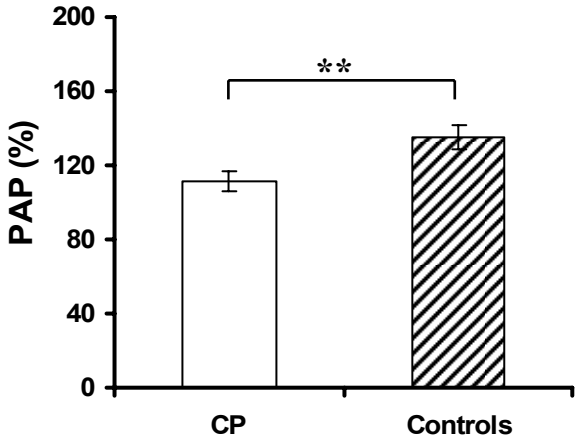

Figure 8. Mean (±SE) post-activation potentiation (PAP) of twitch contraction force of the plantarflexor muscles in children with spastic diplegic cerebral palsy (CP) and controls. ** $p<0.01$.

5.2.3. Twitch maximal rates of force development and relaxation

Electrically evoked twitch maximal RFD and RR of the PF muscles in the resting state were significantly lower in children with spastic diplegic CP compared with the control group (Table 3, see Paper II).

Table 3. Twitch maximal rates of force development (RFD) and relaxation (RR) of the plantarflexor muscles in children with spastic diplegic CP and healthy controls (mean±SE).

Study	Subject group	n	RFD ($N \cdot s^{-1}$)	RR ($N \cdot s^{-1}$)
II	Children with spastic diplegic CP	12	452.6±40.6***	492.1±54.6***
	Controls	12	928.1±110.5	734.4±46.9

CP = cerebral palsy;
*** $p<0.001$ compared with controls.

5.3. Time-course characteristics of the electrically evoked isometric twitch of the plantarflexor muscles

No significant differences (p>0.05) in resting twitch CT and HRT were observed between children with spastic diplegic CP and healthy controls (Table 4, see Paper II).

Table 4. Twitch contraction (CT) and half- relaxation (HRT) times of the plantarflexor muscles in children with spastic diplegic CP and healthy controls (means±SE).

Study	Subject group	n	CT (ms)	HRT (ms)
II	Children with spastic diplegic CP	12	83.4±5.2	87.2±2.1
	Controls	12	83.6±3.8	79.1±6.3

CP = cerebral palsy

5.4. Voluntary isometric force-generation characteristics of the knee extensor muscles

5.4.1. Voluntary activation

As shown in Fig. 9 (see Paper III), VA of the KE muscles in children with spastic diplegic CP was significantly lower compared with healthy controls.

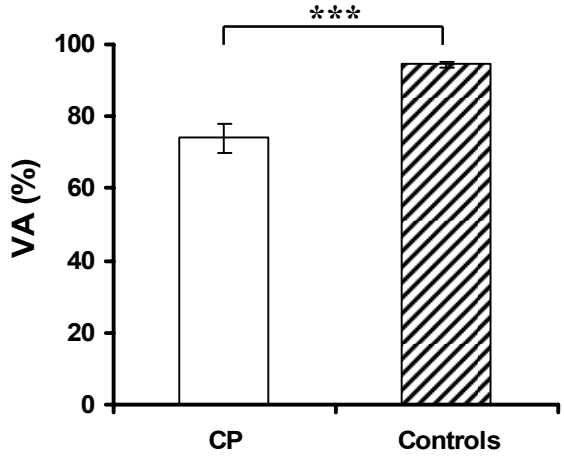

Figure 9. Mean (±SE) voluntary activation (VA) of the knee extensor muscles in children with spastic diplegic cerebral palsy (CP) and controls. *** p<0.001.

5.4.2. Capacity force rapid voluntary isometric force production and relaxation

Isometric RFD_{50} of the KE muscles was significantly lower in children with spastic diplegic CP than in children without disabilities (Fig. 10, see Paper III). There were no significant differences (p>0.05) in LAT_C between the measured groups of children in the present study (Fig. 11). However, children with spastic diplegic CP had a significantly longer LAT_R compared with controls (Fig. 11). As shown in Fig. 12, HRT after isometric MVC in children with spastic diplegic CP was also significantly longer than in children without disabilities.

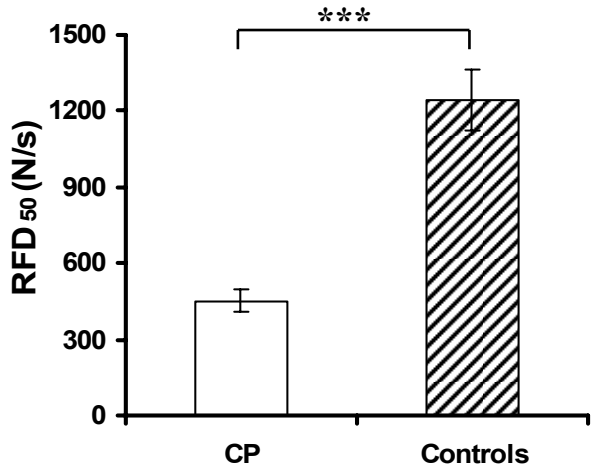

Figure 10. Mean (±SE) rate of isometric force development at level of 50% of maximal voluntary contraction (RFD_{50}) of the knee extensor muscles in children with spastic diplegic cerebral palsy (CP) and controls. *** p<0.001.

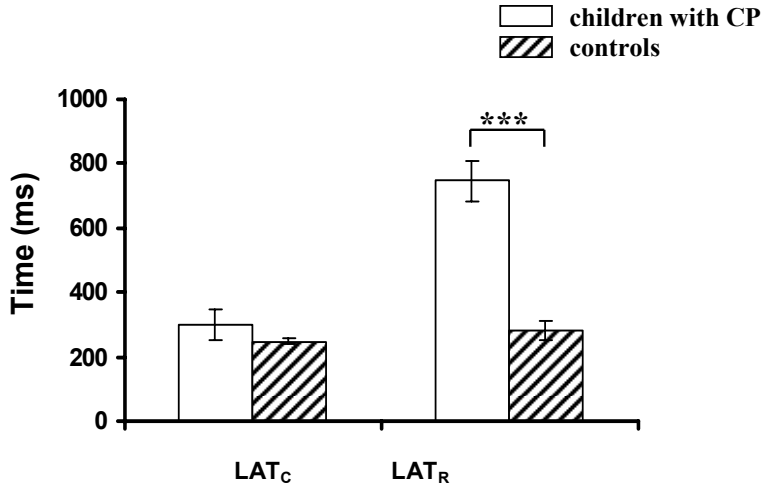

Figure 11. Mean (±SE) latency of contraction (LAT_C) and relaxation (LAT_R) of the knee extensor muscles in children with spastic diplegic cerebral palsy (CP) and controls. *** $p<0.001$.

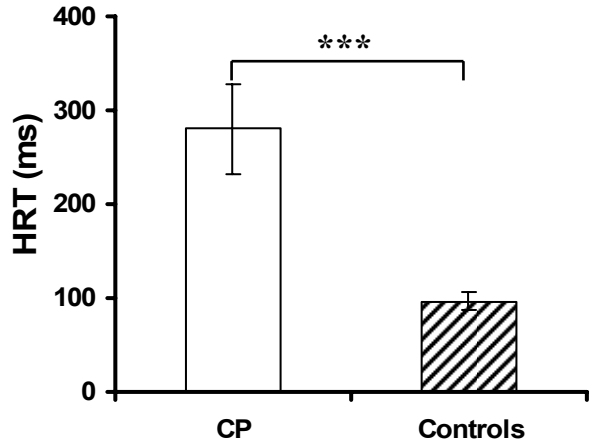

Figure 12. Mean (±SE) half-relaxation time (HRT) after isometric maximal voluntary contraction of the knee extensor muscles in children with spastic diplegic cerebral palsy (CP) and controls. *** $p<0.001$.

6. DISCUSSION

6.1. Isometric maximal voluntary force-generation capacity of the leg muscles

The present data reveals a markedly reduced isometric voluntary force-generation capacity of the LE muscles during bilateral and unilateral contractions (leg press exercise) in 6-year-old children with spastic diplegic CP compared with age- and gender-matched healthy children (Paper I). On average, the children with spastic diplegic CP produced 36% less isometric MVC force of the LE muscles during bilateral contraction than the children without disabilities. The difference between the two groups of children was somewhat smaller (31%) if force was expressed relative to the BM. On average, isometric MVC of the LE muscles of the right and left leg during unilateral contractions in children with spastic diplegic CP was 30% and 37% lower, respectively, compared with healthy controls.

In children with spastic diplegic CP aged 11–12 years a marked isometric voluntary force deficit in the KE muscles of the dominant leg is evident (Paper III). On average, they produced 38% less isometric MVC force of the KE muscles and 37% less MVC force relative to the BM, respectively, during unilateral contraction than the age- and gender-matched healthy controls. These findings are in agreement with the data reported by Damiano *et al*. (1995), who observed an isometric voluntary force deficit of 31% in KE muscles of children with spastic diplegic CP. Moreover, Damiano *et al*. (1995) and Stackhouse *et al*. (2005) have demonstrated an even more pronounced isometric force deficit (46–56%) in the KE muscles of children with spastic diplegic CP. A marked deficit in voluntary force production in the knee extensor muscles in children with spastic diplegia may explain the reduced ability to stretch the knees while standing and walking (Radtka *et al*., 2005).

Similarly to many previous studies (Wiley and Damiano, 1999; Damiano *et al*., 2001; Buckon *et al*., 2002; Elder *et al*., 2003; Rose and McGill, 2005; Stackhous *et al*., 2005), the present results reveal a markedly reduced voluntary isometric force-generation capacity of the PF muscles in children with CP (Paper II). On average, they produced 76% less isometric MVC force and also less MVC force relative to the BM in the dominant leg in comparison with the control group. This finding is in accordance with that of Stackhouse *et al*. (2005), who demonstrated 73% less isometric MVC force of the PF muscles in boys with CP (mean age 10.5 years) compared with the healthy boys. Several studies, which have investigated the pathological gait pattern in children with spastic diplegic CP, have concluded that spasticity of posterior calf muscles is the main reason for toewalking and the inability to push off in the late stance phase during walking. On the other hand, if spasticity is reduced, the gait

pattern does not improve in many children with the above mentioned gait abnormalities, which would let us suggest that plantarflexor muscle weakness could also contribute to poor walking ability (Damiano and Abel, 1998; Wiley and Damiano, 1999; Engsberg and Ross, 2007).

This study reveals a negative BI, i.e. BLD of the LE muscles in 6-year-old children with spastic diplegic CP and in children without disabilities (Paper I). The mean values of BI in children with spastic diplegic CP and their age- and gender-matched controls were similar: –25.4% and –22.0%, respectively. However, there were 4 children with spastic diplegic CP and 2 healthy children who had a positive BI, i.e. bilateral strength facilitation. One possible explanation for this phenomenon is that some children, especially with spastic diplegia, have difficulties performing a reciprocal movement, and their ability to produce bilateral force may develop to a greater degree. Limited information is available on lower extremity BLD in subjects with CP. Tihanyi and Horvath (2000) reported that in patients with spastic CP aged 15–20 years BI of the KE muscles was –32%. However, several investigators have observed BLD in the muscles of lower extremities in healthy adult subjects. Taniguchi (1997) observed that BI ranged from –19% to –7% in male students. Secher *et al*. (1988) reported BI of –20% in untrained persons, –14% in weightlifters and –24% in cyclists. The BI observed by Schantz *et al*. (1989) was –14% in the untrained male group and –8% in the heavy-resistance trained male group.

Neural mechanisms seem to be the cause of the BLD in humans. The nature of the neural mechanisms must ultimately involve altered MU discharge frequency and/or recruitment during maximal voluntary bilateral contraction (Secher *et al*., 1978; Vandervoort *et al*., 1984; Oda and Moritani, 1995, 1996; Ikeda *et al*., 1998; Rose and McGill, 1998, 2005). The BLD may be caused by reduced activation of higher threshold (fast) MUs (Owings and Grabiner, 1998). The unilateral muscle contraction is mainly controlled by the contralateral cerebral hemisphere. The bilateral muscle contraction is considered to be generated by a simultaneous activation of both hemispheres. Although the exact mechanisms of BLD are still unclear, the neural interaction between the two hemispheres connected by commissural nerve fibres may by involved (Koh and Grabiner, 1993; Oda, 1997; Jakobi and Cafarelli, 1998; Janzen *et al*., 2006). It has been shown that BLD was associated with reduced movement-related cortical potentials caused by a mechanism of interhemispheric inhibition (Oda, 1997). It has also been reported that BLD may be related to inhibitory spinal reflexes (Ohtsuki, 1983) and that it may be a consequence of a disproportionate increase in the coactivation of antagonist muscles (Bax, 1964; Howard and Enoka, 1991; Kuban and Leviton, 1994; Oda and Mortiani, 1996; Burtner *et al*., 1998; Ikeda *et al*., 1998; Damiano *et al*., 2000).

Isometric MVC force of the LE muscles during bilateral contractions, expressed in absolute values as well as relative to the BM, correlated ($p<0.05$) negatively with the BI ($r= –0.75$ and $r= –0.78$, respectively) in 6-years-old

children with spastic diplegic CP (Paper I). This finding suggests that BLD is most obvious in children with spastic diplegic CP with a considerably decreased maximal and body mass related voluntary isometric force-generating capacity of the LE muscles during bilateral contraction. No significant correlation was observed between BI and maximal force during isometric bilateral or unilateral contractions of the LE muscles in healthy controls. Therefore, in children without cerebral palsy the leg extensor muscle BLD is obviously not necessarily related to a reduction in isometric force-generating capacity during bilateral contraction.

6.2. Electrically evoked isometric twitch characteristics of the plantarflexor muscles

This study (Paper II) was designed to develop a better understanding of the contractile properties of the skeletal muscles in prepubertal children with and without spastic diplegic CP. The results indicate that the electrically evoked isometric twitch Pf is 40% lower in children with spastic diplegic CP aged 11-12 years compared with healthy children. The decrease in the twitch Pf may be associated with a loss of the muscle cross-sectional area and a decrease in the number of type II muscle fibres (Rose *et al*., 1994; Ito *et al*., 1996., Marbini *et al*., 2002). One indicator of voluntary activation capacity of a muscle is the twitch force:MVC force ratio. In this study, the children with spastic diplegic CP had a 60% greater Pf:MVC force ratio compared with the control group. This finding indicates a significantly reduced VA capacity of the PF muscles in children with spastic diplegic CP. Hence, in children with CP, the isometric voluntary force generation capacity of the PF muscles is relatively more reduced than the electrically evoked twitch force generation capacity.

The present study revealed no differences in time-course characteristics (CT and HRT) of the resting twitch of the PF muscles in children with spastic diplegic CP in comparison with the control group. However, a reduction in twitch maximal RFD and RR in PF muscles in children with spastic diplegic CP in comparison with healthy children, is evident. In children with spastic diplegic CP, the twitch maximal RFD and RR were lower, by 51% and 42% ($p<0.001$), respectively. The time course characteristics (CT and HRT) as well as RFD and RR are considered to be highly related to intracellular Ca^{2+} movement (Klug *et al*., 1988; Westerblad *et al*., 1997; Theroux *et al*., 2002; Hamada *et al*., 2003). Hence, similar values of CT and HRT in children with spastic diplegic CP and healthy children together with decreased RFD and RR values in children with spastic diplegic CP suggest that other mechanisms besides differences in intracellular Ca^{2+} kinetics might be responsible for a reduction in RFD and RR.

The force of an electrically evoked twitch is greater after a brief MVC compared with the corresponding value at rest. This enhancement has been termed PAP (Vandervort *et al*., 1984; Hamada *et al*., 2003). The major finding of our study is that children with spastic diplegic CP have significantly reduced PAP of twitch contraction force in the PF muscles after a brief conditioning isometric MVC than the age- and gender-matched control children. The mean values of PAP of twitch force were 111% and 136% ($p<0.01$) for children with spastic diplegic CP and the control group, respectively. Previous studies indicated that PAP of twitch force in the PF muscles in healthy 9–10-year-old girls and boys was 123% and 138%, respectively (Pääsuke *et al*., 2003), and 144% for 11-year-old boys (Pääsuke *et al*., 2000). The mechanism responsible for twitch PAP is considered to be phosphorylation of myosin regulatory light chains during a conditioning MVC, which renders actin-myosin more sensitive to Ca^{2+} in a subsequent twitch (Grange *et al*., 1993; Sweeney *et al*., 1993). A potential explanation for the reduced capacity of twitch PAP in children with spastic diplegic CP may lie in morphological changes in the skeletal muscles occurring in CP. Such factors, as myopathic changes and type I muscle fibre predominance (Marbini *et al*., 2002), and selective atrophy of type II muscle fibres (Ito *et al*., 1996) can reduce twitch potentiation capacity in skeletal muscles of children with spastic diplegic CP. An alternative potential explanation for reduced capacity for twitch PAP in children with spastic diplegic CP compared with children without CP might be the differences in MU activation during a conditioning isometric MVC. The greater MVC force of the PF muscles in the control group observed in the present study could be partly attributable to a greater activation of the higher threshold fast MUs composed of type II muscle fibres. It was observed that type II muscle fibres exhibit the greater twitch PAP (Hamada *et al*., 2003). Thus, the decreased capacity for twitch PAP in children with spastic diplegic CP may be partly explained by a decreased ability to activate the higher threshold MUs during conditioning activity.

6.3. Voluntary activation and capacity for rapid voluntary force production and relaxation of the knee extensor muscles

The degree of VA is rarely taken into consideration when assessing maximal isometric force in a clinical samples. VA refers to the level of neural drive to a muscle during MVC. A majority of VA studies using the twitch interpolation technique during isometric MVC have concluded that healthy young adult subjects can completely or nearly completely (VA > 95%) activate the KE muscles (Norregaard *et al*., 1997; Knight and Kramer, 2001; Morton *et al*., 2005;

Miller *et al*., 2006). The present study showed a markedly reduced VA of the KE muscles in children with spastic diplegic CP aged 11-12 years compared with healthy children. The mean VA for control children and children with spastic diplegic CP was 94% and 74%, respectively. Our results indicate that normal prepubertal children have near to complete activation of the KE muscles, whereas children with CP demonstrate incomplete activation during MVC. However, Ramsay *et al*. (1990) demonstrated incomplete activation of the KE muscles in healthy prepubertal boys aged 9–11 years using the twitch interpolation technique. This incomplete activation may represent differences in the recruitment of MUs between children and adults. To our knowledge, only Stackhouse *et al*. (2005) have measured the VA of the KE muscles in children with spastic diplegic CP. They found a 33% VA deficit in boys with CP (mean age 10.5 years) compared with age-matched healthy boys. We observed a 20% lower VA in children with spastic diplegic CP in comparison with healthy children of a similar age. The differences between the two studies could partly be attributed to the different methods of measurement of VA. In our study, the twitch interpolation technique was used, however, Stackhouse *et al*. (2005) used the burst superimposition technique with 13-pulse train at 100 Hz. Hence, the VA of the KE muscles is reduced in children with spastic diplegic CP in comparison with healthy children of the same age.

The RDF_{50} of the KE muscles during fast MVC was 64% lower in children with spastic diplegic CP compared with healthy children (Paper III). The difference in isometric MVC between these two groups of children was 37%. Hence the capacity for rapid voluntary force production in children with CP is reduced to a greater extent than isometric MVC force.

The MVC force and RFD of KE muscles are dependent upon the degree of MU activation (Willy and Damiano, 1998; Morton *et al*., 2005), antagonist coactivation (Damiano *et al*., 1995; Elder *et al*., 2003), and peripheral factors (Rose *et al*., 1994).

The reduction in voluntary isometric force-generation capacity of the skeletal muscles in children with CP could be partly attributable to a reduced ability to recruit higher threshold (fast) MUs or to drive lower threshold (slow) MUs to higher firing rates (Rose, 2005). We found that children with spastic diplegic CP were more deficient in RFD than MVC. This finding supports the notion of an inability to adequately recruit fast MUs.

Increased antagonist co-activation could also contribute to measured deficits in voluntary muscle force production in CP (Damiano *et al*., 1995; Elder *et al*., 2003). Specifically, it has been observed that children with spastic CP had a significantly higher co-contraction ratio of KE and hamstrings muscles than normal children during knee extension (Ikeda and Abel 1998). Co-contraction increases joint stiffness, which makes movement more laborious. Damiano *et al*. (1995) suggested that the co-contraction ratio of KE and hamstrings muscles

occurred during testing the isometric knee extension MVC was well as during gait.

In addition, several peripheral factors have an impact on voluntary force production capacity and therefore may explain differences between children with CP and healthy children. For example, an increased incidence of muscle fibre atrophy, increased intramuscular fat and connective tissue in the most involved muscle groups and an increased percent of type I muscle fibres have been demonstrated in CP. Histological and histochemical studies have shown mild myopathic changes in muscles and atrophy of type I and type II muscle fibres in children with CP (Rose *et al*., 1994). Ito *et al*. (1996) reported a selective atrophy of type II muscle fibres in CP. Moreover, during growth there is a progressive fibrosis and the number of sarcomeres does not increase as rapidly as in children without CP. An abnormal variation in the size of muscle fibres and myosin heavy chain expression (Lewis *et al*., 1986; Rose *et al*., 1994) has been found in children with spastic CP. It has been suggested that muscle cells in patients with spasticity are shorter and stiffer than normal muscle cells (Friden and Lieber, 2003).

The central and peripheral processes in the human motor system can be assessed by reaction time to visual or auditory stimuli. In the present study a visual signal was used for this purpose. There was no difference in the LAT_C between the groups of children studied in the conditions of unilateral MVC of the KE muscles. Consequently, the process of movement preparation of children with CP is not impaired in comparison with healthy children.

The novel aspect of the present study was to compare the capacity for rapid voluntary relaxation of the KE muscles following maximal unilateral effort in children with and without CP. The measured time-course characteristics of the voluntary muscle relaxation, LAT_R and HRT, were both 69% longer in children with CP.

Voluntary muscle relaxation, i.e. the termination of an ongoing muscle contraction has an important role in the execution of complex movements in humans. This is particularly relevant during a rapid sequence of movements when activation must switch between different sets of contracting muscles (Buccolier *et al*., 2004). The neurophysiological mechanisms underlying voluntary muscle relaxation in humans are not well understood. A reduction of the cortical motor output can be achieved by the activation of inhibitory cortical areas (Lyders *et al*., 1995). Both primary and supplementary motor areas may be activated during voluntary muscle relaxation (Toma *et al*., 1999). Heinonen *et al*. (1999) used transcranial magnetic stimulation for investigating the paradigm of transcallosal inhibition. They observed a lack of this inhibitory mechanism in adolescent children with spastic diplegic CP. Inhibitory mechanisms could be activated at the spinal level by a pathway descending to the spinal cord. A neuronal population within the motor cortex can cause spinal presynaptic inhibition by activating inhibitory interneurons in the spinal cord

(Schmidt and McIntosh, 1990). A defect of the mechanisms mentioned above may contribute to the impairment of voluntary relaxation of the KE muscles in children with spastic diplegic CP.

In addition to that, increased antagonist coactivation, may contribute to the measured deficits in voluntary muscle relaxation in CP (Ikeda *et al*., 1998; Elder *et al*., 2003).

Moreover, it has been suggested that abnormal reflexes can restrict the execution of voluntary movement in patients with spasticity (Mizrahi and Angel, 1979).

After all, the prolongation of rapid voluntary relaxation observed in the present study may be influenced also by peripheral factors. It has been observed that the duration and rate of muscle relaxation depend on the sarcoplasmic reticulum Ca^{2+} uptake and the rate of cross-bridge kinetics (Westerblad *et al*., 1997). These intracellular processes may be affected by muscle fibre atrophy and myopathic changes in muscles in children with CP.

6.4. Summary

This study examined the peculiarities of force generation and relaxation capacity of the extensor muscles of lower extremities in children with spastic diplegic CP. Weakness in all LE, PF and KE muscles appears to partly result from the inability of the damaged motor pathways to provide sufficient excitatory drive to the motoneuron pool to fully activate all available MUs. High-intensity strength training at levels close to maximal contraction, may be effective for reducing the movement deficit and improving gait by increasing voluntary excitatory drive and muscle activation. Peripheral factors, including changes in muscle contractile properties, also contribute to muscle weakness. Hence, electrical stimulation may facilitate preservation of muscle structure in combination with high-intensity voluntary contraction. PAP increases muscle force-generation capacity. This phenomenon could be used for increasing the efficiency of rehabilitation programmes, particularly for counteracting muscle fibre atrophy and myopathic changes in the muscles of children with spastic diplegic CP. Moreover, hindering muscle fibre atrophy and myopathic changes could improve the capacity of voluntary relaxation of the muscles.

CONCLUSIONS

1. The maximal isometric voluntary force-generating capacity of the leg extensor, knee extensor and plantarflexor muscles is lower in children with spastic diplegic CP compared with age- and gender-matched children without disabilities.

2. The bilateral strength deficit of the leg extensor muscles does not differ in children with spastic diplegic CP in comparison with children without disabilities.

3. Electrically evoked isometric twitch force-generation and relaxation, and postactivation potentiation capacity in plantarflexor muscles is lower in children with spastic diplegic CP compared children without disabilities.

4. The voluntary activation of the knee extensor muscles is lower in children with spastic diplegic CP compared with children without disabilities.

5. The impaired capacity for rapid voluntary relaxation of the knee extensor muscles in children with spastic diplegic CP is dependent on both, the delayed reaction and slowing of the muscle relaxation process.

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SUMMARY IN ESTONIAN

NÄRVI-LIHASSÜSTEEMI FUNKTSIONAALNE VÕIMEKUS SPASTILISE DIPLEEGILISE SÜNDROOMIGA LASTEL

Sissejuhatus

Laste tserebraalparalüüs (*paralysis cerebralis infantilis*, lüh. PCI) on mitte-progresseeruv kompleksne neuroloogiline arengupuue, kus kesksel kohal on motoorikahäire. Tuginedes kirjanduse andmetele võib väita, et motoorne düsfunktsioon tuleneb nii lihaste spastilisusest kui ka nende nõrkusest. Viimasel ajal on jõutud seisukohale, et lihasjõu oluline vähenemine PCI korral tuleneb suurel määral motoorse kontrolli häiretest. Lihasjõudu on PCI korral uuritud nii unilateraalse kui ka bilateraalse tahtelise aktivatsiooni tingimustes, samas on aga puudulikud teadmised bilateraalse jõudefitsiidi osas. Lihasjõu genereerimise võimet on uuritud eelkõige selle tekkemehhanismide osas, kuid puuduvad andmed tahtelise lõõgastuse iseärasuste kohta PCI-ga lastel.

Siiski PCI korral ei ole lihasnõrkus ainult tsentraalse päritoluga, vaid see võib tuleneda ka perifeersetest muutustest lihases eneses. Seoses sellega on aktuaalne uurida lihaste kontraktiilseid omadusi PCI-ga lastel. Lihaste kontraktiilsete omaduste määramine põhineb elektrostimulatsiooni meetodil, mis võimaldab närvi-lihassüsteemi funktsioonide uurimisel eristada lihastes toimuvaid nihkeid muutustest lihaseid juhtivates motoorsetes keskustes.

Käesoleva töö eesmärgiks oli välja selgitada alajäsemete sirutajalihaste jõu-genereerimis- ja lõõgastusvõime iseärasused spastilise dipleegilise sündroomiga lastel tahtelise lihasaktivatsiooni ja elektrostimulatsiooni tingimustes, võrreldes neid samas vanuses tervete lastega (kontrollrühmaga).

Uurimistöö ülesanded

Töös püstitati järgmised ülesanded:

1. Hinnata alajäsemete sirutajalihaste (reienelipealihase, sääremarja-kolmpealihase ja alajäsemete sirutajalihaste summaarset) tahtelist isomeetrilist maksimaaljõudu, samuti bilateraalset jõudefitsiiti.
2. Hinnata sääremarja-kolmpealihase supramaksimaalse elektrostimulatsiooniga esile kutsutud isomeetrilise üksikkontraktsiooni karakteristikuid, sh. aktiivsusjärgset potentseerumist.
3. Hinnata reienelipealihase tahtelist aktivatsiooni.
4. Hinnata reienelipealihase kiire tahtelise isomeetrilise pingutuse ja lõõgastuse võimet.

Vaatlusalused ja metoodika

Uuringus osales kokku 28 tütarlast ja 22 poeglast vanuses 6–12 aastat. Nendest esimese grupi moodustasid spastilise dipleegilise sündroomiga lapsed (n=25) ja teise (kontroll-) grupi moodustasid samas vanuses terved lapsed (n=25). Kõik lapsed suutsid järgida instruktsioone, sh. uuringusse kaasatud PCI-ga lapsed suutsid kõndida iseseisvalt vähemalt 10 m.

Nii alajäsemete sirutajalihaste tervikuna kui ka üksikute lihasrühmade (reie nelipealihase ja sääremarja-kolmpealihase) funktsionaalse võimekuse hindamiseks kasutati spetsiaalseid elektromehaanilisi dünamomeetrilisi seadmeid, mis võimaldavad lihasjõudu määrata isomeetrilise kontraktsiooni tingimustes. Alajäsemete sirutajalihaste summaarset tahtelist maksimaaljõudu hinnati nii uni- kui ka bilateraalse isomeetrilise pingutuse tingimustes, arvutades bilateraalse jõudefitsiidi. Üksikute lihasrühmade (reienelipealihase ja sääremarja-kolmpealihase) tahtelist maksimaaljõudu hinnati unilateraalse isomeetrilise pingutuse tingimustes. Sääremarja-kolmpealihase isomeetrilise üksikkontraktsiooni karakteristikute määramisel kasutati supramaksimaalset indirektset (*n. tibialis* aktivatsiooni kaudu esile kutsutud) elektrostimulatsiooni, kasutades ristkülikimpulssi kestusega 1 ms. Isomeetriline üksikontraktsioon kutsuti esile nii puhkeolekus kui ka vahetult pärast 5 s kestnud tahtelist maksimaalset isomeetrilist pingutust (aktiivsusjärgse potentseerumise tingimustes). Määrati kontraktsioonijõud, kiirus ning kestus, samuti lõõgastusfaasi kiirust ja kestust iseloomustavad karakteristikud. Reienelipealihase tahtelise aktivatsiooni hindamisel sooritas vaatlusalune maksimaalse isomeetrilise pingutuse kestusega 4–5 s, mille käigus kutsuti 1 ms kestusega supramaksimaalse ristkülikukujulise elektriimpulsiga esile antud lihasrühma isomeetriline üksikkontraktsioon. Üksikkontraktsiooni ekstrapolarisatsiooni meetodil arvutati dünamogrammilt tahtelise aktivatsiooni protsent. Reienelipealihase tahtelise isomeetrilise pingutuse ja lõõgastuse kiiruse hindamisel tuli vaatlusalusel reageerida valgussignaalile maksimaalselt kiire ja tugeva lihaspingutusega, hoida maksimaalset lihaspinget signaali vältel (2 s) ning signaali väljalülitamisel lihased kiirelt lõõgastada. Arvutati lihaspingutuse ja lõõgastuse latentsiajad, jõugradient ja lihaste lõõgastuseks kulunud aeg.

Uurimistöö põhitulemused

Töö tulemused näitavad, et spastilise dipleegilise sündroomiga lastel on alajäsemete sirutajalihaste isomeetriline jõud märgatavalt väiksem kui samas vanuses tervetel lastel. Seejuures alajäsemete sirutajalihaste bilateraalne jõudefitsiit spastilise dipleegilise sündroomiga ja tervetel lastel oluliselt ei erine. Elektrostimulatsiooniga esile kutsutud sääremarja-kolmpealihase isomeetrilise üksikkontraktsiooni jõu ja kiiruse ning aktiivsusjärgse potentseerumise näitajad

on spastilise dipleegilise sündroomiga lastel väiksemad kui tervetel lastel. Spastilise dipleegilise sündroomiga lastel on reienelipealihase tahtelise aktivatsiooni näitaja märgatavalt väiksem kui tervetel lastel. Samuti on neil märgatavalt vähenenud reienelipealihase kiire tahtelise lõõgastuse võime maksimaalse isomeetrilise pingutuse tingimustes, mis väljendub nii lõõgastuse latentsiaja pikenemises (pidurdusprotsesside tekke hilinemises) kui ka lihaste lõõgastumise aeglustumises. Seejuures pingutuse latentsiaeg (liigutustegevuse ettevalmistusfaasi kestus) spastilise dipleegilise sündroomiga ja tervetel lastel oluliselt ei erine.

ACKNOWLEDGEMENTS

I wish to express my sincere gratitude and appreciation to all the people who helped me during this effort, and in particular:

– professor *Mati Pääsuke,* my academic supervisor and co-author, for continuous support, valuable advice, and help;
– professor *Vahur Ööpik*, my academic co-supervisor for help;
– *Jaan Ereline,* PhD, my co-author, for co-operation, and technical help;
– *Helena Gapeyeva,* PhD, my co-author, for help in conducting the studies;
– *Mariann Matlep,* my co-author, for co-operation, help, and support;
– *Helen Kaptein,* for language revision.

My family for their continuous support.

PUBLICATIONS

I

Tammik K., Ereline J., Gapeyeva H., Pääsuke M.
Leg extensor muscle strength during bilateral and unilateral contraction
in children with cerebral palsy and without disabilities.
Biology of Sport, 2004, 21 (2): 159–169.

II

Tammik K., Matlep M., Ereline J., Gapeyeva H., Pääsuke M.
Muscle contractile properties in children with spastic diplegia.
Brain and Development, 2007, 29 (9): 553–558.

III

Tammik K., Matlep M., Ereline J., Gapeyeva H., Pääsuke M.
Quadriceps femoris muscle voluntary force production and relaxation capacity in children with spastic diplegic cerebral palsy.
Pediatric Exercise Science (accepted for publication 2007)

QUADRICEPS FEMORIS MUSCLE VOLUNTARY FORCE PRODUCTION AND RELAXATION CAPACITY IN CHILDREN WITH SPASTIC DIPLEGIC CEREBRAL PALSY

Karin Tammik, Mariann Matlep, Jaan Ereline, Helena Gapeyeva and Mati Pääsuke
Institute of Exercise Biology and Physiotherapy, Estonian Centre of Behavioural and Health Sciences, University of Tartu, Estonia

Running head: Voluntary Force Production and Relaxation in CP Children

Correspondence to:
Mati Pääsuke, PhD, Professor
Institute of Exercise Biology and Physiotherapy
University of Tartu
5 Jakobi Street, 51014 Tartu
Estonia
Phone/Fax: +37 27 376 286
E-mail: mati.paasuke@ut.ee

ABSTRACT

Isometric voluntary force production and relaxation capacity of the quadriceps femoris (QF) muscle was compared between 12 children with spastic diplegic cerebral palsy (CP) and healthy controls, aged 11–12-years. Children with CP had less ($p<.05$) maximal voluntary contraction force, voluntary activation and rate of force development than controls. Visual reaction to contraction did not differ significantly in measured groups, whereas the reaction time to relaxation and half-relaxation time were longer ($p<.05$) in children with CP. We concluded that in children with CP, the capacity for rapid voluntary force production and relaxation is reduced to a greater extent than isometric maximal force.

INTRODUCTION

Cerebral palsy (CP) is an umbrella term for a group of frequent disorders of motor function due to a nonprogressive lesion of the developing brain. Many subtypes of CP have been defined, with spastic diplegia and hemiplegia being the most prevalent. A significant weakness of the muscles of lower limbs has been suggested in children with spastic diplegic CP (8, 22 26, 30), which can be associated with difficulties performing everyday functional activities. The majority of studies assessing muscle weakness in children with spastic CP have indicated a markedly reduced isometric maximal voluntary contraction (MVC) force (3, 8, 26, 30) or isokinetic peak torque (5, 9) of different muscle groups as compared to age- and gender-matched healthy children. Reduced force production in children with CP has been attributed to either incomplete recruitment or decreased motor unit discharge rates during MVC (5, 30). An increased muscle cocontraction as the simultaneous activation of agonist and antagonist muscle groups is an important factor of neuromuscular impairment during CP (4, 8, 12). Knowledge of mechanisms underlying muscle weakness in lower extremities in children with spastic diplegic CP is necessary to develop more effective interventions for increasing force production in such children.

A significantly reduced isometric MVC force of the quadriceps femoris muscle (QF) has been observed in children with spastic diplegic CP as compared to age- and gender-matched healthy children (3, 6, 26). A reduced force production of the knee extensor muscles has been shown to be related to diminished functional capacity in children with CP, as evidenced by lower scores on the Gross Motor Function Measure and increased energy expenditure during gait in the weaker children (15). The weakness of the QF muscles in children with spastic diplegic CP can in part be attributed to a central activation failure, i.e., the inability of the central nervous system to fully recruit and optimally activate available motor units. The ability to achieve complete activation of the QF muscle in healthy and clinical population is commonly assessed by twitch interpolation (14, 20) and the burst superimposition (17, 26) techniques, both with superimposing the supramaximal electrical stimulus while a subject performs an isometric MVC. Any increment in force from the stimulus suggests incomplete activation of the muscle. It is assumed that the superimposed stimulation will recruit muscle fibres that are not activated by voluntary effort and thereby will produce an extra force that is superimposed on the voluntary force. However, only one previous study (26) has compared voluntary activation (VA) of the QF muscle in children with and without spastic diplegic CP, indicating a significantly lowered VA in children with CP. Little attention has been paid to investigating the capacity for rapid voluntary force production and relaxation of the QF muscle in children with spastic diplegic CP, which is an important indicator of neuromuscular performance and movement control.

The purpose of this study therefore was to compare voluntary force production and relaxation capacity of the QF muscle in prepubertal children with spastic diplegic CP and age- and gender-matched healthy controls. The QF muscle plays an important role in many movement activities, including gait. This muscle group has a great importance in the function and stability of the knee joint as well as prevention of knee injuries. We hypothesized that the children with spastic diplegic CP would exhibit a reduced isometric MVC force and VA, and impaired capacity for rapid voluntary isometric force production and relaxation of the QF muscle, whereas the capacity for rapid isometric force production and relaxation in children with CP is reduced to a greater extent than isometric MVC force.

MATERIAL AND METHODS

Subjects

Twelve prepubertal children aged 11–12 years (6 girls and 6 boys) with spastic diplegic CP and 12 age- and gender-matched children without disabilities (also 6 girls and 6 boys) as controls participated in this study (Table 1). Inclusion criteria for children with CP included: diagnosis of spastic diplegia; presence of spasticity with a rating of 2 or 3 on the Modified Ashworth Scale (1); ability to ambulate at least 10 meters without stopping and no fixed contractures or previous surgery on the lower limb. The children with spastic diplegic CP were also classified according to the Gross Motor Function Classification System (21). Accordingly, two were on Level I, eight on Level II and two on Level III. All children were able to follow instructions. None of the children had an impairment of visual, somatosensory, hearing or vestibular function. Pubertal stages were determined according to the criteria of Tanner (27) by a pediatrician of the same gender as the subject. The children were classified as prepubertal if pubic hair and genital development for boys and breast development and pubic hair for girls were both scored as stage 1. All children (CP and controls) and parents and guardians were informed of the purpose and experimental methods and gave written and verbal consent to be participants. The study carried the approval of the University Ethics Committee.

Apparatus and Experimental Protocol

During measurement the subjects sat in a custom-made dynamometric chair with the knee and hip angles equal to 90° and 110°, respectively. The body position of the subjects was secured by three Velcro belts placed over the chest, hip and thigh. The unilateral knee extension force was recorded by a chair-fixed standard strain-gauge transducer (DST 1778, Russia) connected with the plate by rigid bar. The strain-gauge transducer pad was placed approximately 3 cm above the apex of the lateral malleolus on the anterior aspect of the leg. Signals

from the strain gauge transducer were linear from 0 to 2500 N. The force signals were sampled at the frequency of 1 kHz and stored on a hard disk of a computer using software WSportLab (Urania, Estonia).

During the testing of isometric MVC force of the QF muscle, the subject was asked to exert knee extension against the pad of the strain-gauge system as forcefully as possible. The maximal contraction effort was held for approximately 3 s. Three maximal attempts were recorded and the best result was taken for further analysis. Strong verbal encouragement and visual online feedback were used to motivate the subject. A rest period of 2 min was allowed between the attempts. Isometric MVC force relative to body mass (MVC:BM) was calculated.

During testing isometric force–time and relaxation-time characteristics of the QF muscle the subject was instructed to react to the visual stimuli (lighting of the signal lamp, placed 1.5 m from the subject) as quickly and forcefully as possible by extending the leg against a cuff fixed to a strain gauge system, to maintain the maximal effort as long as the signal was on (2 s) and to relax the muscles suddenly after the disappearance of the signal. Three attempts were carried out and the trial with higher isometric MVC force was used for further analysis. A rest period of 2 min was allowed between the attempts. The following characteristics were calculated were calculated: latency of contraction (LAT_C) – the time delay between the visual signal and the onset of force production; rate of isometric force development (RFD_{50}) – the first derivate of force development (dF/dt) at the level of 50% of MVC; latency of relaxation (LAT_R) – the time delay between the visual signal stopping and onset of quick decline in force production during relaxation; and half-relaxation time (HRT) – the time of half of the decline in force during relaxation.

During the testing of VA of the QF muscle the transcutaneous electrical stimulation with supramaximal square wave pulses of 1 ms duration was applied using an isolated voltage stimulator (Medicor MG-440, Hungary) and two self-adhesive surface electrodes (5 × 10 cm, Medicompex SA, Ecublens, Switzerland) placed transversely on the proximal (cathode) and distal (anode) third of the anterior thigh. Skin preparation for each electrode included shaving and light abrasion of the skin followed by cleaning with isopropyl alcohol. Voluntary activation of the QF muscle was estimated by twitch interpolated technique (14). Subjects were asked to reach their maximal force level in approximately 3 s and to maintain it after the supramaximal stimulus was delivered and until they were told to relax. The total duration of this contraction was approximately 5 s. Visual feedback was provided by the display of strain gauge amplifier. In fully activated QF muscle no additional force is generated by the muscle as a result of superimposed electrical twitches. If VA of the QF muscle is reduced, additional force can be generated by superimposed twitches (20). This indicates additional activity from motor units not fully activated at the time of stimulus. The intensity for supramaximal stimuli was assessed

during familiarization session and corresponded to 10% of the above level required to evoke a resting maximal twitch contraction (19). Three trials were performed with the interval of 2 min and the trial with the greatest pre-stimulus voluntary force was taken for further analysis. The VA of the QF muscle was calculated from force-time curve by the formula:

$$VA = (F_V : F_{ES}) \cdot 100\ [\%],$$

where F_V is the voluntary isometric force produced immediately prior to the electrical stimulus and F_{ES} is the peak force produced by the electrical stimulus superimposed on the voluntary effort. VA $\geq$ 95% was used as operational definition of full activation of the QF (19, 20).

Subjects were given instructions 24 to 48 hours before data collection, and the testing of isometric MVC force, force-time and relaxation-time characteristics of the QF muscle and electrical stimulation procedures were demonstrated. This was followed by a practice session to familiarize the subjects with the procedures. The subject's dominant leg was determined based on a kicking preference. During the testing, the recording of isometric MVC force of the QF muscle followed with the assessment of isometric force-time and relaxation-time characteristics. After 5 min rest period VA of the QF muscle was recorded. The same researcher with long-term experience in this kind of testing procedure tested all subjects between 11 am and 3 pm.

Statistics

Data are means and standard errors of mean (±SE). One-way analysis of variance (ANOVA) followed by Scheffe post hoc comparisons were used to test for differences between groups. A level of $p<0.05$ was selected to indicate statistical significance. Main differences in three primary measures in the present study (MVC force, RFD_{50} and VA) between children with CP and controls were tested for statistical significance (alpha = 0.05). Statistical power analysis demonstrated that 12 children in each group is a sufficient number to detect a significant difference ($\beta < 0.080$) in MVC force ($\beta = 0.99$), RFD_{50} ($\beta = 0.98$) and VA ($\beta = 0.99$).

RESULTS

As shown in Figure 1, prepubertal children with spastic diplegic CP had a significantly lower ($p<0.05$) isometric MVC force, isometric MVC force:BM ratio and isometric RFD_{50} of the QF muscle compared to the age- and gender-matched healthy controls. In children with spastic diplegic CP, HRT was significantly longer ($p<0.05$) than in controls (Fig. 2A). When compared to controls, VA of the QF muscle in children with spastic diplegic CP was significantly lower ($p<0.05$) (Fig. 2B). There were no significant differences

($p>0.05$) in LAT_C between the measured groups of children in the present study (Fig. 3A). However, children with spastic diplegic CP had a significantly longer ($p<0.05$) LAT_R compared to controls (Fig. 3B).

DISCUSSION

The present study indicated a marked isometric voluntary force deficit in the QF muscle in prepubertal children with spastic diplegic CP. Children with CP produced 38% less isometric MVC force and 37% less MVC force relative to body mass than the age- and gender-matched healthy controls. Damiano *et al*. (4) reported isometric voluntary force deficit of 31% in the QF muscle for children with spastic diplegic CP at the same knee joint angle (90°) during testing as in the present study, whereas Stackhouse *et al*. (26) demonstrated isometric force deficit of 56% in the QF muscle for these children at the knee joint angle of 60°. In the present study, children with CP had 64% less isometric RFD_{50} of the QF muscle during fast MVC compared to controls. This fact supports our hypothesis of a relatively greater deficiency in the capacity for rapid voluntary force production than in isometric MVC force of the QF muscle in children with spastic diplegic CP. Routine measurements of isometric MVC force include many potential sources of error, the most important of which is a possible lack of central drive to the muscles (19). The degree of VA is rarely taken into consideration when assessing maximal isometric force in clinical contingent. VA refers to the level of neural drive to muscle during MVC. A majority of VA studies using twitch interpolation technique during isometric MVC have concluded that adult young healthy subjects can completely or nearly completely (VA > 95%) activate the QF muscle (19, 20). In the present study, the mean VA percentage of the QF muscles for control children and children with spastic diplegic CP was 94% and 74%, respectively. Our results indicated that normal prepubertal children had near by complete activation of the QF muscle, whereas children with CP demonstrated incomplete activation. However, Ramsay *et al*. (22) demonstrated incomplete activation of the QF muscle also in healthy prepubertal boys aged 9–11 years using twitch interpolation technique. This incomplete activation may represent maturational differences in the recruitment of motor units between children and adults. Only Stackhouse *et al*. (26) measured previously VA of the QF muscles in children with spastic diplegic CP by burst superimposition technique, suggesting 33% VA deficit in boys with CP (with mean age of 10.5 years) compared to age-matched healthy boys. The present study indicated 21% VA deficit in children with spastic diplegic CP of similar age, whereas differences between two studies can in part be attributed to the different methods of measurement of VA.

The reduced voluntary isometric force-generation capacity of the skeletal muscles in children with CP could be partly attributable to a reduced ability to recruit higher threshold (fast) motor units or to drive lower threshold (slow) motor units to higher firing rates (23). The present results indicated that children with spastic diplegic CP were more deficient in the capacity for rapid isometric force production than in maximal isometric force during slower voluntary effort, supporting the notion of an inability to adequately recruit fast motor units. Increased antagonist coactivation could also contribute to measured deficits in voluntary muscle force production in CP (4, 8, 12). It has been observed that children with spastic CP had significantly higher cocontraction ratio of QF and hamstrings muscles than normal children during knee extension (12). Cocontraction increases joint stiffness, which makes movement more laborious. Damiano *et al*. (4) suggested that cocontraction ratio of QF and hamstrings muscles during testing isometric knee extension maximal isometric force correlated directly with those during gait. A reduced isometric MVC force and rate of force development of the QF muscle in children with CP can in part be also attributed to peripheral factors. An increased incidence of muscle fibre atrophy, increased intramuscular fat and connective tissue in the most involved muscle groups and increased percent of slow-twitch (type I) muscle fibres (13, 24) have been demonstrated in CP. Histological and histochemical studies also have shown mild myopathic changes in muscles and atrophy of type I and type II muscle fibres in children with CP (24). Ito *et al*. (13) reported a selective atrophy of type II muscle fibres during the development in CP. An abnormal variation in the size of muscle fibres and myosin heavy chain expression (24) has been found in children with spastic CP. It has been suggested that muscle cells in patients with spasticity are shorter and stiffer than normal muscle cells (10).

The movement preparation process can be assessed by reaction time to visual or auditory stimuli. Our data indicated no significant differences in the indicator of visual reaction (LAT_C) when performing unilateral MVC of the QF muscle between the groups of children with and without spastic diplegic CP. These results indicated that the reaction time of isometric muscle contraction was not significantly prolonged in children with CP, suggesting that movement preparation was not affected.

The novel aspect of the present study was to compare the capacity for rapid voluntary relaxation of the QF muscle following maximal unilateral effort in children with and without CP. The measured time-course characteristics of the voluntary muscle relaxation, LAT_R and HRT, were both 69% longer in children with CP as compared to controls. The voluntary muscle relaxation, i.e. termination of an ongoing muscle contraction has an important role in the execution of complex movement in humans, particularly during rapid sequence of movements when activation must switch between different sets of contracting muscles (2). The neurophysiological mechanisms underlying voluntary muscle relaxation in humans are not well understood (2). A reduction of cortical motor

output can be achieved by the activation of inhibitory cortical areas, and both primary and supplementary motor areas may be activated during voluntary muscle relaxation (28). Using transcranial magnetic stimulation to investigate the paradigm of transcallosal inhibition, Heinen *et al*. (11) indicated a lack of inhibitory control of the motor cortex by this inhibitory mechanism in adolescent children with diplegic CP. Inhibitory mechanisms can be activated at the spinal level by pathway descending to the spinal cord. A neuronal population within the motor cortex can cause spinal presynaptic inhibition by activating inhibitory interneurons in the spinal cord (25). A defect of the above mechanisms may contribute to the impairment of voluntary relaxation of the QF muscle in children with spastic diplegic CP. Increased antagonist coactivation, typically observed in CP (4, 8, 12), increases joint stiffness and could contribute to the measured deficits in voluntary muscle relaxation. It has been suggested that abnormal reflexes can restrict the execution of voluntary movement in patients with spasticity (18). The prolongation of HRT observed in the present study can be influenced also by peripheral factors. It has been observed that the duration and rate of muscle relaxation depend on sarcoplasmic reticulum Ca^{2+} uptake and rate of cross-bridge kinetics (29). These intramuscular processes can be affected by muscle fibre atrophy and myopathic changes in muscles in CP.

It has been indicated that maximal voluntary muscle force production capacity of the QF muscle (4, 7) and some aspects of movement function (gait, sit-to-stand, jumping performance) (16) in children with mild-to-moderate CP can be improved by strength training programs. Results of our study suggest that improvement of capacity for rapid voluntary contraction and relaxation of the QF muscle should be considered when designing strengthening exercise protocols for children with spastic diplegic CP. A limitation of this study was a relatively small number of children (6 girls and 6 boys) in both groups and, therefore, the gender differences were not analyzed. More research is needed on the pathophysiologic basis of impaired capacity for rapid voluntary muscle force production and relaxation in spastic diplegic CP, the effect of therapeutic intervention and the functional benefit of reducing this impairment in subjects with CP.

In conclusion, the present study indicated a markedly reduced isometric MVC force and voluntary activation, impaired capacity for rapid voluntary isometric force production and relaxation of the QF muscle in children with spastic diplegic CP. The rate of isometric force development in children with spastic diplegic CP was reduced to a greater extent than isometric MVC force, supporting the notion of a reduced ability to adequately recruit higher threshold motor units. The impaired capacity for rapid voluntary relaxation of the QF muscle following a short-time maximal effort is dependent both on delayed reaction and slowing of muscle force-relaxation process. No significant impairment in movement preparation during rapid MVC of the QF muscle were observed in children with spastic diplegic CP, assessed by visual reaction time.

ACKNOWLEDGEMENT

This study was partly supported by Estonian Science Foundation, Grant No. 7099

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Table 1. Anthropometric Parameters of the Subject Groups

	Groups	
Variable	**Children with CP (*n* = 12)**	**Controls (*n* = 12)**
Age (years)	11.2±0.7	11.2±0.7
Height (cm)	136.8±7.6	138.9±7.6
Body mass (kg)	33.0±11.4	33.7±10.0
Body mass index ($kg \cdot m^{-2}$)	17.4±4.2	17.3±3.5

Note. CP = cerebral palsy. Variables are expressed as mean ± standard deviation. No significant differences ($p>0.05$) were noted among groups.

FIGURES

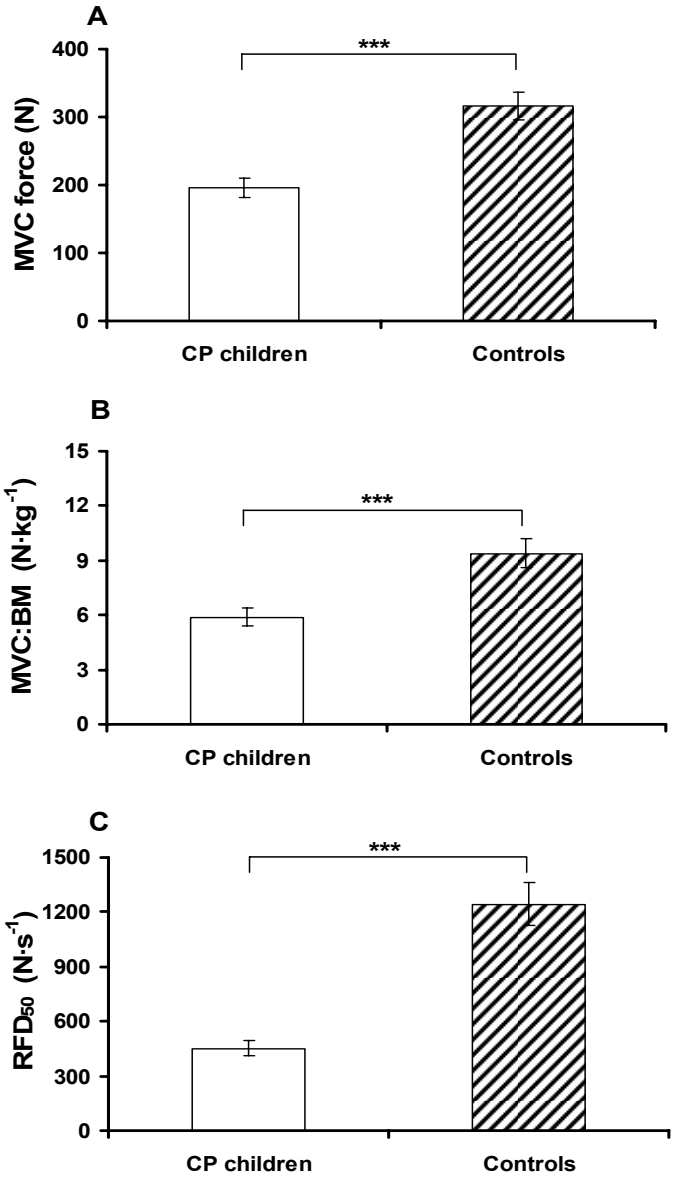

Figure 1. Mean (±SE) isometric maximal voluntary contraction (MVC) force (**A**), MVC force relative to body mass (MVC:BM) (**B**) and rate of isometric force development at level of 50% of MVC (RFD_{50}) (**C**) of the quadriceps femoris muscle in children with cerebral palsy (CP) and controls. *** $p<0.001$.

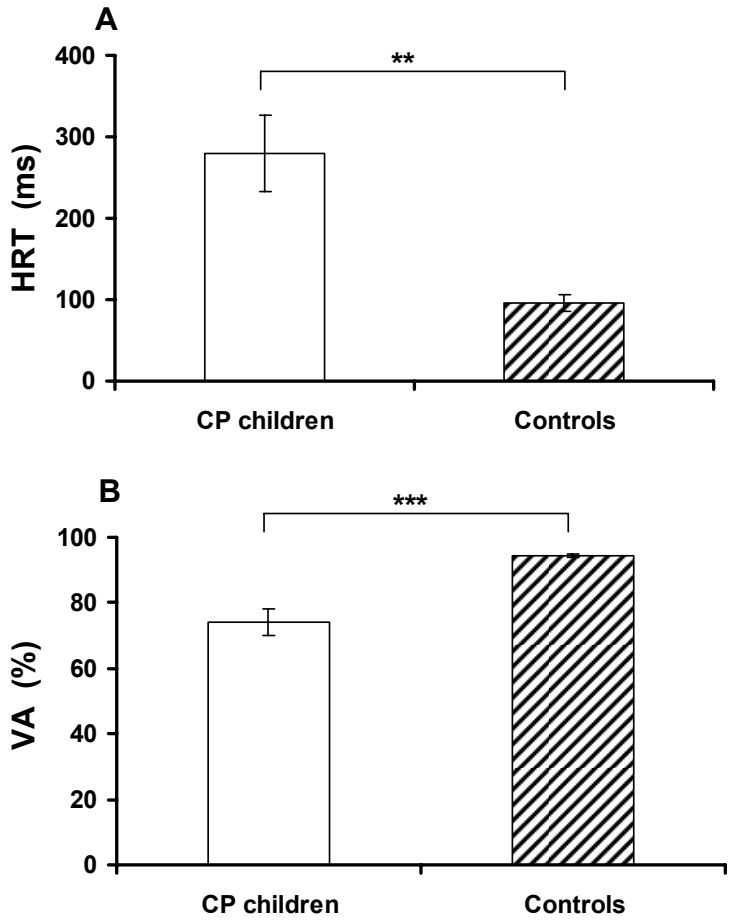

Figure 2. Mean (±SE) half-relaxation time (HRT) (**A**) and voluntary activation (VA) (**B**) of the quadriceps femoris muscle in children with cerebral palsy (CP) and controls. ** $p<0.01$; *** $p<0.001$.

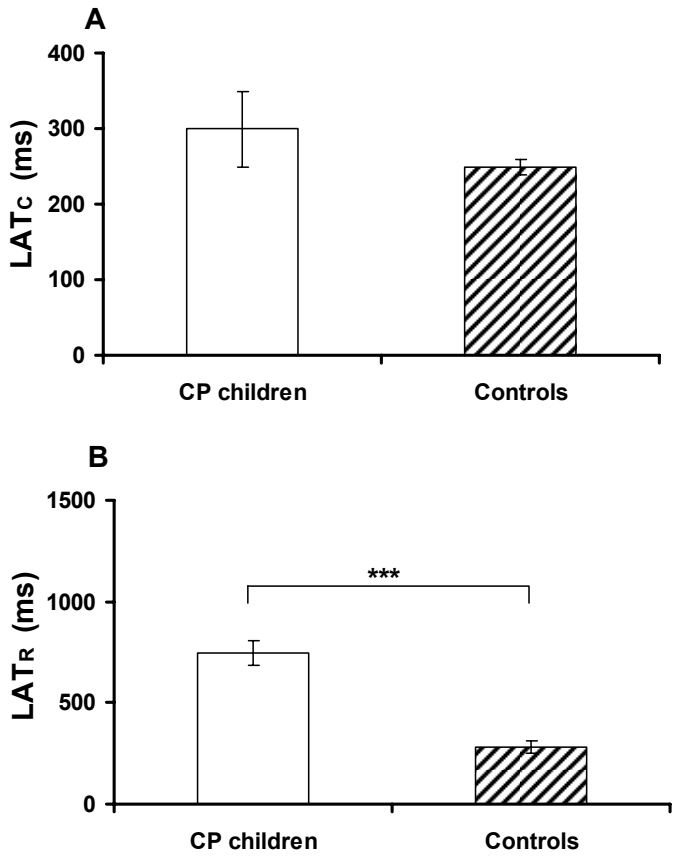

Figure 3. Mean (±SE) latency of contraction (LAT_C) (**A**) and relaxation (LAT_R) (**B**) of the quadriceps femoris muscle in children with cerebral palsy (CP) and controls. *** $p<0.001$.

CURRICULUM VITA

Karin Tammik

Citizenship: Estonia
Born: 10 July 1968, Tartu
Married, daughter Anna, born 2004, sons Oskar, born 2002 and Olar, born 1991
Address: 5 Jakobi Street, Tartu 51014, Estonia
Phone/Fax: +372 7 376 286
E-mail: karin.tammik@ut.ee

Education

1986	Elva Secondary School;
1990–1995	*BSc* (Physiotherapy, *cum* laude), University of Tartu, Faculty of Exercise and Sport Sciences;
1995–1998	*MSc* (Exercise and Sport Sciences), University of Tartu, Faculty of Exercise and Sport Sciences;
1999–2007	PhD-study (Exercise and Sport Sciences), University of Tartu, Faculty of Exercise and Sport Sciences.

Specialized Courses

1995	Kinderfachklinik Satteldyne, Germany, 2-month training in respiratory treatment in patient with cystic fibrosis;
1997	Tartu University Children's Hospital, Tartu, Estonia, Workshop in rehabilitation for cardio-respiratory patients;
1998	Klinik für Kinderneurologie und Sozialpädiatrie, Unna-Königsborn, Germany, 4-week training on neurodevelopment and treatment of children with cerebral palsy (concept of Bobath) and 2-week training on neurokinesiological treatment (concept of Vojta);
2005	University of Tartu, Estonia, Practical assesment and physiotherapy for patients with multiple sclerosis;
2006	The European Cystic Fibrosis Society and The International Physiotherapy Group for Cystic Fibrosis, Copenhagen, Denmark, Pre-Conference course: "Integrating the pulmonary, musculoskeletal and neuromuscular systems: a physical approach to cystic fibrosis";
2006	6th International Congress on Cerebral Palsy, Bled, Slovenia.

Professional Employment

1986–1988 Võnnu Primary School, Physical education teacher;
Since 1994 Tartu University Hospitals, Children's Clinic, Physiotherapist.

Membership in professional organizations

- Estonian Union of Physiotherapists – board member.

Scientific activity

Main research interests:
- Aerobic ability in middle-aged women;
- Twitch contractile properties in children with cerebral palsy;
- Effect of neurodevelopmental therapy on motor functions in children with cerebral palsy;
- Neuromuscular performance in children with spastic cerebral palsy.

Publications:
- Articles in international refereed journals – 4;
- Other scientific articles – 5;
- Abstracts – 7.

ELULOOKIRJELDUS

Karin Tammik

Kodakondsus: Eesti Vabariik
Sündinud: 12. juulil 1968 Tartus
Abielus, tütar Anna, sündinud 2004, pojad Oskar,
sündinud 2002 ja Olar, sündinud 1991
Aadress: Jakobi 5, Tartu 51014
Tel./faks: 7 376 286
E-post: karin.tammik@ut.ee

Haridus

1986	Elva Keskkool
1990–1995	*BSc* (liikumis- ja sporditeadused, *cum laude*), Tartu Ülikool, kehakultuuriteaduskond;
1995–1997	*MSc* (liikumis- ja sporditeadused), Tartu Ülikool, kehakultuuriteaduskond;
1999–2007	Doktoriõpe (liikumis- ja sporditeadused), Tartu Ülikool, kehakultuuriteaduskond.

Erialane enesetäiendus

1995	*Kinderfachklinik Satteldyne*, Saksamaa, 2-kuuline täiendõpe tsüstilise fibroosi korral rakendatava respiratoorne ravi alal;
1997	Tartu Ülikooli lastekliinik, Tartu, kardiorespiratoorsete patsientide rehabilitatsiooni kursus;
1998	*Klinik für Kinderneurologie und Sozialpädiatrie*, Unna-Königsborn, Saksamaa, 4-nädalane täiendõpe tserebraalparalüüsiga laste ravi (Bobath kontseptsiooni) alal ja 2-nädalane täiendõpe neurokinesioloogia (Vojta kontseptsiooni) alal;
2005	Tartu Ülikooli lastekliinik, Tartu, kursus ”Praktiline käsitlus ja taastusravi sclerosis multiplex’i korral”;
2006	*The European Cystic Fibrosis Society and The International Physiotherapy Group for Cystic Fibrosis*, Kopenhaagen, Taani, täiendõppe kursus tsüstilise fibroosi ravi alal;
2006	*6th International Congress on Cerebral Palsy*, Bled, Sloveenia.

Erialane teenistuskäik

1987–1989 Võnnu Põhikool, kehalise kasvatuse õpetaja;
Alates 1994 Tartu Ülikooli Kliinikumi lastekliinik, füsioterapeut.

Erialaorganisatsioonid

- Eesti Füsioterapeutide Liit, juhatuse liige.

Teadustegevus

Peamised uurimisvaldkonnad:
- Motoorne võimekus spastilise tserebraalparalüüsiga lastel;
- Skeletilihaste kontraktiilsed omadused tserebraalparalüüsiga lastel;
- Neuroarengulise teraapia mõju motoorsetele funktsioonidele tserebraalparalüüsiga lastel.

Publikatsioonid:
- Teaduslikud artiklid rahvusvahelise levikuga ajakirjades – 4;
- Muud teaduslikud artiklid – 5;
- Konverentside teesid – 7.

DISSERTATIONES KINESIOLOGIAE UNIVERSITATIS TARTUENSIS

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