Improving Gait in Cerebral Palsy

Effects of a combined Strength, Flexibility and Gait Training Intervention on Lower Limb Gait Kinematics and Kinetics in Children and Young Adults with spastic Cerebral Palsy

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ABSTRACT

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INTRODUCTION. Walking ability is a fundamental skill enabling participation and independence. For people with cerebral palsy (CP) gait can be impaired due to altered musculoskeletal development resulting from a lesion of the developing brain. Neuromuscular impairments like muscle weakness, impaired motor control and reduced range of motion (ROM) are commonly targeted with physical therapy. However, a lack of consistent improvements in motor function requires the development of more evidence-based training interventions to optimally target rehabilitation in CP. The purpose of this thesis is to investigate the effects of a three-month long tailored exercise intervention including strength, flexibility and gait training on lower limb gait kinematics and kinetics, walking endurance and motor function in children and young adults with CP.

METHODS. Seventeen children and young adults with spastic CP (9-22 years, 5 bilateral/13 unilateral, 13/5 GMFCS I/III) participated in two to three individually guided 90 minutes sessions and ten minutes of daily walking on an inclined treadmill at home for twelve weeks. 3D lower limb kinematics and kinetics (Vicon) and six minutes walking test (6MWT) performance were assessed twice before and twice after the intervention in intervals of three months. Gross Motor Function Measure (GMFM) was assessed directly pre and post the intervention. The guided intervention sessions consisted of flexibility, strength and treadmill gait training. Seventeen age and sex matched typically developing (TD) control participants were measured once without participation in the intervention.

RESULTS. CP participants displayed significantly decreased dorsiflexion (DF) during swing and initial contact, reduced ROM of the knee and hip during stance and smaller peak ankle push-off power compared to the control group. There was no statistically significant change in gait kinematics or kinetics in CP after the intervention. Furthermore, there was no statistically significant increase in distance walked in the 6MWT or GMFM score after the intervention.

DISCUSSION. A twelve-week combined strength, flexibility and gait training intervention in children and young adults with CP did not improve gait kinematics or walking function. Despite a lack of significant group effects, analysis of GMFM scores indicated the existence of several responders with clinically relevant improvements in gross motor function. Further studies are needed to investigate the underlying mechanisms behind responders and non-responders to exercise interventions.

Key words: Cerebral Palsy, strength training, inclined treadmill walking, gait analysis

Table of content

Abbreviations

BoNT-A	botulinum neurotoxin type A
CP	cerebral palsy
GMFCS	gross motor function classification scale
GMFM	gross motor function measure
GRF	ground reaction force
ROM	range of motion
TD	typically developed
WHO	world health organization
6MWT	6-minutes walking test

Introduction

Walking on two legs has enabled us to evolve into the humans we are today, carrying tools in our hands while efficiently moving from one place to another (Nielsen, 2003). Shifting our body weight alternatingly between the narrow base of support from one foot to the other. Stabilizing our pelvis and upper body with the stance limb while the other limb swings forward to create step length (Perry, 1992). The healthy human gait is optimized to require so little active control that we have swopped the tools into phones and can walk while answering our mails on them. Only when one element in this elaborate system that composes our walking pattern fails we grasp the complexity of it.

For people with cerebral palsy (CP) walking can be a strenuous activity (Rosenbaum et al., 2006). CP is a motor disorder with its origin in a lesion to the developing brain and presents the most common cause for physical disability with onset in childhood affecting about 2-3 children in 1000 life births (Arnaud et al., 2018). Sensory loss, abnormal muscle tone and impaired motor control undermine musculoskeletal development early on in childhood and persist throughout the entire lifespan (Gage et al., 2009). Despite highly heterogenous manifestations in CP, walking is almost always disturbed decreasing its efficiency, making physical activity more fatiguing and creating barriers for participation (Shikako-Thomas et al., 2012). Reduced physical activity can lead to worsening of secondary symptoms like muscle weakness and create a vicious cycle of further inactivity, further degeneration of function and development of cardiometabolic risk factors (Verschuren et al., 2016).

All children with CP will therefore undergo some form of physical therapy growing up (Graham et al., 2016). The beauty of physical activity is that it gives the patient back some level of control and responsibility for their own well-being and can directly address functional skills necessary for daily life. Various studies have been performed in the past trying to identify the optimal training strategy for addressing impairments like muscle weakness, reduced joint range of motion (ROM), walking kinematics and walking velocity (Booth et al., 2018; Eldridge and Lavin, 2016; Moreau et al., 2016; Verschuren et al., 2011). Since in CP especially distal lower-limb muscles are affected, a main therapeutic goal is to address walking ability (Gage et al., 2009).

Addressing a lack of well-designed training interventions, activity guidelines especially for children with CP have been published by Verschuren and colleagues in 2016 and depict principles for exercise selection and intensity and volume progression for strength training with a CP population. However, increases in muscle strength have not necessarily transferred into improvements of functional tasks like walking in previous studies (Fosdahl et al., 2019; Gillett et al., 2019). Task-specificity is a key requirement for successful motor learning and is needed to promote improved motor patterns (Winstein et al., 2014).

The current study is the first intervention to combine twelve weeks of strength training based on these activity recommendations by Verschuren et al (2016) with task-specific gait training on a treadmill in children and young adults with CP. Additionally, the intervention is supplemented by passive stretching of shortened lower limb muscles. The purpose of this thesis is to examine the effects the tailored intervention has on lower limb gait kinematics, walking endurance and mobility in a cohort of children and young adults with CP.

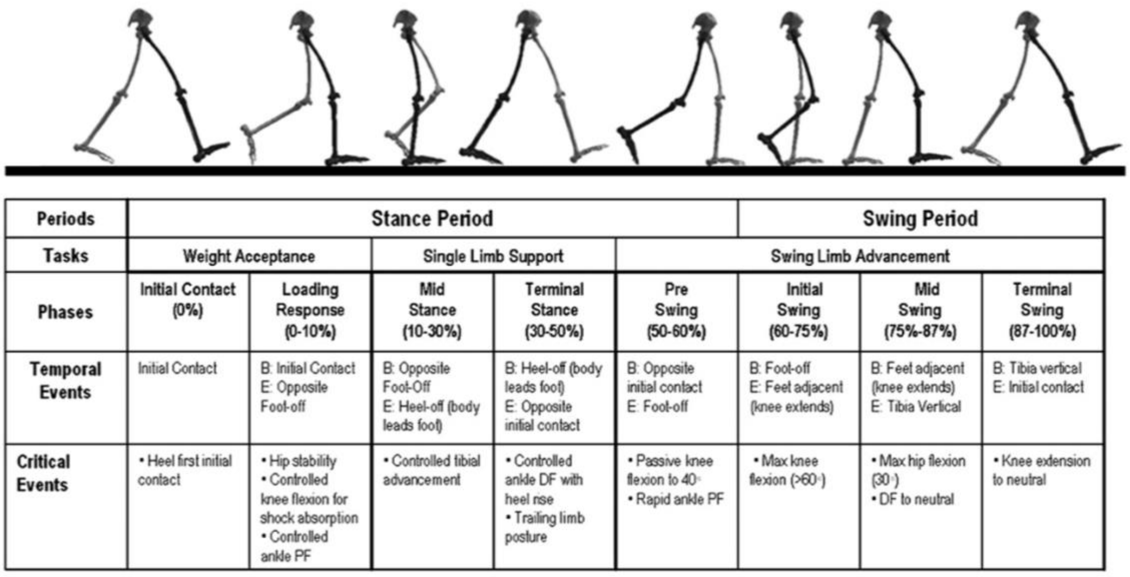
1. Biomechanics of Gait

Gait is our main method of locomotion and characterized by periods of loading and unloading of the limbs to move forward, providing independence (Baker et al., 2016). It is crucial for autonomy in everyday situations and creates the foundation for children to explore their surroundings and interact with others (Shikako-Thomas et al., 2012).

As natural and easy as walking may seem to most people, the human gait is complex and an abundance of bodily systems work hand in hand in perfect harmony to create this fluent and efficient movement pattern (Gage et al., 2009). Gage and Schwartz have defined five prerequisites of healthy gait: 1) stability in stance; 2) foot clearance during swing; 3) prepositioning of the foot before ground contact; 4) adequate step length and 5) energy conservation (Gage et al., 2009, chap. 1.3). Despite high demands, the healthy, mature gait is highly optimized and repeatable. Nevertheless, the complexity of the system makes it vulnerable to pathological deviations.

Gait requires sufficient motor control and integration of sensory information as well as energy sources to generate forces that act on levels to create directed movement (Gage et al., 2009). Gait of bipeds is characterised by the cyclic alternation of stance and swing phases with a double support phase at the start and end of each stance period. During these, in contrast to running, both feet are in contact with the ground for transitioning the base of support from one leg to the other. This pattern is highly symmetrical and repeatable in healthy, typically developed gait patterns.

To facilitate communication and comparison, gait is often categorized into a series of gait cycles. A gait cycle is, by convention, defined as the time between *initial contact* of one foot and repeated ground contact of the same foot after swing phase (Baker, 2013, 9; Chang et al., 2010). This allows for time normalisation of a gait cycle (0-100% as seen in Figure 1), therewith, facilitating the comparison of subjects with different stride characteristics like stride length and walking speed. A gait cycle can be divided into two main periods: stance and swing phases. These can be further subdivided into functional phases each with its characteristics concerning timing, joint angles and posture. Typically developed (TD) walking patterns display a relation of 60% stance phase with the first and last ten percent of it being double support phases where both legs are on the ground to 40% swing phase in one stride. (Perry, 1992)



Periods	Stance Period					Swing Period		
Tasks	Weight Acceptance		Single Limb Support		Swing Limb Advancement			
Phases	Initial Contact (0%)	Loading Response (0-10%)	Mid Stance (10-30%)	Terminal Stance (30-50%)	Pre Swing (50-60%)	Initial Swing (60-75%)	Mid Swing (75%-87%)	Terminal Swing (87-100%)
Temporal Events	Initial Contact	B: Initial Contact E: Opposite Foot-off	B: Opposite Foot-Off E: Heel-off (body leads foot)	B: Heel-off (body leads foot) E: Opposite initial contact	B: Opposite initial contact E: Foot-off	B: Foot-off E: Feet adjacent (knee extends)	B: Feet adjacent (knee extends) E: Tibia Vertical	B: Tibia vertical E: Initial contact
Critical Events	• Heel first initial contact	• Hip stability • Controlled knee flexion for shock absorption • Controlled ankle PF	• Controlled tibial advancement	• Controlled ankle DF with heel rise • Trailing limb posture	• Passive knee flexion to 40° • Rapid ankle PF	• Max knee flexion (>60°)	• Max hip flexion (30°) • DF to neutral	• Knee extension to neutral

Figure 1. A typical gait cycle with description of critical events as described by Jaquelin Perry (Data from Perry J. Gait Analysis: normal and pathological function. Thorofare (NJ): Slack, 1992) taken from Chang et al. 2010.

It is important to note, that despite the time normalization being a useful tool to compare different walking conditions, information is also disguised in the process. Spatiotemporal characteristics of gait cannot be made out from the joint angular curves anymore. Therefore, they are often reported aside of time-normalized characteristics. For example, the analysis of walking speed can provide insights into the abnormality and variability of a gait pattern. Walking speed is the product of cadence and stride length and an indicator of functional ability (Baker, 2013; Middleton et al., 2015). Walking speed below 1m/s has been associated with a history of increased fall risk among healthy and community-dwelling elderly (Kyrdalen et al., 2019). Whereas, faster walking speeds have been associated with increased joint angles, angular velocity and peak power while the pattern stayed the same (Mentiplay et al., 2018). Therefore, any changes in walking velocity should always be reported alongside with kinematic and kinetic changes in walking. Carefully defined and analysed spatio-temporal parameters can give valuable information about an individual's gait. (Chang et al., 2010).

Joint angles, joint angular velocity and acceleration are categorized as kinematic data. The sagittal plane divides the body into left and right and includes all forward and backward directed movements. Joint flexion and extension movements as well as ankle dorsiflexion and plantarflexion occur in the sagittal plane. The coronal, also called frontal plane separates the body into front and back and displays all sideways movements like adduction and abduction and on the foot level inversion and eversion. Motion in the transverse, also called horizontal, plane divides the body into upper and lower parts and is of rotational nature (Figure 2). (Whittle, 2008).

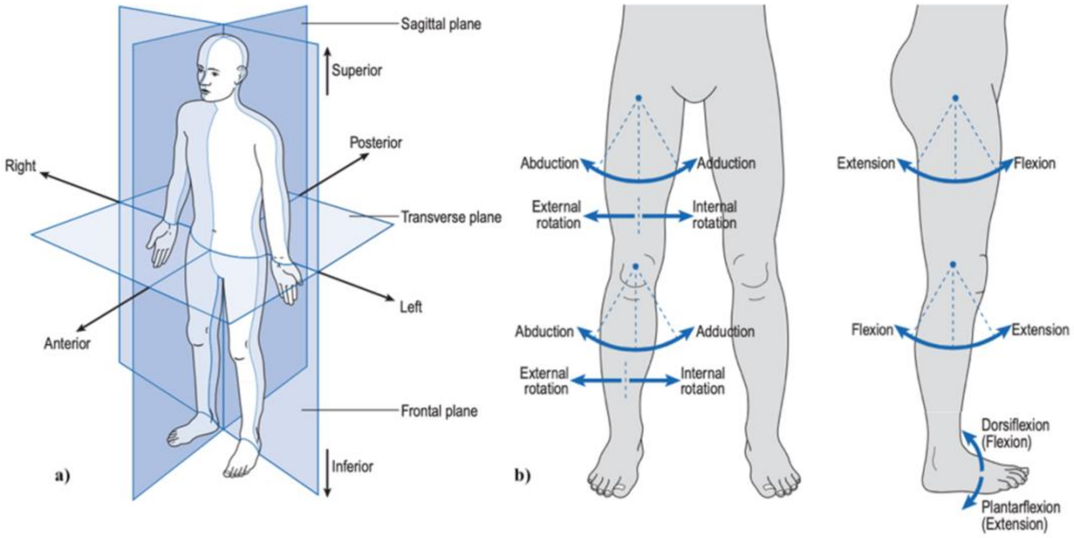


Figure 2. a) Anatomical Position of the reference planes in the human body and the movements in these planes at b) the hip, knee and ankle. taken from Whittle 2007.

An example of such a kinematic description of the gait of a group of TD children can be found in Figure 3. The graph displays the hip, knee and ankle joint motion in all three planes (Chang et al., 2010). The sagittal plane is, due to the forward propelling nature of locomotion, the most prevalent plane in which many changes occur during walking (Perry, 1992).

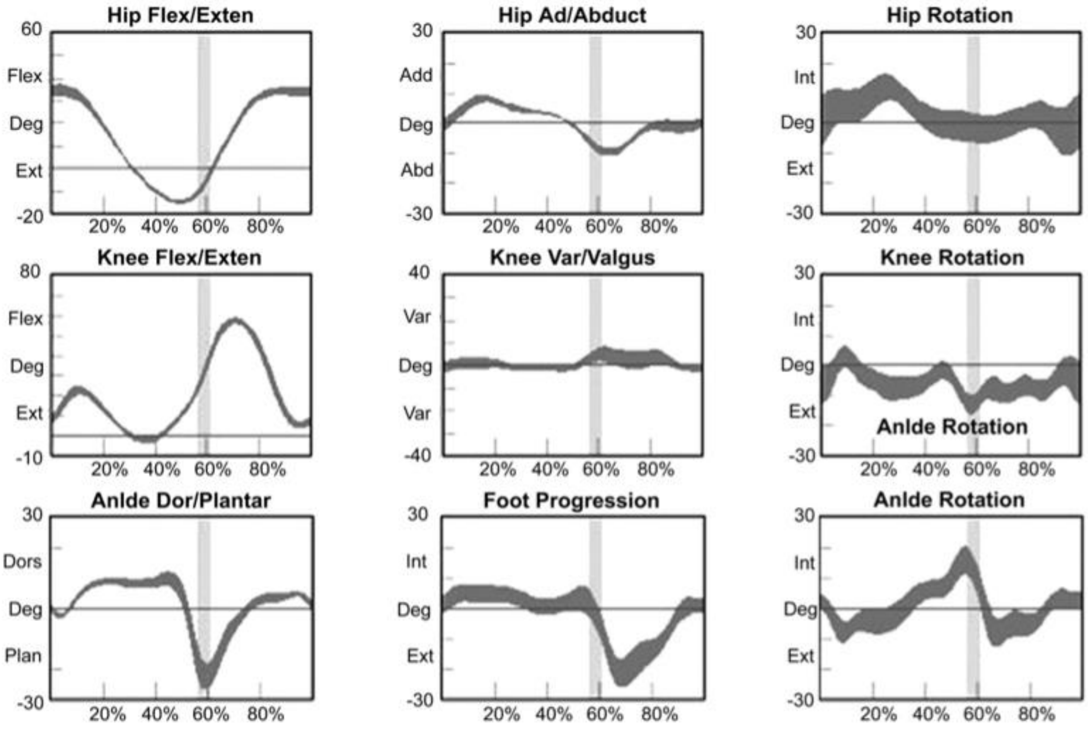


Figure 3. Kinematics of a group of typically developed 13-year-old children. Kinematics includes sagittal, coronal and transverse planes (from the left to the right, respectively). Vertical axis shows degree of motion. Horizontal axis shows the percentage of gait cycle. The vertical light grey bar represents the toe-off and all values show one standard deviation. Figure is taken from Chang et al. 2010.

At the hip joint a single curve leading from flexion to extension in stance phase and back to flexion in midswing is necessary to lift the center of mass (CoM) during stance and allow for leg clearance during swing. The knee joint displays two bumps - the first indicating a small knee flexion peak during weight acceptance and shock absorption. During single leg support the knee extends due to a combination of the plantarflexors eccentrically restricting the forward progression of the tibia and the ground reaction force (GRF) moving anterior to the knee creating an external knee extension moment, also called the "Plantarflexion Knee Extension Couple" (Gage et al., 2009). This way, minimal concentric muscle activity is necessary to extend the knee, while ligaments restricting knee hyperextension and bony alignment keep the knee extended. During midswing the second flexion peak supports limb clearance. The ankle curve in the sagittal plane commonly consists of three curves, also called "rockers" by Perry (Perry, 1974). Starting with the "heel rocker", which originates from a short plantarflexion motion lowering the foot flat to the floor in preparation of weight acceptance. It is followed by the "ankle rocker" which describes an increased dorsiflexion during the transition of the center of mass over the stationary foot. And finally, the third (*toe rocker*) illustrates the rapid ankle plantarflexion during push-off to generate forward propulsion and accelerate the leg for swing phase. Analysing the gait graphs carefully can help understand critical features of typical gait such as the need for a near neutral dorsiflexion of the ankle during swing phase for successful foot clearance without any compensatory movements. (Chang et al., 2010; Gage et al., 2009; Perry, 1992).

In the human body, driver of motion are forces that act around levers. These forces are both the body's own forces like muscles acting on internal structures of the body and external forces like the GRF. The GRF describes the force applied by the ground to the individual's foot during stance phase as a reaction to the force the person exerts on the ground as a combination of gravity and muscular activity (Perry, 1992). Vertical GRF is an important characteristic of walking that can be altered in pathologies. In TD gait, vertical GRF displays two peaks. The peaks relate to the change in centre of gravity during early and late stance phase (i.e. full weight bearing and push-off). During mid-stance, the body weight is partially unloaded when the centre of mass moves over the stationary foot (Whittle, 2008, pp. 80–84). By relating the GRF to the joint kinematics, the work performed at each joint can be calculated using inverse dynamics. Integrating the joint moment with angular velocity results in the measure of power, which relates to the transition from eccentric (negative power) to concentric (positive power) activity (Perry, 1992, p. 475). During a gait cycle, the hip mostly performs positive work to create forward propulsion pulling the leg forward in early swing phase. The knee joint performs little positive mechanical work but rather absorbs energy. However, the active extension of the knee can add to the pulling effect of the leg swinging forward like a pendulum during swing phase. The ankle is an incredibly important joint for achieving and maintaining a healthy gait pattern. It connects the body with the ground in stance and creates the majority of forward propulsion during push-off (Perry, 1992, p. 61). Further, the muscles around the ankle work to: 1) shape the GRF during stance; 2) initiate knee flexion at the end of stance by plantarflexing rapidly; 3) enable foot clearance by dorsiflexing the foot during swing and 4) preposition the foot before ground contact.

2. Cerebral Palsy

2.1 Epidemiology and Classification of CP

Cerebral Palsy (CP) is a physical disability that affects movement and posture caused by an impairment of the brain before, during or shortly after birth. According to numbers of the Australian Cerebral Palsy Alliance, CP is the most common physical disability with onset in childhood with around 17 million people affected worldwide. The prevalence ranges between 2-3 cases per 1000 life births in Europe (Arnaud et al., 2018; Graham et al., 2016) and each patient has an unique set of symptoms. Therefore, CP is utilised as an umbrella term for a group of permanent disorders. In the past, various attempts have been made to define CP, testifying the difficulties of doing so. In 2006, Rosenbaum proposed a definition, which since then has been widely accepted (Rosenbaum et al., 2006):

"Cerebral palsy (CP) describes a group of permanent 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. The motor disorders of cerebral palsy are often accompanied by disturbances of sensation, perception, cognition, communication, and behaviour, by epilepsy, and by secondary musculoskeletal problems."

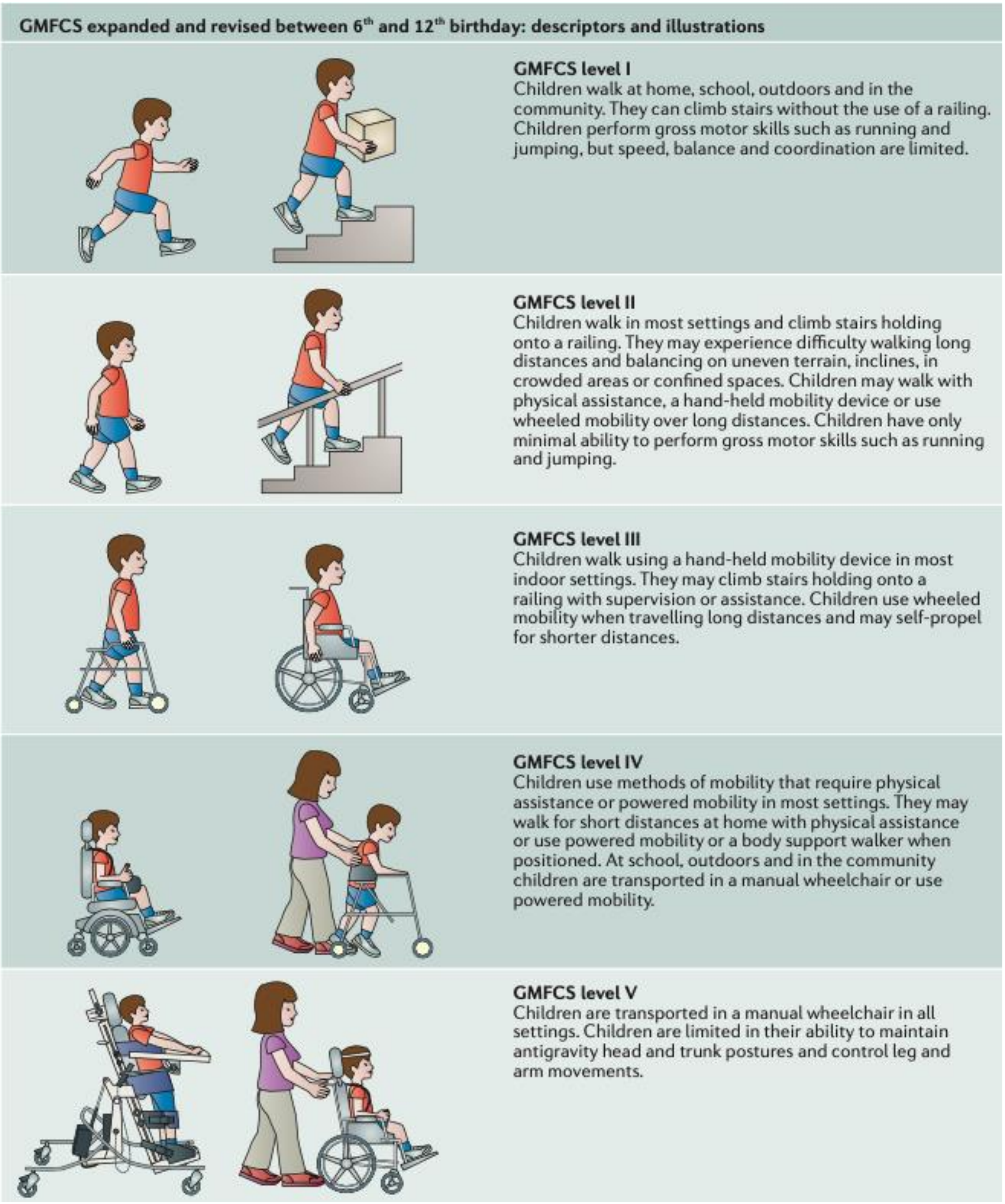
Despite, the primary neurological impairment being non-progressive (Graham et al., 2016), secondary effects of the damaged corticospinal pathways like motor impairments can progress without effective treatment and thus, secondary impairments can largely affect quality of life (Morgan and McGinley, 2014; Shikako-Thomas et al., 2012).

Given the heterogenous manifestation of CP, developing appropriate and reliable classification systems for CP is not easy. Various systems and classification scales have been introduced throughout the past 160 years, some more reliable than others (Rosenbaum et al., 2006). To classify the neuro-motor abnormalities in children with CP, three main types have been widely accepted based on the main site of lesion and resulting motor abnormality. Spastic CP, the most prevalent with around 80% of all CP cases, relates mainly to damage of the brain stem and extrapyramidal tracts of the CNS with impaired inhibition of muscle tone. The second type of CP is the ataxic type, which is traced back to a lesion in the cerebellum and therefore a decrease in fine-motor control and impaired motor learning. Finally, dyskinetic CP is associated with a lesion in the basal ganglia which can emerge into hypokinetic or hyperkinetic disorders depending on the site of the lesion. (Graham et al., 2016). In the following, this review will focus on spastic-type CP, since it was the focus of the present study.

In spastic CP, the anatomical distribution of affected limbs is commonly separated into unilateral and bilateral CP. This categorization has been shown to have good reliability (Arnaud et al., 2018), although, some problems still arise as the distribution of limbs can be blurred. For many unilaterally affected children, the unaffected limb displays a mild impairment as well and in bilaterally affected children a high asymmetry in severity of the limb impairments can be apparent. Therefore, either way, a more affected side is commonly recognizable.

Another important classification concerns the functional motor abilities of an individual. Motor abilities have a direct impact on the ability of performing many important daily activities and, therefore, their classification is crucial. Since upper and lower limbs are structurally as well as functionally very different, separate classification systems were developed for their assessment. For the level of ambulation, and therewith limitations of mostly the lower limbs, the Gross Motor Function Classification System (GMFCS) was developed describing the child's functional mobility and activity limitation across five different age bands. (Palisano et al., 1997, 2008). The classification has shown high interrater reliability and predictive validity. Children are grouped into five groups, with children in Level I and II being able to independently ambulate while children possess decreasing independence in the following three levels (Figure 4).

The age-bands are designed in a way that even with increasing age, children and youth rarely change from one level to another. Therefore, to assess changes in gross motor function over time and due to interventions, the Gross Motor Function Measure (GMFM) was developed specifically for children with CP. A set of 66 items (GMFM-66) is available measuring strength, mobility, motor coordination and balance with the categories D (standing) and E (walking, running, jumping) being the most relevant to walking (Michaelis, 2015; Russell et al., 2000). The GMFM has proven to have high inter- and intrarater reliability and is highly sensitive to change (Wang and Yang, 2006). In fact, increases in GMFM score have been strongly correlated to clinically relevant improvements evaluated by experienced clinicians (Wang and Yang, 2006).



GMFCS expanded and revised between 6th and 12th birthday: descriptors and illustrations

GMFCS level I
Children walk at home, school, outdoors and in the community. They can climb stairs without the use of a railing. Children perform gross motor skills such as running and jumping, but speed, balance and coordination are limited.

GMFCS level II
Children walk in most settings and climb stairs holding onto a railing. They may experience difficulty walking long distances and balancing on uneven terrain, inclines, in crowded areas or confined spaces. Children may walk with physical assistance, a hand-held mobility device or use wheeled mobility over long distances. Children have only minimal ability to perform gross motor skills such as running and jumping.

GMFCS level III
Children walk using a hand-held mobility device in most indoor settings. They may climb stairs holding onto a railing with supervision or assistance. Children use wheeled mobility when travelling long distances and may self-propel for shorter distances.

GMFCS level IV
Children use methods of mobility that require physical assistance or powered mobility in most settings. They may walk for short distances at home with physical assistance or use powered mobility or a body support walker when positioned. At school, outdoors and in the community children are transported in a manual wheelchair or use powered mobility.

GMFCS level V
Children are transported in a manual wheelchair in all settings. Children are limited in their ability to maintain antigravity head and trunk postures and control leg and arm movements.

Figure 4. Gross Motor Function Classification Scale (GMFCS) for the age band 6-12 years according to Palisano.

2.2 Muscle Morphology in Spastic CP

CP is a permanent disorder characterized by a lesion of the brain whose location is decisive for the expression of its manifestations. However, the lesion cannot always be determined and, even if so, may not give sufficient predictability about the exact cause or the development of motor impairments and their severity (Graham et al., 2016). Therefore, each individual’s patient history needs to be taken into account.

Spastic CP is clinically characterized by hyperresistance to passive muscle stretch. In 2017, a European consensus paper, agreed upon by experts, worked out a conceptual framework of the neuromuscular response to passive muscle stretch (van den Noort et al., 2017). Consensus was reached for separating hyperresistance into neural (i.e. related to the central nervous system) and non-neural (i.e. tissue-related, also referred to as passive stiffness) properties. The neural components were further categorized into two subgroups, distinguishing stretch hyperreflexia (i.e. velocity dependent involuntary activation, commonly called spasticity) from non-velocity dependent *involuntary background activation* (also called hypertonia).

Two potential mechanisms have been proposed for this increased stretch reflex response. The first is an increased excitability of the muscle spindles, although there is little evidence that this mechanism is prevalent in humans (Wilson et al., 1999). The more common view is that the sensory information coming from the muscle spindles is abnormally processed at the spinal cord (Trompetto et al., 2014). Furthermore, a loss or reduction in the descending inhibition of lower motoneurons contributes to an increase in stretch reflex activity at rest (Katz and Rymer, 1989; Trompetto et al., 2014). Although, spasticity is seen as one of the major issues in children with CP and therefore targeted with different treatments, the influence of spasticity on functional performance is not consistently reported (Graham et al., 2016; Lin and Brown, 2008; Ross and Engsberg, 2007). However, the loss of antagonist inhibition (i.e. ability of the central nervous system to relax the antagonist muscle) can lead to excessive co-contractions and a loss in effective strength (Graham et al., 2016). Nevertheless, a study comparing the different influences on functional performance in children with CP found little correlations between spasticity and gross motor function whereas muscle weakness was highly correlated (Ross and Engsberg, 2007). This raised the request for more activity-based compared to impairment-based treatments and interventions for children with CP (Verschuren et al., 2016).

The effect of tissue properties, in practice, is often difficult to distinguish from neural aspects like spasticity (de Gooijer-van de Groep et al., 2013). However, its differentiation from neural aspects has large implications on therapeutic approaches and is important to consider. The resistance of a structure to its passive lengthening in the absence of neural activation can be attributed to non-contractile elements like tendons, ligaments and soft tissue (van den Noort et al., 2017). However, the primary root for tissue-related increased passive resistance seems to lay in muscle properties (Lieber et al., 2017).

Drastic changes in the muscle morphology of people with CP include shorter and smaller muscles with muscle fibers of reduced diameter, as shown in Figure 5. Apparently paradoxical, sarcomeres are longer in certain muscles like the medial gastrocnemius (Kalkman et al., 2018) or soleus (Mathewson et al., 2015). Most likely, this derives from a deficiency to add sarcomeres in series as the muscle is stretched during bone growth (Lieber and Fridén, 2019). This stretches out the available sarcomeres while the muscle is hindered in growing to the desirable length which in turn imposes greater stress on the bone during growth and can lead to bony deformations and reduced range of motion (ROM) (Gage et al., 2009). The reduced diameter of muscle fibers lead to a smaller force generating area and, therewith, contributes to a loss in strength in children with CP compared to TD children.

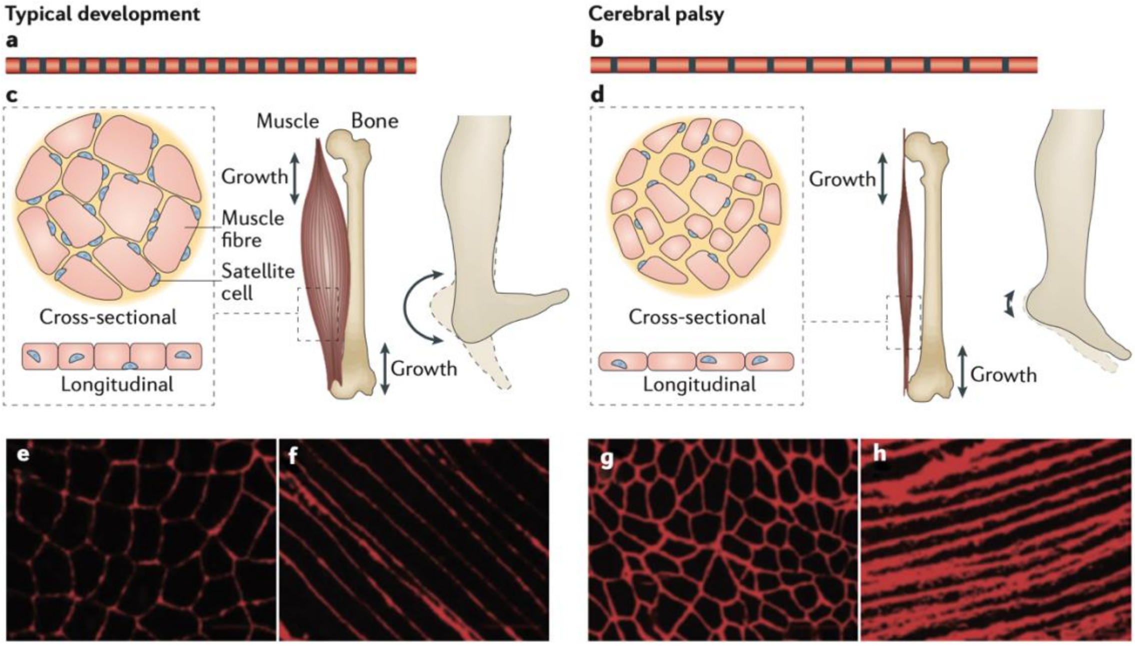


Figure 5. Difference in muscle morphology in typically developing children and children with CP. a, b: schematic muscle fibre with longer sarcomeres in CP compared to TD. c, d: schematic representation of the muscle during growth with CP children developing smaller muscles that work over a reduced ROM. e-h: example of the immunohistochemistry of muscle biopsies indicating increased amounts of extracellular matrix in CP viewed cross-sectionally (e,g) and longitudinally (f,h). Taken from Graham et al (2016)

It is difficult to determine whether the muscle in CP is inherently impaired or if changes in mechanical properties arise from altered neural control, immobilization and modified use of muscle and the surrounding tissue (Lieber et al., 2017; Nielsen et al., 2005). However, Willerslev-Olsen and colleagues (2018) found that growth of the medial gastrocnemius muscle volume was impaired in CP already with 12 months while passive stiffness increased disproportionally more than their peers only with 27 months of age. Thus, supporting the hypothesis that growth is damaged before the onset of contractures (i.e. permanent loss of ROM) and possibly contributes to the development of such. Interestingly, both groups displayed similar stretch reflexes which suggests that spasticity develops later and likely does not play an important part in the formation of contractures. Either way, changes in muscle-tendon mechanical properties and further increases in passive resistance occur gradually over the course of years limiting ROM and potentially leading to the development of contractures, bony deformations and muscle atrophy (Nielsen et al., 2005). These secondary impairments then facilitate sedentarism, forming a vicious cycle of inactivity and further loss of function. (Graham et al., 2016)

2.3 Gait in spastic CP:

CP is the most common cause for motor disability in children, nonetheless, around 70% of children with CP learn to ambulate independently or with the support of assistive devices (Gage et al., 2009, chap. 2.7). Fundamental abnormalities that inflict gait deficiencies include the loss of selective motor control, especially for biarticular and distal muscles, further, balance difficulties and abnormal muscle tone. Loss of selective motor control can lead to increased prevalence of primitive motor patterns while reductions in ROM of the lower limbs due to abnormal muscle tone can inhibit voluntary control of muscles around a joint. This in turn increases the energetic cost of walking for people with CP and lead to fatigue (van den Hecke et al., 2007). The type, location and severity of impairments caused by CP vary a lot between each individual and greatly influence interpretation of gait data and clinical implications. However, the altered musculoskeletal development of every child with CP and its influence on reaching motor milestones lead to all individuals with CP having in common some degree of gait limitation. (Gage et al., 2009, chap. 2.6).

Grouping sets of gait limitations together and grouping individuals according to these attributes naturally has its limitations but it can promote communication among professionals and with patients and their families. In addition, it can facilitate to predict the future development and needs of patients and help evaluate changes over time or due to interventions on a statistical level, hopefully making treatment more efficient in the future. An extensive review of the different gait patterns in CP with possible underlying causes and functional significances is out of the scope of this review and has been done in great detail in other sources (Chang et al., 2010; Gage et al., 2009; Nieuwenhuys et al., 2017; Perry, 1992). However, a general overview will be given in the following to understand common gait patterns in unilateral and bilateral CP.

Gait in unilateral CP. Winters, Gage and Hicks (1987) have suggested a classification system for gait impairments in individuals with spastic hemiplegia (Figure 6). It is based on kinematic patterns of the ankle, knee and hip in the sagittal plane with increasing involvement of the more proximal joints throughout the groups.

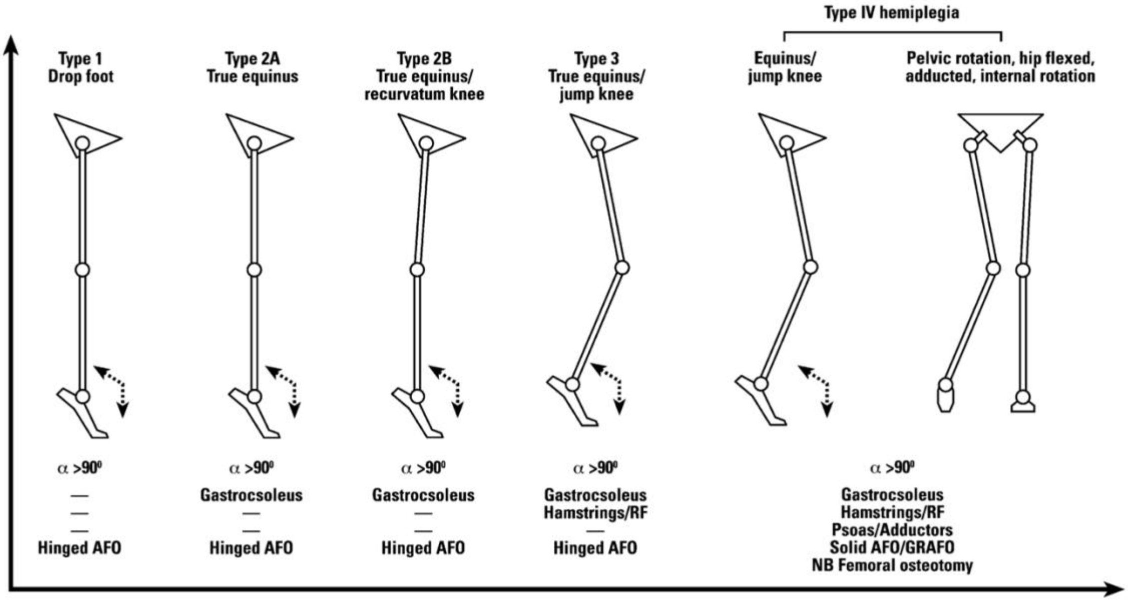


Figure 6. Classification system for gait impairments in individuals with spastic hemiplegia showing increasing proximal involvement from Type 1 to Type 4. Source: Rodda and Graham (2001).

All groups can be viewed to be on one continuum of impairments rather than separate types with clear boundaries (Armand et al., 2016). Drop Foot is very common in CP and refers to excessive ankle plantarflexion during the swing phase often due to weakness of the tibialis anterior muscle and/or high coactivation of the plantarflexors. If dorsiflexion ROM is close to normal during stance, it can be assumed that this inability to dorsiflex the ankle during swing derives from muscle weakness, a lack of selective motor control and/or passive stiffness of the plantarflexor musculature. Drop foot is oftentimes compensated by increased hip and knee flexion during swing and accompanied by a loss of the first heel rocker at initial ground contact due to contact with the toes first instead of the heel. If drop foot during swing is followed by restricted dorsiflexion during stance, it is denominated equinus gait. This is also very commonly seen in children with CP and is usually related to spasticity or a fixed contracture of the plantarflexors. Nevertheless, underlying causes can vary and physical examinations give further insight into this. Thus, toe gait can also be a compensatory mechanism to reduce the external moment arm of the GRF and therewith minimize the internal strain on the Achilles tendon (Kalkman et al., 2020), or present impaired motor learning abilities of children with CP (Lorentzen et al., 2019). Feedforward processes during toe walking show increased co-contraction that usually disappear with age in voluntary toe-walking but can persist in children with CP (Lorentzen et al., 2019). Equinus during stance can lead to an over-active plantarflexion knee extension couple which can favour the extended knee going into recurvatum. However, to compensate for the functional lengthening of the leg during equinus, the knee often displays increased flexion which can be succeeded by a contracture of the hamstrings fixing the knee in a flexed position over time. (Perry, 1992, chap. 4)

Generally, a high asymmetry due to the hemiplegic nature of the impairment can be noted. Treatment will always have to consider impairments of the proximal joints first as more distal treatment will otherwise have little effect. This model has shown high stability and reliability to the identification of gait limitations (Sangeux and Armand, 2015).

Gait in bilateral CP. Based on Sutherland and Davids' (1993) classification of sagittal knee patterns of spastic diplegia, Rodda and Graham (2001) developed a classification for overall sagittal plane gait patterns in children and adults with spastic diplegia (Figure 7). Diplegia is generally more complex as the involvement of sides is typically not symmetrical and every classification of gait makes use of simplifications to allow for easier access and communication. Thus, this one is no exception. However, it has also proven to be of high value for the process of identifying gait impairments in children with spastic CP (Rodda et al., 2004).

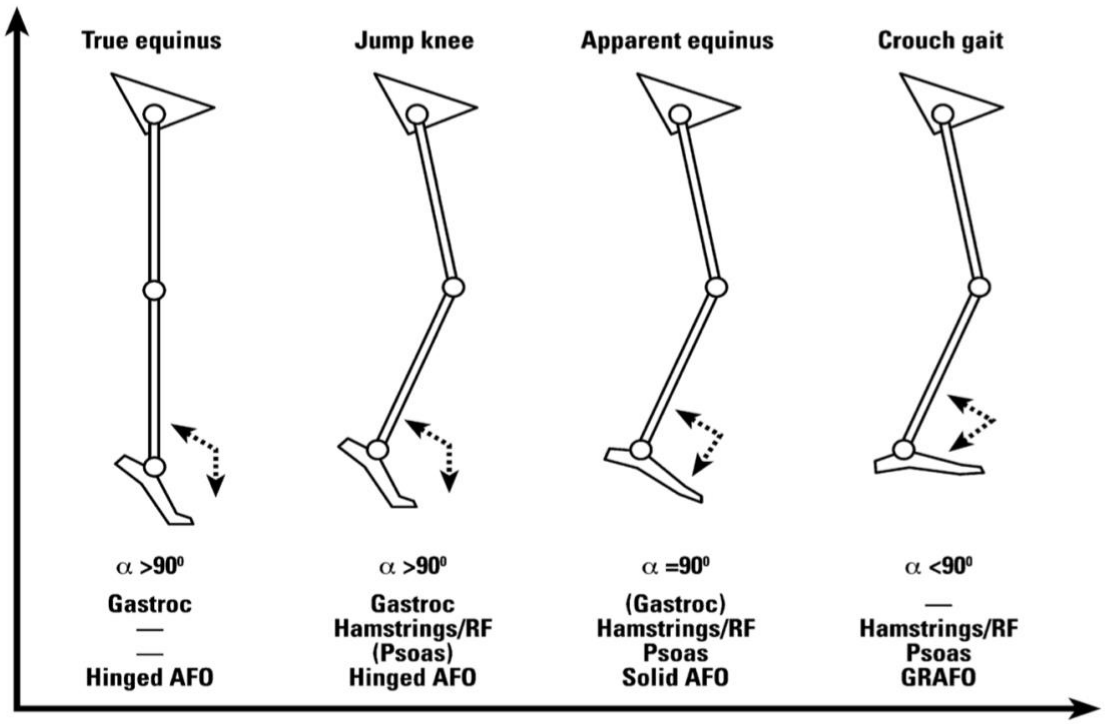


Figure 7. Classification system for gait impairments in individuals with spastic diplegia. Group I to Group IV displays the transition from equinus foot to excessive dorsiflexion. Taken from Rodda and Graham (2001).

The groups are ordered in a progression from increased plantarflexion to excessive dorsiflexion, starting with true equinus. The authors note that true equinus in early stages can be disguised by knee hyperextension. However, true equinus rarely continues when the child grows older as the plantarflexors weaken and cannot withhold the increased forces applied by increasing body weight during growth unless a fixed contracture forms at the ankle (Chang et al., 2010). Treatment with muscle relaxants like botulinum neurotoxin type A (BoNT-A) and the use of orthosis can be enough to prevent maladaptations to the gait pattern without weakening the muscle substantially which can cause problems later in life (Chang et al., 2010). Group II (Jump Gait) combines true equinus with increased knee and hip flexion. A pelvic anterior tilt and lumbar lordosis can often be seen as well as a reduced ROM of the knee during swing. Group III (Apparent Equinus) occurs frequently when the child grows older and the weakening plantarflexors cannot remain in equinus. Equinus decreases while knee and hip flexion increase placing an increasing demand on the plantarflexors. Instrumented gait analysis can be vital to distinguish true from apparent equinus especially in a phase where toe-gait is still apparent but kinematic analysis reveals a near normal functional dorsiflexion ROM. Anti-spasticity treatment weakening the plantarflexors or Achilles tendon lengthening in this phase can do great harm to the walking function of the patient and might lead to crouch gait (Sutherland and Cooper, 1978). Crouch gait, is defined by increased knee and hip flexion combined with excessive ankle dorsiflexion and is connected to increasing deterioration of walking ability (Galey et al., 2017; Rodda and Graham, 2001). Once developed, a rapid decrease in function with increases in knee pain and patellar deformities are the natural progression of symptoms in crouch gait. Complex treatment including bony surgery is often needed to improve and preserve walking function. Additionally, Rodda et al (2004) classified another group of individuals with spastic diplegia as *mild pattern* consisting of individuals whose gait deviations were inside the one standard deviation band of typically developed gait and therefore showed no statistical difference to their peers in the sagittal plane.

3. Improving walking function in Cerebral Palsy

Since there is no cure for CP as of today, therapy plays a vital role in basically all patients diagnosed with CP especially early in childhood until early adolescence (Damiano et al., 2009). The natural history of the condition includes distorted musculoskeletal growth including the development of contractures and bony deformations which, if untreated, lead to lever-arm dysfunction and altered muscular functioning which can result in dislocations of joints and interfere with the ability to ambulate. This can affect participation in daily life activities and lead to a reduced quality of life (Shikako-Thomas et al., 2012). Furthermore, secondary clinical symptoms in patients with CP can worsen over time increasing barriers for an active lifestyle and creating a cycle of inactivity and further loss of function. Therefore, therapeutic interventions play a crucial role to reduce secondary impairments, maintain function and enable independent mobility for people with CP. Therefore, all children with CP depend on some form of clinical and physical therapy after their diagnosis.

In the past, the focus of treatment interventions has been mostly on tackling motor impairments like spasticity and contractures assuming that these corrections would automatically translate into functional improvements. In recent years, however, it has been acknowledged that the relationship between motor impairments and function is not as strong and especially not as linear as assumed in many cases (Abel et al., 2003; Ross and Engsberg, 2007; Sahrmann and Norton, 1977). The world health organization's classification of functioning, disability and health has helped to shift the focus towards functional improvement, participation and quality of life. Motor impairments are still being addressed of course but with a stronger attention for physical therapy, environmental factors and addressing fitness and lifestyle of patients (Verschuren et al., 2016).

Depending on the individual combination of impairments, age and severity of symptoms a personalized therapeutic strategy is developed. Typical treatments include the reduction of spasticity with BoNT-A, tendon lengthening to reduce contractures, osteotomies to correct malformed bones and physical therapy to improve motor control and secondary impairments like muscular weakness (Graham et al., 2016). The heterogeneity of CP complicates treatment selection (Damiano et al., 2009) but clinical gait analysis, functional assessments scales, patient questionnaires and energy cost analysis have made evaluation of outcome more measurable and helped improved treatment (Gage and Novacheck, 2001).

A discussion of treatment options for improving gait in children with Cerebral Palsy has been done extensively in other literature (Damiano et al., 2009; Gage et al., 2009). In the next section, an overview over the most important and common treatments and a detailed review of the current knowledge about physical training interventions to improve gait in children and adolescence with CP is presented.

3.1 Medical Treatments

Limited ROM in lower limb joints affect walking ability greatly. One origin of functionally limited ROM can be spasticity (Rodda and Graham 2001). To reduce spasticity, treatment often consists of BoNT-A injections into the spastic muscle, whereas oral or intrathecal baclofen as well as selective dorsal rhizotomy treat more generalized spasticity (i.e. affecting many muscles; (Brandenburg et al., 2019). BoNT-A directly affects the presynaptic release of the neurotransmitter acetylcholine to effectively prevent muscular activation and is routinely used in young children to reduce the influence of spastic muscles on musculoskeletal growth, delay need for surgery and improve walking function by reducing muscle tone (Multani et al., 2019; Tedroff et al., 2009). However, the loss of muscle function, even if considered reversible, can lead to atrophy and fatty infiltration of the treated muscle (Multani et al., 2019). The long-term effect of denervation and the concomitant atrophy are not yet fully understood and might play a central role in the development of contractures (Armand et al., 2016; Gough et al., 2005; Gough and Shortland, 2012). Selective dorsal rhizotomy is, in contrast to BoNT-A, non-reversible and consists of the sectioning of spastic rootlets of the dorsal sacral roots and leads to a permanent interruption of the signalling pathways. Good care has to be taken when selecting patients for this treatment as functional improvements depend largely on the type of muscle tone abnormality (Damiano et al., 2009). Spasticity is believed to be a contributor to the development of contractures which in turn produce large functional complications concerning gait. However, spasticity does not seem to be the only factor. Over a 10-year period Tedroff and colleagues (2011) found a decline in function and the occurrence of contractures in a group of 19 children with CP despite the absence of spasticity. The paradigm shift towards more focus on functional improvement has increased the debate whether targeted resistance training for weaker muscles can restore muscular balance in a more sustainable manner than weakening dominant and stronger muscles with therapeutic interventions like BoNT-A (Damiano et al., 2009; Fonseca Jr. et al., 2018; Graham et al., 2016). Further, the positive effects of BoNT-A seem to be greater and last longer when combined with physiotherapy (Fonseca Jr. et al., 2018).

Despite good medical care and intensive physiotherapy, many children with CP will sooner or later have to undergo surgery due to fixed contractures, spasticity, bony deformities or joint dislocations or subluxations. There are four general categories for orthopedic surgery for children with CP: 1) musculotendinous or tendon lengthening, 2) tendon transfers, 3) osteotomies and 4) arthrodesis (Damiano et al., 2009). The most common orthopedic surgery for improving gait in children with CP is the lengthening of the gastrocnemius-soleus complex to reduce equinus gait. Gastrocnemius contracture is the common indicator for this approach. Clinical gait analysis is crucial to guide this treatment and to prevent falsely mistaking apparent equinus for true equinus as weakening of the triceps surae will then most likely lead to crouch gait (Armand et al., 2016). Tendon transfers can be used to release the influence of rectus femoris on stiff knee gait and increase ROM especially during swing phase (Armand et al., 2016). Osteotomies refer to correcting rotational abnormalities or shortened bones. The effects are usually long-term and surgery does not need to be repeated. Osteotomies can help treating lever-arm dysfunction like femoral internal torsion and tibial external torsion with foot deformities leading to an ineffective plantarflexion knee extension couple combined with a less rigid foot that is transmitting forces less well. Osteotomy can be very effective and predictable if underlying causes are determined correctly (Gage and Novacheck, 2001).

3.2 Physical Training Interventions

Since CP is a motor disorder, physical therapy is the backbone of all therapies for individuals with CP, usually starting already during infancy and potentially supporting the patient throughout the entire life-span. It offers an unique way for the patient to become active and participate in his or her own well-being and has demonstrated to increase the benefit of other therapies when done in conjunction (Fonseca Jr. et al., 2018). Physical therapy aims to reduce physical impairments and assists the patient with achieving participation needs by increasing strength, aerobic conditioning and enhancing lower limb coordination. Especially, since loss of function begins much earlier in life in individuals with CP compared to their TD peers, it is crucial to build a high strength reserve and delay loss of motor abilities (Gage et al., 2009).

A wide variety of interventions and therapy approaches are used to treat symptoms related to impaired walking ability in patients with CP, some showing greater effects than others (Moreau et al., 2016). As functional tasks require complex interaction of muscular strength, flexibility and motor coordination, isolated strength training interventions have often failed to lead to functional improvements in tasks like gait even despite improvements in strength. Additionally, the benefits of muscle stretching interventions on ROM is highly controversial (Moreau et al., 2016; Verschuren et al., 2011). Furthermore, activity guidelines have been published for children in general and children with CP in particular to help setting appropriate training stimuli (Faigenbaum et al., 2009; Verschuren et al., 2016).

The following section will closely depict the effects of flexibility, strength and gait training interventions on walking in children with CP.

3.2.1 Flexibility Training

As discussed in earlier chapters, muscle growth is impaired in CP resulting in shorter and stiffer muscles (Graham et al., 2016; Smith et al., 2011). This can lead to greatly smaller ROM and decreased mobility which effectively hinders normal gait patterns. The aim of stretch interventions in children with CP commonly is to improve and maintain ROM and reduce joint passive stiffness to delay or prevent the development of contractures and to improve walking function.

Stretch of muscles in CP is commonly applied via (1) passive-static stretching by a physiotherapist or equipment, (2) with ankle foot orthosis or (3) serial casting. Orthosis impose mechanical constraints to the ankle and foot creating a sustained stretch, while serial casting takes this one step further and immobilizes the joint imposing increasing stretch on a joint (Kalkman et al., 2020). However, both also constraint some or any active motion around the joint and inactivity has been connected with the development of contractures which paradoxically is defined as permanently reduced ROM (Gough and Shortland, 2012).

The effectiveness of traditional stretching has been controversially discussed in the literature since there is only weak level of evidence for it increasing ROM and reducing stiffness in muscles in CP (Eldridge and Lavin, 2016). Elongation of the muscle-tendon unit generally can come from a stretch of the tendon, the muscle belly or the muscle fascicles. Kalkman hypothesized that stiffer muscles in CP result in relatively more compliant tendons possibly taking up more of the stretch (Kalkman et al., 2019). Building upon this, Kalkman et al (2019) evaluated the combination of strength training, increasing tendon stiffness, with passive stretching of the triceps surae in a small group of children with CP. The aim was to increase mechanical stretch stimulus on the muscle belly. The experimental group performed four weeks of standing unilateral heel-raises followed by six weeks of unilateral heel raises combined with passive stretching of the calf muscles (four sessions per week) while the control group underwent the same amount of training time but performed seated biceps curls instead of heel raises. Results indicated an increased resting fascicle length in the experimental group while the control group showed no change in resting fascicle length. These results are promising, trying to more precisely and efficiently target stretch interventions in people with CP.

However, muscle morphology is fundamentally different and sarcomerogenesis is impaired in spastic CP muscles. Thus, it is unclear if mechanical stress, even if applied to the muscle, can achieve sufficient adaptability. A study by Matthiasdottir and colleagues (2014) measured fascicle excursion in the gastrocnemius muscle in children with CP compared to TD children when passively moving into dorsiflexion. The study found that in CP shorter fascicles operated through a similar absolute excursion than in the control group leading to an increased relative fascicle excursion. This suggests that muscles in CP work more on the descending side of the force-length curve with sarcomeres being stretched out. Therefore, it is important to evaluate if interventions can also increase strength over the available ROM.

Considering this, there is insufficient evidence that passive stretch interventions have a positive effect on functional outcome measures like gait kinematics or GMFM in CP (Craig et al., 2016).

3.2.2 Strength Training

Lower limb strength has been shown to be moderately to strongly related to self-selected walking speed and GMFM score (Damiano and Abel, 1998; Kramer and Ann MacPhail, 1994) with 50% of the variance in walking speed explained by weakness of the lower limb musculature (Damiano and Abel, 1998).

However, strength training has been subject of controversial discussions regarding the treatment management of CP (Damiano et al., 2002). Although it is commonly acknowledged that weakness is a substantial aspect of children and adults with CP and that even mildly affected individuals display reduced strength especially in distal muscles (Wiley and Damiano, 1998), the consequences of this fact are not as clear. The reasoning against using resistance training in children with CP has ranged from its being ineffective in improving strength and function to its exacerbating spasticity (Damiano et al., 2002; Scianni et al., 2009). Especially the latter has not scientifically been proven up to today and is commonly accepted as to not be true (Scholtes et al., 2010). The former argument seems to present more difficulty to address. Many studies have been conducted so far examining the effect of different strength training protocols on various aspects of muscle strength and functional parameters like walking capacity and quality with varying results (Andersson et al., 2003; Damiano et al., 2010; Gillett et al., 2019; Scianni et al., 2009). Thus, Verschuren et al (2011) examined the quality of present randomized controlled trials assessing the effect of strength training on individuals with CP. The study found deficiencies in intensity and type of exercises as well as the duration of training interventions when compared with recommendations of the National Strength and Conditioning Association (Faigenbaum et al., 2009). Most exercises worked with bilateral exercises only, which may be too complex at the start leading to ineffective loading of the target muscle with the appearance of compensatory movements. Furthermore, functional tasks require complex interactions of strength, flexibility and motor coordination which isolated strength exercises might fail to address if used without additional training tasks. Due to the lack of strength training guidelines specific to individuals with CP, Verschuren and colleagues published according recommendations in 2016 which are largely consistent with the recommendations by the National Strength and Conditioning Association for typically developed children (Faigenbaum et al., 2009; Verschuren et al., 2016). A training volume of 2-4 sessions per week for 12-16 weeks was recommended with 1-3 sets per exercise and 6-15 repetitions at 50-85% of the 1-repetition maximum. Additionally, progressive increase in complexity of the exercises, starting with isolated single-joint exercises was advised (Verschuren et al., 2016). In the future, investigations with adequate exercise protocols following these recommendations and a combination of strength training with functional walking training on the effect of gait, activity capacity and participation in CP are needed which is one goal of the current study.

3.2.3 Gait Training

Gait and walking speed are indicators of functional abilities and quality of life across different populations and walking speed has therefore also been called the sixth vital sign (Middleton et al., 2015). Training walking ability via gait training incorporates the motor learning principles of repetition and task-specificity (Winstein et al., 2014). Generally, the central nervous system displays high levels of adaptability especially in younger years (Winstein et al., 2014). However, the underlying brain lesion in CP might lead to an impaired neural plasticity, reducing the capacity to adapt or newly learn motor patterns (Ismail et al., 2017; Wittenberg, 2009). Nonetheless, studies have shown that people with CP are certainly able to enhance performance and display motor learning capabilities (Booth et al., 2018; Novak et al., 2013; van Gelder et al., 2017). Yet, more repetition might be necessary create automated and long lasting changes in movement patterns than in healthy individuals (Kleim and Jones, 2008).

In CP, selective motor impairment has been reported to increase from proximal to distal (Fowler et al., 2010). Accordingly, one very common factor in CP is the inability to dorsiflex the ankle joint during stance phase (i.e. toe-walking) and in late swing phase (i.e. toe drop) of gait (Fowler et al., 2010; Willerslev-Olsen et al., 2014) interfering with the biomechanics of the entire gait cycle.

A wide variety of interventions and therapy approaches are used to treat symptoms related to impaired walking ability in patients with CP, some showing greater effects than others (Moreau et al., 2016). Specificity of training and repetition are key elements for improving movement patterns and motor learning (Winstein et al., 2014). On this account, reviews concluded that gait training is safe, feasible and effective in improving walking ability in children and young adults with CP and more effective than traditional physical therapy (Booth et al., 2019) or than strength training alone (Moreau et al., 2016).

Insufficient dorsiflexion during gait may be increased by different factors. Firstly, an early plantarflexor pre-activation before ground contact during gait can occur (Willerslev-Olsen et al., 2014). Secondly, data suggests that there is a reduced central drive to the ankle dorsiflexors in children with CP, resulting in weakened dorsiflexor muscles (Willerslev-Olsen et al., 2015). Additionally, the elastic components of the muscles and connective tissue are altered in children with CP (Willerslev-Olsen et al., 2013). Therefore, early therapy aiming to strengthen ankle dorsiflexors and reduce ankle joint stiffness to increase appropriate heal strike is important to work against decreasing range and velocity of motion and to enable a more normal motor pattern. Furthermore, Geertsen and colleagues (2015) found an inverse association of passive ankle joint stiffness with toe lift during gait implying a relationship to impaired gait parameters.

In particular, inclined treadmill training seems to be especially effective in improving walking ability and dorsiflexor strength in people with CP (Lorentzen et al., 2017; Willerslev-Olsen et al., 2014). During uphill walking, the person is forced to dorsiflex the ankle in swing to allow foot clearance and prevent tripping. EMG activity of the tibialis anterior muscle was higher during inclined walking compared to level walking (Willerslev-Olsen et al 2014). Furthermore, due to the incline, the ankle joint undergoes a greater passive dynamic stretch during the stance phase than during over-ground walking. Willerslev-Olsen and colleagues (2014) assessed the effects of inclined treadmill walking on children with CP participating in 30 minutes of inclined treadmill walking at home every day for four weeks. The results demonstrated an increase in toe lift and heel strike. Additionally, ankle joint stiffness was significantly reduced after the four-week intervention in those subjects with previously elevated stiffness compared to the TD controls. The changes in ankle joint passive stiffness were stable over the one-month follow-up period. The same training protocol followed for six weeks in adults with CP resulted in decreased ankle joint stiffness. Simultaneously, the toe lift during swing phase increased in the intervention group from pre to post as well as the maximum gait speed. However, the 6-minute walking test did not improve. Also no changes in passive ankle joint mobility were reported which implies that despite some adaptability of the muscle-tendon unit, the short duration of the intervention might have been insufficient. (Lorentzen et al., 2017)

Willerslev-Olsen et al (2015) demonstrated changes in the intramuscular coherence of the tibialis anterior during level walking after the above mentioned training intervention in children with CP. Walking uphill is associated with higher toe-lift which is partly achieved by a higher activation of the tibialis anterior muscle. The coherence analysis suggests an increased central drive to the tibialis anterior motor units during the gait cycle (Willerslev-Olsen et al., 2015).

While these are very promising results, gait training for 30 minutes everyday may not be feasible for a long-term implementation into most daily routines of children with CP, especially considering other hobbies and time-consuming therapy going along with it. Furthermore, for how long the improvements last after cessation of the intervention is not clear yet. Therefore, developing an intervention program that achieves functional gait improvements while being more applicable for daily life is desirable.

4. Purpose:

The main objective of this thesis was to study the effects of a three month long tailored strength, flexibility and gait training intervention on gait performance in children and young adults with spastic CP. As there is currently no cure for CP, physical rehabilitation programs are crucial for people with CP to maintain ambulatory function for as long as possible to facilitate participation and increase quality of life. Although, many studies have investigated the effects of various training approaches, results remain inconclusive whether gait performance and gait quality can be improved efficiently partly due to limitations in the intervention designs of previous studies. The current project developed an evidence-based exercise therapy intervention based on the physical activity recommendations for children with CP by Verschuren et al (2016) and promising results related to benefits of inclined treadmill walking on ankle joint morphology (Lorentzen et al., 2017; Willerslev-Olsen et al., 2014). Thus, the current study offers a tremendous opportunity to evaluate lower limb gait kinematic and kinetic adaptations after such an intervention in a CP population of children and adolescents in Finland.

The main research question and subsequent hypothesis for this thesis were:

1. **Can the EXECP training intervention improve gait quality of children and adolescents with CP?**
    a.) The stretching of the triceps surae muscle during inclined walking and the strengthening of the ankle plantarflexors and dorsiflexors during strength and gait training will increase passive ankle ROM during stance and active ankle ROM during swing concomitant with larger mean and peak dorsiflexion angle during swing.
    b.) This will facilitate prepositioning of the foot in terminal swing and increase dorsiflexion angle at ground contact.
    c.) The incline of the non-motorized treadmill will increase the demands on ankle push-off and hip extension power and therewith lead to an increase in peak ankle and hip power.
    d.) Participants with CP with increased knee and hip flexion during stance will progress towards values of their TD peers.

2. **Can the EXECP training intervention positively affect overall functional gait performance?**
   a.) Participants with CP will improve their walking distance over the course of the intervention and achieve a higher score in the GMFM category D (standing) and E (walking, running, jumping).

Secondary research question and subsequent hypothesis of the thesis are:

3. **Will measured parameters differ at a group level between CP and TD?**
   a.) CP participants will walk with reduced ROM in the ankle, knee and hip joint compared to TD.
   b.) Participants with CP will walk with decreased dorsiflexion during swing compared to TD.
   c.) Participants with CP will achieve a shorter walking distance in the 6MWT compared to TD.

4. **Will there be a clinically relevant difference in measured parameters in the control period in the CP group?**
   a.) There will be no clinically relevant change between Pre1 and Pre2 in CP.
   b.) Changes of the intervention will be retained over the following 3 months or reduce but not below the initial level from before the intervention.

   Due to small variations from manual placement of the markers and skin movement, only changes above 5° in gait kinematics are viewed as clinically relevant (Perry, 1992, chap. 4).

5. Methods

5.1. Participants

19 participants with spastic CP were included in the study. All participants and legal guardians for participants below the age of 18 provided their written informed consent prior to commencing the study and acknowledged that they participated voluntarily and could withdraw from the study at any point. Ethical approval was given by the ethics committee of the Central Finland Healthcare District (U8/2017) and the study is preregistered in the International Standard Randomization Controlled Trial (ISRC TN69044459).

Two participants did not finish the intervention (1x personal reasons, 1x health problems unrelated to the intervention). Therefore, 17 participants were included in the analysis (age: 14±4 [range 9-22] years) with 5 bilaterally and 13 unilaterally involved (GMFCS I/III: 15/3). Detailed characteristics can be found in Table 1. However, five participants had to be excluded during the analysis of the 3D gait analysis due to missing or invalid data of either the Pre2 or Post1 measurements. Of the remaining 12 participants, 8 were unilaterally and 4 bilaterally affected (GMFCS I/III: 10/2). Due to interruptions of the measurements during the Corona pandemic, only 7 of these 12 participants finished the Post2 measurements. A diagram of the participant recruitment can be found in Figure 8. All participants were recruited in the city of Jyväskylä and neighbouring cities as part of a larger research project, the EXECP research project (Valadão et al. 2021). All participants answered a screening questionnaire to check for compliance with the inclusion criteria. Participants of either gender were eligible to participate in the intervention if they had a confirmed diagnosis of spastic CP (hemiplegia or diplegia, GMFCS I-III, *Palisano et al. 1997*). Exclusion criteria were a) lower limb surgery and/or pharmacological treatments in the past six months, b) selective dorsal rhizotomy, c) serial casting of the lower limbs or d) participation in a guided strength training program for the lower limbs in the past six months. All participants were able to understand and comply with basic instructions and were able to stand with both heels touching the ground. As a control group, 17 age and sex-matched individuals were recruited for the study.

Table 1. Participant Characteristics

Subject	Gender	Age [y]	Height [cm]	Weight [kg]	Hemisphere	GMFCS	Walking Aid
1	m	15	162	59	B	III	Yes
2	m	21	179	72	U	I	No
3	m	22	168	45	B	III	No
4	m	16	164	48	B	I	No
5	f	15	165	62	U	I	No
6	m	10	152	39	U	I	No
7*	m	14	180	71	U	I	No
8º	m	14	171	49	U	I	No
9º	m	9	142	29	U	I	No
10*	f	13	170	81	U	I	No
11º	f	12	159	46	U	I	No
12	m	10	148	38	B	I	No
13*	m	13	144	35	U	I	No
14*	f	22	169	60	U	I	No
15º	f	19	168	76	U	I	No
16º	m	10	140	38	U	I	No
17*º	m	10	143	37	B	III	Yes

*, gait analysis data was excluded; º, without Post2 test, m=male, f=female

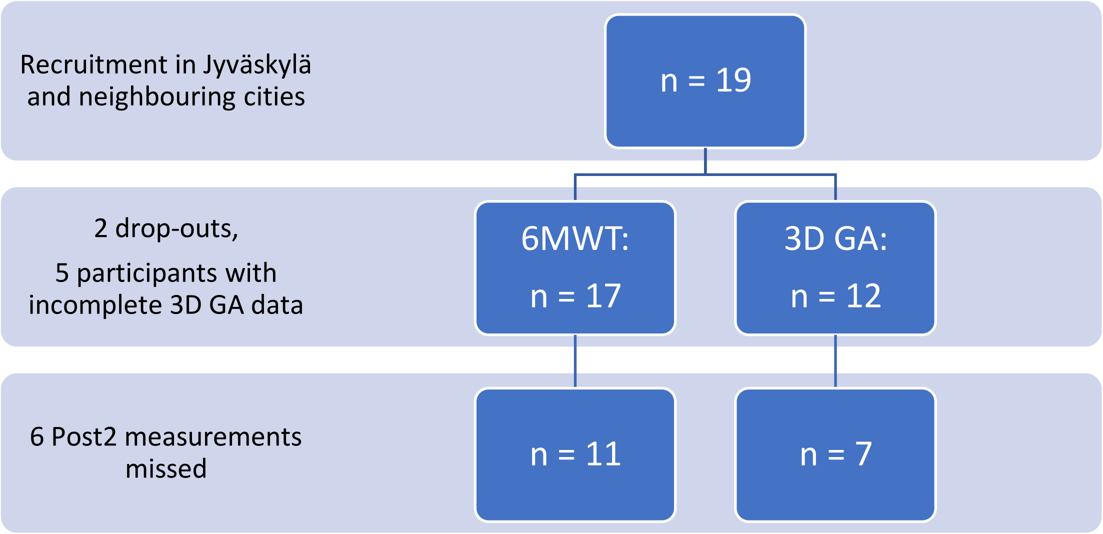


Figure 8. Flowchart of CP participant recruitment and drop-out.

5.2. Study Design

The study followed a non-concurrent multiple-baseline design with four measurement time points (Graham et al. 2012). Two pre-tests separated by three months (control period) were followed by a three-month long guided training intervention and an immediate post-test as well as a follow-up test after additional three months (retention period). In total, CP participants were enrolled in the study for a period of nine months. The control group was measured once without participation in the training intervention. Each period was initiated by a 3D marker-based gait analysis of the lower limbs and a 6-MWT. Figure 9 visualises the measurement timepoints of the study.

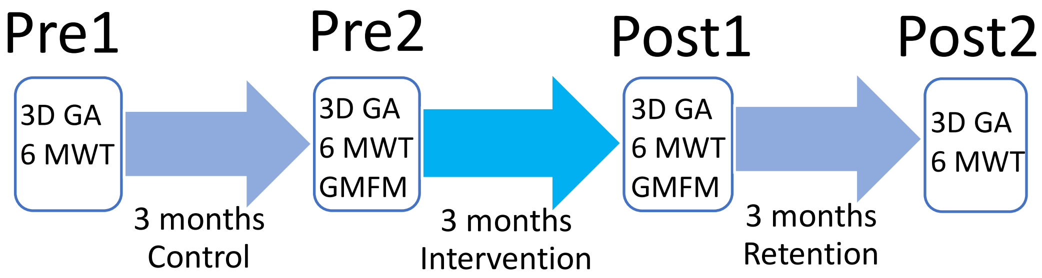


Figure 9. Measurement timepoints for each CP participants in the course of the study.3 dimensional gait analysis (3D GA) and a six minutes walking test (6MWT) were performed during all sessions. Gross Motor Function Measure (GMFM) was only assessed directly prior to and post of the training intervention.

5.3. Intervention protocol

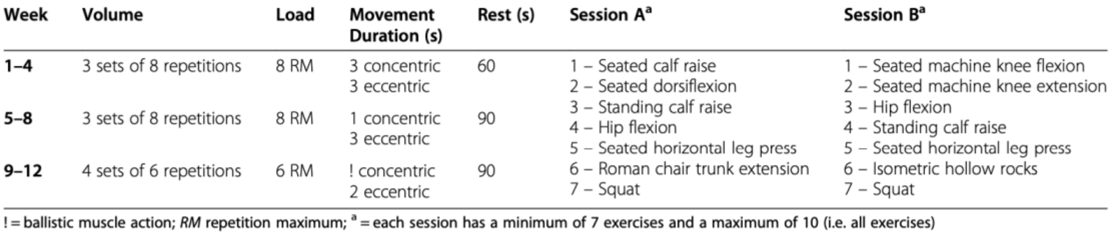
Each participant in the CP group underwent an intervention period of twelve weeks with 2-3 training session á 90 minutes per week interspaced by a minimum of 48 hours. Physically active participants trained 2-3 times per week while sedentary participants trained three times per week. A minimum of 25 sessions was achieved for every participant.

To ensure optimal execution of the training protocol, each participant was individually guided by a coach or physiotherapist with detailed knowledge of the intervention. The structure of each session included 5-10 minutes of walking on an inclined treadmill, 60-75 minutes of strength training and 10-20 minutes of flexibility training.

Gait Training. Each participant received a non-motorized treadmill with a 6° or 7.3° incline (Vida XL, Venlo, Netherlands) to take home together with the instruction to walk on it for 10 minutes every day. Additionally, during each training session the participant walked with a comfortable walking speed on the treadmill for 5-10 minutes as warm-up and cool-down. Verbal encouragement was given throughout to guide the attention towards a best possible heel strike. A non-motorized treadmill was chosen to increase hip-extension and ankle plantarflexion power necessary to create belt movement and thereby train and improve the appropriate timing of these muscles' activation patterns during gait. The incline of the treadmill was chosen to instigate increased need for toe clearance during walking.

Strength Training. Strength training represented the largest block during each intervention session with 60 to 75 minutes. Free weights and weight stack machines were used to include guided as well as free motion exercises and allow for individual adjustment and progression of loading in each session. The protocol and the specific exercises are in accordance with the strength and conditioning guidelines for youth resistance training by the National Strength and Conditioning Association (Faigenbaum et al 2009) and the recommendations by Verschuren et al (2011) for physical activity in children and adolescents with CP.

Ten different exercises were chosen for the lower limbs and trunk of which half were single-joint and the other half multi-joint exercises. Single-joint exercises for better targeting of specific, especially weak, muscles and control of compensatory movements while multi-joint exercises are recommended for a combination of strength and motor control improvements (Verschuren et al 2011). A detailed description of all exercises used can be found in Valadão et al. (2021). The pattern of progression and an example training session plan can be found in Figure 10. Two exercise protocols were created by the coach in conjunction with the wishes and needs of the participant with 7-10 exercises each and performed alternatingly. Weight progression and exact execution of each exercise was individualized to the abilities and limitations of each participant.



Week	**Volume**	**Load**	**Movement Duration (s)**	**Rest (s)**	**Session A**[a]	**Session B**[a]
1–4	3 sets of 8 repetitions	8 RM	3 concentric 3 eccentric	60	1 – Seated calf raise 2 – Seated dorsiflexion 3 – Standing calf raise 4 – Hip flexion 5 – Seated horizontal leg press 6 – Roman chair trunk extension 7 – Squat	1 – Seated machine knee flexion 2 – Seated machine knee extension 3 – Hip flexion 4 – Standing calf raise 5 – Seated horizontal leg press 6 – Isometric hollow rocks 7 – Squat
5–8	3 sets of 8 repetitions	8 RM	1 concentric 3 eccentric	90		
9–12	4 sets of 6 repetitions	6 RM	! concentric 2 eccentric	90		

! = ballistic muscle action; *RM* repetition maximum; [a] = each session has a minimum of 7 exercises and a maximum of 10 (i.e. all exercises)

Figure 10. Pattern of progression of strength training and an exemplary set up of two alternating training sessions. Taken from Valadão et al. (2021).

Flexibility Training. The Flexibility session was performed on muscle groups that indicated shortening during the initial flexibility measurement and, thus, was individualized to every participant. The stretching was carried out passively in four sets of 45 seconds at the pain threshold. Stretched muscle groups included the one- and two-joint hip flexors muscles (e.g. iliopsoas, rectus femoris), hip adductors and hamstrings. The study refrained from stretching the triceps surae complex to not further increase the duration of the training session. Furthermore, the warm-up on the inclined treadmill already forced a dynamic, passive stretching of the triceps surae during walking.

5.4. Testing protocol

The EXECP research project analysed additional variables such as corticospinal excitability, cortical processing of proprioceptive stimuli and daily physical activity levels to create a neuromechanical and metabolic profile of children and adolescents with CP. For a detailed description of all measurements taken during the project please refer to Valadão et al (2021).

At each timepoint, measurements concerning this thesis were collected in a single session. After preparing the participant for the 3D gait analysis, the participant walked for six minutes along a walkway with break intervals as needed. Removing all equipment and giving the participant 15 minutes of rest, the 6MWT was performed subsequently.

Gait Analysis measurement. For measuring overground walking kinematics and kinetics, a marker-based 3D motion capturing system with 8 cameras (MXT40) and a sampling frequency of 200 frames/second was used (Vicon Motion System, Oxford, UK). The participant walked along a 7,41m x 0,6m indoor walking path that was marked on the floor of the laboratory for 6x1 minute. The participant was allowed to request a break whenever needed to prevent a change in walking kinematics due to fatigue, however, walking was always measured for a total of six minutes. In the middle of the walkway, two force plates were mounted into the floor simultaneously collecting data at 1000 Hz sampling frequency (51x46cm, AMTI OR6-6-2000, AMTI Inc., Watertown, USA). Via an Amplifier (AMTI MiniAmp MSA-6, AMTI Inc., Watertown, USA) and Analog-to-Digital converter the force plates were synchronized to the motion capturing unit (MX Giganet). Three to six clean foot strikes on the force plates were obtained for later analysis in a *maximally fast but controlled walking speed*. Due to time constraints, only the more affected leg (based on flexibility and strength measures) was investigated. All participants walked without walking aids or orthosis during the gait analysis.

Preparing the participant, 24 retroreflective markers (diameter: 13mm) were attached to the lower limbs. Of these, 16 markers were placed according to Vicon's Plug-In Gait Model which was used for calculating direct kinematics with Vicon Nexus 2.5 (Kadaba 1989, Davis 1991, Kainz et al 2017). The remaining markers were not used in this analysis. The Plug-In Gait model is an implementation of the conventional gait model and based on the Newington-Helen Hayes model to calculate joint motion of the lower extremities (Plug-In Gait reference guide, Kadaba 1990). Joint kinetics were calculated employing inverse dynamics using Vicon Nexus 2.5.

6MWT. The 6MWT has shown to be a reproducible measure of functional capacity in children with CP with functional mobility score being closely correlated to the distance walked in the 6MWT (r=0.68, p=0.001) (Silva et al 2016).

Following the motion analysis, all equipment was taken off the participant and the participant was able to rest for 15 minutes before starting the 6MWT. For the test, the participant walked along a 30m long indoor rubber track, encouraged to walk as fast as possible for the whole of the six minutes. The whole testing session lasted 90-120 minutes in general.

GMFM. The Gross Motor Function Measure (GMFM-66) is an interval scale providing valid and reliable insight into the motor development of children with CP with a good responsiveness to changes in gross motor function (Russel et al. 2000). The GMFM was measured in two categories: D, measuring Standing, and E, assessing Walking, Running and Jumping. GMFM was only ascertained for the CP group and only at Pre2 and Post1.

5.5. Data Analysis

For kinematics, mean, peak and ROM of dorsiflexion (°) and mean vertical toe clearance during swing (cm) were calculated. Toe clearance was defined as the vertical height of the toe marker minus the toe marker height during single stance. During stance, ROM of the ankle, knee and hip joint (°) and sole angle at initial contact (°) were examined. Sole angle describes the angle between the sole of the foot and the ground, revealing whether the participant touched the ground with the heel, flat or on toes at initial contact. For kinetics, absolute ankle push-off power (region of interest 30-70% of gait cycle) and absolute hip extension power (W/kg) were chosen and the cumulative power of each was calculated by taking the integral of the power output in the given region of interest. Marker data were filtered with a Woltering filter at a smoothing factor of 20. To reduce high frequency noise in the model output, power output data was bidirectionally low-pass filtered at 20Hz with a 4th order Butterworth filter. All data trajectories were time-normalized to 100 data points.

5.6. Statistics

Model output data was imported from Nexus into MATLAB 2021a (The MathWorks Inc., Natick, Massachusetts, USA) and statistical analysis was performed with customized scripts. Normality of data was assessed using a Shapiro Wilk test. Due to the small sample size for some tests and since most discrete parameters did not display a normal distribution, non-parametric tests were used to calculate statistics and group data is displayed as median and 25th and 75th percentile, unless indicated otherwise. Difference between TD and CP was calculated by a Wilcoxin signed-rank test and corrected for familywise inflated error rates with the Holm correction. To assess differences over time in the CP group, discrete kinematics and kinetics, 6MWT, walking velocity and GMFM were analysed using a Friedman repeated measures ANOVA. For kinematics and kinetics, additionally, a trajectory analysis was performed using statistical parametric mapping (SPM). A t-test was used to inspect for significant differences between TD and CP and a repeated measures ANOVA for changes in the CP group over time. Based on random field theory, each time node is checked whether the differences between trajectories exceeds the threshold only 5% of smooth random curves are expected to cut across. Due to autocorrelation of neighbouring data points in biomechanical trajectories, several time nodes usually cross the critical threshold and are called supra-threshold clusters. Clusters are presented as % of gait cycle during which they occur. In case of significance, a post-hoc t-test determined between at which timepoints the difference occurred. The significance level for all tests was set to $P \leq 0.05$.

6. Results

6.1. Gait Analysis Outcome measures:

Walking speed did not differ significantly between timepoints in CP (P=0.933). At all timepoints before and after the intervention, CP participants walked significantly slower than TD participants (P=0.035, P=0.033, P=0.032, P=0.028, respectively). Table 2 depicts the mean walking speed as measured from the most affected leg.

*Table 2. Mean walking speed measured from the most affected leg during the gait analysis. Presented as group median with 25th and 75th percentile. *refers to the difference between Pre2 in CP and TD.*

	CP					TD	
Gait	Pre1	Pre2	Post1	Post2	*P*	Control	*P*
Speed [m/s] iqr:	1.36 (1.14-1.53)	1.29 (1.17-1.53)	1.27 (1.1-1.49)	1.32 (1.17-1.53)	0.933	1.64 (1.43-1.83)	0.033*

CP = Cerebral palsy; TD = Typically Developed; iqr = interquartile range

Kinematics

Joint angles pre and post intervention were highly similar throughout the entire gait cycle in all three joints (i.e. hip, knee and ankle) showing no significant difference (Figure 11). In comparison to TD, several supra-threshold clusters exceeded the critical threshold. At the hip level, two clusters (21–63% and 79–98%) indicating an increase in hip flexion in CP were found (p<0.001 and p=0.016). At the knee level, a cluster between 0-11% (p=0.01) and 79–99% (p<0.001) was evident presenting a significantly larger knee flexion in CP, while the ankle was significantly more plantarflexed during initial ground contact (0-2%, p=0.047) and during late swing (88–99%, p=0.0062) in CP.

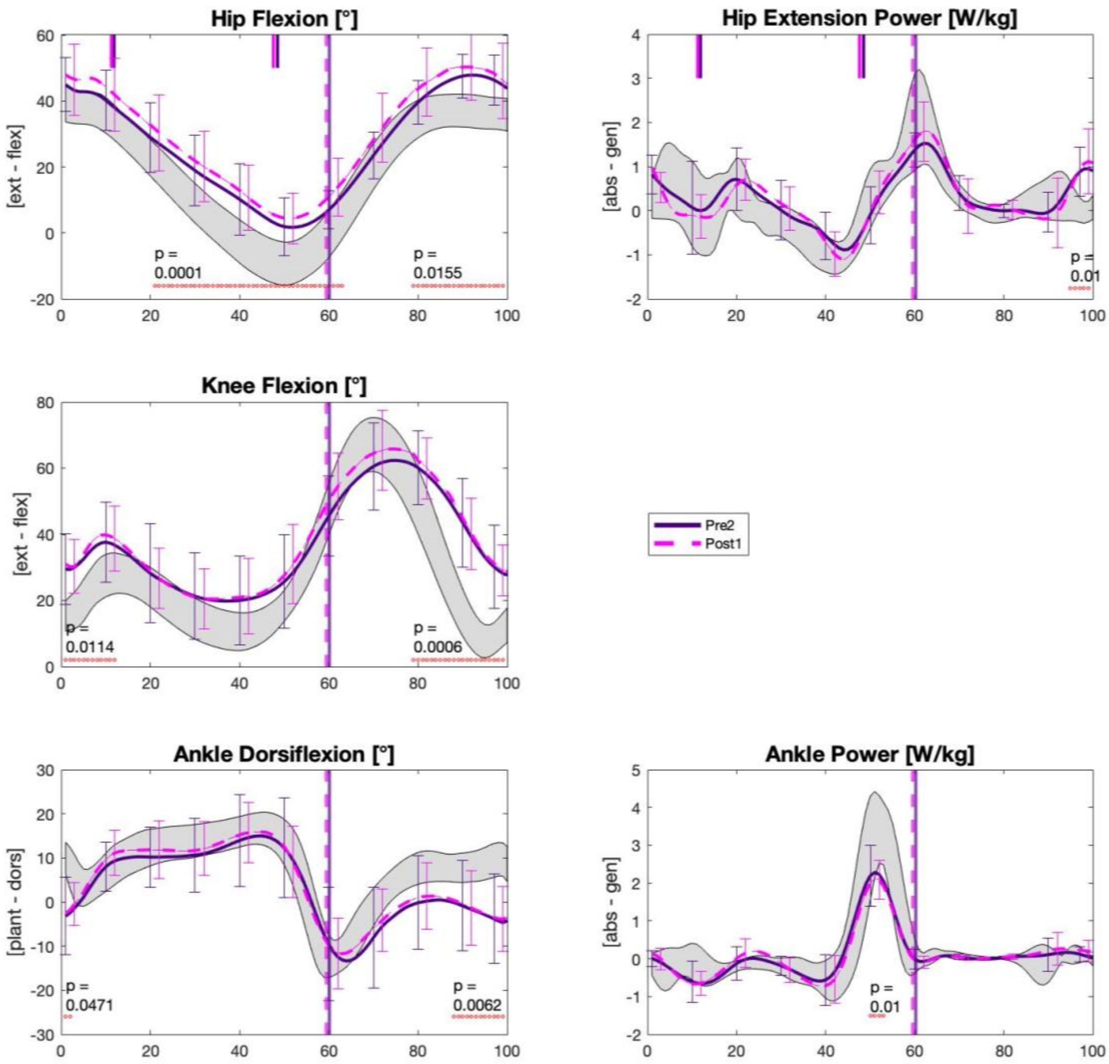


Figure 11. Mean and standard deviation joint angles for hip, knee and ankle joints across a gait cycle for CP pre intervention (Pre2, dark purple) and post intervention (Post1, dashed pink). For easier readability, SD is only displayed every 10%. Grey curve represents TD range of ±1SD. The long vertical lines represent the averaged ipsilateral foot-off, whereas the short vertical lines in the top graphs display contralateral foot-off and ground contact. Red dotted lines indicate supra-threshold clusters between CP post intervention and TD.

Discrete Kinematics

Prior to the intervention (Pre2), participants with CP dorsiflexed their ankle during swing significantly less than their TD peers. Mean dorsiflexion angle during swing was -2.2° (iqr: -6.2 – 0) compared to 6.6° (iqr: 3.8 – 8.7, p<0.001), peak dorsiflexion was 1.5° (iqr: -4 – 5.3) compared to 10.6° (iqr: 8.3 – 12.5, p=0.0053) and dorsiflexion ROM was 16.6° (iqr: 12 – 18.3) in comparison to 24.2° (iqr: 22.7 – 28.4, p=0.0011). Mean toe marker height during swing was significantly reduced in CP compared to TD (19.9mm, iqr: 14.5 – 28.3 compared to 35.5mm, iqr: 25.7 – 44.5, p=0.0081).

Interestingly, this difference, however, was not visible when comparing the mean toe clearance at Pre1 with TD (p=0.163).

The top row of Figure 12. shows the median group values of the measured discrete stance parameters during the different timepoints of the study, while the bottom row displays the individual change of each participant.

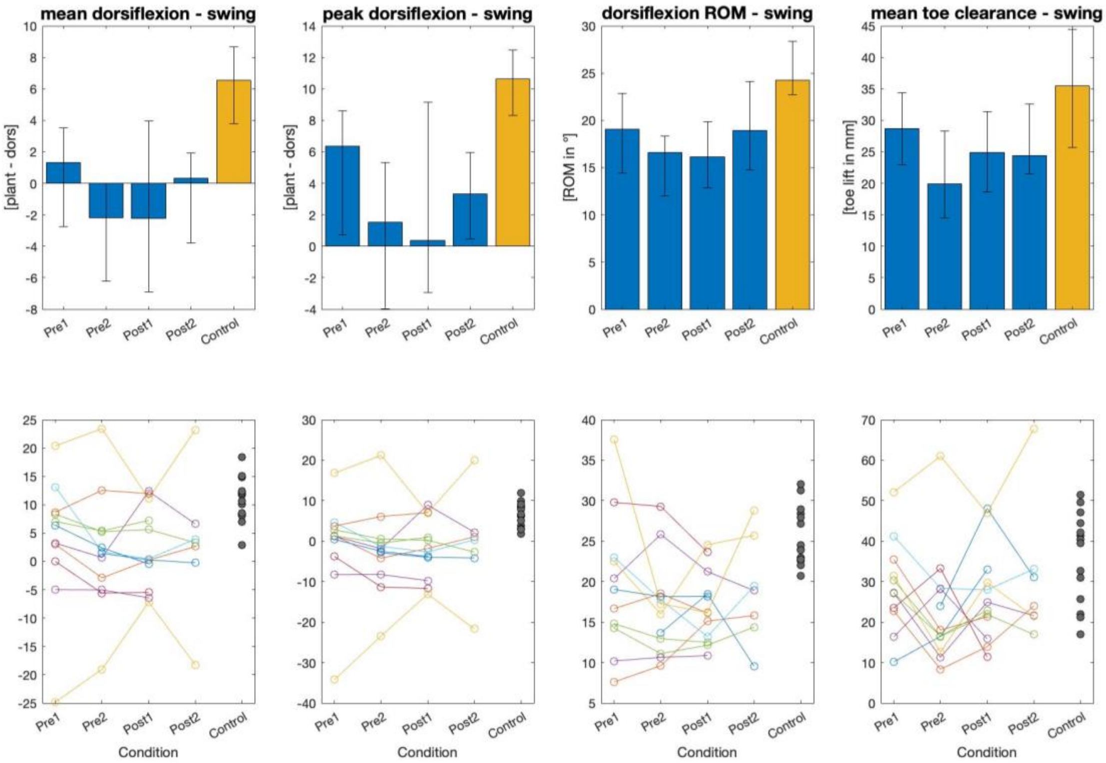


Figure 12. Gait kinematics during swing displayed as (top) group median and interquartile range and (bottom) participants individual development over measurement timepoints. No significant changes were evident between different measurements in CP.

Furthermore, at Pre2, the angle between the sole of the foot and the ground was significantly smaller in CP compared to TD with -87° (iqr: -93– -85) indicating a slight equinus at ground contact in CP compared to -117° (iqr: -118– -107, p<0.001), signalling heel contact in TD. Knee ROM during stance revealed a significant reduction of 4° in Pre2 compared to TD (CP: 30.1, iqr: 25.2–33.2 compared to TD: 34.3 iqr: 32.3–37.7, p=0.019), this significance was not visible when comparing knee ROM at Pre1 with TD (p=0.338).

No significant difference was shown in any of the measured parameters across time in CP (p>0.23).

The top row of Figure 13 shows the median group values of the measured discrete stance parameters during the different timepoints of the study, while the bottom row display the individual change of each participant.

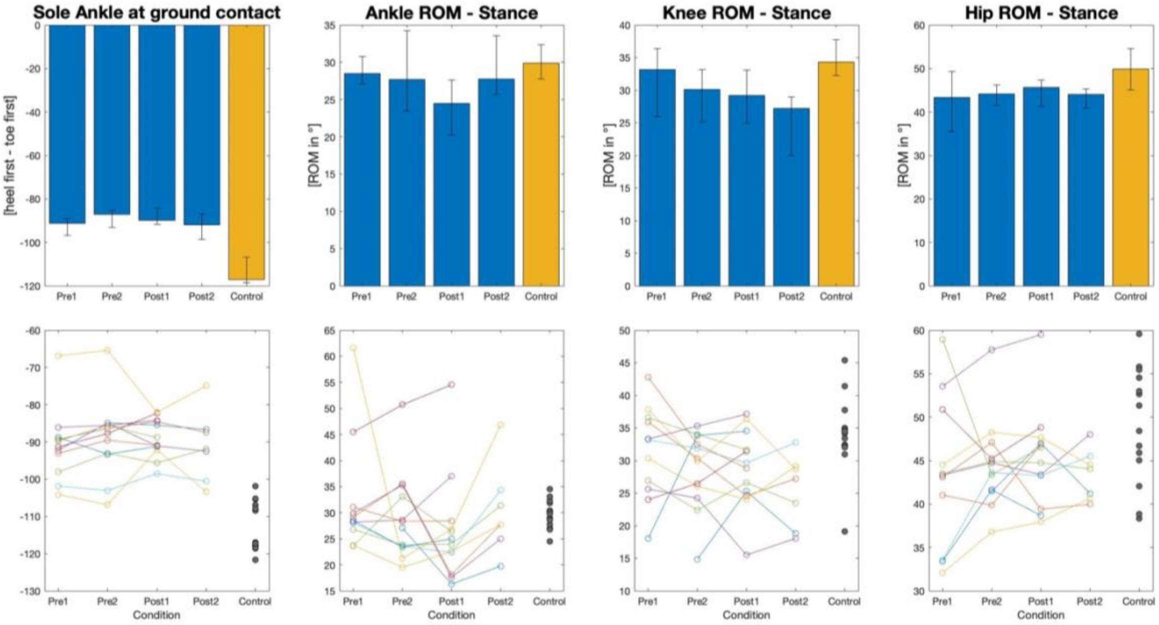


Figure 13. Gait kinematics during stance displayed as (top) group median and interquartile range and (bottom) participants individual development over measurement timepoints. No significant changes were evident between different measurements in CP.

Kinetics

For average joint power output at hip and ankle joints the critical threshold were not exceeded between pre and post intervention (Figure 11). Significant differences in power output between CP post intervention and TD were found. In late swing, a supra-threshold cluster (96-99% of GC) indicates a significantly greater hip extension power in CP. Furthermore, during push-off, CP participants displayed significantly lower ankle power (at 51-53%, p=0.01).

6.2. Functional Outcome measures

6MWT. The distance walked in the 6MWT differed significantly between all timepoints of CP in comparison to TD (p < 0.001). No significant difference comparing CP timepoints was found (Figure 14.).

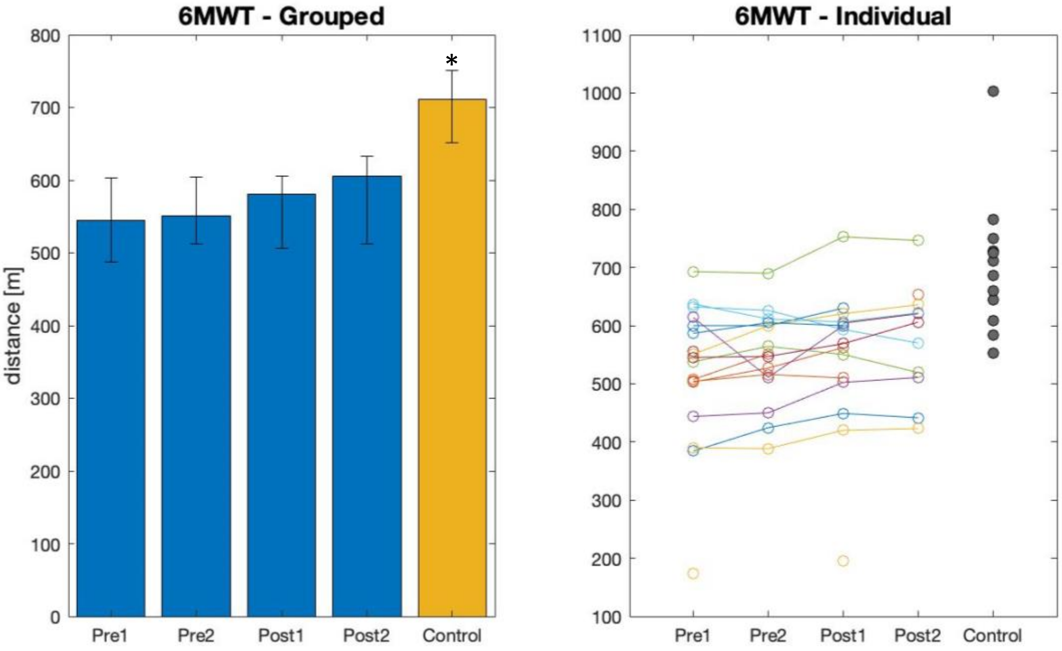


*Figure 14. (left) Median and interquartile range of all timepoints in CP (blue bars) and TD (yellow bar). *, all CP timepoints differ significantly from TD. (right) Individual results for the 6MWT of all participants and timepoints. Coloured dots connected by lines represent one participant each, while grey dots represent each TD participant.*

GMFM. Four participants reached the maximum score in both categories in the Pre-test and were not reassessed since no further improvement was possible. The median improvement for the remaining participants was 1 point in each category with a range of 0–5 points (iqr: 0–3) for category D and 0–8 (iqr: 0–2) points for category E. The difference between pre and post intervention was not statistically significant (p=0.393 and p=0.642, for D and E respectively). Individual scores can be viewed in Figure 15.

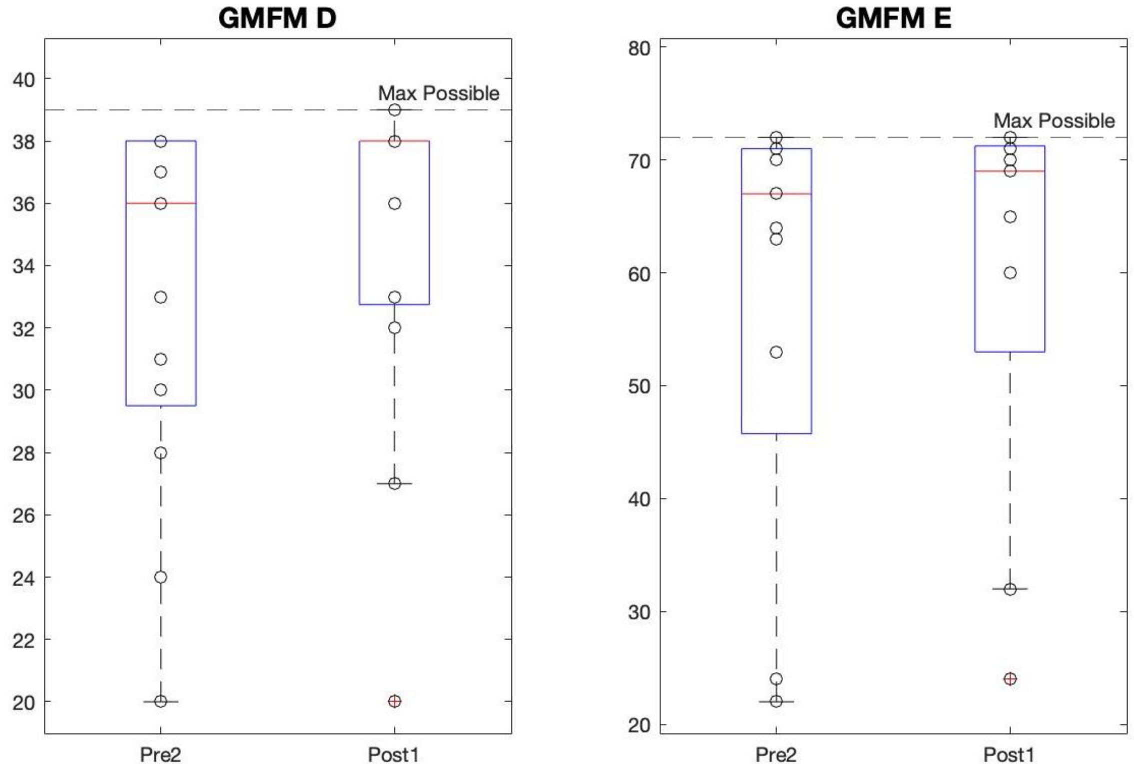


Figure 15. Scores for the GMFM in category D and E of participants that reached submaximal scores in at least one category at Pre2 (N=13). Red line represents the median value. Black circles depict the individual results of each CP participant.

7. Discussion

This study investigated the effects of an 12 week long combined strength, flexibility and gait training intervention on gait kinematics and kinetics in children and young adults with spastic CP. The hypothesis that the training intervention would improve gait quality by increasing dorsiflexion at ground contact and during swing, increasing peak ankle and hip power during push-off and directing knee and hip flexion during stance towards values of TD was not supported by our results. Further, active ROM of the ankle, knee and hip did not change throughout the intervention. Self-selected fast walking velocity did not differ pre-post intervention and was at all timepoints significantly slower than TD. Overall walking function measured as the distance walked in the 6MWT improved by 29.7m on average without reaching statistical significance and GMFM in categories D and E improved by 1 point on median without this change reaching statistical significance.

1. Will the EXECP training intervention improve gait quality of children and young adults with CP?

Drop foot during late swing and loss of the heel rocker due to toe first or flat foot initial contact is common in CP and can be a sign of weak pretibial musculature (Perry, 1992, chap. 11). A main target of the EXECP intervention was to strengthen the ankle dorsiflexors to increase ankle DF during swing and, thereby, improve foot clearance and prepositioning of the foot for ground contact in participants with CP. However, the intervention did not lead to a change in DF during gait on a group level. This lack of kinematic improvement at the ankle joint is in line with previous findings (Gillett et al., 2019). Gillet and colleagues (2019) did not find any change in ankle kinematics after a well-designed 12 week long randomized, controlled intervention including heavy strength training and functional anaerobic exercises. The intervention of the EXECP project was designed to combine task-specific training (daily gait training on an inclined treadmill) with exercises addressing underlying impairments to gait like muscle weakness (strength training) and reduced flexibility (passive stretching) of the lower limbs. We hypothesized that the incline of the treadmill would provide sufficient stimulus for the participant to increase ankle DF during swing and apply passive stretching of the plantarflexors during stance while the strength training would enlarge the muscular capacity of the pretibial muscles. The assumption was that this would translate into kinematic changes during gait. However, the ankle joint kinematics were not altered after the intervention. In contrast to our findings, a different study conducting 12 weeks of explosive resistance training found increases in toe lift during swing and a more dorsiflexed foot at ground contact in adults with CP (Kirk et al., 2016). Participants were asked to perform all concentric actions as fast as possible regardless of actual movement velocity with repetitions until failure in each set. Participants in the ECEXP project only performed explosive exercises in the last four weeks of the training intervention which might have been too short to induce similar changes as seen by Kirk et al (2016). Nonetheless, Kirk et al (2016) also did not find clinically significant increases in functional tasks like the 6MWT. This emphasizes the complexity of walking and the fact that there seems to be a considerable discrepancy between the intervention effects on gait performance and gait kinematics.

Flexed knee gait pattern is commonly seen in CP (Galey et al., 2017) and refers to an inability to fully extend the knee which can be connected to a flexion contracture at the knee or hip or also weakness of the plantarflexors (Perry, 1992, chap. 12). Excessive knee flexion during terminal stance can effectively reduce the passive stability that a vertical alignment of tibia and femur can achieve and simultaneously increase the demand on the knee extensors (Perry, 1992, chap. 12). Mild flexed knee gait (>20° knee flexion) did not increase tibiofemoral forces in an individualized musculoskeletal model in children with CP compared to TD but severe knee flexion (>50° knee flexion) more than doubled peak compressive forces likely due to a high extensor moment of the quadriceps muscle (Steele et al., 2012). Increased joint loadings may in turn increase the risk of developing pain over time which is significantly associated with degeneration of walking function (Opheim et al., 2009), highlighting the importance of interventions reducing the risk of gait deterioration. Our participants walked with increased hip flexion in terminal stance and pre-swing and showed another burst of hip flexion in the second half of swing likely to accommodate for a lack of knee extension and help swing the leg forward in preparation for ground contact. Knee flexion was insufficient in second half of swing possibly as a consequence of the ankle joint moving into excessive PF during the same time. Thus, at ground contact the more affected knee was already flexed on average 10° more than in TD. After weight acceptance, the knee flexion was not statistically different from TD but a trend towards a more flexed knee was visible. The hypothesis of the current study was that the combination of inclined treadmill walking (providing stimulus to increase peak knee and hip extension in stance) and strength training for all lower limb extensor and flexor muscle groups would increase knee and hip ROM in stance was not supported. These findings are in line with a 16 week long RCT by Fosdahl et al (2019) that conducted a strength training and stretch intervention with children with CP and found no kinematic improvements during walking post intervention. However, the study did not include task-specific gait training. Gait training has been found to be effective in improving walking velocity (Booth et al., 2018), but only few studies have investigated the effect of gait training on gait quality. Willerslev-Olsen and colleagues (2014) investigated the effects of four weeks of 30 minute daily gait training on an inclined treadmill on children with CP and found moderate improvements of ankle joint stiffness, toe lift during swing and ankle position at initial contact. Gait kinematics above the ankle were not reported. The strength training in the EXECP intervention complied with activity recommendations and strength training guidelines by the National Strength and Conditioning Association (Faigenbaum et al 2009) and the additions by Verschuren (2016) for people with CP concerning duration, intensity, volume, type of exercises and progression. Further, all participants completed an average of ten minutes daily inclined treadmill training. Therefore, the lack of effect on gait kinematics is most likely not due to deficits in the intervention design.

A recent study found that intervention effects on gait kinematics were greater at higher walking speeds, potentially leading to an underestimation of intervention effects when walking is only tested at comfortable walking speeds (Oudenhoven et al., 2019). During the gait analysis, our participants were asked to walk in their fastest controlled walking speed. However, they walked 15% slower compared to the average walking velocity during the 6MWT indicating that they chose a walking speed probably in between their fast and comfortable walking speed. Thereby, some smaller effects of the intervention on gait kinematics might have been disguised due to our participants walking speed.

Gait impairments in CP can arise from and are enhanced by impaired selective motor control (Gage et al., 2009, chap. 2.4). This loss in motor control roots in the brain lesion underlying CP and occurs before the onset of walking and therefore substantially influences the gait pattern a person with CP acquires in childhood (Rosenbaum et al., 2006). Thus, people with CP have likely never walked with a completely “normal” walking pattern and effective feedback might be necessary to enhance gait quality. Although verbal feedback directing the participant’s focus towards lifting the toes and achieving heel strike was given during walking in the training sessions and parents were asked to do the same during the home-based session this might not have been enough to adapt the motor pattern. A study by van Gelder and colleagues (2017) examined the potential of instant biofeedback in a virtual surrounding on flexed knee gait pattern in 16 children with CP. The participants were able to modify their gait towards increased peak knee and hip flexion based on the feedback and increase ROM of the knee and hip joint. This suggests that with the correct feedback mechanisms, children with CP are capable of adapting their motor patterns. Nevertheless, whether this change in motor pattern as seen by van Gelder et al (2017) could be maintained independently of the feedback after a training period is unclear.

Interestingly, responders in the study had a significantly higher initial gait profile score (i.e. greater overall kinematic gait deviation) than non-responders (responders (n=9): 14.5±5 versus non-responders (n=7): 9.4±1.2, p=0.005) (van Gelder et al., 2017). The gait profile score summarizes the difference of relevant gait kinematics compared to TD gait into an overall index of gait pathology. Responders were classified as such when the participant achieved a clinically relevant change in knee and/or hip kinematics (>5°). Out of the 17 participants of the current study, 14 were classified as GMFCS I and 13 of these were highly functional children. They already operated very close to the TD range concerning functional abilities like the 6MWT and four participants reached the maximum score in the GMFM D and E in the pre-test. These participants might have already achieved a gait pattern that best accommodated their individual deficits and might exhibit a smaller capacity for improvement than more impaired participants. Since CP is a permanent disorder with no cure at present, certain impairments will most likely always influence the motor abilities of people with CP (Graham et al., 2016). Therefore, the question arises whether it is even desirable to aim for a most “normal” gait pattern in more functional people with CP. This is in line with the general shift towards emphasising the improvement of everyday life activities compared to more impairment-focused rehabilitation in children with CP (WHO 2001).

In front of this background, it is important to consider what the goals of therapeutic strategies and training interventions are. With our intervention we hoped to see improvements in gait quality and functional gait performance based on our intervention program. Especially the effect on gait quality was not evident and the effect on functional performance was very limited. However, the median distance walked in the 6MWT was higher in our CP group across GMFCS I and III compared to reference values of CP children with only GMFCS I by Thompson et al (2008). Therefore, a lack of strength and power might not be the main factors influencing gait in this group of CP children. To trace back what the true underlying causes for each participants gait deviations are, more detailed analysis of spasticity, passive ROM and strength assessments would be needed. But is physical training in children with CP obsolete if it fails to improve walking kinematics? Most probably not. Possibly strength training should not be viewed as a measure to improve walking mechanics but rather as a mean to increase strength reserve to delay onset of gait deterioration. A healthy gait pattern utilizes eccentric muscle action and recoil of elastic energy as well as alignment of bony structures for passive stability to minimize the energetic cost of walking (Gage et al., 2009, chap. 1.3). It is said that even with moderate strength values in a physical examination (3+, i.e. fair strength) a healthy gait pattern can be maintained, only a higher percentage of the maximum capacity is used (Perry p. 429, chap.21). In CP, despite the lack of evidence connecting muscular strength increases to improved performance, loss of strength is associated with loss of walking ability and function (Opheim et al., 2009). Thus, a closer examination of the strength improvements of the intervention will give further valuable information about the effectiveness of the intervention.

2. Will the EXECP training intervention positively affect overall functional gait performance?

The ability to ambulate is important in many daily settings to gain independence and especially for children it can decide over whether they can participate in activities with their peers or not. Strength training has not consistently proven to lead to functional improvements like walking endurance measured via the 6MWT with average changes often below the minimal detectable change of 60m reported by Thompson et al (2008): (Taylor et al 2013: ±0m; Fosdahl et al 2019: +46m; Gillet et al 2018: +30m; Kirk et al 2016: +30m). This is in line with our findings as only two participants displayed an increase in walking distance larger than 60m after the intervention. However, gait training has shown to improve gait endurance after seven weeks of 30 minutes twice-weekly treadmill training (Grecco et al 2013). The cumulated weekly duration of treadmill training was similar in this study compared to ours (2x30 min versus 7x10 min). Yet, the intensity of the training was different between the two protocols. In the study by Grecco et al (2013), participants trained at 80% of their maximal walking speed for 20 of the 30 minutes in each session whereas participants in the current study were free to choose their own comfortable walking speed. This might have provided a less intense stimulus for improvement. Nonetheless, participants in the study by Grecco et al (2013) walked 220m on average in the initial test whereas participants in this study walked more than double the distance in the first pre-test. This relates back to the assumption that participants with lower initial abilities have a higher capacity for improvement and might benefit more and after a shorter time from interventions. Therefore, it is difficult to determine whether the larger improvement in the 6MWT is related to this or the higher intensity of the treadmill training.

The GMFM is more difficult to interpret as the different scores are based on an interval scale and the improvement about one point can entail different levels of functional relevance for the participant depending on where they gained it. Addressing this issue, a study by Wang and Yang (2006) reported that on average a change in GMFM-66 of 1.58 points represented a meaningful clinical improvement as evaluated by trained therapists. This change was significantly different to children classified as showing no improvement (average of 0.2 point improvement, $p<0.001$). Children considered to have great clinical improvements gained on average 3.71 points. Although the overall improvements in GMFM scores in this study after the intervention were not significant, five participants improved their score in the category D (standing) by 2 to 3 points and two participants improved their score in the category E (Walking, Running Jumping) by 2 points. One participant gained 5 points in category D, while three participants improved their score in the category E by even 7 to 8 points. This suggests an important and clinically relevant improvement of motor abilities in at least six participants after the intervention.

3. All parameters will differ at a group level between CP and TD.

It was hypothesized that the CP participants would display deviations to the gait pattern of their TD peers including but not limited to a reduction of dorsiflexion during swing. On a group level, the CP participants walked with statistically lower ankle dorsiflexion during the second half of swing during the initial pre-test. However, six participants had mean ankle dorsiflexion values similar to TD. As described above, hip and knee flexion were increased in late swing to prepare the limb for ground contact despite the decreased dorsiflexion. Further, knee flexion was increased during weight acceptance and hip flexion exaggerated during terminal stance. These results indicate that the group of CP participants did show deviations from TD in their gait pattern and therewith fulfilled the basic prerequisite for the intervention to be able to shift CP values more towards TD. Nonetheless, a high level of functionality and gait quality might have made it more challenging for the intervention to show significant improvements over all participants.

4. There will be no difference in measured parameters in the control period in the CP group.

In line with the hypothesis, no significant differences were seen in any of the measured parameters between Pre1 and Pre2 in CP, indicating good repeatability of the measurements. Thus, changes in the intervention period would have likely been attributed to the intervention itself and not merely to biological variability, retest effects and methodological inconsistencies. Nonetheless, there were visible, if not statistically significant variations in parameters especially concerning summary measures of gait kinematics like ROM and toe lift. Knowing these variations assists crucially in interpreting intervention effects and is one important benefit of multiple baseline testing designs.

Limitations

Considering the intricacy of instrumented gait analysis and the complex manifestations of CP, it is important to discuss certain limitations of this study. Instrumented 3D gait analysis can have high inter- and intrarater reliability (Kadaba et al., 1989) but this highly depends on the skills of the investigator (McGinley et al., 2009). Despite substantial piloting, a learning process concerning marker placement and camera calibration might have influenced the Pre1 tests of the first subjects. To keep the error due to differences in marker placement to a minimum, the same person was responsible for applying markers during all measurement sessions throughout the study. A further aspect is that markers are placed on skin and especially in participants with some level of obesity the anterior pelvis markers can be subject to considerable soft tissue artefacts and placement right above the superior iliac spine might not be possible. Although best efforts were put into the analysis to ensure highest data quality, marker-based analysis should always be interpreted with a degree of caution.

Secondly, the training sessions during the intervention were guided individually for each participant which is one strength of the study. However, due to wide geographic dispersion of some participants across central Finland, different physiotherapists and personal coaches were trained to execute the training with the participant at a local gym if the research centre was located too far away. Great care was taken to ensure the technical equipment of each gym was sufficient and that the coach/physiotherapist was well acquainted with the study design and intervention protocol. Nevertheless, a difference in coaching style might have had an influence on the effect of the interventions that is beyond our control.

In the same vein, it is also important to acknowledge that the subjective perception of the intervention and motivation during each training session might have been confounding factors on its effectiveness as well as the compliance to the home-based treadmill training. We did not assess the participants experience of the intervention after each session which permits us to evaluate the influence of motivation. Nevertheless, it is likely that the lengthy nature of the study design mainly attracted participants that had a high internal motivation to improve their walking function to begin with. Yet, this is also a source of bias. The probability that an intervention like this attracts participants that are generally interested in physical activity and are already active themselves is reflected in the amount of participants with GMFCS I (14/17) and high functional abilities. Therefore, the results cannot be generalized to populations with more severe impairments.

Further, motivation of the children during the 6MWT could have influenced the test result. The 6MWT has a high repeatability but in our session design it was conducted after the gait analysis which means at the end of a session with a duration around 1.5 hours. A rest period with time to drink was provided for all participants to minimize fatigue influencing the result. Yet, the test required six minutes of continuous and concentrated effort. It is known that the emotional state and alertness of a person with CP can impact the degree of severity of spasticity (Bonow et al 2018) which could complicate objective evaluation. Thus, despite efforts to encourage all participants throughout the test we cannot rule out that some level of mental fatigue impacted the physical capacity of some participants.

Lastly, an important consideration concerns the diversity of clinical manifestations in CP and our small sample size. Since impairments in CP are based on a neurological impairment that impacts motor abilities in a multitude of ways, a holistic view on the individual might sometimes be needed to fathom the patterns of responders and non-responders to certain interventions. Gait impairments in CP can result both in flexed and stiff knee gait pattern and the ankle can be in equinus for one participant and in excessive DF for another. Averaging participants without clear distinction of these gait patterns can lead to cancelling out of deviations. However, our group of participants was too small to effectively compare subgroups against each other.

Further, the effect of growth was not controlled for. Several studies have shown that the natural progression of gait in CP shows a deterioration of joint ROM, strength and walking ability already starting before the age of 18 in CP (Bell et al., 2002; Johnson et al., 1997). The inability of muscles in CP to grow at the same rate as the bone grows during that time can lead to increases in muscle stiffness. Additionally, increases in body weight can decrease the relative force generating capacity of a muscle. Therefore, growth and increases in body weight over the nine months study period could have impacted the effect of the training intervention especially in the younger participants.

The analysis of something as intricate as gait is a constant balance act between simplifying a complex matter to facilitate it’s interpretation and retaining enough information for it to remain meaningful. Normalization of the gait cycle, for instance, can largely improve comparability of different participants. Nonetheless, it also masks information like the walking velocity of a participant which in turn influences the amplitude of certain gait parameters. As an example, the reduction in peak ankle power during push-off in CP compared to TD in our study is likely related to the significantly slower walking speed of CP.

Future Studies

The goal of our intervention was to increase walking performance and gait quality in children and young adults with CP, hoping this would in a second step increase participation, independence and well-being. However there seems to be a critical gap between the underlying physical prerequisites for walking (i.e. mobility and strength) and functional outcome measures (gait quality and performance). Future studies should aim to further explore the impact of neural control mechanisms and motor learning processes on the effect of such training interventions and the adaptability of movement patterns in CP.

CP entails lifelong impairments and the design of optimal training interventions is therefore crucial to enable patients to actively take part in life with the highest degree of function possible. Targeted training strategies can thereby help create the basis for a healthy lifestyle rather than viewing training as singled out interventions with a clear start and end like surgical treatment. On that note, it should be viewed as an encouragement that our intervention did not lead to worsening of gait parameters and can therewith be noted as safe for children and young adults with CP. Nonetheless, the design for training interventions should be explored further in the future possibly by increasing the focus on feedback-driven gait training in the expectation to maximize positive outcomes on motion patterns after training.

Additionally, investigations with larger sample sizes will enable further exploration of subgroups trying to find the patterns between responders and non-responders to training. This study included participants of different GMFCS levels, lateral involvement and gender which all contributed to the heterogeneity of our participants group. Further the gait pattern was not controlled for beyond the inclusion criterion of passive neutral ankle mobility (flat foot during quiet standing). In the future, studies with more participants might be able to apply machine learning algorithms to identify the influence of initial gait pattern, motivation and initial walking performance on the magnitude of the intervention effect. Accordingly, it can be recommended to include an index of gait pathology into the analysis of gait kinematics in CP to define what clinically relevant changes are. The adoption of a multiple baseline design is hereby recommended to separate intervention effects from other sources of variability.

Conclusion

This thesis investigated the effects of a three-month long tailored strength, flexibility and gait training intervention on gait quality and functional gait performance in a group of children and young adults with spastic CP. We expected the intervention to increase dorsiflexion during swing and initial contact and expand the active ROM of the ankle, knee and hip joint during stance in our participants as well as an increase in the distance walked during the 6MWT. However, this was not the case to an extent possible to detect with our limited sample size and heterogeneity of participants. Nonetheless, a clinically relevant improvement in gross motor function was seen in six participants indicating the presence of responders and non-responders. Whether a similar training intervention with longer duration and a stronger emphasize on feedback-driven gait training can lead to the desired improvements in gait performance and a change in motor patterns remains to be investigated.

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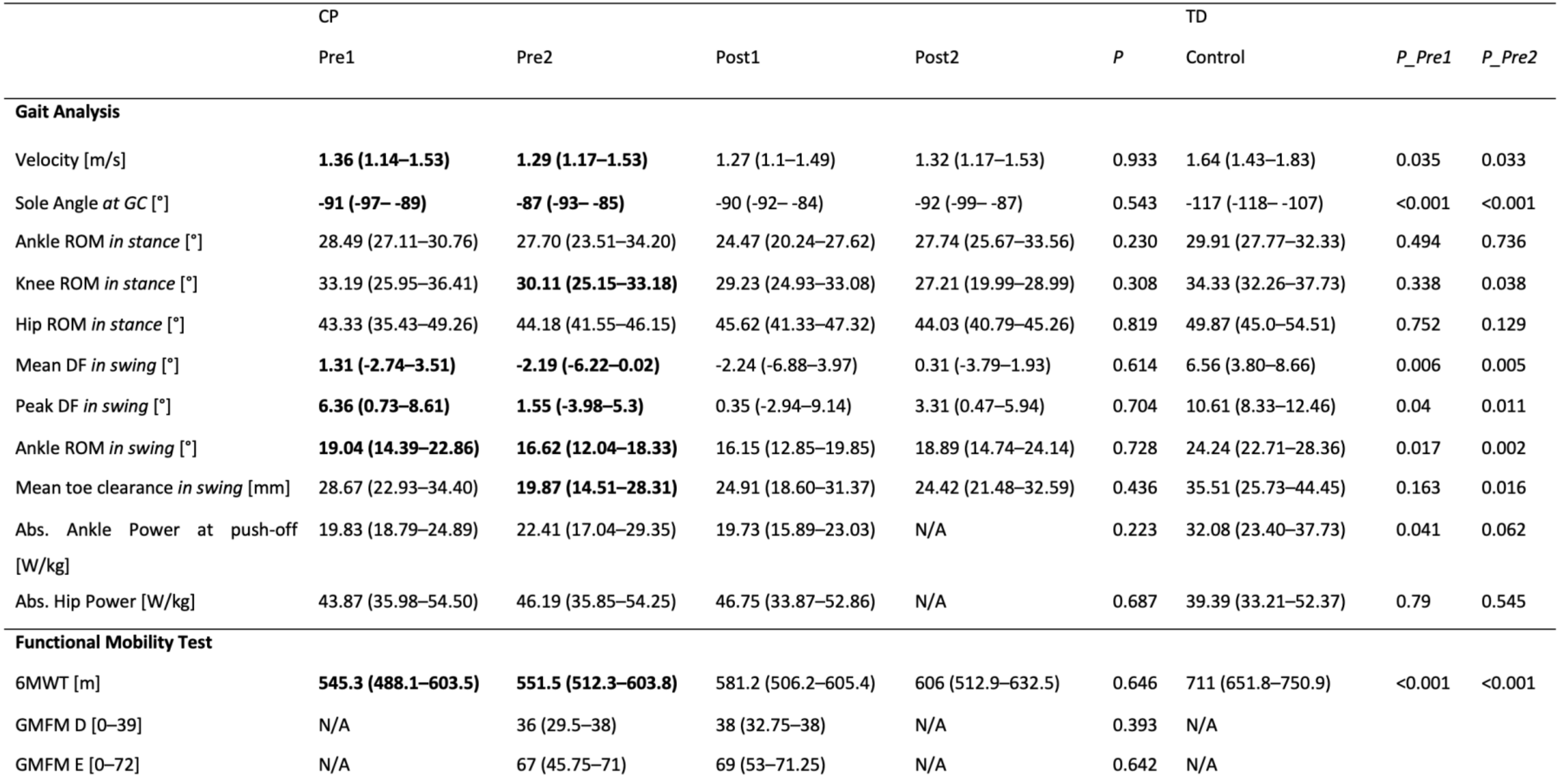
Appendix

Appendix 1. Biomechanical Parameters. Presented as group median with 25th and 75th percentile. Bold values in Pre1 and Pre2 facilitate detecting significant differences compared to TD.



	CP					TD		
	Pre1	Pre2	Post1	Post2	*P*	Control	*P_Pre1*	*P_Pre2*
Gait Analysis								
Velocity [m/s]	**1.36 (1.14–1.53)**	**1.29 (1.17–1.53)**	1.27 (1.1–1.49)	1.32 (1.17–1.53)	0.933	1.64 (1.43–1.83)	0.035	0.033
Sole Angle *at GC* [°]	**-91 (-97– -89)**	**-87 (-93– -85)**	-90 (-92– -84)	-92 (-99– -87)	0.543	-117 (-118– -107)	<0.001	<0.001
Ankle ROM *in stance* [°]	28.49 (27.11–30.76)	27.70 (23.51–34.20)	24.47 (20.24–27.62)	27.74 (25.67–33.56)	0.230	29.91 (27.77–32.33)	0.494	0.736
Knee ROM *in stance* [°]	33.19 (25.95–36.41)	**30.11 (25.15–33.18)**	29.23 (24.93–33.08)	27.21 (19.99–28.99)	0.308	34.33 (32.26–37.73)	0.338	0.038
Hip ROM *in stance* [°]	43.33 (35.43–49.26)	44.18 (41.55–46.15)	45.62 (41.33–47.32)	44.03 (40.79–45.26)	0.819	49.87 (45.0–54.51)	0.752	0.129
Mean DF *in swing* [°]	**1.31 (-2.74–3.51)**	**-2.19 (-6.22–0.02)**	-2.24 (-6.88–3.97)	0.31 (-3.79–1.93)	0.614	6.56 (3.80–8.66)	0.006	0.005
Peak DF *in swing* [°]	**6.36 (0.73–8.61)**	**1.55 (-3.98–5.3)**	0.35 (-2.94–9.14)	3.31 (0.47–5.94)	0.704	10.61 (8.33–12.46)	0.04	0.011
Ankle ROM *in swing* [°]	**19.04 (14.39–22.86)**	**16.62 (12.04–18.33)**	16.15 (12.85–19.85)	18.89 (14.74–24.14)	0.728	24.24 (22.71–28.36)	0.017	0.002
Mean toe clearance *in swing* [mm]	28.67 (22.93–34.40)	**19.87 (14.51–28.31)**	24.91 (18.60–31.37)	24.42 (21.48–32.59)	0.436	35.51 (25.73–44.45)	0.163	0.016
Abs. Ankle Power at push-off [W/kg]	19.83 (18.79–24.89)	22.41 (17.04–29.35)	19.73 (15.89–23.03)	N/A	0.223	32.08 (23.40–37.73)	0.041	0.062
Abs. Hip Power [W/kg]	43.87 (35.98–54.50)	46.19 (35.85–54.25)	46.75 (33.87–52.86)	N/A	0.687	39.39 (33.21–52.37)	0.79	0.545
Functional Mobility Test								
6MWT [m]	**545.3 (488.1–603.5)**	**551.5 (512.3–603.8)**	581.2 (506.2–605.4)	606 (512.9–632.5)	0.646	711 (651.8–750.9)	<0.001	<0.001
GMFM D [0–39]	N/A	36 (29.5–38)	38 (32.75–38)	N/A	0.393	N/A		
GMFM E [0–72]	N/A	67 (45.75–71)	69 (53–71.25)	N/A	0.642	N/A		