FACTORS ASSOCIATED WITH STIFF KNEE GAIT IN CEREBRAL PALSY

by

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Abstract

Stiff knee gait (SKG) is one of a few classified walking patterns which people with cerebral palsy (pwCP) can present with. The characteristic for SKG is delayed and/or reduced peak knee flexion during swing phase, which can reduce walking ability and result in functional restrictions. Through the use of both clinical and laboratory based measures this cross-sectional study aimed to identify the factors associated with SKG, suggest possible treatment options and propose potential directions for future research.

The impact of five variables on knee flexion amplitude during the swing phase of gait was assessed. Data was gathered from a group of 27 pwCP and 20 age-matched controls. Three dimensional motion analysis was used to record the kinetics and kinematics of the pelvis and lower limbs. Isometric strength of the ankle plantarflexors, knee extensors, hip flexors and hip extensors was recorded via maximal voluntary contraction using a dynamometer. Passive and stretch-mediated stiffness of the knee extensors was also recorded using a dynamometer with two set stretch speeds.

 The main findings highlight that several factors are correlated with SKG. The key determinants of which are a crouch positioning of the lower limb in stance phase and spasticity within the knee extensors. Additionally, secondary analysis highlighted the importance of the knee extensors inner/outer range strength ratio. Greater weakness in inner range was linked to increased spasticity, to the degree of crouch and in turn to a smaller degree of knee flexion in swing phase. This study further highlighted that both clinical and laboratory based measures may be used to determine the possible causes of SKG but that laboratory based gait analysis and outcome measures were more sensitive and had higher predictive power. The implications for treatment are to be mindful of the fact that by attempting to improve one impairment it does not have a negative effect upon another. Inter-relationships between impairments need to be looked at in more detail. Future work should evaluate treatments on SKG of strengthening the inner range quadriceps with/without a stretching programme.

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EQUATIONS

ABBREVIATIONS

°/s	degrees per second
3D	three-dimensional
AD	analogue-to-digital
ANCOVA	analysis of covariance
ASIS	anterior superior iliac spine
cm	centimetre/s
COM	centre of mass
COP	centre of pressure
CP	cerebral palsy
EMG	electromyography
EVB	embedded vector basis
EVGS	Edinburgh visual gait score
GMFCS	gross motor function classification system
H	Hoffman
HSP	hereditary spastic paraparesis
Hz	hertz
ICF	international classification of functioning, disability and health
IVH	intraventricular haemorrhage
kg	kilograms
kHz	kilohertz
kN/V	kilonewtons per volt
m	metres
m/s	metres per second
MRC	medical research council
ms	millisecond
MUR	muscle utilisation ratio
MVC	maximal voluntary contraction

N/V	newton's per volt
NICE	national institute for health and clinical excellence
PCA	principle component analysis
PRS	physicians rating scale
PSIS	posterior superior iliac spine
PVHI	periventricular haemorrhagic infarction
PVL	periventricular leukomalacia
pwCP	people with cerebral palsy
SD	standard deviation
SEM	standard error of the mean
SF-GT	Salford gait tool
SKG	stiff knee gait
TDC	typically developing children
TTL	transistor-transistor logic
WHO	world health organisation

APPENDICES

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DEDICATED to all whom believed this was possible for me, thank you.

AUTHOR'S DECLARATION

At no time during the registration for the degree of Master of Philosophy has the author been registered for any other University award without prior agreement of the Graduate Committee.

Work submitted for this research degree has not formed part of any other degree either at Plymouth University or at any other establishment.

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CHAPTER 1: INTRODUCTION AND LITERATURE REVIEW

Introduction

This thesis investigates stiff knee gait (SKG) in people with cerebral palsy (pwCP); the differences in gait between pwCP and healthy matched controls (chapter 3), the relationship between the presence of SKG and impairments such as weakness, passive stiffness and spasticity (chapter 4) and the relative predictive power of laboratory and clinical based outcome measures of impairment (chapter 5). The methods used are described in chapter 2 whilst chapter 6 provides an overall discussion of the thesis and an overview of the study limitations and future directions.

This chapter will firstly describe the definition, epidemiology and classification of cerebral palsy (CP) before describing the causes and impact of common impairments and the changes in gait patterns commonly described in pwCP.

Definition, epidemiology and classification of cerebral palsy

Definition of cerebral palsy

CP is a highly complex disorder and as such it has been proven difficult to define. It was first identified in the 1830's by William Little who described it as 'a brain injury due to oxygen deprivation to the brain at birth'(Dabney & Miller 2012). Subsequently it became known as Little's disease. Since that time medical diagnostic techniques have developed which has enabled a great improvement in the understanding of CP. It became apparent that it would be beneficial to have a definition and classification which would be appropriate for a spectrum of professions and individuals. In 2006 an executive committee, comprising of an international panel, published a report introducing a revised definition. The definition, shown below, is all-encompassing and it covers secondary conditions and related disabilities which previous definitions have not.

> *'Cerebral palsy 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 CP are often accompanied by disturbances of sensation, perception, cognition, communication, and behaviour by epilepsy, and by secondary musculoskeletal problems.'*

> (Rosenbaum et al. 2007)

Although, as highlighted in the definition, the lesion is non-progressive it affects development and the child may therefore find activities more difficult and symptoms may appear to worsen as they age, due to growth spurts and the development of secondary changes such as muscle weakness, muscle shortening and bony deformity (Strobl 2012).

Epidemiology and causes of cerebral palsy

The prevalence of CP is approximately 2 to 2.5 per one thousand children in the western countries (Lin 2003). A promising study focussing on preterm infants reported that there have been decreasing rates of CP among children born over the past twenty years (Robertson et al. 2007).

CP is an umbrella term encompassing a range of developmental and acquired abnormalities of the immature brain. The predisposing and predictive factors that can occur pre-, during and post-pregnancy which can lead to CP are varied. Pre-conceptual risk factors include smoking, alcohol, adverse socioeconomic status and maternal health problems (Sundrum et al. 2005; Jacobsson et al. 2008). In addition, mothers' educational status and those who do not receive parental care have also been found to be factors relating to an increased chance of CP (Qureshi et al. 2010; Wu et al. 2011). These are not direct causes but are likely to be part of a causal chain (Rosenbaum & Rosenbloom 2012). In 1999 a study identified genetic causes, a gene on chromosome 2q24-25 was recognised to be associated with symmetrical spastic CP (McHale et al. 1999). However, the most important risk factors reported for an increased chance of cerebral palsy are low birth weight and prematurity (Sankar & Mundkur 2005). The factors causing CP vary depending on the stage of pregnancy in which lesions arise:

Early antenatal factors:

Only around five per cent of CP patients are believed to have early antenatal causes these include, chromosomal abnormalities, congenital infections and early cerebral malformation syndromes, late in second trimester (Rosenbaum & Rosenbloom 2012). During this phase of development the immature white matter is particularly vulnerable to hypoxia-ischemia (Back et al. 2007). Injury at this stage will disrupt subsequent myelination and result in abnormal and incomplete white-matter development (du Plessis 2004). Further, the functional and the anatomic-structural immaturity of the cerebral vessels are related to the intrinsic vulnerability of the preterm brain to ischemic and haemorrhagic injury (Volpe 2001).

Later antenatal factors:

A primary arterial ischemic injury which occurs to the white matter surrounding the ventricles is known as periventricular leukomalacia (PVL). The window of vulnerability for this to arise

is between 24-34 weeks gestation (Folkerth 2006). PVL is typically bilateral and occurs most frequently towards the posterior aspects of the ventricles in the white matter, as well as in the white matter adjacent to the frontal horns of the lateral ventricles (du Plessis 2004). Since the axons conducting motor input to the lower extremities course through the frontal regions, injury in this location produces the typical clinical picture of spastic diplegia, in which the most prominent motor impairment is in the legs (du Plessis 2004; Shevell et al. 2008). The clinical hallmark of this form of CP is motor developmental delay which is associated with spastic hypertonus that principally affects the lower limbs (Rosenbaum & Rosenbloom 2012).

Periventricular haemorrhagic infarction (PVHI) is usually unilateral but may involve extensive areas of the hemisphere affecting fibres supplying the upper and lower extremities and possibly also the face (du Plessis 2004). This lesion has a poor prognosis, being associated in the long term with a 90% prevalence of neurodevelopmental impairment that is often severe (Bassan et al. 2007).

Post-haemorrhagic hydrocephalus manifests as progressive ventricular distension that may distort or compress the adjacent axonal tracts directly, or cause regional periventricular ischemia and secondary injury to these pathways with those supplying the lower extremities being most affected. Co-existing PVL and PVHI will result in combined hemiparesis and spastic diplegia (du Plessis 2004).

Cerebral insults in the preterm infant:
PVL in preterm infants is caused by a combination of the immaturity of deep cerebral arteries that are easily damaged, impaired autoregulation and a predilection of immature oligodendrocytes to ischaemia (Volpe 2001; Volpe 2009). Preterm babies are at risk of sustaining a germinal matrix haemorrhage, the rupture of immature blood vessels. When this rupture occurs within the lateral ventricles it is known as intraventricular haemorrhage (IVH) (du Plessis 2004). Preterm babies are also at risk of periventricular venous infarction, the common and distinct cause of presumed perinatal ischaemic strokes (Takanashi et al. 2005; Kirton et al. 2008). These can result in motor developmental delay with hypotonia or more severe forms of CP (Kirton et al. 2010). PVL and IVH can occur together (Rosenbaum & Rosenbloom 2012). Poor autoregulation of cerebral blood flow can result in the cerebral circulation being pressure-passive, that is the system does not compensate as well for changes in blood pressure. This means that increases in pressure may rupture small vessels. Fluctuations in perfusion pressure may cause repeated ischemia in the arterial end-zones or the periventricular white matter (du Plessis 2004). In vitro studies have also shown

that in the preterm stage the immature oligodendrocytes are vulnerable to ischaemia resulting poor development of myelin (i.e. leukomalacia) (Volpe 2001).

CP of perinatal origin in term-born infants:
CP can also develop during the perinatal period of term-born infants, usually either by hypoxic-ischaemic injury or perinatal stroke (Nelson 2007; Martinez-Biarge et al. 2010). Hypoxic-ischaemic injury occurs when there is perfusion failure which affects the cerebral hemispheres. Perinatal stroke happens when there is an occlusion of a major cerebral blood vessel, most commonly the left middle cerebral artery. This is usually as a consequence of embolism from a remote site or by thrombosis (Kirton & deVeber 2009). The clinical picture is typically a hemiplegia (Boardman et al. 2005). These infants are at an increased risk of epilepsy, behavioural disturbances and cognitive impairment (Lee et al. 2005; Lynch 2009).

Cerebral insults in the term and postnatal infant:
The principle cerebrovascular lesions in the term infant result from global hypoxia-perfusion insults to the entire brain and focal infarction following embolic occlusion of a cerebral artery (Johnston et al. 2001). Postnatal causes of CP can include bacterial infection, particularly meningitis and inflammatory disorders (Rosenbaum & Rosenbloom 2012).

In summary there are many different causes of CP and symptoms may reflect the combined effects of more than one lesion (Stanley et al. 2000).

Diagnosis and classification of cerebral palsy
CP is termed a disorder as its underlying biological causes vary, as opposed to a disease that has known detectable markers. This can make diagnosis a difficult and lengthy process as there is no single test that can rule out or confirm CP. Therefore, because there is no biological marker or stereotyped syndromic pattern, the diagnosis and classification of CP is mainly phenomenological (Rosenbaum & Rosenbloom 2012). Monitoring the child for the key developmental stages helps with the diagnosis process; key milestones include height and weight, testing their reflexes and monitoring the development of their posture and movement (Krigger 2006; Stevenson et al. 2006). Diagnosis for those with spastic diplegia (see below) tends to be made at 18 months (Rosenbaum et al. 2007), however other forms of CP can be diagnosed soon after birth or much later once the brain is more developed between two and three years of age (Sankar & Mundkur 2005).

There are several ways in which CP may be classified such as according to the topography of symptoms (Table 1.1) and the predominant motor impairment (Table 1.2). Often the topography and symptom classifications are combined; for example a child may be classified as having a spastic diplegia.

Topography	Definition
Hemiplegia	Half (one side) of the body is mainly affected
Diplegia	The lower limbs are more affected than upper limbs
Quadriplegia	The lower and upper limbs (and trunk) are affected

Table 1.1: Definition of CP based on symptom topography

Symptom	Definition
Spastic	This occurs in 70-80% of cases. People present with hypertonia associated with damage to the corticospinal (pyramidal) tract and / or motor cortex
Dyskinetic/ Athetoid	This occurs in 10-20% of cases. People present with involuntary movements and fluctuating muscle tone associated with basal ganglia (extrapyramidal) dysfunction
Ataxic	This occurs in ~10% of cases and results in incoordination of movement and tremor due to dysfunction of the cerebellum

Table 1.2: Definition of CP based on the main motor deficit (Krägeloh-Mann & Cans 2009)

The most common way of defining symptom severity is according to the Gross Motor Function Classification System (GMFCS) (Appendix 1). This assesses self-initiated functional movement with an emphasis on sitting, transfers and mobility. People are classified between levels I – V depending on their ability. As functional ability varies with age the criteria for each level varies from <2 years; 2-4 years; 4-6 years; 6-12 years and 12-18 years. For example, children >6 years old who are able to walk short distances with/without a mobility aid such as a walker or crutches will have a classification between I-III.

This current work focuses on children and adults with CP who have spastic diplegia with minimal upper limb involvement with a GMFCS I-III. The main symptoms seen in children with spastic diplegia will be described in the next section with an emphasis on those that affect walking and balance.

Clinical presentation of cerebral palsy

People with CP can have difficulties with functional tasks such as walking and climbing stairs (Scholtes et al. 2012). The World Health Organisation (WHO) developed the International Classification of Functioning, Disability and Health (ICF) (WHO 2001) which is a tool that provides a framework for describing and organising information on functioning and disability.

It looks at the individuals' health conditions and personal and environmental factors as a dynamic interaction with their level of functioning. Therefore, although the emphasis of the following sections is on the impairment(s) that can lead to functional difficulties in agreement with the ICF classification, it is acknowledged that the cause of deficits in functional ability and participation in CP are often multifaceted.

Motor control deficits: The upper motor neuron syndrome

An upper motor neuron syndrome occurs after some damage to the descending and/or ascending central nervous system pathways (Stevenson & Marsden 2006). An upper motor neuron lesion in either the brain or spinal cord results in positive and negative features. The positive features are those which increase or enhance muscle activity such as; spasticity, co-contraction, clonus, brisk tendon reflexes and involuntary movements. Negative features include weakness and reduced postural responses (Tilton & Graham 2014). The site of the lesion rather than the pathology determines the combination of positive and negative features (Stevenson & Marsden 2006).

Children with a spastic diplegia have an upper motor neuron lesion (Lee et al. 2011) and show at least some of the features or impairments outlined above. In this context "spastic" is used to describe a constellation of features or impairments. Spastic clinical features occur in 70-80% of pwCP (Krigger 2006) and are the focus of this current work. The following section will describe the main features/impairments that are seen in spastic diplegia which may affect functional ability.

1. Spasticity

Spasticity is a neurological impairment resulting from abnormal central nervous system control over skeletal muscle (Lieber et al. 2004). In 1980 Lance proposed a definition for spasticity;

> *'Spasticity is a motor disorder characterized by a velocity-dependent increase in tonic stretch reflexes, with exaggerated tendon jerks resulting from hyperexcitability of the stretch reflex, as one component of the upper motorneuron syndrome'.*

(Lance 1980)

This definition is well-known and is still widely referenced, however, more recently an alternative broader definition which encompasses excessive muscle activity that is not solely caused by an enhanced stretch reflex has been provided:

> *'Spasticity – disordered sensorimotor control, resulting from an upper motor neurone lesion, presenting as intermittent or sustained involuntary activation of muscles'.*

(Pandyan et al. 2005)

The latter definition allows an inclusion of clinical phenomena such as spastic dystonia; ongoing muscle activity at rest. However, the breadth of definition means that it is difficult to quantify. For this reason the definition of spasticity put forward by Lance (1980) will be used in this thesis.

Spasticity is caused by a loss of post- and pre-synaptic inhibition of the stretch reflex and alterations in motor neuron properties, such that the muscle becomes overactive when stretched (Dietz & Sinkjaer 2007). The descending parapyramidal pathways, particularly the dorsal reticulospinal tract, are important in activating inhibitory pathways within the spinal cord such as those mediating reciprocal inhibition and presynaptic inhibition (Stevenson & Marsden 2006). A lesion below the reticular and vestibular nuclei produces spinal spasticity, which is characterised by increased tone, or spasticity, with the tendency to flexor spasms and a flexed posture (Brown 1994). A lesion above the reticular and vestibular nuclei (cerebral lesion) often causes a lesser degree of spasticity than lower lesions, but the altered activity of the vestibular nucleus due to the loss of inhibitory influence from the cortex commonly results in extensor posturing in the lower limbs (Peacock 2004). The level and type of impairment is determined by the extent and location of the lesion (Burridge et al. 2005).

The exact lesions to descending pathways that result in spasticity in humans is unclear (Nielsen et al. 2007). Although damage to descending pathways seems necessary to elicit spasticity it is not sufficient. Spasticity tends to develop over time following a lesion suggesting the development of adaptive/plastic changes (Thompson et al. 2005). More recently adaptive changes in motor neuron properties have been reported in animal models and people with spinal spasticity resulting in prolonged responses, termed plateau potentials, to incoming afferent stimulation (Bennett et al. 2001). These changes may be associated with lesions to descending serotonergic pathways from the raphe nuclei to the spinal cord which normally modulate motor neuron properties (Bennett et al. 2001; Dentel et al. 2013). Additional adaptive increases may also occur in the effectiveness of the Ia afferent-motor neuron synapse leading to reduced post-activation depression (Nielsen et al. 2007). Post-activation depression is the decrease in response with repetitive afferent stimulation. With reduced post-activation depression this decrement does not occur resulting in a sustained response. The reduction in post activation depression correlates with clinical measures of spasticity (Achache et al. 2010).

The mechanisms of spasticity in humans have mainly been elucidated in adults with acquired diseases (e.g. stroke and spinal cord injury). Different disorders and diseases may have different causes of spasticity. In adults with stroke, for example, reduced reciprocal

inhibition in the spinal cord between antagonist and agonist muscles is commonly reported but is normal in adults with CP (Achache et al. 2010). This suggests that a central nervous system lesion acquired during development may have different effects from those acquired as an adult. Clearly more work needs to be performed looking at people with similar lesion locations at different developmental time points and the impact this has on the cause of spasticity and ultimately its treatment.

The increased muscle tone produced by spasticity will lead to an increase in the stiffness of a limb and interfere with movement (Peacock 2004). Spasticity in a growing child is felt to contribute to the development of secondary impairments such as muscle contractures and bony deformity (Dudley et al. 2013). Spasticity may however aid stability and people can use the support it generates to aid anti-gravity activity and walking. Therefore in some cases spasticity could be considered to be a compensation for weakness.

A guideline development group have produced a summary of the National Institute for Health and Clinical Excellence (NICE) guidelines regarding spasticity among children and young people. The areas of focus comprised of; principles of care, physical therapy, orthoses, oral drugs, botulinum toxin type A, intrathecal baclofen, orthopaedic surgery and selective dorsal rhizotomy. Thus covering all of the possible management options (Mugglestone et al. 2012).

2. Co-contraction

Co-contraction occurs when agonist and antagonist muscles contract simultaneously around a joint causing it to hold a certain position (Lewis et al. 2011). This can happen normally to stabilise joints and is more prevalent in the early stages of learning new motor skills (Osu et al. 2002). When co-contraction is excessive and relatively constant it is considered to be a pathological sign.

Muscle co-contraction can occur in the UMN syndrome and interferes with function by making the muscles appear weaker than they are, due to the increased resistance from the antagonist muscle, or by reducing dexterity and co-ordination (Stevenson & Marsden 2006; Pierce et al. 2008). In cases where co-contraction occurs with rapid or rapidly alternating movements the underlying cause of the co-contraction could be a stretch-evoked contraction of the antagonist muscle (Nielsen & Kagamiharat 1992; Morita et al. 2001). Co-contraction can also take place in the absence of activation of the stretch reflex or any muscle stretch i.e. during an isometric contraction. In these cases people with spasticity have an excitatory response at the beginning of a contraction as opposed to the normal relaxation of the antagonist muscle (via reciprocal inhibition) seen in those without spasticity (Nielsen & Kagamiharat 1992; Morita et al. 2001). This excitatory response causes an agonist-antagonist co-contraction. Therefore, the presence of co-contraction could be the result of

the abnormalities (impaired spinal inhibitory pathways) that also lead to increased stretch reflexes (Stevenson & Marsden 2006).

Muscle co-contraction during active movements and during gait have been investigated (Pierce et al. 2008), for example hamstring/quadriceps co-contraction can cause a flexed SKG (Rodda & Graham 2001). The development and change of co-contraction over the course of time has been investigated by comparing the joint movement and electromyography (EMG) patterns of infants both with and without CP (Leonard et al. 1991). To begin with, during supported walking, the patterns of co-contraction and accompanying joint synchronies were similar between both groups. Over time the children with CP retained the pattern of co-contraction during unsupported walking. In contrast the unsupported walking of children without CP eventually developed to show less co-contraction and more "fluid patterns" characterised by physiological joint asynchrony (Leonard et al. 1991).

The degree of co-contraction in CP seems to vary with the clinical presentation. Patients with dystonia have an increased resistance to external motion at slow velocities and a greater degree of co-contraction (Lebiedowska et al. 2004; Sanger et al. 2003). Lebiedowska et al. (2004) compared the degrees of co-contraction between those with dystonia and those with spasticity. They found that those with dystonia had greater co-contraction of antagonist muscles during both isometric flexion and extension. It was hypothesised that the reduction in strength in dystonia may be due to supraspinal-mediated co-contraction rather than a co-contraction of spastic origin (i.e. arising through a stretch-evoked contraction of the antagonist muscle) (Lebiedowska et al. 2004). This in turn may lead to slower walking speeds and reduced range of motion at the knee during stance phase of walking (Lebiedowska et al. 2004).

Although co-contraction is frequently present in pwCP (Pierce et al. 2008; Gross et al. 2013) it may not be detrimental or a pathological action, instead it could actually be an intentional compensation. For example, knee extensors and knee flexors contracting simultaneously could be compensating for hip extensor weakness (Frigo et al. 2010). Therefore, it is important to not only highlight the presence of co-contraction but to try to understand its underlying functional significance.

3. Weakness

Muscle weakness in pwCP is a primary clinical feature of the disorder and occurs as a result of impaired cortical innervation of descending pathways caused by a non-progressive lesion in the brain, which results in secondary adaptations in the muscle (Hussain et al. 2014). The term 'cerebral palsy' means weakness originating from the brain and the suffix 'plegia' used in clinical descriptions describes the anatomic distribution of weakness e.g. diplegia and

hemiplegia (Damiano et al. 2001). Several studies have shown pwCP to have deficient strength (Damiano et al. 1995; Engsberg et al. 1998; Wiley & Damiano 1998) and this relates directly to physical performance (Kramer & MacPhail 1994; Damiano & Abel 1998). Damiano and Abel (1998) found that stronger ambulatory pwCP showed greater performance on the GMFCS, required less ambulatory assistance, walked faster and had an enhanced ability to increase walking speed. Even children with mild diplegic CP have, on comparison with controls, been found to have significant lower limb weakness (Thompson et al. 2011). Specific patterns of walking may also be related to muscle weakness. Wu et al (2011) found that a reduction in plantarflexor moments in children with CP was associated with crouch gait (excessive flexion of hips and knees). This thesis will explore whether muscle weakness contributes to another pattern of walking seen in CP, namely SKG.

The precise aetiology of muscle weakness is a subject of on-going investigation; understanding this is important as it will have direct implications for intervention strategies (Damiano et al. 2001). There are numerous theories reported for the mechanism of muscle weakness in pwCP, however weakness most likely results from multiple factors (Rose & McGill 1998). The most reported possibilities include;

(a) A central deficit in volitional agonist activation (Leonard et al. 1990; Elder et al. 2003; Rose & McGill 2005; Stackhouse et al. 2005; Hussain et al. 2014) caused by damage to motor pathways. Damage to the corticospinal tract, as determined by diffusion tensor imaging for example, is correlated with the degree of muscle weakness in pwCP (Lee et al. 2011).

(b) Agonist-antagonist co-contraction (Ikeda et al. 1998; Elder et al. 2003; Stackhouse et al. 2005; Tedroff et al. 2008; Hussain et al. 2014) (see co-contraction section above).

(c) Spasticity: Spasticity is often reported as a possible cause for muscle weakness (Ross & Engsberg 2002). There are several conflicting assumptions within the literature concerning the relation between strength and spasticity within a single muscle group. Several authors believe a spastic muscle to be a strong muscle and that weakness in antagonist muscle groups is caused by spasticity (Reimers 1990a; Reimers 1990b; Thomas et al. 1996). However, there is some literature highlighting that the spastic muscle is weak and that the amount of damage to the pyramidal tracts or the amount of spasticity affects the amount of weakness present (Rab 1992). In contrast no relation between strength and spasticity was reported by Ross and Engsberg (2002).They found that not all of the pwCP within their study had spasticity present yet muscle weakness remained a consistent finding (Ross & Engsberg 2002). Therefore, muscle weakness might be a fundamental impairment for pwCP, and not directly related to spasticity as originally thought. Ross and Engsberg (2002)

suggest the treatment focus for pwCP should be muscle strengthening as this was felt to be the fundamental deficit.

(d) Secondary muscle atrophy and changes in muscle morphology (Ito et al. 1996; Friden & Lieber 2003; Barber et al. 2012). Histological changes in muscle fibres (Dietz & Berger 1995) such as reduced muscle volume/physiological cross sectional area (Barber et al. 2011), reduced muscle fibre diameter and corresponding contraction of the aponeurosis (Shortland et al. 2002; Malaiya et al. 2007; Hussain et al. 2014) have been described. Spastic muscles tend to have shorter muscle fibres, and an increased variability in fibre size (Foran et al. 2005). Longer muscle fibres can provide larger operating ranges, making muscle fibre length an important determinant of functional ability. Therefore pwCP who have short muscle fibres have a decreased range of motion i.e. contracture (Lieber & Bodine-Fowler 1993).

(e) Changes in muscle fibre type and contractile protein content. Myosin is a contractile motor protein comprised of light and heavy chains; it forms cross bridges with actin and conformational changes in the myosin head produces relative motion of the proteins that underlies a muscle contraction (Jones et al. 2005). The type of myosin heavy chain (MyHC) present determines the speed and force of contraction of individual muscle fibres (Bottinelli et al. 1991; Pette & Staron 2000). Different MyHC expressions can be altered by changes in the neuromuscular activity and the mechanical load of the muscle (Pette & Staron 2000). The expression of MyHCs can also be affected by the severity of the CP (Pontén et al. 2005). Furthermore, changes have been observed in the muscle fibres as a result of other upper motor neuron lesions. It appears the normal matching between type and fibre is lost (Friden & Lieber 2003). The muscle fibre types change from the slow to fast phenotype in CP (Pontén et al. 2007). This reduces the ability to produce a prolonged, sustained contraction, as usually observed during postural maintenance, as the fibres are now less fatigue resistant.

(f) Lever arm dysfunction: Limb movement is produced by the relative movement of limb segments about an axis of rotation (Gage 2004a). Limb motion is produced by a torque which is the product of the force generated by the muscle and the perpendicular distance from the line of pull of the muscle to the joint axis (the lever arm) (Gage & Schwartz 2004). Therefore, a reduction in the lever arm can reduce the torque generated for a given muscle contraction, this is termed lever arm dysfunction (Gage & Schwartz 2004). Reductions in the lever arm may arise with bony deformity which is common in CP (see bone mass and deformity section below). Modelling studies, for example, have shown that tibial torsion reduces the capacity of the muscles which extend the hip and knee and can contribute to a crouch gait (Hicks et al. 2007).

4. Passive stiffness and contracture

Passive stiffness and joint contractures are two complications that often develop secondary to upper motor neuron lesions. As highlighted below research carried out within this field, is often conflicting and has generated yet more questions and highlighted the lack of understanding of these secondary changes that occur within muscle (Pontén et al. 2007). Further work is very much required because the greater our understanding of these changes, the more appropriate the rehabilitation prescription process can be.

Clinical presentation

When muscles are left immobile in a shortened state for prolonged periods of time due to limb weakness, a lack of passive movement and /or incorrect positioning then changes can develop in the muscles, tendons and ligaments. The changes can lead to a loss of passive range at joints, termed contracture, and an increase in the resistance to passive movement that is not associated with a change in muscle activation, termed passive stiffness (Sinkjaer 1997; Stevenson & Marsden 2006). The term passive stiffness is therefore used to distinguish between stiffness caused by other mechanisms such as spasticity or co-contraction, both of which involve muscle contraction.

Contractures can often be painful and they limit patient function because they reduce the range of motion possible. Prevention of contracture development is important as the management of established contractures is difficult and can even require surgery (Karol 2004; Stevenson & Marsden 2006). Prior to any surgical intervention a range of appropriate conservative treatments are often utilised, these include physiotherapy, splinting and electrical stimulation (Friden & Lieber 2003).

Changes occurring in the muscle with CP contributing to contracture and increased passive stiffness

In 2003 it was highlighted that within muscle cells obtained from biopsy in patients with CP and spasticity there are alterations to the structures responsible for passive load bearing and setting of the resting sarcomere length compared to healthy muscles. The spastic muscle cells had reduced resting sarcomere length (i.e. was shorter) and almost double the elastic modulus (i.e. was stiffer) compared to normal cells (Friden & Lieber 2003). The development of contracture could, theoretically, be accounted for by a shorter sarcomere length and in keeping with this Pontén et al (2007) reported that sarcomere length was shorter than normal and that there was a high correlation between sarcomere length and the degree of contracture (Pontén et al. 2007).

Although other works (Tardieu et al. 1982; Elder et al. 2003; Rose & McGill 2005; Stackhouse et al. 2005; Mohagheghi et al. 2008; Pontén et al. 2007) agree that spastic

muscles overall are shorter compared to non-spastic muscles, there are conflicting findings with regards to the sarcomere length (Smith et al. 2011; Pontén et al. 2007). More recently issues with earlier studies by Leiber's group including the differences in the muscles assessed in pwCP and healthy participants and standardisation of the muscle length when a biopsy has been taken have been addressed (Smith et al. 2011). This study compared semitendinosus muscles in pwCP and healthy children undergoing surgery for knee ligament repair. Biopsies were taken with the muscle at a standardised length allowing a direct comparison of resting sarcomere length using laser diffraction. Smith et al (2011) confirmed that the whole muscle fibre was stiffer and shorter than normal in pwCP. However, they found that the sarcomere length was significantly *longer* than the control values. Therefore, it was concluded that shortening of muscle fibres is the result of a reduction of the *number* of sarcomeres in series rather than a reduction in *individual sarcomere length* (Smith et al. 2011).

The observed increase in sarcomere length has several implications. Muscle will not be able to generate as much force if there is only a very short overlap of myosin and actin filaments as the sarcomeres will be stretched out; i.e. the muscle is on the descending arm of the length-tension relationship which is normally an inverted U shape (Pontén 2008). This theoretically could be another cause of muscle weakness. However, we do not know where on the length-tension relationship muscles are in pwCP, it could be that an increase in sarcomere length is beneficial and increases the muscles' force generating capabilities if it is on the ascending limb of the length-tension relationship. As well as possibly affecting force generating capabilities an increase in sarcomere length will also lead to higher passive stresses (Smith et al. 2011) as the increase in resistance to movement is not linear with greater increases being seen as the sarcomere is lengthened i.e. at a given overall muscle length the sarcomeres will be more stretched in pwCP and produce a greater resistance to subsequent movement.

Changes occurring within the extracellular and intracellular proteins
Another change observed amongst people with spasticity is an increase in the total content of the extracellular matrix proteins such as collagen (Smith et al. 2011). The severity of the UMN syndrome has been correlated with this finding (Pontén 2008; Booth et al. 2001). Collagen is the most abundant extracellular matrix protein within connective tissue which envelops muscle within the endo- peri- and epi-mysium (Turrina et al. 2013). Collagen is formed in a dense network within muscle, it arranges around fibres and bundles of fibres. It has a significant role in force transmission between the external tendon and muscle fibres and is a source of passive elasticity in muscle (Friden & Lieber 2003).

Titin is another protein that may potentially contribute to contracture and increased passive stiffness (Rassier et al. 2005). Titin is a giant structural intramuscular protein. It connects the z lines to the myosin filaments and largely determines passive muscle fibre tension i.e. when the muscle fibre is assessed without any surrounding connective tissue; a "skinned preparation" (Rassier et al. 2005). Titin plays a role in signalling stresses that a muscle fibre is subjected to; these signals in turn are felt to result in adaptive changes within the muscle (Pontén 2008). Although changes in titin could theoretically contribute to increased passive stiffness muscle, biopsies of people with spinal cord injury and spasticity (Olsson et al. 2006) and more recently pwCP (Smith et al. 2011) have found no change in titin content.

In summary, in comparison to normal muscles, spastic muscles tend to have shorter and stiffer fibres comprising of faster and more fatigable myosin filaments, increased connective tissue and small muscle bellies. These changes are due to altered neuromuscular signalling and immobilisation. Muscle is an adaptive tissue so it is thought that these changes can be influenced by activity such as stretching or muscle contraction. Whether the use of passive and active movements of the limb have a differing effect on adaptive muscle changes in pwCP and health participants is currently unknown (Pontén 2008).

5. Bone mass and deformity

Young people who have disabilities that limit mobility are at greater risk for osteoporosis, osteopenia and fracture (King et al. 2003; Krigger 2006). CP has varying effects upon mobility and is a predictor of skeletal and muscular compromise (Aronson & Stevenson 2012). Healthy bone mass production is critically important during the early years of life, up to and including the adolescent years. If the production is compromised during this period, for example due to CP, the risk factor for fractures is increased. In order to help prevent fractures, focus should be put on optimising bone density (Aronson & Stevenson 2012). Inactivity, immobilisation and poor nutrition are factors which lead to decreased bone mass in pwCP (King et al. 2003; Chen et al. 2011). Osteopenia in pwCP is considered a growth failure, as opposed to degeneration as it is within the elderly population (Henderson et al. 2005).

In addition to the above mentioned alterations to bone density and mass, further changes can develop. Bone growth is dependent on the size and direction of forces applied to the bone (Wolff's law) (Frost 1994). Muscle contracture, spasticity and altered forces associated with differences in weight-bearing posture and mobility can cause changes in the bone growth and bony deformity in pwCP. Among this population progressive bone and joint radiographic findings are found, they commonly occur as scoliosis and torsion deformities of the hips, knees and feet (Morrell et al. 2002). Recognising progressive deformity during early

stages of development will allow for timely treatment and help prevent irreversible change (Morrell et al. 2002). The majority of these deformities are rotational and treatment can include invasive surgery. An example is tibial torsion, a rotational deformity about the long axis of the tibia (Hicks et al. 2007). There is a relationship between excessive tibial torsion and crouch gait, as they are commonly present together among this population. It is thought the reduced capacity of the muscles which extend the hip and knee, resulting from tibial torsion, are a significant precursor for crouch gait (Hicks et al. 2007).

Femoral anteversion is a term used to describe abnormal internal rotation of the femur, resulting from the head and neck of the femur being angled forward in excess of 15 degrees (Cibulka 2004). Excessive femoral anteversion has been reported to be a major contributor to hip dislocation in pwCP (Laplaza et al. 1993). Abnormal tibial torsion and abnormal femoral anteversion combined are known to cause rotational gait problems and for this reason are typically focused on during treatment and evaluation in clinical practice (Lee et al. 2013). To achieve realignment surgically, rotational osteotomies of the tibia and fibula can be performed.

6. Sensory deficits

In addition to changes of muscles, bones and joints, CP can affect sensory processing as well. Young pwCP can have altered kinaesthetic, tactile and proprioceptive awareness (Van de Winckel et al. 2013). In a study comparing joint-position sense and kinesthesia without vision between a group of pwCP (diplegia and hemiplegia) and a group of age matched controls, it was found that the group of pwCP had proprioception deficits in all limbs apart from the dominant upper extremity (Wingert et al. 2009). In pwCP the *non-dominant* upper limb joint-position sense error magnitude was more than double than that of the controls and there was a three-fold greater error magnitude in the lower limbs compared to the control group. The study concluded that CP leads to varied somatosensory discrepancies and pwCP have proprioception deficits in all of their limbs. This suggests that enhancing vision for pwCP should be a critical part of rehabilitation and once accurate perceptions of body movements have been mastered then skills should be trained without vision (Wingert et al. 2009).

The sensory deficits are felt to be caused by either abnormal organisation or diminished activation of the somatosensory cortex. When compared to aged matched controls, children with spastic diplegic CP demonstrated less response in the somatosensory cortices to foot stimulation when measured using magnetoencephalography (Kurz & Wilson 2011). This is thought to be related to the severity of the injury to the thalamocortical pathways (Hoon et al. 2009; Kurz & Wilson 2011). Interestingly Hoon et al (2009) also found that functional deficits

in pwCP were related to the degree of sensory dysfunction rather than to motor impairment. Somatosensory responsiveness and organisation could possibly be improved among children with CP by utilising sensory-retraining programmes, adapted from previous successful ones used with adults. Encouraging these neurophysiological changes may enhance motor control and capacity to learn new motor skills (Kurz & Wilson 2011).

Walking and gait in cerebral palsy

Walking or gait is characterised by cyclic motion of the legs due to a repetitive pattern of angular joint motions. Walking has been defined as 'a method of locomotion involving the use of the two legs, alternately, to provide both support and propulsion with at least one foot being in contact with the ground at all times' (Whittle 2012). As opposed to the walking process, gait is defined as 'the manner or style of walking' (Whittle 2012). Due to the cyclic motion of the legs walking can be divided into cycles, phases and sub-phases that repeat themselves, this process is known as the gait cycle.

Walking comprises of two phases, stance phase and swing phase, lasting approximately 60% and 40% of the gait cycle respectively. Stance phase refers to the period when the foot is in contact with the ground, from heel strike to toe off of the same leg. Swing phase describes the time when the foot is travelling forwards off the ground, lasting from toe off until heel strike (Figure 1.1). A complete cycle (100%) usually commences when one foot strikes the ground (initial contact) and finishes when the same foot strikes the ground again (Gage 2004a).
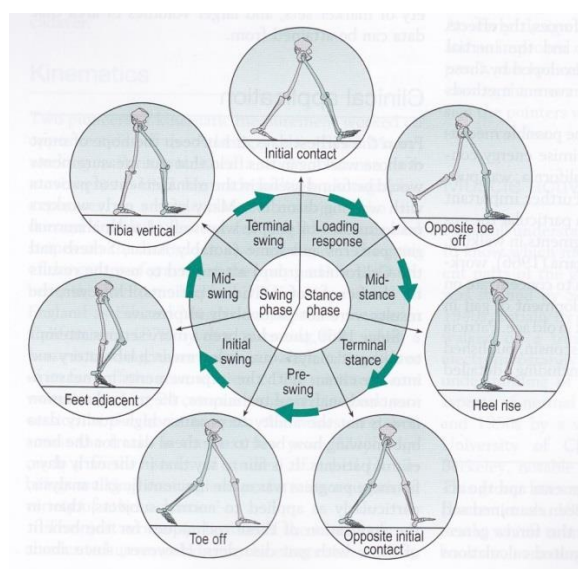
Figure 1.1: Taken from (Whittle 2012) *'positions of the legs during a single gait cycle by the right leg'*

Phases of the gait cycle:

To describe the events that occur during stance and swing phase, the sub-phases will be explained individually. Stance phase is sub-divided into; initial contact, loading response, mid-stance, terminal stance and pre-swing. Swing phase is subdivided into; initial swing, mid-swing and terminal-swing. In broad terms stance phase involves weight acceptance and single limb support and swing phase achieves limb advancement (Perry & Burnfield 2010). Initial contact is the instant one foot makes contact with the ground, also known referred to as heel strike. Loading response is the sub-phase where shock absorption of the impact and deceleration occurs. During mid-stance one foot is on the ground, this sub-phase lasts from opposite toe off to heel rise of the stance leg. Terminal stance lasts from heel rise of stance leg until initial contact of opposite leg. The final event of stance phase is pre-swing, here both legs are in contact with the ground and it occurs from opposite initial contact to toe off of the stance leg. During this sub-phase ankle plantarflexion generates power that helps to propel the body forwards. Initial swing is the first sub-phase of the swing phase, it is the period from toe off to the point at which the feet become adjacent. Mid-swing occurs from time the feet are adjacent to when the tibia of the swinging leg is vertical. The final period of swing phase is terminal swing which lasts from tibia vertical until the next initial contact (Gage 2004a).

Throughout the gait cycle there are periods of double support (when both feet are in contact with the ground at the same time) and single support (when only one foot is in contact with the ground at that time). There are two occurrences of double support within one cycle, between initial contact of one foot and toe off of the opposite foot. Single support occurs when one leg is in contact with the ground whilst the other leg is in swing phase (Figure 1.2) (Whittle 2012).
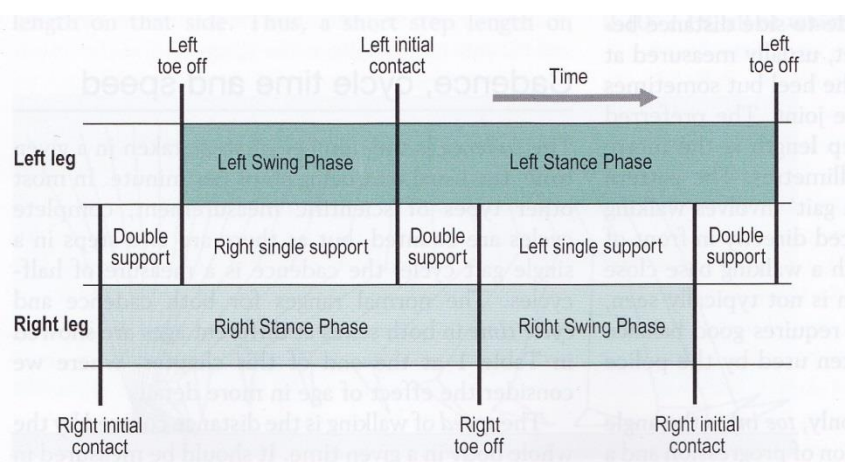
Figure 1.2: Taken from (Whittle 2012) *'timing of single and double support during a little more than one gait cycle, starting with right initial contact'*

Investigating gait in health and disease

There are several methods that have been used to describe and investigate walking in both healthy participants and those with neuromuscular impairment. These will be referred to throughout this thesis.

The pattern of walking can be described following observational analysis. Tools such as the Salford Gait Tool (SF-GT), which is used in the current study, have been developed to aid this. Difficulties with parallax error and in defining events that occur quickly are possible disadvantages with this method. Potentially a more accurate way of recording the movement of joints during walking, termed kinematics, is to use a form of three dimensional (3D) motion analysis. This involves hardware and software that measures the movement of markers placed on standardised landmarks on the limbs.

The addition of force plates can record the amplitude and direction of the ground reaction force as the leg is in contact with the ground. Through a process called inverse dynamics the moments acting at each joint can be estimated. This is termed joint kinetics and requires additional anthropometric data that help to describe the size and centre of mass of limb segments. Joint moments can either be described as external moments representing the effect of the ground reaction force on the joint or internal moments representing the actions of the muscles acting on the joint (Whittle 2003). This thesis will refer to internal moments; these give an indication of what muscles are doing. However, they only describe the net moment and do not describe the cause of a moment. Therefore, if there is co-contraction only the net effect will be measured. Further, the net moment could be caused by passive tension of a muscle or muscle contraction (Whittlesey & Robertson 2004). This in turn could be caused by a stretch reflex or a volitional contraction. Another potential disadvantage with using inverse dynamics when working with people with bony abnormalities is that the anthropometric data used to calculate joint kinetics is derived from cadavers of healthy participants. In people with bony abnormalities the anthropometric data may be inaccurate and result in errors in the estimation of joint kinematics.

To help understand what causes net moments derived using inverse dynamics surface EMG can be applied to lower limb muscles. EMG measures the electrical activity associated with a muscle contraction. To record deep muscles (e.g. tibialis posterior) fine wire electrodes may be inserted within the muscle (Sutherland 2001; Bogey et al. 2003; Murley et al. 2009).

More recently walking has been investigated by using modelling studies (Fonseca et al. 2001; Arnold & Delp 2005; Damiano et al. 2010). As the name suggests the musculoskeletal system and the timing and size of muscle activation are modelled. For example, limb segment lengths, inertia and the associated muscle attachments are defined a priori. Thus a

virtual, computer generated pair of legs are created which, when activated with appropriately timed signals, will produce rhythmic activity. The accuracy of the model in describing walking is then determined by comparing the results of the model with normal data. The advantage of this modelling technique is that once a valid model is produced it is possible to look at the effects of altering one variable. Thus, groups have looked at the effects of producing bony torsion or reducing the activation ("strength") of muscles (Schwartz & Lakin 2003; Hicks et al. 2008). Therefore, modelling studies of walking can help us to understand the relative role of different structures. The disadvantage of this method is that it is difficult to accurately model people with disability due to a series of unknown variables such as the length, stiffness and relative strength of muscles and the conformation of bones.

Gait in cerebral palsy

Differences in patterns of walking often exist between pwCP and typically developing children (TDC). These can be seen by plotting graphs of kinematics and kinetics for both groups together along with indications of the variability within each group. Kinematics describes motion of the legs without regards to its causes whilst kinetics is concerned with the effect of forces and torques on the motion of bodies.

Some of the group differences in kinematics are due to differences in walking speed. Thus it is important to take differences in walking speed into account when comparing groups. This is often addressed by normalising the gait cycle to 100%. Usually, as previously mentioned, stance phase lasts for the first ~60% of the gait cycle. However, pwCP can have longer durations of stance phase and an increase in double support time when both legs are on the ground (Brégou Bourgeois et al. 2014). Therefore in the current study we will account for differences in walking speed in the analysis by using an analysis of covariance. People with spastic diplegia can present with several different patterns of walking as described in Table 1.3 below.

Walking Pattern	Characteristic
Stiff knee Gait	Delayed and/or reduced peak flexion in swing phase
Crouch Gait	Greater than 30 degrees knee flexion in stance phase
Equinus Gait	Toe walking
Jump Gait	Excessive knee flexion at initial contact followed by extension later in stance

Table 1.3: Some walking patterns described for spastic diplegia (Carriero et al. 2009)

These walking patterns were initially descriptions of patterns identified through clinical experience (Sutherland et al. 1990). Other groups have provided alternative classifications based on 3D motion analysis (Hullin et al. 1996). More recently the walking styles of people with spastic diplegia were classified using statistical clustering techniques, such as principle component analysis (PCA) that classified groups of pwCP based on kinematic and temporal gait data. Using this approach Toro et al. (2007a) classified gait of pwCP into 3 main types "crouch", "equinus" and "other" (Toro et al. 2007a). Carriero et al. (2009) used a combined PCA and cluster analysis technique that divided pwCP from TDC. CP subgroups with equinus pattern, jump knee, crouch gait and stiff knee were defined as well as an additional 6 subgroups with abnormalities in the coronal and transverse planes. With this analysis pwCP could belong to several groups at once, for example ~70% of people with SKG also had either jump, equinus or crouch gait characteristics. Therefore, recent quantitative analysis techniques provide some support for the qualitative classifications commonly used.

Although these qualitative and statistical classifications have been used to direct treatment interventions (Rodda & Graham 2001), they do not inform the clinician about the underlying cause of the abnormal walking patterns. This study will look at impairments associated with one aspect of walking, namely SKG.

Stiff knee gait in cerebral palsy
Many pwCP walk with a SKG, it is characterised by reduced knee flexion amplitude during the swing phase of the gait cycle. SKG is associated with reduced walking speeds in pwCP (Carriero et al. 2009) and is clinically associated with an increased incidence of tripping and falls. Over time mid-stance knee flexion, range of knee flexion, peak knee extension in

stance and hamstring length all deteriorate among children with CP, yet maximum and mean hip rotation improve (Rose et al. 2010).

Previous studies have proposed a number of possible causes of reduced knee flexion amplitude during swing phase. Early work concentrated on the role of the rectus femoris muscle, an extensor of the knee, during swing phase (Waters et al. 1979; Perry 1987; Sutherland et al. 1990). Here a SKG was attributed to inappropriately timed activity in rectus femoris caused by a stretch reflex elicited by rapid flexion of the knee in preswing and early swing phase i.e. spasticity. This results in excessive knee extension moments in swing phase that limit flexion of the knee. To support this, rectus femoris stretch reflex activity is poorly modulated in swing phase in people with an UMN syndrome (Faist et al. 1999) and modelling studies suggest that excessive rectus femoris activity can indeed limit knee flexion (Marks et al. 2003; Kay et al. 2004; Arnold et al. 2005; Goldberg et al. 2006; Jonkers et al. 2006; Cimolin et al. 2010). Based on this theory techniques such as rectus femoris transfer, where the distal attachment of the extensor muscle is transferred to become a flexor of the knee, are undertaken with the aim of aiding knee flexion in swing phase. However, rectus femoris transfer procedures have been shown to have inconsistent outcomes with some patients showing improvements in swing phase knee flexion but others showing very little change (Goldberg et al. 2006). Cases that improved did have excessive muscle activity in early swing phase suggestive of stretch reflex activation. This study suggests that in the remaining cases other causes of SKG may be present.

Modelling studies have further shown that reduced knee flexion amplitude in swing is directly related to low knee flexion velocity at the end of stance phase (Goldberg et al. 2006). Thus, factors limiting the initial flexion of the knee (i.e. initiating swing phase) may limit subsequent swing phase knee flexion. Further, modelling studies suggest that low knee flexion velocity at the end of stance may be caused by diminished force generation during the double support phase in the iliopsoas and gastrocnemius muscles that initiate swing phase, and also to excessive forces in the knee extensors (either the rectus femoris and/or the vasti) (Piazza & Delpt 1996; Anderson et al. 2004; Goldberg et al. 2004; Arnold & Delp 2005; Goldberg et al. 2006). The excessive forces within the knee extensors may be attributed to spasticity, as described above but also to increased passive stiffness in the extensor muscle due to changes in the surrounding connective tissue and intramuscular proteins (Dietz & Berger 1983; Booth et al. 2001; Stevenson & Marsden 2006). Distinguishing between these different causes of resistance or stiffness to movement imposed by the knee extensors is clinically important as their treatment varies with spasticity being amenable to pharmacological and surgical interventions (e.g. botulinum toxin injections) and changes in passive stiffness being more amenable to physical interventions such as stretching and

surgical interventions including muscle lengthening. Thus, theoretically SKG could be caused by multiple factors including weakness in the ankle plantarflexors and hip flexors and stiffness (either stretch mediated or due to passive factors) in the knee extensors.

More recent studies have highlighted that a crouch position during stance phase is often associated with a lack of knee flexion during swing phase (van der Krogt et al. 2010). Computer simulations of walking show that a crouch position during stance phase results in altered gravitational moments about the knee leading to reduced knee flexion during swing phase. The model further shows that the effect of crouch on swing phase knee flexion is dominant over the contributions of hip flexion torque and ankle plantarflexor power generation during preswing (van der Krogt et al. 2010). Thus, recording crouch gait and understanding factors contributing to this walking pattern can inform our understanding of the pathogenesis of SKG.

As highlighted above many previous studies investigating the multiple factors associated with a SKG in pwCP have been based on mathematical models (Zajac et al. 2002; Zajac et al. 2003). Clinically based studies in contrast have often looked at the effect of only one impairment, such as muscle strength or spasticity, on walking ability (Kerrigan et al. 1991; Damiano & Abel 1998; Tuzson et al. 2003; Damiano et al. 2006; Thompson et al. 2011). Further, walking has been assessed using gross outcomes such as walking speed or the GMFCS (Goh et al. 2006; Eek & Beckung 2008; Thompson et al. 2011) and the causes of specific components of walking have not been extensively investigated in a prospective, hypothesis driven study (Ross & Engsberg 2007). This approach will be used in the current study to investigate possible contributory factors to a SKG in people with an established diagnosis of CP. The potential contributory impairments/factors assessed will be based on previous models of walking described above i.e. ankle and hip strength, knee extensor stiffness and the degree of crouch.

Understanding the factors that contribute to a SKG in pwCP will have important clinical implications, allowing interventions to be appropriately targeted to that variable in order to improve the impairment and functional walking (Damiano et al. 2010). This will help clinicians to avoid currently used treatments such as surgical rectus femoris muscle transfer and rectus femoris botulinum toxin injections in circumstances where they are likely to be ineffective or harmful. Furthermore, it will lead to more effective clinical trials of different potential interventions by allowing stratification of patients according to their primary deficit.

This study will be performed using gait analysis and laboratory based measures of neurological impairment. Although gait analysis using 3D motion analysis is often performed in the pre-surgical assessment of children with CP the laboratory based measures adopted

(e.g. dynamometry and motor-driven perturbations) are not routinely performed. Further, in clinical practice, it is expensive and sometimes difficult to obtain data from a gait laboratory. This study will therefore also investigate whether clinical measures of impairment (such as manual strength testing) and walking (observation gait analysis) affect the ability to predict factors affecting SKG. If a strong relationship between objective and clinical measures of impairment is found then reliance upon time-consuming, expensive analysis of impairments and gait could be replaced by simpler tests performed in the clinical examination room. This will ultimately save the NHS money and reduce travel to multiple assessments for the patient and family. Finally, the clinical applicability of this study is increased by including children and adults with CP who can walk regardless of the use of walking aids and medical and previous surgical management.

In summary, a review of the literature highlighted that there are multiple potential cases of SKG in pwCP. Although knee flexion amplitude can be delayed in time this aspect was not investigated in the current study. This study will assess the impact of specific impairments on knee flexion amplitude during the swing phase of gait in pwCP. Additionally, this study will compare pwCP and healthy control participants and investigate the role of knee extensor muscle strength in causing a crouch gait and SKG in pwCP. Finally, the relationship between laboratory and clinical outcome measures of neurological impairment and walking pattern will be determined.

CHAPTER 2: METHODOLOGY

Objectives

Primary objective

This study assessed the impact of five variables on knee flexion amplitude during the swing phase of gait in pwCP: i) plantarflexor strength, ii) hip flexor strength, iii) knee extensor spasticity, iv) knee extensor passive stiffness and v) degree of crouch during stance phase.

Secondary objectives

Additionally, this study

- Determined differences in kinematic and kinetic variables and neurological impairments between pwCP and healthy control participants
- Investigated the relationship between knee extensor muscle strength and the degree of crouch (knee flexion) in stance phase; a potential key determinant of SKG
- Investigated the relationship between clinical outcome measures and the degree of SKG as determined using observational gait analysis
- Investigated the relationship between laboratory and clinical outcome measures of neurological impairment.

Participants and eligibility criteria

Children and adults with a clinical diagnosis of bilateral cerebral palsy meeting the following criteria were investigated:

Inclusion criteria

(1) Signs of weakness or increased tone on clinical examination of at least one joint in the lower limbs
(2) Able to walk at least twenty metres independently with or without the need of a walking aid.

Exclusion criteria

(1) Cognitive or behavioural deficits such that the child/adult is unable to follow instructions
(2) Lower limb operation within the last year
(3) Botulinum toxin injections for a lower limb muscle in the last month.

Additionally, twenty healthy age and gender matched control participants were assessed to allow quantification of the severity of impairment and knee flexion while walking. Control participants were included if they had no history of orthopaedic and neurological conditions that affected their walking or balance.

Sample size and power calculations

Prior studies in people with Hereditary Spastic Paraparesis (HSP) found a correlation between the degree of knee flexion and stiffness of the knee flexors and strength of the ankle plantarflexors of R^2=0.37-0.39 (Marsden et al. 2012). Assuming a correlation of R^2 0.3 for at least two predictors, a sample size of 27 pwCP was required (power =0.80 significance =0.05) (Lenth 2006).

With 27 pwCP and 20 healthy controls, a power =0.8 and a significance =0.05 it is possible to detect an effect size on 0.5. Previous work comparing healthy control participants with people with HSP found the following effect sizes (Marsden et al. 2012).

Variable	Effect Size
Trough to peak knee flexion	2.74
Knee extensor total stiffness	1.76
Ankle isometric strength	1.61
Hip flexor isometric strength	1.25

Table 2.1: Effect size findings from previous work with HSP patients

Therefore, it was felt that there was sufficient power to detect differences between the pwCP and the control participants.

Recruitment

Twenty seven people (age 6 to 43 years) with a clinical diagnosis of CP were recruited from clinics of paediatricians and paediatric orthopaedic surgeons of Plymouth Hospitals Trust (Mr Jeffery, Mr Metcalfe and Mr Holroyd) and also from Plymouth child development centre, Devon. The study was briefly explained by the clinician and the parents/guardians were provided with an information sheet (Appendix 2), stamped addressed envelope and reply slip (Appendix 3) to inform the research team whether they were interested in receiving more information and/or volunteering for the study.

Additionally, pwCP on the research database of the Human Movement and Function Laboratory based at Plymouth University who had previously indicated that they would be willing to be approached in the future to take part in research projects were contacted. Parents/guardians were contacted in the cases where the potential participants were under 18 years old. Adults and children were sent a cover letter (Appendix 4 and 2 respectively) and an age appropriate information pack regarding the study (6-10 year olds, 11-16 year olds or adult) (Appendix 5, 6 and 7) and contact information for the research team in order for any queries or concerns to be discussed.

Healthy TDC participants were recruited from a local school. A short written piece explaining the study was included within the school newsletter which was circulated around both the students and their parents/guardians. Shortly afterwards members of the research group presented the study during school assemblies to the age appropriate year groups. Information packs were then sent out to all of the parents/guardians, containing a letter introducing the study and research team, the age appropriate information sheets and a form to return to the school reception stating whether they wished to be included in the study or not (Appendix 8 and 9). Any positive responses were then followed up by a member of the research team and an appointment was made to attend the Human Movement and Function Laboratory. Adult control participants were recruited from staff and students at the School of Health Professions, Plymouth University.

Informed consent

Potential participants (or the parents/guardians if under 18 years of age) were approached by one of the research team prior to attendance at the Human Movement and Function Laboratory, the study was explained to them and an information sheet was provided (Appendix 4 or 2). There was a minimum 24 hour period during which the parents/guardians and relevant others were able to contact the researchers to discuss any potential issues. Informed written consent was taken by a member of the research team at the time of presentation to the Human Movement and Function Laboratory prior to any assessment of the participant occurring. Parents/guardians and adults filled out a consent form (appendix 10) and children, where possible, completed an assent form (appendix 11).

Trial design

A cross-sectional study design was used where pwCP and healthy controls were seen on one occasion for measures of walking ability and impairment profile. Appointments lasted approximately ninety minutes.

Comparisons were made between the pwCP and control groups and a stepwise multiple regression approach was used to investigate the relationship between five measures of neurological impairment and the degree of SKG. The kinematics and kinetics of SKG was assessed. Additionally neurological impairments were assessed using dynamometry and clinical outcome measures, whilst gait was assessed using 3D motion analysis and observational gait analysis.

Measurement of lower limb kinematics and kinetics

Limb kinematics were measured using a 3D motion analysis system (Codamotion Analysis Software, version 6.64-CX1/MPX30, Leicestershire, UK). Two cameras, each capable of

measuring movement of markers in three dimensions were placed perpendicular to a ten metre walkway that housed two force plates (Type 9286A, Kistler Instruments Ltd., Hook, UK). Prior to data analysis the cameras were aligned to a common global coordinate reference frame that was centred to the middle of one force plate. The second force plate was placed at a standard distance from the first so the position of markers relative to either force plate could be calculated (see measurement of kinetics later in this chapter).

Markers were placed in standardised positions on the lower leg (Figure 2.1). Markers were either attached to the skin overlying a bony landmark or to wands that were attached via Velcro straps to the pelvis, thigh or shank. The shank wand was aligned orthogonal to the mediolateral axis of the shank as defined by the middle of the lateral and medial malleolus. The thigh wand was aligned orthogonal to the mediolateral axis of the knee as defined by the centres of the lateral and medial femoral condyles. The pelvis frame was aligned to the plane defined by the right and left anterior and posterior superior iliac spines (ASIS and PSIS).

Ground reaction forces were recorded via the two force plates. Vertical forces from the four piezoelectric sensors in each force plate and from the combined shear forces were amplified. Shear forces (in the anteroposterior and mediolateral directions) were amplified by 50 Newton's per Volt (N/V) whilst vertical forces were amplified by 0.5 kilonewtons per volt (kN/V).

Additionally, muscle activity was measured using surface EMG via a telemetry unit (MT8, MIE Medical Research Ltd., Leeds, UK). The skin was firstly prepared using an alcohol wipe. EMG electrode pads (2.5x2.5 centimetres [cm] with a $0.79cm^2$ diameter recording area) were placed longitudinally 2.5 cm apart on the muscle belly of the rectus femoris, medial hamstrings, tibialis anterior and medial gastrocnemius head. A ground and pre-amplifier was placed adjacent to each electrode array.

Three-dimensional motion analysis and force plate signals were analogue-to-digital (AD) at 200 hertz (Hz) whilst EMG signals were sampled at 2 kilohertz (kHz). Signals were AD converted through the same device (Codamotion active hub) meaning that they were synchronised in time.
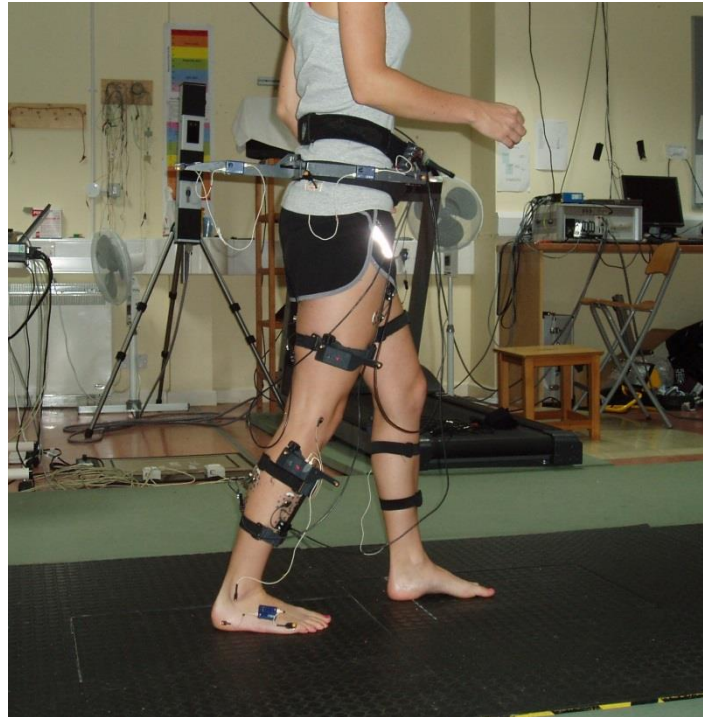
Figure 2.1: Placement of markers on the lower limb. One Codamotion camera is pictured to the left side of the participant

Participants were asked to walk at their normal speed up and down the walkway. At the end of every walk they could rest by sitting or holding onto a support if required. During the rest period the trial was assessed to see if markers were in full view and whether the participant had placed either the right or left leg on a force plate without any walking aid (if present) touching the plate. A few pwCP had short strides and had difficulty in naturally "hitting" each force plate. In these cases advice about positioning to one side or the other of the walkway was given to facilitate this. Some pwCP used rollator frames to walk, this precluded obtaining any data from the force plate. A minimum of three steps on the force plate per leg were measured. Depending on ability participants performed between 10-25 trials to obtain the required data.

Anthropometric Measures:
In order to calculate joint kinetics callipers and a tape measure were used to record the following anthropometric measures (Leva 1996):

(1) the distance between the ASIS and PSIS (termed pelvic depth)
(2) the distance between the right and left ASIS (termed pelvic width)
(3) The width of the knee at the level of the joint line (in line with the knee axis marker)
(4) The width of the ankles at the level of the lateral malleolus marker

Height was measured using a stadiometer and mass was measured using scales; gender and age were additionally noted.

Trials where the joint markers were in view and, if possible, one leg contacted the force plate during stance phase, were identified. Participants' demographics and anthropometric data (weight, height and joint widths) were stored. Lower limb kinematics and kinetics were calculated automatically using Codamotion software using the calculations outlined below.

Calculation of lower limb kinematics

The arrays of markers placed on the legs determined a local coordinate system or embedded vector basis (EVB) for each segment. The EVB consisted of three orthogonal axes (Table 2.2) from which unit vectors were defined. These were used in the measurement of segmental rotations (Ward 2004).

EVB	Principal axis	2nd axis	3rd axis
Foot	Line connecting the heel and toe markers that is offset by ½ inter-malleolar distance (u_x)	Line running from the heel marker to ankle marker and orthogonal to the principal axis (u_z)	Orthogonal to 1st and 2nd axes (u_y)
Shank	Ankle joint centre to knee joint centre (u_z)	Tibial wand orientation orthogonal to principle axis (u_x)	Orthogonal to 1st and 2nd axes (u_y)
Thigh	Knee joint centre to hip joint centre (u_z)	Thigh wand orientation orthogonal to principle axis (u_x)	Orthogonal to 1st and 2nd axes (u_y)
Pelvis	Line between right and left ASIS markers (u_y)	Line connecting mid PSIS to mid ASIS and orthogonal to the principal axis (u_x)	Orthogonal (u_z) to 1st and 2nd axes

Table 2.2: Derivation of embedded vector basis for each segment

MPhil   Factors Associated with Stiff Knee Gait in Cerebral Palsy   Chapter 2

Internal joint centres for the hip, knee and ankle were calculated using joint width measurements using callipers and marker positions over the joints.

Joint Centre	Distance	Direction
Ankle	½ inter-malleolar distance	Perpendicular to shank lateral plane (defined by tibial wands)
Knee	½ knee width distance	Plane defined by virtual hip joint and thigh (defined by femoral wands)
Hip	½ inter ASIS distance - 0.19Wu_x - 0.36Wu_z ± 0.3u_y Where W is the pelvic width, ASIS is the anterior superior iliac spine, u_x, u_y and u_z are the unit vectors describing the pelvic plane (Bell et al. 1990; Ward 2004)	

Table 2.3: Calculation of internal joint centres

Relative segment orientation was described in terms of Euler angles. The orientation of the distal segment relative to the proximal segment was described except for the pelvis and foot which were calculated relative to the global coordinate frame. Distal segment rotations occurred about the proximal segment axes in the following sequential order: Z (internal/external axial rotation) then X (mediolateral bending) then Y (flexion/extension). Once the angles were known, the time derivatives were calculated to give angular velocity and acceleration (Ward 2004; Hamill & Selbie 2004a).

Measurement of lower limb kinetics
Two force plates embedded in the walkway measured the ground reaction forces applied when one leg was in contact with the force plate during the stance phase of gait. An inverse dynamics approach was used to calculate the forces, moments and powers at each joint. The joint inter-segmental forces and net joint moments were calculated for the ankle as follows:

The linear (translational) equations of motion were:

$$\sum \vec{F} = \vec{F}_a + \vec{F}_{GRF} + W_{foot} = m_{foot}\vec{a}_g \quad \textit{(Equ. 2.1)}$$

Solving for $\vec{F}_a$:

$$\vec{F}_a = m_{foot}\ \vec{a}_g - \vec{F}_{GRF} - m_{foot}g \quad \textit{(Equ. 2.2)}$$

Where:

ΣF = sum of all the forces applied to the segment;

$\vec{F}_a$ = the unknown ankle inter-segmental force;

$\vec{F}_{GRF}$ = the ground reaction force;

W_{foot} = weight of the foot;

m_{foot} = mass of the foot;

$\vec{a}_g$ = linear acceleration of the foot centre of mass (COM);

g = gravitational constant.

Taking moments about the COM the rotational equations of motion were:

$$\sum \vec{M}_g = \vec{M}_a + (\vec{r_1}\vec{F}_a) + (\vec{r_2}\vec{F}_{GRF}) + \vec{T}_{GR}$$

$$= I_{foot}\vec{\alpha}_{foot} \qquad \text{(Equ. 2.3)}$$

Solving for $\vec{M}_a$

$$\vec{M}_a = (I_{foot}\vec{\alpha}_{foot}) - (\vec{r_1}\vec{F}_a) + (\vec{r_2}\vec{F}_{GRF}) - \vec{T}_{GR}$$

$$\text{(Equ. 2.4)}$$

Where:

$\sum \vec{M}_g$ = the sum of the moments of force acting about the COM;

$\vec{M}_a$ = the vector of the unknown net ankle moment;

$\vec{F}_a$ = the vector of the joint inter-segmental force;

$\vec{r_1}$ = the vector of the distance from the ankle joint centre to the COM;

$\vec{F}_{GRF}$ = the vector of the joint reaction force;

$\vec{r_2}$ = the vector of the distance from the point of application of the centre of pressure (COP) to the COM;

$\vec{T}_{GR}$ = the vertical ground reaction torque vector that normally acts to resist turning about the vertical axis;

I_{foot} = the centroidal mass moment of inertia of the foot;

$\vec{\alpha}_{foot}$ = angular acceleration of the body segment.

Joint centre positions were calculated as described previously and the COM was located along the principle axis (Tables 2.2 and 2.3). The segment mass, COM locations and the radius of gyration (expressed as a proportion of the segment length) were estimated from anthropometric data based on the subjects' height, weight and gender. Each limb segment was assumed to be rigid and have a uniform distribution of mass around a longitudinal axis connecting the joint centres, to simplify its' inertial properties (Hamill & Selbie 2004b).

The ground reaction force and ground reaction torque were measured using force plates that were embedded into the walkway.

The point of application of the COP was calculated as:

$$COP_x = \frac{[b(\vec{f}_z1+\vec{f}_z2-\vec{f}_z3-\vec{f}_z4)]+(\vec{F}_xA_z)}{\vec{F}_z}$$

(Equ. 2.5)

$$COP_y = \frac{[a(\vec{f}_z1+\vec{f}_z2+\vec{f}_z3-\vec{f}_z4)]+(\vec{F}_yA_z)}{\vec{F}_z}$$

(Equ. 2.6)

Where:

b = (inter-sensor distance in the x direction) /2;

a = (inter-sensor distance in the y direction) /2;

$\vec{f}_z$ *1..4* = vertical force measured by sensor 1..4;

$\vec{F}_x$ = Anteroposterior force;

$\vec{F}_y$ = Mediolateral force;

$\vec{F}_z$ = Vertical force.

Calculation of joint kinetics proceeded in a distal to proximal direction with the net inter-segmental joint forces and net joint moments calculated for the more distal segment being used in the calculation of the next more proximal segment. These moments and forces were expressed in the local coordinate system (EVB) of the proximal segment.

Joint Power

Joint power vectors were calculated from the vector product of the joint moment vectors and the relative inter-segmental velocity (Hamill & Selbie 2004b).

$$\vec{P} = \vec{J}_m(\vec{\omega}_p - \vec{\omega}_d) \qquad\qquad (Equ.\ 2.7)$$

Where:

$\vec{P}$ = the joint power vector;

$\vec{J}_m$ = joint moment vector;

$\vec{\omega}_p$ = proximal segmental angular velocity.

$\vec{\omega}_d$ = distal segment angular velocity

Secondary analysis of lower limb kinematics and kinetics

Segment rotations, joint moments and power calculated in Codamotion software were exported as ascii text files and subsequently imported into MATLAB (MATLAB, version R2009a, The MathWorks Inc., Cambridge, UK). The left and right leg were analysed separately. Initial foot contact and foot lift off were identified via the kinematic data using the foot velocity algorithm described by O'Connor et al (2007). Kinematic data rather than the vertical forces obtained from the force plates was used as some pwCP who used walking aids were unable to place one foot on the plate in isolation. The use of kinematic data therefore allowed a common method of analysis to be used for all participants.

The foot velocity algorithm consisted of low pass filtering (7Hz 4th order zero-phase Butterworth filter) the heel and toe data. The midpoint between the heel and toe markers was then calculated; termed the foot centre. The first derivative of the vertical coordinates of the foot centre was then calculated to give the vertical foot velocity. Characteristic troughs and peaks indicating foot contact and lift off were then identified visually (Figure 2.2 and 2.3) and marked using crosshairs. If available the vertical force trace was used as an additional guide. Pilot work confirmed previous reports (O'Connor et al. 2007) that this technique was simple to use and correctly detected foot contact and lift off in both pwCP and healthy controls with a wide range of walking speeds and symptom severities.
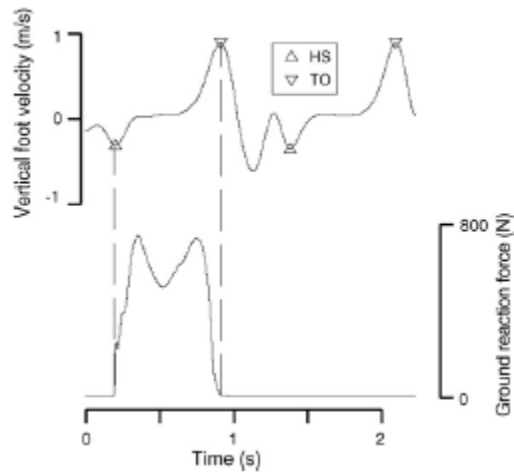
Figure 2.2: Heel strike and Toe off indicated by troughs and peaks as described by O'Connor et al (2007)
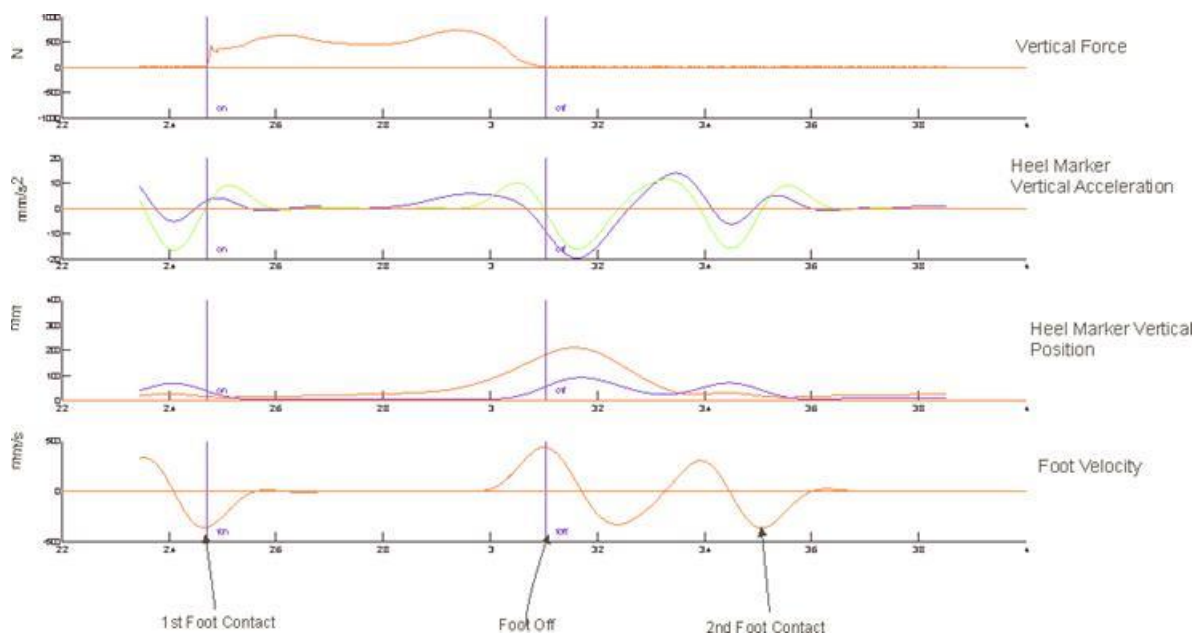
Figure 2.3: Screen shot indicating the graphs used in determining foot contact and lift off. The vertical foot velocity is shown in the bottom trace. Vertical lines indicate the start and end of stance phase as indicated by the vertical force (top trace); these coincide with the troughs and peaks of the foot velocity trace as outlined by O'Connor et al 2007

Definition of gait variables:

The duration of the stance and swing phase was noted. This was used with the measure of the foot marker in the direction of travel over one stride to define walking speed:

Walking velocity = foot marker distance over one stride/duration of one stride

The duration of one gait cycle was then normalised so that its duration was 100% and three gait cycles averaged (Maynard et al. 2003). Phases of gait were defined in Table 2.4 below;

Phase of gait	Definition
Stance Phase	Period between initial ipsilateral foot contact and ipsilateral foot lift off
Swing Phase	Period between ipsilateral foot lift off and second ipsilateral foot contact
Loading phase	Period between initial ipsilateral foot contact and contralateral foot lift off
Mid stance	Period between contralateral foot lift off and contralateral foot contact
Preswing	Period between contralateral foot contact and ipsilateral lift off

Table 2.4: Definitions of the phases of the gait cycle

The gait variables indicated in Table 2.5 (below) were then detected automatically via a MATLAB program written in house.

Gait Variable
Maximal knee extension during the stance phase
Maximal knee flexion during the swing phase
Maximal knee flexion velocity in preswing and swing
Maximal ankle power during preswing
Maximal hip flexor power in preswing and swing phase
Maximal knee extensor moment in preswing

Table 2.5: Gait variables

The trough to peak knee angle was defined as:

Maximal knee flexion during the swing phase - Maximal knee extension during the stance phase.

Measurement of knee extensor stiffness

Knee extensor stiffness was measured using ramp and hold stretches delivered via a dynamometer (a "Biodex") (Biodex Medical Systems, Inc., System 3, New York, USA) as described previously (Marsden et al. 2012). Subjects lay supine with their hips at 20 degrees, their thighs were supported by the chair and their head was supported by a pillow. On the side of interest the knee axis was aligned with the axis of rotation of the dynamometer. The shank was attached to a manipulandum which was attached to the motor. Straps secured the shank and the thigh.

A safety cut off switch was given to the participants and another held by the researcher. The dynamometer had additional software cut offs that limited excessive torques or movements being applied and mechanical stops were present on the manipulandum that would have prevented moving the knee in non-physiological ranges.

The participant was asked to relax and let the motor move them. Visual feedback about the data gathered including surface EMG was provided. The starting position for the stretch was 85 degrees knee flexion (Figure 2.4). The knee was then rotated through 15 degrees into flexion, stretching the knee extensors. Two stretch speeds were used; 5 degrees per second ($^{\circ}$/s) and 175°/s as specified by a positional data file (Biodex dynamometer). The slow stretch was always applied first to make the participant confident that the stretch would not cause discomfort. Six stretches at each speed with a three second inter-stretch period were performed.
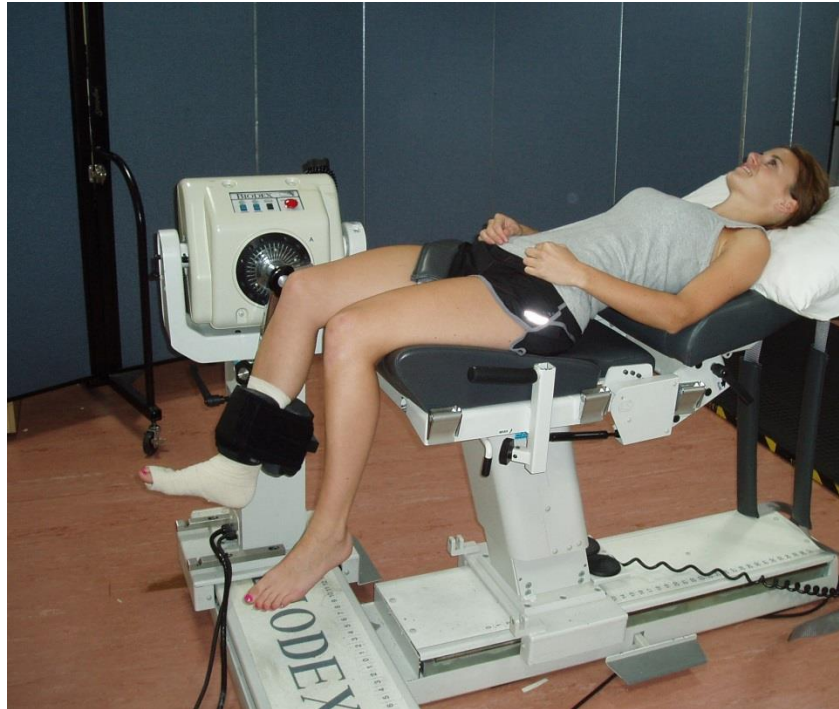
Figure 2.4: Participant and equipment positioning for the measurement of knee extensor stiffness

Surface EMG was recorded from the knee extensors (namely rectus femoris) and medial hamstrings to confirm muscle relaxation at the beginning of the stretch and during the slow stretch. It also detected the presence of stretch reflex activity during the fast stretch.

Torque, velocity and position were collected via the Biodex remote access port. Signals were AD converted using a Power 1401 (Cambridge Electronic Design, Cambridge, UK). Data was sampled at 2000Hz and collected using Spike2 software (Spike2, version 5.06, Cambridge Electronic Design, Cambridge, UK). Stretch data was collected using Spike2 software and exported as text files for analysis using MATLAB programmes written in house.

The data was firstly filtered (30Hz low pass first order butterworth filter) to remove high frequency artefact that could be seen when using the motor. The stretches were aligned to the stretch onset using the position, velocity and derived acceleration data. The last 5 stretches were averaged (Figure 2.5); the first trace being discarded to account for thixotropic effects. The mean torque (Torque $_{total}$) and position was measured over a 300 millisecond (ms) period just prior to the stretch and post stretch onset when the knee had stopped moving (Figure 2.5).

The torque due to the weight of the shank and foot (*Torque $_{shank\ \&\ foot\ weight}$*) was estimated as:

$$Torque_{shank\ \&\ foot\ weight} = mg \sin \theta d \qquad \textit{(Equ. 2.8)}$$

Where:
θ = knee angle relative to vertical;
g = acceleration due to gravity;
m = mass of the shank and foot estimated from anthropometric data based on the subject's mass and gender;
d = the manipulandum length.

The change in torque due to the manipulandum (*Torque $_{manipulandum}$*) was measured directly by moving the manipulandum through the same range at the same speed when the leg was not attached. The torque due to stiffness in the knee-shank complex (*Torque $_{knee\text{-}shank}$*) was defined as:

$$Torque_{knee-shank} = Torque_{total} - Torque_{shank\ \&\ foot\ weight} - Torque_{manipulandum} \qquad \textit{(Equ. 2.9)}$$

Stiffness was calculated as the change in *Torque $_{knee\text{-}shank}$* divided by the change in position.

Stiffness during the slow stretch (5°/s), when there was no muscle activity measured passive stiffness of the knee extensor musculo-tendinous complex. Stiffness measured during the fast stretch (175°/s) was due to a combination of passive stiffness and stretch reflex mediated stiffness and was termed total stiffness. As the hip was extended this test mainly assessed rectus femoris stiffness although a contribution of the other knee extensors cannot be discounted. The difference between the total stiffness and passive stiffness thus provided an estimated of the stretch reflex mediated stiffness.
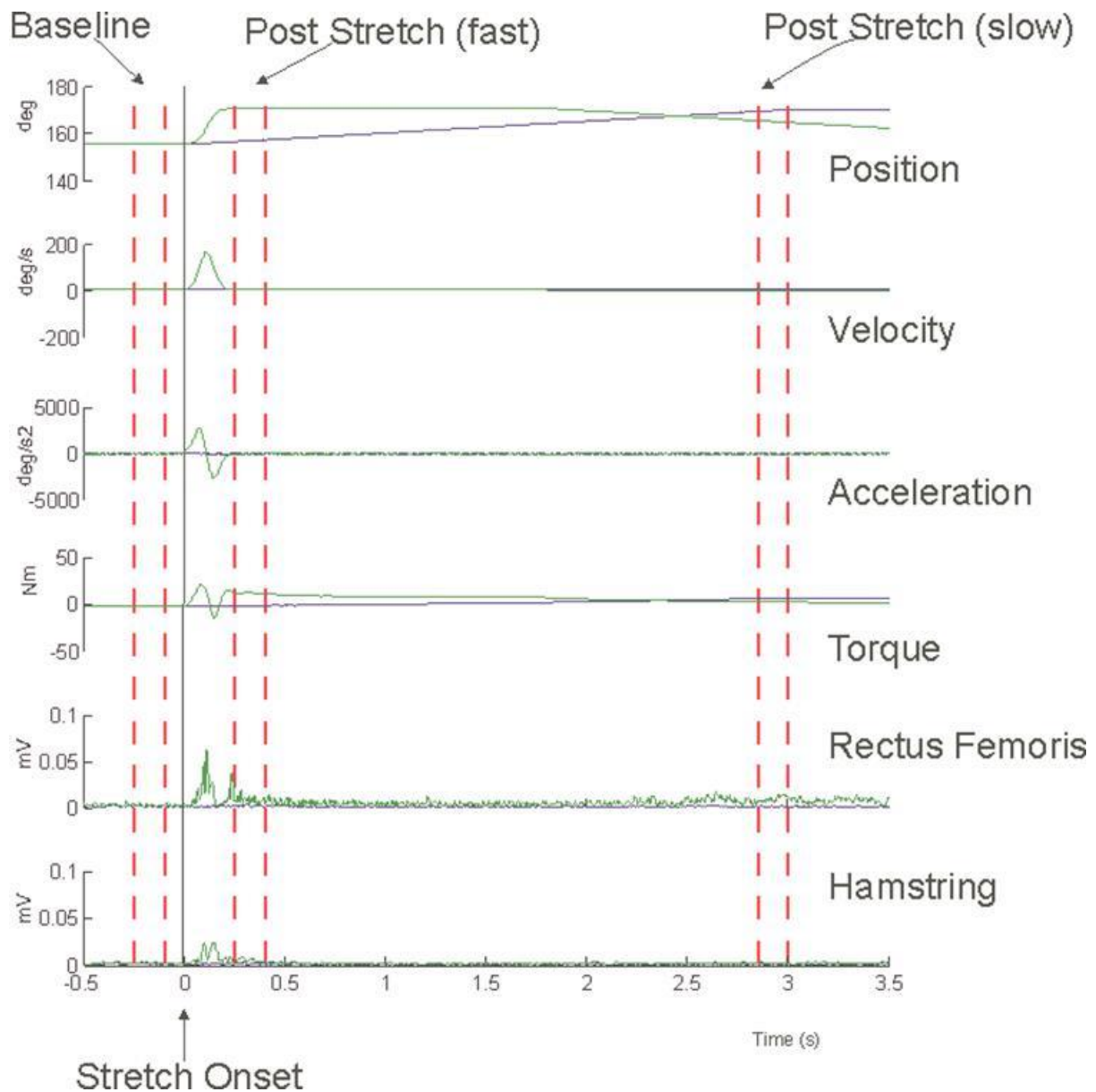
Figure 2.5: An example of the averaged response to a fast (green) and slow (blue) stretch in a participant with CP (cp3). Red lines indicate the time periods over which the mean position and torque data was calculated. Note the lack of EMG activity in the rectus femoris and hamstrings during the slow stretch indicating that this is measuring passive stiffness. With the fast stretch there is a clear stretch reflex elicited in the rectus femoris that leads to an increase in the torque at the end of the movement that is greater than that seen at the end of the slow stretch.

Measurement of lower limb strength

Isometric ankle dorsi- and plantarflexion strength; knee extension and flexion strength; and hip extension and flexion strength were measured using the Biodex dynamometer. Isometric contractions were chosen as opposed to isokinetic contractions at speeds similar to that seen during gait, as the latter would involve stretch of the antagonist muscle. This antagonist stretch may have elicited a stretch reflex activation of the muscle which would thus have affected the torque response measured.

The starting position for each test is indicated in Table 2.6 and Figures 2.6 - 2.8). Strength was tested with the muscle group of interest either in a shortened or a lengthened position; termed inner and outer range. Angles were chosen a priori with the aim that the majority of pwCP could achieve them even with commonly observed contractures. However, some participants could not achieve all positions (e.g. 10° hip flexion) due to muscle contracture.

Muscle Group	General Starting Position	Joint Angle
Ankle dorsiflexors	Position: Sitting with hips at 85° Proximal segment: Thigh supported and knee fixed at 90°	5° plantarflexion 15° plantarflexion
Ankle Plantarflexors	Distal segment: Ankle supported in a manipulandum Axis: Aligned with lateral malleolus	5° plantarflexion 15° plantarflexion
Knee Extensors	Position: Sitting with hips at 85° Proximal segment: Thigh supported on chair and fixed with straps	90° knee flexion 20° knee flexion
Knee Flexors	Distal segment: Shank supported in manipulandum Axis: Aligned with lateral femoral condyle	90° knee flexion 20° knee flexion
Hip Flexors	Position: Supine with head supported on a pillow Proximal segment: Trunk fixed manually at shoulders /pelvis. The contralateral hip was flexed to >90°	10° hip flexion 40° hip flexion
Hip Extensors	Distal segment: Thigh supported in manipulandum Axis: Aligned with greater trochanter Hip starting position was confirmed using a goniometer	10° hip flexion 40° hip flexion

Table 2.6: The starting positions for the objective strength measure tests

Figure 2.6: Positioning for the measurement of ankle dorsi- and plantarflexor strength

Figure 2.7: Positioning for the measurement of knee extensor/flexor strength

Figure 2.8: Positioning for the measurement of hip extensor/flexor strength

Participants were asked to contract as hard as they could, verbal encouragement was provided and visual feedback of the applied torque was displayed on a screen in front of them. Test trials were provided to ensure the participant understood the instructions. This was particularly relevant for the younger pwCP. Some pwCP produced minimal torque during the maximal voluntary contraction (MVC) and could even apply torques in the other direction. To facilitate data analysis the researcher pressed a switch that delivered a Transistor-transistor logic (TTL) pulse to the AD converter at the start of the test and after the rest period.

Signals were AD converted using a Power 1401. Data was sampled at 2000Hz and collected using Spike2 software. Strength data was subsequently exported as text files for analysis using MATLAB programmes written in house. The data was firstly filtered (30Hz low pass first order butterworth filter) to remove high frequency artefact that could be seen when using the motor.

All participants were able to relax prior to the contraction. The weight of the limb and manipulandum prior to the contraction was firstly measured over a 300ms period. Moveable cross hairs then identified the period at the beginning and end of the contraction and the maximal torque in the requested direction recorded. The MVC was defined as:

Maximal isometric torque – torque applied at rest

Therefore, the weight of the lower leg and manipulandum in different positions was taken into account.

Clinical measures of strength and stiffness

Knee Extensor Stiffness:
Knee extensor stiffness was measured using the Duncan-Ely test and graded according to the modified Tardieu scale. The Duncan-Ely test has been shown to be reliable in pwCP and to be able to predict the outcomes of rectus femoris transfer (Kay et al. 2004). The Tardieu scale was originally described in pwCP where it has been shown to be reliable (Haugh et al. 2006). Unlike other clinical scores of stiffness and tone such as the Ashworth scale, the Tardieu scale grades stiffness when the limb is moved at different speeds in order to estimate the passive and stretch-mediated components of stiffness.

Participants lay in prone with their hips in neutral or if hip flexion contractures were present, at their end of range. One of the examiners' hands stabilised the pelvis while the other moved the lower leg flexing the knee (Figure 2.9). Slow (<5 ^{o}/s) and fast (>175°/s) stretches were manually applied through the full range available. The resistance to movement was

graded using the Tardieu scale (Table 2.7). The total range achieved during the slow stretch (V1) was noted and during the fast stretch (V3) the angle at which any catch occurred was also noted. Angles were visually determined in keeping with the guidance for the Tardieu scale. As the hip is extended this test mainly assesses stiffness in the rectus femoris muscle.

Velocities	**V1**: As slow as possible, slower than the natural drop of the limb segment under gravity
	V2: Speed of limb segment falling under gravity
	V3: As fast as possible, faster than the rate of the natural drop of the limb segment under gravity
Scoring	**0**: No resistance throughout the course of the passive movement
	1: Slight resistance throughout the course of passive movement, no clear catch at a precise angle
	2: Clear catch at a precise angle, interrupting the passive movement, followed by release
	3: Fatigable clonus with less than 10 seconds when maintaining the pressure and appearing at the precise angle
	4: Unfatigable clonus with more than 10 seconds when maintaining the pressure and appearing at a precise angle
	5: Joint is immovable

Table 2.7: The Tardieu scale measure of resistance to movement

Figure 2.9: Duncan-Ely test to determine muscle stiffness and spasticity

Ankle and Hip Strength

Strength was graded using manual muscle testing according to the Medical Research Council (MRC) Oxford grading of muscle power scale (Table 2.8). The starting positions for grades 5-3 and 2/1 are indicated in Table 2.9 and shown in Figures 2.10 - 2.14. In all cases the proximal segment was fixed and movement of the distal segment with/without resistance applied was assessed.

Tests of manual muscle strength are used extensively in the clinical situation. They are reliable in people with an upper motor neuron syndrome and in the paediatric population (Florence et al. 1992; Cuthbert & Goodheart 2007). They correlate with objective measures of muscle strength i.e. show evidence of concurrent validity (Cuthbert & Goodheart 2007; Paternostro-Sluga et al. 2008).

Grade	Description
5	The muscle is able to contract through full range of joint movement against gravity, plus a resistance which is maximal for the age, sex and occupation of the subject
4	The muscle is able to contract through full range of joint movement against gravity, plus a resistance which is less than maximal for the age, sex and occupation of the subject
3	The muscle is able to contract through a full range of joint movement against gravity
2	The muscle is able to contract through a full range of joint movement with gravity eliminated
1	A muscle contraction is detectable on palpation. Movement of the joint is minimal or absent
0	No muscle contraction is detectable on palpation

Table 2.8: MRC Oxford grading of muscle power scale

Joint position	Grades 3-5	Grades 0-2
Hip Flexion	Sitting with trunk supported and pelvis fixed manually	Side lying with pelvic fixation. Tested leg upper most and manual support provided to maintain leg position in the coronal plane (between abduction and adduction)
Hip Extension	Prone with fixation of the pelvis	Side lying with pelvic fixation. Tested leg upper most and manual support provided to maintain leg position in the coronal plane (between abduction and adduction)
Knee Extension	Sitting with trunk supported using the participant's upper limbs and the thigh supported on the plinth	Side lying with pelvic fixation. Tested leg upper most and manual support provided to maintain thigh fixed and the shank aligned to the thigh in the coronal plane
Knee Flexion	Prone lying with the thigh supported and the pelvis fixed	Side lying with pelvic fixation. Tested leg upper most and manual support provided to maintain thigh fixed and the shank aligned to the thigh in the coronal plane
Ankle Dorsiflexion	Sitting with trunk and thigh supported. The shank in the vertical position manually stabilised by the assessor	Side lying with thigh and shank support. Assessor maintains the foot in neutral between inversion/eversion
Ankle Plantarflexion	Standing on the tested leg. Light upper limb support provided for balance only	Side lying with thigh and shank support. Assessor maintains the foot in neutral between inversion/eversion

Table 2.9: MRC Oxford grading of muscle power scale: starting positions

Figure 2.10: Hip extensor strength measure

Figure 2.11: Knee extensor strength measure

Figure 2.12: Knee flexors strength measure
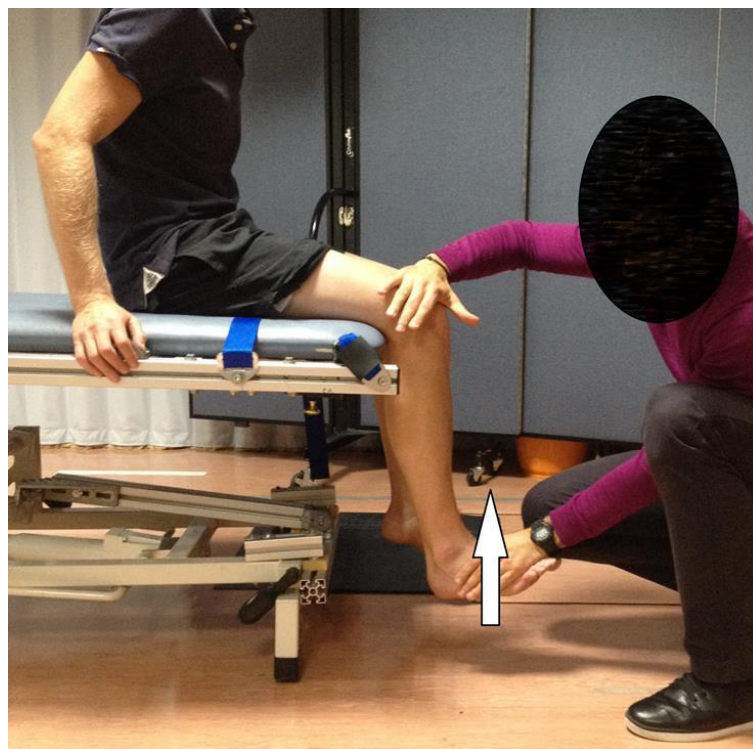
Figure 2.13: Ankle dorsiflexors strength measure

Figure 2.14: Plantarflexor strength measure

Observational gait analysis

The SF-GT sagittal plane view (as described by Toro et al. 2007) was the observation-based clinical gait assessment tool used to determine the degree of knee bend. A visual estimate of knee bend was recorded at mid stance (knee extension) and mid swing (knee flexion) and the difference between the two was determined. The angle estimated was between the longitudinal thigh axis and the longitudinal shank axis. This process was done using video clips and the video was paused at the two positions. The video was taken at right angles to the direction of travel to avoid any parallax error. The same researcher did this for every case.

Demographics and clinical descriptors:

In addition to the above measures of walking and impairment the following clinical descriptors were gathered;

Age, gender, height, weight and functional ability. Functional ability was defined using the GMFCS (Appendix 1), a classification of walking and motor ability that classifies the child into one of five levels.

Participants were further classified on a two point nominal yes/no scale according to whether they have had:

- bony lower limb surgery (e.g. osteotomy);
- muscle lengthening and botulinum toxin injections targeting the ankle plantarflexors or hip flexors;
- muscle lengthening or transfer and botulinum toxin injections targeting the rectus femoris

Analysis

All data was tested for normality using the Kolomgorov-Smirnov test. Comparisons with controls (chapter 3) were made using an analysis of covariance (ANCOVA) taking walking speed as a covariate. A Bonferroni correction was performed when assessing the gait variables to account for the multiple comparisons used.

The associations between the independent variable (trough to peak knee flexion) and the dependent variables (clinical and laboratory based measures of muscle strength and stiffness) were made using Pearson's (parametric) or Spearman's (non-parametric) correlations as appropriate. Correlations between 0.1-0.3 were defined as weak; between 0.4-0.6 as moderate and >0.7 as strong (Dancey & Reidy 2007).

Significant correlations were entered into a stepwise multiple regression with factors that significantly improved the model being retained. Significance was taken as $P<0.05$.

CHAPTER 3: DIFFERENCES IN IMPAIRMENT PROFILE AND WALKING IN PEOPLE WITH SPASTIC CEREBRAL PALSY AND HEALTHY CONTROLS

Introduction

This chapter will look at the differences in impairment profile and walking between pwCP with spastic diplegia and healthy controls.

Methods

As highlighted in chapter 2 data was gathered within the Human Movement and Function Laboratory at Plymouth University. Participants from both the CP and control groups were seen on just one occasion, for approximately 90 minutes. Firstly gait analysis data was obtained using 3D motion analysis equipment (Codamotion, UK), secondly strength and stiffness data was collected using a Biodex dynamometer and thirdly clinical measurements were taken (MRC Oxford grading of muscle power scale, Duncan-Ely test and via video analysis).

Analysis

All data was normally distributed as assessed using the Kolmogorov-Smirnov test.

Analysis of laboratory strength and stiffness data

Some pwCP were unable to achieve all the positions during the strength tests at the ankle, knee and hip due to contracture. Therefore, strength was analysed in each position separately using an unpaired t-test. Further, the ratio between inner range and outer range strength measures were assessed. Where:

Inner-outer range ratio = strength in inner range / strength in outer range.

Therefore for each joint measured, three tests were performed (inner range, outer range and inner-outer range ratio). To account for the multiple comparisons a Bonferroni correction was performed:

Bonferroni correction = 0.05/n Where n= number of tests performed. Therefore results were considered to be significant if $p<0.05/3=0.017$.

Please refer to chapter 2 for the method of analysis of the stiffness data.

Analysis of walking data

There was a difference between the walking speed in the control group and pwCP. As many gait variables are speed dependent an ANCOVA was performed when comparing the different gait variables, with walking speed being the covariate.

The variables that a priori were felt to possibly affect SKG were assessed statistically. The primary outcome measure (trough to peak knee flexion from stance to swing phase) was analysed separately.

Other comparisons between pwCP and controls in kinematic and kinetic variables at the pelvis, hip, knee and ankle in the sagittal, coronal and transverse planes were summarised visually using grand average graphs with +/- 1 standard deviation (SD) bar indicated and a descriptive summary within the text.

PwCP were characterised as having different severities of gait pattern deviation (mild, moderate and severe). Four gait patterns were described (crouch, jump, stiff knee and equinus) according to changes seen in the kinematic data. The classification of the severity of kinematic changes in pwCP was based upon the mean values and their variance seen in comparison with the control group:

Mild changes: control group mean +/- 2 SD to mean +/- 4 SD

Moderate changes: control group mean +/- 4 SD to mean +/- 6 SD

Severe changes: above control group mean +/- 6 SD

The cut off values for each gait parameter are provided in Table 3.1;

Gait	Mild (+/- 2 to +/- 4 SD)	Moderate (+/- 4 to +/- 6 SD)	Severe (+/- 6 SD)
Crouch	+21.0 to +33.0	+33.1 to +46.0	>+46.0
Jump	-4.0 to -16.0	NA	NA
Stiff Knee	+42.0 to +50.0	+35.0 to +42.0	< +35.0
Equinus	-3.0 to +6.0	-11.0 to -3.0	<-11.0

Table 3.1: Definition of mild, moderate and severe kinematic changes. Crouch and jump gait are defined as the maximal knee extension in stance. SKG is defined as the trough to peak change in knee flexion from stance to swing phase. Equinus gait is defined from the foot-floor angle at initial contact. The definitions used were mild: Mean +/- 2SD to +/- 4SD. Moderate: mean +/- 4SD to +/- 6SD. Severe: mean +/- >6SD.

In tables and text the mean +/- SD is indicated and in graphs the mean +/- standard error of the mean (SEM) is indicated.

Results

Participant characteristics:

Twenty Seven pwCP (age 13.6±8.3 years; gender 15 males, 12 females; height 1.4 ±0.2 metres [m]; weight 39.2± 19.4 kilograms [kg]) were compared to 20 controls (age 14.0±3.2 years; gender 13 males, 7 females; height 1.6± 0.12 m; weight 51.7 ±10.9 kg. There was no significant difference between the groups in terms of age ($P>0.05$) although the controls were significantly higher ($P<0.02$) and heavier ($P<0.001$).

Table 3.2 indicates the clinical characteristics of the pwCP. The results of clinical tests of strength, stiffness and range of movement are indicated in chapter 5.

Table 3.3 indicates the classification of gait pattern deviations seen in pwCP.

Participant Code	Age (yrs)	BMI (Kg/m²)	GMFCS	Walking aids	Walking Speed	Operations / Injections
Cpks1	7.9	15.5	II	unaided	1.02	No operations.
Cpks2	12.8	18.9	II	unaided	1.00	Botulinum toxin A injections into bilateral calves (2003-2006). External rotation varus osteotomy right femur (2010).
Cpks3	12.4	17.1	II	unaided	0.72	Botulinum toxin A injections into right gastrocnemius, psoas, hamstrings (2002-2005).
Cpks4	12.4	20.7	II	unaided	1.03	Botulinum toxin A injections into bilateral calves and ?hamstrings (2003-2006). Bilateral gastrocsoleus lengthening (2007).
Cpks5	10.8	12.9	II	unaided	0.93	Right hamstring lengthening and gastrocnemius recession (2008). Serial injections of botulinum toxin A to hip adductors, hamstrings and calf muscles.
Cpks6	11.6	13.4	I	unaided	1.01	Botulinum toxin A injections into bilateral calves (2002-2006).
Cpks7	10.4	14.3	II	unaided	1.36	Botulinum toxin A injections into bilateral calves. A period of serial casting.
Cpks8	6.3	16.2	II	unaided	0.24	Botulinum toxin A injections into bilateral gastrocnemius (2010-2011).
Cpks9	13.2	9.3	II	unaided	0.76	Bilateral psoas lengthening and rectus femoris to sartorius transfer and left gastrocnemius recession (2011).
Cpks10	10.3	15.9	II	unaided	0.68	Botulinum toxin A injections into bilateral calves (2004 & 2007). Bilateral hip adductor tenotomy (2006). Bilateral botulinum toxin A injections into hamstrings and external rotation osteotomy tibia (2007).
Cpks11	10.7	18.9	III	Kaye walker	0.08	External rotation osteotomy proximal femur and 8-plates to anterior distal femur, right (2009).
Cpks12	8.9	17.9	III	Kaye walker	0.24	No operations.
Cpks13	12.2	18.1	II	unaided	0.95	No operations.
Cpks14	7.2	18.8	I	unaided	1.03	AFO's daytime and night splints. Uses a k-walker at school.
Cpks15	10.0	17.8	II	unaided	0.39	No operations
Cpks16	13.4	25.2	II	unaided	0.65	Right gastrocsoleus lengthening (2010).
Cpks17	6.0	16.5	II	unaided	0.61	No operations.
Cpks18	12.7	20.8	III	2 x sticks	0.56	Botulinum toxin A injections into bilateral gastrocnemius x10 and hip adductors x6 (2004-2010).

Participant Code	Age (yrs)	BMI (Kg/m^2)	GMFCS	Walking aids	Walking Speed	Operations / Injections
Cpks19	14.1	17.2	I	unaided	1.17	No operations.
Cpks20	12.4	15.1	I	unaided	1.27	No operations.
Cpks21	43.7	35.7	III	2 x sticks	0.39	Right foot triple arthrodesis (2009).
Cpks22	12.2	15.4	I	unaided	0.90	No operations.
Cpks23	9.75	25	II	unaided	1.15	External rotation osteotomy proximal femur, bilateral (2012).
Cpks24	15.7	19.8	II	unaided	1.13	Botulinum toxin A injections into bilateral calves (2001). Bilateral gastrocnemius recession (2003). Left gastrocsoleus lengthening (2006).
Cpks25	22	21.4	II	unaided	0.59	Botulinum toxin A injections into bilateral calves (1998). Right hip adductor tenotomy, rectus femoris release and gastrocsoleus lengthening (2000). Bilateral external rotation osteotomy proximal femur, psoas and hamstring lengthening and lateral column foot lengthening (2000). Left gastrocnemius recession (2000). Bilateral hamstring lengthening, bilateral (2006).
Cpks26	36.1	28.1	II	unaided	0.81	Bilateral achilles tendon lengthening and hip adductor tenotomy (1980). Left tibialis posterior tendon lengthening (1988). Bilateral hamstring and psoas lengthening, hip adductor tenotomy, rectus femoris release and gastrocnemius recession (1999).
Cpks27	13.1	15.3	II	unaided	0.89	No operations.
Controls	**14.0 (±3.2)**	**19.9 (±2.5)**	**I**	**unaided**	**1.26 (±0.16)**	

Table 3.2: Clinical characteristics of the pwCP

Participant	Crouch/Jump	Stiff Knee	Equinus
Cpks1	Mild	Mild	Moderate
Cpks2	Normal	Severe	Severe
Cpks3	Mild	Moderate	Severe
Cpks4	Normal	Mild	Mild
Cpks5	Mild	Moderate	Severe
Cpks6	Normal	Normal	Moderate
Cpks7	Normal	Moderate	Severe
Cpks8	Jump	Normal	Severe
Cpks9	Normal	Mild	Moderate
Cpks10	Normal	Severe	Severe
Cpks11	Moderate	Severe	Severe
Cpks12	Severe	Severe	Severe
Cpks13	Mild	Severe	Moderate
Cpks14	Normal	Normal	Mild
Cpks15	Moderate	Severe	Moderate
Cpks16	Mild	Moderate	Moderate
Cpks17	Normal	Normal	Severe
Cpks18	Severe	Severe	Severe
Cpks19	Normal	Normal	Normal
Cpks20	Normal	Normal	Normal
Cpks21	Normal	Mild	Normal
Cpks22	Normal	Normal	Normal
Cpks23	Normal	Normal	Moderate
Cpks24	Normal	Mild	Normal
Cpks25	Severe	Severe	Severe
Cpks26	Mild	Severe	Moderate
Cpks27	Mild	Normal	Moderate

Table 3.3: Classification of gait pattern deviations seen in pwCP

Pelvic grand average kinematics

Figure 3.1: Grand average plots of pelvic joint angles in the sagittal (column 1), transverse (column 2) and coronal (column 3) planes.

Motion on the side analysed, the subjectively defined more severe side is indicated.

Descriptive differences in lower limb kinematics and kinetics

The grand average responses for the pwCP and controls are shown in Figures 3.1 to 3.5. Common gait abnormalities in pwCP are listed in Table 3.3. The description of the grand average differences between groups will be emphasised when the +/- 1 SD bars do not overlap. It should be emphasised that the grand average responses highlight group differences only. It will hide individual differences as highlighted by the large standard deviations for some variables (e.g. pelvic tilt, ankle plantarflexion and knee extensor moments). Furthermore, the following descriptive analysis may include differences that are due to differences in walking speed; this will be taken into account during the selective statistical analysis.

Pelvic abnormalities

Sagittal plane:
In pwCP the pelvis tends to be more anteriorly tilted and a double bump pattern is present, where there is more posterior tilt in periods of double stance (Figure 3.1).

Coronal plane:
There were no marked group differences in pelvic obliquity (Figure 3.1).

Transverse plane:
The pelvis tended to be more retracted on the right side compared to the control group (Figure 3.1).

Sagittal plane grand average kinematics and kinetics
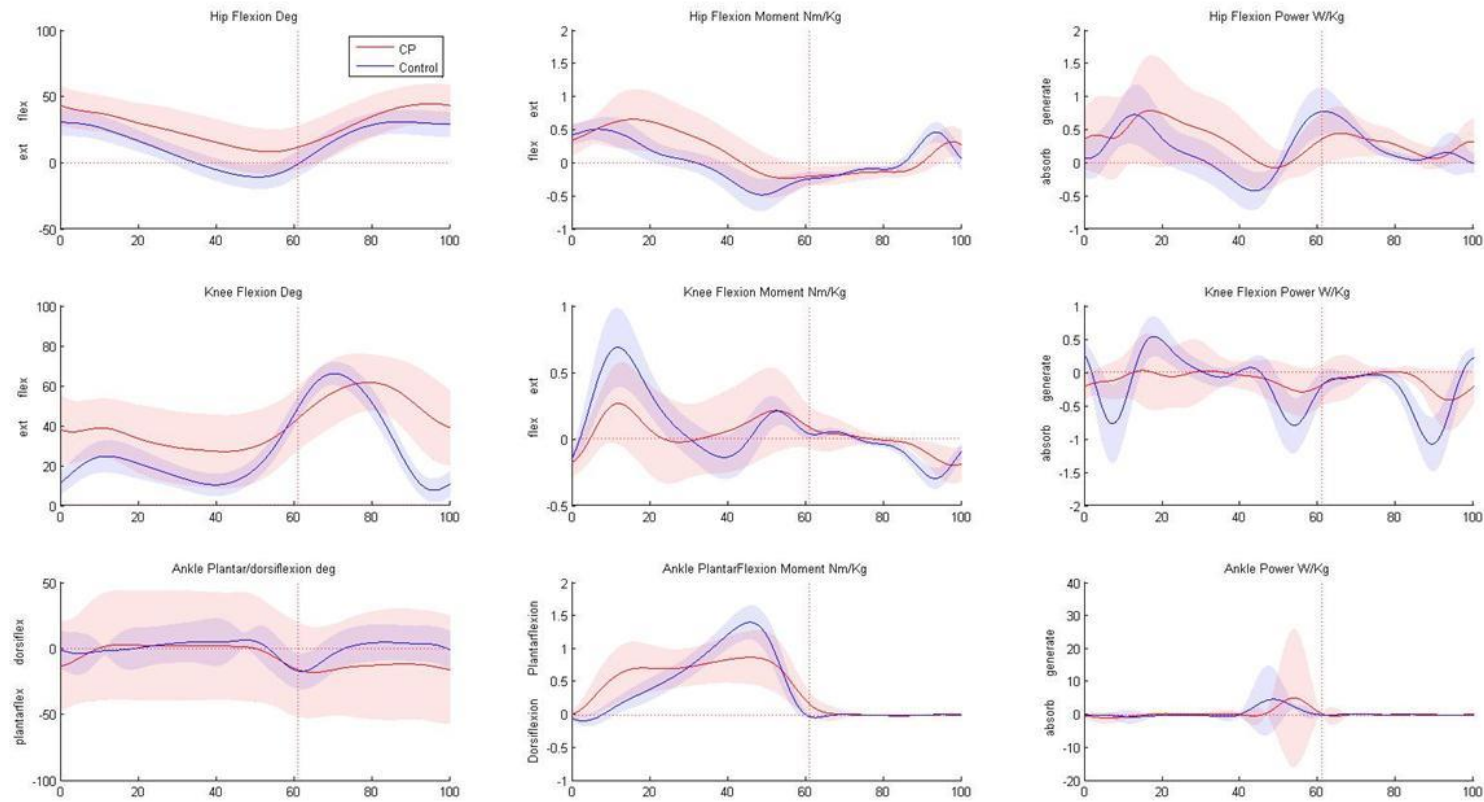
Figure 3.2: Grand average plots of sagittal plane joint angles (column 1), joint moment (column 2) and joint power (column 3) for the hip (row 1), knee (row 2) and ankle (row 3)

Sagittal plane abnormalities

Hip:

The hips are in more flexion in pwCP and this reflects the increased anterior pelvic tilt. There is slightly less excursion of the hip into extension in stance phase. The hip extensor moment and power generation is increased in pwCP at the beginning of stance phase. Hip flexor power generation is lower in preswing in pwCP but slightly higher than the controls in swing phase (Figure 3.2).

Knee:

The position of the knee is more flexed in pwCP throughout the gait cycle. The movement of the knee into flexion is less in pwCP during loading phase. The excursion of the knee into flexion from stance to swing phase is less in pwCP, indicative of a SKG. The degree of knee extension at the end of swing phase is also less in pwCP as highlighted by the non-overlap of the SD bars (Figure 3.2).

The knee extensor moment and power absorption during loading the phase is less in pwCP. Interestingly, the knee extensor moment in preswing is similar between the two groups although pwCP show less power absorption because the knee is flexing slower. At the end of stance phase there is less power absorption in pwCP reflecting slower extension of the knee and lower knee flexor moments (Figure 3.2).

The variability of the knee extensor moment in stance phase is quite large in pwCP reflecting the contribution of different effects such as jump versus crouch gait and the presence/absence of knee extensor spasticity (Figure 3.2). This will be further explored in chapter 4.

Ankle:

PwCP tend to be plantarflexed at the start of stance phase, their ankles move from plantarflexion into dorsiflexion, compared to the controls that move from dorsiflexion into plantarflexion (first rocker). There is not much subsequent dorsiflexion during the second rocker in pwCP and the excursion of the ankle into plantarflexion is less in pwCP during the third rocker. During swing phase the ankle remains plantarflexed in pwCP (Figure 3.2).

The plantarflexor moment is higher in pwCP at the beginning of stance phase. PwCP show a large variability in their plantarflexor moment. The average power generation in preswing is similar between groups but delayed in pwCP. Power generation in pwCP therefore predominately occurs when the opposite leg is in contact with the ground i.e. during the period of double support phase (Figure 3.2).

Coronal plane grand average kinematics and kinetics
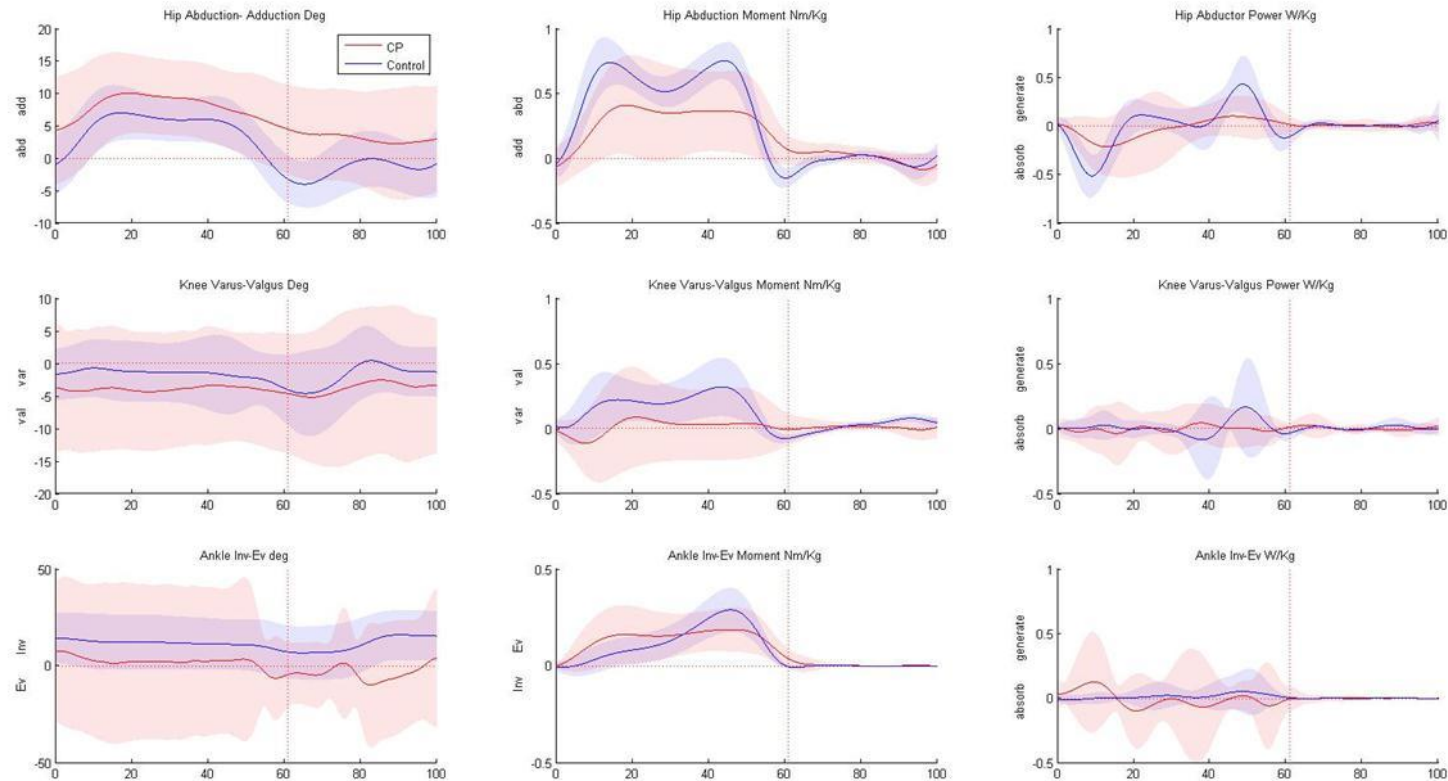
Figure 3.3: Grand average plots of coronal plane joint angles (column 1), joint moment (column 2) and joint power (column 3)

for the hip (row 1), knee (row 2) and ankle (row 3)

Coronal plane abnormalities

Hip:

The hip was more adducted in both stance and swing phase in pwCP. There was a reduced abductor moment during both peaks that are normally seen during stance phase (Figure 3.3).

Knee:

Whilst the controls had a valgus moment at the knee at the start of stance phase the pwCP showed a varus moment. With an associated valgus position of the knee this suggests that this moment may result from passive stretch to structures on the medial side of the knee. The knee moment was close to zero during the period of single support (Figure 3.3).

Ankle:

As a group pwCP had a more everted foot position. This is in keeping with the more valgus knee position at the start of stance phase (Figure 3.3).

Transverse plane grand average kinematics and kinetics
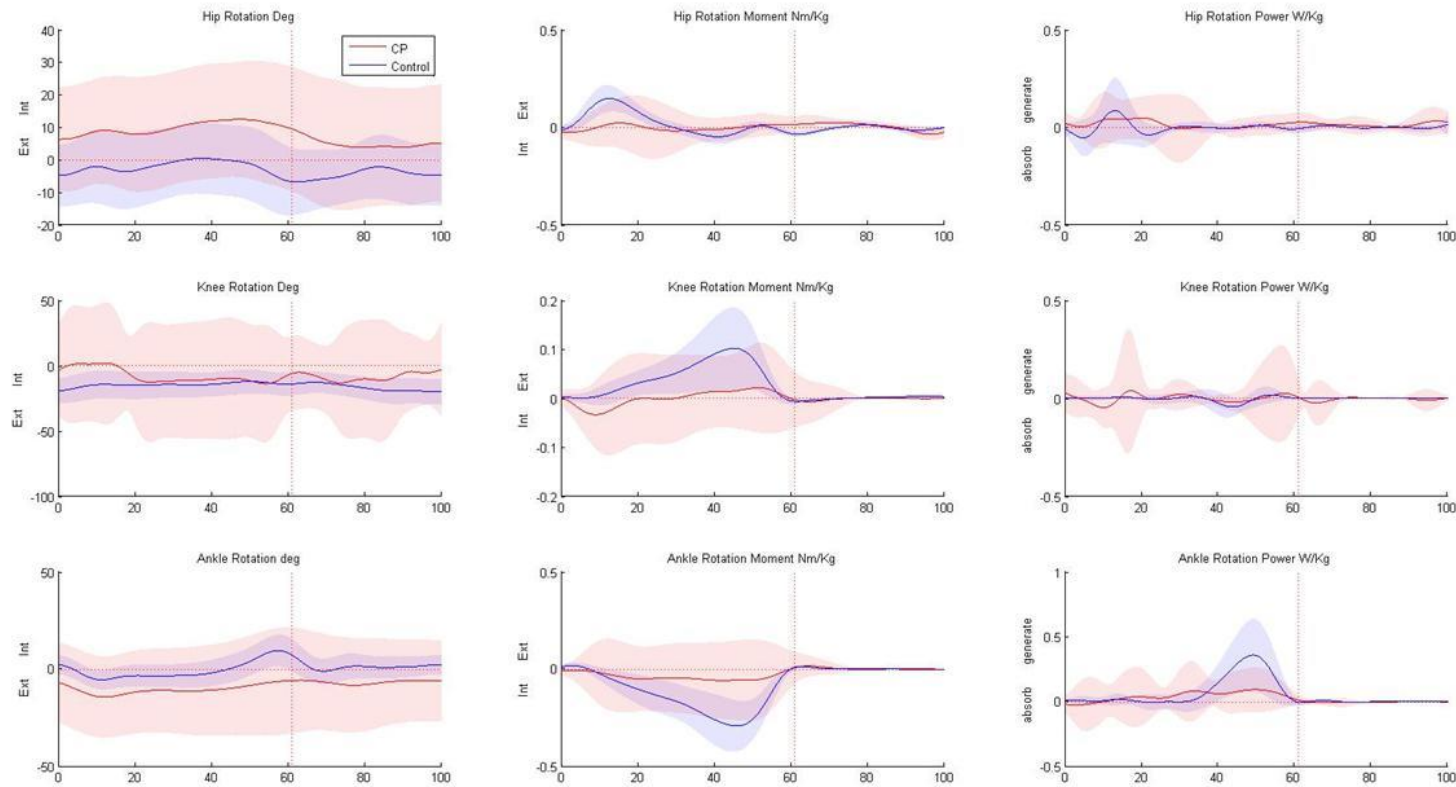
Figure 3.4: Grand average plots of transverse plane joint angles (column 1), joint moment (column 2) and joint power (column 3) for the hip (row 1), knee (row 2) and ankle (row 3)

Transverse plane abnormalities

Hip:

The hips tended to be internally rotated in pwCP. Hip rotation moments were close to zero throughout stance phase (Figure 3.4).

Knee:

At the start of stance phase the knee was more internally rotated in pwCP. Knee rotation moments were close to zero throughout stance phase (Figure 3.4).

Ankle:

As a group the ankles were externally rotated in pwCP relative to the shank. Ankle rotation moments were close to zero during stance phase (Figure 3.4).

Walking related outcome measures

Walking speed and double support time

PwCP walked significantly slower than the controls (pwCP 0.80 ± 0.33 metres per second [m/s] (n=27), control 1.26 ± 0.16 m/s (n=20) t=-6.3 P<0.0005). The percentage of the gait cycle in double support was significantly longer in pwCP (32.6 ± 11.4%) compared to the controls (22.2 ± 2.6%).
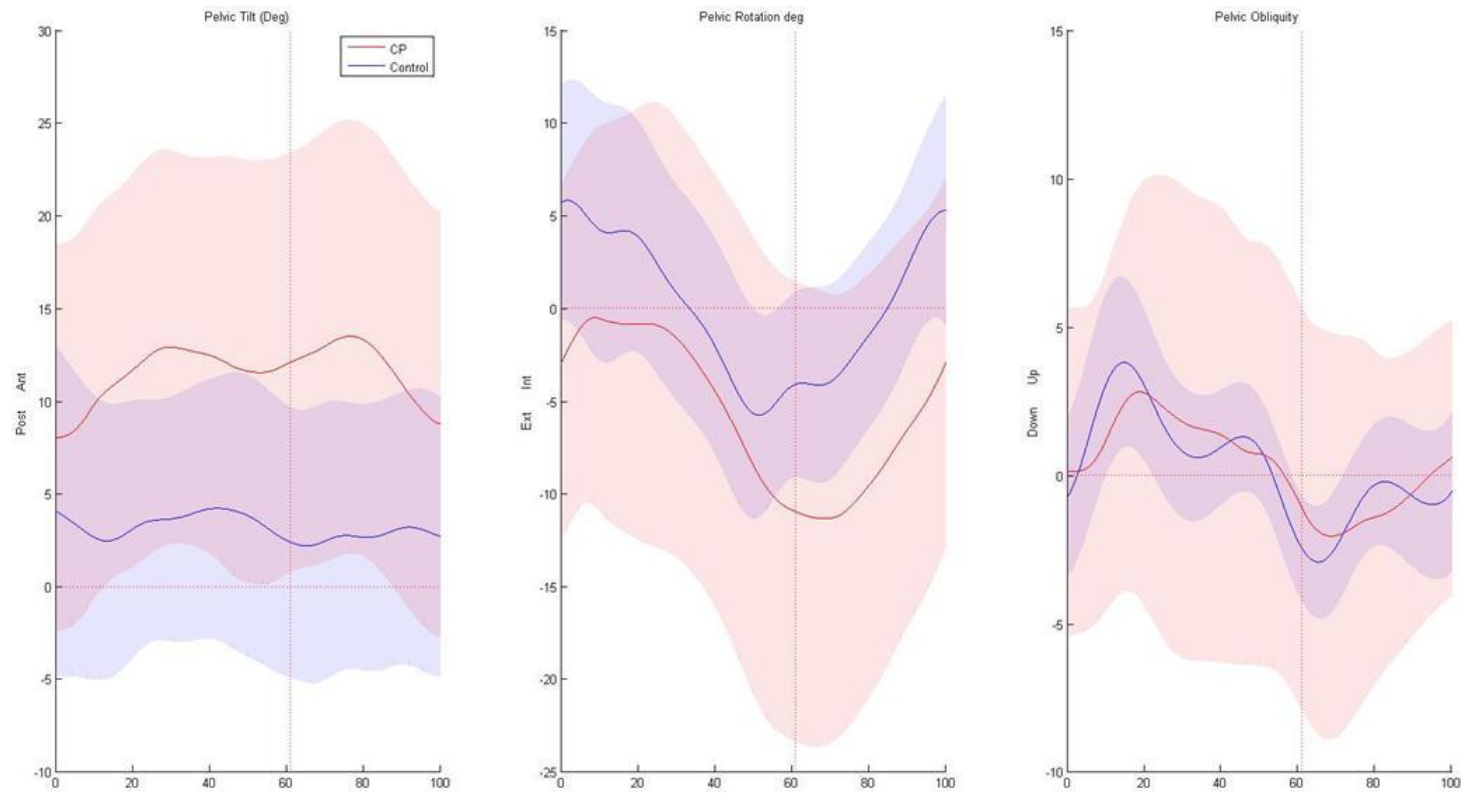
Foot-floor grand average kinematics
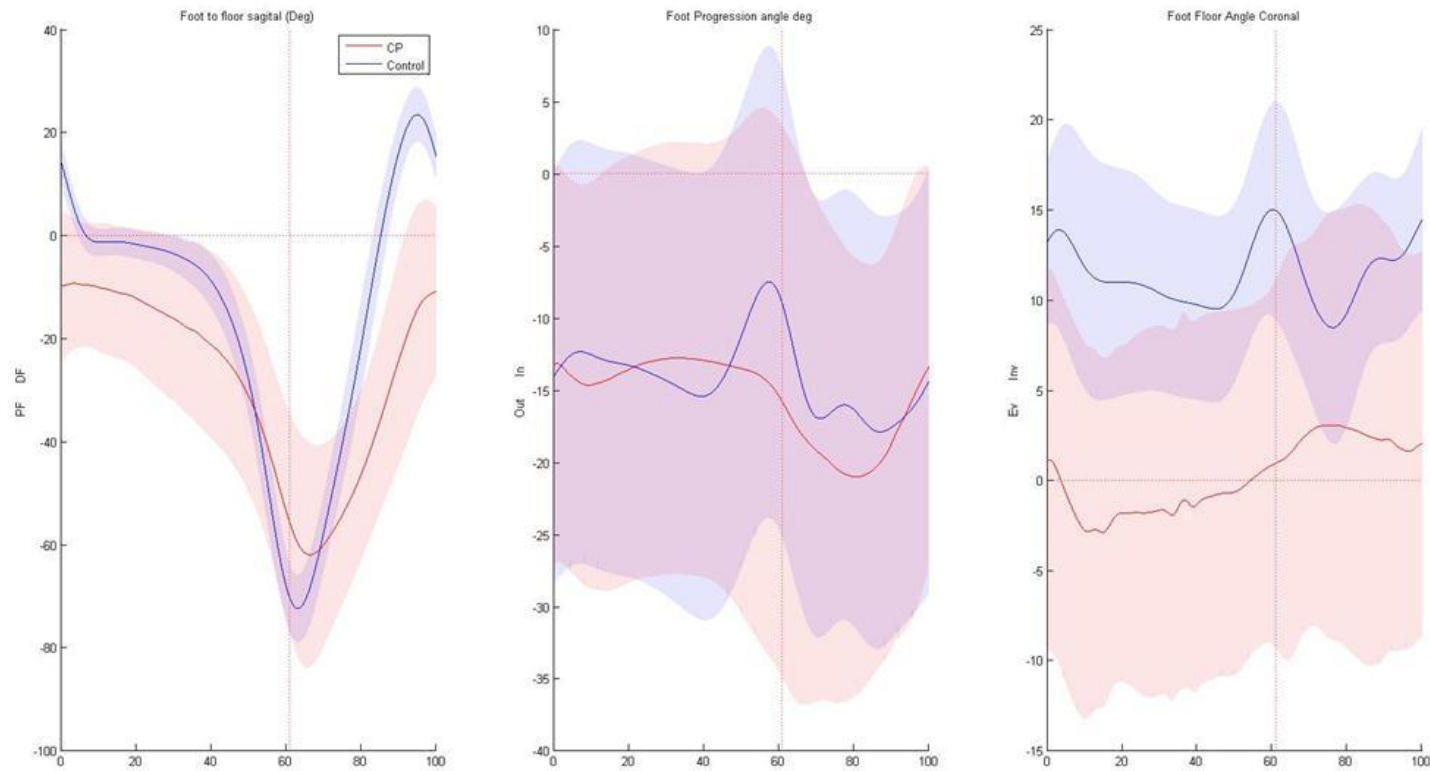
Figure 3.5: Grand average plots of foot-floor joint angles in the sagittal (column 1), transverse (column 2) and coronal (column 3) planes.

Motion on the side analysed, the subjectively defined more severe side is indicated.

Differences in kinematics and kinetics

The following section explores the statistical differences between pwCP and the control group of selective variables relevant to the assessment of SKG. In these analyses the effects of walking speed have been accounted for using an ANCOVA.

Trough to Peak knee flexion

Trough to peak knee flexion was significantly lower in pwCP (n=27) after taking into account differences in walking speed between the groups (control n=20) using an ANCOVA $(F_{(1,44)}=5.8\ P<0.05)$.
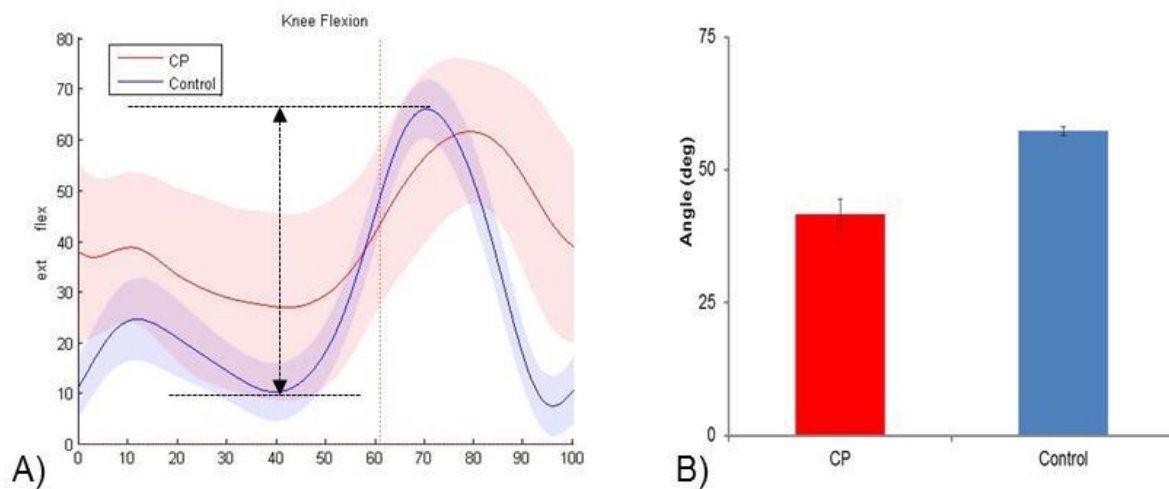
Figure 3.6: Trough to peak knee flexion A) Grand average response (+/- 1 SD). Arrows indicate the measure taken. B) Mean differences in trough to peak knee flexion in pwCP and controls

Knee extension in stance

After taking into account differences in walking speed between the groups (pwCP n=27 control n=20) using ANCOVA $(F_{(1,44)}=1.2\ P>0.05)$ no significant difference was shown in knee extension during stance.
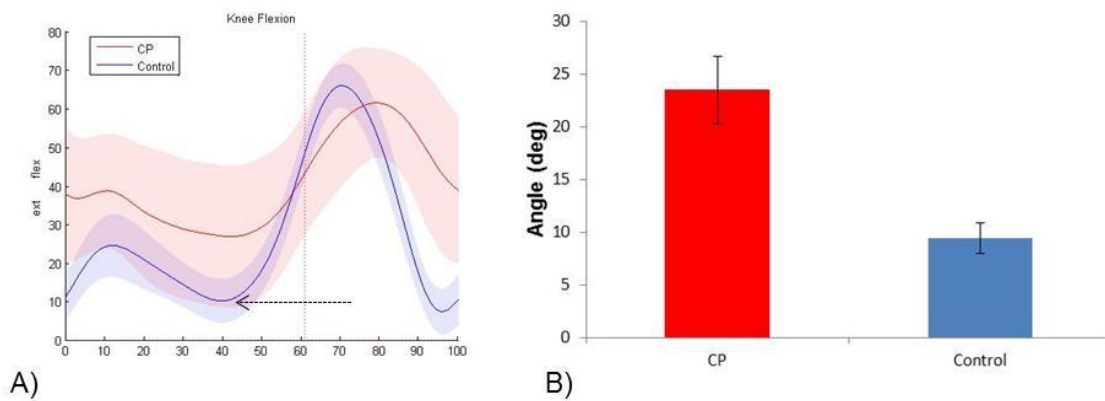
Figure 3.7: Knee extension in stance A) Grand average response (+/- 1 SD). Arrow indicates the measure taken. B) Mean differences in knee extension angle in stance in pwCP and controls

Knee flexion velocity in preswing

After taking into account differences in walking speed between the groups (pwCP n=27 control n=20) using ANCOVA $(F_{(1,44)}=0.6\ P>0.05)$ no significant difference was shown in knee flexion velocity in preswing.
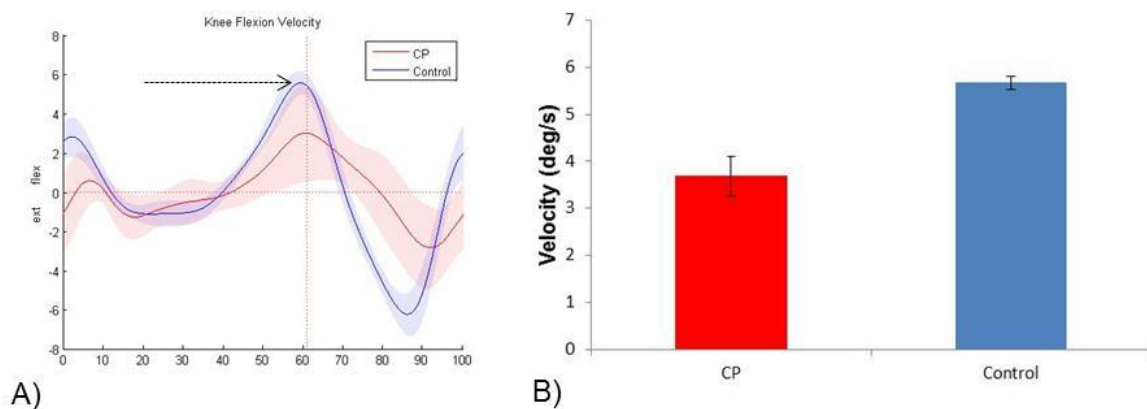
Figure 3.8: Knee flexion velocity in preswing A) Grand average response (+/- 1 SD). Arrow indicates the measure taken. B) Mean differences in knee flexion velocity in preswing in pwCP and controls

Ankle power in preswing

Peak ankle power in preswing was significantly lower in pwCP (n=25) after taking into account differences in walking speed between the groups (control n=20) using ANCOVA ($F_{(1,42)}=7.4$ $P<0.05$).
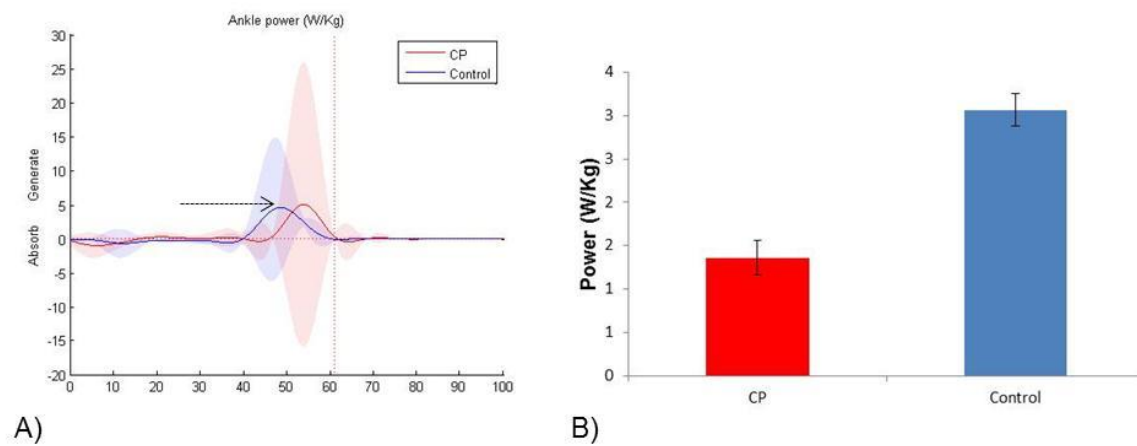
Figure 3.9: Ankle power in preswing A) Grand average response (+/- 1 SD). Arrow indicates the measure taken. B) Mean differences in ankle power in preswing in pwCP and controls

Hip flexor power in preswing

After taking into account differences in walking speed between the groups (pwCP n=25 control n= 20) using ANCOVA ($F_{(1,42)}=0.31$ $P>0.05$) no significant difference was found in hip flexor power in preswing.
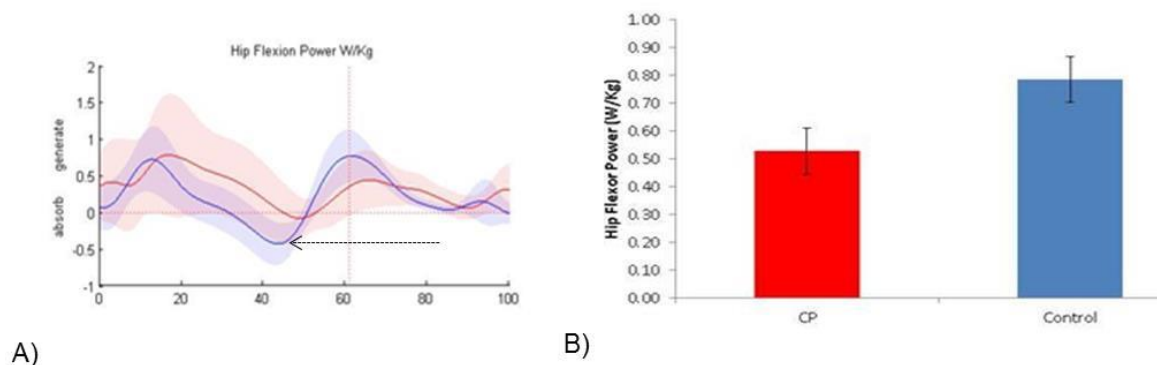
Figure 3.10: Hip flexor power in preswing A) Grand average response (+/- 1 SD). Arrow indicates the measure taken. B) Mean differences (+/-SEM) in hip flexor moment in preswing in pwCP and controls

Knee extensor moment in preswing

After taking into account differences in walking speed between the groups (pwCP n=25 control n=20) using ANCOVA ($F(1,42)=0.04$ $P>0.05$) no significant difference was shown in knee extensor moment in preswing.
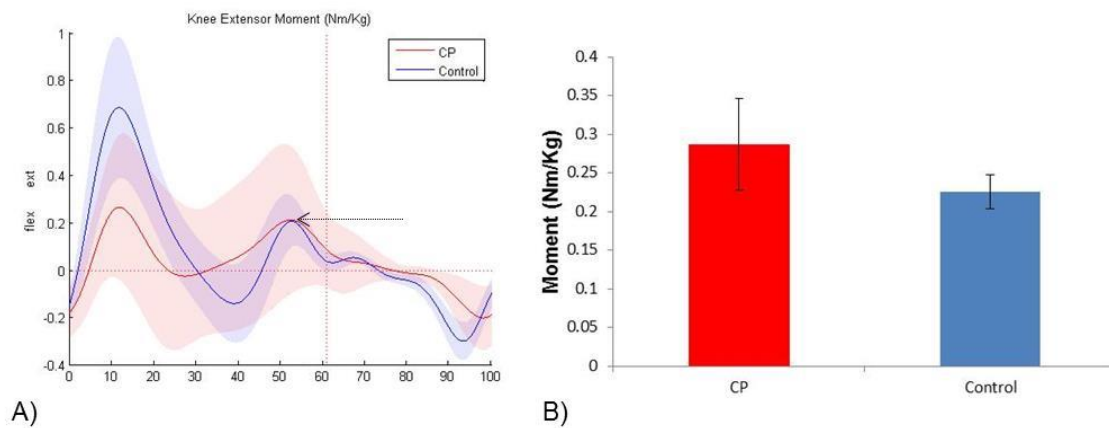
Figure 3.11: Knee extensor moment in preswing A) Grand average response (+/- 1 SD). Arrow indicates the measure taken. B) Mean differences in knee extensor moment in preswing in pwCP and controls

Measures of Stiffness in the knee extensors

The grand average response to stretching the knee extensors at different speeds in the pwCP (n=27) and the controls (n=18) is indicated in Figure 3.12.
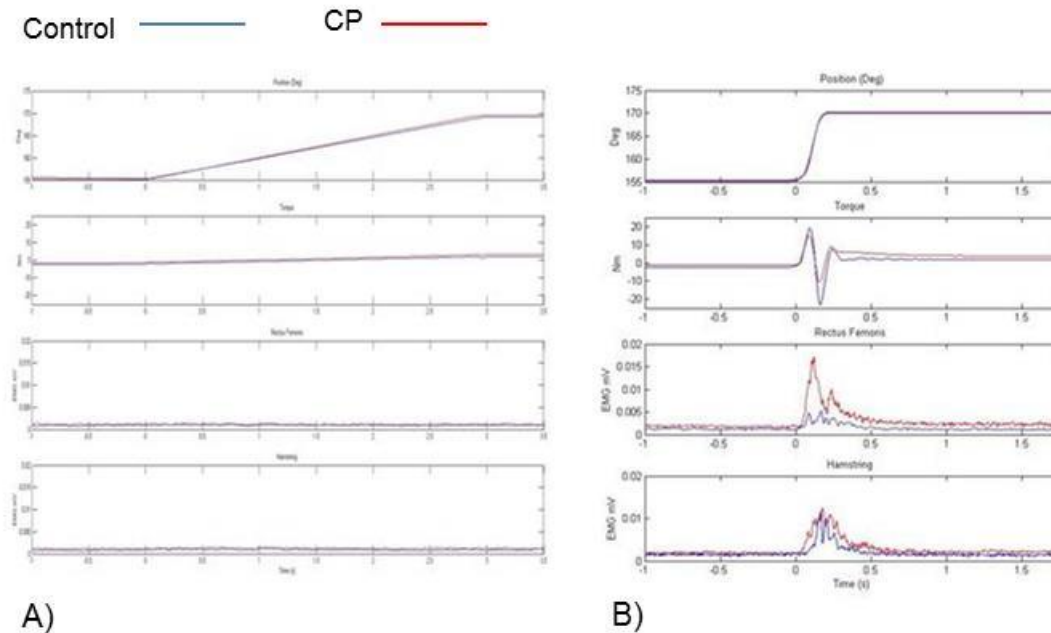
Figure 3.12: Measure of stiffness in the knee extensors A) Grand average response to a 5 ^{o}/s. B) 175 ^{o}/s stretch

PwCP had significantly higher total stiffness t= 5.6 P<0.001, passive stiffness t= 3.5 P<0.002 and stretch-mediated stiffness t= 5.3 P<0.001 (Figure 3.13).
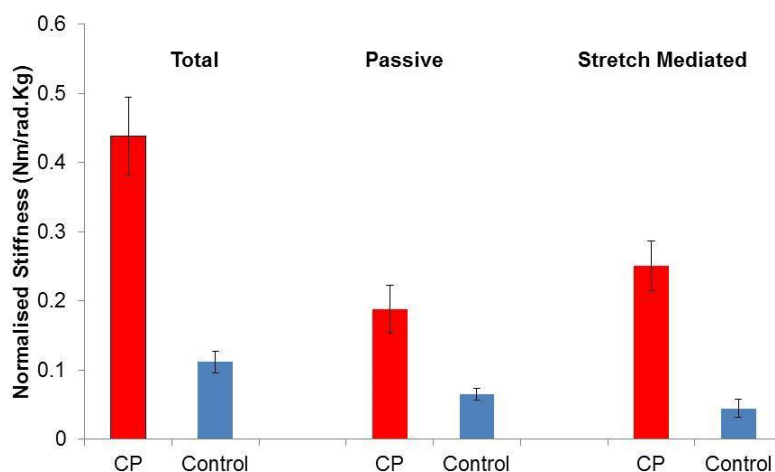
Figure 3.13: Differences in normalised stiffness between pwCP and controls

Measures of Strength

Ankle plantarflexion

Isometric ankle plantarflexion strength was significantly weaker in pwCP when measured at both 15 degrees (t= -6.9 P<0.001) and 5 degrees (t= -5.9 P<0.001, Figure 3.14) compared to the controls. [Ankle 5 degrees pwCP n=17, control n=19. Ankle 15 degrees pwCP n=24, control n=20].

In both groups the mean ratio (15/5 degrees) was below 1 indicating that the ankle plantarflexors tended to be stronger when they were lengthened. There was no significant difference between the groups (t= 1.7 P>0.05).
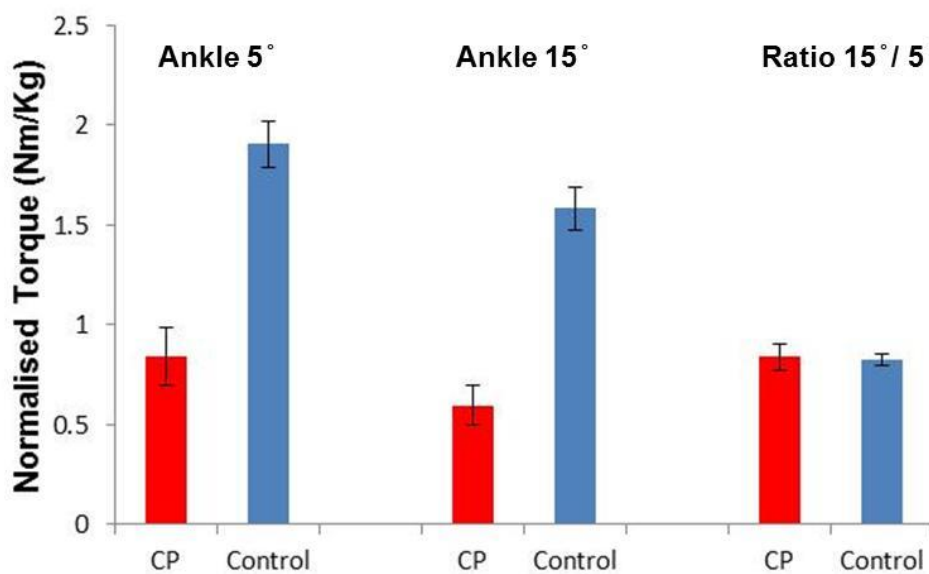
Figure 3.14: Differences in MVC at the ankle between pwCP and controls

Knee extension

Isometric knee extension was significantly weaker in pwCP at both 20 degrees (t= -9.3 P<0.001) and 90 degrees (t= -4.4 P<0.001) compared to the controls. [Knee 20 degrees pwCP n=23, control n=20. Knee 90 degrees pwCP n=24, control n=20].

Knee strength was higher at 90 degrees in both groups (Figure 3.15) i.e. when the muscle was lengthened. The ratio of knee extension (20/90 degrees) was lower in pwCP compared to the control group (t= -6.0 P<0.001). This indicates that pwCP were relatively weaker when the knee was at 20 degrees compared to 90 degrees in comparison to the control group (Figure 3.15).
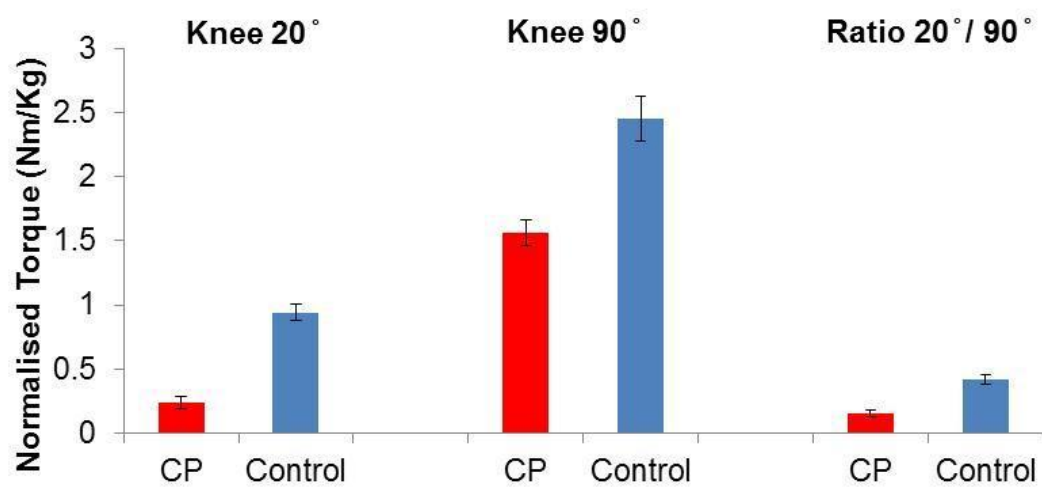
Figure 3.15: Differences in knee extension at different joint angles in pwCP and controls

Hip flexion

Isometric hip flexion was significantly weaker in pwCP at both 10 degrees (t= -2.7 P<0.001) and 40 degrees (t= -4.9 P<0.001) compared to the controls. [Hip 10 degrees pwCP n=22, control n=19. Hip 40 degrees pwCP n=25, control n=20].

Both groups were stronger with the hip at 10 degrees (Figure 3.16). The ratio of hip flexion (10/40 degrees) was lower in the control group compared to pwCP, indicating that the controls were relatively stronger when the hip was at 10 degrees. There was no significant difference between the groups (t= 1.5 P>0.05).
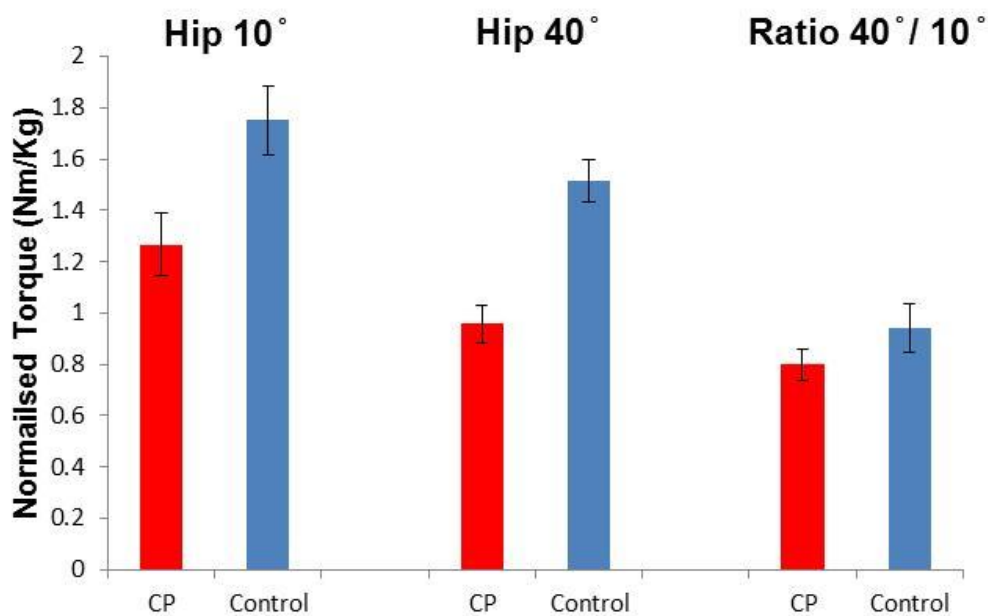
Figure 3.16: Differences in hip flexion at different joint angles in pwCP and controls

Hip extension

Isometric hip extension in pwCP was significantly weaker at both 10 degrees (pwCP n=21 t= 2.6 P<0.05) and 40 degrees (pwCP n=24 t= 1.7 P<0.001) compared to the controls. [Hip 10 degrees pwCP n=15, control n=18. Hip 40 degrees pwCP n=16, control n=19].

Both groups were stronger with the hip in 40 degrees (Figure 3.17). The ratio of hip extension (40/10 degrees) was similar between the two groups, showing no significant difference (pwCP n=21 t= 0.4 P>0.05).
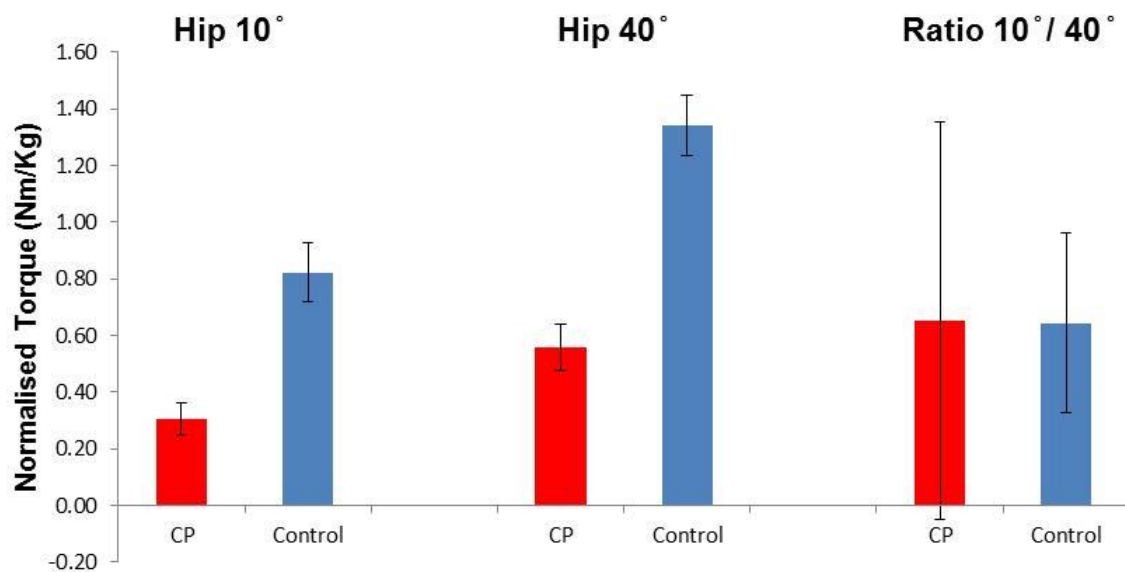
Figure 3.17: Differences in hip extension at different joint angles in pwCP and controls

Discussion

General differences in walking

This chapter looked at the general differences in walking between pwCP and healthy controls and then focussed on specific changes in knee motion while walking and impairments that have a priori been hypothesised to cause SKG. The general differences that were descriptively highlighted will be discussed prior to discussing differences in specific gait patterns and impairments.

Sagittal plane differences

A double bump pattern is present in pwCP, this term refers to the increased anterior pelvic tilt which occurs once in midstance phase and once in midswing phase, therefore twice in total during a complete gait cycle (Ounpuu 2004). The CP group become less anteriorly tilted during periods of double support (i.e. initial contact and midstance) and more anteriorly tilted during single support phase when the contralateral leg is swinging forwards. Peak anterior tilt may occur when spastic/contracted hip flexors and/or weak hip extensors cause the pelvis to tilt forwards during single stance. The peak posterior tilt occurs during double stance when the hamstrings (on the leading leg) are stretched. Thus, pelvic motion may result from both hip flexor and extensor (including the hamstrings) involvement (Ounpuu 2004). These two peaks give the double bump appearance on a kinematic graph (Figure 3.1).

Contracture in the hamstrings could also limit the knee extension at the end of swing phase. However, as with knee flexion during swing phase the factors affecting knee extension in swing are multifactorial. Early modelling studies of normal walking have shown that much of the pattern of knee flexion and extension during swing phase is passive in nature reflecting the motion of multilinked joints that are provided with an initial impulse at the beginning of swing phase (Mochon & McMahon 1980). More recent studies have modelled the action of different muscles during swing phase (Jonkers et al. 2006). They have highlighted that muscle activity is important in modulating the amplitude and rate of joint motion. Eccentric contraction of the hamstrings, for example, can limit extension of the knee. It is interesting to note that the knee flexor moment at the end of swing phase was reduced in pwCP. This may reflect a compensatory decrease in eccentric hamstring muscle activity with the aim of aiding the slow and reduced amplitude knee extension.

An increased hip extensor moment was present in pwCP between 10 and 55% of the gait cycle, in comparison to the control group (Figure 3.2). This could possibly be due to increased flexion at both the hip and knee, requiring more antigravity activity and/or

compensation for lack of plantarflexor power generation during push in the contralateral leg to help with antigravity function and progression.

Deficits in distal control were clearly evident in pwCP. The action of the foot and ankle during stance phase can be described in terms of three foot rockers. The first two rockers aid deceleration of the body and leg so the respective muscles (ankle dorsiflexors and plantarflexors) are working eccentrically. The third rocker is an acceleration rocker, aiding propulsion, so the respective muscles (ankle plantarflexors) are working concentrically. The first rocker acts as a shock absorber, from the initial contact through to loading response. The second rocker refers to the midstance sub-phase where the shank moves forward on the stationary leg. The purpose of second rocker is to control the position of the ground reaction force. In third rocker the fulcrum moves from the ankle forwards to the metatarsals and initiates a heel raise caused by the concentric actions of the ankle plantarflexor muscles (Gage 2004a). The high plantarflexor moment witnessed within pwCP during early stance phase (Figure 3.2) contributes to a reduced dorsiflexion during the second rocker. As ankle moments are calculated through inverse dynamics (see chapter 2) the cause of the high plantarflexor moment is unclear. The increased plantarflexor moment and subsequent poor second rocker could result from either increased passive stiffness or spasticity in the ankle plantarflexors or volitional activity. EMG would help determine whether active muscle contraction contributes to the high moment but would not be able to easily identify voluntary contractions from stretch reflex induced responses. The late ankle power generation in pwCP occurred when the contralateral leg was in contact with the ground. Thus the delayed ankle power generation may reflect a combination of a high plantarflexor moment and a relatively slow and passive ankle plantarflexion as the leg lifts off the ground at the start of swing phase (Shortland, A., 2014 personal communication, Guy's Hospital). Thus the delay in ankle power generation may reflect a relatively passive process that contributes little to progression and swing phase initiation.

Coronal and Transverse plane differences
The common themes within these planes are highlighted below. This study showed, in comparison with the controls, that in pwCP the hip abductor moment was low during stance (coronal plane, Figure 3.3). This could possibly be due to weakness in the hip abductors, leading to a trendelenburg gait. Alternatively it could reflect leaning of the trunk towards the side of the stance leg. This would bring the ground reaction force close to the hip joint centre thus reducing the hip abductor moment. Increased trunk motion was often observed on the videos taken but no markers were placed on the trunk to support/refute this hypothesis. Increased trunk motion in the coronal and transverse planes can aid in motion of the pelvis

(Inman et al. 2006) and thus limb motion during swing phase. Additionally it can help to position the ground reaction force close to the joint centres thus reducing the required limb muscle activity.

Internal rotation at the hip is greater in pwCP (transverse plane, Figure 3.4), this could be due to a combination of dynamic muscle pull and femoral anteversion. As mentioned in chapter 1, femoral anteversion describes the abnormal internal rotation of the femur, resulting from the head and neck of the femur being angled forward in excess of 15 degrees (Cibulka 2004). It is commonly seen in pwCP and spastic diplegia. As this study focused on the causes of SKG, clinical markers of femoral anteversion such as the range of internal and external hip rotation and the femoral anteversion test were not performed. Increased knee valgus and ankle eversion were also present (coronal plane, Figure 3.3) among pwCP. In other patient groups with an upper motor neuron syndrome (stroke) increased ankle eversion has also been described in cross-sectional studies (Forghany et al. 2011) and was felt to reflect ankle planovalgus. The current study modelled the foot as one segment therefore it cannot determine the relative segment motion that contributed to the ankle eversion (e.g. hind foot vs forefoot). Planovalgus has been described in pwCP who walk with a crouch gait (Kadhim & Miller 2014) and 12/27 pwCP were classified as having some degree of crouch gait in the current study.

In summary, the gait differences seen in pwCP reflect those previously described either clinically or in retrospective or prospective gait analysis studies. In many cases however the causes of gait abnormalities are unknown or there are several possible reasons. Future work in healthy controls, pwCP and other patient populations should explore different aspects of walking in more detail. An experimental approach could be beneficial here. For example, exploring in healthy controls how they compensate for bilateral stiffening of the knee (e.g. with altered trunk motion) will help us to understand which changes may arise from primary pathology and which changes may reflect compensatory strategies. Examination of pathologies, such as neuropathies and myopathies for example, where there is deficient distal control with relatively normal proximal control and no signs of an upper motor neuron syndrome can help us understand the effects of distal weakness on walking.

Specific gait abnormalities

Some of the apparent kinematic gait differences between the control group and pwCP such as the degree of crouch (knee extension in midstance) and knee velocity in preswing were not statistically significant once the effects of walking speed were accounted for. This highlights that at least some differences seen between the groups could be explained by differences in walking speed. Slower speeds are associated with (a) a reduction in the

required joint torques and (b) a reduction in joint angular velocity that would lead to a reduction in stretch reflex induced muscle activation (i.e. spasticity). Thus, as hypothesised elsewhere (Nielsen et al. 2007) the reduction in walking speed may in part be a compensatory strategy to avoid spasticity and/or reflect the limitations imposed by weakened muscle groups.

Despite appearing reduced (compared to the control group) no significant difference was shown in the hip flexor power once walking speed was taken into account (Figure 3.10). In contrast a significantly lower ankle power generation was observed. Both muscle groups however generated significantly reduced torque during isometric testing. The differential effects of hip flexor moment and ankle power generation may reflect two interrelated factors namely a difference in the degree of weakness seen in the hip flexors and ankle plantarflexors in pwCP and the effects of reduced walking speed. Although both muscle groups were weaker with isometric testing, the ankle plantarflexors were relatively more impaired than the hip flexors. The ratio between isometric strength for the controls/pwCP (when tested in the most lengthened position) was 2.25 for the ankle plantarflexors but only 1.3 for the hip flexors. Thus there was a greater impact on distal compared to proximal muscle groups. This may in part reflect differences in the descending control of proximal and distal leg muscles. Proximal muscles, for example, have a higher proportion of innervation by both ipsilateral and contralateral corticospinal fibres whilst the innervation of distal muscles is predominately contralateral (Kuypers 1964). The higher proportion of bilateral control for proximal muscles means that these muscles are more resistant to the effects of focal pathology as some tracts may be spared. Previous work in stroke has recorded the maximal strength in the hip flexors and ankle plantarflexors during isokinetic contractions at speeds similar to that seen during walking (Milot et al. 2008). They then related the peak torques achieved to those achieved during walking, as determined using inverse dynamics. The ratio of the peak torque during walking/peak isokinetic torque was termed the muscle utilisation ratio (MUR) and reflects the "spare capacity" of the muscle to generate torque during walking. Healthy participants during level walking have MURs of 51.3-62.6% in the ankle plantarflexors and 2.7-49.9% in the hip flexors (Requião et al. 2005). At higher cadences the MUR for the hip flexors reach the values of the plantarflexors indicating an increased usage of these muscles with an increase in walking speed. Post stroke the MUR are similar to controls at self-selected speeds (64%+/- 18.7) and (46%+/-27.6) for the ankle plantarflexors and hip flexors respectively (Milot et al. 2007). However, there is a marked increase in MUR when people are asked to walk at their maximal speed (77%+/- 23.6) and (72%+/- 33.0) for the ankle plantarflexors and hip flexors respectively. Milot et al have also shown that the ankle plantarflexors are often working close to 100% capacity while walking

and weakness in this muscle group can limit maximal walking speed. Further, people with relatively spared hip flexor strength post stroke were able to compensate for the weakness in the ankle plantarflexors to a certain extent and achieved greater maximal walking speeds (Milot et al. 2008). In summary, the reason why ankle power generation was more affected than hip flexor power generation while walking may reflect relative sparing of the hip flexors and the fact that the ankle plantarflexors were working at close to 100% of their capacity. In future it would be useful to look at joint power/moments both at self-selected and maximal walking speeds. It would be predicted that group differences would be more marked when pwCP walk at their maximal speed. Whether joint power increases with walking speed, as would be expected in the healthy population, would also provide an indication of whether a muscle is working close to their maximal capacity and possibly limiting any further increase in walking speed. This could then aid decisions about which muscle groups to target with therapy.

Importantly trough to peak knee flexion was significantly lower in pwCP (Figure 3.6), even when walking speed was taken into account. This highlights that SKG was, as a group, a significant problem. SKG was seen in 18/27 (66%) of pwCP with 33% (9/27) being classified as having a severe limitation. This is higher than the proportion of some other gait changes (e.g. crouch gait 12/27). This difference may however reflect recruitment bias as pwCP and families may have been more likely to participate if they had a SKG. As the presence of SKG is not explained by walking speed it suggests that it is mainly caused by the direct effects of pathology. The factors affecting SKG will be explained more in chapter 4.

Stiffness

PwCP had significantly higher total stiffness, passive stiffness and stretch-mediated stiffness (Figure 3.12/13). This is in keeping with the literature (Ranatunga 2011; de Gooijer-van de Groep et al. 2013; Willerslev-Olsen et al. 2013; Bar-On et al. 2014). In pwCP increases in passive stiffness have been reported in children as young as three years old highlighting that it can develop quite early.

The presence of both increased passive and stretch-mediated stiffness contributing to the total stiffness has implications for the assessment and rehabilitation for both passive stiffness and spasticity. Firstly, these findings highlight that clinical scales, such as the Ashworth scale, that only rate the perceived resistance to stretch are only able to provide a global rating of limb stiffness and cannot differentiate between the different components. Further, it highlights that the speed of passive limb movement during an assessment is important as this will determine whether only passive stiffness is being assessed or a combination of both components.

The different components of stiffness may require different interventions. Typical interventions for spasticity, for example, would involve pharmacological input or surgical procedures, such as dorsal rhizotomy. In contrast typical treatment for passive stiffness would be a physical intervention, such as stretching. The literature for stretching is inconclusive (Katalinic et al. 2011) but there is evidence that stretching at the ankle for pwCP using serial casting may be effective (McNee et al. 2007; Jain et al. 2008). Whether these techniques are appropriate for knee stiffness is debateable as they would be associated with considerable reduction in functional ability while the cast was in situ. Other options such as night splints could be a preferable option.

Although there are interventions that can potentially improve passive and stretch reflex mediated stiffness it is not certain which, if any, require targeting. Some studies and case reports in other patient populations (e.g. HSP and multiple sclerosis) have highlighted that some degree of stiffness is beneficial as it can aid in stability and transfers (Marsden & Stevenson 2013). Understanding the impact of these impairments on a functional activity such as walking is thus vital and will be explored in chapter 4.

Strength

PwCP were found to be significantly weaker at both positions measured for the ankle, knee and hip (Figure 3.14-17). There are several reasons why pwCP could be weak and they include neurological deficits, peripheral atrophy, altered sarcomere length and lever arm dysfunction as discussed in chapter1. Unfortunately it is not possible to distinguish between these possible reasons using the techniques used within this study. To distinguish between these components it would require techniques such as twitch interpolation that assesses the additional torque generated during a MVC by maximally stimulating the peripheral nerve. If there is a large increase in torque this implies that there is reduced central drive i.e. descending signals are not able to activate the muscle to its full potential.

This study highlighted differences between the strength generated when the joint was at different angles. Differences in torque generation with joint angle reflects two factors (a) changes in the lever arm with movement and (b) changes in the length-tension relationship in the muscle. With a change in joint angle, for example in the knee, the axis of rotation and the line of pull of the muscles alters, both of which will alter the lever arm and thus torque generated for a given force. Changes in applied torque will also in part reflect differences in the length-tension relationship. This describes the relationship between the tension that a muscle can generate and the length of the muscle. It has been explored in animal preparations in the isolated muscle where factors such as lever arm change and changes in the weight of the limb relative to gravity are avoided (Edman 2010). The length-tension

relationship has an inverted U shaped curve and is caused by the degree of overlap between the actin and myosin filaments. Tension is maximal when there is maximal overlap of the filaments and drops with subsequent lengthening and shortening. Normally muscles are felt to work on the ascending arm of the length-tension relationship although factors such as sarcomere length, which may be longer in pwCP, makes it hard to conclude whether this is true in this patient population.

In the present study people were assessed with the muscle either in inner range, when the muscle is shortened, or outer range when the muscle is lengthened. Not all participants could achieve the positions required due to contracture and the differences reported were seen when the subgroup that performed both tests were described. In all cases the inner range was found to be weaker than the outer range. This could be explained by the length-tension relationship, in inner range there is less overlap between the actin and myosin filaments.

For both groups (CP and control) the hip flexors, hip extensors, knee extensors and plantarflexors were all found to be stronger in the outer range muscle position, compared with their respective inner range positions.

Measuring hip extension had some practical difficulties. There was sometimes not a large enough space between their lower limb and the plinth when measuring hip extension. It was noted that sometimes the participants' heel would reach and therefore push down on the plinth or the strap around the participants' thigh would sometimes become squashed against the plinth. In some cases there was also difficulty with fixing the pelvis, despite one researcher attempting to counteract this by applying a downward pressure. Other studies have tested hip extension strength in prone standing (Damiano & Abel 1998; Taylor et al. 2004; van der Linden et al. 2004). Prior to 2011 prone standing had not been tested in young people with CP (Dyball et al. 2011), however these techniques were not deemed appropriate for the current participants with CP due to their limited mobility and stability in standing. Dyball et al (2011) assessed the reliability of measuring hip extensor strength in three different testing positions; supine, prone and standing. They found that the supine position was the most reliable and can monitor change with sufficient reliability as long as three trials were used during testing. It is worthy to note that the starting positions used in that study (hip 90°, knee 90°) differed to the current study (hip 40° inner range and 10° outer range). Due to the difficulties found in standardising the position for hip extension in the current study the alternative method of measuring strength in prone standing could have been preferable.

In pwCP the ratio at the knee extensors is less than the controls, whereas with the hip flexors, hip extensors and the plantarflexors the ratio is similar. The difference with the knee extensors could possibly be a result of the pwCP not using the inner range knee extensors habitually during everyday activities. They have the range to do so but they are not seen to use it as many of the participants walked with a crouch gait. The effects of gravity should not be underestimated with regards to the CP group, it will be pushing them down while they walk and it may be the case that they do not have the same strength as the controls to withstand it. The relationship between the inner/outer strength ratio and crouch gait will be further explored in chapter 4.

As well as an alteration in habitual use of the knee extensor muscles the difference in inner/outer range ratio could be influenced by a change in the lever arm. Patella alta, a condition where the patella runs outside of the intercondylar groove due to the patella ligaments' high position on the femur (Schejbalova et al. 2011) is commonly seen in pwCP. It may result from having a shorter, stiffer muscle and a more compliant in series patellar tendon as has been described for the plantarflexor muscles in pwCP (Wren et al. 2010; Gao et al. 2011). The effect of patella alta on the lever arm and extensor muscle mechanism will be explored in more detail in chapter 4.

Summary

PwCP present with alterations in the pattern of walking that can be interpreted as arising from deficits in muscle weakness and hypertonia as well as compensatory strategies to maintain walking ability. Some kinematic and kinetic patterns can be attributed to a reduction in walking speed that may arise due to limitations in muscle strength or an avoidance of stretch reflex activation. However, some features such as SKG are present even when walking speed is accounted for as a covariate.

CHAPTER 4: FACTORS AFFECTING STIFF KNEE GAIT IN PEOPLE WITH SPASTIC DIPLEGIA

Introduction

In chapter 3 it was found that strength was reduced and knee stiffness (both stretch reflex related and passive) was increased in pwCP compared to the controls. It was also found that the trough to peak knee flexion was significantly reduced in pwCP; this pattern is indicative of a SKG. This chapter will look at factors affecting SKG in people with spastic diplegia.

Methods

As highlighted in chapter 2 all data was obtained within the Human Movement and Function Laboratory (Plymouth University) and participants were seen on one occasion for approximately 90 minutes. Gait measurements were recorded via 3D motion analysis equipment (Codamotion, UK) and strength and stiffness measures were recorded via a dynamometer (Biodex, USA). Muscle stiffness and spasticity in the knee extensors were measured objectively during controlled passive flexion of the knee. Slow movements of 5°/s measured the passive stiffness and much faster movements of 175°/s measured total stiffness from which the contribution of the stretch reflex related stiffness was estimated.

Analysis

The trough to peak knee flexion and potential predictors were normally distributed. The relationship between the predictors and the trough to peak knee flexion from stance to swing phase were assessed using a Pearson's correlation analysis. The following predictors were assessed defined a priori based on previous literature in this area (see chapter 1);

- Ankle plantarflexor strength
- Hip flexor strength
- Passive stiffness in the knee extensors
- Stretch reflex related stiffness in the knee extensors
- Knee extension in stance phase

Predictors that had a significant correlation with the trough to peak knee flexion while walking were entered into a stepwise multiple regression. Factors were accepted when they significantly increased the final model.

To provide a general description of the differences between pwCP with different degrees of SKG, participants were divided into three groups according to the criteria outlined in chapter 3: normal range (n=8); mild/moderate impairment (n=9); severe impairment (n=8). The two people who used frames to walk (participants 13 and 14) were excluded from this analysis as kinetic recordings could not be obtained from them; they were classified as having severe and normal SKG respectively.

Results

Descriptive differences between different severities of SKG in pwCP are indicated in Figures 4.1-4.3.

As well as a clear difference in trough to peak knee flexion, the variable used to produce this classification, the following gradations from normal to severity were noted. In particular with an increase in SKG severity there was:

- a decrease in the degree of knee extension in mid stance (Figure 4.1)
- an increase in knee extensor moment in preswing (Figure 4.1)
- an increase in hip internal rotation in stance phase (Figure 4.2)
- an increase in knee external rotation in stance phase (Figure 4.2)
- a reduction in the hip abductor moment in stance phase (Figure 4.3)
- an increase in the knee varus moment in stance phase (Figure 4.3)
- an increase in the ankle eversion moment in stance phase (Figure 4.3)
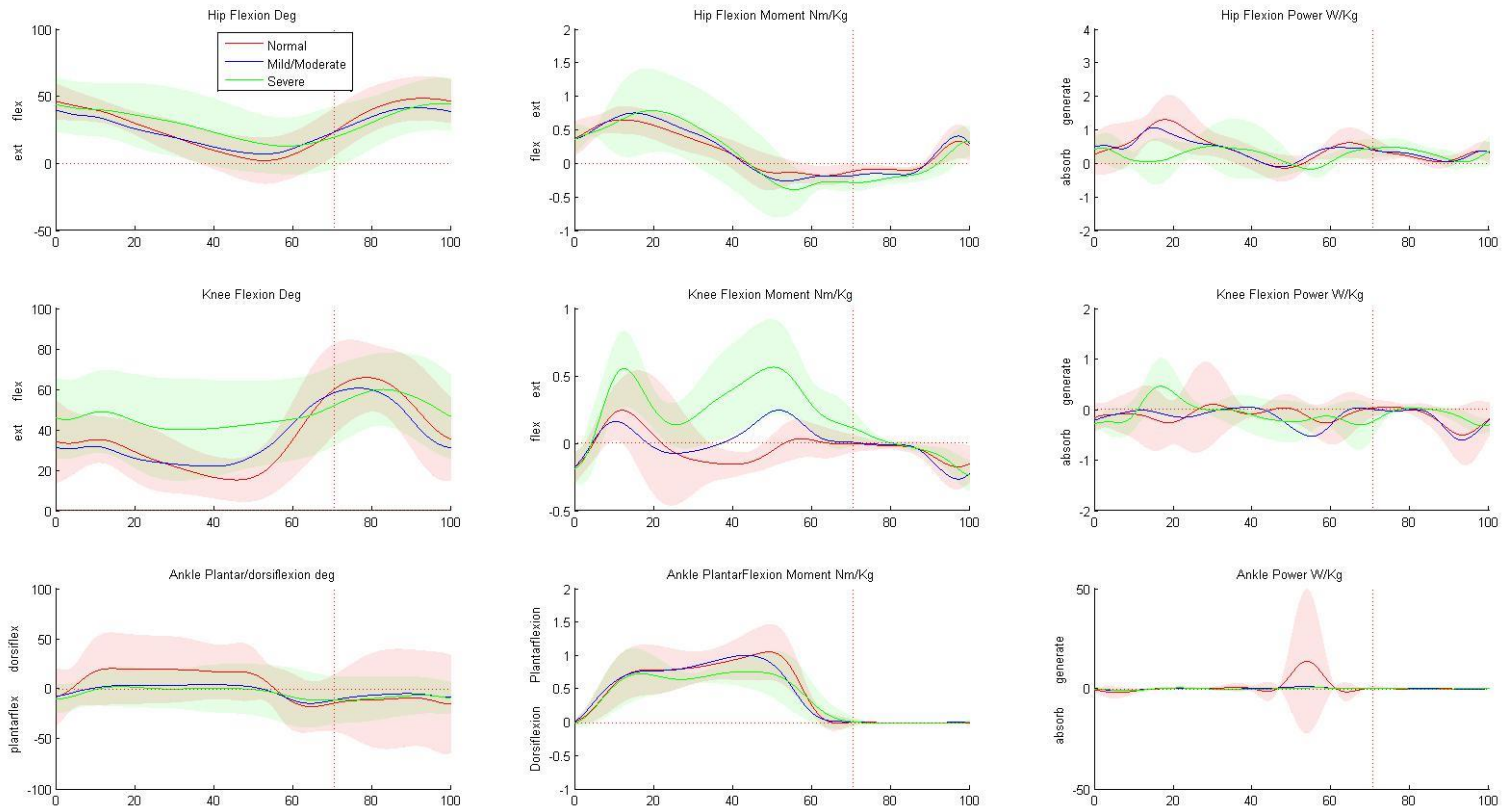
Figure 4.1: Comparison of sagittal plane joint kinematics and kinetics for pwCP with trough to peak knee flexion classified as normal, mild/moderate and severe
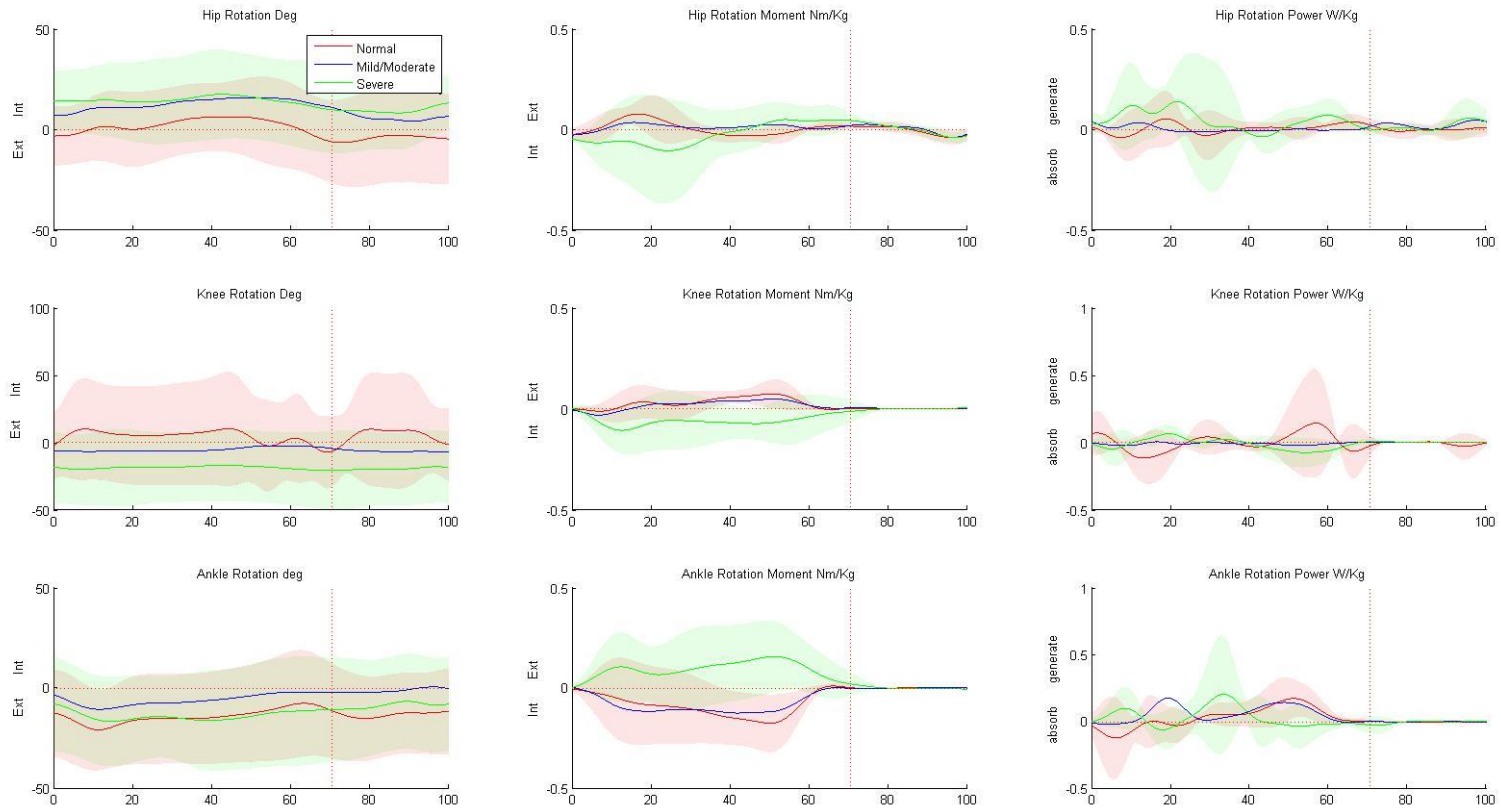
Figure 4.2: Comparison of transverse plane joint kinematics and kinetics for pwCP with trough to peak knee flexion classified as normal, mild/moderate and severe

Factors Associated with Stiff Knee Gait in Cerebral Palsy
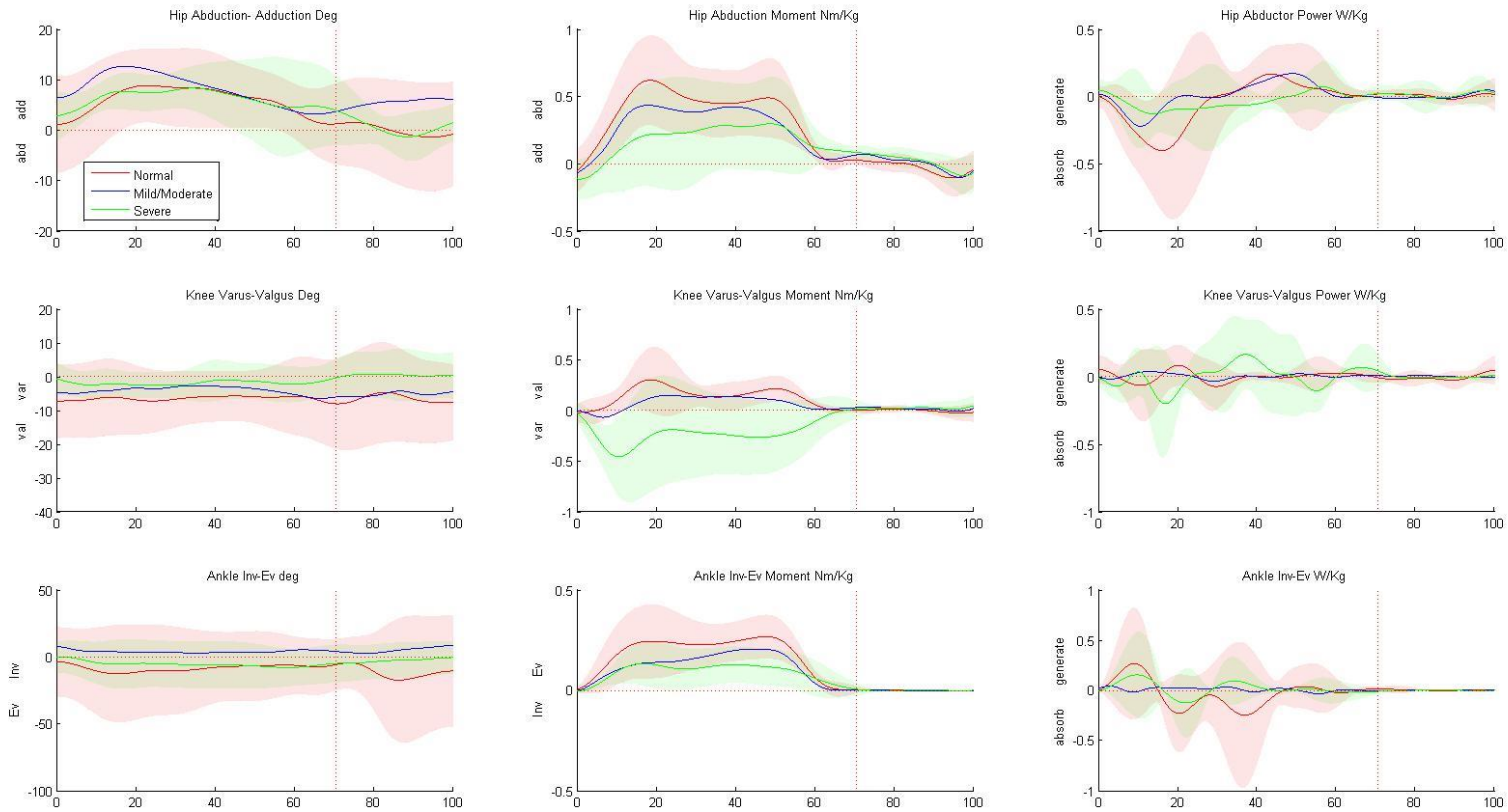
Figure 4.3: Comparison of coronal plane joint kinematics and kinetics for pwCP with trough to peak knee flexion classified as normal, mild/moderate and severe

Correlation with individual predictors

Two participants did not perform the strength measures due to difficulty with compliance and comprehension of the test requirements, although data was obtained for knee extensor stiffness in these cases.

Ankle plantarflexor strength

Due to ankle plantarflexor contracture not everyone could perform the test with the ankle in 5 degrees plantarflexion (n=17) or with the ankle in 15 degrees plantarflexion (n=23).

There was a weak non-significant positive correlation between trough to peak knee flexion and ankle strength in 5 degrees plantarflexion (r= +0.40, R^2=0.16, P= 0.11, Figure 4.4). Lower trough to peak knee flexion was associated with lower strength in the ankle plantarflexor.
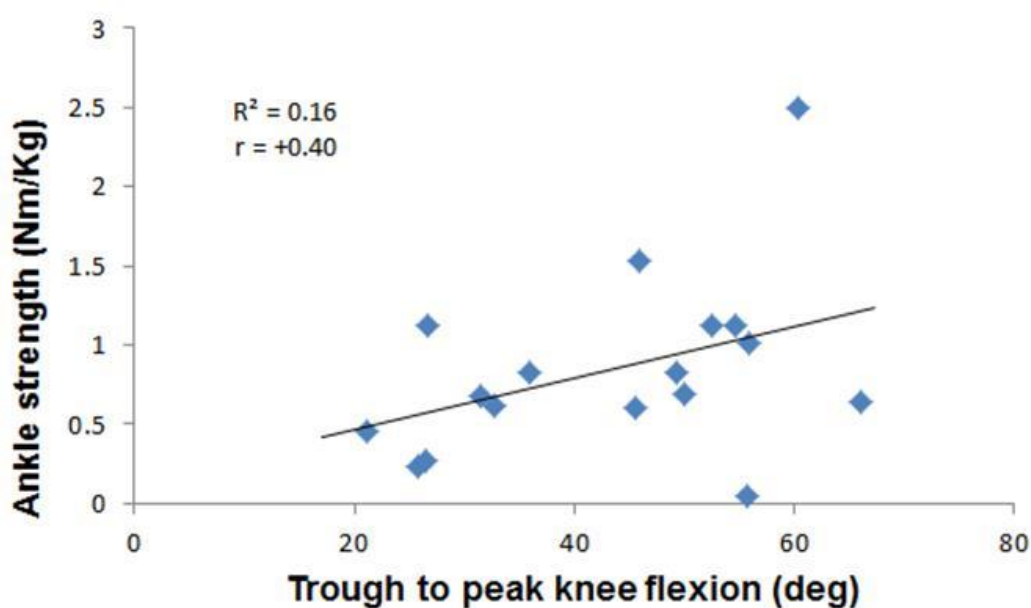
Figure 4.4: Correlation between trough to peak knee flexion and ankle strength in 5 degrees dorsiflexion

There was no significant correlation between trough to peak knee flexion and ankle strength in 15 degrees plantarflexion (r= +0.23, R^2=0.05, P>0.05).

Ankle power generation

Due to the lack of isometric strength measure data on all participants the correlation between trough to peak knee flexion and ankle power generation in preswing was also exported. This was obtained in 25 people, the remaining 2 required a frame to walk which prevented the gathering of kinetic data. There was a significant moderate positive correlation between trough to peak knee flexion and ankle power generation (r= +0.48, R^2=0.23, P<0.05, Figure 4.5). Lower ankle power generation was associated with less trough to peak knee flexion.
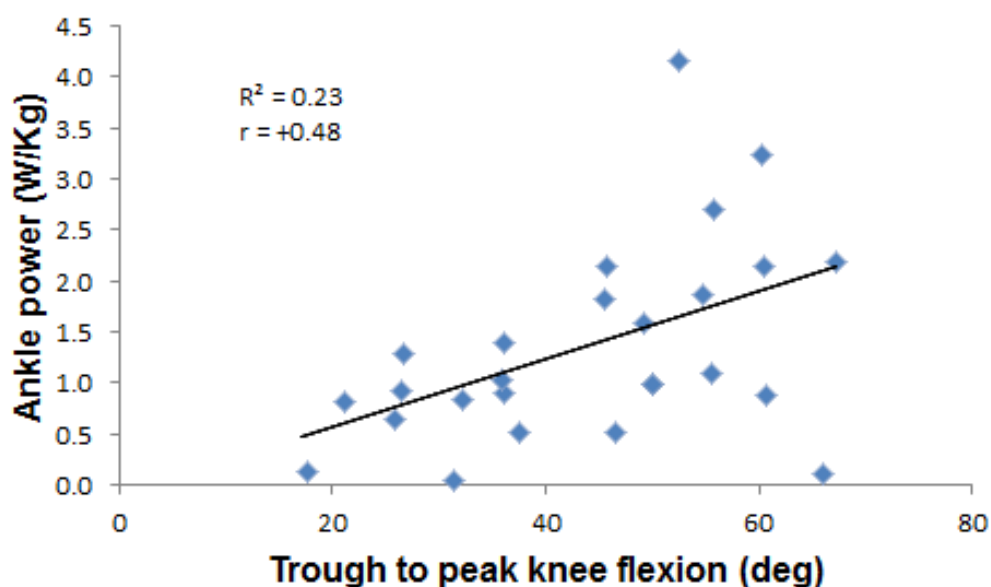
Figure 4.5: Correlation between trough to peak knee flexion and ankle power generation

Hip flexor strength

Due to hip flexor contracture not everyone could perform the test with the hip in 10 degrees flexion (n=22). There was a non-significant positive weak-moderate correlation between trough to peak knee flexion and hip flexor strength in either 10 degrees (n=22, r= +0.34, R^2=0.11, P>0.05) or 40 degrees flexion (n=25, r=0.00, R^2=0.00, P>0.05).

Passive stiffness in the knee extensors

There was a non-significant weak negative correlation between trough to peak knee flexion and knee extensor passive stiffness when normalised to body weight (r= -0.30, R^2=0.09, P>0.05). Assessment of the scatter plot (Figure 4.6) suggests that above a certain threshold knee extensor passive stiffness may limit trough to peak knee flexion i.e. there may be a non-linear correlation. On Figure 4.6 the red line indicates the control +2 standard deviations.
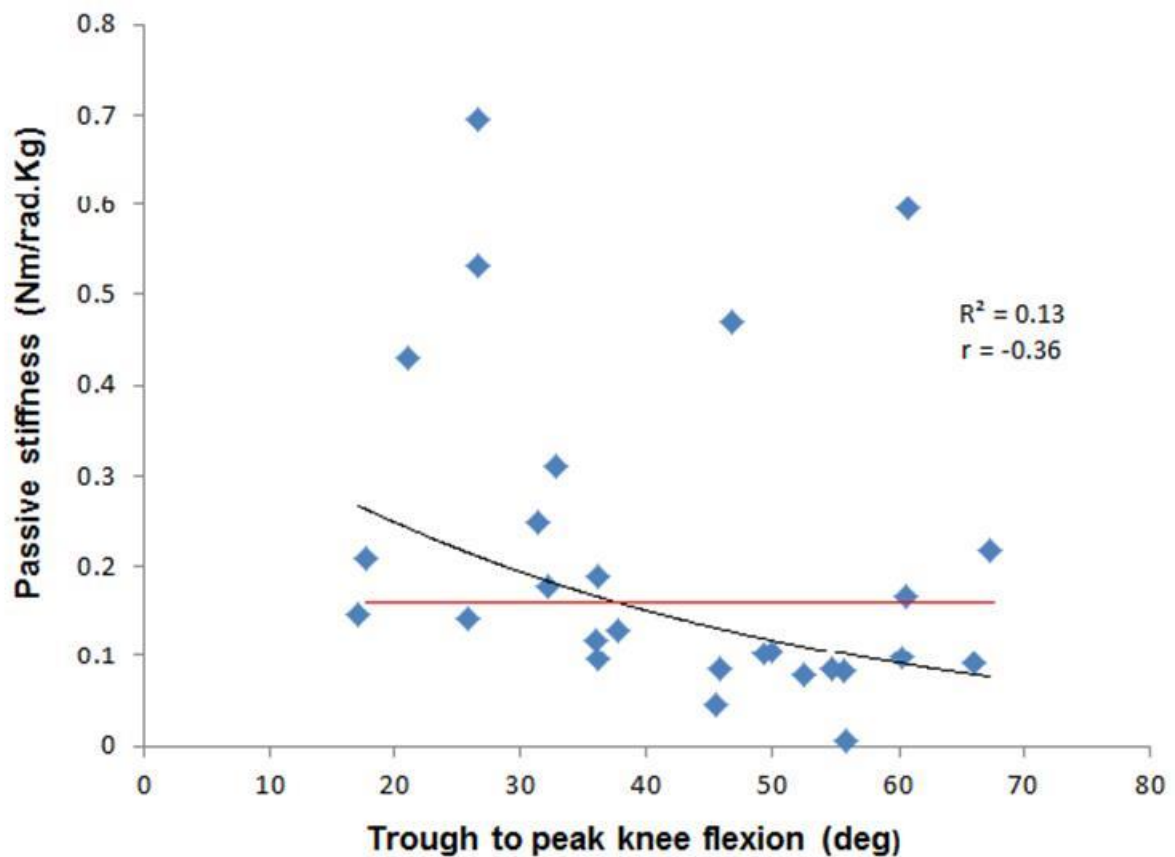
Figure 4.6: Correlation between the trough to peak knee flexion and the knee extensor passive stiffness

The data was close to significance (P=0.06) when the correlation between the trough to peak knee flexion and the natural logarithm transformed slow stretch data was assessed (r= -0.36, R^2=0.13, P>0.05, Figure 4.7). Removal of the outlier (circled) does not greatly affect the correlation (r= -0.35, R^2=0.12).
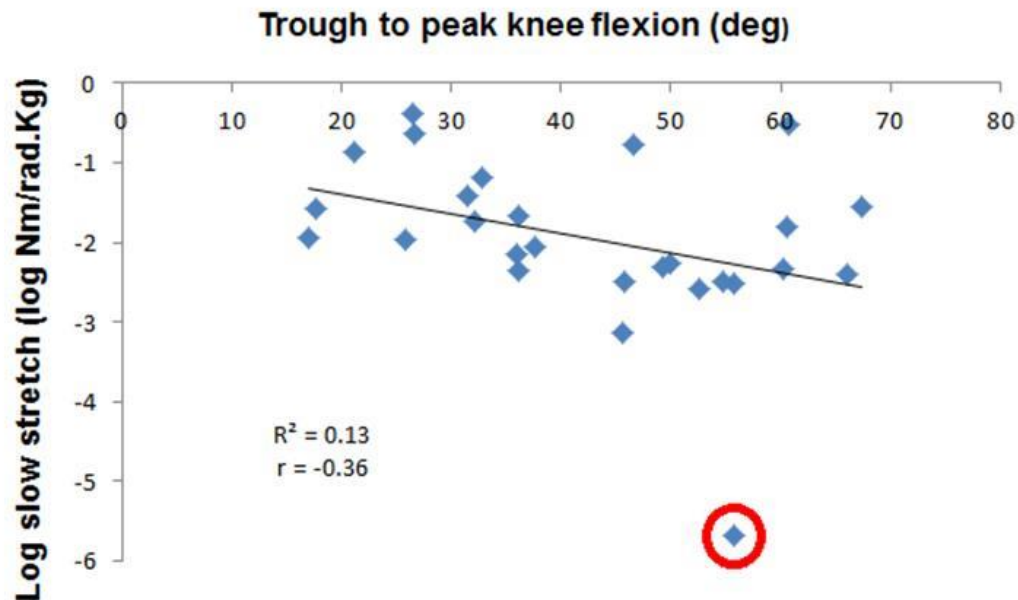
Figure 4.7: Correlation between the trough to peak knee flexion and the natural logarithm transformed slow stretch data

The trough to peak knee flexion was higher for people with passive stiffness within the control range (<control mean +2SD <0.16, 45.9 degrees +/- 13.23) compared to above this range (>control mean +2SD >0.16, 38.3 degrees +/- 16.6).

Total stiffness in the knee extensors

There was a significant moderate negative correlation between trough to peak knee flexion and knee extensor spasticity when normalised to body weight (r= -0.57, R^2=0.33, P<0.05, Figure 4.8). Greater stiffness following the fast stretch was associated with smaller trough to peak knee flexion.
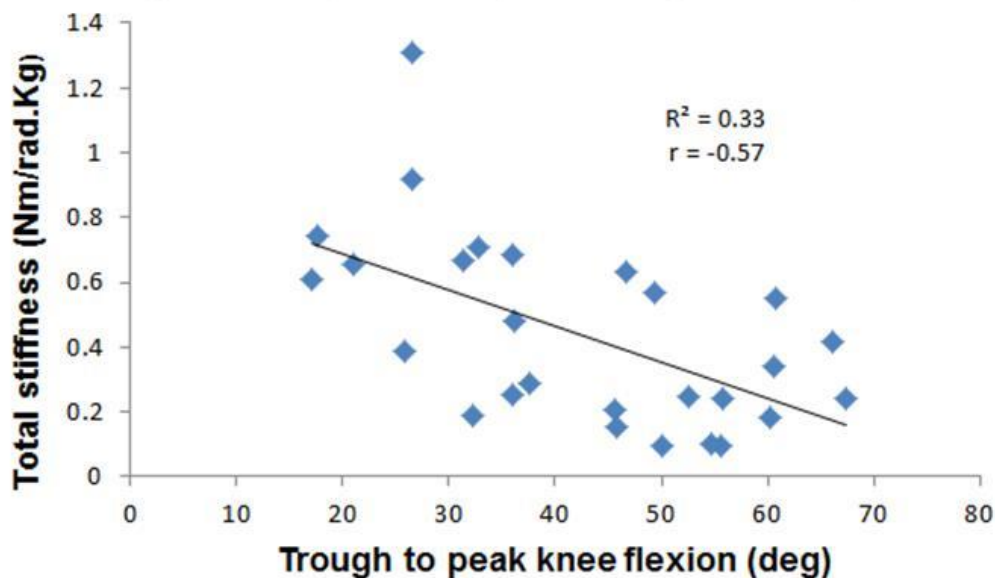
Figure 4.8: Correlation between the trough to peak knee flexion and total stiffness

There was a significant moderate negative correlation between trough to peak knee flexion and the difference between the stiffness measured with fast and slow stretch (stretch reflex related stiffness), indicative of spasticity (r= -0.59, R^2=0.35, P<0.05). Greater stretch reflex related stiffness was associated with smaller trough to peak knee flexion (Figure 4.9).
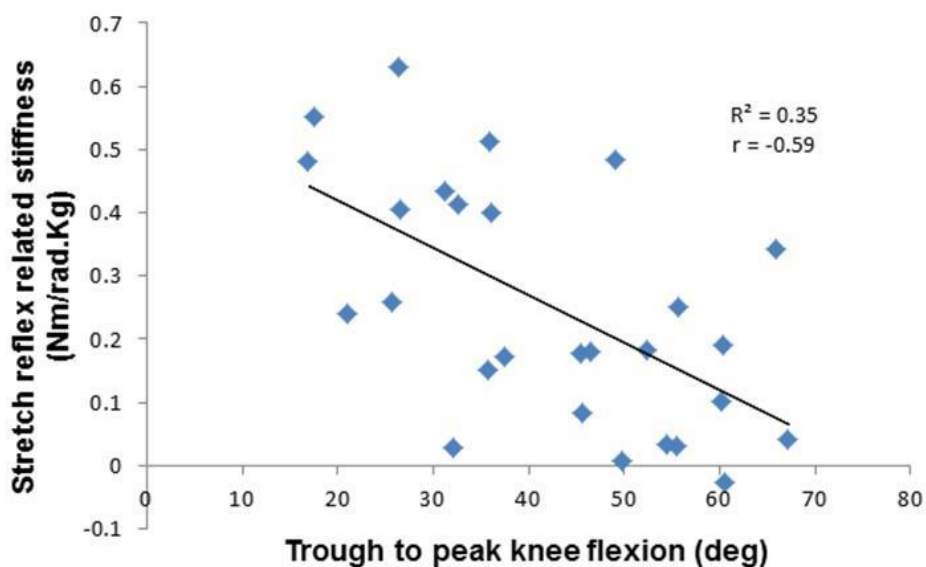
Figure 4.9: Correlation between trough to peak knee flexion and the stretch reflex related stiffness

Knee extension in stance

There was a significant moderate negative correlation between trough to peak knee flexion and knee extension in stance (r= -0.61, R^2=0.37, P<0.05, Figure 4.10). Lower knee extension in stance was associated with less trough to peak knee flexion.
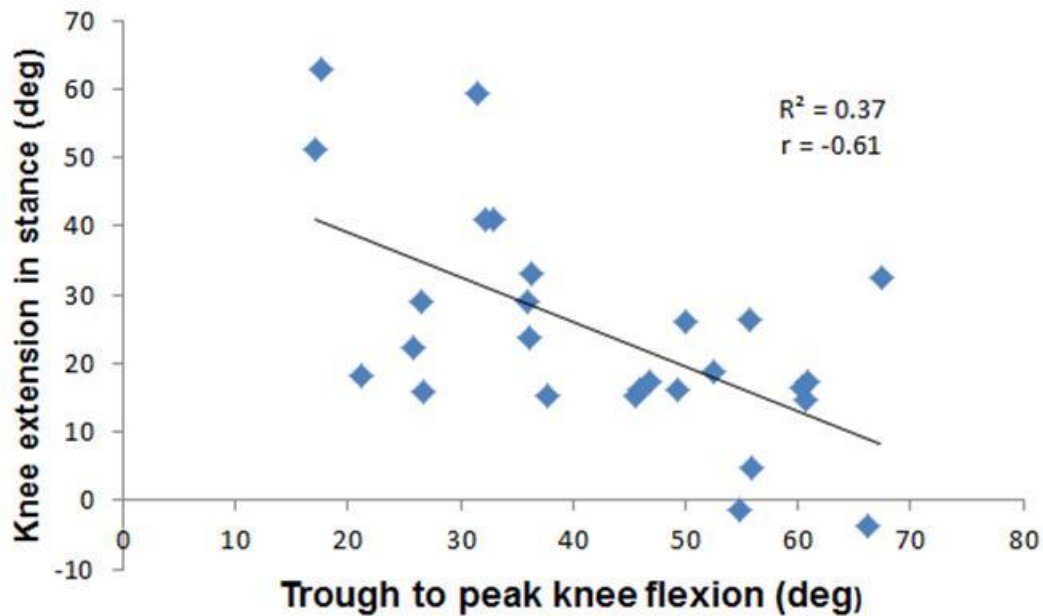
Figure 4.10: Correlation between trough to peak knee flexion and knee extension in stance phase

Relationship between multiple predictors and SKG

The following predictors were significantly correlated with trough to peak knee flexion and were entered into a stepwise multiple regression: ankle power; total stiffness; stretch reflex related stiffness; and maximal knee extension in stance.

A stepwise multiple regression revealed that total stiffness and maximal knee extension in stance accounted for 47% of the variance in trough to peak knee flexion (r= -0.69, R^2=0.47, P<0.01).

When stretch reflex related stiffness was entered into the stepwise multiple regression instead of the total stiffness an r value of -0.68 and an R^2 of 0.46 was found. This highlighted that the spasticity component of stiffness significantly contributed to the stepwise multiple regression.

Factors associated between knee extensor strength and knee extension in stance phase

As maximal knee extension in stance phase (i.e. the degree of crouch) significantly predicted trough to peak knee flexion an assessment was made of factors that could explain why pwCP walked with a crouch gait.

It was predicted that people with crouch gait were weaker in antigravity muscles namely their hip, knee and ankle extensors especially when the muscle is shortened in inner range i.e. the position required for upright standing.

The correlations between knee extension in stance phase and ankle plantarflexor and hip extensor strength in either inner or outer range were low and non-significant (P>0.5). Knee extension in stance phase was significantly correlated with isometric knee extensor strength when measured at 20 degrees (r= -0.41, R^2=0.17, P<0.05) but not at 90 degrees (r= -0.04, R^2=0.002, P>0.05). There was a significant negative correlation between knee extension in stance phase and the ratio between inner and outer range knee extensor strength (r= -0.55, R^2=0.30, P<0.005, Figure 4.11). Greater inner/outer range knee extensor strength ratio was associated with lower knee flexion in stance i.e. a more upright posture.
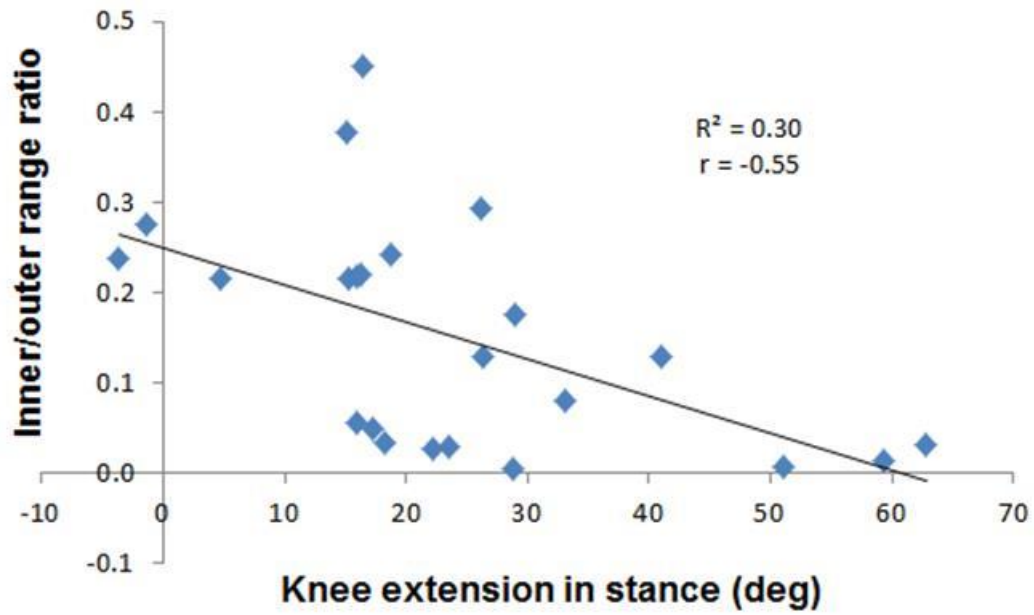
Figure 4.11: Correlation between knee extension in stance phase and the ratio between inner and outer range knee extensor strength

Correlation between knee extensor strength and SKG

In light of the significant negative correlation between knee extensor inner range strength and inner/outer range strength ratio and the degree of crouch in stance phase (Figure 4.11) the correlation between these variables and the trough to peak knee flexion was explored. A strongly significant positive correlation was found for both inner range knee extension strength (r= +0.69, R^2=0.47, P<0.0001) and the inner/outer range knee extension ratio (r= +0.76, R^2=0.58, P<0.0001, Figure 4.12A) with trough to peak knee flexion. Greater inner/outer knee extension strength ratio was associated with greater trough to peak knee flexion (Figure 4.12A).
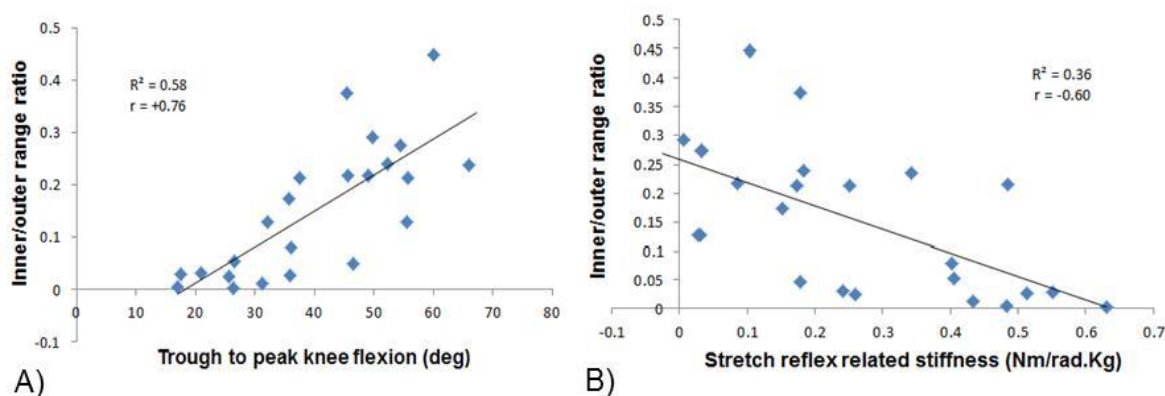
Figure 4.12A: Correlation between inner/outer range knee extension ratio and trough to peak knee flexion

Figure 4.12B: Correlation between inner/outer range knee extension ratio and degree of knee extensor stretch reflex related stiffness

The inner/outer range knee extension strength ratio was also correlated to the degree of knee extensor stretch reflex related stiffness (r= -0.60, R^2=0.36, P<0.002, Figure 4.12B). Due to this correlation a stepwise multiple regression with knee extensor stretch reflex related stiffness and inner/outer range knee extensor strength ratio as predictors and trough to peak knee flexion as the independent variable was performed. This highlighted a strongly significant relationship with lower inner/outer knee extensor strength ratio being related to lower trough to peak knee flexion (r=-0.77, R^2=0.59, P<0.0001).

Discussion

Chapter 3 showed that trough to peak knee flexion was reduced in pwCP, which is indicative of a SKG. Therefore this chapter looked at factors affecting SKG in people with spastic diplegia. The analysis and interpretation of the results in this chapter highlighted three main findings which relate to trough to peak knee flexion; total and stretch reflex related knee extensor stiffness, the degree of crouch (maximum knee extension in stance) and interestingly the inner/outer range knee extension strength ratio.

Impact of knee extensor muscle stiffness

Within this study both slow and fast stretches of the knee extensors were performed, the difference of the stiffness measured between them was found and this difference is known as the stretch reflex related stiffness. The total stiffness gave the best correlation in the multiple regression with trough to peak knee flexion for the measures of stiffness. Greater total stiffness was associated with smaller trough to peak knee flexion (Figure 4.8). The stretch reflex related stiffness also demonstrated a significant association (Figure 4.9) whereas the passive stiffness only had a weak relationship that tended to be non-linear in nature (Figure 4.6 and 4.7). This suggested that when passive stiffness was high then it greatly affected the amount of knee bend but when it dropped below a certain level, it no longer affected knee bend. To explore this further post hoc power calculations suggest that for a correlation $R^2 = 0.13$ that 58 participants are required (power=0.8 and α=0.05) for the relationship between passive stiffness and trough to peak knee flexion to be significant.

In summary, the findings are in keeping with previous studies that highlight the importance of spasticity affecting the knee extensors and in particular the rectus femoris muscle (Marks et al. 2003; Jonkers et al. 2006; Cimolin et al. 2010). Here, it is hypothesised that rectus femoris activity would be elicited by stretch of the muscle at the start of swing phase and that this would limit subsequent knee flexion. In keeping with this there is a gradual increase in the extensor moment in preswing in people with increasing severity of SKG (Figure 4.1). However, this could reflect the increased crouch in mid stance that requires ongoing knee extensor activity.

The relationship between stretch reflex related stiffness and trough to peak knee flexion would suggest that interventions that can decrease/alter the effects of rectus femoris activation, such as the use of botulinum toxin injections and rectus femoris transfers, may be useful interventions. However, it should be noted that the relationship between stretch reflex related stiffness and trough to peak knee flexion is only moderate at best explaining only 35% of the variance (Figure 4.9). This may explain why techniques such as a rectus femoris transfer are not always successful; it is not a problem in *all* pwCP and SKG. Other factors

such as ankle weakness (as supported by the relationship with ankle power generation) and posture during stance (as supported by the relationship with stance phase knee extension) can also be important. However, the low relationship with stretch reflex related stiffness and with passive stiffness may reflect other methodological factors.

Passive and stretch reflex related stiffness were measured with the participant resting in a semi-supine position. The starting position and the degree of activation of the muscle is clearly different from the task of walking under investigation, although the maximal speed of motion (175°/s) was similar to the pwCP group average obtained while walking (195°/s). Several groups have demonstrated that the size of stretch reflexes and the resistance to movement in people with spasticity is relatively normal when the muscle is stretched after it has been pre-activated to a small amount (e.g. 10% of the person's MVC) (Ada et al. 1998; Burne et al. 2005). This is felt to be because in healthy participants the degree of reciprocal inhibition between the agonist and antagonist decreases when a muscle is pre-activated making the stretch reflex size similar to that seen in people with spasticity (Morita et al 2001). Further, with pre-activation there is the formation of active cross bridges within the muscle that contribute significantly to the overall resistance felt to passive movement. This has led to some authors asking whether spasticity is simply a disorder of resting muscle (Ada et al. 1998; Burne et al. 2005).

Stretch reflexes have also been shown to modulate in healthy people with starting position and task. For the ankle plantarflexors, the most commonly investigated muscle, stretch reflex amplitude is lower in standing than in sitting (Cattagni et al. 2014). Further, during walking the plantarflexor and the knee extensor stretch reflex modulates with the phase of walking. It is larger in stance phase than in swing phase (Dietz et al. 1990). This is, in part, because the muscle is more active in stance phase and so the motor neurons supplying the muscle are closer to the threshold for activation. However, changes in pre and post synaptic inhibitory mechanisms have also been reported. Ultimately the modulation of the stretch reflex is felt to have a role in aiding stance stability (when their threshold is low/amplitude high) and in facilitating motion in swing phase (when their threshold is high/amplitude low). This implies that testing stretch reflexes at rest will not provide an accurate picture of how they perform during functional tasks. This is further complicated by differences in stretch reflex modulation in people with spasticity. In people with spasticity (spinal cord injury and stroke) there is a lack of modulation of the stretch reflex with task and position, with less modulation in people with more severe spasticity (Sinkjaer et al. 1995; Sinkjaer et al. 1996; Faist et al. 1999) i.e. the stretch reflex is high during both stance and swing phase.

In summary, there are several factors that may influence why higher (or lower) correlations were not seen between the stretch reflex related stiffness and SKG. Importantly the tests performed in the study simply reflect those that are performed during a clinical assessment. Here, a clinician assesses factors such as tendon reflexes, tone and strength when the participant is in a non-functional position and then makes inferences as to how this impacts on functional tasks such as walking to inform their clinical decision making. This implies that functional tests of stiffness and strength may be more applicable to inform clinical decision making.

Crouch gait and SKG

The relationship with the degree of crouch and trough to peak knee flexion was based on recent findings from a modelling study highlighting its importance in causing SKG (van der Krogt et al. 2010). This was felt to be because the alteration in leg posture with increasing crouch was associated with a reduction in the gravitational moment that aids the initial flexion of the knee in swing phase (Figure 4.1). The impact of crouch gait was more significant than the contribution of other factors such as weakness in the ankle and hip flexors (van der Krogt et al. 2010). This finding was supported in the current study.

The significant relationship between knee extension in stance phase and trough to peak knee flexion may seem at first sight self-explanatory as the degree of knee extension in stance is part of the equation used to calculate the trough to peak knee flexion (i.e. it is the trough). Therefore one may expect that a reduction in the knee extension (greater crouch) is associated with less trough to peak knee flexion as was found in the present study. However, the relationship between the knee extension in stance phase and the trough to peak knee flexion is not only a result of less knee extension occurring in stance but additionally less knee flexion in swing. Therefore the "trough" is higher on comparison with the controls but the "peak" is also lower. With regards to the gravitational forces aiding swing phase initiation, there is less torque due to gravity if the individual has a crouch gait (van der Krogt et al. 2010). As well as affecting the action of gravitational torques, a crouch gait position will be associated with contraction of the knee extensors acting in an anti-gravity function. Therefore, the lack of knee bend might also be due to the knee extensors already being active while the individual attempts to bend the knee. In effect if the knee extensors do not switch off quickly enough then the high background activity remains.

The strong significant relationship between the degree of crouch and trough to peak knee flexion led to a further exploration of factors affecting crouch gait. The current study found that pwCP who are weaker in inner range relative to outer range do not bend their knees in swing phase as much. In keeping with this Thompson et al (2011) found that the strength of

the knee extensors when measured at 30 degrees differentiated independent walkers from those dependent on walking aids with higher strength being seen in independent walkers.

There are several possible reasons for the relative weakness in inner range knee extension. As mentioned in the previous chapter it could be associated with factors such as disuse muscle atrophy. It could also be influenced by the position of the patella. Measures of moment arms in healthy participants suggest that patella alta may increase the knee extensor moment arm and increase knee extensor efficiency (Ward et al. 2005) although it is unclear the impact of additional torsional deficits has on this in pwCP. Patella alta is felt to be associated with elongation and increased compliance of the patella tendon. This could be caused by the long term effects of walking in a crouched position where the hip and knee extensors are under increased strain putting pressure on the patella mechanism, gradually leading to elongation of the patella tendon which causes patella alta (Gage 2004b). A not mutually exclusive scenario is that a shortened, stiff spastic muscle could lead to tendon elongation and an increase in compliance over time; this will be expanded upon further below.

Regardless of the cause, an increase in the compliance of the patellar tendon would also lead to a delay in force development as tension has to be taken up within the tendon before it becomes taut. The tendon can then effectively transmit the forces generated by the muscle to the attached bone. This could mean that the resultant torque development at crucial parts of the gait cycle such as loading phase is delayed leading to increased knee flexion i.e. crouch. This in turn might lead to individuals not using their knee extensors within inner range leading to weakness (Thompson et al. 2011). Crouch gait commonly develops during the adolescent growth spurt because the rate of growth (body mass) increases quicker than muscle power and the ratio of strength to mass falls.

It is acknowledged that not all factors affecting crouch gait were investigated within this study. For example, tibial torsion has been shown to affect the force generating capacity of other lower limb muscles (e.g. soleus/gastrocnemius) to extend the knee while walking. Here, the movement of tibial tubercle due to the tibial torsion may affect the moment arm (Hicks et al. 2007). Femoral torsion has also been shown to affect crouch gait (Sobczak et al. 2013). Weakening of the soleus, either through pathology or surgery, is also a common factor leading to crouch gait (Gage 2004b). This causes excessive ankle dorsiflexion during the second rocker altering the positioning of the ground reaction force to a significant distance behind the knee which then requires a large internally generated extensor moment to counteract this alteration; this can be over twice that seen in health individuals (Gage 2004b;

Whittle 2012). In summary, as with the investigation of SKG, a lack of knee extension in stance is not simply due to the effects of one muscle (Hicks et al. 2007).

Inner/outer range knee extensor strength ratio and spasticity
An additional interesting finding in this chapter was the relationship between the inner/outer range knee extensor strength ratio and spasticity. Weaker inner range strength was associated with greater spasticity (R^2=0.36). Two hypotheses for this relationship are considered below.

Firstly, muscles with spasticity tend to be shorter and stiffer and associated with a more compliant in series tendon. As highlighted above this in turn could lead to crouch gait by affecting the rate of effective torque generation during the loading phase of the gait cycle.

Secondly, the relationship may reflect a functionally useful role of spasticity during stance phase. With weak inner range knee extensors there will be an initial stretch of the muscle when weight is applied to the leg at the start of stance phase. This could elicit a stretch reflex, especially in the presence of spasticity. The stretch evoked contraction here would be functionally useful in helping to stabilise the knee and provide anti-gravity support. Therefore, it could be considered that individuals in crouch gait may actually be using their stretch reflexes and spasticity to remain upright.

These two hypotheses have different implications for potential interventions. If short stiff, spastic muscles are implicated in causing tendon elongation which in turn affects the rate of force generation leading to a crouch gait, this would imply that a reduction in spasticity and normalisation of muscle and tendon compliance could be functionally useful. In contrast, if spasticity is felt to aid in stabilisation of the knee and anti-gravity control then a reduction in knee extensor spasticity may actually impair function. In this case there may need to be a trade-off between a reduction in spasticity to allow mobility (e.g. by preventing stretch reflex activation at the start of swing phase as discussed above) and retaining spasticity to aid stability. If both of these factors are indeed present in variable degrees in different people this may further explain why pharmacological and surgical spasticity reduction techniques are not universally successful at improving function. With baclofen, for example, a GABAergic anti-spasticity medication that can be administered orally or intrathecally, people can report that they feel weaker when the dose is titrated up and this can impair their walking (Lambrecq et al. 2007). Peripheral effects on strength have been reported for baclofen (Nielsen & Sinkjaer 2000) but this could also reflect the importance of spasticity in maintaining stability while walking.

Summary

This chapter has shown that increased stiffness of the knee extensors in pwCP is associated with a reduction in trough to peak knee flexion. Crouch gait has also been shown to be a potential contributing factor and this in turn was associated with a reduction in the inner/outer range knee extensor strength ratio. Together total knee stiffness and crouch gait explained 47% of the variance in trough to peak knee flexion whilst the inner/outer range knee extensor strength ratio alone explained 58% of the variance. In both cases ~50% of the variance remains unexplained. The primary stepwise multiple regression was hypothesis driven looking at the potential role of ankle plantarflexor and hip flexor strength, passive and stretch reflex related stiffness in the knee extensors and the degree of crouch in stance phase. Other predictors could be used in future analyses such as age, gender and inner/outer knee extensor strength ratio. The addition of these factors may result in improved predictive ability.

It is important to acknowledge that these findings only reveal associations rather than cause and effect relationships and as discussed there are several mechanisms that may explain these findings. The need for future work to further elucidate these associations and implications for the treatment of SKG will be discussed in further detail in the last chapter.

CHAPTER 5: RELATIONSHIP BETWEEN LABORATORY BASED AND CLINICAL OUTCOME MEASURES IN DETERMINING PREDICTORS OF STIFF KNEE GAIT

Introduction

In chapters 3 and 4 it was found that strength was reduced and knee extensor stiffness (stretch reflex related and passive) was increased in pwCP compared to the controls. It was also found that selected measures of impairment correlate with SKG as measured using 3D motion analysis (Codamotion, UK).

The laboratory measures were obtained using expensive, bulky and non-portable equipment in comparison to the clinical outcome measures which were performed by the same researcher requiring no equipment, other than a plinth.

This chapter explores the following points within the subgroup of pwCP:

(a) The relationship between SKG identified using observational analysis of videos taken while walking and measures taken using 3D motion analysis

(b) The relationship between clinical measures of strength and stiffness and clinical measures of SKG

(c) The relationship between clinical measures of strength and stiffness and kinematic measures of SKG

These points have important implications for the requirement for laboratory based measures of impairment and function when defining possible treatment options in the clinical setting.

Methods

Clinical measures

The SF-GT sagittal plane view was the observation based clinical gait assessment tool used to determine the degree of knee bend (Toro et al. 2007c). A visual estimate of knee bend was recorded at mid stance (knee extension) and mid swing (knee flexion) and the difference between the two was determined. The angle estimated was between the longitudinal thigh axis and the longitudinal shank axis. This process was done using video clips and the video was paused at the two positions. The video was taken at right angles to the direction of travel to avoid any parallax error. The same researcher did this for every case.

The Duncan-Ely test (Marks et al. 2003) was used to determine stiffness and spasticity of the knee extensors but due to the extended hip position it mainly targeted the rectus femoris.

The Duncan-Ely test was graded using the Tardieu scale (Table 2.7) which rated the resistance to movement when the limb is moved at different speeds and also identified a catch if one was present. This test was performed on all of the study's participants and was carried out by the same researcher for each individual. Please see chapter 2 for more detail and an example photograph.

The MRC grading of strength manual muscle testing technique (Table 2.8) was used for scoring the muscle strength in both the controls and pwCP. The same researcher performed these tests on each individual. Please see chapter 2 for more detail and example photographs.

Laboratory measures

Measurement of lower limb kinematics and kinetics were done using a 3D motion analysis system (Codamotion, UK). Limb stiffness and muscle strength were measured using dynamometry (Biodex, USA). Please refer to chapter 2 for further information regarding these measures.

Analysis

The relationship between clinical measures of impairment and SKG were assessed using parametric (Pearson's) and non-parametric (Spearman's) tests for categorical data as appropriate. Correlations between 0.1-0.3 were defined as weak; between 0.4-0.6 as moderate and >0.7 as strong (Dancey & Reidy 2007).

Results

Relationship between observational gait analysis and 3D motion analysis

There was a significant moderate positive correlation between the trough to peak knee flexion assessed using the SF-GT and that measured using 3D motion analysis (r= +0.68, R^2=0.46, P<0.0001 Figure 5.1).
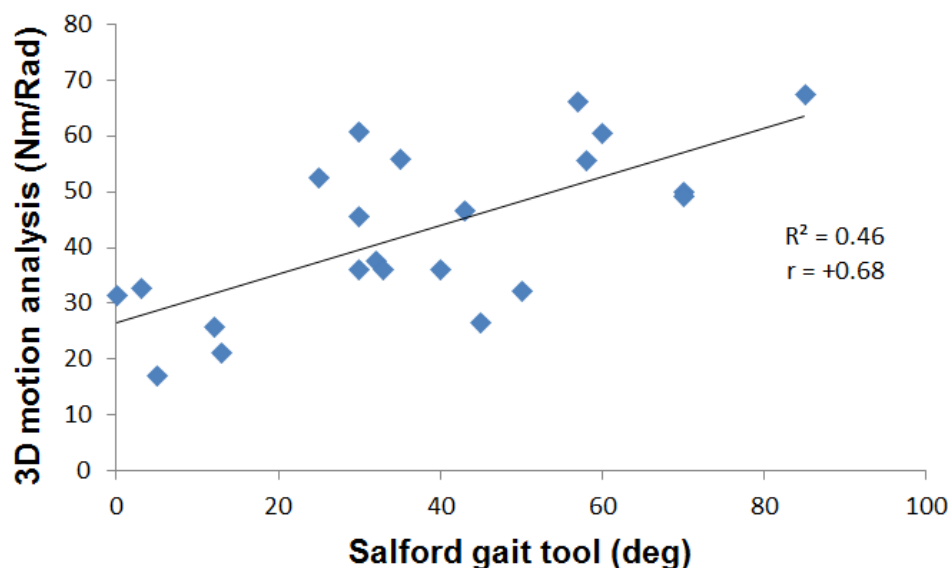
Figure 5.1: Correlation between the trough to peak knee flexion assessed using the SF-GT and the use of 3D motion analysis

Relationship between clinical measures of strength and stiffness and clinical measures of SKG

The relationships between the degree of SKG, as defined by the SF-GT and the following variables were explored using non-parametric tests as appropriate:

- Knee extension in mid stance
- Hip flexor, knee extensor and ankle plantarflexor strength
- Knee extensor stiffness as determined using the Duncan-Ely test at slow and fast speeds

Only the degree of knee extension in mid stance correlated with the trough to peak knee flexion. Here greater knee extension in stance phase was associated with greater trough to peak knee flexion (Figure 5.2A). There was a tendency for greater trough to peak knee flexion to be seen in people with stronger knee extensors and lower stiffness following a Duncan-Ely fast stretch of the knee extensors (Table 5.1). A definite catch following a Duncan-Ely fast stretch of the knee extensors (mainly rectus femoris) was recorded in 9 people. In these 9 there was a moderate but non-significant negative correlation with peak knee flexion; an earlier catch was associated with less knee flexion (Figure 5.2B).

Clinical Parameter	R^2	r	P
Mid stance knee extension (via SF-GT)	0.51	0.71	<0.005
Hip flexion strength	0.02	0.15	>0.05
Knee extension strength	0.15	0.39	P=0.09
Ankle plantarflexion strength	0.10	0.32	>0.05
Duncan-Ely slow	0.06	0.25	>0.05
Duncan-Ely fast	0.13	0.36	P=0.11
Catch (n=9)	0.31	0.56	P=0.11

*Table 5.1: Regression results: Relationship between **observational gait analysis** and clinical measures of impairment*
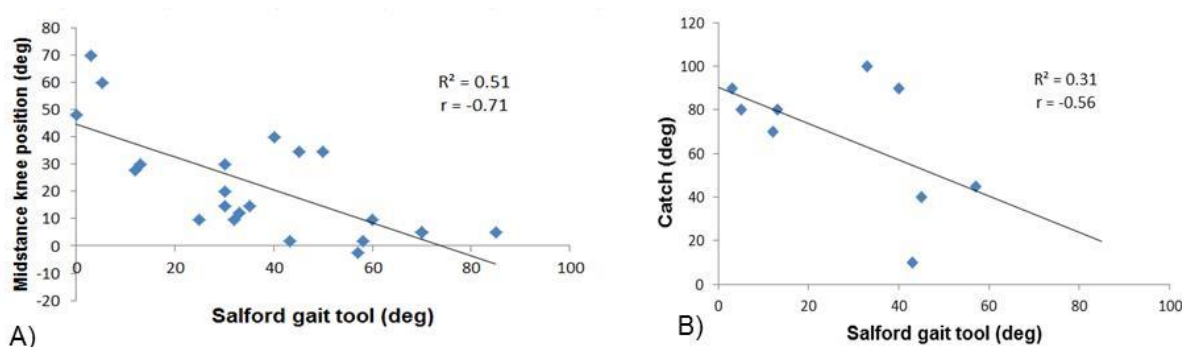
Figure 5.2A: Correlation between the degree of knee extension in mid stance and the trough to peak knee flexion measured via the SF-GT

Figure 5.2B: Correlation between the degree of catch and trough to peak knee flexion measured via the SF-GT

Relationship between clinical measures of strength and stiffness and kinematic measures of SKG

The relationships between the degree of SKG, as defined by 3D motion analysis and the following clinical measures were explored using Spearman's correlation analysis reflecting the fact that the clinical data were categorical.

- Knee extension in mid stance
- Hip flexor, knee extensor and ankle plantarflexor strength
- Knee extensor stiffness as determined using the Duncan-Ely test at slow and fast speeds

The 3D motion analysis produced stronger correlations when compared to the SF-GT. Using 3D motion analysis the knee extensor strength showed a significant weak positive correlation and the stiffness recorded using a Duncan-Ely fast stretch showed a significant moderate negative correlation with the degree of SKG (Figure 5.3A and B).

Further, there was an increase in the correlation with the Duncan-Ely test measured using a slow stretch, with greater passive stiffness being associated with less trough to peak knee flexion although this was not significant (P=0.08). There remained a significant correlation between the trough to peak knee flexion (as measured using 3D motion analysis) and knee extension in mid stance as measured using the SF-GT (Table 5.2).

Clinical Parameter	R^2	r	P
Mid stance knee extension (via SF-GT)	0.54	0.73	<0.0005
Hip flexion strength	0.05	0.22	>0.05
Knee extension strength	0.24	0.49	<0.05
Ankle plantarflexion strength	0.08	0.28	>0.05
Duncan-Ely slow	0.15	0.39	>0.05
Duncan-Ely fast	0.30	0.55	<0.01
Catch (n=9)	0.19	0.43	>0.05

*Table 5.2: Spearman's correlation results: Relationship between **3D gait analysis (trough to peak)** and clinical measures of impairment*
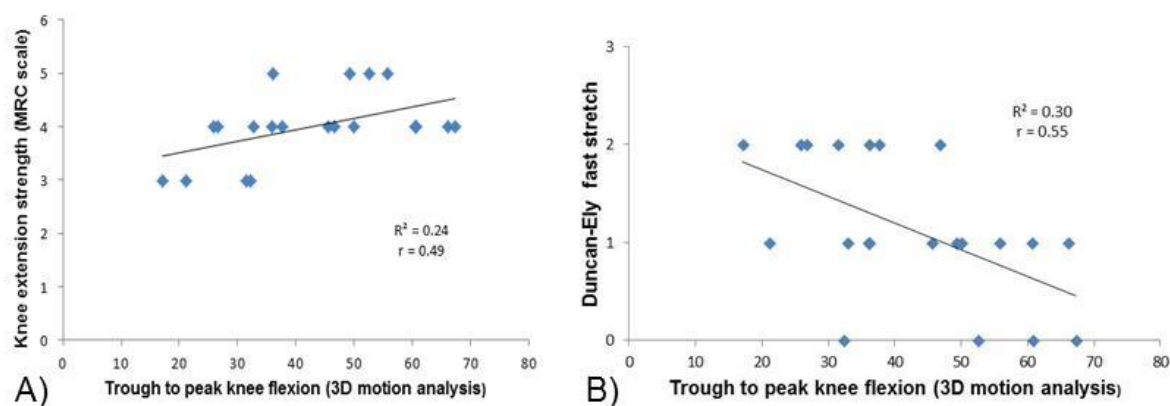
Figure 5.3A: Spearman's correlation between knee extension strength and trough to peak knee flexion measured via 3D motion analysis

Figure 5.3B: Spearman's correlation between the Duncan-Ely fast stretch and trough to peak knee flexion measured via 3D motion analysis

Discussion

This chapter investigated the relationship between laboratory based and clinical outcome measures in determining predictors of SKG. It focussed on the relationships between; observational gait analysis and 3D motion analysis; clinical measures of strength and stiffness and clinical measures of SKG; and clinical measures of strength and stiffness and kinematic measures of SKG. The findings showed that trough to peak knee flexion assessed via the SF-GT and measured using 3D motion analysis was significantly positively correlated. It was also demonstrated that the relationship between kinematic measures of SKG (obtained via 3D motion analysis) and clinical measures of strength and stiffness produced stronger correlations than the relationship between observational measures of SKG (obtained via the SF-GT) and clinical measures of strength and stiffness.

This study has demonstrated that clinical (SF-GT) and kinematic (3D motion analysis) measures of SKG provide similar results with regards to the trough to peak knee flexion, producing a significant positive correlation between them. This is an interesting finding particularly as the researcher who performed the video analysis was unexperienced prior to the task. Further, this finding is promising from a clinical point of view because the SF-GT is fast and cheap in comparison to 3D motion analysis. 3D motion analysis is an expensive and timely process as it is performed in a human movement laboratory and uses multiple pieces of equipment. It also requires a specialist to set it up, run the data collection and interpret the data. Although a significant and positive correlation was found only 46% of the variance was explained. This suggests that the tests were measuring slightly different constructs. The relationship between the clinical and kinematic measures of SKG will be further discussed throughout this discussion.

The clinical measures of SKG (SF-GT) did not produce the same results as the kinematic measures of SKG (3D motion analysis) when related to clinical measures of strength and stiffness (manual muscle testing and the Duncan-Ely test; see Tables 5.1 and 5.2). The SF-GT only had a significant correlation with mid stance knee extension, whereas the 3D motion analysis was significantly correlated with knee extension strength, the Duncan-Ely fast stretch as well as mid stance knee extension. Interestingly the SF-GT results do hint towards an effect with the Duncan-Ely fast stretch and knee extensor strength but they are not significant. Neither the SF-GT nor the 3D motion analysis results showed an effect on hip strength, ankle strength, passive stiffness or spasticity. A possible reason for the differences between the clinical and kinematic measures of SKG and their correlations with the clinical measures of strength and stiffness could be due to the psychometric properties of the SF-GT.

It should be considered whether the SF-GT is reliable, valid and also capable of being sensitive enough to show differences between groups and with interventions i.e. responsive.

Salford Gait Tool

The SF-GT was developed for therapists who work with children with CP and manage their gait problems within a clinical setting. The designers (Toro et al. 2007c) describe it as a clinically orientated observational gait assessment tool. When setting the category boundaries Toro et al took into account previous gait literature and clinical observation (Sutherland et al. 1988; Whittle 1991; Perry 1992). It was acknowledged that the defining angular positions needed to be great enough to be recognised via observation of a video clip yet small enough to be sensitive to alterations from clinical interventions and variances of thirteen different gait styles. A drawback of the original assessment of this tool was that the recording for the kinematic gait analysis was separate to the recording for the observation analysis. This was due to the reflective markers, needed for the kinematic analysis, getting in the way for the observational analysis so therefore had to be removed. Another noteworthy point is the kinematic data had several trials whereas only one video clip was analysed. These two points reflect the recording practice adopted in the current study.

There are other tools available for assessing gait via observation, for example the Edinburgh visual gait score (EVGS) (Read et al. 2003) and the Physician Rating Scale (PRS) (Koman et al. 1993; Maathuis et al. 2005). The SF-GT has been found to have greater interobserver and intraobserver agreement compared to both the EVGS and the PRS (Toro et al. 2007b). The SF-GT also has more scoring categories for describing joint or gait pathology (Toro et al. 2007b). To summarise, the SF-GT is valid, it measures what it claims to measure and it is reliable. The main factor which needs to be investigated is whether this test is sensitive enough to extract the relevant information. When discussing clinical tests, sensitivity refers to the tests ability to accurately detect the impairment or disease in question. The sensitivity is measured in percentage making it quick and easy to interpret, for example a clinical test with 70% sensitivity identifies 70% of patients with the impairment. Leaving the remaining 30% of patients with the impairment unidentified (Lalkhen & McCluskey 2008). It is important to question the sensitivity of the SF-GT as it is an ordinal measure and groups the data into quite large categories, therefore making it less sensitive than 3D motion analysis as it has got a different scaling system. For example the SF-GT offers three categories (0, 1 and 2) for the degree of knee flexion; -5 to 10 degrees, 11 to 45 degrees and 46 degrees or more (respectively). These are very broad categories in comparison with 3D motion analysis which can provide a precise degree of movement at a joint. However, that is not to say that 3D motion analysis is error-free, a slightly misplaced marker on the participants leg could skew the data, for example 5 degrees may actually be 10 degrees. The differences in the rating

could explain why the correlation is slightly lower between the clinical measures of SKG and the clinical measures of strength and stiffness compared to the correlations between the kinematic measures of SKG and the clinical measures of strength and stiffness.

Duncan-Ely, Tardieu scale and manual muscle testing

This study uses two clinical tests of impairment; manual muscle testing and the Tardieu scale which was used to quantify the Duncan-Ely test. A systematic review of the instruments used for clinical assessment of spasticity claims only the Tardieu scale is sufficiently valid and reliable (Scholtes et al. 2006). Reliability of the Tardieu scale has specifically been assessed in pwCP and it has shown to be reliable in grading spasticity of the knee flexors, ankle plantarflexors and elbow flexors (Gracies et al. 2010; Numanoğlu & Gunel 2012).

The results from this current study relating to the Duncan-Ely test are largely non-significant. Only the Duncan-Ely fast stretch demonstrated a significant correlation with the 3D motion analysis, although there are trends towards significance for other results (catch and slow stretch). These findings are in-keeping with the previous literature (Marks et al. 2003; Jonkers et al. 2006). The Duncan-Ely test, for example, has been reported to be a positive predictor upon the success of distal rectus femoris transfer operations (Kay et al. 2004). Individuals with a positive preoperative Duncan-Ely test demonstrated a significant increase in knee arc and also a greater improvement in the peak knee flexion in swing timing compared to individuals with a negative preoperative Duncan-Ely test. The Duncan-Ely test also has been shown to predict rectus femoris dysfunction during gait. In particular the Duncan-Ely test can predict a decreased range of knee motion, abnormal electromyography of the rectus femoris during swing phase and the delayed timing of the peak knee flexion in swing phase (Marks et al. 2003).

The clinical impairment measures (Duncan-Ely and manual muscle testing) predicted the gait analysis range of knee flexion (trough to peak) to a very similar standard as the laboratory based measures (Biodex, USA). This suggests that the clinical impairment measures are a suitable option to use, which is reassuring from a clinical perspective. Overall this also fits with what was highlighted within the previous chapter with regards to, the relationship with knee extension in stance phase and measures of knee extensor spasticity.

This chapter suggests that when measuring SKG the most sensitive measure should be used where possible (as long as other factors such as validity and reliability are accounted for). However, this chapter also suggests that the clinical measures of impairment which were used, such as the Tardieu scale, have clinical utility. Thus, a combination of both

clinical and laboratory measures may be most effective. For example, clinical measures of strength and stiffness combined with kinematic measures of SKG. As mentioned previously the equipment required for the laboratory testing is non-portable, expensive and time consuming making the laboratory based work unfeasible from a clinical perspective. However, patients will often attend a laboratory for gait analysis and the Duncan-Ely and strength measure tests are performed routinely as part of this process.

Possible future work

This chapter explored the relationship between clinical tests and measures of SKG obtained from clinical observation and 3D motion analysis. Due to the categorical nature of the clinical tests a Spearman's correlations was used. An alternative method of analysis could be to compare the size of stiff knee associated with each clinical category using a non-parametric test (e.g. Mann-Whitney U test). It could also be possible to explore the specificity and sensitivity, positive and negative predictive values for individual and combined clinical measures. In this case a cut off value could be used for a clinical measure (e.g. ≥ 2 on the Duncan Ely test) and the ability to predict moderate-severe SKG (as defined in previous chapters) could be explored.

It would be interesting to find out whether the sensitivity of tests of SKG could be further improved whilst avoiding costly, non-portable equipment. There are other more sensitive clinical measures available for analysing kinematics that may be more readily available in the clinical setting other than 3D motion analysis. The use of an electronic goniometer, for example, may be used to quantify knee movements. This method has distinct benefits if one specific aspect of gait is focussed upon. However, within this study and within the clinical setting the focus is usually on recording (either through observation or instrumentation) multi-joint motion in multiple planes. Other potential measures which have may have increased sensitivity in comparison with the clinical observational measures used within this study include the use of accelerometers and video vector analysis and other video based systems (e.g. Xbox Kinect). The video vector analysis combines video recording of the participant with a superimposed image of the size and line of action of the ground reaction force. From this it would be possible to further estimate kinetics of walking as well as kinematics, although it does require the use of a force plate. It would be interesting to investigate whether these methods provide enough sensitivity to match that of 3D motion analysis. Although it is unlikely that video recordings such as the use of Xbox Kinect will be as precise with regards to the joint positioning it is predicted that they will provide greater sensitivity than the gross banding used within the current clinical measures (e.g. SF-GT). The video recording products are commercially available, relatively cheap and could be set up and used within a clinic. These tests could then be used routinely in combination with

clinical measures such as the Duncan-Ely test. As access to gait analysis laboratories is somewhat limited (Toro et al. 2003), video recording measures may be able to offer an appropriate and suitable alternative in the future.

Summary

In conclusion, the results of the laboratory based impairment measures for predicting the gait analysis trough to peak were reproduced by the clinical impairment measures (i.e. mid stance knee extension, tests of stiffness). This is encouraging from a clinical perspective as it indicates that the laboratory equipment and methods are not necessarily required and the clinical measures should continue to be used. However, it did highlight that 3D motion analysis resulted in improved predictive capability compared to the SF-GT. The main problem with the clinical impairment measures appears to be their gross banding systems (Marks et al. 2003).

From this study it seems the best assessment tool combination would be the use of clinical impairment measures with 3D motion analysis in terms of cost (both time and money) and predictive abilities. However, not every child can attend a gait laboratory clinic as they are not readily accessible. Consequently attention should turn to new technology such as the use of accelerometers and video recordings which may be useful in this field and are therefore suggested as new possible alternative measures.

CHAPTER 6: DISCUSSION

Brief summary of findings

This study has shown the key determinants of SKG are a crouch positioning of the lower limb in stance phase and spasticity within the knee extensors. A non-significant trend for a non-linear relationship between passive stiffness and SKG was also seen. Additionally, the secondary analysis highlighted the importance of the knee extensors inner/outer range strength ratio. Greater weakness in inner range was linked to increased spasticity, to the degree of crouch and in turn to the degree of SKG; the weaker the inner range knee extensors, the greater the degree of knee bend in stance phase. Finally, this study highlighted that both clinical and laboratory based measures may be used to determine the possible causes of SKG but that more sensitive measures of joint motion (3D motion analysis) results in stronger correlations and predictive power.

Interactions between determinants of SKG

The main findings of this study highlighted that several factors are correlated with SKG. This section will firstly review possible reasons for these relationships and suggest further work to elucidate the mechanism of SKG.

Crouch and SKG

It is hypothesised that the degree of crouch directly influences the degree of SKG i.e. the events earlier in the gait cycle have an influence upon those later on. This may occur by the crouched position affecting the size of gravitational torques that can aid in swing phase initiation and/or producing excessive knee extensor activity in stance phase that limits fast, early swing phase initiation. Of course, as walking is repetitive it could be argued that the relationship is circular i.e. factors occurring in swing phase (e.g. a lack of terminal swing phase knee extension) may influence the degree of crouch in stance phase.

Inner/outer range knee extensor strength

Deficits in the inner/outer range knee extensor strength was related to crouch and also related to spasticity. Two theories outlining how these variables may be related have been explored in chapter four:

1) Inner/outer range knee extensor strength deficit gives rise to crouch gait and that spasticity may subsequently aid in the control of stance in mid swing.

2) Spasticity is integral to the development of inner range knee extensor weakness and thus crouch gait by causing patellar tendon lengthening and subsequent patella alta.

It is important to acknowledge however that crouch may due to other factors, for example tibial torsion as this has been found to lead to reduced extensor muscular capacities (Hicks et al. 2007). There is also the possibility that the spasticity and weakness are not related, they could just be markers of the disease severity. For example among individuals with an upper motor neuron syndrome (CP/brain damage) there is a broad number of impairments that may be seen, dependent upon location, degree and type of injury. A correlation of spasticity and weakness could therefore just be coincidental and a reflection of the injury severity.

Spasticity and SKG

This study found a significant moderate negative relationship between stretch reflex related stiffness of the knee extensors and trough to peak knee flexion. It also found a non-significant trend between passive stiffness and trough to peak knee flexion. This relationship may be causative, that is, knee extensor stiffness resists flexion of the knee during preswing and early swing phase. In support of this, previous modelling and clinical studies have shown both theoretically that SKG can be caused by increased knee extensor stiffness of either origin. In people with HSP, for example, higher passive stiffness was associated with less knee flexion (Marsden et al. 2012). Other groups have found that clinical or laboratory based markers of knee extensor spasticity are associated with less knee flexion in swing phase.

Musculo-tendinous stiffness and spasticity

This study measured gross limb stiffness. The whole limb was moved by a dynamometer (Biodex, USA) and the overall level of stiffness was determined. Although it is acknowledged this is a gross measure it is an accepted method and has been used in other studies (Bolteau et al. 1995; Damiano et al. 2002; Pierce et al. 2008). There are studies and commentaries discussing this topic and highlighting the difficulties of determining between passive stiffness and spasticity in pwCP (Desloovere & Bar-On 2013; Willerslev-Olsen et al. 2013). The gross measure of passive stiffness used within this study did not produce a significant relationship with SKG (P=0.06) but the potential importance of passive stiffness needs to be taken into account. It could be that any relationship was affected by the gross stiffness measures used. As highlighted below other additional methods could be used in future that may be more specific and sensitive to the changes occurring in the muscle and tendon.

There is literature reporting changes within muscle at a cellular level among individuals with CP. It has been found that the muscle fascicle lengths are shorter and stiffer (Matthiasdottir et al. 2014), the sarcomere lengths are longer (Pontén et al. 2007; Smith et al. 2011) and

there is an increased amount of connective tissue within the muscle, compared to normal (Booth et al. 2001; Smith et al. 2011). The greater amount of connective tissue and fascicle shortening leads to increased passive stiffness. Of these findings some, such as the sarcomere length and the degree of connective tissue, require analysis of invasive muscle biopsies. This, due to ethical reasons, precludes most pwCP who are not having surgery. Other measures such as muscle and tendon length can be assessed non-invasively using ultrasound. These studies, for example, have shown overall muscle size and individual muscle fibres to be shorter than normal in pwCP. These studies have also found that the tendon in spastic muscles can be longer than normal in pwCP (Wren et al. 2010; Gao et al. 2011).

More recently ultrasound techniques have been employed to measure muscle and tendon compliance (Maganaris et al. 1998; Herbert et al. 2011; Diong et al. 2012; Kwah et al. 2012). Here individual portions of the muscle fascicle or tendon are tracked over time while the muscle-tendon unit is put under tension. The tension can be applied either by stretching the musculo-tendinous unit (in a stereotyped way usually using a motor) or by contracting the muscle, either voluntarily or via electrical stimulation. By tracking the tendon and/or muscle fascicle over time it is possible to calculate how much it has elongated; with a stereotyped perturbation (induced via a stretch or contraction) this will give a measure of stiffness (or the inverse compliance). Some groups have further estimated the force in the in-series muscle-tendon (Maganaris 2002). As the force applied by the muscle is measured as joint torque this requires a transformation from angular to linear based measures. An estimation of the linear force applied as well as total muscle and tendon length allows a direct estimation of;

Strain= fascicle (or tendon) elongation/overall length
Stress= fascicle (or tendon) elongation/applied force

These techniques have to date mainly been performed in the ankle plantarflexors in pwCP. They have shown that the muscle fascicles are stiffer and the tendons are longer and more compliant with changes similar to that seen in tendinopathy on biopsy (Gagliano et al. 2013).

Understanding the finer structural changes rather than simply describing gross changes in muscle-tendon stiffness has the following implications for the understanding of the genesis of SKG:

1) Genesis of patella alta and its relationship to crouch gait and knee extensor spasticity:

   Patella alta has been mentioned previously in chapters three and four, it is a condition where the patella shifts superiorly up the femur and it is associated with the

lengthening of the patellar tendon (Gage 2004b). This change of positioning of the patella may alter the line of pull of the muscle and the patella's positioning relative to the femur and the knee joint axis. It is hypothesised to be caused by passive stiffness and spasticity in the knee extensors leading to a short stiff muscle and/or excessive and repeated contractions of the knee extensors during crouch walking, causing the patella to track proximally. The altered positioning and line of pull of the knee extensor mechanism may subsequently lead to lever arm dysfunction and muscle weakness.

Further work should look into the presence and impact of patella alta among pwCP. Here longitudinal studies would be useful relating factors such as walking pattern (i.e. degree of crouch gait) with knee extensor related impairments. This could involve both simple clinical measures of patellar tendon length (tibial tuberosity to patella pole) as well as direct recordings of muscle and tendon compliance and structure using ultrasound. A longitudinal study would help to identify how different impairments develop and how they impact on crouch and SKG. They could be combined with direct magnetic resonance imaging recordings to quantify changes in the lever arm.

2) Effects of stiffness on stability and mobility:

It has been hypothesised that increased muscle stiffness may be useful for standing stability in pwCP, for example, during the loading response. Early theories of how healthy people balance during quiet bipedal stance suggested that stance was mainly controlled by the action of the ankle plantarflexors as the body swayed like an inverted pendulum. It was felt that contraction of the plantarflexors was sufficient to hold and stabilise the load of the body (Winter et al. 1998; Fitzpatrick 2003). Recent work has however highlighted that this scenario is not possible because the compliance of the tendon is too high (Loram & Lakie 2002a). Therefore during a static muscle contraction the tendon would simply elongate preventing the person from remaining stable. Further work by (Loram & Lakie 2002b; Loram et al. 2009) highlighted that quiet bipedal stance is due to anticipatory contractions of the ankle plantarflexors producing predictive contractions to prevent the body swaying too far forwards. This anticipatory activity is under central nervous system control.

There are clearly several factors that may change in pwCP when considering their ability to balance and stabilise. Firstly, factors such as muscle contracture and deformity mean that the body cannot be modelled as an inverted pendulum and balancing presumably requires motion about several joints. Secondly, in pwCP the

anticipatory control of balance may be impaired by lesions to ascending and descending pathways i.e. pathways carrying signals about how the person is moving (required for anticipatory control) and pathways carrying signals leading to contraction of appropriate muscles. Thus there is a need to rely on other factors such as increased muscle-tendon stiffness. Thirdly, tendon compliance may increase but overall muscle-tendon stiffness, as measured in the current study, may be higher. Whether this means that pwCP are able to balance in part using their increased passive stiffness or whether elongation of an extra compliant tendon makes pwCP even more unstable is unclear. This may mean that pwCP require an additional stiffening mechanism namely enhanced stretch reflexes. In healthy people stretch reflex activity is usually too low to influence standing balance (Fitzpatrick 2003). However, in pwCP the increased gain of the response to stretch may be sufficient to at least aid standing balance. Clearly this is insufficient as balance is worse than normal in pwCP but it may be useful. Thus, by taking direct measures of tendon and muscle stiffness and muscle activity during stance and relating this to the ability to balance in standing, it would be possible to understand the relationship between stiffness and stability in pwCP.

Importantly, although there has been much interest recently in changes in muscle and tendon architecture in pwCP the primary pathology arises from damage within the central nervous system. Enhanced stretch reflex mediated stiffness was associated with SKG. It is equally important to understand the longitudinal changes in spasticity and their impact on function. Recent work highlighting that adults with CP and spasticity show different changes in spinal cord inhibitory circuits compared to adults with acquired disorders suggests that spasticity in the developing child may be different in nature from that seen in later life (Achache et al. 2010). When these changes occur and how they affect functional movement needs to be elucidated in more detail. This may require not only the combined electromyography-biomechanical approach used in the current study but also the use of electrophysiological techniques such as the Hoffmann (H) reflex.

These current hypotheses about what causes SKG have been derived from a cross-sectional study looking at associations between variables. Thus cause and effect cannot be identified. To understand the relationship between factors such as muscle weakness and stiffness requires longitudinal or intervention studies that aim to alter one or more of these variables and to assess the impact on SKG and overall function. Studies of relevant interventions to date and suggestions for the future will be explored in the next section.

Targeting the main problem

Targeting the main problem associated with SKG remains a challenge because it is not yet known what the main problem is. The findings from this study suggest that the weakness of the inner range knee extensors is important as suggested by a moderate correlation (R^2=0.58) between this variable and trough to peak knee flexion. However, the causes of this relationship are yet to be looked at in more detail. Studies are beginning highlight the importance of inner range weakness (Thompson et al. 2011) but it is felt that greater degrees of inner range should be tested at speeds comparable to that seen during walking. Future work also needs to focus on whether the weakness is central or peripheral. A central cause of weakness refers to the inability to activate a specific muscle via descending commands. The peripheral component refers to the effects of muscle atrophy and/or changes in force generation caused by longer sarcomeres and a longer more compliant tendon. As discussed below potential future treatments may differ depending on the primary cause of muscle weakness.

Weakness

Previous literature has targeted weakness of the knee extensors in pwCP by carrying out strength training or progressive resisted exercises. The parameters of training have tended to follow the guidelines of the American College of Sports Medicine (Ratamess et al. 2009). Systematic reviews highlight that this can lead to an improvement in strength but that function does not markedly improve. This lack of function change could be because the inner range knee extensors were not targeted (Scianni et al. 2009). If the strength training programme did not include any focussed inner range work then the participants inner range strength will not have been improved. In healthy participants improvements in strength with isometric training are specific to the range trained (Folland et al. 2005).

One difficulty in training inner range knee extension in pwCP is that (a) there is the presence of knee flexor contractures precluding training in this zone (b) people can be so weak that they have minimal or no activation in this range even if the range is still available.

Potential treatments for targeting the inner range could be electrical stimulation of the muscle or electrical/magnetic stimulation of the femoral nerve. Both of these techniques would cause the participant to contract and work within the desired inner range. There are a few considerations for stimulating the knee extensors. As a rule the key to eliciting a strong muscle contraction is to stimulate the peripheral (femoral) nerve; this will achieve a larger contraction compared to stimulating the muscle directly. For example, to target foot drop the electrodes are placed on the common peroneal nerve and the foot dorsiflexes accordingly once stimulated (Burridge et al. 1997). Direct electrical stimulation of the quadriceps muscle

requires large electrodes placed over the muscle. To achieve high forces with stimulation, comparable to that achieved during a maximal contraction in sitting/standing when the muscle is acting in outer range can be uncomfortable as high currents are required to activate the whole of the muscle. It is hypothesised that electrical stimulation techniques have been misguided in the past with the positioning of the limb and aims of treatment. For example if the leg is positioned in a mechanically strong position then the electrical stimulation will not be able to match what the participant is already able to do alone. Thus, the stimulation will be likely to be ineffective as it is not overloading the muscle, a key principle of progressive resisted exercises. Current evidence suggests that for strength training to be effective and for hypertrophy to occur the muscle needs to be working at 80% of its 1 repetition maximum for 6 to 8 repetitions (Ratamess et al. 2009). If an individual is not able to tolerate stimulations at a level equivalent to this then the training will not be sufficient. However, if the limb is positioned in a weaker position, for example targeting inner range and is then stimulated, even if the current is low it should have a beneficial effect providing the resultant contraction is greater than what the individual was capable of producing voluntarily. Once the individual has sufficient voluntary control within a range that comfortably exceeds the level which can be achieved via electrical stimulation, then they can move on to progressive resisted exercises.

Electrical stimulation of the femoral nerve requires the electrodes to be placed over the nerve where it is accessible in the groin. This can be uncomfortable and more importantly when working with children possibly unfeasible due to the electrode positioning required. An alternative is to directly stimulate the nerve using magnetic stimulation. Currently magnetic stimulators are mainly used to stimulate the cerebral cortex (transcranial magnetic stimulation). The discharge of a large capacitor is used to evoke a rapidly changing current within an attached coil which in turn leads to a changing magnetic field at right angles to the coil. The coils are designed to provide a focused magnetic field. It is the magnetic field that induces a current in the underlying tissue (e.g. the peripheral nerve). This technique has the advantage that, unlike the electrical stimulation, it does not have to be in direct contact with the skin. Therefore the participant may wear underwear and a pair of shorts as the magnetic field can pass through these. There are now magnetic stimulation coils that are flexible and can mould to the limb, additionally they can have an intrinsic water cooling device to prevent the coil from overheating and the stimulator automatically cutting out during repetitive stimulation for a period of time (Imetum, Transcranial Magnetstimulation 2014). The disadvantage of this technique is that it requires the participant to attend a clinic to receive the treatment compared to electrical stimulation which can be used at home. However,

magnetic peripheral nerve stimulation could be combined with an intensive strength training programme of two to three times per week for six weeks.

To date most strength training regimes in pwCP have used concentric training or eccentric training during closed kinetic chain exercises (e.g. squats) (Dodd et al. 2002; Mockford & Caulton 2008; Verschuren et al. 2008; Scianni et al. 2009). Eccentric muscle work could be very effective among pwCP. Pilot work in TDC has already shown that this can not only increase muscle strength but also increase fascicle length (Crill et al. 2014). Thus this eccentric training may potentially address both muscle weakness and increased passive stiffness (Mohagheghi, A. 2014 personal communication, Brunel University). Although this is an exciting concept it needs further work before it can be considered the ideal solution for muscle weakness among pwCP and there are potential drawbacks. Eccentric training often leads to delayed onset muscle soreness caused by the training inducing mild muscle damage and localised inflammation. The repair of this muscle damage involves activation of satellite cells that fuse with the multinucleated muscle cell resulting in repair and muscle hypertrophy. In pwCP it has recently been suggested that satellite cells are less active than normal (Smith et al. 2013). This may explain why there are fewer in series sarcomeres present and why difficulties often occur during rapid growth spurts when the muscle must lengthen by the addition of sarcomeres in series. Therefore, it remains to be seen whether eccentric exercise has the same beneficial effects seen to date in TDC. It may be that with insufficient satellite cell activity that this form of training just causes further muscle damage and should be avoided as is recommended for types of myopathy. Therefore, during and after training there should be indirect measures of muscle damage such as phosphocreatine kinase, a muscle enzyme involved in energy provision that is released into the blood stream when there is muscle damage.

Both peripheral muscle/nerve stimulation and progressive resisted exercise involving eccentric contractions predominately target the peripheral component of muscle weakness. However with progressive resisted exercise in healthy participants central changes have been reported (i.e. in the size of the response to cortical stimulation). Similarly, task related training may also directly affect weakness by improving central control. Task related training involves training on a targeted task, such as walking. As walking is so complex, involving activation of multiple muscle groups to achieve propulsion and maintain stability, it is clear that targeting one component (e.g. inner range quadriceps strength) may not necessarily carry over into functional gains as much as expected. In pwCP the task could be modified during therapy so they can exercise either different muscle groups or within ranges that are not usually achieved. One way of doing this could be through supported treadmill training. Here a harness would provide support to the person which would reduce the antigravity

requirements. In combination with guidance from a therapist pwCP could then focus on specific aspects of leg extension e.g. during the loading response. Treadmill training has additional effects on cardiovascular fitness and has been shown to be effective for this in pwCP and other upper motor neuron syndromes (Martin et al. 2010).

Another novel method of targeting muscle weakness could be via direct stimulation of the motor cortex. This technique would be directly addressing central, rather than peripheral, causes of weakness. Most of the work in this area has been performed to date in stroke (Le et al. 2014; Liew et al. 2014; Raffin & Siebner 2014). Studies in primates and humans have shown that after a stroke the areas adjacent to the damage increase their activity and directly influence recovery (Grefkes & Ward 2014). Stimulation of these areas using either repetitive transcranial magnetic stimulation or transcranial direct current stimulation has provided promising results that this can increase cortical activity and have behavioural effects (Le et al. 2014; Liew et al. 2014; Raffin & Siebner 2014). Thus this could be a potential adjunct to treatments using progressive strength training, peripheral muscle and nerve stimulation and task related training.

Passive stiffness

As there was a trend towards a significant relationship between the passive stiffness and SKG potential treatments of this impairment will be briefly discussed as recent work suggests that passive stiffness and muscle atrophy may be intrinsically interlinked (Li et al. 2008). Potential treatments for passive stiffness could be aimed at increasing tendon stiffness and increasing fascicle length thus reducing muscle stiffness. As discussed previously an important initial stage is to clearly define longitudinal changes in tendon compliance and muscle stiffness with the development of SKG and crouch gait.

Increases in passive stiffness, as found in the current study, are potentially amenable to physical interventions such as splinting or stretching. A recent Cochrane review however suggested that there is no evidence for the effectiveness of stretching in people with neurological deficits (Katalinic et al. 2011). Although this review has been criticised in terms of the breadth of patient groups (both lower and upper motor neuron syndromes were included and different muscle groups were assessed) and the inclusion criteria (many groups had minimal spasticity and/or contracture at the start of treatment) the review methods are robust and the findings hold, even when the effect of stretching one muscle group (the plantarflexors) is assessed in people with an upper motor neuron syndrome (Ofori 2012).

It is particularly important to assess the effects of stretching in pwCP as this is a developmental disorder. Deficits in satellite cell function and thus the ability to increase in

series sarcomere number may be present as discussed above. Therefore, pwCP may behave differently to stretching compared to adults with acquired central nervous system disorders. There are some positive recent findings suggesting that stretching can be effective in pwCP and can help both muscle and tendon stiffness/compliance. A passive stretching programme performed simultaneously with active-movement training, for example, has been shown to have positive effects upon the calf muscle-tendon biomechanical properties in children with CP (Zhao et al. 2011). A six week treatment of passive stretching and active-movement training reduced the stiffness of the fascicles, lengthened the fascicles and also decreased the tendon length and increased the tendon stiffness. It was an intensive programme involving three 1 hour sessions per week for six weeks, each session comprised twenty minutes of passive stretching, thirty minutes of active-movement and a further ten minutes of passive stretching, the calf muscle was strenuously strained towards extreme dorsiflexion. All elements of the training were performed using an intelligent ankle-stretching device which was attached to a chair and the muscle-tendon changes were measured using ultrasound combined with biomechanical measurements. Although this study showed very promising results with regards for future effective treatments, the methods used are still laboratory based and may not easily transfer to a home programme. Nevertheless Zhao et al. demonstrated that combining strength and stretch training produces the desired results which other pure strength or stretch studies have often failed to do (Katalinic et al. 2011).

As previous systematic reviews have found that stretching alone may not be an effective treatment plan (Katalinic et al. 2011), it may be that combined approaches are required. This combination concept could possibly be explained by the understanding that strength and stiffness are related. The molecular pathways regarding muscle atrophy and how they affect muscle fibrosis and stiffness are now beginning to be understood (Li et al. 2008). For example, during bed rest muscles atrophy. Muscle cell nuclei usually produce intramuscular proteins (e.g. actin and myosin) but when the muscles are resting and not being used (e.g. bed rest) then the protein production is greatly reduced and this leads to the muscle breaking down. There is a cascade of molecular events underling this effect. As more is being discovered about this molecular pathway it is becoming apparent that certain molecules link in with the fibrosis pathway (Li et al. 2008). For example, one molecule central to muscle atrophy, myostatin, has also been shown to activate fibroblasts which in turn cause fibrosis and increased passive stiffness. Thus muscle atrophy and muscle fibrosis/stiffness pathways seem to be interlinked (Li et al. 2008). Therefore it could be postulated that if muscle atrophy is occurring that it will in turn cause stiffness (Smith et al. 2011). An older animal based study showed that muscle atrophy and fibrosis can be

targeted by a combination of stretching and electrical stimulation (Williams et al. 1988). As part of the study rabbit soleus muscles were immobilised and shortened which caused a reduction in the number of sarcomeres and an increased amount of connective tissue. The muscles were also immobilised, shortened and electrically stimulated which caused a reduction in the number of sarcomeres but the amount of connective tissue did not change in relation with the control. Therefore, although this was only an animal study, stretching and strengthening in combination looks to be a potentially beneficial approach (Mugglestone et al. 2012).

Functional Training

Another possibility is to take a functional approach where treatments aim to encourage knee flexion without targeting the underlying impairment. One example of this could be to encourage children to walk over uneven ground. Walking over uneven ground is associated with a decrease in walking speed and cadence. However, walking over uneven ground is associated with a 12 degree average increase of knee flexion whilst compared to even ground, among a group of participants with CP. There were additional increases in hip flexion, anterior pelvic tilt and outward foot rotation (Böhm et al. 2014). This highlights a functional training strategy for stiff knee walkers with the potential of improving the degree of knee flexion. Walking over uneven ground may also have beneficial effects on balance.

Limitations

Static impairment measures

The main limitation of this study is considered to be the fact that the laboratory and clinical measures of impairment are static, as opposed to dynamic which would reflect the task under investigation, namely waking. As described in chapter two, the participants were assessed in a seated position for strength and in a relaxed supine position for stiffness during the laboratory measures and moved through several different positions for the clinical measures. Therefore it can be said that this study has taken static measures and related them to dynamic ones, this issue has already been raised in previous work (Desloovere & Bar-On 2013) and discussed in chapter four.

This highlights that the stretch reflex is not actually the stereotype response it is often thought to be. This study found a correlation with spasticity whilst measured statically, however if the stretch reflex was measured during gait it may produce different results. Following on from this study it would be interesting to look at the modulation of stretch reflexes during the gait cycle among individuals with CP. However, this is technically difficult and involves imposing stretches at specific parts of the gait cycle. The static dynamometry-based methods used in this study quantify tests that are commonly used clinically. In a gait

laboratory setting the walking is often assessed in detail then the impairment measures are performed statically. Therefore, the flaws in this study's approach are resultant from the flaws of current clinical decision making.

This study looked at the potential causes for SKG using current clinical assessment techniques. As demonstrated between chapters four and five the clinical impairment measures of strength and stiffness were just as good at predicting SKG as the laboratory measures were. However, the 3D motion analysis was shown to be superior to the observational analysis, so in light of this it is suggested that the clinical impairment measures are used in combination with 3D motion analysis where possible.

Gross measures

The dynamometry measures of gross limb strength used within this study are a further limitation. This study did not measure the moment angles throughout the range of movement, instead they were recorded at just two points (see chapter two for details). This was performed to avoid stretch reflex activation by stretching the antagonist muscle. However, it resulted in a less dynamic measure of muscle strength. Previous authors have used isokinetic dynamometry which, in combination with measuring lower limb kinetics while walking, allows one to calculate the MUR. This informs the clinician of the relative capacity of the muscles while walking (Milot et al. 2007; Milot et al. 2008).

Additionally, it could be argued this study used a gross measure of passive stiffness. It was measured using a dynamometer and also utilised EMG but it did not use ultrasound to assess passive stiffness of the muscle and tendon as other studies have done (Herbert et al. 2011; Diong et al. 2012). As mentioned above future work should focus on the changes in muscle and tendon stiffness and how this relates to the development of SKG and crouch gait.

These gross measures were chosen for this study because multiple impairments were being investigated and the majority of the participants were children which imposed a time constraint. It was important to keep the data collection appointment as short as reasonably possible, usually it was an hour and a half contact time. It is true that some of the measures were gross but had they all been as specific as possible the participants, whom were all volunteers, would have had to donate more of their time and it was considered unfeasible for the children to be able to concentrate for that length of time and could have caused fatigue.

Too specific

The overall aim for any child with CP is to offer them the best quality of life possible, opinions on what this is exactly will vary from child to child. Individual children and parents/carers will have differing desired outcomes from treatments and rehabilitation. For example, the child's

wish from a participation aspect could be to participate in sports at school and access a cinema which has stairs. Other goals commonly encountered include the desire to walk faster or further, or be more efficient and delay/avoid the onset of tiredness and/or pain in muscles. Children with CP do not tend to attend a clinic complaining that their knee does not bend enough. Instead they tend to say they are not able to run as fast as other children or complain that they often trip.

This current study hones in on very specific aspects, the underlying theory is that if SKG is improved and the overall gait is more normal then the child will see their desired improvements and have fewer secondary complications. These interventions may all improve SKG but it may not necessarily make an impact unless community ambulation is improved, something which is important, measurable and functional for pwCP.

This study looked at the correlation between a very specific measure of walking and several impairments but what might be useful is to also look at the correlation between the impairment and larger scales such as community ambulation scales. The difficulty with these measures is that the causative links are more complex and unknown. There could be a relationship between the two but it would be difficult to hypothesise the cause and effect and provide implications for treatment.

Normalising

The study approach could be flawed by the opinion that in the long term the attempt is to normalise pwCP. Throughout this study, in clinical practice and clinical decision making, pwCP are compared to healthy controls and when differences between the groups are found it is considered that it would be beneficial if the CP group could be "altered" (e.g. with rehabilitation, surgery or pharmacological interventions) to match the results of the control.

However, it could be argued that pwCP and control groups are two very different biological (as well as psychosocial) entities. The fact is that a child whom has grown up with a brain injury has adapted to live and ambulate in the best possible way for them. Their control of movement could be very different to that of TDC and their optimum/most efficient way of walking might actually be with a SKG.

The only comparator this study has is the control group but if more was known about what makes pwCP walk more optimally i.e. what it is they are trying to control, then that could be used as a comparator/bench mark instead. For example, attempting to improve walking efficiency may not require scrutiny of joint angles or enforcing "normality", there may be different approaches if this route was explored. What is optimal may vary over time and between people. Theories of what is being controlled in "normal" movement include

movement efficiency or a minimization of jerk (the derivative of acceleration) (Rosenbaum 1991; Rosenbaum et al. 1999). In pwCP it could be that stability in standing achieved through minimal muscle activity could be a fundamental aim that requires optimal positioning of the ground reaction force, using body movements unique to that patient population/situation.

Normalising and the aim to improve and maintain walking has further implications upon the approach to children and adults with CP. Within this study and in gait clinics in general, the children with CP are being compared to TDC and this may not be a good thing as it instantly classes the children with CP as abnormal and the controls as normal. This demonstrates that there are also sociological factors to be aware of.

Not causative

This study does not examine causative factors, it only looks at correlations. This study only took measurements on one occasion and did not look at the effect of a treatment plan, e.g. a strengthening programme and its effect on SKG, nor did it follow up participants longitudinally. It is suggested that future work focusses on this and upon the inner range quadriceps strength in particular. Therefore this study can be considered to be a preliminary investigation of the mechanisms underlying movement patterns in pwCP and is speculative in many of its findings.

Healthy participants

The majority of the healthy control participants were very fit due to their sporting background. The school from which all of the under eighteen year old healthy control participants were recruited from is associated with an elite swimming programme and several participants were members of this programme. The differences between the control and CP group could have been exaggerated due to this. Additionally, it is important to note that increased amounts of sport training (e.g. long distance running) can alter factors such as tendon compliance and muscle stiffness due to changes in the amount and content of connective tissue (Kubo et al. 2000). Running over time, for example, is associated with stiffer tendons although the effects of swimming have not been assessed to date (Kubo et al. 2000). Therefore the difference in passive stiffness may not be as much as expected because the chosen 'healthy sample' may be stiffer than the general 'healthy population' i.e. they were aged matched controls but possibly the healthier side of healthy!

Summary

In summary this study found correlations between total stiffness, degree of crouch and inner range strength with trough to peak knee flexion. It also looked at the relationships between

the clinical and laboratory measures and it is suggested that clinical measures of impairments are used in combination with 3D motion analysis for the assessment of SKG.

The implications for treatment are to be mindful of the fact that by attempting to improve one impairment it does not have a negative effect upon another. It is believed the impairments studied could be interrelated. The implication of this is that the causation needs to be looked at in more detail. In parallel with this there should be an evaluation of treatments such as the strengthening and stretching on walking patterns and function. Future work should be targeted at strengthening the inner range quadriceps and also combining this with a stretching programme.

APPENDICES

Appendix 1   Gross Motor Function Classification System for Cerebral Palsy

Gross Motor Function Classification System for Cerebral Palsy

Robert Palisano, Peter Rosenbaum, Stephen Walter, Dianne Russell, Ellen Wood, Barbara Galuppi

Introduction & User Instructions

The Gross Motor Function Classification System for cerebral palsy is based on self-initiated movement with particular emphasis on sitting (truncal control) and walking. When defining a 5 level Classification System, our primary criterion was that the distinctions in motor function between levels must be clinically meaningful. Distinctions between levels of motor function are based on functional limitations, the need for assistive technology, including mobility devices (such as walkers, crutches, and canes) and wheeled mobility, and to much lesser extent quality of movement. Level I includes children with neuromotor impairments whose functional limitations are less than what is typically associated with cerebral palsy, and children who have traditionally been diagnosed as having "minimal brain dysfunction" or "cerebral palsy of minimal severity". The distinctions between Levels I and II therefore are not as pronounced as the distinctions between the other Levels, particularly for infants less than 2 years of age.

The focus is on determining which level best represents the child's present abilities and limitations in motor function. Emphasis is on the child's usual performance in home, school, and community settings. It is therefore important to classify on ordinary performance (not best capacity), and not to include judgments about prognosis. Remember the purpose is to classify a child's present gross motor function, not to judge quality of movement or potential for improvement.

The descriptions of the 5 levels are broad and are not intended to describe all aspects of the function of individual children. For example, an infant with hemiplegia who is unable to crawl on hands and knees, but otherwise fits the description of Level I, would be classified in Level I. The scale is ordinal, with no intent that the distances between levels be considered equal or that children with cerebral palsy are equally distributed among the 5 levels. A summary of the distinctions between each pair of levels is provided to assist in determining the level that most closely resembles a child's current gross motor function.

The title for each level represents the highest level of mobility that a child is expected to achieve between 6-12 years of age. We recognize that classification of motor function is dependent on age, especially during infancy and early childhood. For each level, therefore, separate descriptions are provided for children in several age bands. The functional abilities and limitations for each age interval are intended to serve as guidelines, are not comprehensive, and are not norms. Children below age 2 should be considered at their corrected age if they were premature.

An effort has been made to emphasize children's function rather than their limitations. Thus as a general principle, the gross motor function of children who are able to perform the functions described in any particular level will probably be classified at or above that level; in contrast the gross motor functions of children who cannot perform the functions of a particular level will likely be classified below that level.

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Gross Motor Function Classification System for Cerebral Palsy (GMFCS)

Before 2nd Birthday

Level I   Infants move in and out of sitting and floor sit with both hands free to manipulate objects. Infants crawl on hands and knees, pull to stand and take steps holding on to furniture. Infants walk between 18 months and 2 years of age without the need for any assistive mobility device.

Level II   Infants maintain floor sitting but may need to use their hands for support to maintain balance. Infants creep on their stomach or crawl on hands and knees. Infants may pull to stand and take steps holding on to furniture.

Level III   Infants maintain floor sitting when the low back is supported. Infants roll and creep forward on their stomachs.

Level IV   Infants have head control but trunk support is required for floor sitting. Infants can roll to supine and may roll to prone.

Level V   Physical impairments limit voluntary control of movement. Infants are unable to maintain antigravity head and trunk postures in prone and sitting. Infants require adult assistance to roll.

Between 2nd and 4th Birthday

Level I   Children floor sit with both hands free to manipulate objects. Movements in and out of floor sitting and standing are performed without adult assistance. Children walk as the preferred method of mobility without the need for any assistive mobility device.

Level II   Children floor sit but may have difficulty with balance when both hands are free to manipulate objects. Movements in and out of sitting are performed without adult assistance. Children pull to stand on a stable surface. Children crawl on hands and knees with a reciprocal pattern, cruise holding onto furniture and walk using an assistive mobility device as preferred methods of mobility.

Level III   Children maintain floor sitting often by "W-sitting" (sitting between flexed and internally rotated hips and knees) and may require adult assistance to assume sitting. Children creep on their stomach or crawl on hands and knees (often without reciprocal leg movements) as their primary methods of self-mobility. Children may pull to stand on a stable surface and cruise short distances. Children may walk short distances indoors using an assistive mobility device and adult assistance for steering and turning.

Level IV   Children floor sit when placed, but are unable to maintain alignment and balance without use of their hands for support. Children frequently require adaptive equipment for sitting and standing. Self-mobility for short distances (within a room) is achieved through rolling, creeping on stomach, or crawling on hands and knees without reciprocal leg movement.

Level V   Physical impairments restrict voluntary control of movement and the ability to maintain antigravity head and trunk postures. All areas of motor function are limited. Functional limitations in sitting and standing are not fully compensated for through the use of adaptive equipment and assistive technology. At Level V, children have no means of independent mobility and are transported. Some children achieve self-mobility using a power wheelchair with extensive adaptations.

Between 4th and 6th Birthday

Level I   Children get into and out of, and sit in, a chair without the need for hand support. Children move from the floor and from chair sitting to standing without the need for objects for support. Children walk indoors and outdoors, and climb stairs. Emerging ability to run and jump.

Level II   Children sit in a chair with both hands free to manipulate objects. Children move from the floor to standing and from chair sitting to standing but often require a stable surface to push or pull up on with their arms. Children walk without the need for any assistive mobility device indoors and for short distances on level surfaces outdoors. Children climb stairs holding onto a railing but are unable to run or jump.

Level III   Children sit on a regular chair but may require pelvic or trunk support to maximize hand function. Children move in and out of chair sitting using a stable surface to push on or pull up with their arms. Children walk with an assistive mobility device on level surfaces and climb stairs with assistance from an adult. Children frequently are transported when travelling for long distances or outdoors on uneven terrain.

Level IV   Children sit on a chair but need adaptive seating for trunk control and to maximize hand function. Children move in and out of chair sitting with assistance from an adult or a stable surface to push or pull up on with their arms. Children may at best walk short distances with a walker and adult supervision but have difficulty turning and maintaining balance on uneven surfaces. Children are transported in the community. Children may achieve self-mobility using a power wheelchair.

Level V   Physical impairments restrict voluntary control of movement and the ability to maintain antigravity head and trunk postures. All areas of motor function are limited. Functional limitations in sitting and standing are not fully compensated for through the use of adaptive equipment and assistive technology. At Level V, children have no means of independent mobility and are transported. Some children achieve self-mobility using a power wheelchair with extensive adaptations.

Between 6th and 12th Birthday

Level I   Children walk indoors and outdoors, and climb stairs without limitations. Children perform gross motor skills including running and jumping but speed, balance, and coordination are reduced.

Level II   Children walk indoors and outdoors, and climb stairs holding onto a railing but experience limitations walking on uneven surfaces and inclines, and walking in crowds or confined spaces. Children have at best only minimal ability to perform gross motor skills such as running and jumping.

Level III Children walk indoors or outdoors on a level surface with an assistive mobility device. Children may climb stairs holding onto a railing. Depending on upper limb function, children propel a wheelchair manually or are transported when travelling for long distances or outdoors on uneven terrain.

Level IV   Children may maintain levels of function achieved before age 6 or rely more on wheeled mobility at home, school, and in the community. Children may achieve self-mobility using a power wheelchair.

Level V   Physical impairments restrict voluntary control of movement and the ability to maintain antigravity head and trunk postures. All areas of motor function are limited. Functional limitations in sitting and standing are not fully compensated for through the use of adaptive equipment and assistive technology. At level V, children have no means of independent mobility and are transported. Some children achieve self-mobility using a power wheelchair with extensive adaptations.

Distinctions Between Levels I and II

Compared with children in Level I, children in Level II have limitations in the ease of performing movement transitions; walking outdoors and in the community; the need for assistive mobility devices when beginning to walk; quality of movement; and the ability to perform gross motor skills such as running and jumping.

Distinctions Between Levels II and III

Differences are seen in the degree of achievement of functional mobility. Children in Level III need assistive mobility devices and frequently orthoses to walk, while children in Level II do not require assistive mobility devices after age 4.

Distinctions Between Level III and IV

Differences in sitting ability and mobility exist, even allowing for extensive use of assistive technology. Children in Level III sit independently, have independent floor mobility, and walk with assistive mobility devices. Children in Level IV function in sitting (usually supported) but independent mobility is very limited. Children in Level IV are more likely to be transported or use power mobility.

Distinctions Between Levels IV and V

Children in Level V lack independence even in basic antigravity postural control. Self-mobility is achieved only if the child can learn how to operate an electrically powered wheelchair.

Want to know more? Contact:

CanChild
Centre for Childhood Disability Research

Institute for Applied Health Sciences, McMaster University
1400 Main Street West, Rm. 408, Hamilton, ON, Canada L8S 1C7
Tel: 905-525-9140 Ext. 27850 * Fax: 905-522-6095
E-mail: canchild@mcmaster.ca
Website: www.fhs.mcmaster.ca/canchild

Appendix 2 Study information sheet

Faculty of Health

University of Plymouth
Peninsula Allied Health Centre
Derriford Road, Plymouth
Devon, PL6 8BH

tel +44 (0) 1752 587590
fax +44 (0) 1752 238 874
www.plymouth.ac.uk/healtheducation

Date 11/01/11 Version 1

Ref 11/H0206/10

Paediatric Orthopaedic Research Team

Child + Parents
Address

11ᵗʰ Jan 2011

Dear ***Child + Parents***,

We are a team of Orthopaedic Surgeons and Research Scientists with a special interest in Cerebral Palsy (CP). We have contacted you either because you have discussed the project with one of the Orthopaedic Paediatric Team or you have attended a gait assessment at the Human Movement and Function Laboratory, MARJONS, Plymouth and indicated that you would be interested in details about future research projects.

We are conducting a research project which aims to identify the reasons why some children with CP walk with stiff knees. The aim of this project is to provide us with information which will improve our management of walking difficulties in people with CP.

We are writing to ask whether your child would be interested in participating in the study. This would involve attending our gait research centre for a period of approximately 90 minutes. A series of tests will be performed looking at the way your child walks and his/her leg muscle power. These tests will involve small sensors being attached to the legs with Velcro, it is entirely painless. Any costs incurred through travel will be re-imbursed. People are welcome to leave the study/decide against volunteering at any stage and do not have to mention a reason why. This will

not affect their medical care or any participation in future research studies. We have enclosed an information sheet outlining the study.

If you have any further queries regarding this study or have any concerns about your child taking part, please do not hesitate to contact us at the address below.

If you and your child are interested in participating could you fill out the reply slip and return it in the stamped addressed envelope.

Yours sincerely

Mr Ben Bradley, *Specialist Registrar in Trauma and Orthopaedic surgery*
Mr Robert Jeffery, *Consultant Orthopaedic surgeon*
Professor Jon Marsden, *Professor in Rehabilitation Medicine*

Appendix 3 Reply slip

Faculty of Health
University of Plymouth
School of Health Professions
Peninsula Allied Health Centre
College of St Mark and St John
Derriford Road
PL6 8BH

Tel 01752 587 590
jonathan.marsden@plymouth.ac.uk

Date 11/1 2011 / Version 1 / 11/H0206/10

Factors associated with stiff-legged gait in Cerebral Palsy

Name…………………………………………………………………

	Please Tick Relevant Box
YES I would be willing to participate in the study	
NO I would not like any further contact about this study	

If you would like to participate in the study please fill out the following section

Please insert contact details here	
Address	
Telephone / e mail	
Child's Name / age	

Signature …………………………………….

Please return slip in the stamped addressed envelope provided.

Appendix 4 Cover letter for adults with CP

Faculty of Health
University of Plymouth
Peninsula Allied Health Centre
Derriford Road, Plymouth
Devon, PL6 8BH

tel +44 (0) 1752 587590
fax +44 (0) 1752 238 874
www.plymouth.ac.uk/healtheducation

Date 11/01/11 Version 1 Ref 11/H0206/10

Orthopaedic Research Team

28th November 2012

Dear

We are a team of Orthopaedic Surgeons and Research Scientists with a special interest in Cerebral Palsy (CP). We have contacted you either because you have discussed the project with one of the Orthopaedic Paediatric Team or you have attended a gait assessment at the Human Movement and Function Laboratory, MARJONS, Plymouth and indicated that you would be interested in details about future research projects.

We are conducting a research project which aims to identify the reasons why some people with CP walk with stiff knees. The aim of this project is to provide us with information which will improve our management of walking difficulties in people with CP.

We are writing to ask whether you would be interested in participating in the study.

This would involve attending our gait research centre for a period of approximately 90 minutes. A series of tests will be performed looking at the way you walk and your muscle power. These tests will involve small sensors being attached to the legs with Velcro, it is entirely painless. Any costs incurred through travel will be reimbursed. People are welcome to leave the study/decide against volunteering at any stage and do not have to mention a reason why. This will not affect your medical care or any participation in future research studies. We have enclosed an information sheet outlining the study.

If you have any further queries regarding this study or have any concerns about taking part, please do not hesitate to contact us at the address above.

If you are interested in participating could you fill out the reply slip and return it in the stamped addressed envelope.

Yours sincerely,
Miss Elle Compton, *Research student*
Mr Robert Jeffery, *Consultant Orthopaedic surgeon*
Professor Jon Marsden, *Professor in Rehabilitation Medicine*

Appendix 5 6-10 year olds study information pack (CP)

Version 1.0

Date 11/01/11

Ref: 11/H0206/10

Patient Information Sheet Age 6-10 yrs Old

Study Title: Why some children with cerebral palsy walk with stiff knees

What is research? Why is this project being done?

Research is a way we try to find out the answer to questions. We want to find out why children with cerebral palsy can have difficulties bending their knee while walking.

Why have I been invited to take part?

We want to find out why some children with cerebral palsy find it difficult to bend their knees when they walk.

Did anyone check the study was OK to do?

Before any research is allowed to happen, it has to be checked by a group of people called a research ethics committee. They make sure that the research is fair. This project has been checked by the South West 2 Research Ethics Committee.

Do I have to take part?

No. It is up to you. Only take part if you want to. You can stop at any time without giving a reason.

What will happen to me if I take part?

We want to see you once. The tests take 90 minutes.

We want to test the strength and stiffness of your legs. This involves pushing and pulling against a machine or resting while the machine moves your legs

We want to test the way you walk by measuring the movement of lights that are attached to the legs with Velcro straps

Will the tests upset me?

No, we will give you lots of rest but you might feel slightly tired afterwards. This will only last a day at the most.

Will joining in help me?

We cannot promise that the study will help you but the information we get might help treat young people with cerebral palsy in the future.

What happens when the study stops?

We will send a summary of the study to you and your parents / guardian. We will also tell other people involved other people who care for children with cerebral palsy.

What happens if something goes wrong during the project?

If there is a problem or something goes wrong; we will talk to you and your parents/ guardians about it. We will also tell your doctor and the people who keep an eye on the project.

Will my medical details be kept private if I take part? Will anyone know I'm doing this?

If you say we can, we will tell your doctor you are taking part in the study. We will not tell anyone else about you talking part in the study.

What happens if I don't want to do the research any more?

If at any time you don't want to do the research anymore, just tell your parents, doctor or nurse. They will not be cross with you.

Appendix 6   11-16 year olds study information pack (CP)

**Faculty of Health
& Social Work**

University of Plymouth
Peninsula Allied Health Centre
Derriford Road, Plymouth
Devon, PL6 8BH

tel +44 (0) 1752 587590
fax +44 (0) 1752 238 874
www.plymouth.ac.uk/healtheducation

Version 1.0

Date 11/01/11

Ref: 11/H0206/10

Patient Information Sheet Age 11-16 yrs Old

Study Title: Why children with cerebral palsy walk with stiff knees

We are asking if you would take part in a research project to find out why children with cerebral palsy can have difficulties bending their knee while walking. Before you decide if you want to join in it's important to understand why the research is being done and what it will involve for you. So please consider this leaflet carefully. Talk about it with your family, friends, doctor or nurse if you want to.

Why are we doing the research?
People with cerebral palsy often experience difficulty walking. This study will investigate the factors that limit bending of the knee while walking in children with cerebral palsy. An understanding of the causes of walking difficulties in children with cerebral palsy will allow clinicians in the future to target their treatments more effectively.

What is being tested?
We are measuring the strength and stiffness of children's leg muscles and recording the way children walk.

Why have I been invited to take part?

We want to find out why some children with cerebral palsy find it difficult to bend their knees when they walk. We are recruiting children from specialised clinics in Devon and Cornwall that see people with cerebral palsy. We need to see 40 children with cerebral palsy between 6-16 years old.

Do I have to take part?

No. It is up to you. If you do your doctor will ask you to sign a form giving your consent or assent. You will be given a copy of this information sheet and your signed form to keep. You are free to stop taking part at any time during the research without giving a reason. If you decide to stop this will not affect the care you receive.

What will happen to me if I take part?

If you agree to take part we will need to see you on one occasion lasting 90 minutes. These tests are commonly used in specialised hospitals to assess and help treat children and adults with walking difficulties.

Part 1

We firstly want to see how walking is affected by strength at the ankle and hip. To measure strength we ask people to push or pull as hard as they can against a machine that measures the force people can produce. At the same time we will also measure when the muscles are active by recording placing pads over the muscles.

Part 2

We also want to measure how walking is affected by the stiffness in the knee. To measure stiffness we will move the knee back and forwards very slowly or very quickly using a machine

Part 3

We would then like to measure children's walking by measuring the movement of lights that are attached to the legs with Velcro straps. We are interested in how the knee bends while walking

Finally we will measure your weight, height and the size of your legs. We will use this data to help calculate the forces going through the legs while walking.

What will I be asked to do?

Shorts and a t-shirt, which we can supply, will need to be worn for the tests. All usual medication should be continued.

Are there any side effects?

There are no risks with this study. The tests may be tiring and cause some slight muscle soreness but we will give rests to minimize this as much as possible. Any fatigue should wear off within one day and should not affect walking ability.

What are the possible benefits of taking part?

We cannot promise the study can help you but the information we get might help treat young people with cerebral palsy in the future.

Contact for further information please contact :

Prof Jon Marsden School of Health Professions

Faculty of Health and Social work Peninsula Allied Health Centre

Derriford Road Plymouth PL6 8BH Tel 01752 587 590

Email jonathan.marsden@plymouth.ac.uk

Thank for reading so far- if you are still interested, please go to part 2.

Part 2 Study Title: Why children with cerebral palsy walk with stiff knees

What happens when the research stops?

A summary of the data will be sent to all children. We will share the results of the study with other medical professionals through reports in journals and presentations.

What if there is a problem or something goes wrong?

If there is a problem or something goes wrong; we will discuss it fully with you and your parents / guardian. We will also tell, your GP and the ethics committee that oversees this project. If you are unhappy with this study please approach the researchers or your doctor. The Patient Advice and Liaison Service PALS are also there to help.

Telephone the free phone help desk on 0845 155 8121

Email: pals.pct@plymouth.nhs.uk

Patient Advice and Liason Service (PALS)

Nuffield Clinic, Baring Street, Greenbank, Plymouth PL4 8NF

Will anyone else know I'm doing this?

We will keep your information in confidence. This means that we will only tell those that have a need or a right to know. Wherever possible, we will only send out information that has your name and address removed.

Will taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential. Data will be stored within the University of Plymouth and Prof J Marsden, the chief investigator, will be responsible for the security of the data. Any data we gather will have your name and address removed so that you cannot be recognised from it. You will not be identifiable in any way from any publication arising from the study. With your permission a letter would be sent to your GP informing them of your participation in the study.

Who is organising and funding the research?

The research has been funded by the Plymouth Orthopaedic Research and Training fund and the Plymouth Hospitals General Charity fund.

Who has reviewed this study?

Before any research goes ahead it has to be checked by a research ethics committee. They make sure that the research is fair. This project has been checked by the South West 2 Research Ethics Committee.

Thank you for reading this. Please ask any questions if you need to.

Appendix 7 Adult study information pack (CP)

**Faculty of Health
& Social Work**

University of Plymouth
Peninsula Allied Health Centre
Derriford Road, Plymouth
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fax +44 (0) 1752 238 874
www.plymouth.ac.uk/healtheducation

Version 1.0

Date 11/08/11

Ref: 11/H0206/10

Study Title: Factors associated with stiff-legged gait in Cerebral Palsy

You are being invited to take part in a research study. Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Please ask if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part.

What is the purpose of the study?

People with cerebral palsy often experience difficulty walking. This study will investigate the factors that limit bending of the knee while walking in children and adults with cerebral palsy. To understand the differences in walking pattern and its relationship to the person's leg strength and stiffness we will compare the results to children and adults of a similar age without cerebral palsy. An understanding of the causes of walking difficulties in people with cerebral palsy will allow clinicians in the future to target their treatments more effectively.

Why have I been chosen?

You have been chosen because you have cerebral palsy and are over 16 years old. You should have some weakness in the legs and be able to walk at least 20m non-stop with or without a walking aid. You should not have had any operation on the legs within the last 1 month.

Do I have to take part?

It is up to you to decide whether or not you will take part. If you do decide to take part you will be asked to sign a consent form. If you decide to take part them you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect your current and future medical care or inclusion on any future research projects.

What will happen if we choose to take part?

The study takes place at the Peninsula Allied Health Centre, which is opposite Derriford Hospital in Plymouth. We will provide a map and directions if you choose to participate. The study will take 1 ½ hours to perform.

We will firstly measure the strength and stiffness of the legs. We will measure this in two ways. The first way will be to estimate strength and stiffness using clinical test. These will involve pushing or pulling against a manually applied resistance or relaxing as the leg is moved back and forth by the examiner.

The second way will be to use a dynamometer; this is a motor that is commonly used to measure strength in clinical practice. This will involve fixing the leg and trunk with straps so that only the joint of interest (the ankle, knee or hip) can move. The foot or thigh will be strapped into a support that is attached to a computer controlled motor.

When we measure muscle strength using the dynamometer we will ask you to push or pulls against the support as hard as possible. The amount of force generated will be measured by the motor. When we measure limb stiffness the motor will move the ankle or knee either quickly or slowly while you are relaxing as much as possible. The resistance to movement will be measured. The activity of the muscles in the leg will be measured using stick on electrode pads that attach via wires that attach to an amplifier box. There are several safety features built into the dynamometer such as electrical and mechanical stops which will prevent the motor from over stretching any joint. You will have a switch that can cut off the motor at any time.
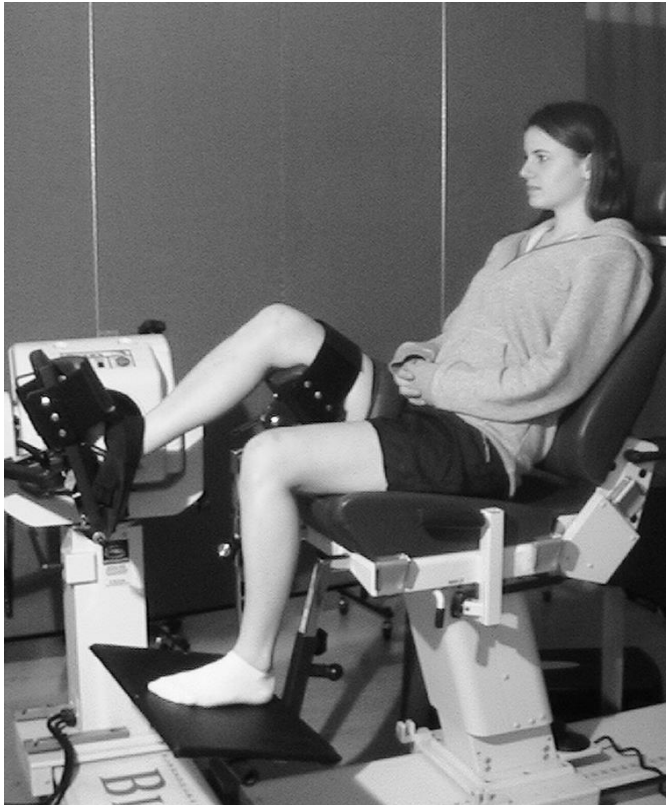
Using a dynamometer to measure ankle strength

We will then measure walking. The movement of small lights attached to the legs will be detected by a camera system and will be used to measure how the legs move. We will also measure muscle activity using the same pads we used in the first part of the study. We will ask you to walk up and down a walkway if possible we will record the forces going through the legs while walking using plates embedded into the walkway. To record the walking data may take several minutes; we will provide rest periods whenever they are required. Finally we will measure your weight, height and the size of your legs. We will use this data to help calculate the forces going through the legs while walking.

What do I have to do?
Shorts and a t-shirt, which we can supply, will need to be worn for the tests. All usual medication should be continued.

Are there any side effects?
The tests may be tiring and may result in some temporary fatigue and slight muscle soreness. This should wear off within one day and should not affect walking ability.

Measuring the movement of the legs while walking

What are the possible risks and benefits of taking part?

There are no direct benefits or risks of taking part in this study.

Will taking part in this study be kept confidential?

All information which is collected about you during the course of the research will be kept strictly confidential. Data will be stored within the University of Plymouth and Prof J Marsden, the chief investigator, will be responsible for the security of the data. Any data we gather will have your name and address removed so that you cannot be recognised from it. You will not be identifiable in any way from any publication arising from the study.

We may consult your medical notes to record the results of any brain scans you may have had in the past. With your permission a letter would be sent to your GP informing them of your participation in the study.

Withdrawal from the project

Your participation in the trial is entirely voluntary. You are free to decline to enter or to withdraw from the study any time without having to give a reason. If you choose not to enter the trial, or to withdraw once entered, this will in no way affect your future medical care. All your information will be treated as strictly confidential.

What if something goes wrong?

If you are harmed by taking part in this research project, there are no special compensation arrangements. If you are harmed due to someone's negligence, then you may have grounds for a legal action but you may have to pay for it. Regardless of this, if you wish to complain, or have any concerns of this study, the normal National Health Service complaints mechanisms should be available to you If you are unhappy with this study please approach the researchers or your doctor.

The Patient Advice and Liaison Service PALS are also there to help.

Telephone the free phone help desk on 0845 155 8121
Email: pals.pct@plymouth.nhs.uk
Patient Advice and Liason Service (PALS)
Nuffield Clinic
Baring Street
Greenbank
Plymouth
PL4 8NF

What will happen to the results of the research study?

A summary of the data will be sent to all participants. The results of this study aim to be published in medical journals by 2013 and presented at relevant national and international conferences. We will ask if you want to be set a copy of any publications at the time of the study. You will be sent a separate summary of the study when it is completed.

Who is funded and reviewed the research?

This research has been funded by the Plymouth Hospitals charitable fund and Plymouth Orthopaedic Research Trust (PORT). Ethical approval has been gained for this study from the NHS South West 2 Research Ethics Committee

For further information please contact :
Prof Jon Marsden

School of Health Professions

Faculty of Health and Social work

Peninsula Allied Health Centre

Derriford Road Plymouth PL6 8BH

Tel 01752 587 590

Email jonathan.marsden@plymouth.ac.uk

Thank you for reading this.

Appendix 8 Information pack for parents/guardians and students aged 6-10 years

Date 11/01/11 Version 1

Ref 11/H0206/10

Paediatric Orthopaedic Research Team

14th January 2013

Dear *Parents/Guardian*,

We are a team of Orthopaedic Surgeons and Research Scientists with a special interest in
Cerebral Palsy (CP). We are conducting a research project which aims to identify the
reasons why some children with CP walk with stiff knees.

Recent studies investigating CP walking patterns have thrown doubt on assumptions
currently used to guide treatments decisions. Many of these studies have been based on
computer models, whereas we aim to identify the causes of stiff-knee walking patterns using
people with an established diagnosis of CP.

The long-term aim of this project is to provide us with information which will improve our
management of walking difficulties in people with CP. We plan to publish this information
and present it at National and International conferences.

In order to make this a valid and relevant study we need to recruit a large number of healthy
children into our study to act as comparisons to children with a diagnosis of CP. We hope
that your child might be happy to volunteer to help us gather the information we need.

This would involve attending our gait research centre for a period of approximately 90
minutes. A series of tests will be performed looking at the way your child walks and his/her
leg muscle power. These tests will involve small sensors being attached to the legs with
Velcro, it is entirely painless. Any costs incurred through travel will be reimbursed. The

students are welcome to leave the study/decide against volunteering at any stage and do not have to mention a reason why. This will not affect their studying, medical care or any participation in future research studies. We have enclosed an information sheet outlining the study; this is aimed to be read by children age 6-10 yrs.

If after reading the information sheet your child agrees to take part and you are willing for them to do so, please sign and return the attached return slip to the school reception as soon as possible.

If you have any further queries regarding this study or have any concerns about your child taking part, please do not hesitate to contact us. Our contact details are attached. Alternatively you can speak to Mr Gatherer who is fully briefed on this project.

Yours sincerely

Professor Jon Marsden, *Professor in Rehabilitation Medicine*
Mr Robert Jeffery, *Consultant Orthopaedic surgeon*
Elle Compton, Research student

Contact for further information:

Prof Jon Marsden School of Health Professions
Faculty of Health and Social work Peninsula Allied Health Centre
Derriford Road Plymouth PL6 8BH
Tel: 01752 587 590
Email : jonathan.marsden@plymouth.ac.uk

Faculty of Health

University of Plymouth
School of Health Professions
Peninsula Allied Health Centre
College of St Mark and St John
Derriford Road
PL6 8BH
Tel 01752 587 590
jonathan.marsden@plymouth.ac.uk

Date 11/3/ 2011 / Version 1 / 11/H0206/10

Factors associated with stiff-legged gait in Cerebral Palsy

Name……………………………………………………………………

	Please Tick Relevant Box
YES I would be willing for my child to participate in the study	
NO I would not like any further contact about this study	

If you would like your child to participate in the study please fill out the following section

Please insert contact details here	
Address	
Telephone	
Child's Name / age	

Signature of   Parent / Guardian ……………………………………

Please return slip to Elle Compton at School Reception.

**Faculty of Health
& Social Work**
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Peninsula Allied Health Centre
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fax +44 (0) 1752 238 874
www.plymouth.ac.uk/healtheducation

Version 1.0

Date 11/01/11

Ref: 11/H0206/10

Healthy Participant Sheet Age 6-10 yrs Old

Study Title: Why children with cerebral palsy walk with stiff knees

What is research? Why is this project being done?

Research is a way we try to find out the answer to questions. We want to find out why children with cerebral palsy can have difficulties bending their knee while walking.

Why have I been invited to take part?

We want to compare the way you walk with a child with cerebral palsy.

Did anyone check the study was OK to do?

Before any research is allowed to happen, it has to be checked by a group of people called a research ethics committee. They make sure that the research is fair. This project has checked been checked by the South West 2 Research Ethics Committee.

Do I have to take part?

No. It is up to you. Only take part if you want to. You can stop at any time without giving a reason.

What will happen to me if I take part?

We want to see you once. The tests take 90 minutes.

We want to test the strength and stiffness of your legs. This involves pushing and pulling against a machine or resting while the machine moves your legs

We want to test the way you walk by measuring the movement of lights that are attached to the legs with Velcro straps

Will the tests upset me?

No, we will give you lots of rest but you might feel slightly tired afterwards. This will only last a day at the most.

Will joining in help me?

We cannot promise that the study will help you but the information we get might help treat young people with cerebral palsy in the future.

What happens when the study stops?

We will send a summary of the study to you and your parents / guardian. We will also tell other people involved other people who care for children with cerebral palsy.

What happens if something goes wrong during the project?

If there is a problem or something goes wrong we will talk to you and your parents/ guardians about it. We will also tell your doctor and the people who keep an eye on the project.

Will my medical details be kept private if I take part?

All information which is collected about you during the course of the research will be kept strictly confidential. Data will be stored within the University of Plymouth and Prof J Marsden, the chief investigator, will be responsible for the security of the data. Any data we gather will have your name and address removed so that you cannot be recognised from it. You will not be identifiable in any way from any publication arising from the study.

Will anyone know I'm doing this?

If you allow, we will tell your doctor you are taking part in the study. We will not tell anyone else about you talking part in the study.

What happens if I don't want to do the research any more?

If at any time you don't want to do the research anymore, just tell your parents, doctor or nurse. They will not be cross with you.

Appendix 9 Information pack for parents/guardians and students aged 11-16 years

Faculty of Health

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www.plymouth.ac.uk/healtheducation

Date 11/01/11 Version 1

Ref 11/H0206/10

Paediatric Orthopaedic Research Team

11th May 2011

Dear *Parents/Guardian*,

We are a team of Orthopaedic Surgeons and Research Scientists with a special interest in Cerebral Palsy (CP). We are conducting a research project which aims to identify the reasons why some children with CP walk with stiff knees.

Recent studies investigating CP walking patterns have thrown doubt on assumptions currently used to guide treatments decisions. Many of these studies have been based on computer models, whereas we aim to identify the causes of stiff-knee walking patterns using people with an established diagnosis of CP.

The long-term aim of this project is to provide us with information which will improve our management of walking difficulties in people with CP. We plan to publish this information and present it at National and International conferences.

In order to make this a valid and relevant study we need to recruit a large number of healthy children into our study to act as comparisons to children with a diagnosis of CP. We hope that your child might be happy to volunteer to help us gather the information we need.

This would involve attending our gait research centre for a period of approximately 90 minutes. A series of tests will be performed looking at the way your child walks and his/her leg muscle power. These tests will involve small sensors being attached to the legs with Velcro, it is entirely painless. Any costs incurred through travel will be reimbursed. The

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students are welcome to leave the study/decide against volunteering at any stage and do not have to mention a reason why. This will not affect their studying, medical care or any participation in future research studies. We have enclosed an information sheet outlining the study; this is aimed to be read by children age 11-16 yrs.

If after reading the information sheet your child agrees to take part and you are willing for them to do so, please sign and return the attached return slip to the school reception as soon as possible.

If you have any further queries regarding this study or have any concerns about your child taking part, please do not hesitate to contact us. Our contact details are attached. Alternatively you can speak to Miss Dunn who is fully briefed on this project.

Yours sincerely

Professor Jon Marsden, *Professor in Rehabilitation Medicine*
Mr Ben Bradley, *Specialist Registrar in Trauma and Orthopaedic surgery*
Mr Robert Jeffery, *Consultant Orthopaedic surgeon*

Contact for further information please contact :

Prof Jon Marsden School of Health Professions
Faculty of Health and Social work Peninsula Allied Health Centre
Derriford Road Plymouth PL6 8BH Tel 01752 587 590
Email jonathan.marsden@plymouth.ac.uk

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Date 11/3/ 2011 / Version 1 / 11/H0206/10

Factors associated with stiff-legged gait in Cerebral Palsy

Name…………………………………………………………………

	Please Tick Relevant Box
YES I would be willing for my child to participate in the study	
NO I would not like any further contact about this study	

If you would like your child to participate in the study please fill out the following section

Please insert contact details here	
Address	
Telephone / e mail	
Child's Name / age	

Signature of   Parent / Guardian ……………………………………

Please return slip to Ms Elle Compton at Main school Reception
Or email ecompton@plymouth-college.co.uk

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Version 1.0

Date 11/01/11

Ref: 11/H0206/10

Healthy Participant Information Sheet Age 11-16 yrs Old

Study Title: Why some children with cerebral palsy walk with stiff knees

We are asking if you would take part in a research project to find out why children with cerebral palsy can have difficulties bending their knee while walking. Before you decide if you want to join in, it's important to understand why the research is being done and what it will involve for you. So please consider this leaflet carefully. Talk about it with your family, friends, doctor or nurse if you want to.

Why are we doing the research?
People with cerebral palsy often experience difficulty walking. This study will investigate the factors that limit bending of the knee while walking in children with cerebral palsy. To understand the differences in walking and its relationship to the child's leg strength and stiffness we will compare the results of children of a similar age without cerebral palsy. An understanding of the causes of walking difficulties in children with cerebral palsy will allow clinicians in the future to target their treatments more effectively.

What is being tested?
We are measuring the strength and stiffness of children's leg muscles and recording the way children walk.

Why have I been invited to take part?

In order to understand the reasons why some children with cerebral palsy walk with a stiff knee we need to compare them with people who don't have cerebral palsy. We are recruiting healthy children from local schools in the Plymouth area with the permission of the school's head teacher. We need 20 children between 6-16 years old to take part.

Do I have to take part?

No. It is up to you. If you do, your doctor will ask you to sign a form giving your consent or assent. You will be given a copy of this information sheet and your signed form to keep. You are free to stop taking part at any time during the research without giving a reason. If you decide to stop this will not affect the care you receive.

What will happen to me if I take part?

If you agree to take part we will need to see you on one occasion lasting 90 minutes. These tests are commonly used in specialised hospitals to assess and help treat children and adults with walking difficulties.

Part 1

We firstly want to see how walking is affected by strength at the ankle and hip. To measure strength we ask people to push or pull as hard as they can against a machine that measures the force people can produce. At the same time we will also measure when the muscles are active by recording placing pads over the muscles.

Part 2

We also want to measure how walking is affected by the stiffness in the knee.

To measure stiffness we will move the knee back and forwards very slowly or very quickly using a machine

Part 3

We would then like to measure children's walking by measuring the movement of lights that are attached to the legs with Velcro straps. We are interested in how the knee bends while walking

Finally we will measure your weight, height and the size of your legs. We will use this data to help calculate the forces going through the legs while walking.

What will I be asked to do?

For the tests, you will need to wear shorts and a t-shirt, which we can supply. All usual medication should be continued.

Are there any side effects?

There are no risks with this study. The tests may be tiring and cause some slight muscle soreness but we will give rests to minimize this as much as possible. Any fatigue should wear off within one day and should not affect walking ability.

What are the possible benefits of taking part?

We cannot promise the study can help you but the information we get might help treat young people with cerebral palsy in the future.

Contact for further information please contact:

Prof Jon Marsden School of Health Professions
Faculty of Health and Social work Peninsula Allied Health Centre
Derriford Road Plymouth PL6 8BH Tel 01752 587 590
Email jonathan.marsden@plymouth.ac.uk

Thank for reading so far- if you are still interested, please go to part 2.

Part 2 Study Title: Why children with cerebral palsy walk with stiff knees

What happens when the research stops?
A summary of the data will be sent to all families. We will share the results of the study with other medical professionals through reports in journals and presentations.

What if there is a problem or something goes wrong?
If there is a problem or something goes wrong; we will discuss it fully with you and your parents / guardian. We will also tell, your GP and the ethics committee that oversees this project. If you are unhappy with this study please approach the researchers or your doctor.

The Patient Advice and Liaison Service PALS are also there to help.
Telephone the free phone help desk on 0845 155 8121
Email: pals.pct@plymouth.nhs.uk
Patient Advice and Liason Service (PALS)
Nuffield Clinic, Baring Street, Greenbank, Plymouth PL4 8NF

Will anyone else know I'm doing this?
We will keep your information in confidence. This means that we will only tell those that have a need or a right to know. Wherever possible, we will only send out information that has your name and address removed.

Will taking part in this study be kept confidential?
All information which is collected about you during the course of the research will be kept strictly confidential. Data will be stored within the University of Plymouth and Prof J Marsden, the chief investigator, will be responsible for the security of the data. Any data we gather will have your name and address removed so that you cannot be recognised from it. You will not be identifiable in any way from any publication arising from the study. With your permission a letter would be sent to your GP informing them of your participation in the study.

Who is organising and funding the research?
The research has been funded by the Plymouth Orthopaedic Research and Training fund and the Plymouth Hospitals Trust General Charities fund.

Who has reviewed this study?
Before any research goes ahead it has to be checked by a research ethics committee. They make sure that the research is fair. Your project has been checked by the South West 2 Research Ethics Committee.

Thank you for reading this. Please ask any questions if you need to.

Appendix 10 Consent form

Faculty of Health

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11th January 2011 Version 1.0

Ref: 11/H0206/10

Study Number
Patient Identification Number

Title of Project: Factors associated with stiff-legged gait in Cerebral Palsy

Name of Researcher: Professor Jon Marsden

Please initial Box

1. I confirm that I have read and understand the information sheet dated 02/11/10 (Version 2) for the above study. I have had the opportunity to consider the information, ask questions and have had these answered satisfactorily

2. I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason, without my medical care or legal rights being affected

3. I agree to my GP being informed of my participation in the study

4. I agree to take part in the above study

Name of patient   Date   Signature

Name of person taking consent   Date   Signature

When completed: 1 for patient 1 for researcher site file

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Appendix 11 Assent form

**Faculty of Health
& Social Work**

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Version 1.0

Date 11/01/11

Ref: 11/H0206/10

Study Title: Why children with cerebral palsy walk with stiff knees

Child (or if unable, parent on their behalf) / young person to circle all they agree with:

Have you read (or had read to you) about this project?	**Yes**	**No**
Has somebody else explained this project to you?	**Yes**	**No**
Do you understand what this project is about?	**Yes**	**No**
Have you asked all the questions you want?	**Yes**	**No**
Have you had all your questions answered in a way you understand?		
	Yes	**No**
Do you understand it's OK to stop taking part at any time?		
	Yes	**No**
Are you happy to take part?	**Yes**	**No**

If <u>any</u> of the answers are "no" or you don't want to take part, don't sign your name!

If you <u>do</u> want to take part, you can write your name below

Your name_____

Date_____

The doctor who explained this project to you needs to sign too:

Print name_____

Sign_____

Date_____

Thank you for your help.

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