Kinematics and kinetics of people with Joint Hypermobility Syndrome during activities of daily living. Do they move differently?

by

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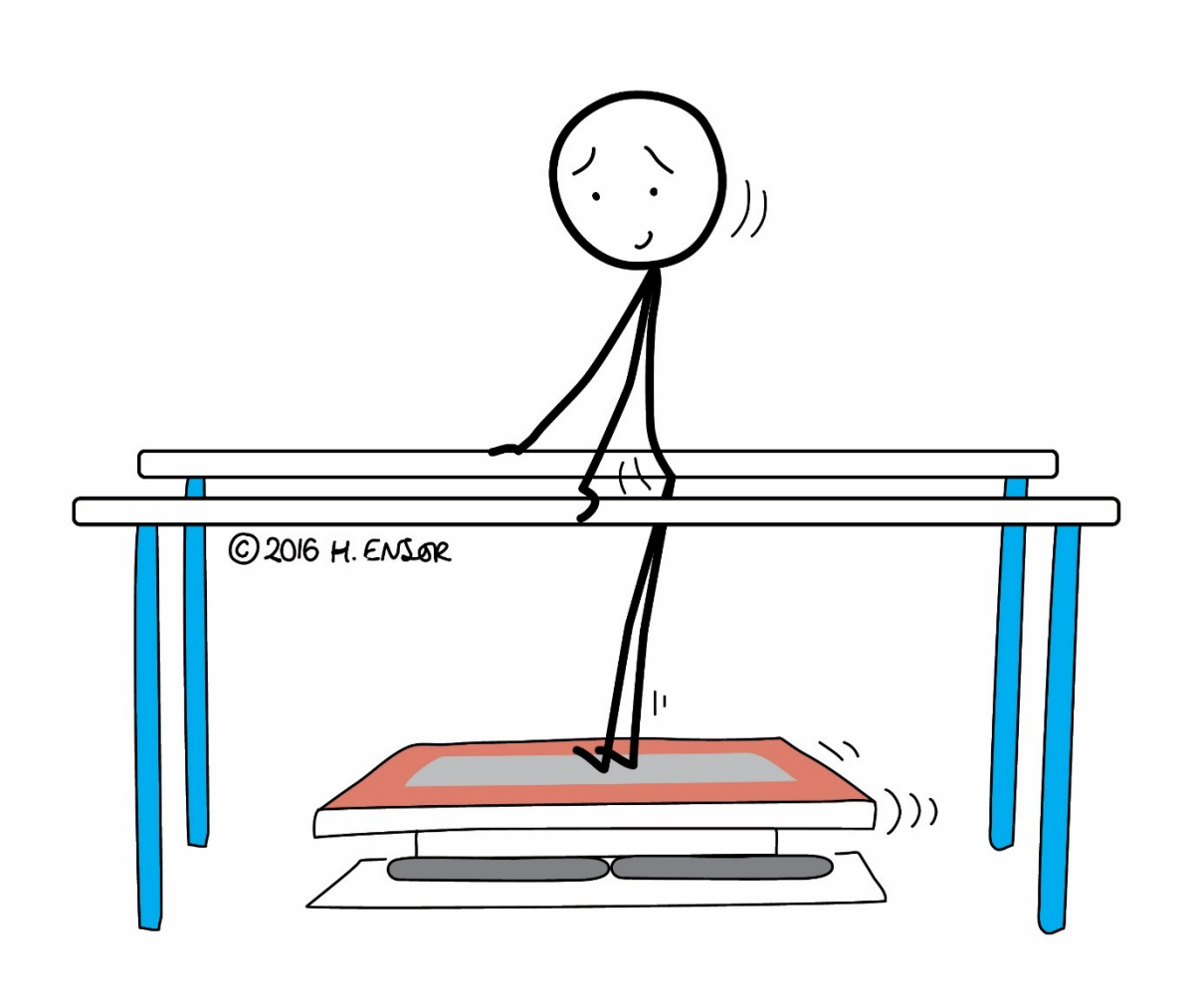
Submitted as partial fulfilment for the degree of PhD at Imperial College London

Declaration of originality

The following thesis and research is my own work, and has been appropriately referenced.

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"The wobble board" by Hannah Ensor, Stickman Communications.

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Abstract:

Introduction: Joint Hypermobility Syndrome (JHS) is a heritable disorder of connective tissue characterised by increased laxity of the joints associated with chronic and widespread arthralgia, along with many other extra-articular symptoms[1]. The hypermobility cannot be changed; instead treatment focuses on the management and improvement of symptoms and expectations of the patient[2]. Physiotherapy is the mainstay intervention, although there is no consensus, and little evidence, to say that a particular type of physiotherapy is effective[3]. Part of the problem is that it is unknown how the symptoms and factors of JHS interplay to affect movement and pain. This is important to understand as without understanding the deficits it is not possible to target treatment. Comparing how people with JHS move to people who are hypermobile and do not have symptoms (GJH), or to people with normal flexibility (NF) may highlight impairments and differences in movement, which could then be targeted with physiotherapy.

Aim: This thesis investigated movement of people with JHS, with the aim to provide information about how people with JHS move during activities of daily living. This information may help clinicians to target differences in movement with the physical therapies, and further our knowledge of this under-recognised condition.

Methods: A systematic review was conducted; research investigating kinematics and/or kinetics of hypermobile movement were reviewed. To progress to measuring movement in JHS, a reliability study was performed; 14 GJH and 13 normal flexibility participants completed three sessions of 3D gait analysis. The main study used 3D movement analysis and EMG to compare 23 JHS participants, 23 GJH participants, and 22 NF participants. Participants completed perturbation, prolonged standing, gait and stair-climbing activities.

Results: The systematic review identified a lack of investigation into any activity other than gait, and in gait there was no consensus as to how people with JHS move differently to NF/GJH. There was no difference in the reliability of 3D movement analysis in GJH people compared to NF people. The main study found differences in movement parameters in each of the tasks. People with JHS had different reactions to perturbations, different behaviour during prolonged standing, and showed impairments in gait and stair climbing. Many of the differences between JHS and NF/GJH were in ankle movement parameters.

Conclusion: Movement during the activities investigated differs between JHS and GJH/NF groups, whereas there is no difference in movement between GJH and NF groups. Since there was only one significant difference between GJH and NF across all tasks, hypermobility per se does not cause the change in movement and therefore pain. It is not clear whether the differences in movement of JHS cause the pain, or are due to pain avoidance. Either way, the results provide guidance to physiotherapists to normalise the movement in treatment.

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Publications from this PhD

Journal papers:

Alexander V. Bates, Caroline M. Alexander, Kinematics and kinetics of people who are hypermobile. A systematic review, In Gait & Posture, Volume 41, Issue 2, 2015, Pages 361-369.

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Acronyms

AAM Ankle ascent moment

AAP Ankle ascent power

ADM Ankle descent moment

ADP Ankle descent power

ANOVA Analysis of variance

AP Anterioposterior

BF Biceps femoris

BIoH Bristol Impact of Hypermobility

BJHS Benign Joint Hypermobility Syndrome

BW Bodyweight

CA Cumulative angle

CoM Centre of mass

CTSIM Clinical test of sensory interaction and balance

EDS Ehlers Danlos Syndrome

EMG Electromyography

HDCT Heritable Disorder of Connective Tissue

hEDS Hypermobility type Ehlers Danlos Syndrome

ICC Intra-class correlation

iEMG Integrated electomyograph

GA Gastrocnemius

GJH Generalised Joint Hypermobility

GM Gluteus medius

GRF Ground reaction force

HAM Hip ascent moment

HAP Hip ascent power

HDM Hip descent moment

HDP Hip descent power

HMS Hypermobility Syndrome

HSD Hypermobility Spectrum Disorder

JHS Joint Hypermobility Syndrome

KAM Knee ascent moment

KAP Knee ascent power

KDM Knee descent moment

KDP Knee descent power

MANOVA Multiple analysis of variance

MDC Minimum Detectable Change

ML Mediolateral

MVC Maximum voluntary contraction

NF Normal flexibility

RF Rectus femoris

RMS Root-mean-square

RoM Range of Motion

SEM Standard error of the mean

TA Tibialis anterior

UD Unable to determine

TTR Time to reversal

TTP Time to peak

VAS Visual Analogue Score

VL Vastus lateralis

VM Vastus medius

Chapter 1: The Joint Hypermobility Syndrome

1.1 What is JHS

The protein that gives humans, and all animals, their tensile strength is collagen. Collagen is the most abundant protein in animals and makes up 25% of total body protein in humans[5]. It is the main protein component of all connective tissues; teeth, bone, fascia, cartilage, ligaments, skin, and extracellular matrix. Given the abundance and many uses of collagen in the body, it is perhaps not surprising that defects in collagen, or a departure from normal, can cause a wide spectrum of health defects. This is the case in a range of disorders collectively termed Heritable Disorders of Connective Tissue (HDCT); Marfan's syndrome, Osteogenesis Imperfecta, Ehler's Danlos syndrome, Stickler syndrome and Joint Hypermobility Syndrome (JHS). Joint hypermobility, where a joint exhibits a range of motion greater than what would be expected in a given population[2,6], is a common factor of all these clinical conditions. However, joint hypermobility is not always a sign of a clinical disorder that is associated with symptoms. Many people exhibit hypermobility in multiple joints and have little or no associated symptoms, a condition labelled Generalised Joint Hypermobility (GJH). GJH can even be an asset, for example in performing arts or in sports where a high degree of flexibility is advantageous[6].

1.2 Classification of hypermobility and Joint Hypermobility Syndrome

GJH is classified using the Beighton Score[1]. A score out of a maximum of 9 is awarded depending on whether a person can perform certain movements; passively bending the little finger past 90° (1 point for each side), passively bending the thumb to touch the forearm (1 point for each side), straightening the elbow to or beyond 10° hyperextension (1 point for each side), straightening the knee to or beyond 10° hyperextension (1 point for each side), and bending forward at the waist to place the palms of the hands on the floor with knees fully extended (Figure 1.1). Although the Beighton score has been shown to have good reproducibility[7] and validity[8], criticisms are that it only samples a few joints and provides no information relating to the degree of joint hypermobility[2]. The test was designed for clinical use and therefore the validity of the Beighton score has been measured when a clinician is administering the test; the self-reported validity is unknown. In an effort to remove the need for a clinician and to address the fact that hypermobility declines with age, Hakim & Grahame[9] developed a five-point questionnaire (Table 1.1). This questionnaire is not commonly used in the literature however.

Item number	Question	Response
1	Can you now (or could you ever) place your hands flat on the floor without bending your knees?	Yes/No
2	Can you now (or could you ever) bend your thumb to touch your forearm?	Yes/No
3	As a child or teenager did your shoulder or kneecap dislocate on more than one occasion?	Yes/No
4	As a child did you amuse your friends by contorting your body into strange shapes or could you do the splits?	Yes/No
5	Do you consider yourself double jointed?	Yes/No

Table1.1: The five-point hypermobility questionnaire. Answering 'Yes' to two or more items suggests hypermobility[9].

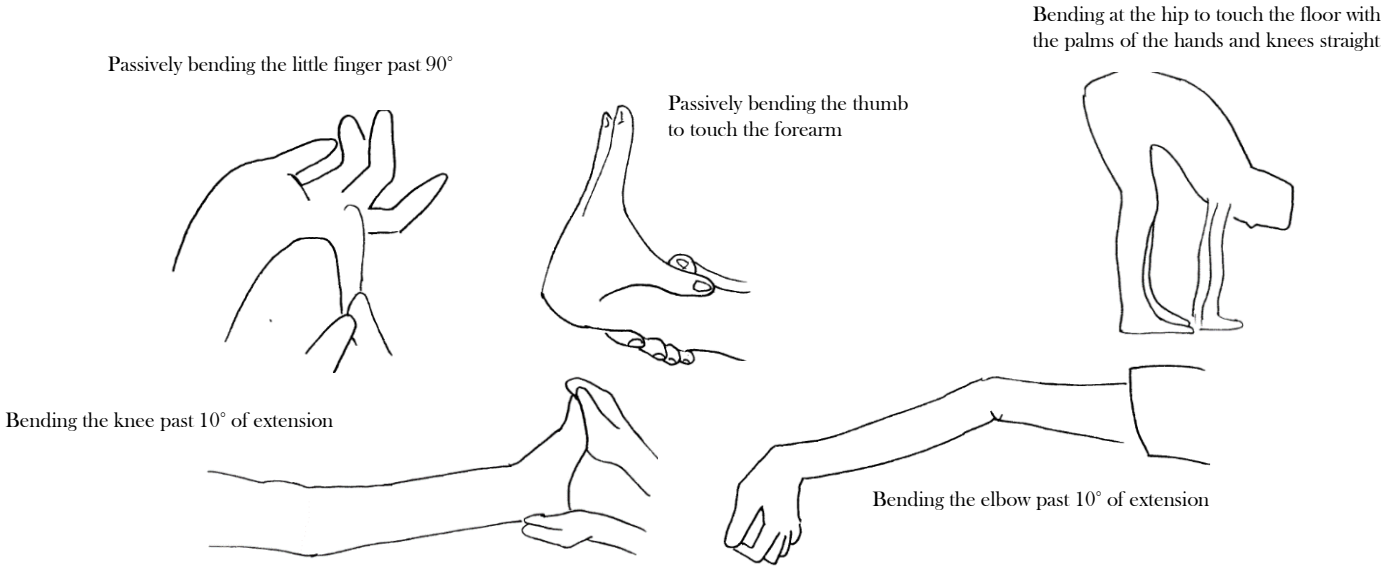


Figure 1.1: The Beighton Score, 1 point is awarded for each movement that can be completed.

Turning to JHS, to date, despite a number of studies investigating genetics of JHS, no definitive genetic profile has been found[10]. The fact that no specific genetic phenotype for JHS has been found, combined with a diverse range of symptoms and clinical presentations, means that making a classification of JHS is a significant challenge[11]. Since the genetic profile of JHS is unknown, and the other HDCTs have specific genetic profiles or clear clinical features[11], a classification of JHS tends to be made by exclusion of other HDCTs. Classification is further made difficult by the fact that there are a range of terms used for what is considered to be the same clinical entity[12]; in recent years the terms

Hypermobility Syndrome, Benign Joint Hypermobility Syndrome, Ehlers-Danlos syndrome Type III, Ehlers-Danlos syndrome Hypermobility Type and Joint Hypermobility Syndrome have all been used. For the remainder of this thesis the term Joint Hypermobility Syndrome (JHS) will be used. In the interests of readability, in reviewing and referencing other studies, the term JHS is used regardless of the term used in the original research paper.

The Beighton Score is a method of defining someone as having GJH, it does not consider any symptoms and is not used to classify JHS. The most common method of classifying JHS is probably the Brighton Criteria. In using the Brighton Criteria, a person's symptoms are marked against major and minor criteria. Major criteria are: (1) Beighton score of 4 or more out of 9, and (2) Arthralgia for 3 months or more in at least 4 joints. Minor criteria are (1) A Beighton Score of 1 to 3 out of 9, (2) Arthralgia for 2 months or longer in at least one joint, or back pain, and/or spondylolysis/spondylolisthesis, (3) Dislocation or subluxation in more than one joint, or in one joint on more than one occasion. (4) Soft tissue rheumatism; three or more lesions (e.g. epicondylitis, tenosynovitis, bursitis). (5) Marfanoid habitus. (6) Abnormal skin striae, hyperextensibility, thin skin, papyraceous scarring. (7) Eye signs: drooping eyelids or myopia or antimongoloid slant. (8) Varicose veins or hernia or uterine/rectal prolapse. A person is classified as JHS if they score positive for 2 major criteria, 1 major and 2 minor, or 4 minor. The Beighton Score features in both major and minor criteria of the Brighton Criteria, and so testing for hypermobility forms part of the diagnostic makeup of the Brighton Criteria. The Brighton Criteria has been shown to have generally good reproducibility[7] and validity[8], however this validity has been measured against healthy individuals, and not other classification systems or disorders. The consequence of this is that although the Brighton Criteria may be valid when comparing against a healthy population, it is not known how well the criteria distinguish someone with JHS from other HDCTs, or other chronic, widespread painful conditions.

Other classification methods include the Villefranche criteria[13], which is typically used for classification of the Ehlers-Danlos syndromes, of which Hypermobility Type is considered synonymous with JHS[14]. Similar to the Brighton Criteria, the Villefranche Criteria incorporate major and minor criteria of clinical manifestations (Beighton score ≥ 5, hyperextensible skin, recurring joint dislocations, chronic pain for 3 months or more, and a positive family history) to classify an individual. The Villefranche criteria also incorporates specific genetic and/or protein abnormalities[13], whereas the Brighton score incorporates more extra-articular symptoms. Other methods of classification of GJH include the Contompasis score[15] and the Bulbena/Barcelona Score[16]. They are used less in the literature, possibly due to the time-consuming nature of the tests[2], or the fact they are rarely discussed in scientific publications written in English[17]. In a survey of UK physiotherapists by Billings *et al.*[17], only approximately 3% of respondents used Contompasis or Barcelona scores for classifying JHS, versus approximately 54% of respondents used the Brighton Criteria. The difficulties of classification are known, and a recent symposium addressed these concerns and reported a new set of diagnostic criteria.

The results of which have recently been published[18]. The authors summarised conditions relating to hypermobility and the problems caused with having multiple terms. Despite there being a relatively large number of terms to describe JHS already, they suggest removal of the term JHS and use of yet a further term Hypermobility Spectrum Disorder (HSD), which is further split into Generalised HSD, Localised HSD, Peripheral HSD and Historical HSD. In addition, they suggest that a new classification of people at the most symptomatic end of the spectrum of disorders will be called hypermobile Ehlers Danlos Syndrome (hEDS). The criteria for hEDS have been tightly specified in order to prevent over classification. It is too early to say whether these terms will be adopted. The investigations presented here occurred before the new classification; it is difficult to know how many JHS participants would now be classified as having HSD or hEDS. For this reason, as well as clarity of reporting the terms used in this thesis will remain as JHS, GJH and NF.

The Brighton Criteria does not measure severity or impact of JHS on the patient. Recently there has been an effort to address this. The Bristol Impact of Hypermobility (BIoH) questionnaire is a series of 55 questions designed to assess the impact JHS has on an individual[19]. Rather than classifying the condition, the BIoH will in theory allow for an accurate assessment of the effectiveness of treatment in JHS, as other questionnaires may not be condition specific[19]. The clinically meaningful difference in BIoH score has not yet been established.

1.3 Prevalence

The prevalence of GJH is difficult to estimate, as incidence varies by population depending on gender, age, sex, and ethnicity, and studies use different criteria for defining hypermobility. A study of US blood donors found a prevalence of 5%[20], a Swedish working population had a prevalence of approximately 17% in females and 6% in males[21], and prevalence was as high as 25-38% in Iraq[22]. JHS is far less prevalent; although no specific population survey has been conducted, the incidence in the general population is estimated to be between 0.75 and 2%[23], and listed as 1 in 5000 by Camerota *et al.*[24], but it is not clear where any of these figures are derived from. Importantly, although the incidence in the general population is low, the prevalence within musculoskeletal health clinics is much higher[25]. For example, the prevalence of JHS was 33% in patients presenting at a UK gastrointestinal clinic[26], and in referrals to a West-London rheumatology clinic, the JHS phenotype was present in 58% of females and 29% of males[27]. Given the high proportion of patients presenting with JHS, it is perhaps surprising that JHS is an under recognised and poorly managed disorder[2] and a recognised area of neglect in rheumatology[6].

1.4 Symptoms of JHS

As may be expected with a disorder of connective tissue, symptoms of JHS are diverse, and JHS patients tend to present with a wide spread range of articular and extra-articular symptoms[2]. Some of these symptoms are summarised in Table 1.2.

Joint	Soft Tissue	Spine	Extra-articular
Hip Dysplasia	Ligament/muscle/meniscus tear	Loose-back syndrome	Stretchy skin
Late walking			Thin scars
Growing Pains	Epicondylitis	Disc prolapse	Hernia
Arthralgia/Myalgia	Tendonitis/capsulitis	Pars defects	Varicose veins
Dislocation/subluxation	Tenosynovitis	Spondylolysis	Uterine/rectal prolapse
	Entrapment neuropathy		
Joint Synovitis	Fibromyalgia	Spinal anomalies	Chronic pain syndrome
Osteoarthritis	Bakers cyst	Spinal stenosis	Depression/anxiety
		SIJ instability	
Chondromalacia patellae		Dysautonomia	

Table 1.2: The Symptoms of JHS. Reproduced from Hakim and Grahame 2003[6].

Articular symptoms include pain, and dislocation and/or subluxation of joints[6]. The most common presenting symptom of JHS is pain, which may be both chronic and acute[2]. Surveys have found that the most common site of pain is the knee[28,29], however pain is typically widespread in a person with JHS; a typical presentation of pain in a JHS participant is shown in Figure 1.2.

The cause of pain in JHS can vary. Pain may be due to overuse or injury caused by the connective tissue being more lax and less resilient[30]. Alternatively, the excessive range-of-motion of joints may cause pain by increasing stress on joint surfaces and related structures[28]; for example joint laxity could cause mechanical overload of tendons[31]. Differences in movement may also cause pain indirectly; in changing their movements to adapt to the symptoms of JHS such as pain or instability, people with

JHS might overload other joints and/or muscles[32]. These mechanisms of pain generation are rooted in differences in movement and/or movement control; altered biomechanics can stress the joints and increase the likelihood of injury. This form of pain is nociceptive in nature, i.e. pain arises from damage or disease to body tissues. Pain in JHS may also have neuropathic characteristics, where pain arises from dysfunction of the nerves themselves. Camerota *et al.*[24] examined 29 patients with JHS, and found 68% suffered with "probable" neuropathic pain. Neuropathic pain might be associated with neural compression caused by excessive movement[33,34], and it has been suggested that changes to collagen in the connective tissue distributed throughout peripheral nerves may influence pain, although the mechanism has not been identified[34].

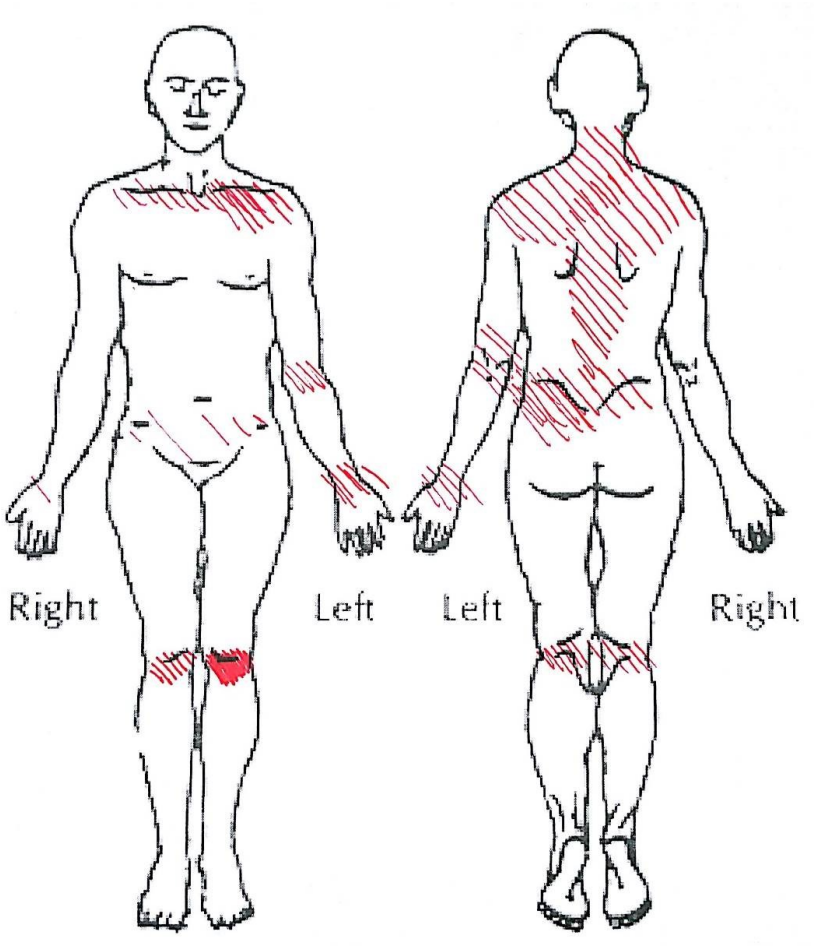


Figure 1.2: Example of chronic pain in a JHS participant (from a Case Report Form used in this study). Participants were asked to shade areas where they experience pain.

Another articular symptom of JHS is joint laxity and hypermobility. However, even with this prominent feature of JHS, the biomechanics causing the hypermobility are not fully understood. Magnusson *et al.*[31] sampled passive muscle-tendon stiffness of the hamstring in 9 women with JHS. There were no differences in stiffness, though JHS participants had a greater subjective tolerance to

joint loading, which had the effect of the JHS group having a greater maximal joint angle of stretch, total energy absorption, and peak moment. A similar result was found in a cohort of people with GJH: Jensen *et al.*[35], who used another method of measuring muscle-tendon stiffness (electromechanical delay), found there was no difference in stiffness between GJH and a normal flexibility control group. These results would indicate that muscle/tendon stiffness in both JHS and GJH cohorts is similar to those with normal flexibility, and it is stretch tolerance that allows the extra range of motion observed in hypermobile joints. A possible mechanism for this is abnormalities of muscle spindles; the structures used to indicate muscle length and influence muscle tone. The results of Magnusson *et al.*[31] and Jensen *et al.*[35] are contradicted by Rombaut *et al.*[36], who found that during a passive range-of-motion task, JHS had a greater maximal range of motion, but no significant difference in the magnitude of torque applied, indicating that the muscle tendon unit had lower stiffness (the same force produced a greater range of motion). Interestingly Rombaut *et al.*[36] only found differences between groups towards maximum range, and there was no significant difference in stiffness at a smaller range of motion. A reason for this could be that small movements do not stretch the connective tissue surrounding the muscle. During a muscle stretch the individual sarcomeres lengthen first. When the sarcomeres are fully stretched collagen fibres in the surrounding perimysium align themselves with the force, and further stretch occurs. The smaller range movement may be able to be performed with increasing sarcomere length, and differences in tension only showing when the connective tissue is stretched. The result supports the theory that it is changes to the connective tissue which cause differences/symptoms in JHS. For example Voermans *et al.*[37] found the ratio of type III collagen tended to be greater than normal in a sample of 10 JHS individuals[38].

Muscle weakness is present in JHS, and symptoms may develop from deconditioning through inactivity[30,39]. Women with Joint Hypermobility syndrome had significantly lower knee extensor and flexor strength than healthy controls with NF, even after adjusting for differences in physical activity[39]. Since there was no difference in lower limb muscle mass, the authors conclude that muscle weakness must be due to muscle dysfunction and/or pain and fatigue in the JHS group.

JHS is associated with impaired lower limb proprioception, in both children[40] and adults[32,41–43]. Less research has been conducted on the upper limb, and the results are inconclusive, or at least vary by joint; one study found no significant difference in shoulder proprioception[42], whereas another found a JHS group had significantly less finger joint proprioception[44]. Significantly, Hall *et al.* [41] found that knee joint proprioception was particularly poor toward the end of range. This not only alludes to a mechanism of injury (JHS individuals may increase risk of acute injury by being more likely to progress beyond end-of-range) but links to results from Magnusson *et al.*[31], who found that JHS individuals were more tolerant of stretch toward the end of range, further supporting the theory that JHS have abnormalities in the stretch sensory organs.

Balance has been found to be impaired in JHS individuals in both static standing[45,46] and walking conditions[47]. During standing, the largest differences between JHS and control groups were observed in eyes-closed conditions[45,46], which is perhaps not surprising given the reduced proprioception of JHS individuals. It may be that they use relatively more visual input to balance, and with eyes closed rely more on their impaired proprioception[46]. Ferrell *et al.*[32] used a balance board to measure balance in JHS individuals before and after a physiotherapy intervention. JHS individuals did improve their balance, but since there was no control group, it is not possible to say if they improved their balance to a level that would be considered normal.

As well as articular symptoms, JHS is correlated with a large number of extra-articular problems and impairments. JHS may manifest as a problem of the nervous system; there is evidence that people with JHS suffer with dysautonomia, with cases of syncope, presyncope, palpitations, chest discomfort, fatigue, heat intolerance and postural orthostatic tachycardia syndrome all correlated with JHS[48]. Extra-articular symptoms also include problems with the gastric system; in a survey of referrals to a neurogastroenterology clinic, almost 50% of patients had hypermobility[49]. Symptoms relating to the gastrointestinal system include bloating, nausea, reflux, vomiting, constipation and diarrhoea[49]. Joint hypermobility is a risk factor for developing venous insufficiency, such as varicose veins[50]. In a group of gynaecology clinic patients, subjects with hypermobility were more likely to have cystocele, rectocele or uterine prolapse than women with normal flexibility[51]. In a small sample of JHS women attending a rheumatology clinic, mitral valve prolapse had a prevalence over three times greater than what would be expected in a normal adult population[38].

Symptoms of JHS even progress into mental health; anxiety and panic attacks are more common in people with JHS. When groups of panic-disorder patients, fibromyalgia patients, psychiatric patients, and a healthy group, were screened for JHS, a significant correlation between severity of JHS and anxiety was found[52]. Similarly, Bulbena *et al.*[53] found that JHS was highly associated with panic disorder, agoraphobia, and simple phobia. Further, JHS subjects with mitral valve prolapse are 3 times more likely to suffer with anxiety[53], which may indicate that anxiety symptoms are linked to the severity of other features of JHS. Interestingly, there is some evidence that brain structure is different in hypermobile people, which may explain why JHS individuals are more likely to suffer anxiety and panic attacks. Eccles *et al.*[54] performed MRI scans on the brains of 72 healthy individuals with and without hypermobility, they found that bilateral amygdala volume was greater in the hypermobile group. These results, however, should be interpreted with caution, as typically a smaller amygdala volume is associated with anxiety[55]. In addition, not only were no symptomatic or JHS individuals included, but the hypermobile cohort was defined as a Beighton score >1, whereas the usual classification for hypermobility in adults is a score of ≥4.

1.5 Treatment of the Joint Hypermobility Syndrome

The large number of symptoms and clinical presentations of JHS necessitates a variety of treatment strategies, and may result in a high consumption of medications[56,57]. Particularly high is the consumption of analgesics, which is perhaps not surprising given the common symptom of pain experienced in JHS[57]. Physiotherapy is the de facto treatment for JHS[6]. Physiotherapy and exercise has been shown to offer a generally moderate improvement in patients' visual analogue pain scores, taken before and after an exercise programme, in both adults[32,43,58] and children[59]. In a recent systematic review, however, Palmer *et al.*[3] found that the methodological qualities of these studies were lacking, particularly in regard to providing adequate control groups and statistical power. Other research groups have stated that there is a lack of evidence-based treatment for JHS[4], and generally the treatment of a JHS patient relies on the experience of the physiotherapist[57]. Another finding of the Palmer *et al.*[3] review was that there is no consensus that a specific type of physiotherapy is more beneficial than another; no difference in improvement was found when comparing generalised exercise to joint specific exercises, and there was a call for further quality research to find what is effective. Perhaps it is this uncertainty surrounding physiotherapy as a treatment, that is the reason a large proportion of JHS patients do not find physiotherapy effective[6,57]. Alternatively, it may be that physiotherapy really is not effective in relieving symptoms.

Another reason some patients do not perceive physiotherapy as effective could be due to the experience and understanding of the condition by physiotherapists. In a survey of UK physiotherapists, almost 20% had not heard of the Brighton Criteria[17]. A review by Russek *et al.*[60] of American physiotherapists' knowledge about JHS, found that although recognition of the Beighton score for classifying joint hypermobility was relatively high, therapists were not as familiar with the Brighton Criteria. Furthermore, only 11-19% were familiar with the extra-articular features of JHS. Similar results were found in a survey of Flemish physiotherapists[4]; confidence in assessment and management of JHS was low, and although a range of different treatment strategies were used, physiotherapists perceived them all as effective; showing a lack of agreement over what type of physiotherapy is most effective. There is common understanding between physiotherapists and JHS patients that physiotherapy is not effective when only acute injuries or specific joints are treated[61]. But since referral to physiotherapy is commonly made for an acute injury[61], practitioners may not recognise the chronic nature of the condition, and patients may not be put on the best treatment pathway. Both patients and physiotherapists have reported that successful treatment depends on a swift diagnosis of JHS, as once chronic symptoms develop treatment becomes less effective[3]. This is likely to be problematic as the time to diagnosis of Ehlers Danlos Syndrome from first presentation has been reported as 14 years for 50% of people surveyed[62].

Researchers have suggested that improving strength, instability, proprioception, and correcting badly adapted posture/movements will improve symptoms of JHS[63]. And in focus groups of JHS patients and healthcare professionals, it was recognised that the prevention of patients assuming abnormal posture and movement was important to stop progression of symptoms[61]. General exercise and/or strengthening programmes may not be optimal; in a study at Imperial College Healthcare NHS Trust, a physiotherapist led leg strengthening programme was shown to increase the strength of people with JHS[64], and although this increase in strength correlated with a reduction in pain[65], it took three to four months to reach the starting mean strength of the GJH group[64], suggesting a need for more effective interventions. Indeed, although people with JHS are weak, therapy may need to be directed at additional factors for better effect. It follows that, for the successful amelioration of symptoms in JHS, therapists need to know what postures and movements JHS patients assume, to normalise the movements. A reason that physiotherapy has only shown a moderate improvement is that we do not know how people with JHS move compared to people with normal flexibility, and how they move compared to people with GJH. Given that people with GJH are hypermobile but generally do not experience pain, it is interesting to see if they move differently to people with JHS, in order that physical therapies can aim to normalise the movement and therefore hopefully ameliorate the patient's symptoms. Indeed, where some researchers have found differences in movement and movement control, specific targeted physiotherapy has been suggested to correct these movements[45]. In another single patient case, pain was abolished in a JHS patient immediately following a correction of movement[56].

Physiotherapists will be aided by the study of movement in JHS; investigating how JHS individuals move during activities that cause them discomfort compared to people who do not experience pain. With this in mind kinematic and kinetic analysis would seem like an ideal tool to differentiate movement in JHS. Furthermore, there is a lack of understanding of the mechanisms that cause pain and its persistence[11]; studying movement and understanding the differences between people with JHS and people who are equally flexible but not in pain may help explain why people with JHS experience pain, or show how JHS affects movement in everyday tasks and show physiotherapists impairments to target with therapy.

1.6 The biopsychosocial model and JHS

The traditional biomedical model of healthcare follows the process of recognising symptoms, diagnosing underlying pathology, treating that pathology, and finally expecting the patient to recover[66,67]. The biomedical model does not consider psychological and societal impacts on illness. This makes the biomedical model limited, for example where the original health condition is the premier cause of

symptoms and illness, but symptoms are influenced by psychosocial factors[67]. Conditions are better understood and managed when taking into account the social and psychological aspects of the condition[67]. The biopsychosocial model includes both psychological and societal factors which can affect a person's health/illness, and thus is a more extensive appraisal of health. The model complements the flag system, where different "coloured flags" are used as markers of risk factors in musculoskeletal disorders. Red flags concern pathology and relate to the "Bio" part of the model. Psychosocial factors are indicated by yellow flags, examples include peoples' attitudes, beliefs and emotions. Blue flags relate to the person's perception of how work affects their illness. Black flags concern working conditions that could be detrimental to treatment (e.g. prolonged standing times or heavy lifting). Finally, Orange flags denote abnormal psychological factors or drug abuse. There is now a wealth of research regarding how the biopsychosocial model can be applied and used to understand health problems[68], and Waddell *et al.*[67] state that "It is now widely accepted that biopsychosocial factors contribute to the development and maintenance of chronic pain and disability".

Applying the biopsychosocial model is useful in understanding JHS, where the underlying pathology and cause-effect relationship between symptoms is not understood, people can wait a long time for a diagnosis, and there is no definitive treatment. As stated earlier in this chapter, the mechanisms that cause pain and loss of function in JHS are not fully understood[69]. Particularly relevant to this thesis is the relationship of pain, loss of function and movement; to what degree abnormalities cause differences in movement and pain, and vice-versa. It is well documented that pain can influence movement, for example people with fibromyalgia have slower walking speed, with shorter stride length and cadence[70], as well as impaired balance and increased fall frequency[71]. On the other hand, some of the proposed mechanisms of pain in JHS relate directly to differences in movement; for example the earlier discussed mechanism of the excessive range-of-motion of joints may cause pain by increasing stress on joint surfaces and related structures[28], possibly by causing mechanical overload of tendons[31]. Chaitow *et al.*[72] have proposed that this ongoing microtrauma is a mechanism that may lead to repeated pain experience and disordered pain responses. This theory is strengthened by the fact that there is some evidence that increasing the stability of hypermobile joints can reduce the excessive range of motion and improve pain[58], although the study does suffer from methodological issues[3]. The multifactorial nature of people who suffer pain such as people with JHS makes the relationship between pain and movement complex, with a range of biological and psychosocial factors that influence pain beyond differences in movement. Therefore, the cause-and-effect relationship between movement and pain cannot be straight forward and is essentially unknown. This makes treatment of JHS a significant challenge, and due to the wide range of symptoms and factors associated with JHS, each patient may require a unique combination of treatments from a range of healthcare professionals that ideally could be tailored to individual requirements[56,69].

Moving now to how the psychosocial features of JHS could affect movement and pain. People with JHS are significantly more likely to have a range of psychological symptoms including depression, agoraphobia, anxiety, and panic disorders than controls[73]. These factors have been correlated with other musculoskeletal chronic pain conditions. In addition, studies of other musculoskeletal conditions have found that prior psychological symptoms are associated with the development of chronic pain, for example McBeth and Jones[74], Diatchenko *et al.*[75], and Fillinim *et al.*[76]. Similarly, it is not clear how the psychological factors of JHS interplay with the physical symptoms to affect pain and movement. For example anxiety could at least be partly responsible for people with JHS having an increased fear of falling[46], which in turn can affect gait parameters such as velocity. It is not clear whether the anxiety is inherent in JHS or is in itself caused by pain[69]. In addition, depression is known to affect gait; people with depression tend to walk slowly and take shorter steps[77]. However, this difference was measured in people with major depression and may not be comparable to JHS individuals en masse. There are similar complications surrounding the interplay between physical and psychological symptoms in other aspects of JHS. JHS is correlated with various cardiovascular symptoms, including palpitations and dizziness. These conditions are also associated with anxiety, which is prevalent in people with JHS. It is not clear how these factors affect each other; is it that people with JHS have anxiety which increases the chance of cardiovascular anomalies such as palpitations, or that the cardiovascular factors are a direct result of JHS?

There is the potential for these interactions to form a feedback loop, for example there are cases of people with JHS having repeated injuries which causes anxiety and the worry about the next incident[78]. This in turn could potentially affect how people behave, causing them to move less and deconditioning to occur, which would further exacerbate the problem. A similar scenario was described by Rombaut *et al.*[46], where fear of falling leads to self-limiting of activities, leading to muscle weakness and ultimately increasing the risk of future falls.

In terms of social influences on JHS, people with JHS have stated that there is a lack of awareness of JHS in healthcare and wider society[78]. This could feasibly affect how they seek and respond to treatment.

In summary the relationship among the articular, extra-articular, and psychological symptoms of JHS are complex. In all cases the interplay and direction of causality has not been established, and the nuances of the symptoms between JHS and GJH is not known. This is complicated by the fact that the mechanisms of differences in movement and how they relate to pain may be due to a variety of reasons, such as pain, impaired balance, joint-instability, impaired proprioception, differences in the circulatory system, fatigue, and psychological effects such as depression and anxiety. The complexity means that when investigating JHS controlling confounding factors is a challenge. Given the complexity, there is recognition that differences in movement are not likely to be the only factor relevant to pain in people with JHS.

1.7 Summary

JHS is as an under recognised and poorly managed disorder and a recognised area of neglect in rheumatology[2,6]. Although there are many studies that have shown various symptoms and impairments correlate with JHS, the aetiology, prevalence, and arguably most importantly, treatment of JHS is not known. Physiotherapy is a mainstay of treatment and has shown success in being part of effective treatment of conditions such as fibromyalgia[79] and other musculoskeletal chronic pain conditions[80], but further research is required to determine what is effective in the treatment of JHS.

The aim of this PhD is to investigate movement in JHS: to find how, and why, people with JHS move differently to people with normal flexibility and people with GJH. This information will help physiotherapists and healthcare professionals target movement differences and better understand the condition, and in turn help to inform improved treatment.

1.8 Aims of this PhD

Joint Hypermobility Syndrome is complex with many interacting symptoms and factors that could influence pain and movement. As has been covered in this chapter, how the physical, neurological and psychological factors interplay to affect pain and function is unknown. Physiotherapy is the mainstay of treatment, but it is not always effective. It is possible that pain may be caused or maintained, even if in part, by JHS individuals having different movement parameters compared to normal. Equally, other physical or psychological factors may also be influencing movement. There has been little research about how people with JHS move compared to GJH and NF groups, and this information could help therapists target impairments and help the understanding of pain in JHS. Part of the problem is that it is not clear whether it is the joint hypermobility itself that causes pain in JHS, or if it is some other factor. The interplay and cause-and-effect relationship between the factors is likely to be complex, however investigating how people with JHS move may provide a piece of the puzzle about how pain and poor function manifests in JHS.

This PhD aims to improve the understanding of how people with JHS move compared to two groups of people; people who are hypermobile but do not have symptoms (GJH), and people with normal flexibility (NF). Quantifying movement in JHS and comparing it to these two groups will improve the understanding of differences in movement that physiotherapists may be able to target. Specific aims relating to relevant chapters/sections of the thesis are given in each chapter. Broadly speaking, this study sought to answer two questions.

1) What is currently known about how people with JHS move?

2) Do people with JHS move differently to people with GJH and NF?

Chapter 2: Literature review

2.1 Introduction

Given that people with JHS and GJH exhibit joint laxity and hypermobile joints, it could be hypothesised that their kinematics and kinetics of functional activities vary from normal; they have a greater range of motion, and kinematics/kinetics have been affected in other conditions causing laxity such as anterior cruciate ligament injuries[81]. Therefore, the study of kinematics and kinetics of people with JHS and GJH could further our understanding of potential impairments and allude to possible treatment plans using physical therapies. As there are a range of studies investigating movement in JHS and GJH individuals, it is now timely to systematically review the literature. The aim is to identify which movements have been examined and whether these movements can now be described in a consistent manner. If movement patterns during different tasks differ to normal, a review will help identify which movement parameters could be targeted in treatment. Finally, since there are a variety of terms used to describe JHS, a review is useful in grouping literature so that future researchers are less likely to miss information by missing a specific term, or using an out-dated term.

This systematic review concerns studies of lower limb functional tasks that have compared kinematics, kinetics, and/or electromyographic activity (EMG) parameters of people with JHS or GJH with healthy controls; it aimed to determine the quality of research completed so far and to collate what information is available regarding these factors in JHS and GJH. This will complement and build on the work by Palmer *et al.*[19]; helping to identify gaps in current knowledge and provide direction for determining which activities are to be measured in this thesis. The systematic review of gait has been published in Gait & Posture[82].

The aims of this systematic review were:

- To collate and critically evaluate studies describing movement during activities of daily living in JHS and GJH cohorts.
- To identify gaps in knowledge/the current understanding of movement in JHS, and so provide direction for what to research in this thesis.

2.2 Methods

2.2.1 Search strategy.

Key search terms were identified as 'joint hypermobility', 'kinetics', 'kinematics' and 'EMG'. Alternative terms were identified by using MeSH headings, checking keyword lists of relevant published studies and team discussion. The list of search terms used is shown in Table 2.1. An electronic search of databases AMED, CINAHL, EMBASE and MEDLINE was conducted between 13th February 2014 and 25th March 2014. The original search only identified studies that had used 3D movement analysis as an outcome measure. The search was expanded on 12th February of 2017 to include more recent research, and studies that had investigated movement but had not used 3D movement analysis.

Category 1	Category 2	Category 3
Joint hypermob*	Kinematic*	Joint
Benign joint hypermobility syndrome	Kinetic*	Knee
JHM	Gait	Hip
JHS	Gait analysis	Ankle
HMS	Gait disorder*	Lower limb
BJH	Biomechanics	Lower extremity
Joint laxity	Jump*	Leg
Ehlers Danlos	Stair*	Talo-crural
Ehlers-Danlos	Hop*	Talo crural
EDS	Activities of daily living	Tibio-femoral
Hypermobility Syndrome	ADL*	Tibio femoral
Generalised Joint Hypermobility	Perturbation*	
GJH	Step*	
	Squat*	
	Lung*	
	Rest*	
	Walk*	
	Stand*	
	Balance	
	Postur*	
	EMG	
	Electromyograph*	
	GRF	
	Ground reaction force	

Table 2.1 Search Terms. * indicates a 'wild card' operator. For example "Postur*" would return results for both "Postural" and "Posture".

2.2.2 Inclusion and exclusion criteria.

Papers from the search were assessed by Alex Bates (Author) and Caroline Alexander (Supervisor) independently and any discrepancies were resolved by discussion. Papers were included if they satisfied the following criteria:

(1) The study included JHS and/or GJH participants.

(2) The study was in the English language.

(3) Functional tasks involving the lower limbs were investigated.

(4) The study used kinematic, kinetic, spatial, EMG, or temporal data as an outcome measure.

(5) The study compared a JHS and/or a GJH group to a control group.

Inclusion criteria were applied to the titles of the electronic search and any irrelevant papers were excluded. The abstracts of the remaining papers were reviewed and the same inclusion/exclusion criteria applied again. Hand searching and checking the reference lists of relevant articles was used to identify any papers that may have been overlooked by electronic database searching.

2.2.3 Quality and risk of bias

As there is no standardised or validated tool for this type of review, a customised quality checklist was developed. This was heavily based on the Downs & Black 'Quality Index' checklist[83], which has been used in a variety of systematic reviews of gait and movement analysis[84–89] and has been rated as having a moderate to good inter-rater reliability[90]. It was originally designed to assess the methodological quality of randomised and non-randomised studies of interventions however it has been developed by removing items 4, 9, 13, 14, 17, 19, 21, 23 and 26 as they were not relevant to these types of study. For example, item 4 relates to interventions (there was no intervention in any of the reviewed studies) and item 23 relates to randomisation of subjects prior to intervention. In addition item 27 was changed from a scoring scale of 0-5 to a score of 0-1, with a positive score being if a power calculation or sample size calculation was performed[91]. This gave a maximum score of 18. The Quality Index does not provide specific categories for labelling studies as low, moderate or high quality. One method of rating that has been proposed is rating studies based on their percentage score[90], which was successfully implemented by Ratcliffe *et al.*[91]; studies scored as high quality achieve a score >66.8%, medium quality 33.4-66.7%, with low quality studies achieving <33.4%. Based on this method, studies were rated as high quality if achieving a score ≥12, moderate quality if scoring between 7-11, and low quality if achieving a score ≤6. These scoring brackets were defined in advance and both authors independently used the checklist to evaluate the quality of each study. Any discrepancies in scoring were resolved by discussion using the original article as reference.

2.2.4 Data extraction

Data extraction was undertaken from the studies by the author and reviewed by one of the project supervisors (Dr. Caroline Alexander). Key details of each study were extracted using a customised data extraction form based on extraction forms used in similar reviews of gait and movement[3,92,93]. Data extraction categories were study design; subject characteristics; movement analysed; kinematic, kinetic and spatio-temporal outcome measures; equipment used; marker set and anatomical model used and significant results.

2.3 Results

2.3.1 Search results and study selection

The initial combined search listed 230 papers. After reviewing titles and abstracts this list was reduced to one; Simonsen *et al.*[94]. The majority of papers were excluded because they either did not report kinematic, kinetic, or other movement parameters, or did not investigate movement. A further twelve studies were found using hand-searching and checking reference lists[95-99]. Full text was obtained for all thirteen studies.

2.3.2 Downs and Black results

The thirteen papers were scored using the modified Quality Index tool. Table 2.2 lists the overall Quality Index score and Appendix A gives each scoring sheet for individual studies, along with reasons for negative scores. Quality scores ranged from 2 to 15. Four studies were classified as low quality[45,96,97,100], six were classified as moderate quality[94,95,98,99,101,102], and three were classed as high quality[46,103,104]. There were two items in the modified Quality Index tool where none of the six studies scored positively, these were: (8) Not reporting/stating there were no adverse effects; and (12) Not describing the population from where participants were recruited.

All studies scored positively for item 1; "Is the hypothesis/aim/objective of the study clearly described?".

Nine of the thirteen studies scored positively for item 2; describing the outcome measures of the study. The main reason for scoring negatively was not giving enough detail when defining outcome measures. For example, in one study (Galli *et al.*[96]) twenty-six outcome measures were used. The majority are described in the methods section, however maximum ankle dorsiflexion during swing and pelvic tilt range-of-motion, are not listed in the methods and yet are reported in the results section. For

both these measures significant differences were observed between JHS and control groups. Since they were not mentioned in the methods it is unclear whether these measures were planned prior to the collection of results, or included afterwards, once significant differences were observed. The other reason for scoring negatively was a lack of detail; many studies listed "kinematics" or "kinetics" of joints as outcome measures, but generally specific parameters were not listed.

Nine of the studies adequately described the patient characteristics (Item 3 of Downs & Black). Three of the studies did not explain how hypermobility and/or JHS was classified, and one study classified their participants incorrectly (they used the term Benign Joint Hypermobility Syndrome for people with asymptomatic GJH)[101]. In another study different values are given for participant age, sex, and height in separate sections of the paper[97].

Eight studies scored positively for Item 5 of Downs and Black, and adequately listed confounding factors in participant groups (for example pain and any previous surgery). Where a negative score was given, generally other factors which could affect the movement investigated were not listed.

For Item 6, eight of the thirteen studies failed to score. Where no score was awarded, generally this was for not reporting results for outcome measures reported in the Methods, or a lack of clarity. For example, Celletti *et al.*[100] state that their outcome measures include a Fatigue Severity Scale questionnaire, the absorbed power in early stance, generated power at push-off, maximum power at push off, and maximum vertical ground reaction force during stance phase. Unfortunately, the results for these parameters are not reported; the authors report whether each variable is statistically correlated with fatigue, but do not list any actual values or results. The authors state that the results will be compared to a control group, and in the methods state the JHS and control group were compared with a Mann-Whitney U-test. The results of this test, however, are not reported, and the control group is not mentioned in the Results or Discussion sections of the paper. Another example is found in Nikolajsen *et al.* [99]; their tabulated results differ to the results reported in figures. For example, the tabulated result for the second peak of ankle dorsi/plantar flexor moment falls outside of the scale of the associated figure. The consequence of this is that it throws into dispute the validity of the results; it is not possible to know whether the results reported in the text are correct and the wrong figure has been used, or if the figure is correct and the wrong results reported. It is difficult therefore to compare the results to other studies. Simonsen *et al.*[94] suffers with similar problems of presentation; although graphs are marked with an asterisk to indicate where significant differences occur, it is unclear as to which results the asterisk corresponds to. For example in the text Simonsen *et al.*[94] specify that there was a significant difference in knee flexion/extension angle at heel strike, for the corresponding kinematic graph an asterisk is placed at 10% of stance phase. It is unclear if this asterisk is in the wrong place, is correct and subjects walked with a 'toe-contact' gait, or if it corresponds to a different result.

Ten of the thirteen studies scored positively for Item 7; "Does the study provide estimates of the random variability in the data for the main outcomes?" The three studies which scored negatively did not provide standard deviations for results and/or error bars on figures. It was uncommon for studies to report exact probabilities (Item 10); only five of the studies reported exact p values for their results.

Items 11 & 12 relate to whether the recruitment pool and those recruited were representative; only three studies scored positively for Item 11, and only one study scored positively for Item 12. Generally this was due to a lack of detail about the recruitment and participant population. In some cases however, there were more pronounced problems. For example, Galli *et al.*[96] state that control group participants were "age and sex matched", however their JHS group consisted of 1 male and 11 females, whereas their control group consisted of 10 males and 10 females.

Only two of the studies reported that they blinded the researcher testing the participants (Item 15), the other studies did not state whether any blinding had occurred.

Seven studies scored positively for Item 16. Where a study scored negatively, insufficient information was given in the study regarding the outcome measures, and typically specific outcome measures were not given. For example, Galli et al.[96] presents results for outcome measures that are not defined in the methods section (maximum ankle dorsiflexion during swing and pelvic tilt range of motion), raising the question of whether the parameter was defined beforehand, or included after analysis after significant differences were observed.

Only three studies were scored negatively for Item 18 ("Were the statistical tests used to assess the main outcomes appropriate?"). Two negative scores were given for not adjusting for multiple comparisons[45,102]. The third negative score was Celletti *et al.*[100], who stated in their 'Methods' section that a JHS and a control group would be compared, but in the analysis only report results for the JHS group. The only study to score negatively for Item 20 ("Were the main outcome measures used accurate (valid and reliable)?") was Celletti *et al.*[100], since they did not report the results they specified in their Hypothesis/Methods. In seven studies it is not clear whether participants in control and JHS/GJH groups were recruited over the same period of time (Item 22). In regards to Item 27, only one study included a power calculation[98].

Table 2.2. Downs & Black quality index results for the reviewed studies.

Quality Index item Number	Fatoye *et al.* 2011[95]	Galli *et al*. 2011[96]	Celletti *et al.* 2012[100]	Simonsen *et al*. 2012[94]	Rigoldi *et al*. 2012[97]	Celletti *et al*. 2013[98]	Nikolajsen *et al*. 2013[99]
1	1	1	1	1	1	1	1
2	0	0	0	1	1	1	1
3	1	1	0	1	0	1	1
5 (out of 2)	0	0	1	2	0	0	1
6	0	0	0	0	0	0	0
7	1	1	0	0	1	0	1
8	0	0	0	0	0	0	0
10	1	0	0	1	0	0	1
11	1	UD (0)	UD (0)	1	UD (0)	UD (0)	UD (0)
12	1	UD (0)	UD (0)	UD (0)	UD (0)	UD (0)	UD (0)
15	UD (0)	UD (0)	0	UD (0)	UD (0)	UD (0)	UD (0)
16	0	UD (0)	UD (0)	UD (0)	UD (0)	1	1
18	1	1	0	1	1	1	1
20	1	1	0	1	1	1	1
22	1	UD (0)	UD (0)	1	UD (0)	0	1
25	UD (0)	0	0	0	0	0	0
27	0	0	0	0	0	1	0
TOTAL SCORE (out of 18)	9	5	2	10	5	7	10
PERCENTAGE SCORE	50%	28%	11%	56%	28%	39%	56%
QUALITY CATEGORY	Moderate	Low	Low	Moderate	Low	Moderate	Moderate

Table 2.2 continued

Quality Index item Number	Rombaut *et al.* 2011[46]	Galli *et al.* 2011[45]	Cimolin *et al.* 2011[102]	Luder *et al.* 2015[104]	Greenwood *et al.*[101]	Schmid *et al.*[103]
1	1	1	1	1	1	1
2	1	1	1	1	0	1
3	1	0	1	1	0	1
5 (out of 2)	2	0	1	2	1	2
6	1	0	1	1	1	1
7	1	1	1	1	1	1
8	0	0	0	0	0	0
10	1	0	0	1	0	1
11	UD (0)	UD(0)	UD (0)	UD (0)	UD (0)	1
12	UD (0)	UD(0)	UD (0)	UD (0)	UD (0)	UD (0)
15	UD (0)	0	0	1	UD (0)	1
16	1	1	1	0	1	1
18	1	0	0	1	1	1
20	1	1	1	1	1	1
22	1	UD(0)	UD(0)	UD(0)	1	1
25	1	0	0	1	1	1
27	0	0	0	0	0	0
TOTAL SCORE (out of 18)	13	5	8	12	9	15
PERCENTAGE SCORE	72%	28%	44%	67%	50%	83%
QUALITY CATEGORY	High	Low	Moderate	High	Moderate	High

UD = Unable to determine.

1. Is the hypothesis/aim/objective of the study clearly described?
2. Are the main outcomes to be measured clearly described in the Introduction or Methods section?
3. Are the characteristics of the patients included in the study clearly described?
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?
6. Are the main findings of the study clearly described?
7. Does the study provide estimates of the random variability in the data for the main outcomes?
8. Have all important adverse events that may be a consequence of the intervention been reported?
10. Have actual probability values been reported (e.g.0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?
11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?
12. Were those subjects who were prepared to participate, representative of the entire population from which they were recruited?
15. Was an attempt made to blind those measuring the main outcomes of the intervention?

16. If any of the results of the study were based on "data dredging", was this made clear?
18. Were the statistical tests used to assess the main outcomes appropriate?
20. Were the main outcome measures used accurate (valid and reliable)?
22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?
27. Was a power calculation or sample size calculation provided?

2.3.4 Characteristics of the studies

Table 2.3 shows the characteristics of each study. All the reviewed studies were cohort studies. Two of the studies measured gait in children, eight measured gait in adults, three measured standing posture, and one investigated stair ascending and descending. Of the studies of children, one compared children with JHS to a NF control group[95] and one compared children with GJH to a NF control group[99]. For the studies investigating adults gait, six compared JHS subjects with a NF control group[46,96-98,100,102], and two compared GJH with a NF control group[99,103]. One study evaluated muscle activity during standing posture in people with GJH[101], and two studies quantified balance during standing in JHS[45,46]. Luder *et al.*[104] investigated stair ascent/descent in GJH. Sample sizes ranged from 12[96,97] to 128[104].

There was variation in how hypermobility was diagnosed. Studies with child participants used a higher Beighton score to define hypermobility (Beighton score ≥5 for Nikolajsen *et al.* [99] and ≥6 in Fatoye *et al.* [95]). For the studies concerning adults, Luder *et al.*[104] and Schmid *et al.*[103] defined hypermobility as a Beighton Score ≥6, Simonsen *et al.* [94], Greenwood *et al.*[101], and Galli *et al.*[96] as a Beighton score ≥4. Celletti *et al.*[98,100] used the Villefranche and Brighton Criteria to classify JHS and used Beighton score to classify hypermobility, they do not specify what cut off score was used. In addition Celletti *et al.*[98] also assessed 'additional extra-articular features', no further details are given. Rombaut *et al.*[46] use the Villefranche criteria to classify JHS. Rigoldi *et al.*[97] do not specify how JHS was classified. Luder *et al.*[103] and Schmid *et al.*[103] further classified their participants as asymptomatic GJH or symptomatic GJH, based on their responses to a survey completed 6 months after the testing session. If participants answered positively to experiencing symptoms whilst descending stairs in the 6 months post session, they were counted as a symptomatic participant. Since the participants were not classified as JHS, and were asymptomatic on the day of testing, their results have been interpreted as testing of a GJH cohort.

Where listed, exclusion criteria tended to be conditions that could potentially affect the movement of interest. These included; leg or spinal surgery, balance disorders, arthritis, obesity, and other neurological conditions. Two studies had solely female participants by design[46,104]. Where the gender of participants was listed, all studies had a greater number of female participants than male.

Of the studies investigating gait, six use an optoelectronic measuring system, and kinematic, kinetic and spatiotemporal outcome measures were investigated. Three different marker sets/biomechanical models were used (Table 2.3). One study used a pressure sensitive walkway and measured spatiotemporal outcome measures[46], and one used instrumented force plates and EMG to investigate gait[103]. Of the three studies investigating standing posture, two measured sway parameters using a force plate[45,46], and one used surface EMG to investigate muscle activity[101]. Force plates were used in the stair-ascent study to measure temporal and ground reaction force parameters.

Table 2.3. Characteristics of the reviewed studies

	Fatoye *et al.*[95]	Galli *et al.*[96]	Simonsen *et al.*[94]	Celletti *et al.*[98]	Nikolajsen *et al.*[99]
Study Design	Cohort	Cohort	Cohort	Cohort	Cohort
Testing group	Children with HMS	Adults with JHS	Adults with GJH	Adults with JHS	Children with GJH
Diagnostic method and inclusion criteria	Beighton score ≥ 6 and multiple joint pain (present or historic)	Beighton score (actual score not given). Age >30 years. ability to walk without devices	Beighton score of ≥4, at least one hypermobile knee (>10° hyperextension)	Villefranche and Brighton Criteria. Inclusion criteria not specified.	Beighton score of ≥5
Exclusion criteria	Ehlers-Danlos syndrome (EDS), musculoskeletal disorders, history of trauma to knee joint, vestibular system disorders.		Severe present knee pain. No hereditary diseases such as Ehlers-Danlos. BMI <25.	Exclusion criteria not specified.	Previous/current serious knee trauma, hereditary diseases such as Ehlers-Danlos Syndrome or Osteogenesis Imperfecta, BMI index >25.
Group characteristics; male/female, mean age (S.D.), where recruited from.	HMS Group: 8m/21f, 11.9 ± 1.8 years, rheumatology department at the Royal Hospital for Sick Children, Edinburgh.	JHS Group: 11f/1m, 43.08 ± 6.78 years, not specified.	17 subjects, 39.3±5.4 years, two Danish municipalities.	21 subjects, gender not specified, 36.1±12.7 years, Umberto I University hospital and San Camillo-Forlanini Hospital (Rome, Italy)	10f/9m, age 9-11 years, not reported.
Movement analysed	Walking barefoot, 7m walkway. Self-selected walking speed.	Walking barefoot, 10m walkway. Self-selected walking speed.	Walking barefoot, 10m walkway. Specific walking speed (4.5km/h)	Walking barefoot, 10m walkway. Self-selected speed.	Walking barefoot, 10m walkway. Specific walking speed (4.4km/h)
Spatio-temporal outcome measures	Walking speed	% stance: duration of the stance phase (as % of the gait cycle) Velocity: mean velocity of progression Step length: longitudinal distance from one foot strike to the next one, normalised to participant's height Step width.	None	Foot progression Gait Variable Score	Maximum step width, step length

Table 2.3. continued: Characteristics of the reviewed studies

	Fatoye *et al.*[95]	Galli *et al.*[96]	Simonsen *et al.*[94]	Celletti *et al.*[98]	Nikolajsen *et al.*[99]
Kinematic outcome measures	Peak ankle dorsiflexion, peak ankle plantar flexion, peak knee flexion LR, peak knee extension, peak knee flexion swing, peak hip flexion, peak hip extension, peak knee adduction, peak knee abduction	Ankle, knee and hip angles and range of motion.	Ankle, knee and hip angle in the sagittal plane. Hip angle in the frontal plane.	Gait Variable Scores; Pelvis tilt, Hip flex/ext, Knee flex/ext, Ankle Dor/pla, Pelvic Obliquity, Hip Rotation. Overall Gait Profile Score.	Angles of the hip, knee and ankle in the sagittal plane during stance phase.
Kinetic outcome measures	None.	Ankle moment, ankle power	Ankle, knee and hip moments in the sagittal plane. Hip and knee moment in the frontal plane. Shear, medial, lateral and total compression force at the knee.	None.	Ankle, knee and hip moments throughout stance phase. Ground reaction forces.
Measurement system (type of camera system, number of cameras, type and number of force plates)	612 Vicon 3-D motion analysis system, eight M8 Vicon cameras, 100Hz sampling rate.	Optoelectronic, no details of number of cameras, 2 Kistler force plates, 2 TV cameras.	Five digital video campers (Canon MV 600), 50Hz. AMTI OR6-5-1 force platforms.	Optoelectronic (ELITE2002, BTS, Milan, Italy), sampling rate of 100Hz, two force platforms (Kistler, CH), 2 TV cameras (BTS, Italy)	Five digital video campers (Canon MV 600), 50Hz. AMTI OR6-5-1 force platforms.
Marker set and anatomical model used	Vicon plug-in-gait, Knee alignment device to define knee joint functional axes.	Davis *et al.* [29]	Vaughn *et al.* [30]	Davis *et al.* [29]	Vaughn *et al.* [30]

Table 2.3 Continued. Characteristics of the reviewed studies

Authors	Luder *et al.*[104]	Galli *et al.*[45]	Cimolin *et al.*[102]	Rombaut *et al.*[46]	Greenwood *et al.*[101]
Study Design	Cohort	Cohort	Cohort	Cohort	Cohort
Testing group	Adults with GJH (differentiated into asymptomatic and symptomatic)	Adults with JHS	Adults with JHS	Adult women with JHS	Adults with GJH (listed as BJHS)
Diagnostic method and inclusion criteria	Beighton score of ≥6 and positive score for knee hyperextension and palms flat to floor. NF group as Beighton score ≤1	Not specified	The Brighton Criteria.	Villefranche Criteria	Beighton score ≥4
Exclusion criteria	Leg or spinal trauma or surgery within 2 years prior, pregnancy, BMI > 30kg/m2, over 4 hours intensive exercise per week, diagnosis of another HDCT.	Not specified	Not specified	Recent inflammation of the ear or a known disorder of the organ of balance (such as Méniere's disease). Pregnancy.	Any neurological or painful musculoskeletal conditions involving the lower limbs, rheumatoid or any other systemic arthritis and obesity
Group characteristics; male/female, mean age (S.D.), where recruited from.	GJH group: 128 female subjects (0 male), 25.8±5.6 years, Bern University Hospital	JHS Group: 22 participants (gender not specified, 40.8±11 years, San Rafael Piassa Hospital (Rome)	JHS group: 20 subjects (2 male), 33.2±13.8 years, Umberto I Hospital (Rome)	JHS group: 22 subjects (0 male), 39±10.6 years, Ghent University Hospital.	GJH group: 8 participants (3 male), age not listed, Imperial College Healthcare NHS Trust.
Movement analysed	Stair climbing	Standing posture; eyes-open and eyes-closed.	Barefoot walking, natural pace.	Standing for 30 seconds, eyes-open and eyes-closed, hard and soft surface. Barefoot walking in three conditions.	Standing for 30 seconds, in two stances (both feet and singe leg standing), and in two conditions (eyes-open and eyes closed)

Table 2.3 Continued. Characteristics of the reviewed studies

Authors	Luder *et al.*[104]	Galli *et al.*[45]	Cimolin *et al.*[102]	Rombaut *et al.*[46]	Greenwood *et al.*[101]
Spatio-temporal outcome measures	Time in stance, time to peak ground reaction force, and cadence	NA	% time in stance, velocity, anterior step length.		NA
Kinematic outcome measures	NA	NA	Mean and range of motion for hip, knee and ankle. Angle at initial contact. Maximum and minimums during stance and swing phases.	NA	NA
Kinetic outcome measures	Maximum ground reaction force during weight acceptance,		Peak ankle plantarflexion moment during second half of stance, ankle power during terminal stance. Joint stiffness.	NA	NA
Other outcome measures	EMG intensity of lower limb muscles; peak, mean, and intensity at peak ground reaction force	Standard deviation of sway in anterioposterior and mediolateral directions, sway length, frequency analysis of sway.	NA	Postural: Centre of pressure measures; sway velocity, standard deviation, and elliptical area. Gait: velocity, cadence, step length, stride length, % swing, and % stance.	EMG intensity of lower limb and erector spinae muscles. Co-contraction of Tib ant/Gastroc, and Rec Fem/Semiten
Measurement system (type of camera system, number of cameras, type and number of force plates)	Force plates and wireless surface EMG	Force plate	12 Camera optoelectronic system	Force plate for posture analysis. Gaitrite Walking System for gait.	Wireless surface EMG.
Marker set and anatomical model used	NA	NA	Davis *et al.*[105]	NA	NA

Table 2.3 continued. Characteristics of the reviewed studies

Authors	Celletti *et al.*[100]	Rigoldi *et al.*[97]	Schmid *et al.*[103]
Study Design	Cohort	Cohort	Cohort
Testing group	Adults with JHS	Adults with JHS	Adult women with GJH (differentiated into asymptomatic and symptomatic)
Diagnostic method and inclusion criteria	Villefranche and Brighton Criteria (included if they classified positive to either criteria)	Not specified	Beighton score of ≥6 and positive score for knee hyperextension and palms flat to floor. NF group as Beighton score ≤1
Exclusion criteria	Not specified	Not specified	Leg or spinal trauma or surgery within 2 years prior, pregnancy, BMI > 30kg/m2, over 4 hours intensive exercise per week, diagnosis of another HDCT.
Group characteristics; male/female, mean age (S.D.), where recruited from.	11 participants (1 male), 43.08±6.78 years, not specified.	12 participants (1 male), 43.08±6.78 years, San Raffaele-Pisana (Rome)	128 participants (all female), 24.8±5.4 years, University of Applied Sciences (Switzerland) and local physiotherapy association.
Movement analysed	Walking barefoot, 10m walkway. Self-selected speed.	Walking barefoot, 6, walkway, self-selected speed.	Walking barefoot, self-selected speed.

Table 2.3 continued. Characteristics of the reviewed studies

Authors	Celletti *et al.*[100]	Rigoldi *et al.*[97]	Schmid *et al.*[103]
Spatio-temporal outcome measures	NA	% stance: duration of the stance phase (as % of the gait cycle) Velocity: mean velocity of progression Step length: longitudinal distance from one foot strike to the next one, normalised to participant's height Step width.	Stance time (absolute time of stance phase). % stance: duration of the stance phase (as % of the gait cycle). Swing time (absolute time of swing phase). % swing: duration of the swing phase (as % of the gait cycle)
Kinematic outcome measures	NA	Ankle, knee and hip angles and range of motion.	NA
Kinetic outcome measures	Absorbed work during early/midstance, generated work terminal stance, peak power during push-off, peak ground reaction force at push-off.	Ankle moment, ankle power	Force peaks in vertical direction during weight acceptance and push-off. Time to respective peaks. Weight-acceptance and push-off force peaks, Loading rate and unloading rate. Force peaks in the anterioposterior direction during weight acceptance and push-off.
Other outcome measures	Fatigue Severity Scale questionnaire.		EMG Parameters; maximum, mean, and minimum activity during stance phase, and activity at heel strike and 100ms preceding heel strike.
Measurement system (type of camera system, number of cameras, type and number of force plates)	Optoelectronic (ELITE2002, BTS, Milan, Italy), sampling rate of 100Hz, two force platforms (Kistler, CH), 2 TV cameras (BTS, Italy)	Optoelectronic (ELITE2002, BTS, Milan, Italy), sampling rate of 100Hz, two force platforms (Kistler, CH), 2 TV cameras (BTS, Italy)	Force plates

Table 2.3 continued. Characteristics of the reviewed studies

Authors	Celletti *et al.*[100]	Rigoldi *et al.*[97]	Schmid *et al.*[103]
Marker set and anatomical model used	Davis *et al.* [29]	Davis *et al.* [29]	NA

2.3.5 Data Extraction

The reviewed studies were heterogeneous in their outcome measures, necessitating a narrative review rather than meta-analysis. Even for activities such as gait, where the objectives and measuring systems are similar, there was little overlap in specific outcome parameters reported. The results from reviewed studies are shown in Tables 2.4 to 2.6.

Studies of gait in children

There were no common spatiotemporal measures between Fatoye *et al.*[95] and Nikolajsen *et al.*[99], and Fatoye *et al.*[95] did not measure kinetics. The only outcome measure common to both studies was peak knee extension during stance phase, where Fatoye *et al.*[95] found that children with JHS had greater extension than a normal flexibility group, and Nikolajsen *et al.*[99] found no significant difference between GJH and normal flexibility.

Studies of gait in adults

Across the eight studies that investigated adult gait, a total of 70 kinematic, kinetic, and spatiotemporal outcome measures were used; 6 spatio-temporal, 38 kinematic, 22 kinetic and 4 other. For these outcome measures there was no definitive pattern in how JHS/GJH gait differed from normal, and for many factors studies reported conflicting findings, these are described in Table 2.4.

For spatio-temporal measures, all of the four studies which measured step length found a significant difference between JHS and NF control groups; three found that JHS had a shorter step length, and Rigoldi *et al.*[97] found that JHS had a longer step length. Unfortunately, there appears to be an error in the calculation: Rigoldi *et al.*[6] normalised step length to height (normalised step length = step length/height). The JHS group are listed as having a normalised step length of 386.8, and the normal flexibility group as a normalised stride length of 0.88. Rigoldi *et al.*[6] list the mean height of the JHS group as 162.83cm. Therefore, to produce a normalised stride length of 386.8, the actual stride length would be approximately 0.63km. Perhaps unsurprisingly, the authors list a significant difference between JHS and NF groups. Unfortunately, it is impossible to say whether there is in fact a genuine difference, and the mistake merely a typographical error, or is due to an error in calculation.

For kinematic and kinetic measures, at the pelvis significant differences were found in two of the four studies which investigated pelvis kinematics, however the specific kinematic parameter where differences occurred was not common between studies (Table 2.4). At the hip, only Celletti *et al.*[98]

found significant differences in kinematics, and these were in Gait Profile Score; a method of comparing joint angles by averaging the gait cycle[106]. Differences in hip moment were observed in a GJH cohort[94], and these differences were not found in JHS cohorts.

At the knee, there was no consistent way JHS movement differed from NF. Celletti *et al.*[98] found a significant difference in Gait Profile Score for knee flexion/extension, and Cimolin *et al.*[102] observed that the JHS group had a lower peak flexion during the swing phase of gait. Simonsen *et al.*[94] also found that their GJH cohort showed lower knee flexion at various points in the gait cycle, however no significant difference was observed in the other studies of JHS cohorts by Galli *et al.*[96] and Rigoldi *et al.*[97]. Only Simonsen *et al.*[94] reported on knee moments, and found these to generally lower in a GJH group than NF.

At the ankle, there is again no clear agreement between studies, for either kinematics or kinetics. Where differences are found, JHS individuals tend to be less plantarflexed than NF groups. Of the three studies that report on ankle stiffness, all three found that ankle stiffness was lower in JHS groups.

Turning to studies that measured EMG, only the study by Schmid *et al.*[103] used EMG as an outcome measure. They found that at heel-strike GJH had significantly greater activity in the Vastus Lateralis, Vastus Medius, and Gastrocnemius, and significantly lower activity in the Semitendinosus. The Gastrocnemius muscle also showed significantly higher activation levels during stance phase.

Table 2.4 Outcome measures and data extraction table for studies that investigated gait. Results are highlighted in bold where the study found a significant difference between groups. Empty cells indicate the parameter was not measured.

Authors	**Fatoye *et al*.**[95]	**Nikolajsen *et al*.** [99]	**Simonsen *et al*.** [94]
Comparison groups	**Children with JHS, control group (mean ± SD)**	**Children with GJH vs. control group (mean ± SD)**	**Difference between GJH and control group**
<u>Spatio-temporal</u>			
Mean velocity	No significant difference (1.2 ± 0.1m/s, 1.2 ± 0.4m/s). p=.496		
Anterior step length		No significant difference (0.62m ± 0.04, 0.61 ± 0.02m)	
Step width		**0.12 ± 0.01, 0.13 ± 0.01. p<.001**	
<u>Hip Joint</u>			
Mean angle (coronal plane)			**Lower and more adducted for most of stance phase (no %age or absolute figure given). p=.02**
Mean angle (sagittal plane)		No significant difference. -9.1 ± 6.9, -8.7 ± 8.1°. p=.445	
Peak flexion	No significant difference (36.8 ± 5.7°, 37.2 ± 7.5°). p=.842		
Peak extension	No significant difference (-6.7 ± 5.5°, -8.2 ± 7.0°). p=.400		
Hip angle at initial contact (sagittal plane)		No significant difference. -31.5 ± 6.7, -30.6 ± 8.4°. p=.262	
Hip range of motion (sagittal plane)		No significant difference. 41.7 ± 5.5, 41.6 ± 5.4°. p=.329	
Angle at peak knee flexion (sagittal plane)		No significant difference. -26.8 ± 5.9, -26.2 ± 9.9. p=.186	
First peak of hip extensor moment		**-57.8 ± 10.7, -64.7 ± 14.6 Nm/(Kg*m)*100. p=.006**	No significant difference (from figure)
Peak flexor moment		No significant difference. 92.8 ± 21.8, 86.3 ± 15.7 Nm/(Kg*m)*100. p=.460	No significant difference (from figure)
First peak hip abductor moment		**46.5 ± 6.9, 48.4 ± 8.7 Nm/(Kg*m)*100. p=.007**	No significant difference (from figure)
Hip abductor moment (middle of stance phase)		No significant difference (from figure)	**13% higher in GJH group. p=.008**
Second peak hip abductor moment		**45.2 ± 8.3, 48.5 ± 10.6 Nm/(Kg*m)*100. p=.017**	No significant difference (from figure)
Angular impulse (coronal plane)			**Higher in GJH group (no %age or absolute figure given). p=.043**

Table 2.4 continued Outcome measures and data extraction table for studies that investigated gait. Results are highlighted in bold where the study found a significant difference between groups. Empty cells indicate the parameter was not measured.

Authors	Fatoye *et al.*[95]	Nikolajsen *et al.* [99]	Simonsen *et al.* [94]
Comparison groups	**Children with JHS, control group (mean ± SD)**	**Children with GJH vs. control group (mean ± SD)**	**Difference between GJH and control group**
Knee Joint			
Mean knee angle (sagittal plane)		No significant difference. -14.3 ± 5.9, -14.1 ± 6.7°. p=.943	
Knee flexion at heel strike		No significant difference. -3.7 ± 5.5, -4.0 ± 6.8°. p=.580	**More flexed in GJH group (2.2°). p=.001**
Peak flexion during first half of stance phase		No significant difference. -15.4 ± 6.7, 15.6 ± 9.1°. p=.915	**More flexed in GJH group (3.1°). p=.002**
Peak extension during stance phase	**-1.0 ± 3.5°, 4.2 ± 5.5°, p<.001**	No significant difference. -3.8 ± 6.4, -2.5 ± 7.6°. p=.663	**Greater in GJH group (0.42°). p=.02**
Peak knee flexion during loading response	**12.6 ± 4.7°, 20.0 ± 6.1°. p<.001**		
Peak knee flexion during swing	**53.5 ± 4.6°, 60.4 ± 6.6°. p<.001**		
Knee flexion/extension range of motion		No significant difference. 51.5 ± 5.5, 51.5 ± 5.8°. p=.859	
Peak knee adduction	No significant difference (-2.5 ± 4.5°, -2.8 ± 5.5°). p=.801		
Peak knee abduction	No significant difference (9.6 ± 5.5°, 11.0 ± 6.3°). p=.343		
First flexor peak moment during stance		No significant difference. -17.2 ± 8.0, -19.6 ± 7.9 Nm/(Kg*m)*100. p=.050	No significant difference (from figure)
First extensor peak moment during stance		No significant difference. 30.4 ± 13.6, 30.4 ± 11.8 Nm/(Kg*m)*100. p=.781	**10% (2.8Nm/mass × height) higher in GJH group. p=.023**
Flexor moment at middle of stance phase		**-0.8 ± 8.9, -6.7 ± 13.1 Nm/(Kg*m)*100. p=.005**	**27% (2.1Nm/mass × height) lower in GJH group. p=.014**
Second extensor peak during stance		No significant difference. 44.8 ± 15.6, 44.3 ± 11.1 Nm/(Kg*m)*100. p=.851	No significant difference (from figure)
First peak of internal abductor moment		No significant difference. 25.1 ± 8.8, 28.2 ± 9.4 Nm/(Kg*m)*100. p=.073	**13% (4.7Nm/mass × height) higher in GJH group. p=.03**
Second peak of internal abductor moment		**23.1 ± 8.3, 29.2 ± 9.3 Nm/(Kg*m)*100. p=.003**	No significant difference (from figure)

Table 2.4 continued Outcome measures and data extraction table for studies that investigated gait. Results are highlighted in bold where the study found a significant difference between groups. Empty cells indicate the parameter was not measured.

Authors	**Fatoye *et al*.**[95]	**Nikolajsen *et al*.** [99]	**Simonsen *et al*.** [94]
Comparison groups	**Children with JHS, control group (mean ± SD)**	**Children with GJH vs. control group (mean ± SD)**	**Difference between GJH and control group**
Compression force			**Total (p=.034), medial (p=.008) and lateral (p=.036) compression force higher in GJH group just after heel strike**
Shear force			No significant difference
Ankle Joint			
Mean angle (sagittal plane)		No significant difference. -4.2 ± 5.7, -4.2 ± 4.9. p=.0498	
Peak ankle plantarflexion	**-15.3 ± 6.6°, -11.7 ± 6.0°. p=.024**		
Peak ankle dorsiflexion	No significant difference (12.6 ± 4.8°, 13.4 ± 5.1°). p=.546		
Ankle angle at initial contact (sagittal plane)		**1.5 ± 7.2, -0.1 ± 4.9. p=.034**	
Dorsi/plantarflexion range of motion		No significant difference. 31.0 ± 5.9, 29.6 ± 6.8°. p=.454	
Angle at peak knee flexion (sagittal plane)		**1.9 ± 6.2, 3.4 ± 5.8°. p=.048**	
Dorsiflexor moment shortly after heel strike		No significant difference (9.4 ± 5.3, 7.3 ± 3.0 Nm/(Kg*m)*100.) p=.182	**38% (1.1Nm/mass × height) higher in GJH group. p=.017**
plantarflexor moment during stance		**-82.9 ± 14.1, -83.4 ± 8.3 Nm/(Kg*m)*100. p=.029**	No significant difference (from figure)
Angular impulse (coronal plane)			**Higher in GJH group (no %age or absolute figure given). p=.031**
Other			
Knee pain	**2.5 ± 5.3, 0.0 ± 0.0. p<.001**		**53%, 0%. p<.001**

Table 2.4 continued: Outcome measures and data extraction table for studies that investigated gait. Results are highlighted in bold where the study found a significant difference between groups. Empty cells indicate the parameter was not measured.

Authors	Schmid *et al.*[103]	Galli *et al.*[96]	Rigoldi *et al*[97]
Comparison groups	**GJH group vs. control group (mean ± SD)**	**JHS group vs. control group (mean ± SD)**	**JHS vs. control group vs. down syndrome (mean ± SD)**
Spatio-temporal			
% stance phase	60.3±1.6%, 60.1±1.3%	No significant difference (59.83 ± 3.42%, 59.65 ± 3.19%)	No significant difference (59.7±4.65,59.65±3.19)
Mean velocity		No significant difference (0.96 ± 0.25m/s, 1.12 ± 0.18m/s)	No significant difference (0.89 ± 0.32m/s, 1.12 ± 0.18m/s)
Anterior step length		**0.34 ± 0.12, 0.88 ± 0.21. p<.05**	**386.8 ±147.7, 0.88 ± 0.21. p<.05**
Step width		No significant difference (131.64 ± 42.42, 123.29 ± 27.84)	
Stance phase duration	626.4±48.2ms, 636.3±51.9ms		
Swing phase duration	**410.9±25.2ms, 421.5±24.6ms. p=.005**		
Pelvis			
Mean pelvic tilt		No significant difference (8.64 ± 4.99°, 6.53 ± 6.97°)	No significant difference (8.6 ± 5.14°, 6.53 ± 6.97°)
Range of motion of pelvic tilt		**6.2 ± 3.87°, 3.62 ± 0.86. p<.05**	No significant difference 6.8 ± 3.95°, 3.62 ± 0.86
Range of motion of pelvis (coronal plane)		No significant difference (7.58 ± 3.27°, 6.01 ± 2.53°)	
Range of motion of pelvis (transverse plane)		No significant difference (10.29 ± 4.41°, 10.72 ± 5.32°)	
Hip Joint			
Hip angle at initial contact (sagittal plane)		No significant difference (28.45 ± 8.35° in EDSG, 27.23 ± 9.57° in CG)	No significant difference (29.64 ± 9.15° in EDSG, 27.23 ± 9.57° in CG)
Hip range of motion (sagittal plane)		No significant difference (40.37 ± 5.99° in EDSG, 43.52 ± 4.76° in CG)	No significant difference (41.55 ± 5.82° in EDSG, 43.52 ± 4.76° in CG)
Minimum hip flexion in stance phase (sagittal plane)		No significant difference (-11.07 ± 7.9° in EDSG, -14.83 ± 9.6° in CG)	No significant difference (-9.5 ± 8.09° in EDSG, -14.83 ± 9.6° in CG)
Hip maximum flexion			30.91±7.2° in EDSG, 33.45±6.89°
Hip range of motion (coronal plane)		No significant difference (11.82 ± 4.75°, 10.71 ± 3.06°)	
Hip stiffness		**Reduced (values not given, expressed in figure). p<.005**	**0.015±0.006, 0.02±0.007 Nm/Kg/°**
Knee Joint			
Knee flexion at heel strike		No significant difference (4.07 ± 7.19° in EDSG, 4.39 ± 6.53° in CG)	No significant difference (5.96± 7.34° in EDSG, 4.39 ± 6.53° in CG)
Peak flexion during first half of stance phase			
Peak extension during stance phase		No significant difference (-2.44 ± 6.92°, 0.12 ± 3.82°)	No significant difference (-0.3± 6.71°, 0.12 ± 3.82°)
Peak knee flexion during loading response			
Peak knee flexion during swing		No significant difference (53.99 ± 9.23°, 57.08 ± 6.63°)	No significant difference (58.32 ±°, 57.08 ± 6.63°)
Knee flexion/extension range of motion		No significant difference (59.03 ± 7.44°, 59.07 ± 6.31° in CG)	No significant difference (56.84 ± 6.03°, 59.07 ± 6.31° in CG)
Ankle Joint			
Ankle angle at initial contact (sagittal plane)		**-4.74 ± 5.53°, 1.81 ± 6.87°. p<.05**	No significant difference (-4.10 ± 5.48°, 1.81 ± 6.87°. p<.05)
Maximum dorsiflexion during stance phase (sagittal plane)		**9.89 ± 4.79°, 21.04 ± 5.16°. p<.05**	**10.66 ± 4.16°, 21.04 ± 5.16°. p<.05**
Minimum dorsiflexion during stance phase		No significant difference (-13.79 ± 7.35°, -9.73 ± 9.4°)	No significant difference (-14.29 ± 7.35°, -9.73 ± 9.4°)

Table 2.4 continued: Outcome measures and data extraction table for studies that investigated gait. Results are highlighted in bold where the study found a significant difference between groups. Empty cells indicate the parameter was not measured.

Authors	Schmid *et al.*[103]	Galli *et al.*[96]	Rigoldi *et al*[97]
Comparison groups	**GJH group vs. control group (mean ± SD)**	**JHS group vs. control group (mean ± SD)**	**JHS vs. control group vs. down syndrome (mean ± SD)**
Dorsi/plantarflexion range of motion		No significant difference (23.68 ± 6.74°, 25.72 ± 6.56°)	No significant difference (22.75 ± 4.26°, 25.72 ± 6.56°)
Maximum dorsiflexion during swing		**3.02 ± 5.26°, 7.89 ± 9.93°. p<.05**	
plantarflexor moment during terminal stance		**1.17 ± 0.16Nm/kg, 1.51 ± 0.18 Nm/kg. p<.05**	
Maximum ankle power during terminal stance		**2.04 ± 0.88 W/Kg, 3.14 ± 0.88 W/Kg. p<.05**	
Maximum ankle power during terminal stance (normalised to velocity of progression)		**1.88 ± 1.15 m/s2, 2.89 ± 0.93 m/s2. p<.005**	
Ankle Stiffness		**Reduced (values not given, expressed in figure). p<.005**	**0.056±0.03,0.083±0.03 Nm/Kg/°**
Ground reaction force parameters			
Peak vertical GRF during loading response	111.1±7.1% bodyweight, 110.2±6.9% bodyweight		
Peak vertical GRF during push-off	116.1±5.7% bodyweight, 115.0±6.2% bodyweight		
Unloading force between loading response and push off	75.5±6.1% bodyweight, 75.7±7.0% bodyweight		
Vertical GRF loading response rate	1032.7±184.5% bodyweight/second, 1027.8±225.6% bodyweight/second		
Vertical GRF unloading response rate	1075.3±172.2% bodyweight/second, 1047.4±159.3% bodyweight/second		
Time from heel strike to peak vertical GRF, loading response	144.6±20.2ms, 146.6±24.2ms		
Time from heel strike to minimum vertical GRF	298.4±20.8ms, 304.6±26.1ms		
Time from heel strike to peak vertical GRF during push-off	478.3±31.1ms, 485.6±37.0ms		
AP peak braking force	20.8±7.2% bodyweight, 21.0±6.3% bodyweight		
AP peak propulsive force	-24.3±8.2% bodyweight, -23.9±7.2% bodyweight		
Time to peak braking force	95.9±11.7ms, 96.0±12.3ms		
Time to peak propulsive force	543.6±35.3ms, 552.9±44.1ms		
EMG parameters			
Tibialis anterior max	74.2±10.5% peak, 72.9±9.8% peak		
Tibialis anterior mean	13.4±3.4% peak, 12.6±3.2% peak		
Tibialis anterior Heel strike	150.5±13.2% peak, 48±12.3% peak		
Tibialis anterior Pre-swing	29.6±8% peak, 29±7.6% peak		
Gluteus Medius max	77.2±8.4% peak, 78.3±7.4% peak		
Gluteus Medius mean	**20.5±4.6% peak, 22.1±4.3% peak**		
Gluteus Medius Heel strike	**17.1±4.8% peak, 8.6±4.8% peak**		
Gluteus Medius Pre-swing	5.7±4.7% peak, 6.6±4% peak		

Table 2.4 continued: Outcome measures and data extraction table for studies that investigated gait. Results are highlighted in bold where the study found a significant difference between groups. Empty cells indicate the parameter was not measured.

Authors	Schmid *et al.*[103]	Galli *et al.*[96]	Rigoldi *et al*[97]
Comparison groups	**GJH group vs. control group (mean ± SD)**	**JHS group vs. control group (mean ± SD)**	**JHS vs. control group vs. down syndrome (mean ± SD)**
Semitendinosus max	59±16.3% peak, 56.1±16.8% peak		
Semitendinosus mean	13.4±5.2% peak, 13.9±5.8% peak		
Semitendinosus Heel strike	**136.3±13.8% peak, 32.2±12.7% peak**		
Semitendinosus Pre-swing	35.7±11.3% peak, 36.1±9.9% peak		
Biceps femoris max	59±14.5% peak, 56±15.5% peak		
Biceps femoris mean	15.8±5.1% peak, 16±6.1% peak		
Biceps femoris Heel strike	137.6±15% peak, 35.6±12.9% peak		
Biceps femoris Pre-swing	34.6±12.5% peak, 34.5±10.7% peak		
Vastus medialis max	71.1±11% peak, 73.4±9.1% peak		
Vastus medialis mean	**14.9±4.5% peak, 16.4±5.4% peak**		
Vastus medialis Heel strike	128.2±11% peak, 29.8±11.4% peak		
Vastus medialis Pre-swing	21.9±9.1% peak, 22.7±9.5% peak		
Vastus lateralis max	74.2±7.9% peak, 75.9±8.1% peak		
Vastus lateralis mean	15±3.9% peak, 16.5±4.4% peak		
Vastus lateralis Heel strike	130.6±11.5% peak, 32.5±12.3% peak		
Vastus lateralis Pre-swing	22.7±9.9% peak, 22.4±8.9% peak		

Table 2.4 continued: Outcome measures and data extraction table for studies that investigated gait. Results are highlighted in bold where the study found a significant difference between groups. Empty cells indicate the parameter was not measured.

Authors	Celetti *et al.*[98]	Celletti *et al.* [100]	Cimolin *et al.*[102]	Rombaut *et al.*[46]
Comparison groups	JHS group vs. control group	JHS group vs. control group (mean ± SD)	JHS group vs. control group (mean ± SD)	JHS group vs. control group
Spatio-temporal				
% stance phase			No significant difference (59.37±3.19%, 59.45±1.45%)	No significant difference
Mean velocity			No significant difference (0.99±0.24, 1.12±0.18)	**109.49±16.7cm/s, 122.82±19.18cm/s**
Anterior step length			**0.34±0.12, 0.88±0.21**	62.41±6.0cm, 68.2±6.1cm
Foot progression (Gait Variable Score)	No significant difference			
Cadence				**104.86±8.46 steps/min, 107.83±12.23 steps/min**
Pelvis				
Mean pelvic tilt	No significant difference		No significant difference (8.16±4.28, 6.53±6.97)	
Range of motion of pelvis (coronal plane)			No significant difference (8.20±3.32, 6.01±2.53)	
Range of motion of pelvis (transverse plane)			No significant difference (11.88±4.95, 10.72±5.32)	
Pelvic obliquity (Gait Variable Score)	**Significant difference in pelvic obliquity. p<.05**			
Pelvic rotation (Gait Variable Score)	**Significant difference in pelvic rotation. p<.05**			
Hip Joint				
Hip angle at initial contact (sagittal plane)			No significant difference (28.47±8.06, 27.23±9.57)	
Hip range of motion (sagittal plane)			No significant difference (41.43±5.95, 43.52±4.76)	
Minimum hip flexion in stance phase (sagittal plane)			No significant difference (-10.97±6.98, -14.83±9.6)	
Hip range of motion (coronal plane)			No significant difference	
Hip flexion/extension (Gait Variable Score)	**Significant difference in Hip Flex/Ext. p<.05**			
Hip adduction/abduction (Gait Variable Score)	**Significant difference in Hip Add/Abb. p<.05**			
Hip rotation (Gait Variable Score)	**Significant difference in Hip rotation. p<.05**			
Hip stiffness			No significant difference	
Knee Joint				
Knee flexion at heel strike			No significant difference	
Peak extension during stance phase			No significant difference	
Peak knee flexion during swing			**52.86±8.48, 58.01±6.18, p<.05**	
Knee flexion/extension range of motion			54.76±9.14, 60.28±6.31, p0.05	
Knee flexion/extension (Gait Variable Score)	**Significant difference in knee flex/ext. p<.05**			
Ankle Joint				
Ankle angle at initial contact (sagittal plane)			**-4.06±5.27, 1.81±5.87**	
Maximum dorsiflexion during stance phase (sagittal plane)			**10.41±5.27, 21.04±5.16**	
Minimum dorsiflexion during stance phase			**-13.67±7.63, -8.74±9.4**	

Table 2.4 continued: Outcome measures and data extraction table for studies that investigated gait. Results are highlighted in bold where the study found a significant difference between groups. Empty cells indicate the parameter was not measured.

Authors	Celetti *et al.*[98]	Celletti *et al.* [100]	Cimolin *et al.*[102]	Rombaut *et al.*[46]
Comparison groups	**JHS group vs. control group**	**JHS group vs. control group (mean ± SD)**	**JHS group vs. control group (mean ± SD)**	**JHS group vs. control group**
Dorsi/plantarflexion range of motion			No significant difference	
Maximum dorsiflexion during swing			**3.61±5.19, 8.63±9.93**	
Ankle dorsiflexion/plantarflexion (Gait Variable Score)	**Significant difference in ankle dor/pla. p<.05**			
Maximum ankle power during terminal stance			No significant difference	
Ankle Stiffness			**Significant difference (p<.05), exact figures are not listed.**	
Other				
Gait profile score	**JHS had significantly higher Gait Profile Score. p<.05**			
Knee pain				
Fatigue Severity Scale		Greater in JHS group (6.2±0.9 versus 2.3±0.7; p<.05)		
Fatigue Severity Scale; correlation with ankle power		No significant correlation		
Fatigue Severity Scale; correlation with peak ground reaction force		**Negative correlation (greater FSS correlated with smaller GRF), r = 0.66, p<.05.**		

Studies of standing balance

Results from studies of balance are reported in Table 2.5. Both of the studies that measured standing balance in JHS found that balance was impaired, as evidenced by increased values of mediolateral and anterioposterior sway[45,46]. Greenwood *et al.*[101] found that during quiet standing GJH had significantly greater co-contraction in Biceps femoris/rectus femoris muscles during quiet standing in both eyes open and eyes closed conditions, and significantly lower Erector Spinae activity during single leg standing with eyes closed.

Table 2.5: Outcome measures and data extraction table for studies that investigated postural/balance tasks. Results are highlighted in bold where the study found a significant difference between groups. Empty cells indicate the parameter was not measured.

Authors	Galli *et al.*[45]	Rombaut *et al.*[46] (JHS cohort)	Greenwood *et al.*[101] (GJH cohort
Comparison groups	JHS group vs. control group	JHS group vs. control group	GJH group vs. control group
COP measures			
AP Sway	**Significantly greater in eyes-open and eyes closed conditions.**	**Significantly greater than controls in eyes open and eyes closed conditions.**	
ML Sway	**Significantly greater in eyes-open and eyes closed conditions.**	**Significantly greater in Eyes closed condition.**	
Sway velocity		**Significantly greater in both eyes-open and eyes-closed conditions.**	
Sway area		**Significantly greater in eyes-closed condition.**	
Frequency Measures			
Frequency of sway, AP	No significant difference		
Frequency of sway, ML	No significant difference		
EMG measures			
Overall muscle activity			**Erector Spinae and Semitendinosus activity greater in single leg standing, eyes-closed.**
Co-contraction			No significant difference in Tib Ant/Gastroc for any task. **GJH Semitendinosus/Rectus femoris significantly greater in quiet standing tasks.**

Studies of stair climbing

Results from the Luder *et al.*[104] stair climbing study are reported in Table 2.6. There were no differences in GRF parameters between GJH and NF during stair ascending and descending. Nor were there any significant differences in ground reaction force variables.

Table 2.6: Outcome measures and data extraction table for studies that investigated stair climbing. Results are highlighted in bold where the study found a significant difference between groups.

Authors	Luder *et al.*
Comparison groups	GJH group, control group **(mean ± SD)**
Temporal and ground reaction force measures	
Maximum force-peak during weight acceptance - ascent	109.5±6.5% bodyweight, 109.6±7.5% bodyweight
Time to maximum force peak - ascent	196.2±30ms, 195.4±32.6ms
Stance time – ascent	717.8±97.2ms, 725.2±106.8ms
Cadence - ascent	103.0±12.6 steps/min, 102.9±12.6 steps/min
Maximum force-peak during weight acceptance - descent	149.0±28.5% bodyweight, 147.5±24.4% bodyweight
Time to maximum force peak - descent	152.0±20.5ms, 152.3±24.0ms
Stance time – descent	675.9±103.1ms, 690.7±111.4ms
Cadence - descent	111.9±15.8 steps min, 111.3±16.3 steps min
EMG Measures during stair ascent (%MVC)	
Tibialis anterior peak	18.0±9.4, 16.5±7.1
Tibialis anterior mean	4.3±2.0, 3.9±1.6
Tibialis anterior at max GRF	4.0±3.8, 3.4±2.3
Gastrocnemius medialis peak	67.3±15.7, 64.5±14.7
Gastrocnemius medialis mean	18.4±4.8, 18.4±5.1
Gastrocnemius medialis max GRF	9.8±7.2, 9.9±7.2
Semitendinosus peak	22.8±9.1, 20.0±9.9
Semitendinosus mean	4.8±2.0, 4.5±2.1
Semitendinosus at max GRF	4.2±2.5, 3.9±2.6
Biceps femoris peak	26.7±17.9, 25.7±21.0
Biceps femoris mean	7.2±4.4, 7.3±4.6
Biceps femoris at max GRF	8.8±7.6, 8.9±7.2
Vastus medialis peak	110.2±43.9, 93.9±39.2
Vastus medialis mean	22.6±9.6, 19.6±7.7
Vastus medialis at max GRF	26.6±13.5, 22.7±10.0
Vastus lateralis peak	91.4±44.3, 78.1±29.4
Vastus lateralis mean	18.6±8.9, 16.5±6.3
Vastus lateralis at max GRF	22.2±11.7, 19.6±8.0
EMG Measures during stair descent (%MVC)	
Tibialis anterior peak	22.0±9.1, 22.4±8.3
Tibialis anterior mean	4.6±2.5, 4.3±2.0
Tibialis anterior at max GRF	5.0±4.1, 4.5±3.4
Gastrocnemius medialis peak	41.7±10.1, 40.6±10.2
Gastrocnemius medialis mean	7.9±2.8, 7.9±2.5
Gastrocnemius medialis max GRF	6.0±4.5, 6.5±3.4

Table 2.6: Outcome measures and data extraction table for studies that investigated stair climbing. Results are highlighted in bold where the study found a significant difference between groups.

Authors	Luder *et al.*
Comparison groups	GJH group, control group **(mean ± SD)**
Semitendinosus peak	37.6±23.0, 29.6±17.4
Semitendinosus mean	7.7±3.7, 6.4±3.3
Semitendinosus at max GRF	4.6±3.0, 4.3±2.7
Biceps femoris peak	42.6±27.1, 39.6±25.6
Biceps femoris mean	11.5±7.5, 12.0±8.6
Biceps femoris at max GRF	9.1±7.1, 10.1±8.0
Vastus medialis peak	42.8±23.9, 35.9±19.9
Vastus medialis mean	11.3±5.5, 10.3±5.7
Vastus medialis at max GRF	11.0±6.6, 11.0±6.9
Vastus lateralis peak	77.7±28.7, 68.8±28.3
Vastus lateralis mean	20.0±6.4, 19.2±7.7
Vastus lateralis at max GRF	22.2±11.7, 19.6±8.0

2.4 Discussion

2.4.1 Overall study comments.

Overall, there is a concern about the quality of studies and the quality of reporting, and therefore, whether their results are accurate. Fatoye *et al.*[95] and Nikolagsen *et al.*[99] are the better quality studies which investigated kinematics/kinetics of gait, and so their results would seem more reliable, however their cohorts were children, and since this thesis concerns movement in adults their results are not directly comparable. Rombaut *et al.*[46] produced a high quality study of adults, but only temporal outcome measures were used, meaning that although the lower velocity, cadence, and shorter step length may be indicative of impaired gait in JHS, conclusions cannot be drawn as to how or why their gait may differ from normal.

Unfortunately, there is no standard test or tool applicable to the rating of movement analysis studies. Therefore, this review and other systematic reviews in the motion analysis field must adapt other checklists or tools. Here the Quality Index test was used to measure study quality[83]. It should be noted that this is a strict set of criteria, and although modified, may not be wholly suitable for judging gait analysis studies. This is evidenced by the fact that ten questions were considered irrelevant and were removed, which may affect the validity of the scale. Even with removing 10 of the original questions,

there was still a number of questions where none or very few of the studies scored positively (Items 11, 12, and 15) which might indicate that the questions are not relevant to movement analysis studies. Item 11, "Were the subjects asked to participate in the study representative of the entire population from which they were recruited?"; all studies scored negatively simply because there is very little information about what the characteristics of the JHS population are. Since hypermobility varies with age, sex, and gender, studies would need to report these for the recruited group and the background population, which seems unfeasible. This is the same reason why the majority of studies scored negatively for Item 12; "Were those subjects who were prepared to participate, representative of the entire population from which they were recruited?". None of the studies specified whether the assessor was blinded to whether participants were from the GJH/JHS group or the control group (Item 15). Therefore, it should be considered that assessor bias could influence the results. Although it seems unrealistic to blind the researcher who is taking measurements/recording the trials to be blinded to the participant group, movement trials could be anonymised before analysis. This should be considered when performing research in future. Another potential inaccuracy of the Quality Index checklist is that there was an element of repetition between Item 2 (relating to describing outcome measures) and Item 16 (relating to data-dredging). In some cases, if outcome measures were not clearly described, then it was not possible to say if data-dredging may have occurred.

The Quality Index checklist does not include factors unique to kinematic analysis, for example the accuracy of the kinematic model or whether the same person affixed markers in the testing session, which otherwise has been shown to introduce error[107]. In their systematic review, Mcginley *et al.* (2009) recognised that assessor characteristics were rarely mentioned in the studies of reliability of 3D movement analysis. The same situation was found in this review; three studies[95,97,98] did not state whether the same assessor placed markers on all subjects, an important factor as misplaced markers can be a source or error and variability in the results [108].

Another reason why it is difficult to compare the results of the studies is due to the different terms and classification methods used. There was a range of classification methods used to define JHS and GJH, which may add variability when comparing the results of studies. Classification of JHS has been recognised as a significant challenge[18], this difficulty is highlighted by Greenwood *et al.*[101] labelling their participants incorrectly, and how Luder *et al.*[104] and Schmid *et al.*[103] classified their participants. At the time of testing participants recruited to the GJH group were not assessed for pain. Subsequent to participating, participants were defined as symptomatic or asymptomatic based on their responses to a pain survey, with people that had experienced pain during the following 6 months placed in the symptomatic group. In both these studies the pain survey and/or characteristics of participant pain is not included, and so it is impossible to know how the 'pain participants' relate to JHS. There is also no information regarding the accuracy and reliability of the questionnaire used to classify people as being in

pain. Due to this, and the fact that joint pain after testing was not considered in other GJH studies, their results are taken in the context of comparing GJH participants to normal flexibility.

2.4.2 Studies of gait

Whilst a study may report significant differences in a particular gait factor, other studies reported no significant difference. These differences could be due to the different characteristics of groups tested (JHS vs. GJH), age (adults vs. children), experimental procedures, or equally it could be due to confounding factors such as pain, the large number of outcomes measured, or the low power of the studies.

There is a lack of consistency in how studies relating to the gait of hypermobile people report methods and results. The heterogeneity of outcome measures and how results are reported makes direct comparisons of studies difficult. In addition, results should be compared with caution due to one of the studies being rated as low quality, and errors in the reporting of results in general. In particular, data-dredging may be a problem across the six papers reviewed, as in many cases specific measurement outcomes were not identified in the methods. Of the 70+ outcome measures used in the studies of gait, not one is common to all five papers. The most common kinematic factor reported was peak extension of the knee in stance phase, which was reported in four studies[94-96,99]. Knee flexion at heel strike was reported in three studies[94,96,99]. Twenty-five outcome measures were common to two studies, and over forty unique to individual studies. Whilst this is partly because studies investigated different aspects of movement, it could also highlight how data-dredging, when applied to the large amount of data recorded in movement analysis, can present a large number of results simply through type I error.

At first glance there appears to be six separate studies investigating gait in JHS, and so a reader may assume that the movement has been well studied. It is interesting to note however, that the JHS and control participants in Galli *et al.*[96], Rigoldi *et al.*[97], and Celletti *et al.*[100] have identical characteristics (age, weight, and height). It is also noted that the Galli *et al.*[96] and Rigoldi *et al.*[97] share the majority of outcome measures, and the results reported for these measures are very similar. As it is unclear whether the three studies are reporting results from the same cohort of JHS and control participants, for the purpose of this discussion the results of Rigoldi *et al.*[97] and Celletti *et al.*[100] are disregarded to avoid duplication. In addition to the duplication of the JHS cohort, the two other studies from the research group, Cimolin *et al.*[102] and Celletti *et al.*[100], appear to share the same control group. This is important, as from reading each paper individually, it appears that the control group was tested at the same time as each of the JHS groups, for example Galli *et al.*[96] states: "20 adult participants, age and sex matched, were recruited as healthy controls...". Whether participants and controls were recruited from the same time period is one of the questions in the Downs and Black quality index. It is particularly relevant to

studies of movement, in that it is not clear whether the same researcher placed markers on participants in all of the studies, if not then measurement error could be introduced[109]. In addition, some studies are listed as taking part in different movement analysis laboratories[102], introducing the fact that different equipment, environment, researcher placing markers, and testing procedure could all cause error in observed results. The effect of this uncertainty, is that the differences observed between groups in these studies could be at least partly due to differences in experimental procedure. A concern which is underlined by the fact that although Galli *et al.*[96] and Rigoldi *et al.*[97] share the same laboratory, testing procedure, control and JHS groups, and outcome measures, they report some identical outcome measures as significantly different in one study, and not significantly different in the other (for example ankle angle at initial contact).

Only Schmid *et al.*[103] used EMG as an outcome measure; they compared GJH and NF gait. No studies have investigated EMG in JHS gait. Schmid *et al.*[103] state that the increased activation level they observed in various muscles at heel strike complements other studies; that the increased activation corresponds to the increased joint moment observed by Simonsen *et al.*[94] However, the increased joint moment has not been observed in the other studies of gait. Similarly a potential reason for the increased activity in the Gastrocnemius is linked to the results of Galli *et al.*, who observed an increase in plantarflexion at heel strike, and a decrease in dorsiflexion in stance and swing phases. Again, these ankle results have not been consistently found in other studies of JHS or GJH gait.

When considering the results of these studies in general, there does not appear to be a consistent way in which gait of JHS differs from normal flexibility gait. There was no consistent finding for kinematics or kinetics in any joint. The most commonly reported significant difference was that of step length; Galli, Cimolin and Rigoldi all found that JHS tended to walk with shorter steps. Simonsen *et al.*[94] found the most differences between their cohorts (GJH and normal flexibility). An interesting prospect, is that the reason a greater number of differences between GJH and NF gait were observed, than in studies comparing JHS and NF, is that people with GJH are adapting their movement to compensate for increased joint laxity. If JHS individuals do not perform this compensation, then it may indicate why they experience pain. The way to test this would be to measure JHS, GJH, and NF participants in the same study. To date, the three groups have not been directly compared within a single study, and so this is a direction for future research.

2.4.3 Studies of balance

Both Galli *et al.*[45] and Rombaut *et al.*[46] found that balance was impaired in JHS, and link this to reduced proprioception. In quantifying balance, both studies used well-known protocols, where standing is measured for a relatively short period of time (30 seconds). Muscle activity of posture

control has only been measured in a GJH cohort. There is no research to show how this relatively poor balance of JHS manifests in an important activity of daily living such as prolonged standing, thus indicating a possible direction for future research.

Only one study had measured muscle activity during a standing task[101]. Greenwood *et al.*[101] found their GJH group had significantly lower Erector Spinae activity than NF controls during the one-leg eyes-closed task, which the authors state may potentially indicate differences in lumbo-pelvic control. There are various spinal problems that have been associated with joint hypermobility syndrome[1]. However, the distinction between hypermobility of the lumbar region and lumbar instability is not clear[110]. Thus investigating lumbar and/or spinal instability and movement control is a potential avenue for future research. There was also a significant difference between GJH and NF groups in Rectus Femoris and Semitendinosus co-contraction; where GJH showed higher co-contraction during the quiet standing tasks. The authors propose that this strategy is used in the GJH cohort in a relatively low-level task to stabilise the knee joint; there was no difference in co-contraction between groups in the higher-level tasks. It is interesting that differences in EMG activity and co-contraction have been observed in a GJH group without symptoms. There has not been any investigation using EMG to measure muscle activity in a JHS cohort during standing, and it may be that the adaptations observed here are somehow different in JHS.

2.4.4 Studies of stair climbing

Only one study of stair ascending and descending was found in this review. No significant differences were found in ground reaction force (GRF) parameters between GJH and a control group, which is interesting as in the same cohort of women, differences were found in some EMG and temporal parameters during gait[103]. It may be thought that a more demanding task, i.e. stair climbing, would result in greater differences between the groups. In comparing the results of the two studies, stair ascending/descending seems to be more demanding than gait, at least in some muscles, as mean and peak activation of the quadriceps muscles are greater during the stair exercise. However, this increasing demand does not seem to relate to more significant differences between groups. One reason for this could be due to the much greater variability between participants in the stairs exercise. For example, the standard deviation of the peak activity of the Vastus medialis muscle in gait was 9.1% MVC in the GJH cohort, in stair ascending the standard deviation was 39.5% MVC. This may indicate that people use a variety of different strategies and hence muscle activation patterns when presented with a demanding activity, and the study may not have been sufficiently powered to detect these variations. This may be pertinent, given only one of the reviewed studies performed a sample size calculation.

There have not been any studies of stair climbing in people with JHS, and this is another direction for future research.

2.5 Conclusion

At present the main treatment to alleviate pain in JHS is physiotherapy, but there is no consensus as to which type of physiotherapy is most effective[3]. The study of how people with JHS move compared to people with normal flexibility, may highlight differences in movement and give direction to healthcare professionals regarding possible treatments. This systematic review demonstrates a lack of investigation of kinematics and kinetics during activities of daily living in people with JHS. The majority of studies of hypermobile movement have focused on gait, yet there is insufficient evidence to determine if JHS gait differs from NF and/or GJH in a consistent manner, and therefore little information upon which to influence treatment.

Although EMG activity has been investigated in GJH cohorts, it has not been used to assess movement during activities of daily living in JHS cohorts. Therefore, there is little understanding of if or how muscle activity differs during activities of daily living in JHS cohorts. This is surprising given the many features of JHS which could affect muscle control and activity, for example pain, muscle weakness, joint instability, hypotonia, and impaired proprioception. Since GJH participants in the studies did not have joint pain, it would hint that the differences in EMG observed in the reviewed studies are compensation for joint hypermobility, for example increasing co-contraction to increase joint stiffness. A potential avenue for future research is measuring if the same differences are exhibited by people with JHS, which would allude to whether the differences in EMG are used to compensate for the hypermobility, or some other factor.

In conclusion, this review demonstrates a variety of directions for future research. Firstly, there is a need to compare JHS, GJH, and NF groups in the same study. To date no study has measured all three groups. By measuring all three groups in the same study, it may be possible to identify movement strategies JHS individuals are, or are not performing compared to NF and GJH groups. This will highlight impairments during activities which physiotherapists can target and may in turn help explain why they experience pain. Secondly, there has been a lack of investigation into activities of daily living other than gait. By identifying and measuring activities that people with JHS find particularly challenging, we may be able to highlight differences in movement that can then be targeted with treatment. Thirdly, by bringing together kinematic, kinetic, and EMG measures a more complete picture of movement can be developed. Finally, there were a large number of outcome measures used in the reviewed studies, some of which may not be clinically relevant. There is a need to determine what kinematic and kinetic factors are clinically relevant and would assist healthcare professionals in the treatment of JHS. Only one of the six studies reviewed did this[98].

Chapter 3: Reliability study

3.1 Introduction

Three dimensional (3D) movement analysis has been used to investigate differences in kinematics and kinetics between people with normal flexibility and either people with JHS or people with GJH[94-99]. Although these studies have found a range of differences between normal, JHS and/or GJH gait, but these differences have not been consistent[82].

As found in the previous chapter, the majority of studies of movement of people with GJH and/or JHS did not provide a sample size calculation or provide any information about the statistical power of their study. This may contribute to the fact that there were many conflicting findings between studies of movement in hypermobile cohorts. Understanding variability and reliability of measured gait parameters is key to interpreting 3D movement analysis, particularly when comparing between groups or over time[109]. If the reliability of gait parameters is unknown, relatively small differences may be considered significant, or alternatively actual differences may be obscured by error[111]. Variability in 3D movement analysis can arise from intrinsic and extrinsic sources. Intrinsic variability is the natural variability of a subject's gait, and is measured by intra-session repeatability (a subject's stride to stride variability during one 3D movement analysis session). Extrinsic variability arises from methodological sources, for example errors in palpation, anthropometric measurements, and joint centre determination. Extrinsic reliability is measured by the inter-session variability (the variability between separate 3D movement analysis sessions)[68]. Intra and inter-session reliability of lower limb 3D kinematics during gait in normal populations is well documented, and has been measured in other patient groups with movement disorders; cerebral palsy[112], stroke[113], hemiplegia[114], and in children with spasticity[115]. How GJH affects the reliability of 3D movement analysis measurements is unknown. Knowing the reliability of 3D movement analysis measurements in GJH people is particularly relevant given that the characteristics of GJH may affect the repeatability of measurements. For example, hypermobile joints, by definition, have a greater range of motion than normal, and skin of hypermobile people tends to be hyperextensible[6], which may affect how the skin slides over the underlying skeleton; a significant cause of error in 3D movement analysis[116].

Typically, clinical gait analysis aims to differentiate between populations (i.e. normal/abnormal gait), to differentiate an individual from a normal population, or to measure change in gait over time, for example when assessing physiotherapy treatment or a surgical intervention[117]. Physiotherapy is a common method for treating symptoms of JHS, although further studies are required to determine what is effective[3]. 3D movement analysis could be used as an outcome measure for assessment, as is the case for stroke[118] and fall prevention in frail older people[119]. For this to be the case, as well as an understanding of variability and measurement error, it is necessary to know the magnitude by which a

gait variable must change, in order to be sure the change is real and not simply due to measurement error[120]. So far, this minimal detectable change (MDC) and reliability of 3D movement analysis in GJH people has not been studied. Quantifying these parameters would 1) aid interpretation of existing and future studies of gait in hypermobile cohorts, and 2) provide guidance on what 3D movement analysis outcome measures can be used with confidence, to ensure that the change observed during/after an intervention, is greater than the MDC.

The main objective of this study was to measure the intra- and inter-session reliability of gait kinematics in GJH participants compared to people with normal flexibility. From quantifying this reliability, the study aims:

- To determine if GJH affects the reliability of 3D movement analysis measurements.
- To determine what movement parameters (i.e. what joint angles and in what planes) can be feasibly investigated in future studies of movement.
- To determine the minimal detectable change of movement parameters. This will aid future studies using 3D movement analysis to investigate change in movement, for example following a physiotherapy intervention.

3.2 Methods

3.2.1 Subjects

Ethical approval for the study was granted from NRES London-West Ethics Committee. Informed, written consent was obtained from all participants. Inclusion criteria were ambulatory people aged 18-55 years. The upper age-limit was specified as flexibility (and the incidence of hypermobility) reduces with age. Exclusion criteria were designed to remove participants with any condition that may affect their gait, these included lower-limb pain, lower-limb surgery, Joint Hypermobility Syndrome (classified using the Brighton criteria), and any other neuromuscular condition. A priori testing indicated a sample size of 13 in each group was required to reach sufficient power ($\beta = 0.2$) when measured over three time points. 27 participants were recruited; 14 GJH (Beighton score >4) and 13 with normal flexibility (Beighton Score <4).

3.2.2 Lower limb model

In 3D movement analysis, misplacement of reflective markers can cause error in measurement of kinematic parameters[107]. It follows therefore that a standardised placement protocol and a researcher able to place markers consistently will reduce error. All markers were placed by the same researcher (AB). Prior to this study, AB gained experience in motion analysis during a six-month project. For the

purposes of this study AB underwent training by an experienced (28 years) senior clinical specialist physiotherapist (Dr. Caroline Alexander) to identify relevant anatomical landmarks by palpation. In addition, training was given using human cadavers to gain knowledge of underlying anatomy. To minimise error standardised placement procedures were developed (Table 3.1).

Marker	Placement
Posterior superior iliac spine	Most prominent bony process
Anterior superior iliac spine	Most prominent bony process
Lateral femoral epicondyle	Mid-point between most prominent anterior and posterior surface
Medial femoral epicondyle	Mid-point between most prominent anterior and posterior surface
Lateral tibial condyle	Mid-point between most prominent anterior and posterior surface, just below the joint line
Medial tibial condyle	Mid-point between most prominent anterior and posterior surface, just below the joint line
Lateral malleolus	Most prominent bony point
Medial malleolus	Most prominent bony point
Calcaneus	Mid-point between the medial and lateral edge, just above fat pad
Head of 1st metatarsal	Most superior surface
Head of 4th metatarsal	Most superior surface

Table 3.1. Marker placement details.

A customised biomechanical model was used capable of measuring each segment in 6 degrees of freedom. The CODA pelvis (Charnwod Dynamics Ltd., UK) was used to estimate position of hip joint centres. The femoral coordinate system was defined using the knee joint centre (mid-point between lateral and medial femoral epicondyle markers) as the origin, *y*-axis as the line passing from knee joint centre to hip joint centre, *z*-axis following the line joining medial and lateral femoral epicondyle markers (positive laterally in the right femur and medially in the left femur) and orthogonal to the *y*-axis, and finally an *x*-axis as orthogonal to both the *y* and *z*-axes (following a right-hand coordinate system). Shank origin was defined as the mid-point between medial and lateral tibial condyle markers, *y*-axis as the line passing from ankle joint centre (mid-point between the medial and lateral malleolus markers) to the origin, z-axis along the line joining the lateral and medial tibial condyle markers (positive laterally in the right shank and medially in the left) and orthogonal to the *y*-axis, and the *x*-axis orthogonal to the *y* and *z* axes. The foot coordinate system was defined using the ankle joint centre as the origin, a *y*-axis as the line from the mid-point between the head of the first and fourth

metatarsals, a *z*-axis following the line between the medial and lateral malleolus and orthogonal to the *z*-axis, and finally an *x*-axis orthogonal to the *y* and *z* axes. Clusters of four markers were placed on the lateral aspects of each thigh and shank. In a static trial, the position of the femoral epicondyle markers was measured relative to the thigh cluster, and similarly position of the tibia condyle markers measured relative to the shank cluster. For dynamic trials the knee markers were removed, and the position of the markers inferred from thigh and shank clusters. ISB recommended coordinate frames and Euler rotation sequence were used to determine joint rotation angles[78]. VICON Nexus and Bodybuilder software (Oxford Metrics Ltd., Oxford, UK) were used to compute joint angles.

3.2.3 Testing procedure and data analysis

Subjects were asked to walk unshod along a 6m walkway with two force plates (Kistler Instruments Corp., Amherst, USA) embedded. For analysis five full strides of the dominant limb were used, from foot strike to ipsilateral foot strike. The force plates were used to determine initial contact, and subsequent initial contact was determined using the method proposed by O'Connor *et al.* [121]. Trials were recorded using a 10-camera VICON system (Oxford Metrics Ltd., Oxford, UK) at 100Hz. For each cohort, intra- and inter-session variability was calculated for each point throughout the gait cycle. Participants were measured three times, on separate days/with 1–2 weeks between each session. The ratio of inter-session to intra-session error is reported ($\sigma^{ratio} = \sigma^{inter} / \sigma^{intra}$). This ratio can be used as a guide to the reliability of kinematic measurements; larger ratios indicate a greater amount of methodological error[111].

To determine MDCs of the hypermobile cohort, intra class correlation coefficients (ICC) were calculated (two-way mixed, absolute measures, 95% confidence) for relevant gait parameters. Standard error of the mean (SEM) was calculated as[122]:

$$SEM = SD \times \sqrt{1 - ICC}$$

Where SD is the average standard deviations for sessions 1 – 3. Finally the MDC was calculated as[122]:

$$MDC = SEM \times 1.962 \times \sqrt{2}$$

All data were analysed in SPSS v22 (Armonk, NY:IBM) using a single factor ANOVA. Significance was set at 0.05.

3.3 Results.

Subject characteristics of normal flexibility and GJH groups are given in Table 3.2.

	NF (n=13)	GJH (n=14)
Beighton Score	0.82 ± 1.2	5.6 ± 1.6
Age (years)	25.6 ± 5.1	25.8 ± 4.7
Males/females	5/8	5/9
BMI	21.9 ± 2.4	21.4 ± 2.6

Table 3.2. Participant characteristics. There were no significant differences between groups.

For each cohort, intra- and inter-session variability throughout the gait cycle is shown in Figure 3.1. In addition, mean intra- and inter-session variability for each group are listed in Table 3.3. There was no significant difference between GJH and normal flexibility groups in both intra- or inter-session variability in any of the joint angles.

The σ^{ratio} for normal flexibility and GJH groups followed a similar pattern. Since this study is focused on hypermobile gait, we report the σ^{ratio} of the generalised joint hypermobility group. Similar to Shwartz et al.[68] we found that pelvic rotation was most reliable (σ^{ratio} = 0.73), followed by pelvic obliquity (σ^{ratio} = 1.6) and pelvic tilt (σ^{ratio} = 2.0)

Of the hip angles, adduction/abduction was most reliable (σ^{ratio} = 2.1), followed by flexion/extension (σ^{ratio} = 2.3). The least reliable parameter was internal/external rotation (σ^{ratio} = 3.1), showing there is a relatively large degree of methodological error.

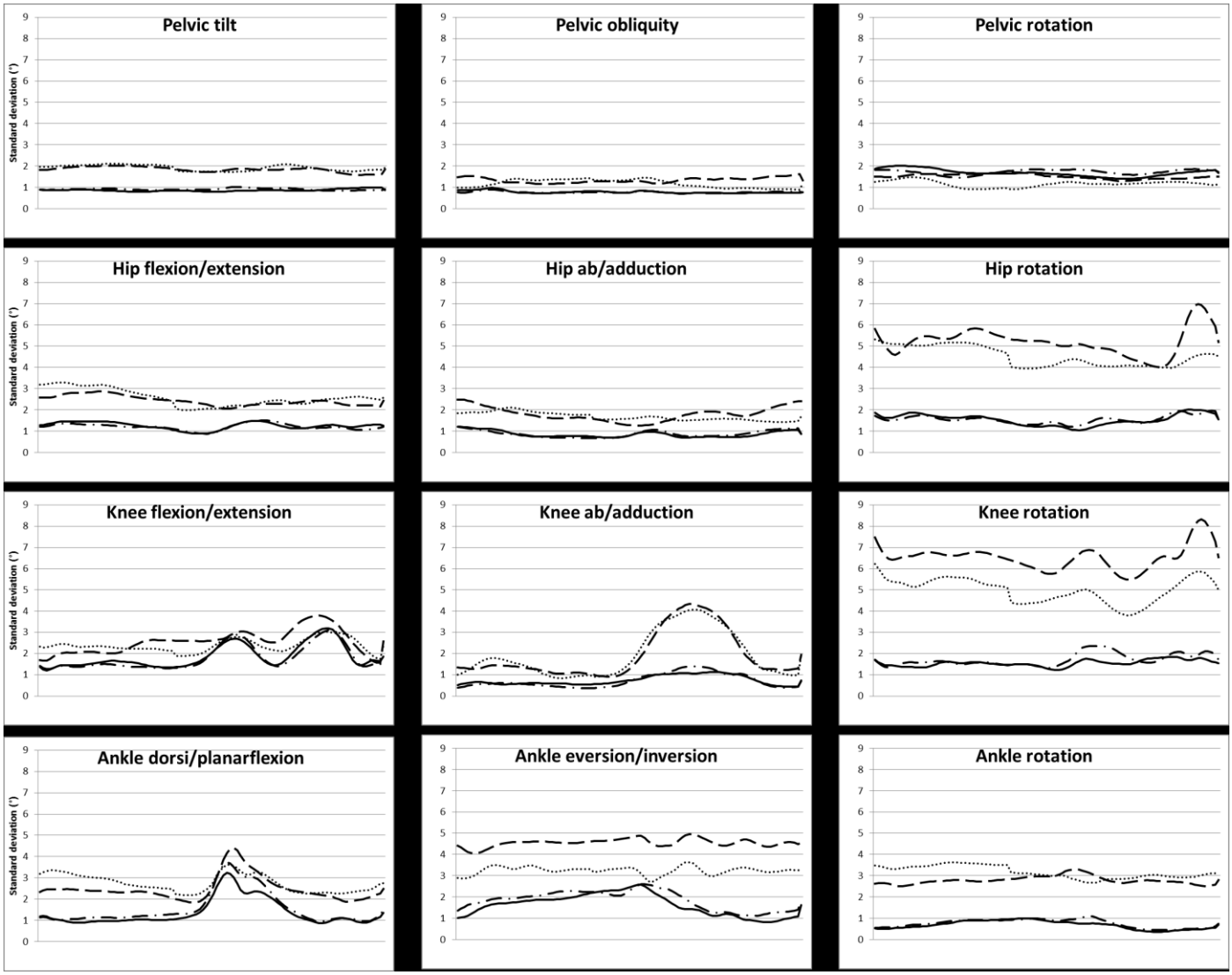


Figure 3.1. Variability in pelvis, hip, knee and ankle kinematics in GJH and normal flexibility cohorts. X axis is gait cycle from 0–100%. Solid line is normal flexibility intra-session variability, dashed & dotted line is GJH intra-session variability, dashed line is normal flexibility inter-session variability, and dotted line is GJH inter-session variability.

	Intra-session reliability			Inter-session reliability		
	NF	GJH	P value	NF	GJH	P value
Pelvic tilt	0.89°	0.91°	0.785	1.75°	1.99°	0.54
Pelvic obliquity	0.82°	0.77°	0.972	1.69°	1.24°	0.528
Pelvic rotation	1.72°	1.72°	0.444	1.36°	1.20°	0.133
Hip flexion	1.32°	1.21°	0.508	2.32°	2.62°	0.388
Hip ab/adduction	0.87°	0.88°	0.321	2.13°	1.75°	0.478
Hip rotation	1.63°	1.56°	0.185	5.36°	4.57°	0.411
Knee flexion/extension	2.02°	1.81°	0.291	2.43°	2.47°	0.534
Knee ab/adduction	0.74°	0.73°	0.523	1.89°	2.04°	0.421
Knee int/ext rotation	1.59°	1.72°	0.981	5.59°	5.05°	0.378
Ankle dorsi/plantarflexion	1.48°	1.55°	0.127	2.13°	2.79°	0.926
Ankle eversion/inversion	1.59°	1.85°	0.33	4.07°	3.43°	0.691
Ankle int/ext rotation	0.69°	0.76°	0.895	2.85°	3.23°	0.612

Table 3.3. Mean intra- and inter- session variability. There were no significant differences between normal flexibility and hypermobile groups.

Table 3.4. Intra-class correlation coefficients (ICC) and Minimal Detectable Changes (MDC) for gait parameters of the GJH cohort.

Gait parameter	ICC	MDC
Pelvic angle at initial contact	0.888	3.97
Pelvic tilt peak	0.856	4.37
Pelvic tilt ROM	0.810	1.34
Pelvic obliquity peak	0.404	3.40
Pelvic obliquity ROM	0.912	1.94
Peak pelvic rotation peak	0.925	2.36
Pelvic rotation ROM	0.962	1.88
Hip angle at initial contact	0.791	6.33
Hip flexion peak	0.792	6.04
Hip extension peak	0.812	4.70
Hip flexion/extension ROM	0.920	2.51
Hip adduction peak	0.625	4.54
Hip abduction peak	0.675	3.88
Hip add/abd ROM	0.956	1.48
Hip external rotation peak	0.731	11.95
Hip internal rotation peak	0.853	9.26
Hip rotation ROM	0.912	4.35
Knee angle at initial contact	0.801	4.80
Knee extension peak	0.818	4.65
knee flexion peak	0.741	5.79
knee flexion stance phase peak	0.719	6.83
Knee flexion/extension ROM	0.658	5.34
Knee adduction peak	0.706	4.90
Knee abduction peak	0.686	8.06
Knee add/abd ROM	0.398	7.19
Knee external rotation peak	0.839	11.84
Knee internal rotation peak	0.804	12.78
Knee external/internal ROM	0.611	5.64
Ankle dorsi/plantarflexion angle at initial contact	0.475	9.11

Table 3.4. continued. Intra-class correlation coefficients (ICC) and Minimal Detectable Changes (MDC) for gait parameters of the GJH cohort.

Gait parameter	ICC	MDC
Ankle dorsiflexion stance peak	0.799	6.20
Ankle dorsiflexion swing peak	0.690	7.35
Ankle plantarflexion peak	0.861	8.69
Dorsi/plantarflexion ROM	0.961	3.60
Ankle eversion peak	0.903	5.59
Ankle inversion peak	0.721	7.33
Ankle external rotation peak	0.540	8.15
Ankle internal rotation peak	0.326	8.59
Ankle int/ext rotation ROM	0.741	2.98

Knee flexion/extension was relatively reliable (σ^{ratio} = 1.4), whereas knee adduction/abduction and internal/external rotation exhibited some of the largest errors seen (σ^{ratio} = 3.0 and 3.2 respectively), again showing that methodological error is comparatively large.

At the ankle, the sagittal plane was again the most reliable (σ^{ratio} = 1.8); eversion/inversion was also relatively reliable (σ^{ratio} = 2.0). In contrast, ankle rotation was the least reliable of all the joint angles measured (σ^{ratio} = 4.44), indicating methodological error is high.

ICC and MDC results are reported in Table 3.4. The range of MDC values was relatively large; ranging from 1.34° to 12.78°. MDC values follow the general pattern of σ^{ratio}, with sagittal plane parameters generating relatively low MDCs, and frontal and transverse plane parameters generating relatively high MDCs.

3.4 Discussion

This study aimed to quantify the reliability of 3D movement analysis in GJH gait and compare to people with normal flexibility. We observed that there were no significant differences between the reliability of GJH and normal flexibility gait, in both mean joint angles and at specific peaks. Variations between gait measurements of individuals are not always due to differences in movement; observed differences are a combination of actual differences and variability introduced during the measuring process. The test-retest reliability of gait in normal populations is well documented[109], and this study furthered current knowledge by investigating reliability of 3D movement

analysis in GJH people compared to people with normal flexibility. Since no significant differences were observed between people with normal flexibility and people with GJH for both intra- and inter-session variability, it follows that 3D movement analysis measurements of GJH people can be interpreted with the same confidence as normal flexibility gait data. Furthermore, we observe that reliability of lower-limb kinematics in GJH people reported in this study are comparable to other studies that have reported reliability in a normal population[111,123,124]. It should be pointed out that care should be taken in interpreting results of this study in absolute measures, as the absolute values will depend on the biomechanical model used, specific lab protocols, and different researchers placing markers, amongst other factors. The general pattern and trends however, can be seen as common[111].

With the exception of the pelvis, sagittal plane angles tended to be most reliable in terms of absolute variability, σ^{ratio}, and MDC. This is a common finding of reliability studies, and reflects the method by which joint angles are calculated from the position of reflective markers[111]. Another source of error in knee angles is crosstalk between sagittal and frontal planes[125], it is likely that this is a factor here as inter-session error for knee adduction/abduction is considerably greater in swing phase (see Figure 3.1), where crosstalk is at a maximum due to a large flexion angle. It is also worth noting that the biomechanical model used in this study is hierarchical; errors are passed downstream via the kinematic chain. The effect of this is that inconsistent placement of the knee markers has a relatively large effect on reliability, which is most apparent in the frontal and coronal planes of hip, knee and ankle joint angles[111].

We reported variability as standard deviations and the ratio of the inter-session/intra-session error, as recommended by McGinley *et al.*[109] and Schwartz *et al.*[111]. Two other techniques which are commonly used to measure reliability in gait are coefficient of multiple correlation and intra class correlation. Here the coefficient of multiple correlation was not used as it has several problems; its value is connected to the range of motion of the joint measured[124], and it is sensitive to the number of subjects and test situations[126]. Similarly problems with reporting reliability solely using intra class correlation is that it cannot be used to cover the whole gait cycle, and necessitates defining key kinematic parameters beforehand. Furthermore, similar to the coefficient of multiple correlation, the intra-class correlation is a ratio and is dimensionless, which can be difficult to interpret clinically[127]. The approach used here, which followed the procedure given by Schwartz *et al.*[111], seems an efficient way of providing information regarding the reliability and variability of joint angles over the entire gait cycle, in a way that is clinically relevant and easy to interpret.

When reporting variability as ICC or coefficient of multiple correlation values, the cut-off value for what is considered reliable is an arbitrary choice. For example, in the case of ICCs, generally a value greater than 0.75 is considered good reliability, 0.5-0.75 moderately reliable, and less than 0.5 poor reliability[128]. Although reporting the σ^{ratio} does give understanding of the relative reliability of the gait parameter in question, it suffers from the same problem that whether it is 'reliable' enough is an arbitrary choice. We therefore used MDC to quantify reliability in terms of how much change is

necessary to occur to be confident that the change is real, and not due to measurement error. Calculated MDCs followed the overall pattern that sagittal plane MDCs are generally lower then frontal and transverse plane joint angles. Unfortunately, MDCs we have reported are relatively large, and it seems likely that for the majority of gait parameters the MDC will exceed the difference that would be expected to be observed if assessing or treating people with JHS relative to healthy controls. For example, Simonsen *et al.*[58] found that knee flexion at heel strike was significantly different between GJH and normal flexibility cohorts. This difference was measured on average as 2.2°, however, the MDC we measured as 4.8°. It is interesting that high ICC values were not always correlated with low MDCs. For example, peak knee internal rotation and peak knee external rotation both have ICC values greater than 0.8, which would be considered as excellent reliability. Their MDCs however, were some of the largest we reported (12.8° and 11.84° respectively). This highlights how researchers should take care in interpreting reliability results; a high ICC does not always indicate that a parameter is suitable as an outcome measure. Conversely, a low MDC can occur when a variable has relatively low reliability. This highlights how useful reporting variability as σ^{ratio} across the gait cycle can be, as it allows clinicians/researchers to interpret results of 3D movement analysis more effectively than what can seem like abstract values that are only relevant for one specific point in the gait cycle.

Whether 3D movement analysis is reliable enough will depend on various factors; in particular the outcome measures used, the similarity between groups tested, and the clinical question. The results of this study suggest that sagittal plane joint angles show the most promise in differentiating between cohorts and measuring change in gait following an intervention.

As was identified in Chapter 2, a potential problem in current 3D movement analysis studies of hypermobile gait, is that they did not provide power calculations. By determining the variability of outcome measures, it will allow for a power calculation to be performed in the main study (chapters 4-8).

3.5 Conclusion

This study indicated good between session reliability of 3D movement analysis of the lower limb during gait in hypermobile subjects, particularly in sagittal plane joint angles. This indicates that the biomechanical model used is a reliable tool to quantify movement in people who have GJH. The variability of joint angles in the three planes of motion can be used to inform sample size calculations in future studies of movement. The MDC values calculated for joint parameters were relatively large compared to differences observed in studies of JHS vs NF and JHS vs GJH gait, which highlights how careful consideration of outcome measures will be needed if 3D movement analysis is to be used to investigate differences following an intervention.

Chapter 4: Methods of main study

In Chapter 2, it was identified that there has been a lack of investigation into activities of daily living other than gait. In addition, in studies of hypermobile movement, the authors generally have not provided their motivation for measuring movements concerned; only Luder *et al.*[104] provided justification for choosing to investigate stair ascending and descending. To understand if, and how movement of JHS individuals differs from normal, and whether this difference is relevant to their complaints, it is necessary to select activities that would likely show differences in movement between JHS and NF individuals. Therefore, the next stage was to select a range of activities that would be investigated in the main study. The reasoning and methodology of selection activities is the subject of this chapter, along with the general methodology of the testing session (a detailed method of each of the activities investigated is given in the respective chapters). The aim of this chapter is to select a range of activities that are would provide interesting information, feasible to be tested, and different information for each activity.

A range of approaches were adopted to select the activities. The researcher (AB) observed an experienced physiotherapist (May To, 12 years' experience and specialist JHS physiotherapist) treating JHS patients during physiotherapy appointments at the Physiotherapy Department at Imperial College Healthcare NHS Trust. Furthermore, potential activities were discussed with two experienced physiotherapists Caroline Alexander (NIHR Senior Clinical Lecturer and Clinical Specialist Physiotherapist) and May To (Research Assistant Physiotherapist) to determine what activities were feasible to be performed by JHS participants, what information about movement the physiotherapists wanted to know to inform treatment, and what specific information could potentially be realised from each activity. Based on this information, it was decided that a testing session limited to two hours, including explaining the protocol, completing participant information sheets, consent, rests/breaks, and performing the activities, would be feasible and suitable for most JHS individuals.

Further guidance for selecting activities came from Palmer *et al.*[19], who in collaboration with people with JHS, developed a questionnaire which measures the impact of the syndrome. There are 55 items on the BIoH questionnaire, the majority feature a Likert scale where respondents rate the impact of their symptoms on their day to day life. The questionnaire is split into nine sections (A – I), with each section focusing on a different aspect, for example section A relates to what parts of the body respondents had experienced pain, section B relates to pain and fatigue over the previous 7 days. In development of the questionnaire, they used focus groups of JHS individuals to identify what physical activities people with JHS found challenging. Their answers were then streamlined using thematic analysis. Combined with analysing over 600 responses from people with JHS, the authors identified which activities had the most severe impact on patients' daily lives. The activities were defined and then included in the BIoH questionnaire. Sections E and F of the BIoH each feature 10 questions that relate

to physical activities. Section E deals with specific activities, for example Squatting, Reaching up to high shelves, and Peeling and chopping vegetables. Section F with more general activities such as Standing up for more than 30 minutes, and Walking briskly for a few miles. The focus chosen was on activities contained in Section F of the BIoH for a number of reasons. Firstly, all the activities relate to lower-limb. Secondly, they fit well with prior literature (both in hypermobility research and other musculoskeletal conditions) meaning that comparisons can be made with other studies, whereas some of the activities listed in Section E would be more difficult to interpret (e.g. peeling and chopping vegetables). Thirdly, after discussion and input from physiotherapists (Caroline Alexander and May To), the activities contained in section F of the BIoH were functionally relevant from a physiotherapist's perspective. The ten questions contained in Section F of the BIoH are:

1) Standing up for more than 30 minutes.
2) Sitting in a chair for more than 30 minutes.
3) Standing up after sitting for more than 30 minutes.
4) Climbing several flights of stairs.
5) Going down several flights of stairs.
6) Walking at your own pace for a few miles.
7) Walking briskly for a few miles.
8) Wandering around shops or museums.
9) Bending or twisting.
10) Squatting.

People completing the questionnaire are asked to rate the above activities on a 5 point scale from 'No discomfort' to 'Could not do it'[19]. In theory, the list of ten activities listed above would be an ideal selection, however it would not be feasible to ask participants to perform all the tasks in a single testing session for several reasons:

- A symptom of JHS is increased fatigue[129], so if asked to perform a large number of activities, fatigue would become a confounding factor.
- Asking participants to perform all tasks would likely cause some participants discomfort/pain. Therefore, consideration is required to ensure that useful data is obtained whilst minimising participant discomfort.
- Testing all activities would take considerable time, which would not be feasible and may mean potential volunteers avoided the study.
- Participants with more severe JHS may not be able to complete some of the more demanding activities, as evidenced by the 'Could not do it' option in the BIoH questionnaire. Inclusion of the more demanding activities may cause people with severe symptoms to avoid the study, causing selection bias.

For the above reasons, it was necessary to select a range of activities that: 1) Would be logistically possible for volunteers to perform in a testing session. 2) That most people with JHS could perform (to reduce selection bias), but would find demanding enough for differences in movement to be measured. 3) Potentially provide useful information about movement that could aid healthcare professionals. 4) Have outcomes that are measurable using 3D motion analysis equipment and using a realistic sample size.

In deciding which activities to investigate, data from a priori testing, advice from physiotherapists, input from people with JHS, results of the BIoH questionnaire, findings from the systematic review, and the results of the reliability study were collated. As a result, four activities were chosen. These activities and the rationale for choosing them are described here. Each activity and specific aims and methods are described in more detail in their respective chapters.

Balance perturbations. Whereas balance has been measured in JHS cohorts during standing, dynamic postural responses to perturbation have not yet been measured. Although this activity was not specifically mentioned in the BIoH, it is interesting in terms of balance control. When a person's balance is perturbed, the central nervous system must sense the direction and magnitude of the perturbation, and initiate a sufficient muscular response to maintain the body's centre of mass over its base of support. Given the joint instability[6], reduced proprioception[43,130], muscle weakness[39], and differences in reflexes[130] of people with JHS, it is possible that this response to perturbation will be insufficient. This activity is particularly interesting given that JHS is associated with increased fall risk, fear of falling, and impaired balance[46]. Given the increased risk and fear of falling, a reason for this may be that their balance reactions are lacking and they are less able to respond to disturbances in balance equilibrium. Disturbing posture and recording reactions to these disturbances is a useful tool in understanding control of posture[131].

Prolonged standing. JHS is associated with decreases in a variety of physiological factors that may affect how people with JHS behave during prolonged standing; balance, fatigue, joint-instability, proprioception, and differences in the circulatory system. Two items of the BIoH questionnaire may be considered to be similar; "Standing up for more than 30 minutes" and "Wandering around shops or museums". They are similar in that wandering around shops and museums involves a considerable amount of standing, interspersed with periods of low velocity gait. The inclusion of prolonged standing activities in the BIoH means that the activity has a relatively large impact on people with JHS, and in talking with JHS patients prior to the study, activities such as queuing, shopping, and standing around were often identified as painful activities. How people move during standing can affect pain[132], The difficulty people with JHS have with standing alludes that it is an activity where differences might become apparent between JHS, GJH, and NF groups.

There are several studies that have investigated standing posture in hypermobile cohorts, in terms of both balance[45,46], and muscular control[101]. These studies have found impaired balance in JHS[45,46], and potentially a different strategy in muscular control in a GJH cohort[101]. Rombaut *et al.*[46] found

increased fall frequency and impaired balance in people with JHS, and state the results imply "a decrease in the safety of standing in everyday life situations.". Therefore, by including prolonged-standing as an activity, we aim to see how this deficiency in balance manifests during an activity of daily living.

Gait. Although the majority of studies which have investigated movement in hypermobile cohorts have measured gait, the results of these studies were not consistent[82]. Potential causes of this inconsistency could have been a lack of statistical power, which was addressed in Chapter 3, the large number of outcome measures used between studies, and/or the fact that GJH and JHS cohorts have not been compared in the same testing session. As a result there is a lack of information about lower limb kinematics and kinetics during JHS gait. In addition, no studies have measured EMG during JHS gait, which is surprising given the connection of co-contraction to joint stability. For this reason, there is a need to compare the gait of JHS, GJH and NF groups.

Although the BIoH identified "Walking at your own pace for a few miles" and "Walking briskly for a few miles", it was not feasible to measure miles of participant walking in the gait lab. Furthermore, to aid comparison with other clinical gait studies, a more typical protocol and distance was used (detailed information in Chapter 7).

Stair climbing. Stair ascending and descending was selected as an activity as it is specifically mentioned in Section F of the BIoH[19]. In addition, Luder *et al.*[104] has compared ground reaction forces and EMG parameters between GJH and NF groups; they did not observe any significant differences between groups. During stair ascent the muscles must work to raise the centre of mass and knee joint moments can be 25% greater than during level gait[134]. Accelerometer-measured shockwaves caused during stair descent are 2.5 times greater than level gait[135], and the muscles must work to support and stabilise the knee[104]. Given that stair climbing is much more of a demanding activity than level walking, it seems feasible that any impairments in the JHS group would become more apparent, which might help physiotherapists target these differences.

General procedure

All testing reported in Chapters 5, 6, 7 and 8 took place during a single session for each participant at the movement analysis laboratory at Charing Cross Hospital, Imperial College Healthcare NHS Trust. Informed written consent was obtained from all participants and the study protocol was approved by the NRES London-West Ethics Committee (reference number 13/LO/0270).

Sample size was calculated from the reliability study (Chapter 3) and was based on knee flexion/extension angle. The sample size calculation was based upon recruiting to three groups; JHS, GJH and NF. With a standard deviation of 2.4°, 20 participants per group were required to reach sufficient power ($\beta = 0.8$) and significance of 0.05. JHS participants were recruited from the physiotherapy department of Charing Cross Hospital, through the Hypermobility Syndromes

Association and Ehlers-Danlos Support UK. GJH participants were recruited from posters placed in Charing Cross Hospital, Imperial College campuses, and local yoga, gymnastics, running, and dance clubs. NF participants were recruited from posters in the same locations, and staff/students of the Department of Surgery and Cancer, Imperial College London.

JHS and GJH were classified using the Brighton Criteria[136]. People with JHS fulfilled the Brighton Criteria where as people with GJH did not fulfil the Brighton Criteria. People with GJH were further classified using the Beighton Score; a score ≥4 was considered as GJH, and a score <4 as normal flexibility[136]. In addition, since we were particularly interested in lower limb kinematics, those in the GJH and JHS group had to score positively for at least one of their knees showing hypermobility. Similarly, NF participants were excluded if they had a Beighton Score <4 , but either of their knees were hypermobile.

Inclusion criteria for all groups were people who could walk unshod and unaided for more than 6 metres, and aged between 18 and 55 years of age. The upper age limit was specified to limit structural joint changes due to arthritis, and the fact that flexibility diminishes with age[137]. Exclusion criteria were neurological or other rheumatological diagnoses or musculoskeletal disorders and pregnancy. NF and GJH participants were additionally excluded if they had any lower-limb joint conditions at the time of testing.

Pain was assessed by two methods. Firstly participants were asked to shade any areas of pain on a map of the body, showing both anterior and posterior aspects. Additionally, participants rated the severity of pain in both of their knees by placing a mark on a visual analogue scale[138]. Leg dominance was determined using a modified version of the test used by Vaunik *et al.*[139], the questions were (1) What foot would you use to kick a football? (2) What foot would you use to draw a diamond on the floor? (3) What foot would you use to stamp on a bug. The dominant leg was defined as the one used in two or more of the tasks.

Reflective markers were affixed to participants' skin as per the method reported in Chapter 3. All movement were recorded with a 10 camera VICON (Oxford Metrics Ltd., Oxford, UK) motion capture system. A wireless EMG system (Myon AG, Schwarzenberg, Switzerland) was used to measure lower limb muscle activity. Eight EMG electrodes (AMBU neuroline 720) were attached to one of the legs using SENIAM guidelines over the following muscles; tibialis anterior, gastrocnemius, rectus femoris, rectus medius, rectus lateralis, bicep femoris, and gluteus medius. For the JHS group the leg with the greater knee pain was selected for EMG analysis. For GJH and NF groups, the dominant leg was selected.

In comparing EMG between people, it is necessary to normalise the EMG signal, as the intensity of the signal will vary depending on electrode placement and participant characteristics (for example fat and hair)[140]. There are a myriad of methods of normalising EMG data, perhaps the most common are the peak dynamic method, and the isometric maximum voluntary contraction (MVC) method[141]. In the peak dynamic method, the EMG is normalised to the peak value recorded during the

activity. A problem with using this method, is that it does not provide any information about the degree to which the muscle in question is contracting[142]. In the MVC approach, a muscle's maximal EMG activity is recorded whilst the participant performs a maximal isometric contraction. This allows the activity of each muscle to be expressed as a percentage of its maximum, which reduces the inter-person variability[143]. Although there are different researchers who advocate each method, on balance the MVC method seems the most effective at reducing the variability between individuals and producing reliable results[141]. For this reason, the MVC method was used. The method used to obtain MVCs was as follows:

- Tibialis anterior. Participant supine with back supported at approximately 45° and a support under the knee causing slight knee flexion. Participants were asked to generate an isometric MVC by resisting the researcher who applied a plantarflexion force to the forefoot.
- Gastrocnemius. Participant laying prone with a support under the ankle to cause a small amount of knee flexion. The participants were asked to generate an isometric MVC by resisting the researcher who applied a dorsiflexion force through their sole.
- Quadriceps. Participant sat on the end of a bench with the lower limbs dependant (keeping knee in 90° flexion). The participants were asked to generate an isometric MVC by resisting the researcher who applied a flexion force against the lower anterior tibia of the participant. The participants were asked to push against the researcher with the knee in neutral rotation, rotated medially, and rotated laterally to bias the contraction to the rectus femoris, vastus medialis and vastus lateralis muscles respectively.
- The same position was used to measure MVC for the hamstrings as was used for the quadriceps; instead of pushing, participants were asked to pull against an extension force applied to the heel.
- Gluteus medius. The participant was instructed to lay on the side of their non-test limb with their test limb raised slightly into abduction, with the hip in neutral flexion/extension and with the knee in a small amount of flexion. To ensure the Gluteus medius was being recruited, their pelvis was stabilised to ensure it was not rotated too far anteriorly or posteriorly. The participants were asked to push into abduction against the researcher pushing down on the thigh.

Participants then performed the four tasks in the following order; perturbation task, walking, prolonged standing and stair climbing. Detailed descriptions of the protocol, method, outcome measures, and data analysis for each task, is given in the respective chapters. The entire testing session was conducted unshod.

Statistical analysis for each activity was undertaken in SPSS. The specific tests used are described in each individual chapter.

Chapter 5: Adaptation of postural reactions following anterior perturbations in people with Joint Hypermobility Syndrome.

5.1 Introduction

As discussed in the preceding chapters, the symptoms and presenting features of JHS are diverse. One of the features of JHS is impaired balance[46], this impairment could be caused by several factors of JHS; neurophysiological differences[37], muscle weakness in knee extensors[144], pain[33], reduced proprioception in the lower limbs[41,43,145], increased reflex latency[130], and joint instability[4]. These factors may combine to affect the ability of JHS individuals to respond to unpredicted perturbations by making the necessary postural adjustments, which is particularly relevant considering people with JHS are more likely to suffer falls; in a study by Rombaut *et al.*[46], 95% of JHS participants had fallen in the previous 12 months.

In the context of balance used in this chapter, The Merriam-Webster dictionary describes stability as "the quality, state, or degree of being stable: such as the property of a body that causes it when disturbed from a condition of equilibrium... to develop forces or moments that restore the original condition."[146]. To balance effectively a person must keep their centre of mass within their base of support. When a person's balance is perturbed the body centre of mass moves in relation to its base of support, and postural adjustments are required to normalise the position of the centre of mass. To achieve this, it is necessary for a person to sense the direction and magnitude of the perturbation, and make the necessary postural adjustments to correct the position of the centre of mass[147]. Key to these postural adjustments is functional joint stability. Functional joint stability is dependent on the relationship of the articulating surfaces of bones, muscles, ligaments and tendons, and the central nervous system's ability to integrate sensory information from vestibular, visual and proprioceptive sources[148,149]. Given the many features of JHS that relate to these factors, it seems likely that ability to correct their posture following a perturbation will be impaired. EMG and kinematic measurements of postural response to perturbations have been used to assess other groups; elderly[147,150–152], intellectual disability[153], Huntington's disease[154], Parkinson's disease[155], and in healthy adults[156]. To our knowledge no study has tested the ability of people with JHS to respond to a postural perturbation. Recording a person's response to a postural perturbation can give information about the control of balance[131]. Therefore, the aim of this study was to compare postural responses of JHS individuals following a forward perturbation, with those of people who are hypermobile without symptoms (GJH) and people with normal flexibility (NF). Specifically:

- Can people with JHS recover their balance as effectively as controls following perturbations?
- Do people with JHS have different muscular responses following perturbation?

- Can people with JHS learn/adapt/improve their balance reactions with repetition?

5.2 Methods

5.2.1 Participants

The participant groups and their characteristics are reported in Chapter 4.

5.2.2 Testing procedure

Reflective markers were affixed to the participants' lower limbs and pelvis, as described in chapter 4. EMG electrodes were affixed to the lower limbs as per Chapter 4. Trials were recorded using a 10 camera Vicon (Oxford Metrics Ltd., Oxford, UK) which synchronised kinematic and EMG data. Kinematic data was sampled at 100Hz, EMG data at 1000Hz.

A custom platform measuring 120cm × 120cm (Figure 5.1) was developed capable of producing perturbations in four directions. For this study, only forward perturbations (where the platform moves to the anterior of the participant) were used as they have been reported by participants to be the most difficult[11]. Furthermore, in a priori testing, clear responses were observed at lower perturbation acceleration than mediolateral or posterior perturbations. An accelerometer (sampling at 1000Hz) was attached to the platform and synchronised to EMG and kinematic data using the Vicon system. Perturbation start time was determined from visual inspection of the accelerometer data.

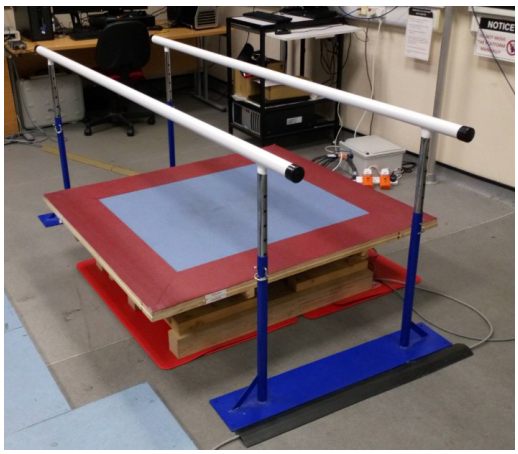


Figure 5.1. The perturbation platform used in this study.

Participants were asked to stand on the platform with their feet hip-width apart and their arms by their sides. The position of the feet was marked on the platform; if a participant needed to take a step to balance following a perturbation, they were asked to return to the same starting position.

Participants wore a shoulder harness attached to the ceiling and had parallel bars available should they need to balance to save them from a fall. Participants reported that neither shoulder harness nor bars impeded movement. Participants were told that the platform would move forwards in relation to them, they were not told the exact timing of the perturbations to limit anticipatory responses. Six perturbations were performed, with 3-10 seconds between each perturbation. The translation distance was 4.0cm, time 0.2 seconds; the perturbation consisted of an acceleration to peak velocity at 0.1 seconds, followed by a deceleration phase to stopping. The perturbation characteristics were chosen so the displacement and velocity/acceleration were large enough to initiate a response from the participant, but low enough to reduce the risk of a fall. These parameters were determined during the building and testing of the platform, and from other studies of balance perturbation[147].

A recovery step was recorded if the participant performed a step with either foot within 1 second of perturbation start. This was determined visually from playback of the kinematic data within Vicon Nexus.

A MatLab (The MathWorks, Natick, United States) function was written to process EMG and kinematic data. EMG data was band-pass filtered between 20 and 500Hz and full-wave rectified. EMG variables analysed were onset latency, time-to-peak amplitude of the rectified response, and integrated EMG (iEMG). A muscle was considered active if its rectified EMG intensity was greater than 2 standard deviations above its mean intensity during the 200ms prior to perturbation onset. Onset latency was defined as the time taken for a muscle to become active from perturbation onset. Time-to-peak was defined as the time taken for a muscle to reach peak amplitude from muscle onset. iEMG was calculated by dividing the area of muscle intensity between onset and off-set, by the area below the mean background EMG:

$$iEMG_{muscle} = (iEMG_{interval} - iEMG_{baseline}) / iEMG_{baseline}$$

Unfortunately, it was not possible to compare groups on all aspects of the amplitude of their EMG normalised to maximal voluntary contraction (MVC). This was due to the fact that in the JHS group the EMG amplitude recorded during a MVC was much lower than the amplitude recorded following a perturbation. The objective of performing a MVC is to obtain the maximum possible EMG amplitude, allowing a muscle's activity during the task of interest to be expressed as a percentage of MVC, and allowing comparisons between individuals or groups. In some participants the EMG amplitude following perturbation was three times greater than that produced from the MVC. It is well known that people in pain may not be able to produce MVCs, and that the MVC normalisation method may not be appropriate in pain cohorts[157].

Kinematic data was low-pass filtered at 15Hz. Kinematic variables analysed were the cumulative sum of change in angle (CA), and time-to-reversal (TTR), for ankle dorsiflexion/plantarflexion, knee extension/flexion, and hip extension/flexion. These were analysed from perturbation onset to 1 second

post perturbation. The period of 1 second was chosen from visual inspection of participants' kinematic data after the perturbation. The limb that was instrumented for EMG was used for analysis.

Typically, in studies of postural responses following perturbation, the greatest adaptation is found between the 1st and 2nd perturbation (P1 and P2). Here, the difference within groups between the 1st and 2nd perturbation to measure initial adaptations, and between the 2nd and 6th perturbations (P6) to determine if groups continued to adapt their response, were analysed. A Sharpiro-Wilks test was used to test variables for normality. EMG parameters were not normally distributed; a Kruskal-Wallis test was used to test for significant difference between medians, and Mann-Whitney U tests used for pair-wise comparisons. The Bonferroni method was used as a post-hoc test for multiple comparisons. Kinematic parameters were normally distributed. A mixed design ANOVA test was used to test for significance between groups and perturbations. Where Mauchly's Test of Sphericity was violated Greenhouse-Geisser adjustments were made. Where significant differences were found, these were investigated by pairwise comparisons and a Bonferroni correction applied for multiple comparisons.

5.3 Results

5.3.1 Participant characteristics.

Three cohorts were recruited in this study; 23 people with JHS, 23 people with GJH without joint pain, and 22 people with normal flexibility without joint pain (see Chapter 3 for an explanation of sample size). Participant characteristics are shown in Table 5.1. There were no adverse events during any of the tasks.

	JHS (n=23)	GJH (n=23)	NF (n=22)
Age (years)	33±9	28±6	28±5
Sex (f/m)	20/3	19/4	16/6
Height (cm)	169±8	169±10	172±8
BMI	25.5±5.6	22.9±4.4	22.0±2.8
Beighton Score	**6.8±2.1**	**6.6±1.3**	**0.3±0.7**
Visual analogue score knee pain, scored from 0-10.	**3.2±2.2**	**0.0±0.0**	**0.0±0.0**

Table 5.1: Participant characteristics. Significant differences found in Beighton Score between JHS / GJH and NF and in pain between JHS and NF /GJH . Rows highlighted in bold indicate there was a significant difference between groups.

There were no significant differences between groups in sex (p=.463). Similarly, there was no significant differences between groups in age, height, or BMI. The NF group has a significantly lower Beighton Score than JHS (p<.001) and GJH (p<.001), but there was no significant difference between JHS and GJH (p=1.000). The JHS group had a significantly greater VAS score than GJH (p<.001) and NF (p<.001), whereas there was no significant difference between GJH and NF (p=1.000).

Typically, joint hypermobility is defined as "a range-of-motion that would be considered greater than normal for a given age, ethnicity, or gender"[22]. Whereas all the studies of movement reviewed in chapter 2 listed participant ages and gender, none reported on the ethnicity of the cohorts. Given that the incidence of hypermobility varies with ethnicity, it seems good practice to report the ethnicity make-up of cohorts to aid interpretation of results and facilitate comparisons with other studies. The ethnicity of participants is shown in Figure 5.2.

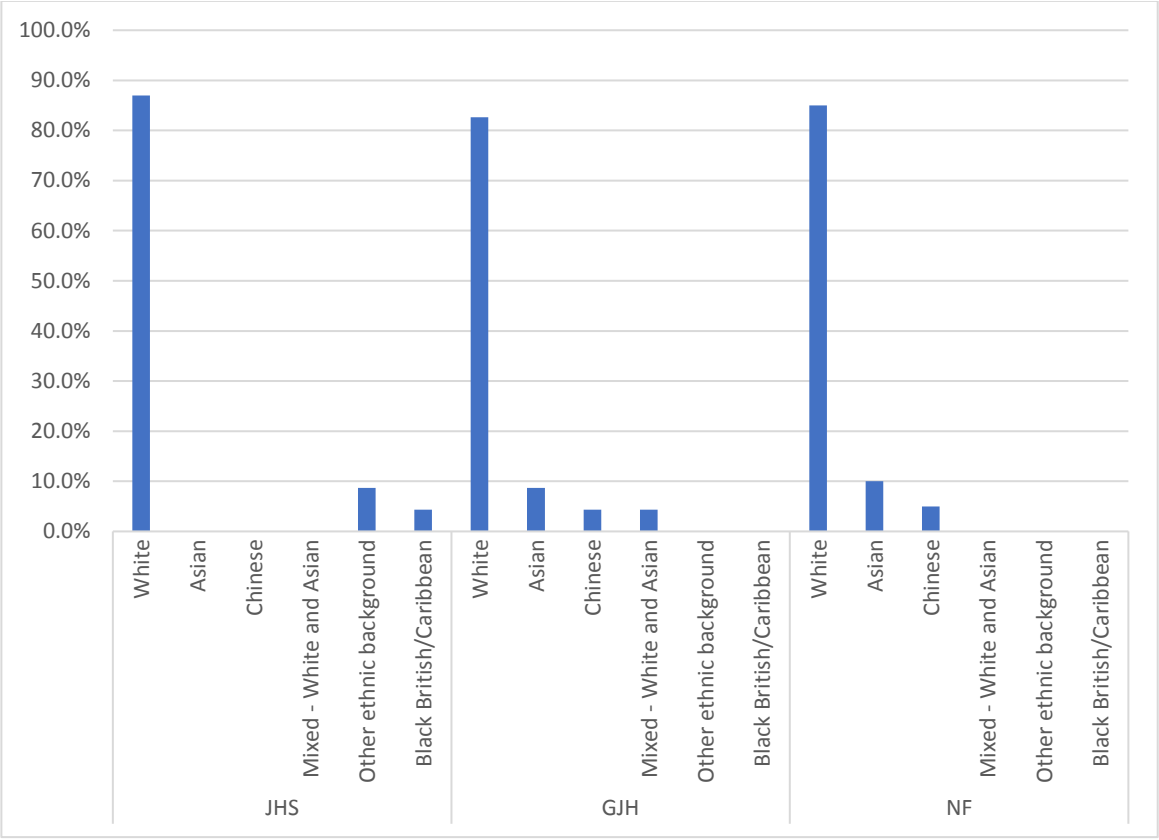


Figure 5.2. Ethnicity percentages for each cohort that took part in the study.

Sites of pain are shown in Figure 5.3. The most common site of pain was the knee, which although was one of the inclusion criteria for JHS participants, all JHS volunteers who volunteered presented with knee pain, and none were excluded from the study for not having knee pain. The median number of pain sites was 7, with an interquartile range of 4-9.

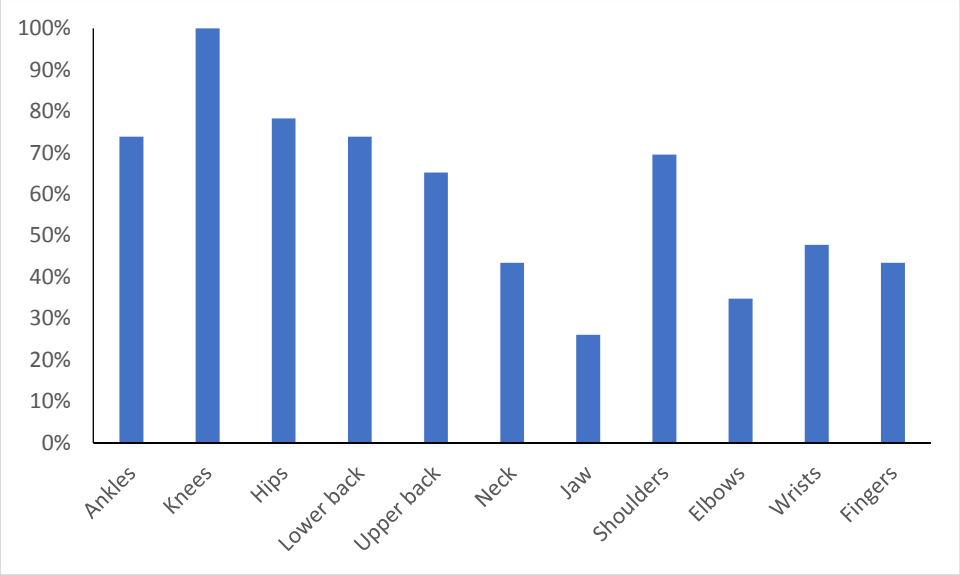


Figure 5.3. Joint pain sites and the frequency of JHS participants who experienced pain at these sites.

5.3.2 Perturbation results

One JHS participants was unable to perform the perturbation task, and another was too uncomfortable to continue after the third perturbation due to fear of falling, meaning our JHS sample size for analysis was reduced to 21 participants.

Percentages of participants who took a recovery step following perturbation are shown in Figure 5.4. A greater proportion of JHS participants took a recovery step on the 1st perturbation (P1). The majority of JHS participants did not perform a recovery step from P2 onwards, with the exception of two participants who performed steps up to P4, and one participant who consistently performed a step on every perturbation. One GJH participant also performed a recovery step on every perturbation, and one NF participant performed a recovery step on P1.

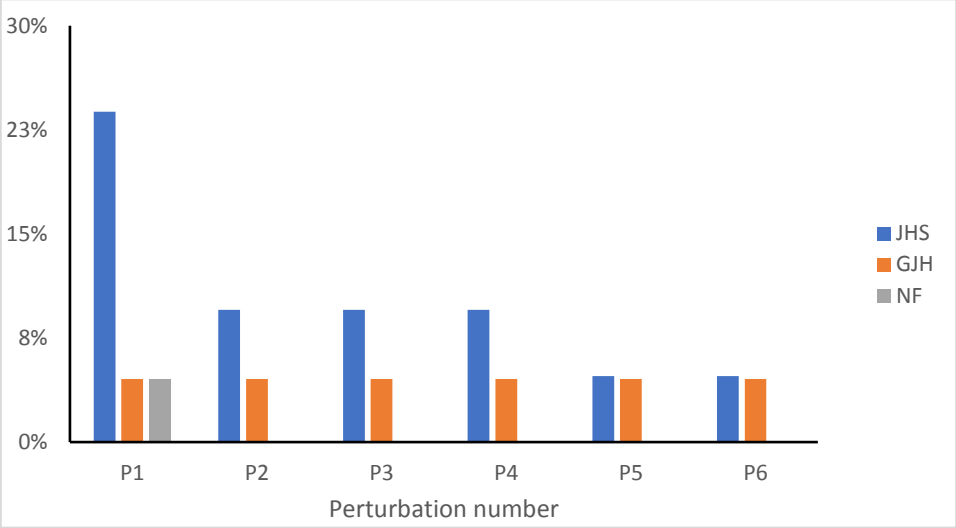


Figure 5.4. Percentage of participants who took a recovery step following a perturbation.

EMG parameters

For the parameters muscle onset, time-to-peak, and iEMG the results were not normally distributed; medians and quartiles are shown in Table 5.2.

For muscle onset, the only significant difference between groups was in Rectus Femoris onset, which was later at P1 (p=.033) in the JHS group, although no significant differences were observed in the pairwise tests after correcting for multiple comparisons.

For muscle time-to-peak, significant differences were observed in P1 for TA, GM, RF, VM, VL (Kruskal-Wallis p values .025, .001, .007, .026, and .002 respectively). After Bonferroni adjustments were made on pair-wise comparisons, JHS time to peak was significantly later than NF in TA (p=.020), RF (p=.002), VM (p=.011), and VL (p=.002), and significantly later than GJH in GM (p=.001) and VL (p=.008). There were no significant differences between JHS and NF groups for P2 and P6 perturbations; the JHS group time-to-peak had reduced such that it was similar to NF. At P6 the later time-to-peak only persisted in GM (p=.003) between JHS-GJH groups (p=.007). There was no significant difference between GJH-NF at any perturbation.

iEMG did not differ over the sequential perturbations or between groups. No significant differences were found between groups in any of the muscles investigated at any perturbation number.

Table 5.2

		P1			P2			P6		
		JHS	**GJH**	**NF**	**JHS**	**GJH**	**NF**	**JHS**	**GJH**	**NF**
TA	Onset (ms)	88(79.3,96)	86(76,99)	88(82,99)	89(80.8,93.5)	88.5(75,97)	87.5(76,103)	88(79.5,94.3)	84(73,91)	79(76,89)
	TTP (ms)	**175(119,298.5)†**	119(72,152)	**101(74,135) †**	103(85.5,149.3)	99(75,138)	89(62,117)	108(83.8,134.8)	93.5(73,121)	102(82,119)
	iEMG	13.1(10.4,18.5)	15.1(9.3,20.2)	16.5(10.3,21.8)	14.4(10.3,19.8)	11.9(6.6,17.4)	11.9(8.5,17.6)	10.8(6.9,16.5)	10.6(7.7,14.8)	12.1(8,17.6)
GM	Onset (ms)	130(113.5,148.5)	116(101,135)	130.5(111,148)	131(101.3,154.3)	113(85,135)	128(114,153)	134(68.5,151)	128(89,147)	129(105,152)
	TTP (ms)	**167(103.8,226.5)***	**78(63,84)***	93.5(68,129)	89(75,149.8)	79.5(35,101)	70.5(56,89)	**89(45.8,136.5)***	**51.5(22,82)***	60(30,71)
	iEMG	2.6(2.1,5.6)	2(1.3,3.6)	2.3(1.6,3.8)	2.6(1.8,5.3)	1.7(0.5,3.2)	1.8(1,3.3)	1.2(0.8,3.1)	1(0.7,1.9)	0.9(0.7,1.8)
RF	Onset (ms)	117(108,123.5)	110(100,118)	119(102,126)	116(99,130.3)	110(88,121)	113.5(102,126)	107(87,124.3)	108(96,118)	112(97,121)
	TTP (ms)	**153(109.5,196.5)†**	99(81,140)	**82(75,107) †**	115(84,231.3)	86(69,99)	93(74,104)	81(59.5,140.3)	80.5(70,94)	79(71,89)
	iEMG	6.1(3.6,8.1)	6(3.9,9.3)	8.1(4.8,11)	4.6(3.1,7.1)	3.8(2.8,5.9)	5(3.4,6.8)	3.5(2,7.6)	3.4(2.3,6.4)	3.7(2.4,6.3)
VM	Onset (ms)	121(110,128.5)	118.5(105,141)	126(109,147)	118(99.5,136)	116(100,149)	114.5(97,133)	123(92.3,129.3)	115.5(94,147)	115.5(90,137)
	TTP (ms)	**133(77,240)†**	117.5(83,150)	**85.5(68,100) †**	93(61.8,196)	88(74,114)	70(45,101)	78(46.3,211.8)	70(56,99)	56(25,85)
	iEMG	5.5(3.3,7)	4.8(3,7.9)	3.5(1.6,4.8)	3(2.2,5.2)	2.4(1.5,4.7)	2.1(0.8,4.6)	2.5(0.9,4.6)	2.1(1.1,2.9)	1.5(0.9,4)
VL	Onset (ms)	114(109.3,132)	106.5(94,114)	112.5(102,123)	116(103.5,137.8)	109.5(89,127)	116(98,126)	116(99.8,123.5)	99.5(92,127)	104(91,120)
	TTP (ms)	**193(114.5,292.3)†**	90(73,125)	**95(77,122)†**	140(85,192.3)	88.5(72,112)	88(72,101)	79(61.5,147.5)	76(66,84)	82.5(68,93)
	iEMG	5.7(4.2,7.5)	3.5(2.6,7.5)	4.4(3.1,5.9)	3.9(3.2,5.6)	2.3(2.1,3.4)	3.2(2.2,4.3)	2.2(1.3,4.3)	2.5(1.8,4.9)	2.2(1.7,4.5)

Table 5.2 continued

		P1			P2			P6		
		JHS	GJH	NF	JHS	GJH	NF	JHS	GJH	NF
BF	Onset (ms)	106(97.8,119.8)	95.5(82,121)	108(82,134)	110(103,120)	96(78,117)	103(88,128)	106(92.5,141)	104.5(83,123)	102.5(66,134)
	TTP (ms)	105(82.8,219.8)	100(61,167)	99.5(69,150)	127(81.5,156.3)	89(66,123)	102(84,148)	69(53.8,101.5)	70.5(45,87)	77(53,88)
	iEMG	5.4(2.9,7.2)	2.6(2,5.7)	3.6(2.5,4.8)	3.9(2.1,8.7)	2.3(1.4,4.8)	2.5(2,5.5)	2.3(1.3,4.2)	1.8(0.9,3)	1.7(1,2.6)
ST	Onset (ms)	99(92.8,111.3)	91(84,115)	92.5(75,153)	110(88.3,128.3)	91.5(71,110)	105.5(63,134)	120(84.3,141)	112.5(86,133)	86(59,142)
	TTP (ms)	86(69.3,151)	91(66,194)	100(72,163)	98(72,129.3)	85(56,131)	81.5(57,119)	67(40,83)	61.5(44,84)	82.5(39,104)
	iEMG	5.3(2.7,7.9)	3.6(1.9,5.3)	4(2.1,6.4)	3.6(1.9,5.4)	2.8(1.4,4)	2.1(1.1,2.9)	2.1(1,4.1)	1.8(1,2.5)	1.5(0.9,2)

Table 5.2. Median (1st quartile, 3rd quartile) for EMG parameters. Onset and TTP are in milliseconds. TA = Tibialis anterior, GM = Gluteus medius, RF = Rectus femoris, VM = Vastus medialis, VL = Vastus lateralis, BF = Biceps femoris, ST = Semitendinosus. P*(i)* = perturbation number. * = significant difference between JHS and GJH, † = significant difference between JHS and NF. Significance set at P<=.05 (see text for exact p values) and Bonferroni corrections were made for multiple comparisons.

Kinematic parameters

In terms of kinematics the same initial response was seen across all participants. As the platform moves forward, the feet move with it and combined with the inertia of the lower limbs, caused plantarflexion at the ankle, and flexion at the hips and knees. Time-to-reversal (TTR) is the time taken for the participant to reverse these initial responses to perturbation.

There was no significant difference between groups for TTR for any joint at P1, P2 or P6 (Table 5.3.). Furthermore, there was no significant difference within groups between P1, P2 and P6.

		JHS	GJH	NF
P1	Hip	27±8	26±8	28±7
	Knee	31±7	29±5	27±4
	Ankle	32±5	32±6	31±8
P2	Hip	27±5	27±5	29±13
	Knee	27±6	30±6	26±5
	Ankle	27±6	30±6	32±9
P6	Hip	27±6	27±7	27±12
	Knee	30±5	29±5	28±7
	Ankle	32±11	32±7	33±12

Table 5.3. Time-to-reversal mean ± standard deviation (milliseconds). There were no significant differences between groups or between perturbations.

In all groups, the first perturbation elicited the greatest magnitude of cumulative angle (CA). The greatest difference between perturbations was between P1 and P2, and differences between subsequent perturbations relatively smaller. See Table 5.4 and Figure 5.5 to 5.7 for a summary of the results. Although differences were compared at P1, P2, and P6, data for all perturbations is displayed in Figure 5.4, to include as much data as possible and show the overall pattern.

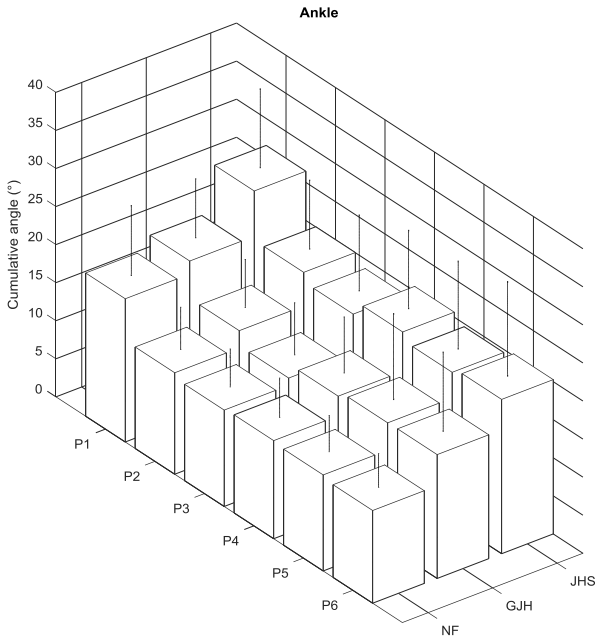


Fig 5.5: Mean cumulative angle ± SD following perturbation for the ankle joint. NF is Normal Flexibility, GJH is Generalised Joint Hypermobility, JHS is Joint Hypermobility Syndrome. P*(i)* = perturbation number.

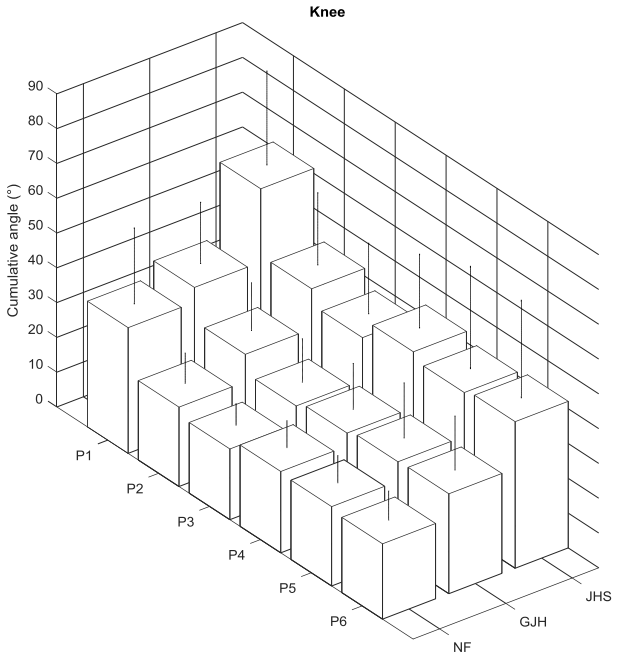


Fig 5.6: Mean cumulative angle ± SD following perturbation for the knee joint. NF is Normal Flexibility, GJH is Generalised Joint Hypermobility, JHS is Joint Hypermobility Syndrome. P*(i)* = perturbation number.

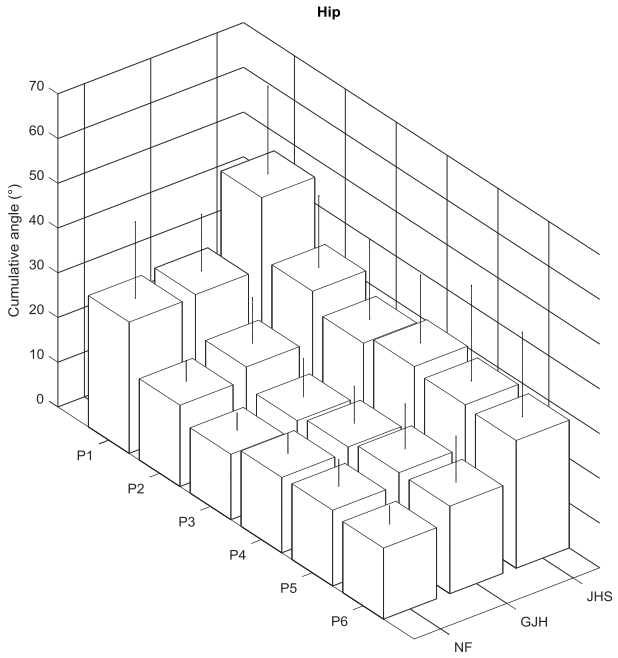


Fig 5.7: Mean cumulative angle ± SD following perturbation for the hip joint. NF is Normal Flexibility, GJH is Generalised Joint Hypermobility, JHS is Joint Hypermobility Syndrome. P*(i)* = perturbation number.

		JHS	GJH	NF
P1	Hip*†	45.8±20.3°	29.8±13.1°	29.3±17.7°
	Knee*†	61.4±28.0°	40.4±18.3°	36.1±22.6°
	Ankle†	26.5±10.8°	20.5±8.1°	18.8±9.6°
P2	Hip*†	32.3±16.7°	21.0±10.6°	18.2±5.0°
	Knee†	42.2±21.6°	30.7±14.3°	22.8±9.1°
	Ankle†	20.0±9.4°	15.6±6.6°	13.3±5.8°
P6	Hip†	28.6±19.6°	19.6±10.8°	15.6±4.5°
	Knee†	42.1±29.1°	28.7±16.1°	21.4±8.6°
	Ankle†	20.3±12.9°	16.3±10.8°	12.1±4.5°

Table 5.4: Mean cumulative joint angles ± standard deviation. * = significant difference between JHS and GJH, † = significant difference between JHS and NF, ^ = significant difference between GJH and NF groups. Significance set at P<.05 and Bonferroni corrections were made for multiple comparisons.

There was a significant difference between groups (p=.001), and significant differences within groups across P1, P2 and P6 (p<.001). Following up on this interaction, JHS had significantly greater CA than NF at P1 (p=.042), P2 (p=.000), and P6 (p=.018), and significantly greater CA than GJH at P1 (p=.041) and P2 (p=.003), but not at P6 (p=.118). There was no significant difference between GJH and NF groups at any perturbation number. Within the JHS group, P1 CA was significantly greater than P2 (p=.022), and P2 CA significantly greater than P6 (p=.011). In GJH and NF groups, P1 CA was significantly greater than P2 (p .033 and .004 respectively), but no significant difference between P2 and P6 (p=.743 and .608 respectively).

There was a significant difference between groups (p=.001), and a significant difference within groups across P1, P2 and P6 (p<.001). JHS had significantly greater CA than NF at P1 (p=.009), P2 (p=.000), and P6 (p=.009), and than GJH at P1 (p=.035) and P2 (p=.028), but not at P6 (p=.134). There was no significant difference between GJH and NF groups at any perturbation. In the JHS group P1 CA was significantly greater than P2 (p=.001), but there was no significant difference between P2 and P6 (p=1.0). The same pattern was observed in GJH and NF groups, in each group P1 CA was significantly greater than P2 (p=.037 and .002 respectively), but there was no significant difference between P2 and P6 (p=1.0 and 1.0 respectively).

There was a significant difference between groups (p=.017), and a significant difference across P1, P2 and P6 (p<.001). The only significant difference observed between groups was at P2, where the JHS group had significantly greater CA than NF (p=.006). In all groups P1 CA was significantly greater than P2 (p=.004, .001 and .000 for JHS, GJH and NF respectively), and no significant difference between P2 and P6 in any group.

5.4 Discussion

To stop a fall following a perturbation, a person must retain their centre of mass over their base of support. This can either be achieved through muscular contractions only, and keeping the same base of support, or by taking a step and increasing the base of support area[147]. Although the perturbation characteristics in this study could be considered as moderate (only one NF participant took a recovery step), more JHS individuals took a recovery step on the first perturbation than NF or GJH participants. This indicates that they either have impaired ability to perform the muscular response necessary to counter the perturbation, or they are more anxious of falling and take a step 'just in case'. Although a relatively high proportion of JHS participants took a recovery step at P1, only one JHS participant took a recovery step for P2-P6. This shows that JHS participants were able to 'learn' to improve their postural response, or were less afraid of falling and so deemed a recovery step unnecessary.

Our results conform with those of other studies of postural perturbations, where postural reactions were found to occur between 70 and 180ms post perturbation[158,159]. Some studies of perturbation response in other patient cohorts have shown differences in muscle onset timing (for

example de Freitas *et al.*[147] and Hale *et al.*[160]), but here we did not find any significant difference in muscle onset times. The delays in onset of postural responses observed in other cohorts have been attributed to several potential impairments; reduced function of the somatosensory system[161], slowed spinal cord conduction, or a delay in central processing[21]. Despite people with JHS having reduced proprioception[27], and deficiencies in the neurophysiological system[8], they were able to initiate a muscular response to the same timing as healthy individuals. This indicates that these mechanisms are not impaired to a degree that would affect the ability of JHS patients to initiate a timely muscular response. If differences in onset latencies were observed at the first perturbation, but were then reduced to normality, then it could be argued that an impairment is being compensated for. However, no significant differences in onset latencies were observed at P1 between any of the groups.

Where significant differences did arise, these were in time-to-peak parameters in anterior leg muscles and gluteus medius, and in cumulative angle. Hughes *et al.*[20] states that the TA and quadriceps muscles are used to arrest and stabilise movement following forward perturbation. It is therefore interesting that it was in these muscles where significant differences were found between JHS-NF groups and JHS-GJH. At P1 the JHS group took significantly longer to reach peak muscle intensity in the TA and quadriceps muscles, this is combined with a significantly larger CA in all joints at P1. The fact that the muscles used to stabilise forward momentum take longer to reach peak intensity, may explain the relatively large difference in CA between JHS and NF/GJH groups at P1; JHS participants are taking longer to produce a peak force, and so are less able to arrest the momentum of the centre of mass.

Whereas onset latencies are a common outcome measure in studies of postural response, time-to-peak (TTP) is reported less frequently. Delays in TTP have been observed in an elderly cohort; De Freitas *et al.*[11] hypothesized that the delayed TTP results they observed were due to differences in the ratio of Type I to Type II muscle fibres. In addition, the delay could be a difference in the recruitment of Type I and Type II fibres. To date, there has not been an investigation of the composition of muscles in JHS, at least in terms of the ratio of Type I/Type II fibres. In terms of the pattern of recruitment, Henneman's size principle states that during an increasing isometric contraction, type I fibres have a lower activation threshold than Type II, and so are activated first[29]. A delayed TTP could therefore be explained by type I fibres predominating in these postural corrections. The force generated by a muscle is also dependent on recruitment (the number of motor units activated in a contraction), and the rate at which motoneurones discharge action potentials[30]. The maximum rate at which motoneurones can discharge is known as the maximum unit discharge frequency. A reduction in maximum unit discharge frequency is associated with lower torque development in faster contractions[31]. Therefore, an explanation for a delayed TTP is that type I fibres predominate in the response to this perturbation due to lower force production, and consequently less effective correction and balance of posture. Another potential mechanism De Freitas *et al.*[11] suggest for causing a delay in TTP is a reduction in the number of doublet action potentials. A "doublet" is two action potentials produced by a motoneurone within a short period (under 10ms)[32]. During fast or strong contractions, like those seen

in postural responses, an increased frequency of doublets are observed[33]. Doublets increase the rate of force production, and it could be that JHS have differences in the motorneurone excitability, which cause a reduction in their production. Both a decrease in maximum motor unit discharge frequency and a reduction in the production of doublets could feasibly cause the delay in reaching peak muscle intensity, as these mechanisms have been shown to reduce force production in other groups, for example in older adults[31,34]. De Freitas *et al.*[11] found that older adults did not normalise their TTP with experience, whereas in the results here JHS normalised their TTP from P2 onwards. Postural responses are not purely reflex, but are a motor skill that can be learned and improved[21]. The improvement observed here may be due to JHS participants learning to compensate for an impaired system.

Another potential mechanism is hypotonia, which may be one of the features of JHS[35]. A longer TTP could be explained by the JHS group having less tone in their muscles than NF and GJH groups. This could mean that the muscle spindle's poles are not held as taught, and consequently group Ia and II afferent feedback to the central nervous system may be less effective resulting in the muscle taking longer to reach the peak that the other groups attained. Postural responses can be altered by anticipatory control[21], and JHS participants might increase the tension in their muscles from P2 onwards, as a way of adapting to hypotonia. It is unfortunate that the JHS participants were not able to produce a reliable MVC, which would have enabled better measurement by normalising EMG amplitude.

It is interesting that, except for the GM muscle at P6, the JHS group could match their time-to-peak response to the other groups from P2 onwards. Importantly, whilst the time-to-peak parameters of the JHS group normalised, this did not translate to normalisation of cumulative angle parameters. At each perturbation measured, the JHS group had significantly higher CA than NF in all joints (figure 2), indicating that their movement control was deficient and remained more unstable than NF and GJH groups.

In all groups, P1 produced the greatest magnitude of CA. Between P1 and P2, all groups significantly reduced their CA in all the joints measured, showing that all groups adapt their postural response. For NF and GJH groups, there was no significant difference in any joint between P2 and P6, indicating that there is little or no further adaptation to the perturbation. In the JHS group, hip CA at P2 was significantly greater than P6, which may mean that they are slower, or unable, to adapt their responses as quickly as the two control groups.

Interestingly, on visual inspection of Figures 5.5 – 5.7, the GJH cumulative angle is consistently between JHS and NF cumulative angles. Although differences between GJH and NF were not significant, the fact that the GJH group had consistently greater CA values than NF may indicate that hypermobility has a contributory effect on instability. Alternatively, the results may reflect issues in classification; it could be that some participants had aspects of JHS but were placed in the GJH group due to not meeting the full criteria. Indeed, since recruitment to this study there has been consensus

that the classification of GJH and JHS should change to a spectrum disorder leading up to hypermobile Ehlers Danlos Syndrome (hEDS) with tighter requirements (the changes to the classification system are discussed in Chapter 9). For example, it is interesting that the GJH participant who consistently took a recovery step fulfilled 3 minor criteria of the Brighton criteria (scoring positively for 4 minor criteria would have resulted in classification as JHS). However, since no significant differences between GJH and NF groups were recorded in any joint at any perturbation, it seems unlikely that it is joint hypermobility per se that is responsible for the increased instability, but rather another factor that is present in JHS but not in GJH. Due to the wide range of symptoms of JHS it is difficult to pinpoint a specific reason for this. There is evidence that there are neurophysiological abnormalities in people with JHS; differences have been shown in proprioception[5–7], autonomic dysfunction[36], and in musculoskeletal reflexes[8]. It could be that through reduced proprioception JHS participants may have been less able to sense the magnitude of the perturbation and/or the position of the joints that result in a stable base of support following the perturbation. The fact that Ferrell *et al.*[8] reported that JHS individuals had a longer spinal reflex latency than normal flexibility participants is interesting, particularly given the differences between JHS and GJH/NF time-to-peak in P1 we found in this study. Postural responses to perturbation, however, tend to be under control of the cerebellum[37], and the muscle onset timings found in this study would indicate cortical control is involved here. Given that all JHS participants had knee pain and GJH and NF participants were pain free, it could also be that pain is affecting postural responses. Rombaut *et al.*[46] highlighted mechanisms of how pain could limit a person's response to perturbations, namely by increasing reflex inhibition around the knee joint[162], and limiting their ability to respond by reducing loading in painful joints. Alternatively, the reason for increased instability could simply be due to muscle weakness, which would limit the ability to control the inertia and momentum produced by the perturbation.

5.5 Conclusion

In conclusion, the results of this study indicate that muscular postural responses are impaired in JHS, as evidenced by the fact that their time-to-peak was slower in 5 of the 8 muscles measured at the first perturbation. Although in the subsequent perturbations the JHS group were able to normalise their muscular response, and reduce the CA excursion in all their joints, they did not reduce the cumulative excursion to the levels seen in the control groups. The greater muscle time-to-peak during P1, and overall greater CA translates into greater instability in the JHS group. This may explain why JHS individuals have a risk of falling – they are less able to perform the corrections required to remain stable following a perturbation. Physiotherapy is the mainstay treatment for JHS, and the results of this study raise the question whether perturbation based training could be used to help improve balance in people with JHS. Ferrell *et al.*[27] found that a strengthening exercise programme improved proprioception in JHS individuals. Training would seem a promising strategy, as Horak & Nasher[23] have found that there

are several strategies for addressing forward perturbations, and that these responses are not hard-wired but instead can be learned. In addition, perturbation based training has produced improvements in other cohorts when responding to perturbations. In older adults, perturbation training has shown to reduce centre of mass displacement[163], and improve compensatory stepping[164]. The improvements in perturbation response through training also translate into a reduction in falls risk within this cohort[165]. A one-day perturbation training period also improved compensatory stepping in Parkinson's disease patients, and these improvements were retained when tested 24 hours later[166]. These improvements seen in other cohorts may allude that a direction for future research would be to test if perturbation based training would similarly improve JHS perturbation responses. The multifactorial nature of JHS however, means that it is difficult to determine the relationship between the many symptoms that could account for the differences observed in postural responses (for example pain, impaired proprioception, impaired balance, joint instability, hypotonia, and weakness). The results observed here could be important for planning targeted interventions, however careful consideration of the other factors relating to perturbation response/balance recovery is required.

Chapter 6: Characterising prolonged standing behaviour in JHS.

6.1 Introduction

There are different aspects to balance. In the previous chapter, a definition of balance from The Merriam-Webster dictionary was used; "the quality, state, or degree of being stable: such as the property of a body that causes it when disturbed from a condition of equilibrium... to develop forces or moments that restore the original condition."[146]. Another factor of remaining stable is *maintaining* a balanced posture. To balance effectively during standing, a person must keep the body's centre of gravity over its base of support; the less sway and greater steadiness of the centre of gravity, the better the person's balance[167]. There is a wealth of research about standing balance and posture. The vast majority of this research had been conducted into quiet standing, where a person is asked to stand 'still'. The typical pose of quiet standing, is where the feet are placed side by side and in parallel. In this position, anterioposterior sway is controlled by the ankle plantarflexors and dorsiflexors, and mediolateral sway is controlled by a load/unload mechanism on each leg[168]. The load/unload mechanism is controlled by the hip abductors/adductors[168].

To balance effectively, information is integrated from several sensory systems; the vestibular, somatosensory, and visual systems[169]. Typically, in studies of posturography, quiet standing is analysed in various conditions, for example with eyes open or closed, on different surfaces, and/or the feet in different positions. The amount of sway observed during these trials is viewed as an error signal, reflecting the body's ability to control posture[168]. There are a variety of techniques used to measure sway during posturography, for example accelerometers, 3D movement analysis, and pressure insoles[170]. The most common method used in the literature is using a force plate to measure the centre of pressure (COP). Typically, participants are asked to stand in various positions for a short period of time, and their COP parameters are measured. By comparing the amount of sway in the different conditions, it can be inferred whether the person is more reliant on a particular control system, implying that one of the other control systems is deficient. For example, in a commonly used posturography test, the modified Clinical Test of Sensory Interaction on Balance (CTSIB)[171], standing balance is assessed for 30 second periods. The CTSIB quantifies how the vestibular, proprioceptive, and visual systems contribute to balance, and if any particular system is impaired. It does this by measuring balance in various conditions; with eyes open and eyes closed on firm and a foam surface. A person is scored on how they perform standing in each condition for a 30 second period. If, for example, someone has greater sway than expected in the situations where eyes were closed, it would show that the person is overly dependent on vision for effective balance, and that one of the other sensory systems is impaired. Similarly, if the participant performed poorly on the soft surface, it is inferred that they are more dependent on somatosensory input[46].

Analysing quiet standing where the person is asked to stand still, is useful for testing if particular sensory systems are impaired, but it does not show how people behave during day-to-day standing tasks. An alternative way of measuring standing posture and balance is during unconstrained natural standing. As the name implies, during unconstrained standing no constraints are put on the participant in terms of their fidgeting, sway, or posture. This type of standing is common in everyday life, for example during queueing, shopping, and in certain jobs, and therefore has received attention particularly in ergonomics research. Prolonged standing is a demanding activity which can cause a wide range of both short and long-term effects. Physical symptoms include; an increase in blood pressure causing venous distension (swelling of the blood vessels) and superficial venous insuffiency[50], lower back pain[172], muscle fatigue[173], venous pooling[174], joint compression[175], and vertigo[176]. There are also psychological factors such as increased tension, mental fatigue, and stress[177,178].

Researchers have investigated movement during prolonged standing to see how people behave to alleviate these symptoms. As opposed to the poses traditionally analysed during posturography, people tend to adopt asymmetric postures during prolonged standing, but change their posture regularly[179]. Carlsoo[180] found that when adopting asymmetrical positions there was little to no muscle activity in the unloaded leg, allowing the leg to relax, and so changing posture is a way of spreading load across different muscles and passive structures. Alexander[169] proposed that these changes in position, or 'fidgeting', was a method to reduce joint pressure by circulating synovial fluid in the joints, something that may be particularly relevant as prolonged standing can cause thinning and compression of the cartilage in the load-bearing areas of the joints[175]. The fidgets may also aid the gathering of information about the local environment using the visual system[181] and prevent the occlusion of blood from the soles of the feet[182]. Duarte *et al.*[177] has investigated these factors by measuring healthy adults during prolonged standing in four conditions; normal, under load, vision restricted, and on a soft surface, with the aim to determine if any of these factors were the main contributor to fidgeting. There was no significant difference in the number of fidgets between any of the conditions, and the authors conclude that people do not fidget to overcome a specific factor. However, this was the first investigation into conditions that may affect prolonged standing, and the authors point out that the lack of a difference between conditions could be because the load was not great enough to increase joint compression enough to cause more fidgeting. The authors also state that the laboratory was 'visually constant', which may mean people did not need to fidget to gather visual information. Other researchers have also found difficulties in connecting prolonged standing behaviours to causes of pain; Gregory & Callaghan[183] found that periods of prolonged standing can cause pain, even in healthy individuals, but were not able to find specific variables of movement that were correlated to the development of back pain. Although in a later study they found that static standing (i.e. not fidgeting) was associated with inducing low back pain[132].

Moving to standing balance in JHS, posturography studies have focused on short periods of quiet standing, and there has not been any investigation of how people with JHS behave during prolonged standing. In their study of balance during quiet standing in JHS, Rombaut *et al.*[46] found that JHS individuals scored poorly in conditions when eyes were closed, and when they stood on a soft surface. The authors attribute this to people with JHS having a lack of sensory information from the lower limbs, which may be explained by the fact that people with JHS exhibit reduced proprioception[145]. The results of Rombaut *et al.*[46] compliment the results of Galli *et al.*[45], who found that JHS participants had greater ML and AP sway than a normal flexibility control group during a short period of quiet standing, particularly in eyes-closed conditions. These results would again infer that people with JHS are more reliant on input from the visual system to compensate for an impairment in other sensory systems. Galli *et al.*[45] state that JHS participants increased their ML sway as a compensation for the fact that they had greater AP sway, and to reduce the risk of a fall. It is not clear how they deduced this mechanism from their results, and they do not explain why this mechanism would reduce fall risk. Interestingly, Galli *et al.*[45] also measured the frequency of sway, but did not find any significant differences between groups. Frequency analysis of sway is another measure of balance, used to deduce if specific sensory systems are impaired. Impairments in the visual system typically manifest in an increase in the power band of 0.01-0.1Hz[184]. The fact that Galli *et al.*[45] did not find a significant difference between groups, contrasts the findings of their sway results. A power calculation was not performed, so it may be that the study was not sufficiently powered to detect a difference. Standing balance has also been measured in GJH cohorts; during single leg standing ML sway was greater in GJH participants than NF controls, however there was no difference in AP sway[185]. There is also some evidence that people with GJH have different activation patterns in lower limb muscles during standing[101].

Whereas current studies of JHS standing balance have shown balance is impaired, it is not clear how this impairment affects how people with JHS behave during prolonged standing. In addition, there has been no comparison between JHS and GJH people. The study of prolonged standing in JHS is particularly relevant given that people with JHS find prolonged standing difficult; one of the questions of the Bristol Impact of Hypermobility questionnaire concerns prolonged standing[19]. As was discussed in Chapter 4, the questions regarding activities in the Bristol Impact of Hypermobility Questionnaire represent activities that people with JHS find particularly challenging. The study of prolonged standing in hypermobile cohorts is relevant because people with hypermobility have shown an increase in incidence of venous insufficiency[50]. Azma *et al.*[50] found that the incidence of venous insufficiency (measured by varicose veins and spider veins) was significantly greater in soldiers with GJH than those with normal flexibility. Furthermore, after completing the army training programme, which the authors state includes a daily standing time of 12h, the prevalence significantly increased in the hypermobile group, but there was no significant increase in the normal flexibility group. This may indicate that prolonged periods of standing have a more adverse effect on hypermobile people than normal flexibility

people. Furthermore, joint hypermobility is a risk factor in the development of venous disease and insufficiency[186].

One reason that JHS people find prolonged standing difficult, is that they may not be performing behaviours that address the effects of prolonged standing. Rombaut *et al.*[46] found an increased fear of falling in JHS and it could be that people with JHS are less likely to perform changes of posture due to upsetting balance. Alternatively, impaired afferent information from the lower limbs may mean that they do not recognise when a change of posture is beneficial, or are holding their posture in 'incorrect' poses, for example knee hyperextension, which may in turn cause pain[33,34]. Combined with some of the other symptoms of JHS; fatigue, pain, low-muscle tone, joint laxity, and reduced proprioception, it is possible that people with JHS are more affected by prolonged standing tasks[33,34,48,145]. With this in mind, the aim of this study is to characterise prolonged standing in people with JHS and compare their behaviour to people with GJH and people with NF. The analysis of prolonged standing will be split into two aims arising from two questions:

i) To characterise the frequency and magnitude of fidgets; are JHS individuals performing behaviours to cope with the demands of prolonged standing?

ii) To characterise how people stand during the periods of quiet standing in between fidgets; are JHS individuals holding their posture in positions that may contribute to pain?

A comparison of JHS and NF prolonged standing was disseminated as an oral presentation at the European Society of Biomechanics and an abstract in Gait & Posture[187].

6.2 Methods

The participants tested here are the same as those described in chapter 5. Participants performed the prolonged standing exercise after the perturbation and gait activities. All participants had a minimum of two minutes sit-down rest between gait and standing activities.

Participants were instructed to stand over two Kistler force plates (Kistler Instruments Corp., Amherst, USA) sampling at 50Hz. Kinematic data was recorded using the same Vicon system and biomechanical model as described in Chapters 3 and 5. Subjects were told to stand with one foot on each of the force plates, and were told they could change position to remain comfortable, so long as they did not place both feet on a single force plate. At the start of the standing task, subjects were asked to rate their pain on a numeric scale from 0 to 10, with 0 awarded for no pain and a score of 10 awarded for the 'worst pain imaginable'. Subjects stood on the force plates for a maximum of 15

minutes, or until their pain score had increased by two points, which has been shown to be a clinically meaningful change[188]. Participants were instructed to say when they felt that their pain had increased by two points, and the researcher asked every two minutes "Has the pain in any of your joints increased to x?" (where x is the participant's starting pain score + 2). Since the task of prolonged standing is usually performed secondary to another task, all participants were instructed to watch a documentary on a tablet computer, placed 50cm in front of the participant.

The outcome measures for the prolonged standing task fall into two categories: (i) the number of changes of position, and (ii) the sway and knee kinematic characteristics during 'quiet periods of standing', i.e. the periods of relatively static posture in-between fidgets. Separating these variables represented a challenge. When a participant changes position, they move one of their feet and/or shift their bodyweight, this generates a change in the Fz signal from the relevant force plate. Detecting changes in position can therefore be thought of as detecting periods of change in the Fz time series. There are many methods of detecting change in time-series data, here an algorithm based on the cumulative sum (CUSUM) method was used[189]. This algorithm allows for tuning to detect changes of events at different thresholds, and was successfully used by Prado *et al.*[190] in their investigation into age-related differences in prolonged standing. The CUSUM algorithm relies on two user inputs; the magnitude of the change to be detected (h), and a 'drift' variable (v) to prevent false positives caused by small-scale changes. The algorithm calculates the cumulative sum of both the positive and negative changes (gt+ and gt-) in the Fz time series and compares the change to the threshold (h), when the threshold is passed a change is detected, and the cumulative sum resets to zero:

$$\Delta_{Fz} = Fz_t - Fz_{t-1}$$
$$g_t^+ = \max(g_{t-1}^+ + \Delta_{Fz} - v, 0)$$
$$g_t^- = \max(g_{t-1}^+ - \Delta_{Fz} - v, 0)$$

Where t is the timepoint in the Fz data series. If either g_t^+ or g_t^- exceed the threshold h, then a change is detected and g_t^+ and g_t^- are reset to zero.

Fidgets were quantified at three bodyweight thresholds; greater than 50%, 25-50%, and 10-25% and were normalised to fidgets per minute. These thresholds were determined by visual inspection of a selection of participants' Fz data. The greater than 50% threshold was included as it contains the largest fidgets; in theory, the largest fidget to be recorded would be 100% bodyweight, a shift from standing with all weight on one leg to all weight on the other leg. The 10% cut off was selected as it was the smallest fidget able to be separated from the Fz signal generated by sway during quiet standing periods. The remaining fidget of 25-50% was selected to capture 'medium' size fidgets. In fine tuning the algorithm to correlate with visual interpretation the variable v was set as 0.001% of bodyweight, which is the same value used by Prado *et al.*[190].

To calculate sway parameters, the two force plates were combined to take an average COP. The point of average centre of pressure (Px_{av}, Py_{av}) was calculated by:

$$(Px_{av}, Py_{av}) = \frac{(Px_1, Py_1).Fz_1}{Fz_{TOT}} + \frac{(Px_2, Py_2).Fz_2}{Fz_{TOT}}$$

Where (Px_n, Py_n) is the coordinate of the centre of pressure on force plate n, Fz_n is the force recorded by each force plate in the vertical axis, and Fz_{TOT} the combined total force in the vertical axis.

Of interest were other variables commonly used in posturography; anterioposterior (AP) and mediolateral (ML) sway, sway area, and sway velocity. These variables are traditionally extracted when a participant is asked to stand still, for example during the Romburg test, and would be affected by the changes of posture during prolonged standing. Therefore, periods of 'quiet standing' were extracted, i.e. the periods between fidgets where participants had adopted a relatively static posture. To achieve this, the positions of fidgets of 10% bodyweight or more were identified using the CUSUM formula, data ± 1.5 seconds from the fidget was removed for the analysis of quiet standing. This left a time series for each variable containing only periods of quiet standing. In addition to sway parameters, kinematic parameters concerning the knee were analysed. One of the theories of the cause of pain in JHS is that people with JHS hold their posture in positions of hyperextension; 'locking out' the joints and causing pain. To measure this, knee joint kinematics and mean difference in limb loading were analysed during the periods of quiet standing. The outcome measures analysed during quiet standing are given in table 6.1.

Outcome measure	Description
Anterioposterior (AP) sway	The standard deviation of COP in the anterioposterior axis.
Mediolateral (ML) sway	The standard deviation of the COP in the mediolateral axis
Sway area	The elliptical area containing 95% of the COP points.
Sway velocity	The velocity at which the COP moves in the AP/ML plane
Mean difference in limb loading	The mean difference in loading between each limb
Knee flexion/extension variability	The standard deviation of the knee flexion/extension angle
Mean knee flexion/extension	The mean angle of the knee joint in the flexion extension axis
Peak knee extension	The greatest amount of knee extension observed during the activity
% time in hyperextension	The % time the participant spent with at least one knee showing <2° hyperextension

Table 6.1. The outcome measures analysed during periods of quiet standing.

Force plate and kinematic data was exported from Vicon and processed in MatLab (The MathWorks, Natick, United States). Statistical analysis was performed in SPSS version 24. Data was tested for normality using a Shapiro-Wilk test. A one-way ANOVA was used to investigate the effect of group on variables that were normally distributed. A Kruskal-Wallis test was used to compare outcome measures that were not normally distributed. Where significant differences were found, pair-wise comparisons were made using Mann-Whitney U tests. Corrections for multiple comparisons were performed using the Bonferroni method. Significance was set at $p<.05$.

6.3 Results

The cohort characteristics were described previously in Chapter 5. All participants completed the prolonged standing activity.

Peak knee extension and mean knee joint angle were normally distributed in all groups. All other outcome measures were not normally distributed. Table 6.2 shows the median and interquartile range for each outcome measure.

	JHS (n=23)	GJH (n=23)	NF (n=22)
Standing time (minutes)*^	**7.35 (4.15 – 14.18)**	**15**	**15**
Starting pain (0-10) *^	**1 (0-3)**	**0**	**0**
Fidgets per minute (>50% bodyweight)	1.19 (0.24 - 2.06)	0.41 (0.27 - 1.41)	0.26 (0 - 1.28)
Fidgets per minute (25-50% bodyweight)	2.12 (0.79 - 4.68)	1.04 (0.73 - 3.1)	0.7 (0.22 - 1.79)
Fidgets per minute (10-25% bodyweight)	5.8 (1.4 - 11.21)	3.87 (2.75 - 7.59)	2.39 (1.34 - 6.41)
AP sway (mm)*	**30.45 (17.82 - 39.54)**	**23.79 (17.38 - 27.1)**	**16.32 (10.34 - 28.75)**
ML sway (mm)	32.51 (16.76 - 56.96)	30.29 (17.52 - 50.12)	16.87 (9.58 - 66.5)
Sway area (cm^2)	170.1 (48.63 - 419.02)	109.94 (57.26 - 162.73)	48.31 (18.91 - 249.26)
Velocity (mm/s)	65.11 (25.92 - 98.74)	94.35 (89.14 - 118.3)	88.09 (73.79 - 117.27)
Knee angle variability (°)	5.45 (1.81 - 8.02)	4.5 (2.46 - 5.95)	1.52 (1.01 - 6.77)
% time in hyperextension	68.6 (33.49 - 80.82)	72.04 (47.04 - 87.84)	84.17 (28.79 - 96.96)
Mean angle (°)	-3.37 (-6.04 - 0.25)	-4.48 (-5.42 - -0.93)	-3.33 (-6.68 - -1.18)
Peak extension (°)	-12.25 (-16.32 - -6.6)	-9.41 (-12.69 - -6.86)	-8.7 (-11.69 - -4.78)
Mean difference in loading	1.17 (0.75 - 2.27)	0.96 (0.62 - 1.65)	0.63 (0.41 - 1.95)

Table 6.2. Median (interquartile range) of outcome measures for each group. Interquartile ranges of Standing time and Starting are not listed for GJH and NF groups as they all completed 15 minutes of standing and did not have any joint pain. * indicates a significant difference between JHS and NF groups, ^ indicates a significant difference between JHS and GJH groups. Significance was set at p<.05 and Bonferroni corrections for multiple comparisons were made.

All GJH and NF participants stood for the full 15 minutes, whereas only 7 JHS participants completed the full 15 minutes. The range of standing times of JHS participants are shown in figure 6.1. The standing time represents the time taken for a participant's pain score to increase by 2 points on a pain numerical rating scale (participants reaching a standing time of 15 minutes did not score an increase in pain score). A Kruskal-Wallis test showed that there was a significant difference in standing time between groups ($p < 0.001$). For pair-wise comparisons, JHS stood for a significantly shorter time than NF ($p<.001$) and GJH ($p<.001$), and there was no significant difference between GJH and NF ($p=1.000$). Starting levels of pain of JHS participants are shown in figure 6.2; all GJH and NF scored 0 out of 10 for starting pain. A Kruskal Wallis test also showed a significant difference between groups in starting pain ($p<.001$); JHS had significantly greater starting pain than both GJH and NF groups ($p<.001$ in both cases).

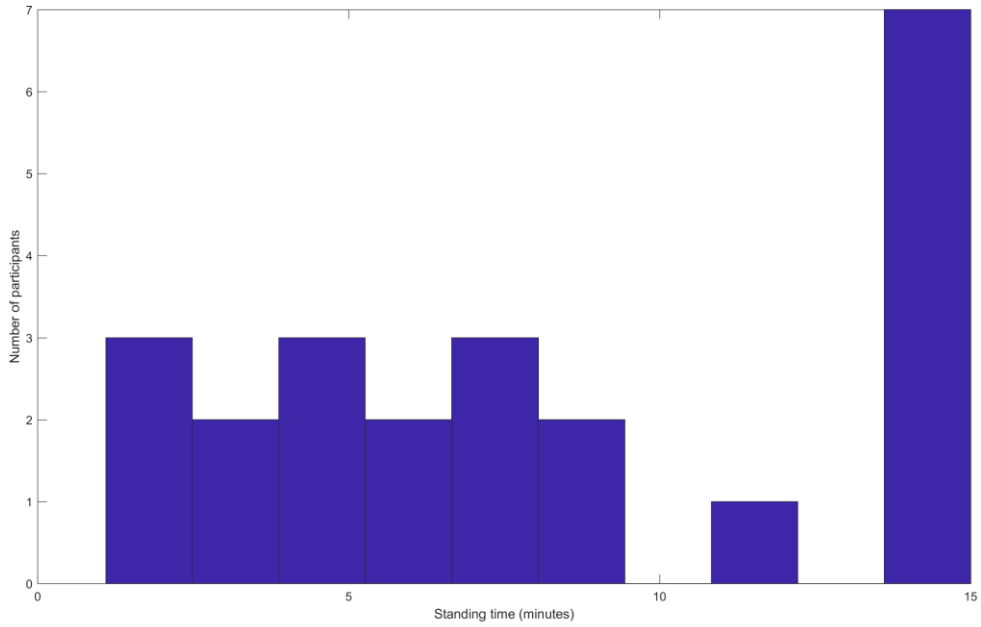


Figure 6.1. Histogram showing the standing time for JHS participants. All GJH and NF participants completed the 15 minutes of standing time.

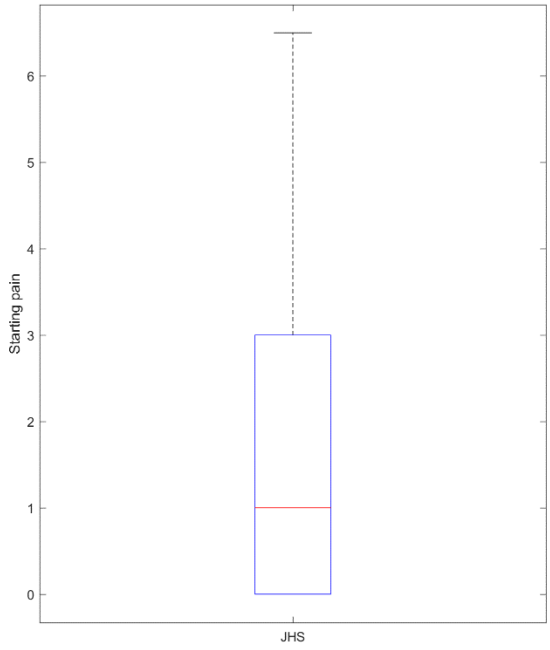


Figure 6.2. The range of starting pain scores for JHS participants. Participants were asked to rate their pain on a numerical scale from 0-10. All GJH and NF participants rated 0 for starting pain.

Figure 6.3 shows the number of fidgets per minute at each fidget magnitude. Generally, the JHS group showed a greater mean number of fidgets per minute, and a wider variability in the number of fidgets per minute, at each bodyweight magnitude. These differences however, were not significant. In the NF group, there were several outliers to the distribution.

In terms of the sway characteristics during the quiet standing periods (figure 6.4), there was no significant difference between any of the groups in ML sway, sway area, or sway velocity. The Kruskal-Wallis test did show a significant difference between groups in AP sway ($p=.029$). For pair-wise comparisons, there was a significant difference between JHS and NF groups ($p=.041$), and no significant difference between JHS and GJH ($p=.190$) or NF and GJH ($p=1.00$).

For the kinematic parameters of the knee joint during quiet standing (figure 6.5), there were no significant differences between groups in peak knee extension, mean knee joint angle, time in hyperextension, or variability. There was also no significant difference between groups in terms of the mean asymmetric loading during the quiet standing periods (figure 6.6).

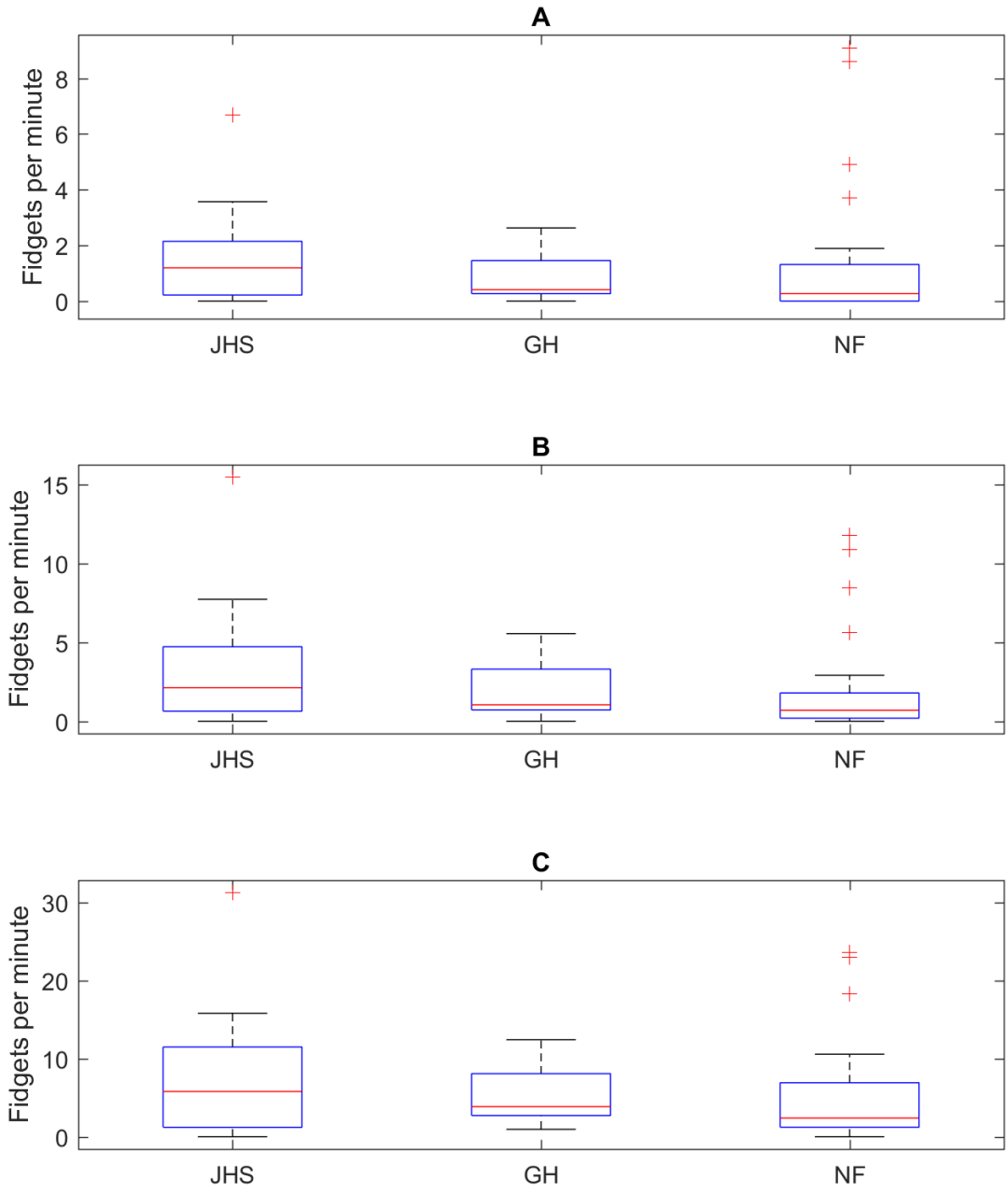


Figure 6.3. Fidgets per minute for each group at the different fidget magnitudes. A = fidgets at over 50% bodyweight, B = Fidgets 25-50% bodyweight, C = Fidgets 10-25% bodyweight. All data, including outliers, is included.

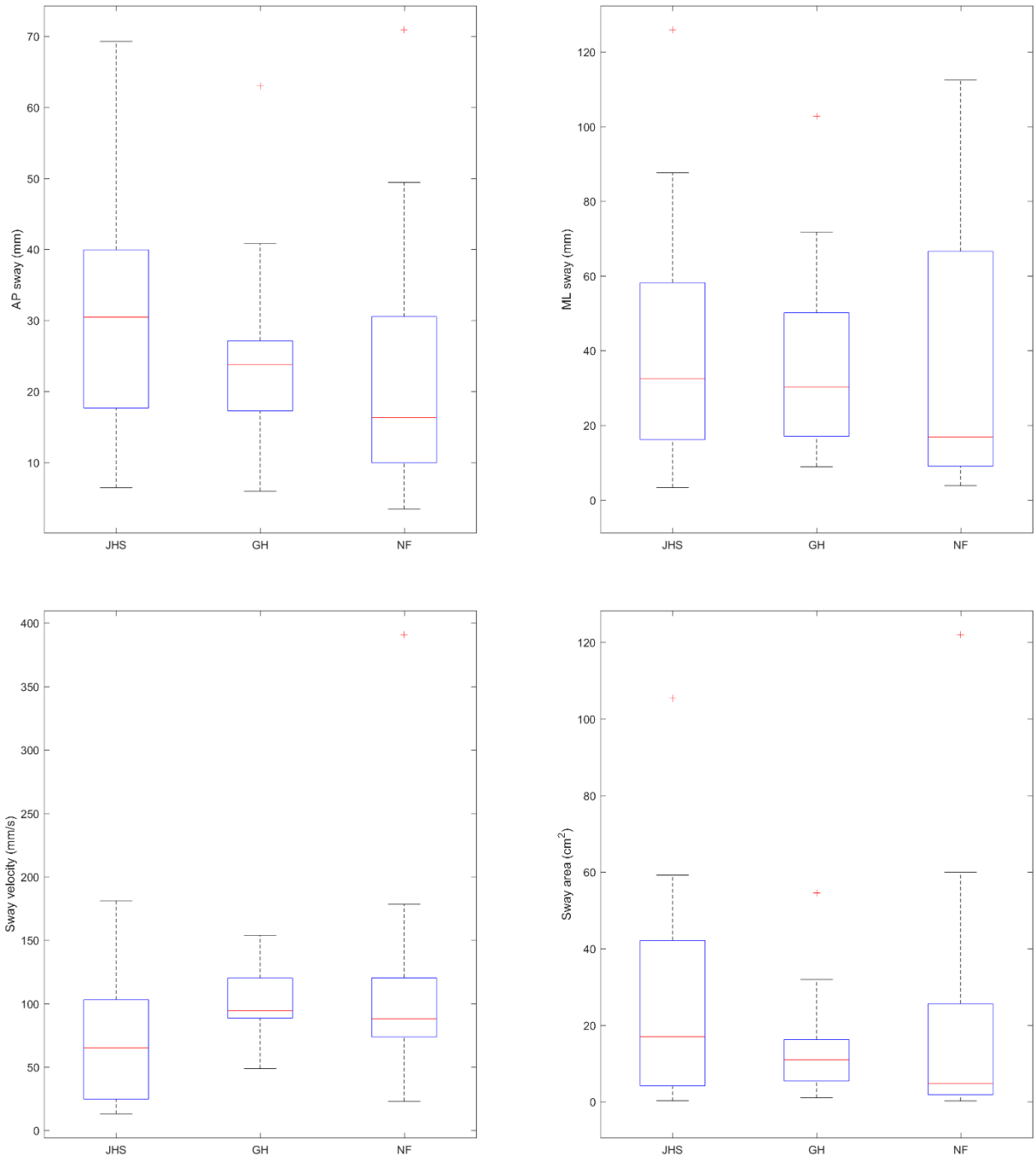


Figure 6.4. Sway parameters during prolonged standing. Anterioposterior (AP), Mediolateral (ML) sway, Sway velocity, and Sway area for each cohort. Parameters calculated during quiet standing.

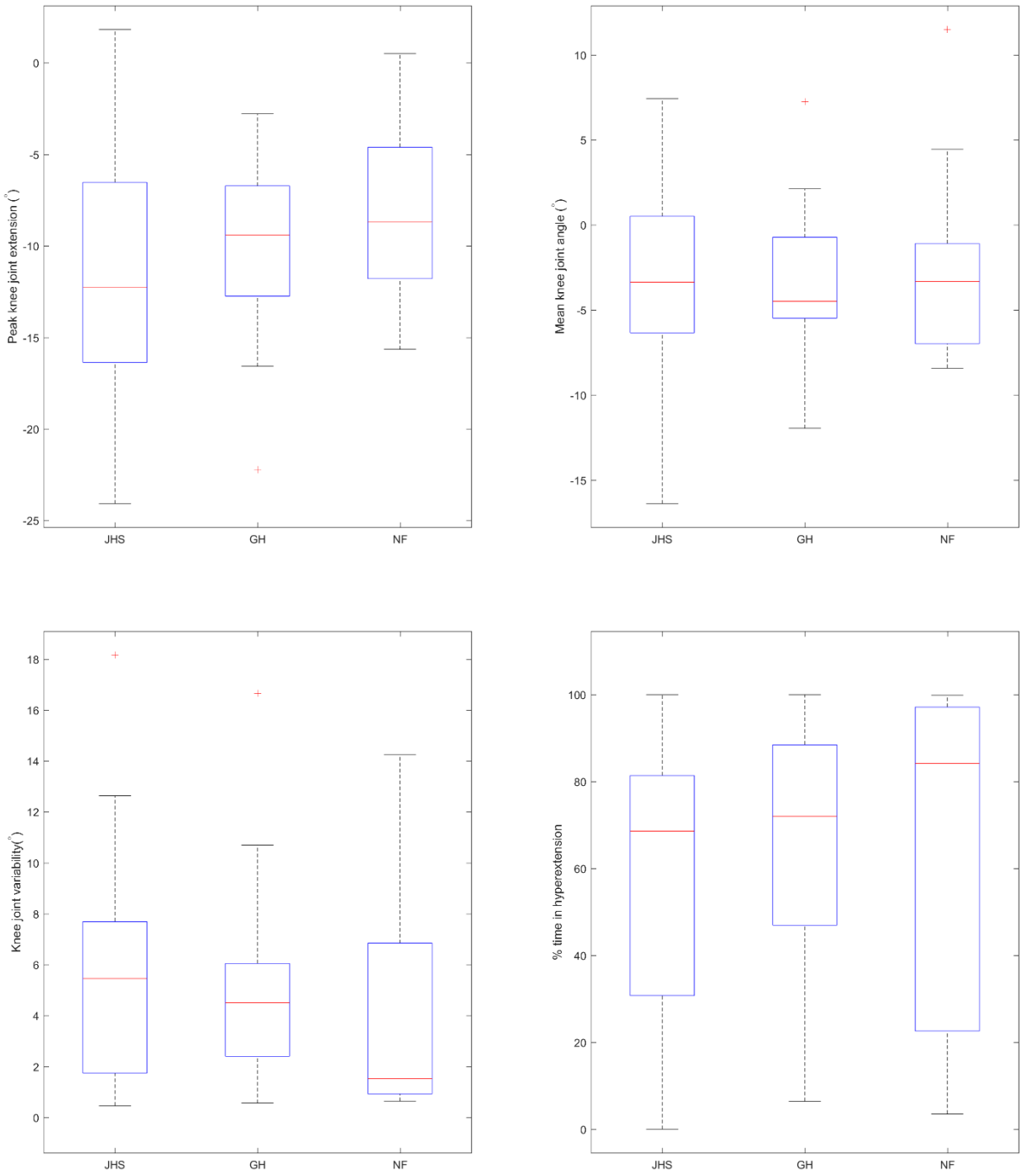


Figure 6.5. Knee joint parameters during prolonged standing. Peak knee extension, mean knee flexion/extension angle, knee flexion/extension variability, and % time in hyperextension.

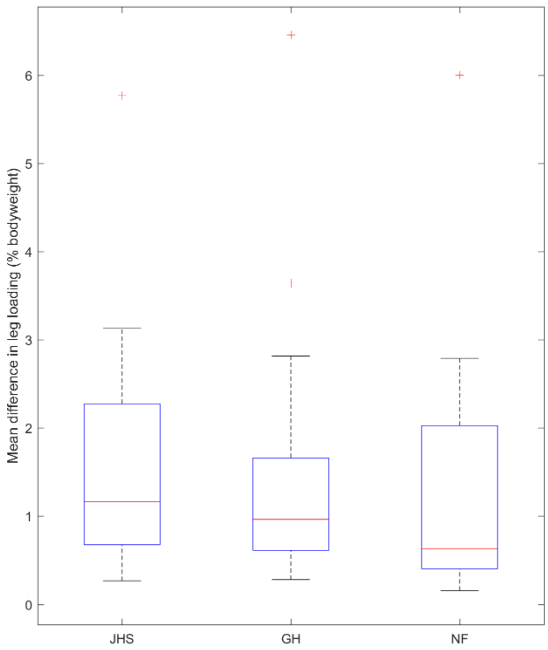


Figure 6.6. Mean difference in loading between each limb during prolonged standing.

6.4 Discussion

In this chapter, prolonged standing in people with JHS was characterised and compared with GJH and NF groups. Fidgets per minute were quantified at different magnitudes, a method was proposed for extracting periods of quiet standing, and sway and knee kinematic parameters during quiet standing were analysed.

The mean standing time of the JHS group was significantly less than both GJH and NF groups. Since participants were asked to stop once their pain had increased by 2 points on a numerical scale, this shows that the JHS group found the task irritable. Since GJH and NF participants all completed the full 15 minutes of standing, it shows they did not find the task painful. Prolonged standing forms one of the questions in the Bristol Impact of Hypermobility questionnaire[19], and so has been highlighted as an activity that JHS subjects say causes discomfort. The results of this study emphasise how difficult they find the activity. Anecdotally, in testing JHS participants over the four activities (perturbations, prolonged standing, gait, and stair climbing), a common consensus was that this prolonged standing task was the most difficult for them.

The aim of this chapter was to see if there were differences in standing behaviour, which might explain why JHS find prolonged standing so discomforting. There was no difference in the frequency of fidgets per minute between groups. A reduction in the number of fidgets has been linked to fear of falling, lower stability, and a lack of somatosensory information[172,177,190]. A lack of fidgeting and movement has also been linked to the development of pain in musculoskeletal conditions such as lower back pain[132]. It is interesting that, although other studies have found that JHS individuals have an increased fear of falling[46], impaired balance[45,46], reduced proprioception in the lower limbs, and pain that these impairments and factors of JHS do not manifest as a change in fidgeting behaviour during prolonged standing. In fact, although the differences were not significant, the JHS median fidgets were actually greater than other groups at each of the fidget magnitudes measured. Considering the functional purpose of fidgets described previously, it may be that JHS individuals perform more fidgets to relieve their symptoms of pain and fatigue, or to gather more visual information about the environment. Although the median and interquartile range of NF fidgets was lower than JHS, there were several outliers in the NF group who performed a relatively large number of fidgets; outside the range of the JHS and GJH groups. It may be that there are clusters of fidgeting behaviour; some people stand relatively still, whereas some people fidget a lot. It was not the intention of this study to investigate this, however it would be a possible question for future research.

The only significant difference found between groups in sway parameters was that of AP sway, where the JHS group had greater sway than the NF group. The GJH group had a median AP sway between the JHS and NF groups, and there was no significant difference between GJH and either of the

other groups, showing they occupied a mid-point between JHS and NF groups. Both Rombaut *et al.*[46] and Galli *et al.*[45] found that JHS participants had greater AP sway than NF participants during a short period of quiet standing, and it is interesting that this difference is also observable during unconstrained standing. This increased AP sway may be indicative of impaired balance; it is considered that the less sway during standing, the better a person's ability is to control their centre of gravity within their base of support[167]. In quiet standing, AP sway is controlled by the ankle dorsiflexors and plantarflexors[168]. The increased sway here may reflect muscle weakness, or alternatively reduced proprioception in the lower limbs. Both are factors associated with JHS[129,145]. Alternatively, since hypotonia is a feature of JHS[102], it may be that people with JHS have more AP sway in order to maintain or increase muscle tone.

Whereas there was a significant difference between JHS and NF in AP sway, there was no significant differences observed in ML sway. ML sway is controlled by a different mechanism than AP sway, a load/unload mechanism for each limb controlled by the hip adductors and abductors[168]. The fact that there were no differences between groups, is evidence that this mechanism is functioning relatively normally in JHS individuals. In addition, it was Carlsoo[180] who first noted that adopting asymmetrical standing positions allowed the leg supporting least bodyweight time to relax. In theory, a potential reason why JHS individual find prolonged standing difficult could be because they do not adopt these postures. However, there was no significant difference between groups in the difference in loading between limbs, showing that the JHS group did not differ in their behaviour in regard to loading/unloading each limb.

One theory of pain aetiology in JHS is that they hold their bodies in ill-advised postures, and "lock out" their joints in positions of hyperextension. This in turn causes wear and tear on the joints, and may cause nerve compression[33,34]. To measure if this occurred during unconstrained standing, this study measured the mean flexion/extension angle of the knee joint, peak extension, and the percentage of time the knee was held in hyper-extension. There was no significant difference between groups in any factor. In addition, there was no significant difference between groups in the variability of the knee flexion/extension angle. These results do not support the hypothesis that JHS individuals are adopting different postures and remaining in 'locked out' postures, at least during prolonged standing.

It should be noted however, in the knee joint outcome measures, the variability within groups was relatively large. For example, for the percentage time the knee joint was in hyperextension, some individuals never entered hyperextension, and some held their joints in hyperextension almost 100% of the time. The results are likely to be influenced by marker placement error. From the reliability study in Chapter 3, sagittal knee joint angle error was approximately 2.5°. It is plausible that the difference between groups in knee parameters, and the difference between being in hyperextension or within normal range, is too small a difference to measure considering the error. For peak extension, given the mean knee joint error is 2.5°, we would expect a range of 5° degrees to be observed, purely by marker placement error. The interquartile range of GJH and NF is 5.83° and 6.91° respectively, suggesting that

marker placement error accounts for a significant proportion of this variability. The variability of the JHS is larger (interquartile range of 9.72), suggesting that they do have a greater range of motion to utilise, and some individuals do go into this range of motion. Unfortunately, a more nuanced analysis is not possible due to the variability within groups and the error. Analysis could potentially be improved by measuring participant's peak knee extension prior to them performing standing protocol. This would give a baseline to measure how long they spent in end-of-range, and is a further direction for future research.

A problem of studying unconstrained standing, as highlighted by other researchers[190], is that it is a highly variable activity. In other activities, such as the perturbation study in the previous chapter, confounding factors are limited. For example, the perturbation velocity, number of perturbations, and standing posture. By the nature of analysing a natural behaviour, it was not possible to control confounding factors in this activity. For example, how someone behaved during prolonged standing might be influenced by how interesting they found the documentary they were asked to watch. It is clear from the results that the variability is relatively large in all the parameters measured. Within each of the groups, there were some people who did not perform any fidgets, whereas others performed a relatively large number. The problem of confounding factors is exacerbated by the multifactorial nature of JHS; there are a wide range of factors and symptoms that could affect behaviour and movement during prolonged standing. Whereas research has linked fidgeting during prolonged standing to factors such as lower stability, lack of somatosensory information[172,177,190], and the development of pain[132], other factors present in JHS such as fear of falling, anxiety, and fatigue could influence behaviour. These factors were not measured as part of the current study.

It is worth noting that there may be differences in prolonged standing behaviour, but the differences were eclipsed by the large variability in outcome measures. The power calculation performed to inform sample size for this study was based on the knee joint variability during gait, and therefore it may be the study was not sufficiently powered to detect a change.

6.5 Conclusion

There are many features of JHS that could influence standing behaviour, these were summarised in the study of quiet standing by Rombaut *et al.*[46] and include pain, fatigue, and muscle weakness. Despite these impairments and symptoms, and the fact that differences between JHS and controls have been observed during short periods of quiet standing, there were no significant differences between JHS and control groups in their fidgeting behaviour during prolonged standing. This is surprising given how uncomfortable people with JHS found the task. As increased fidgeting has been observed in other cohorts it could mean that people with JHS are not performing behaviours that would

help alleviate the discomfort of prolonged standing, perhaps showing unwilling which could be due to the many symptoms of JHS. Many factors could interplay to affect their standing behaviour, and the specific reason JHS find prolonged standing so irritable remains unanswered. A clue may be found in the fact that JHS participants did show more AP sway than controls, which is interesting as this increased sway has been observed in other studies and may point to differences in ankle control.

Chapter 7: Gait

7.1 Introduction

Current studies of gait of hypermobile cohorts were discussed in Chapter 2. Of the four studies that have used 3D movement analysis to investigate gait in adults with joint hypermobility, three compared a JHS group to normal flexibility controls[96-98], and one compared GJH to normal flexibility controls[94]. Although significant differences in movement between JHS/GJH and a control group were found in each study, as discussed in Chapter 2, these findings were not consistent between studies, which means there is uncertainty as to if or how JHS gait differs from GJH and NF gait. Part of the problem, is that for a clear comparison of JHS, GJH, and NF gait to be made, it is necessary to test all three groups within the same study. To date, this has not been performed, and the lack of consistency between published studies could be due to differences in experimental setup. For example; variations in experimental protocol, definition of GJH, data analysis, sample size, and/or research question; all may have led to different observations. Alternatively, movement of JHS and/or GJH people, may be highly variable between individuals, causing differences in observed results between studies. Finally, it may be that there is no consistent way in which movement differs. With this lack of clarity in mind, the broad aim of this study was to compare gait of JHS, GJH and NF groups. Comparing all three groups, may enable conclusions of what factor is causing differences in movement in people with JHS. There are many physical and psychological factors of JHS that can affect gait. One of these factors is joint hypermobility. To date JHS gait has been compared to NF gait, and GJH gait has been compared to NF gait, but JHS and GJH cohorts have not been directly compared. Without including a GJH control group of people who are hypermobile and do not have symptoms, it is impossible to say whether observed differences in gait are due to joint hypermobility, pain, or some other factor that is present in people with JHS. For example, if people with JHS move differently to both people with NF and people with GJH (and GJH/NF move the same), then it could be theorised that it is not the hypermobility per se that is causing the differences in movement, but rather some other factor of JHS. Conversely, if GJH and JHS gait is similar, but different to NF gait, then it would allude to movement not being so relevant to the pain, and other factors of JHS are the cause. Or alternatively that GJH have mechanisms that allow them to 'cope' better with the hypermobility.

For someone to perform gait successfully they need to combine coordination, neurological control of movement, balance, and generation of power[133]. 3D movement analysis, combined with EMG, allows measurement of a huge number of parameters that relate to these factors, and part of the problem with current literature relating to hypermobile gait, was the diverse range of outcome measures used; over 70 outcome measures used across 5 studies[94-96,98,99], of which only 2 were common to all

studies[191]. Broadly, these parameters can be split into temporal-spatial, kinematic, kinetic, stiffness, and EMG measures. An overview of the movement parameters of interest are given below.

7.1.1Temporal-spatial parameters

Temporal spatial features of gait such as stride length, stride width, stride time and velocity are a measure of the quality of gait[192]. Furthermore, the variability of these measures can be indicative of the stability of gait[193].

7.1.2 Kinematics and kinetic parameters

Kinematics shows how the joints of the body move. Kinematic measures seem particularly relevant for hypermobile gait given the extra range of motion available due to joint laxity, and one of the theories of the cause of pain in JHS is that the extra range-of-motion causes more stress on the joints[28]. Measuring joint kinematics during gait will enable us to see if hypermobile individuals do go into their excessive range of motion during gait. Kinetic parameters concern forces passing through the joints. An example of typical joint angles and moments over the gait cycle are shown in figure 7.1.

The objective of gait is forward progression of the body, or can be thought of as the progression of the centre of mass forward. Any displacement of the centre of mass in a direction other than the direction of travel, is inefficient[133]. For this reason, the process of gait aims to minimise the movement of the centre of mass in the vertical and mediolateral directions during walking[133], and in normal gait the kinematics and kinetics of the body reflect this aim. For the purposes of describing kinematics and kinetics of gait, it is necessary to describe the gait cycle. The gait cycle is the interval between two successive occurrences of the same event during gait, typically initial contact; where the foot first contacts the floor. The gait cycle has been described in detail throughout the literature, such as the summaries by Winter[168] and Kirtley[133]. An overview of the gait cycle follows and is shown in Figure 7.1.

<u>Initial contact.</u>

Occurs between 0-2% of the gait cycle. Initial contact is the instant the foot contacts the floor, which in non-pathological gait is with the heel. The limb is positioned for stance with a heel rocker, and impact deceleration occurs.

<u>Loading response.</u>

Occurs between 0-10% of the gait cycle, and constitutes the double support phase. Provides shock absorption, weight-bearing stability, and the preservation of progression.

Mid-stance.

Occurs between 10-30% of the gait cycle, the contra-lateral foot has been lifted off the ground, and so the body is in single limb support. The objectives are progression over the support foot, whilst maintaining limb and trunk stability.

Terminal stance.

Occurs between 30-50% of the gait cycle. Begins with ipsilateral heel rise and ends when the contra-lateral foot contacts the floor. This phase progresses the body beyond the supporting foot, whilst maintaining limb and trunk stability.

Pre-swing.

Occurs between 50-60% of the gait cycle. Starts with contralateral foot contact and ends with ipsilateral toe-off. This positions the limb ready to accelerate forwards.

Initial swing.

Occurs between 60-75% of the gait cycle, when the ipsilateral foot is lifted from the floor and ends when the ipsilateral foot is level with the supporting foot. Objectives are ipsilateral foot clearance and advancement of the trailing limb.

Mid- swing.

Occurs between 75-87% of the gait cycle. Ends when the limb has progressed forward and the tibia is vertical. Objectives are continuation of foot clearance and limb advancement.

Terminal swing.

Occurs between 87-100% of the gait cycle. Ends with ipsilateral initial contact with the floor. This phase completes limb advancement and prepares the limb for stance phase.

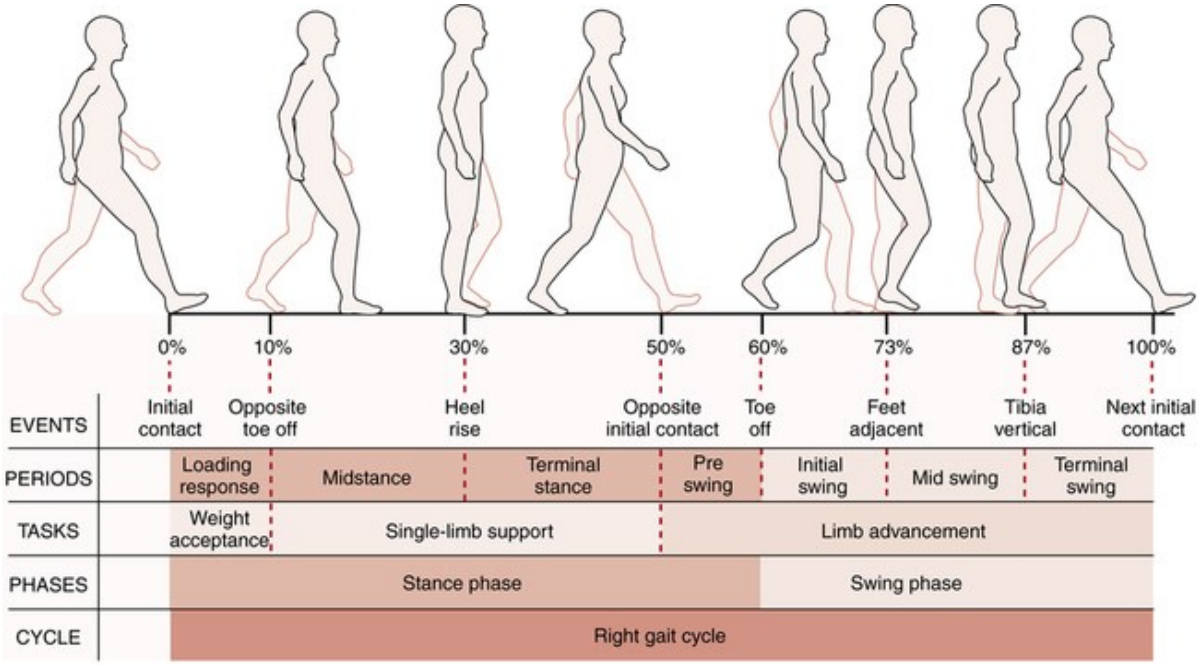


Figure 7.1. The phases of the gait cycle. Reproduced with permission from Kirtley *et al.*[133].

7.1.2 Joint power

Where joint moment shows whether the flexors or extensors are contracting, mechanical power can additionally show whether the contraction is eccentric or concentric[133], i.e. if power is being absorbed or generated at a joint. Power is defined as the joint moment multiplied by the angular velocity[140]. Power can be either positive or negative; positive when joint moment and angular direction are the same, negative when joint moment and direction are in opposite directions. Power is positive when the body is generating energy through the concentric contraction of muscles, and negative when the body's tissues absorb energy[140]. Peaks and features of the joint power curves have been identified and described by Winter[140], and are illustrated in figure 7.2. At the ankle, there is a large positive power peak where the plantarflexors contract concentrically to propel the body forward in pre-swing (AP1 on figure 7.2). At the knee, there are two peaks in negative power; KP1 caused by the rectus femoris, and KP3 which corresponds to the hamstrings eccentric contraction. At the hip HP1 is a period of positive power, where concentric hip activity contributes to forward propulsion. The extensor moment during the first half of stance serves to stabilise the trunk by preventing it from flexing forward due to a posterior reaction force at the hip, and hence helps the knee extensors in preventing collapse of the knee joint. HP1 is a period of negative power corresponding to hip flexor eccentric activity, this stabilises trunk posture. Finally, HP2 is a period of positive power caused by concentric contraction of the hip flexors, this generates force to move the thigh into swing phase, and has been labelled a "pull-off".

7.1.3 Dynamic Joint stiffness

Stiffness is a measure of how an object resists deformation when a force is applied. In conventional mechanics, the stiffness of a spring can be calculated by the ratio of the magnitude of the force applied and magnitude of displacement, or by the slope of the graph showing force applied and displacement. This concept can be applied to the joints of the body; stiffness of a joint can be calculated by the change in joint moment (M) divided by the change in joint angle (θ), or the slope of the graph of joint moment and joint angle[194]:

$$Joint\ stiffness = \frac{\Delta M}{\Delta \theta}$$

This concept has been used in many studies of biomechanics, to investigate and understand movement[194]. The human body, however, is more complex than this simple model; joint stiffness when measured using 3D movement analysis is dependent on both the passive stiffness of soft tissues and the contribution of both eccentric and concentric muscle contractions[194]. In addition a number of assumptions are made; the method does not take into account tissues' ability to store elastic energy, or any forces that oppose the movement that is generated by muscles[195]. For this reason, the term Dynamic Joint Stiffness tends to be used to differentiate from the classical definition of stiffness. These limitations effectively mean that only linear portions of the moment/angle plot can be interpreted as a true measure of the resistance muscles and soft tissues oppose movement[196]. In the study of gait these periods of linearity have been well established; Ankle and hip stiffness has been measured during the second rocker phase of gait (from approximately 10-30% of the gait cycle)[194], and knee stiffness during loading response (approximately 3-15% of the gait cycle)[197,198].

To date ankle and hip dynamic joint stiffness have been measured in JHS individuals[96,102]. However, neither study investigated dynamic joint stiffness at the knee. Interestingly, Galli *et al.*[96] and Cimolin *et al.*[102] observed that JHS participants had significantly lower dynamic joint stiffness than a normal flexibility control group at both the hip and ankle, and attribute this to the increased joint laxity and hypotonia.

7.1.4 EMG co-contraction

Co-contraction is where there is simultaneous contraction of two, or multiple, muscles across a joint. Co-contraction contributes to joint stability by allowing the body to adjust to disturbances and maintain a more constant joint load[199]. Given the joint instability present in JHS, EMG co-contraction would seem an interesting parameter to investigate, particularly as there is evidence of reduced dynamic

joint stiffness during gait[96], which could be related to co-contraction. To date there have not been any studies of EMG activity during gait in a JHS cohort, despite other researchers calling for more research[99].

Although EMG co-contraction during gait has not been measured in a hypermobile group, differences in muscle co-contraction have been found in other tasks in people with GJH, such as sitting knee flexion[35] and in postural tasks[101]. Jensen *et al.*[35] found increased co-contraction of knee flexor and extensor muscles in GJH, and attribute this to people with GJH needing to stabilise the knee joint in the anterioposterior direction. They state that this stabilisation may be task dependent, as no difference in co-contraction ratio was found between GJH and NF groups during knee extension. Interestingly, Jensen *et al.*[35] state that their results show that isometric knee flexion is more challenging that isometric knee extension. Fortunately, we can measure joint stiffness and co-contraction during loading response to mid-stance, where the knee flexes whilst supporting the bodyweight. Greenwood *et al.*[101] found that people with GJH had greater co-contraction of semitendinosus and rectus femoris muscles than the NF group in a simple standing exercise. The NF group only performed the co-contraction during more demanding tasks, the authors attribute these results to the GJH group finding the simpler task demanding, and using co-contraction to stabilise the joint. It should be noted that neither Jensen *et al.*[35] or Greenwood *et al.*[101] included a JHS group in their studies, meaning it is not clear if these stabilisation strategies are present in JHS individuals. Co-contractions of interest are vastus medialis and vastus lateralis (VM/VL). VM/VL co-contraction stabilises the patellofemoral joint of the knee (Rainoldi, Bullock-Saxton, Cavarretta, & Hogan, 2008). Gastrocnemius and tibialis anterior co-contraction can stabilise the ankle[200], and finally bicep femoris and rectus femoris co-contraction, which can stabilise the knee joint in the anterioposterior direction[35]. Co-contraction of the hip Ilio-psoas was not measured as it is difficult to record from these muscles using surface EMG[201].

To measure the amount of co-contraction present, typically an index of co-contraction is used. There are a wide range of different indexes which have been used in the literature. Two of the most common are (1) where the lower of the two EMG signals is divided by the mean between the agonistic and antagonistic muscle activations, and (2) where the ratio between the two muscles' activation is calculated[202]. Of these, the ratio method has proved most reliable[202]. Although in some studies of EMG coactivation the EMG signal has not been normalised with respect to MVC, in a comparison of different methods of calculating EMG co-contraction, the non-normalisation method was criticised as being unreliable[203]. In a priori testing, JHS participants were unable to generate a reliable MVC, and in some cases the EMG activity recorded during activities was much greater than the theoretical maximum of 100%.

7.1.5 Aims of study

As stated previously, the aim of this study is to compare gait of JHS to two control groups; people with normal flexibility and people with generalised joint hypermobility. Data dredging may have been an issue for the studies that have investigated hypermobile gait[82], for this reason the specific aims of investigating gait are:

1) To determine if there are differences in temporal-spatial measures that indicate reduced gait function.
2) To determine if there are differences in variability of temporal-spatial and kinematic parameters, indicative of gait stability.
3) To characterise JHS gait by features of the kinematic, moment and joint power charts over the gait cycle.
4) To characterise dynamic joint stiffness at the ankle, knee and hip.
5) To quantify co-contraction of lower limb muscles during the same periods dynamic joint stiffness are measured.

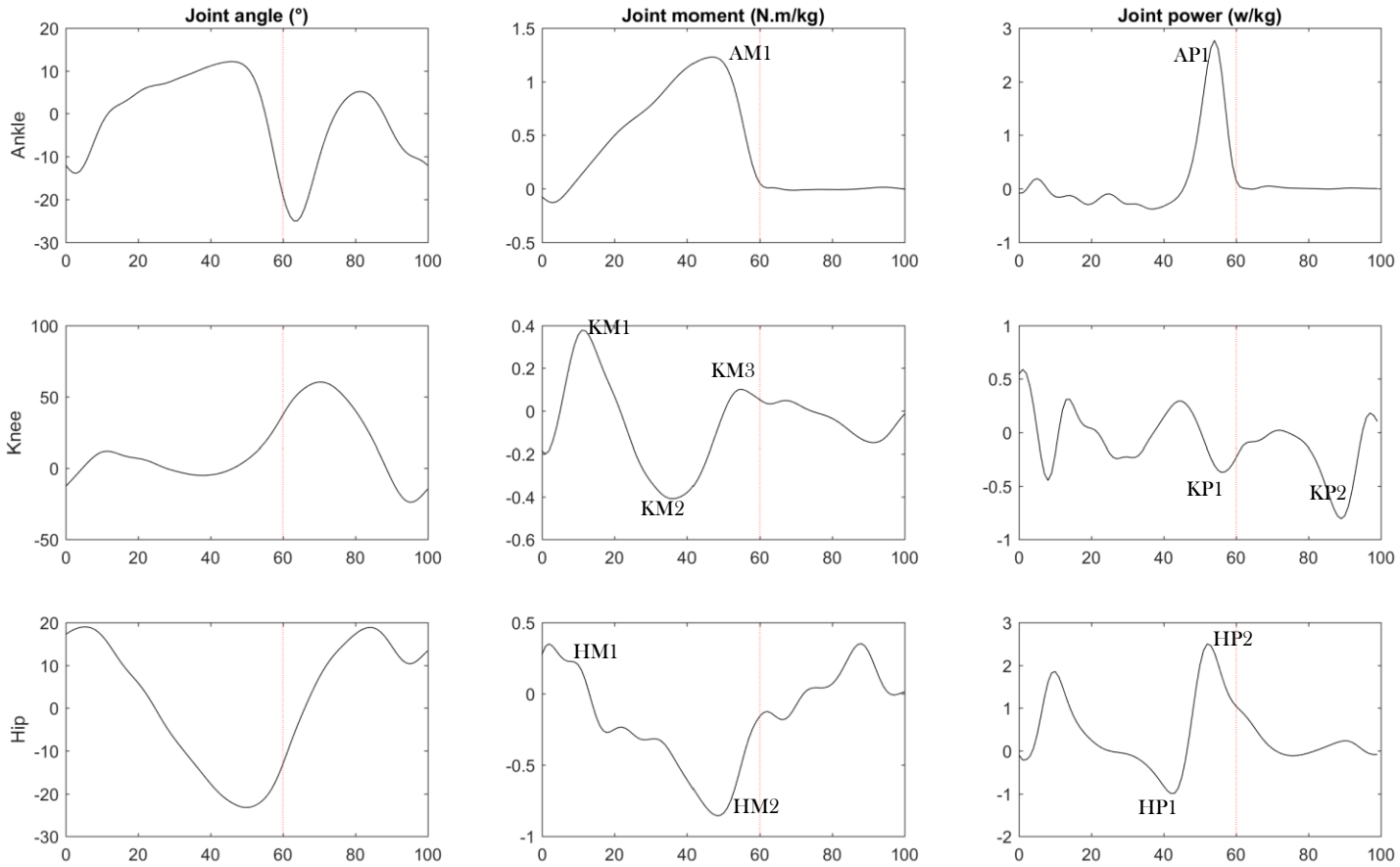


Figure 7.2: Example of joint kinematics, moments and powers during gait. The x-axis is 0-100% of the gait cycle, vertical line indicates the termination of stance phase. Flexion and dorsiflexion are positive, extension and plantarflexion are negative. Platarflexor and extensor moments are positive. Power is positive when generated at the joint, negative when energy is absorbed. Labelled features are explained in the 'Methods' section of this chapter.

7.2 Methods

7.2.1 Experimental procedure

Recruitment and participant characteristics were described in Chapter 5. In this gait task participants were asked to walk along a 6m wooden walkway that had two force plates embedded (Kistler Instruments Corp., Amherst, USA). Five strides from foot strike to ipsilateral foot strike were used in analysis to determine mean parameters over the gait cycle for each participant. Only steps where the foot made full contact with the force plate were used in analysis. Force plates were used to determine initial contact and heel strike by the method proposed by O'Connor *et al.*[121]; initial contact is defined as a peak in the vertical velocity of the midfoot (the point equidistant between the markers on the 1st and 5th metatarsals).

7.2.2 Data analysis

Joint angles and moments were calculated using Vicon Nexus 1.8.5 using the model described previously in Chapter 3. A custom Matlab (The MathWorks, Natick, United States) process was used in post processing to calculate gait parameters of interest. Joint angle, moment, power, and dynamic joint stiffness graphs were normalised to percentage of gait cycle. Statistical analysis was performed using IBM SPSS version 24.

7.2.3 Spatio-temporal parameters

Spatiotemporal methods calculated were stride length, stride width, stride time and gait velocity. Mean values for each parameter and its variability were calculated. Stride length was defined as the distance between the position of the calcaneus marker at initial contact, to the position of the calcaneus marker at the following ipsilateral initial contact. Stride width was defined as the distance between midfoot markers at initial contact. Stride time was defined as the time taken from heel strike to ipsilateral heel strike. Velocity was defined as the mean velocity of the pelvis segment in the direction of progression.

7.2.4 Kinematic & kinetic parameters

Kinematic parameters analysed were sagittal plane joint angles of the hip, knee, and ankle. Only sagittal plane joint angles were considered as frontal and transverse angles are generally less reliable[191].

Mean angle during stance phase and mean variability throughout the gait cycle was calculated for each joint. Joint moment and power outcome measures are illustrated on Figure 7.2.

Ankle parameters measured were peak dorsiflexion during stance phase, peak plantarflexion angle, peak plantarflexor moment (AM1), and peak power generated (AP1). Knee parameters analysed were peak flexion during weight acceptance, peak knee flexion and extension, mean angle during stance, mean variability, peak moment during loading response (KM1), peak moment which occurs between 30-50% gait cycle (KM2), peak moment 45-60% gait cycle (KM3). Power outcome measures at the knee were the peaks KP1 and KP2 (labelled on Figure 7.2). Hip parameters measured were peak flexion and peak extension, peak extension moment shortly after initial contact (HM1), peak flexor moment (HM2), and the power peaks at H1 and H2 (Figure 7.2). All joint moments are expressed as external joint moments.

Root-mean-squared (RMS) power was also measured at each joint to give a measure of the overall power contribution of each joint during the gait cycle.

In addition, variability of gait patterns were investigated by the researcher (AB) inspecting the graphs of hip, knee, and ankle sagittal plane joint angle for each of the five steps.

7.2.5 Dynamic joint stiffness

Ankle and hip dynamic joint stiffness were calculated between 10 and 30% of the gait cycle, and knee dynamic joint stiffness between 3 and 15%, these periods are where there is a linear relationship between joint angle and joint moment. Linear regression was used to calculate the gradient of the line, using the method described by Davis & De Luca[194].

7.2.6 EMG co-contraction

During testing, it became apparent that the participants with JHS were unable to produce maximal voluntary contractions (MVC). This meant that normalization of the EMG data could not be carried out using the preferred method of normalising to peak intensity during an MVC. This in turn meant that the established indices of co-contraction could not be used. There are other methods of EMG normalising EMG, for example normalising to the peak intensity observed during an activity. However, this method loses the variation in EMG between individuals caused by differences in strength[157]. Since JHS individuals have been found to have muscle weakness, and therefore differences in strength between groups are likely to be significant, this method of normalisation is not appropriate here. Instead, to measure co-contraction, a custom Matlab (The MathWorks, Natick, United States) routine was developed. EMG data for of each step of each participant was low-pass filtered at 500Hz

(Butterworth 4th order, zero lag) and rectified. The data was low-pass filtered at 6Hz using a 4th order, zero-lag Butterworth filter to obtain the linear envelope. Graphs of each participants mean linear envelope were displayed for each muscle, and the researcher (AB), manually identified a period where the EMG intensity was at its lowest. The muscle was considered active when the EMG intensity rose 2 standard deviations above this baseline. Co-contraction muscle pairs analysed were gastrocnemius and tibialis anterior (GA/TA), biceps femoris and rectus femoris (BF/RF), and vastus medialis and vastus lateralis (VM/VL). The pair were considered co-contracting if both muscles were active simultaneously. Since the EMG could not be normalised to an MVC, this method does not give a ratio of co-contraction, but rather gives the time the two muscles were contracting at the same time, with no information about relative activation levels. Since co-contraction is linked to joint stiffness and stabilisation, it was measured for the same periods of the gait cycle as joint stiffness; 10-30% for GA/TA, and 3-15% for BF/RF and VM/VL; and expressed as a percentage of time.

7.2.7 Statistics

Where parameters were normally distributed, a one-way multivariate analysis of variance was used to determine the effect of group (JHS, GJH, and NF) on gait. Where parameters were not normally distributed, a Kruskal-Wallis test was used and pair-wise comparisons made with a Mann-Whitney U test. A Bonferroni correction was performed for multiple comparisons. Analysis was performed in IBM SPSS 24.

7.3 Results

Participant characteristics have been described previously in Chapter 5. The MANOVA test indicated there was a significant difference between groups p=.036. Mean results ± standard deviation for all parameters investigated are listed in Table 7.1.

	JHS (n=23)	GJH (n=23)	NF (n=22)
Temporal spatial			
Stride time mean (s)†*	**1.21±0.10**	**1.11±0.07**	**1.11±0.10**
Velocity mean (m/s)†*	**1.01±0.12**	**1.2±0.15**	**1.14±0.13**
Stride width mean (m)	0.09±0.02	0.08±0.02	0.08±0.02
Stride length mean (m)^*	**0.73±0.04**	**0.79±0.06**	**0.74±0.04**
Stride length mean variability (m)†	**0.03±0.02**	**0.02±0.01**	**0.02±0.01**
Sagittal plane joint angles (°)			
Ankle peak stance phase	14.42±0.8	12.74±0.77	12.17±0.78
Ankle peak plantarflexion	-15.64±1.48	-17.48±1.41	-14.12±1.44
Ankle mean weigh bearing	5.31±0.67	3.77±0.64	3.81±0.65
Ankle mean variability†	**-2.75±0.81**	**-3.57±0.78**	**-3.46±0.8**
Knee peak weight acceptance	12.59±1.4	14.21±1.34	9.85±1.37
Knee peak flexion*	**60.09±1.06**	**63.62±1.01**	**61.08±1.04**
Knee peak extension	-5.23±1.14	-6.05±1.09	-7.35±1.11
Knee Mean during weight bearing	9.5±1.08	9.62±1.03	7.63±1.06
Knee mean variability*	**3.2±0.28**	**2.12±0.27**	**2.26±0.28**
Hip peak flexion	32.39±1.33	31.49±1.27	27.99±1.3
hip peak extension†*	**-7.5±1.33**	**-12.19±1.27**	**-12.38±1.3**
Hip mean during weight bearing†	**8.35±1.23**	**4.96±1.18**	**3.37±1.21**
Hip variability†*	**2.09±0.13**	**1.35±0.13**	**1.39±0.13**
Joint moments (Nm/kg)			
Ankle peak plantarflexion moment (AM1)	1.18±0.04	1.25±0.03	1.30±0.04
Knee extensor moment, 0-30% gait cycle (KM1)	0.37±0.05	0.47±0.05	0.34±0.05
Knee flexor moment 30-50% gait cycle (KM2)	-0.24±0.03	-0.31±0.03	-0.32±0.03
Knee extensor moment 45-60% gait cycle (KM3)	0.15±0.03	0.20±0.03	0.20±0.03
Hip peak extensor moment (HM1)†*	**0.53±0.06**	**0.84±0.06**	**0.82±0.06**
Hip peak flexor moment (HM2)†	**-0.35±0.04**	**-0.47±0.04**	**-0.50±0.04**
Joint powers (W/kg)			
Ankle power RMS	0.35±0.03	0.41±0.02	0.39±0.02
Ankle power (AP1)*	**2.81±0.22**	**3.6±0.21**	**3.27±0.22**
Knee power RMS†*	**0.24±0.03**	**0.37±0.03**	**0.35±0.03**
Knee power (KP1)†	**-0.62±0.11**	**-0.89±0.11**	**-1.03±0.11**
Knee power (KP2)*	**-0.89±0.14**	**-1.47±0.13**	**-1.3±0.13**
Hip power RMS†*	**0.23±0.03**	**0.36±0.03**	**0.35±0.03**
Hip power (HP1)†*	**-0.34±0.05**	**-0.59±0.05**	**-0.58±0.05**
Hip power (HP2)†*	**0.75±0.11**	**1.13±0.11**	**1.24±0.11**
Dynamic joint stiffness			
Ankle	5.68±0.43	6.13±0.41	6.02±0.42
Knee*	**4.72±0.41**	**6.25±0.39**	**6.04±0.4**
Hip	1.84±0.19	2.02±0.19	2.4±0.19

Table: 7.1: Results for the outcome measures investigated during gait. † = significant difference between JHS and NF groups, * = significant difference between JHS and GJH groups, ^ = significant difference between NF and GJH groups. $\alpha = 0.05$ and Bonferroni correction was used.

7.3.1 Temporal spatial

For temporal spatial measures, stride time was significantly longer in JHS than NF (p=.002) and GJH (p=.001), gait velocity was significantly slower in JHS than NF (p=.006) and GJH (P<.001), JHS had significant shorter stride length than GJH (p<.001), but not significantly different from NF. JHS had greater stride length variability than NF (p=.022) but not GJH (p=.093).

7.3.2 Kinematic parameters

Kinematic parameters have been illustrated as graphs in figures 7.3 to 7.5. At the ankle, JHS had significantly greater variability than NF (p=.029). There were no significant differences between groups for any other of the ankle kinematic parameters measured. JHS had significantly lower peak knee flexion (p=.049), and significantly higher knee variability (p=.019) than GJH. There were no significant differences between the groups for any other knee joint kinematic parameters. Hip peak extension was lower in the JHS group than both the NF group (p=.028) and the GJH group (p=.035). The mean hip angle during weight bearing was significantly greater in JHS than the NF group (p=.015), showing that JHS participants had greater hip flexion during the support phase of gait. Hip variability was greater in JHS than both NF (p=.001) and GJH (p=.001).

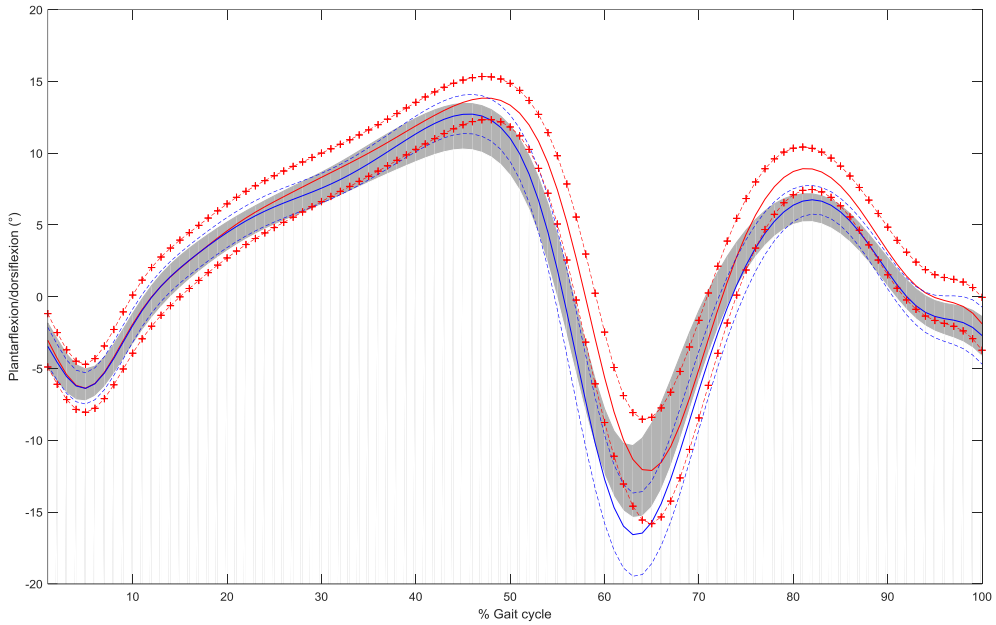


Figure 7.3. Ankle plantarflexion/dorsiflexion. Grey area is within one standard deviation of NF mean. Red line JHS mean with one standard deviation marked as + line. GJH blue with standard deviation marked with blue dashed line.

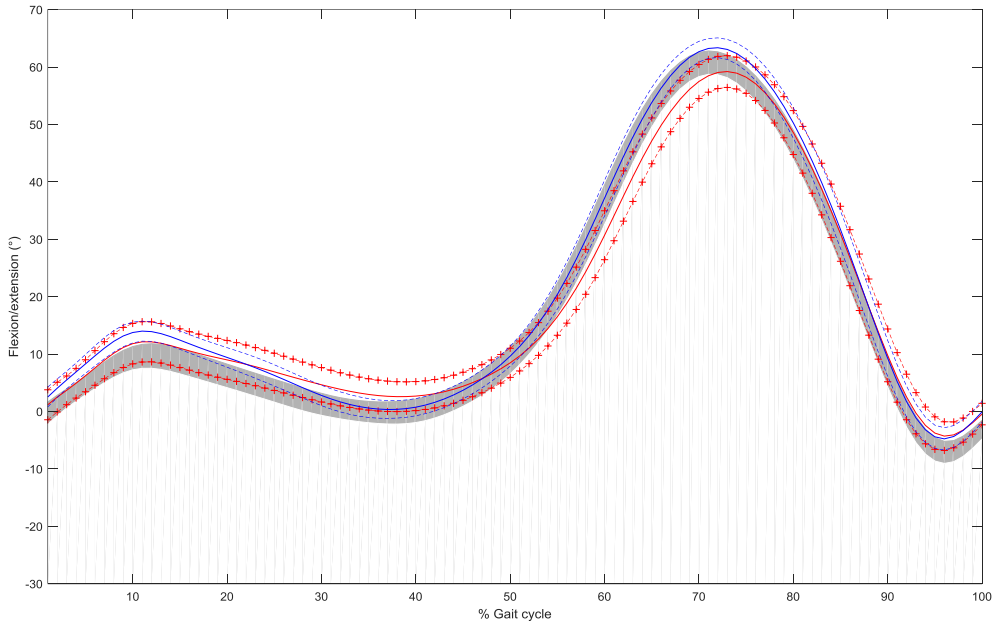


Figure 7.4. Knee flexion/extension. Grey area is within one standard deviation of NF mean. Red line JHS mean with one standard deviation marked as + line. GJH blue with standard deviation marked with blue dashed line.

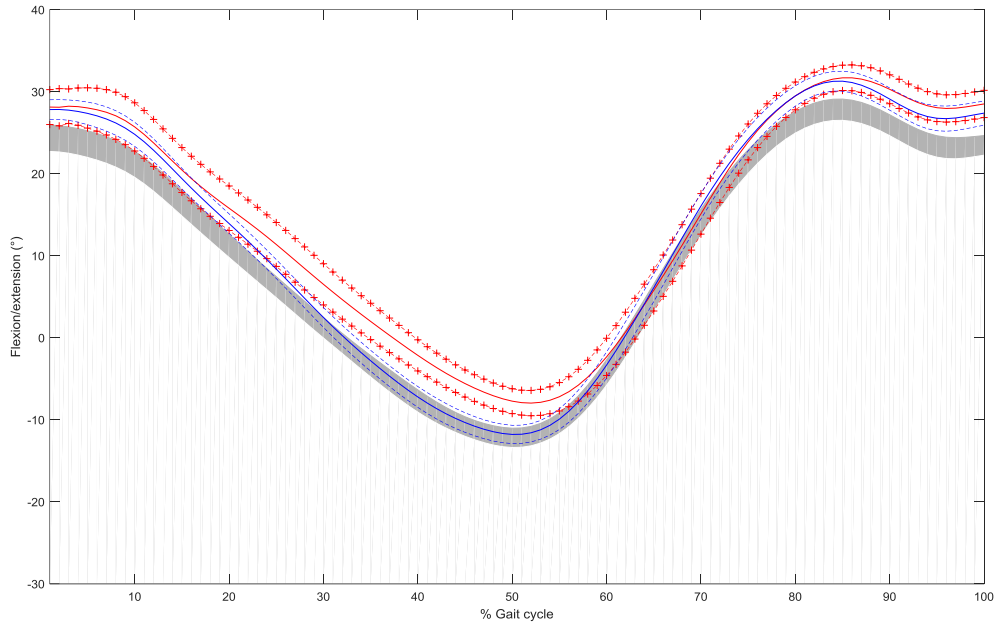


Figure 7.5. Hip flexion/extension. Grey area is within one standard deviation of NF mean. Red line JHS mean with one standard deviation marked as + line. GJH blue with standard deviation marked with blue dashed line.

To illustrate the variability further, an example of a JHS gait trial is shown in figure 7.7.

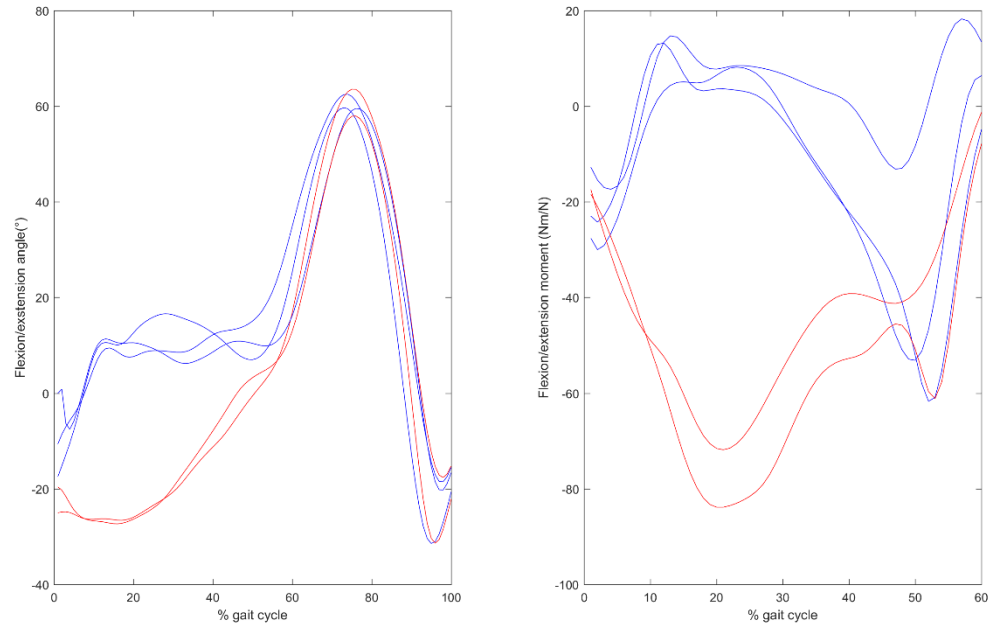


Figure 7.6. Knee flexion/extension angle and moment for one JHS participant. 5 steps are shown, and two different movement strategies observed: Blue line shows a more 'normal' gait cycle, with the knee showing a 'double knee action' and flexion shortly after initial contact. Red lines show a more

pathological gait, where double knee action is no longer present, and the knee moment changes from extensor to flexor. Steps 1, 2, and 4 are shown with blue lines, steps 3 and 5 with red lines. This indicates the different strategies JHS 15 used during gait.

7.3.3 Joint moments

Joint moments have been illustrated throughout the gait cycle in figures 7.7 to 7.9. JHS had a significantly smaller peak hip extensor moment at HM1 than NF (p=.002) and GJH (p=.001), and a significantly smaller peak flexion moment than NF at HM2 (p=.015). There were no significant differences in knee joint or ankle joint moment parameters.

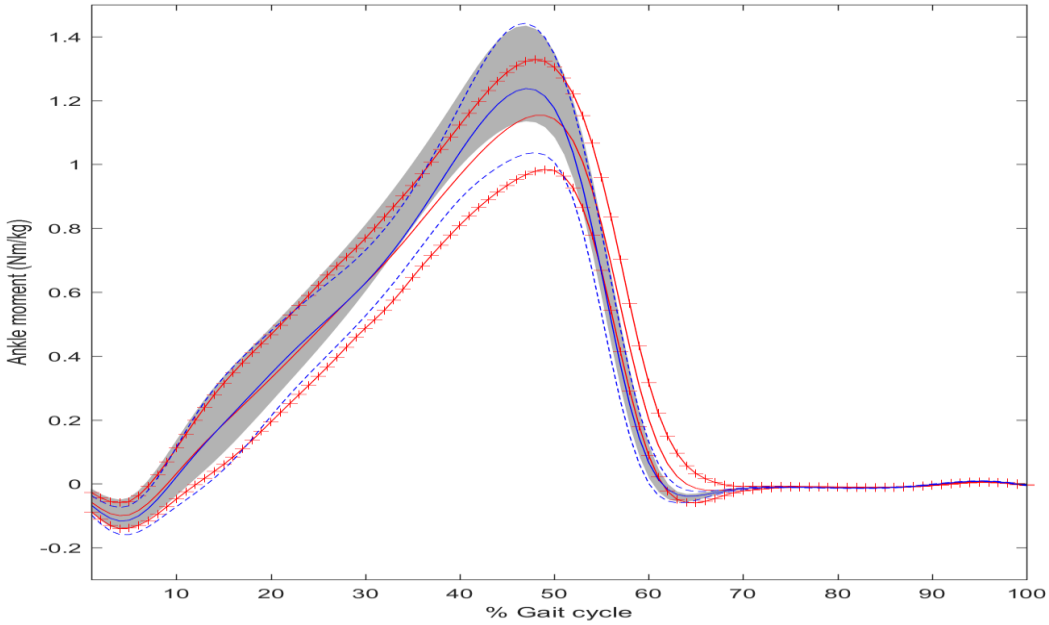


Figure 7.7. Ankle dorsiflexor/plantarflexor moment. Grey area is within one standard deviation of NF mean. Red line JHS mean with one standard deviation marked as + line. GJH blue with standard deviation marked with blue dashed line.

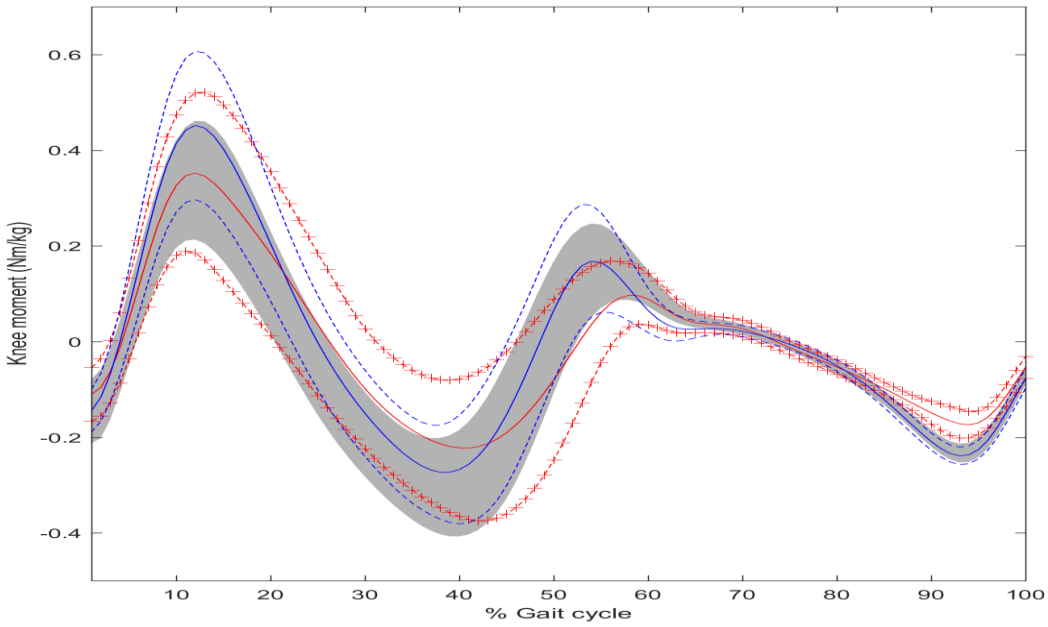


Figure 7.8. Knee flexor/extensor moment. Grey area is within one standard deviation of NF mean. Red line JHS mean with one standard deviation marked as + line. GJH blue with standard deviation marked with blue dashed line.

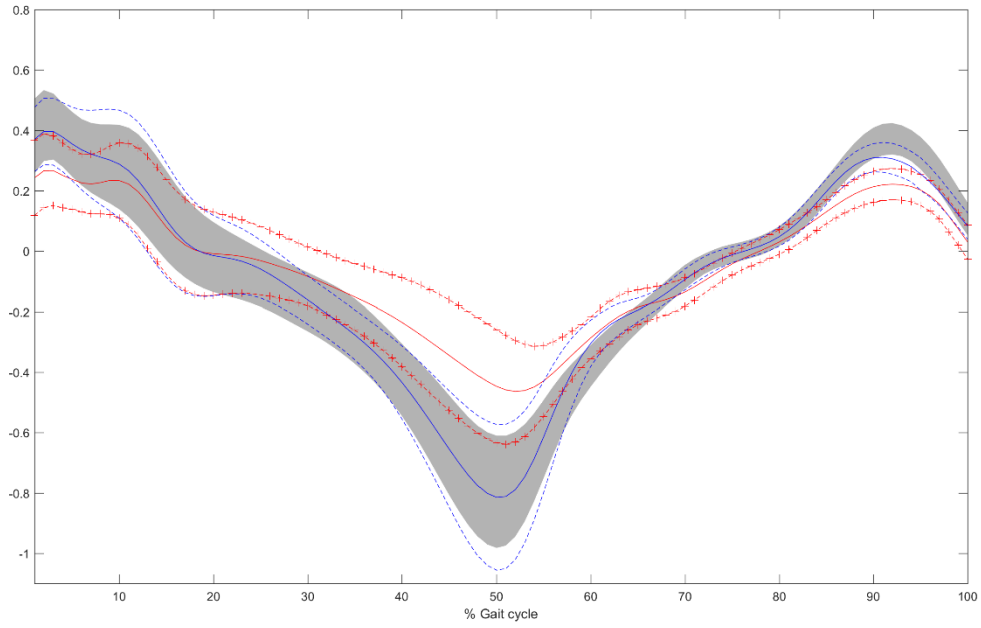


Figure 7.9 Hip flexor/extensor moment. Grey area is within one standard deviation of NF mean. Red line JHS mean with one standard deviation marked as + line. GJH blue with standard deviation marked with blue dashed line.

7.3.4 Joint powers

For ankle power, JHS group has a significantly smaller AP1 peak than GJH (p=.033). Knee power RMS was significantly lower than NF (p=.020) and GJH (p=.004), peak KP1 was significantly lower in JHS than NF (p=.030) and peak KP2 was significantly lower in JHS than GJH (p=.009). At the hip, RMS power was significantly lower in JHS than NF (p=.018) and GJH (p=.006). HP1 and HP2 peaks were significantly smaller in JHS than NF (p=.006 and .006 respectively) and GJH (p=.005 and .040 respectively).

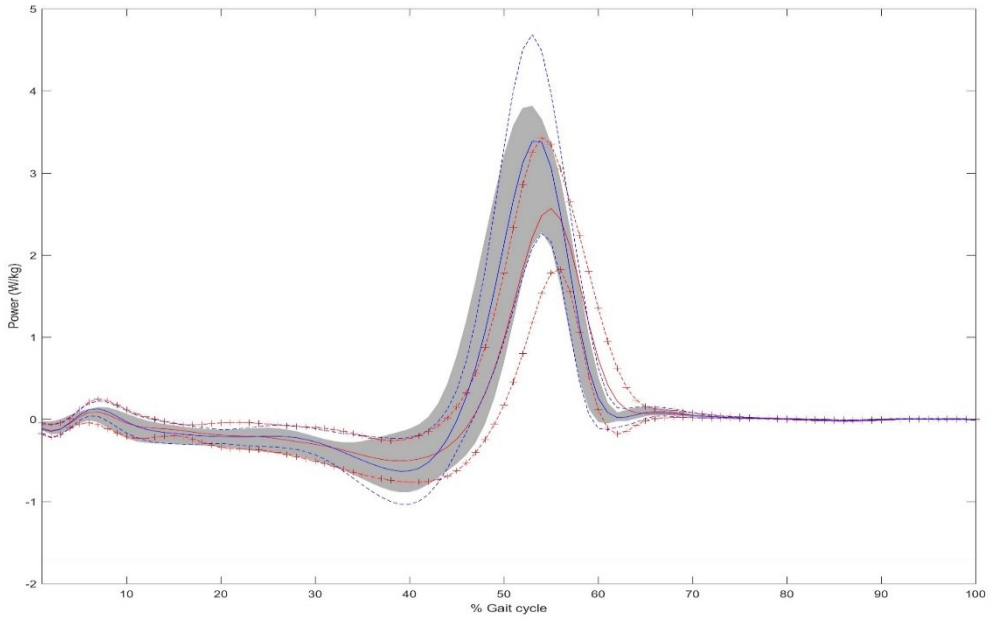


Figure 7.10. Ankle Joint Power. Grey area is within one standard deviation of NF mean. Red line JHS mean with one standard deviation marked as + line. GJH blue with standard deviation marked with blue dashed line.

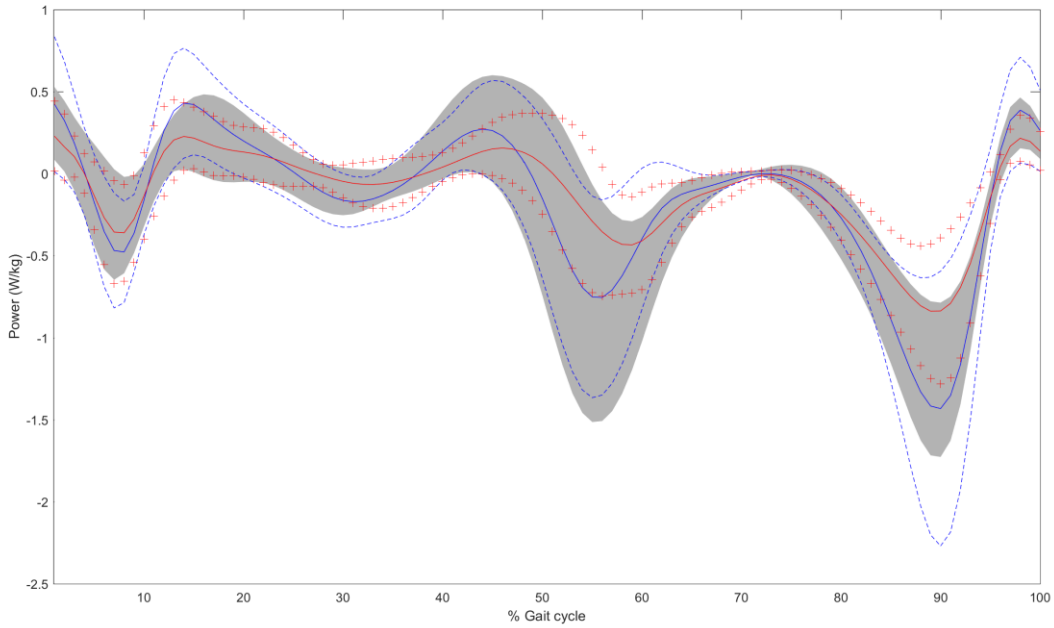


Figure 7.11. Knee Joint Power. Grey area is within one standard deviation of NF mean. Red line JHS mean with one standard deviation marked as + line. GJH blue with standard deviation marked with blue dashed line.

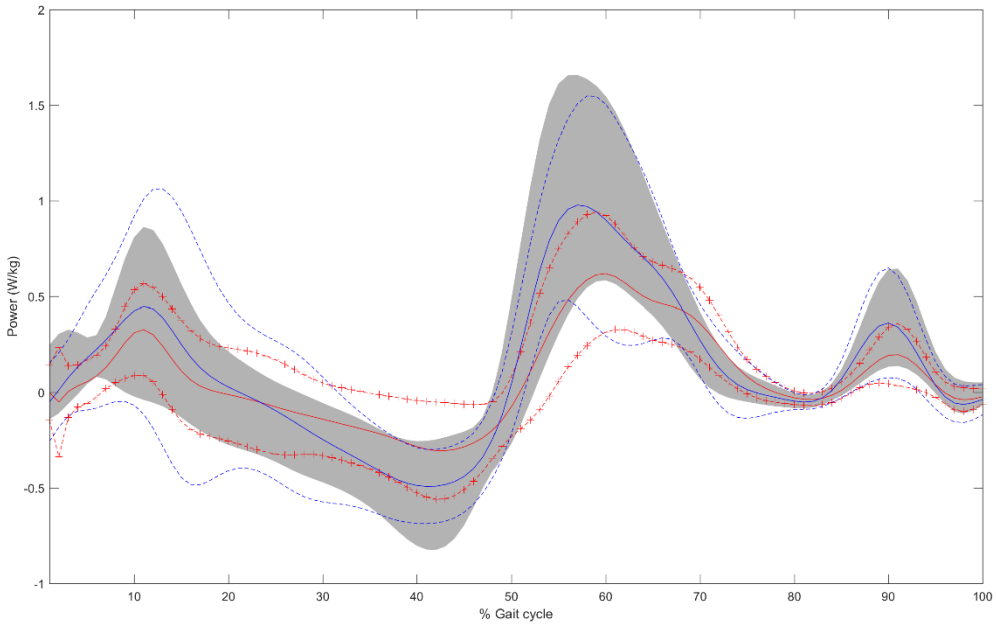
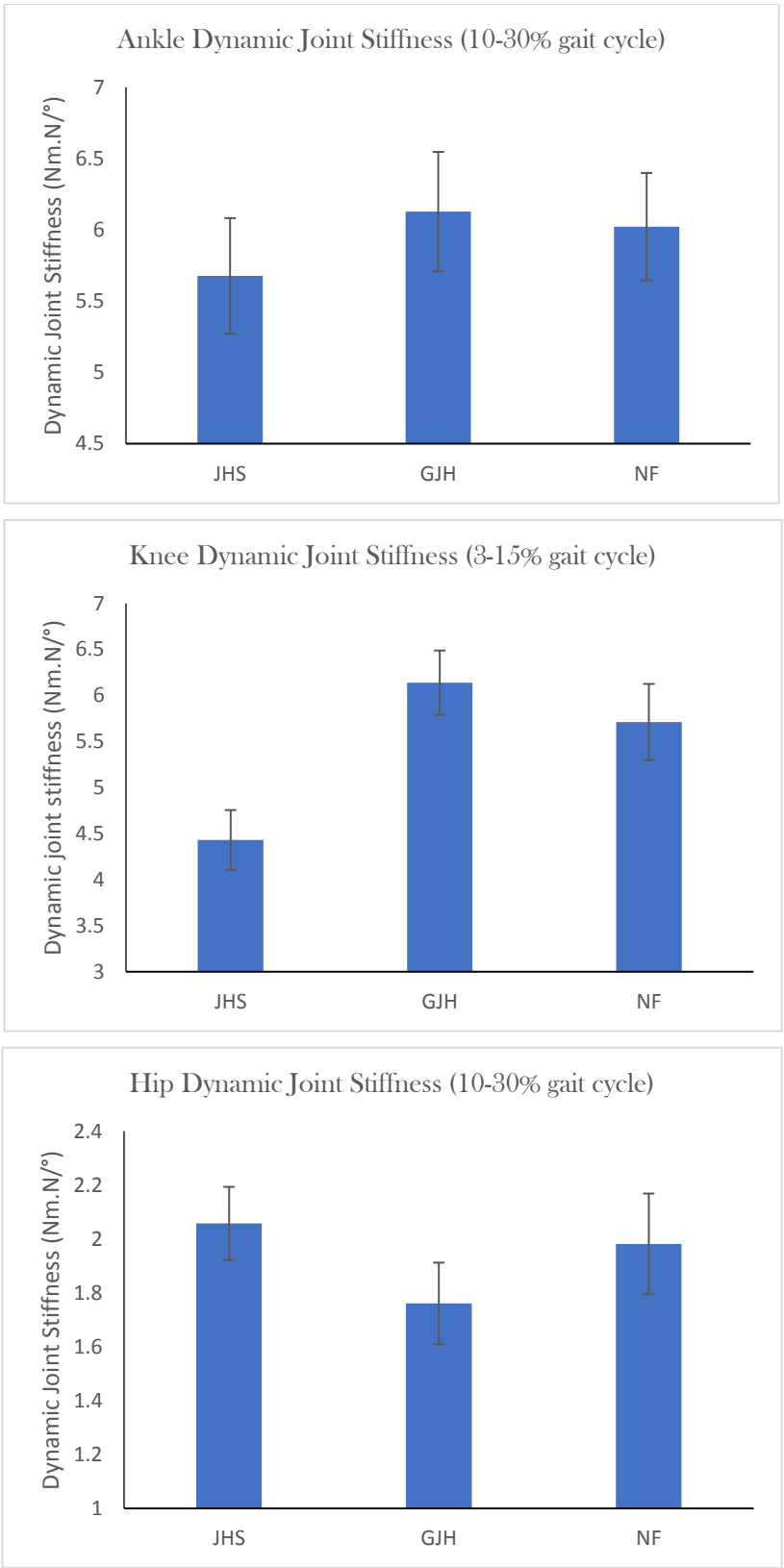


Figure 7.12. Hip Power. Grey area is within one standard deviation of NF mean. Red line JHS mean with one standard deviation marked as + line. GJH blue with standard deviation marked with blue dashed line.

7.3.5 Joint stiffness

Dynamic joint stiffness values are shown in figures 7.13 to 7.15. There were no significant differences between groups in ankle or hip stiffness. The JHS group had significantly lower knee dynamic joint stiffness than GJH ($p=.023$). JHS knee stiffness was also lower than the NF group, and although the difference was not statistically significant, it was close to becoming significant ($p=.051$).



Figures 7.13 – 7.15. Mean ± standard deviation of dynamic joint stiffness for the ankle, knee, and hip. A significant differences was observed in knee stiffness between JHS and GJH groups, all other comparisons were not significant.

7.3.6 Co-contraction

Co-contraction parameters were not normally distributed, and so are illustrated using box plots in figures 7.16-7.18. The Krukal-Wallis test showed that there were no significant differences between groups in VM/VL co-contraction (p=.569), or in RF/BF co-contraction (p=.766). There was a significant difference between groups in GA/TA co-contraction (p= .031). Post-hoc Mann Whitney tests, however, failed to show a significant difference between groups after adjusting for multiple comparisons. The p values for each comparison were p=.206 for NF vs GJH group, p=.058 for NF vs JHS group, and p=.525for GJH vs JHS group.

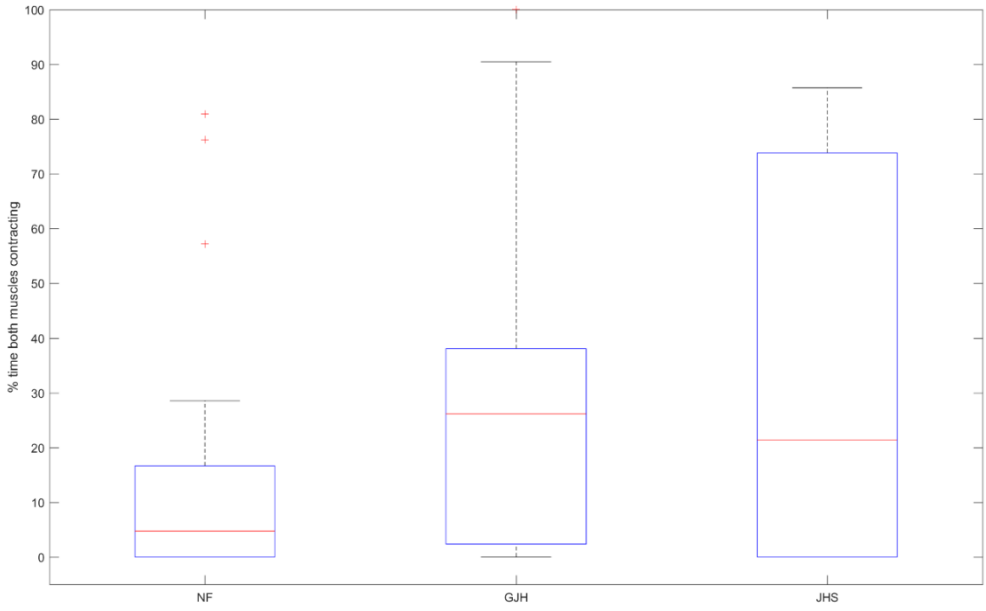


Figure 7.16. GA/TA Co-contraction during 10-30% of the gait cycle.

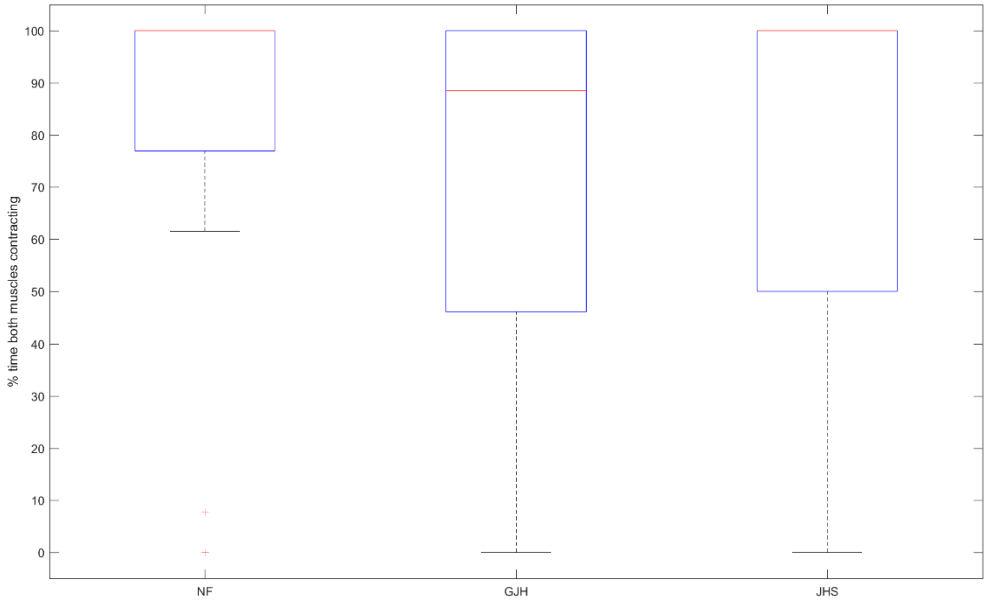


Figure 7.17 VM/VL co-contraction during 3-15% of the gait cycle.

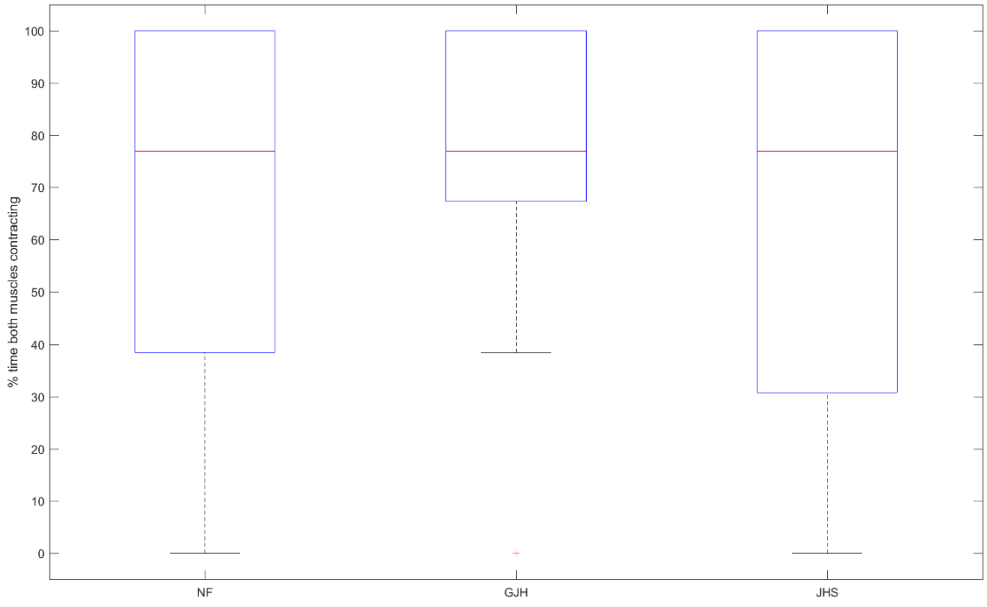


Figure 7.18. BF/RF co-contraction during 3-15% of the gait cycle.

7.4 Discussion

7.4.1 Temporal-spatial and gait variability

Temporal-spatial measures are typical measures of the quality of gait. Although on average the JHS group had a slower stride time, greater mean stride width, lower velocity, and smaller stride length than NF and GJH groups, just velocity and stride time were significantly different in separating the JHS group from both the GJH and NF groups. These results indicate that the JHS group have impaired gait function. Furthermore, variability of temporal-spatial measures can be seen as a measure of gait stability, with an increase in variability being indicative of instability[193]. The JHS group showed more variability in all temporal-spatial measures, of which stride length variability was significantly larger than the NF group, indicating that their gait may be less stable. The other method of measuring variability employed in this study was inspection of the kinematic charts for each joint for each step. It was noticed that it was common for JHS participants to employ more than one movement strategy for gait, for an example see figure 7.6. Using the example in Figure 7.6, two different strategies were used; in three steps a relatively normal strategy where the knee flexes after initial contact, in two steps there was little to no knee flexion following initial contact. Interestingly, this may have been noticed by other researchers; Cimolin *et al.*[102] in their study of JHS gait state in the methods "starting from the five trials collected, three consistent trials able to evidence the same gait pattern...were selected", which implies that more than one gait pattern was observed. In this analysis, we included all gait trials regardless of whether a different gait pattern was observed. The reason for this is two-fold; firstly, since variability of kinematic and spatio-temporal parameters was an outcome measure, limiting a participant to a particular gait pattern would artificially reduce variability; secondly, when presented with two or more gait patterns for an individual, there is an issue of how to choose the gait pattern which is representative of their gait. Interestingly, knee flexion during stance is one of the determinants of gait, its function is to limit deviation of the centre of mass during stance, without this flexion the centre of mass would rise and cause inefficient gait[133]. Anecdotally, this same pattern was observed in several of the JHS participants, but not observed in the NF and GJH groups. The cause may be quadriceps weakness; the quadriceps muscles are responsible for the control of the knee during loading by eccentrically contracting, if they are not strong enough, the plantarflexor-knee extensor couple is used instead[133]. In the plantarflexor-knee extensor couple, under load the plantarflexors can apply a knee extensor moment to stabilise the knee[204], as is observed in the moment chart in figure 7.7; when the knee doesn't flex during stance the moment at the knee reverses to extensor rather than flexor. It would be interesting to quantify the incidence of these different gait patterns in JHS individuals compared to the control groups, and multiple gait strategies were observed in at least 8 of the 23 JHS participants. However, since data-dredging was identified as a potential problem in the study of JHS gait[82], the data was not retrospectively analysed.

7.4.2 Kinematics

In terms of kinematics, the JHS group were significantly more variable than NF at the ankle and hip, and more variable than GJH at the hip and knee. This again indicates that the JHS participants walked with greater instability. There were no significant differences in variability between GJH and NF at any joint. The fact that the GJH group had similar variability to people with NF suggests that hypermobility either is not a factor in causing instability, or that GJH individuals are better at controlling any contribution to instability hypermobility makes. There were no other significant differences in kinematics at the ankle. At the knee, the GJH group had significantly greater peak flexion than JHS, but there was no significant difference between JHS and NF or GJH and NF. Peak knee flexion occurs in swing phase, to provide limb clearance for the swing limb, it can be reduced by pain, muscle weakness, and lower walking velocity[205,206]. It is therefore surprising that the JHS group, despite all individuals having knee pain, and evidence that people with JHS generally suffering from muscle weakness[39,64], did not reduce their peak knee flexion compared to NF participants. The GJH group did have significantly greater peak knee flexion than JHS, however they also walked with significantly greater velocity than NF and JHS groups. Since peak knee flexion increases with velocity it is feasible that this is the cause of the observed difference. Reduced hip moments during gait have been associated with reduced peak knee flexion[207]. It is therefore interesting, that although JHS has a significantly lower peak hip extensor moment than NF and GJH, and a significantly lower peak flexor moment than NF, these differences did not result in lower peak knee flexion when comparing JHS to NF.

At the hip JHS had significantly lower peak extension of over 4° than both NF and GJH groups, and during weight bearing had greater flexion than the NF group. Reduced peak hip extension is commonly seen in deficient gait, and can be attributed to muscle weakness of the hip flexors[208]. Hip extension can also be reduced by forward trunk lean, by tilting the pelvis forward anteriorly, an adaption to take work away from the hip flexors by negating the effort used to support the trunk[133]. Flexing the trunk moves the body's centre of gravity/ground reaction line anteriorly relative to the knee joint, which stabilises the knee joint and aids hip flexion, which aids the pull-off of the limb during pre-swing[133]. Although the position of the trunk was not measured in this study, this adaption has been seen in stair climbing of JHS individuals[104]. Reduced hip extension has also been associated with pain[209].

7.4.3 Moments and powers

Evidence of JHS having hip weakness is supported by moment data; both the hip extensor and flexor moment peaks were significantly lower in JHS than NF cohorts, and there was no significant difference between NF and GJH groups. The peak extensor moment functions to stabilise the trunk from flexing forward during the first half of stance phase[168], since the moment is reduced it is feasible

that the trunk is being allowed to flex forward, as per the mechanism to stabilise the knee and aid pull-off. Equally however, the reduction in hip moments could show a reluctance to generate muscular force due to pain. If pain were the cause however, it would be expected to see reduced moments at the knee and hip, this was not the case; there were no significant differences between any of the groups in knee or ankle joint moments.

The results for joint power, support muscle weakness being a factor in causing the differences in JHS gait, with the JHS group producing lower power in many of the power parameters measured. RMS power, a measure of the mean power generated throughout the gait cycle, was significantly lower in JHS than NF and GJH at the knee, and significantly lower than NF at the hip. Although ankle RMS power was lowest in the JHS group, this difference was not significant. JHS had a lower peak power at A2, which is where the foot plantarflexes to provide a 'push-off'. For knee power, the JHS group was significantly lower than NF at KP1 peak, and GJH at KP2 peak. Peak KP1 corresponds to a knee extensor moment that limits the amount of knee flexion in late stance, and KP2 corresponds to knee flexor activity to decelerate the swing limb for initial contact[140]. The reduction of power could again show an inability to create a greater joint moment due to muscle weakness, or a reluctance to create larger magnitude moments due to pain. A similar pattern was observed at the hip, with JHS having significantly less power than both NF and GJH groups at peaks HP1 and HP2. Peaks HP1 and HP2 correspond to hip moments that serve to stabilise the trunk and knee[140], the fact that these peaks are reduced may explain why we found evidence of increased instability. Interestingly, the significant differences in power peaks were all found in late stance and swing phase, the late stage peaks are where the body generates energy to propel the body forward, and muscle weakness of JHS could be limiting the amount of power produced.

7.4.4 Dynamic joint stiffness

Although JHS dynamic joint stiffness was the lowest of the three groups at each joint, these differences were never significant between JHS and NF groups, the only significant difference observed was between JHS and GJH at the knee. This result contrasts the findings of Galli *et al.*[96] and Cimolin *et al.*[102], who found that JHS participants had reduced ankle and hip stiffness compared to normal flexibility controls. The fact that differences were not significant in this study may be due to the large variability of joint stiffness observed. As discussed previously, Galli *et al.*[96] and Cimolin *et al.*[102] chose to analyse steps with a similar gait pattern instead of including all of a participant's steps. Since all a participant's steps were included in this analysis, it could be that JHS individuals used a variety of gait patterns, and the inclusion of all patterns led to an increase in variability of dynamic joint stiffness measured. The differences in methodology and results highlight the difficulty in comparing studies.

7.4.5 EMG co-contraction

There were no significant differences between any of the groups in VM/VL or BF/RF co-contraction. Although the Kruskal-Wallis test showed there was a significant difference between groups in GA/TA co-contraction, there were no significant differences for the pairwise comparisons, after adjusting for multiple comparisons. This situation can arise when the study is underpowered. The difference between JHS and NF groups was closest to significance (p=.058). The sample size for this study was based on the kinematic outcome measures, therefore it may be that there is a significantly difference between JHS and NF groups, but this study was not sufficiently powered to measure the difference.

An increase in GA/TA co-contraction could function to stabilise and stiffen the ankle joint, as is the case in other groups with diminished gait function, such as the elderly[210]. It has also been suggested that co-contraction could function to enhance proprioception by increasing the afferent information from muscle spindles[211]. In contrast there is evidence that people with less proprioceptive acuity have lower GA/TA co-contraction[200], which would indicate that joint instability rather than reduced proprioception was the drive behind JHS/GJH groups increasing their co-contraction. At the knee there was no significant difference between groups for BF/RF and VM/VL co-contraction in all groups, however knee stiffness in JHS was significantly lower than GJH. This could be indicative of muscle weakness; JHS are not able to generate the force necessary to stiffen and stabilise the knee. Future research could investigate whether increasing lower limb muscle strength would normalise these parameters.

It should be noted that the method of determining co-contraction we used in this study is a rather blunt approach; it does not measure the magnitude of the co-contraction as other methods used in the literature aim to do. The method we have used simply shows that both muscles are active at the same time. Although this method may lose some of the nuances of co-contraction, other methods were not available, as the JHS group were unable to create maximum voluntary contractions. This means that the co-contraction magnitudes would be unreliable and uncomparable[202]. Similar problems regarding the determination of co-contraction in the absence of EMG normalisation have been faced by other researchers. For example, Lamontagne *et al.*[212] were unable to normalise EMG in a cohort of stroke patients, and used a similar method to that used here in that they calculated the % time of co-contraction in relation to the gait cycle. It should be noted however that there are limitations regardless of the method of measuring co-contraction when using EMG, namely that the magnitude of EMG observed is not necessarily indicative of the joint forces; a muscle can be more active than another and still generate less force, due to a range of factors such as pennation angle and fibre length[203].

7.5 Conclusion

The results of this study indicate that gait is impaired in JHS individuals. For temporal-spatial, kinematic, kinetic, dynamic joint stiffness, and EMG measures significant differences were observed between JHS participants, and/or NF and GJH participants, but no significant differences were observed between NF and GJH groups. The results in general support the current literature that gait of JHS individuals is impaired. There are a multitude of both physical and psychological factors of JHS that could cause changes in gait in JHS. These include fear of falling, muscle weakness, pain, instability, fatigue, and balance impairments. The fact that significant differences were observed between the JHS and NF/GJH groups, but no significant differences observed between NF and GJH groups, indicates that joint hypermobility *per se* is not detrimental to gait. It could be theorised that GJH individuals use mechanisms to 'overcome' their hypermobility, and JHS individuals do not employ these mechanisms. Since there were no significant differences between NF and GJH groups in any of the temporal-spatial, kinematic, or kinetic parameters measured it would appear that GJH gait is the same as NF gait, and such adaptations do not need to be made. The sample size was determined from the reliability study of hypermobile gait (Chapter 3), it is therefore unlikely that the study was under-powered for kinematic variables. Sample sizes were not considered for EMG and dynamic joint stiffness variables however, and so the study may not have been fully powered to detect a meaningful change in these parameters.

The results of this study would point to another factor other than hypermobility, present in JHS, but not present in GJH. This factor(s) may cause pain or this factor may be the existing pain. The GJH group was included as a control group to control for the confounding factor of hypermobility. Other confounding factors are pain, muscle weakness, impaired balance, fear of falling, and fatigue. A benefit of future work would be to see if increasing muscle strength of JHS individuals leads to a normalisation of gait parameters, using 3D gait analysis as an outcome measure. Interestingly, a study at Charing Cross Hospital found that a physiotherapy treatment programme increased the strength of people with JHS[64,213], but this change in strength was only weakly (but significantly) correlated to the reduction in pain. This may highlight the multifactorial nature of JHS and the wide range of its associated symptoms that could influence movement and pain.

Chapter 8. Stair ascending and descending.

8.1 Introduction

Stair climbing in hypermobile cohorts

To date, only one study has investigated stair climbing in a hypermobile cohort; Luder *et al.*[104] measured ground reaction forces and lower-limb EMG parameters in people with GJH. They did not find any significant differences between GJH and NF groups in ground reaction force parameters, and stated that the global movement pattern of the two groups was comparable. Significant differences were found in some EMG parameters; women with GJH had a significantly lower peak activity in Vastus Medialis during stair ascent, and a significantly smaller peak activity in Semitendinosus during stair descent. The authors attributed this to women with GJH walking with a 'cautious movement pattern'[104]. The authors provided several potential reasons for this; pain causing inhibition of muscles, avoidance of activation, or a muscle effusion. As discussed in Chapter 2, these results should be interpreted with some caution, since the participants may have not had symptoms during testing. Kinematic and kinetic measurements were not part of the study by Luder *et al.*[104], and they state that these measures should be included in future research in order to gain a more detailed understanding of movement and biomechanics of hypermobile people. It could be that differences in movement are not shown in ground reaction forces, but may be revealed by investigating kinematics, joint moments, and joint powers. Furthermore, there has been no research into characterising the movement strategy of people with JHS during stair climbing, and so the three groups (JHS, GJH and NF) have not been compared. As stated in Chapter 4, by comparing JHS to GJH and NF groups, a more thorough picture of how hypermobility affects movement may be observed. The objective of this study was therefore to characterise stair ascent and descent in people with JHS, to identify possible adaptations and further the understanding of movement in JHS.

Why study stair climbing

Stair climbing is a challenging activity, and places different demands on the body than level walking. Not only is a greater range of motion of lower limb joints required in order to place the foot on the next step in sequence, but joint moments are greater[214]. For example, during stair ascent, knee joint moments have been found to be up to 25% greater than level walking[134], and a study using accelerometers to measure shockwaves during stair climbing, found that the shockwaves caused by stair descent were 1.3 times greater than during stair ascent and 2.5 times greater than level walking[135].

It is the increased physical demands of stair climbing that makes it an interesting activity to investigate, and stair climbing has been measured in musculoskeletal conditions such as osteoarthritis[215-217], patellofemoral pain syndrome[218], and people with knee replacements[219]. Overall, these investigations tend to emphasise upon the knee. For example, in the study of stair climbing in a hypermobile cohort by Luder *et al.*[104], they only discussed compensatory strategies concerning the knee and hip, and the ankle was not considered. In another study of stair climbing kinetics in healthy individuals by Costigan *et al.*[220], the ankle joint was again ignored. Where it has been studied, it has been shown that the ankle plantarflexors play a substantial role in accelerating the centre of mass upwards during stair ascent[221].

In stair ascent, lower-limb muscles must work to accelerate the body upwards. Peak activity has been found to be greater in the soleus, rectus femoris, hamstrings, and gluteus maximus during stair ascent when compared to level walking[134]. During stair descent, the soleus and rectus femoris are more active, as they work to stabilise the knee[134]. The high forces incurred and demands on the musculoskeletal system mean stair climbing is a challenging task, and as such it can be used to aid therapists in clinical examination and treatment of patients who have lower limb dysfunction[214,222]. Considering that features of JHS include joint pain, instability, muscle weakness, and fatigue[1,223], such an activity that places relatively high demand on the lower limb joints, would potentially show differences in movement between people with JHS and people with GJH/NF. Furthermore, stair climbing features in one of the questions in the Bristol Impact of Hypermobility questionnaire[19], and so it is reasonable to say that people with JHS find stair climbing challenging. In addition, Luder *et al.*[104] found significant differences in lower limb EMG parameters between women with GJH and women with NF; these differences were more pronounced in the GJH participants who later developed symptoms.

Given that there have been adaptions to stair climbing found in a range of other conditions, such as knee osteoarthritis[215-217] and patellofemoral pain syndrome[218], I hypothesise that people with GJH and JHS also adapt their movement during stair climbing. By characterising if, and how, movement differs we may further the understanding of the syndrome and its functional deficits. This information will be valuable to provide insight in recognising impairments in JHS individuals, and highlight factors to target using physiotherapy. In addition, understanding of stair climbing and descent mechanics is important in furthering the knowledge of lower limb pathogenesis[134], it could direct treatment to the appropriate correction of kinematics and kinetics. Therefore, this study explores lower-limb kinematics and kinetics during stair climbing in JHS individuals compared to GJH and NF. The aim is to characterise and identify adaptations of people with JHS when ascending and descending stairs. The specific research question is:

- Do people with JHS present kinematic and/or kinetic alterations at the hip, knee, and ankle during stair climbing?

Describing stair climbing

Level gait has been well defined in terms of phases of the gait cycle and the normal joint range of motions, moments, powers, and the functional objectives have been described in detail. There is less consensus in the current literature as to how stair ascent and descent are described. This may be because the specific movement patterns generated during stair climbing are likely to depend on several factors. For example, the inclination of the staircase affects joint moment and joint power; the steeper the stair, the more energy needs to be generated by muscles to raise the centre of mass during ascent, and in descent more energy needs to be absorbed[224]. Considering there are additional dimensions of the stairs to consider; step height, step depth, and the number of steps in the staircase; it is perhaps not surprising that there is relatively large variability in absolute values found between studies. Additionally, there is not universal agreement whether stair ascent or descent is the more demanding activity. Andriacchi *et al.*[134] found that stair descent generated the greatest moments and joint powers. In contrast, Protopapadaki *et al.*[214] state that ascent is the more demanding activity. In the study by Luder *et al.*[104], peak ground reaction force was greater during descent than ascent in both NF and GJH cohorts. Riener *et al.*[224] found that peak knee extensor moment was greater during ascent at all three different stair inclinations measured. Whereas McFadyen & Winter[225] reported broadly similar knee moments in stair ascent vs stair descent.

Added to the fact that physical characteristics of the staircase affect the movement observed, there are also several approaches a person may use to climb stairs. Common methods include "step-over-step", where each foot is placed on the next step of the stair in sequence, and "step-by-step", where both feet are placed on the same step (Figure 8.1)[226]. Combined with the fact that a person may use a handrail during stair climbing, there are a huge variety of methods of stair climbing, which may explain the variability of results observed in the literature. Interestingly, there is evidence that stair ascent is considerably more variable than stair descent[134]. This variability has been attributed to people adopting a variety of different movement patterns during ascent, for example using a forefoot only or full-foot contact[214].

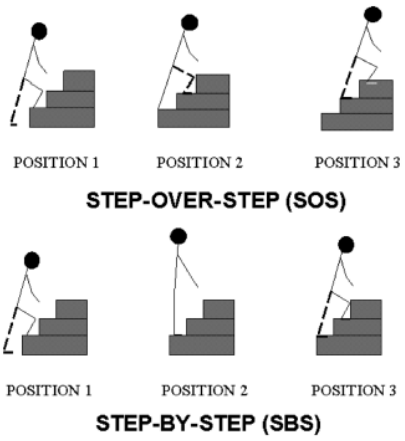


Figure 8.1: Two different methods of stair climbing; the "step-over-step" and "step-by-step" method. Reproduced with permission from Reid *et al.*[226].

Phases of stair climbing

To aid understanding and interpretation of movement, the gait cycle is commonly split into separate functional phases (see Chapter 7). There is less consensus in describing stair climbing, with researchers defining the cycle in different ways. Andriacchi *et al.*[134] and McFadyen *et al.*[225] both describe stair ascent as beginning and ending with initial contact of the ipsilateral limb, but define stair descent as the opposite; as starting and ending with toe-off of the ipsilateral limb. In contrast, Protopadaki *et al.*[214] use initial contact as the start of the cycle for both ascent and descent. In other studies, such as Reid *et al.*[226], Igawa *et al.*[216], and Costigan *et al.*[220], the start and end point of the stair-cycle is not defined. The effect of this is that it is relatively difficult to compare the results of these studies at a glance.

To address this problem, the stair cycle is described in the following paragraphs. In terms of kinematic studies, two of the first to describe stair climbing was Andriacchi *et al.*[134] and McFadyen & Winter[225]. Their descriptions form the basis of the following phases, to which the results of a more recent 3D movement analysis study by Protopapdaki *et al.*[214], and information about the role of joint powers from Wilken *et al.*[227], have been integrated. The standard step-over-step method of stair climbing is described.

Stair ascent:

Example moments and powers for lower limb joints are presented in Figure 8.3.

Initial contact and weight acceptance.

On initial contact the hip and knee are in flexion. Shortly after initial contact knee flexion and ankle dorsiflexion increases[134], as weight is transferred from the contralateral limb to the ipsilateral limb.

For knee power, there is a small negative power peak on initial contact, as the knee works to absorb bodyweight, followed by an increase as the knee extensors work to raise the body[227].

Pull-up.

Pull-up starts with the ipsilateral foot losing contact with the floor and marks the beginning of single limb support. The hip and knee extend to raise the body centre of mass. During Pull-up, the ankle stays at a relatively constant dorsiflexion, as the contralateral foot makes contact on the next step and double support is resumed, the ankle enters platarflexion. There is a large knee extensor moment, which can be double that of level walking[228], as the centre of mass is propelled upwards[228]. There is a relatively large peak of positive power at the knee[227,228].

There is a peak in ankle power in late stance during the double support phase[227,228]. This peak in power corresponds to a vertical acceleration of the centre of mass, as the platarflexors work to raise the body upwards[227].

Swing.

Shortly after toe-off, the ankle dorsiflexes to provide clearance for the swing limb to pass over and above the step. At the same time, knee flexion provides clearance, and the hip flexes to progress the swing limb.

Foot placement.

On foot placement the hip and knee extend, and the ankle begins to plantarflex, as the limb is prepared for initial contact and weight acceptance. In terms of hip moment, there are a variety of patterns that have been observed in the literature[214], which have been attributed to the position of the trunk; whether the trunk is positioned with anterior or posterior lean will affect the line of centre of gravity passing through the hip joint, and would cause the variability of hip moment seen across studies[214].

Stair descent

The main functional difference between ascent and descent, is that the lower limbs do not need to work to raise bodyweight, but rather their function is to stabilise and safely lower bodyweight[134,215]. As discussed previously, there is a large amount of variability in joint angles and moments observed during stair descent. The phases, joint powers, moments, and kinematics listed below have been collated from various investigations of stair climbing[134,214,226,229,230]. An example of hip, knee, and ankle moment and powers are shown in Figure 8.4.

Initial contact and weight acceptance.

At initial contact, the hip is in a small amount of flexion, the knee extended, and the ankle plantarflexed. As the foot is placed on the step and weight is transferred onto the ipsilateral limb from the contralateral limb, the quadriceps muscles and soleus contract eccentrically combined with a dorsiflexion and knee flexion. Power generation comes from the hip, and there is an external hip extensor moment (HDM). There is an external flexion moment at the knee (KDM1), and external dorsiflexion moment at the ankle (ADM1). These moment peaks correspond to negative power peaks KDP1 and ADP1 where energy is absorbed at the joints.

Single limb support.

At the start of single limb support, the hip and knee remain extended to aid ipsilateral limb clearance. As the ipsilateral limb and the centre of mass move forward, the hip and knee flex to lower the centre of mass for ipsilateral initial contact. The ankle dorsiflexes as the centre of mass passes over the support limb. The knee reaches peak external flexion (KDM2) and a peak in negative power (KDP2), these peaks correspond to a peak in ankle dorsiflexion moment (ADM2) where the plantarflexors contract to provide positive power to accelerate the limb into swing phase (ADP2).

Swing phase.

Just after toe-off, the knee reaches peak flexion to clear the step, which is combined with concentric contraction of Biceps Femoris. The hip flexes as the contralateral limb is pulled forward towards the next step. In early swing, Tibialis Anterior contracts to bring the ankle into dorsiflexion. From mid to late swing phase, the hip and knee extend to meet the next step of the stair, and to prepare for initial contact and loading. The ankle enters plantarflexion in midswing.

8.2 Methods:

An instrumented staircase comprising of three steps was used (Figure 8.2). The height of each step was 25cm, width 60cm and tread depth 25cm. At the top of the stair was a platform measuring 60 by 60cm. A Kistler force plate was inserted into the first and second step.



Figure 8.2. The instrumented staircase.

Participants were instructed to ascend and descend the staircase. To facilitate the gathering of comparable data, participants were asked to climb the stairs in the same manner; using the step-over-step method, without using the hand rail. Five complete ascent and descent steps were used for analysis.

Movement parameters differ for step-to-step, and step-to-floor steps[134]. In addition, floor-to-stair steps (and vice versa) are less reproducible than mid-staircase steps[222]. Furthermore, in a priori testing some participants would begin turning around (to re-ascend/descend the stairs) whilst completing the final step in the sequence, whereas the middle step in the stair was completed in a 'straight ahead' motion. For these reasons, only steps making contact with the middle step of the stair-case were analysed.

The stance phase, where the foot is in contact with the stair, was analysed. Stance phase was defined from initial contact to lift-off of the supporting limb.

Kinematic data was collected at 100Hz, force plate data at 1000Hz. Joint angles and moments were calculated using Vicon Body Language software, using the model described in Chapter 3. Results for each participant were analysed in MatLab (The MathWorks, Natick, United States). Kinematic and kinetic parameters were low-pass filtered at 6Hz using a Butterworth 4th order filter with zero phase lag, and normalised to percentage stance phase. Spatiotemporal variables of interest were stance time, gait velocity, and stride width. Kinematic parameters were the mean joint angle and range-of motion for the ankle, knee, and hip. Joint moments were normalised to bodyweight. Joint moment and power parameters of interest during stair ascent were: At the hip, the peaks in extensor moment, the first occurring at 22% stance phase (HAM1), the second just after 80% stance phase (HAM2); At the knee,

the peak flexion moment in the first half of the gait phase (KAM1), and peak extensor moment in the second half of stance phase (KAM2); At the ankle, peak plantarflexion moment in the first half of stance phase (AAM1) and peak plantarflexion moment in the second half (AAM2); Peak hip, knee, and ankle power generated (HAP1, KAP1, and AAP1).

Joint moments and powers of interest during stair descent were: At the ankle, peak dorsiflexion moment at the end of stance phase (ADM1); At the knee, peak flexor moment in the first half and second half of stance phase (KDM1 and KDM2); At the hip, peak extensor moment during stance (HDM1); For knee power, negative peaks of power absorption (KDP1 and KDP2); For ankle power, the negative peak in early stance phase (ADP1) and peak power generated (ADP2). The root-mean-square (RMS) power for each joint was calculated for both ascent and descent.

Five trials for both ascent and descent were averaged for each participant. Individual participant results were then averaged to give the group mean and standard deviation throughout the stance phase.

Variables were analysed with SPSS version 24. A MANOVA test was used, with group (JHS/GJH/NF) as the independent variable and the outcome measures as dependent variables. Post-hoc tests were corrected for multiple comparisons using the Bonferroni method, and significance was set at 95% ($\alpha = 0.05$).

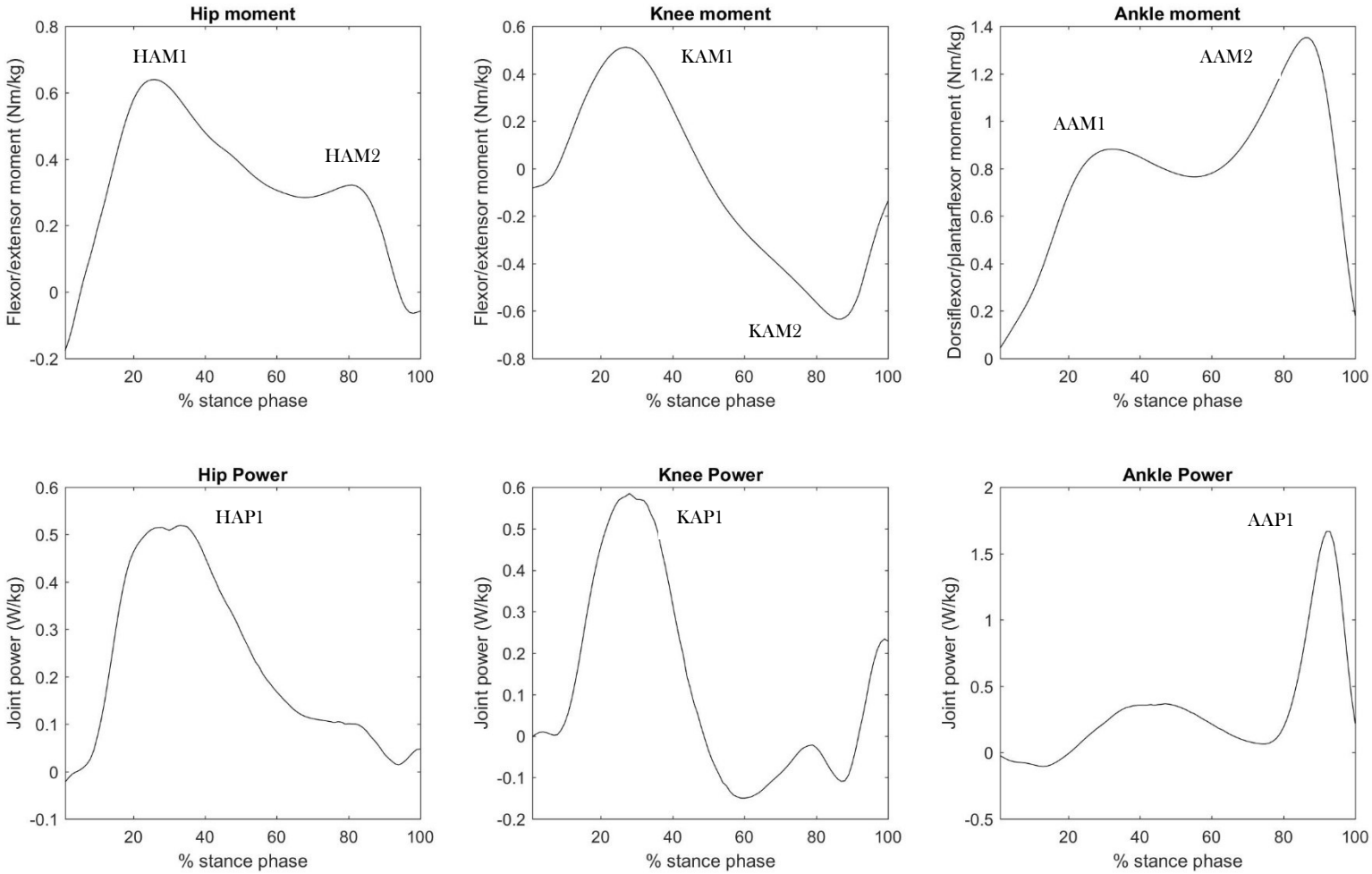


Figure 8.3. Typical joint moments and powers observed in a normal flexibility group during stair ascent. Flexion (and dorsiflexion) positive, extension (and plantarflexion) negative.

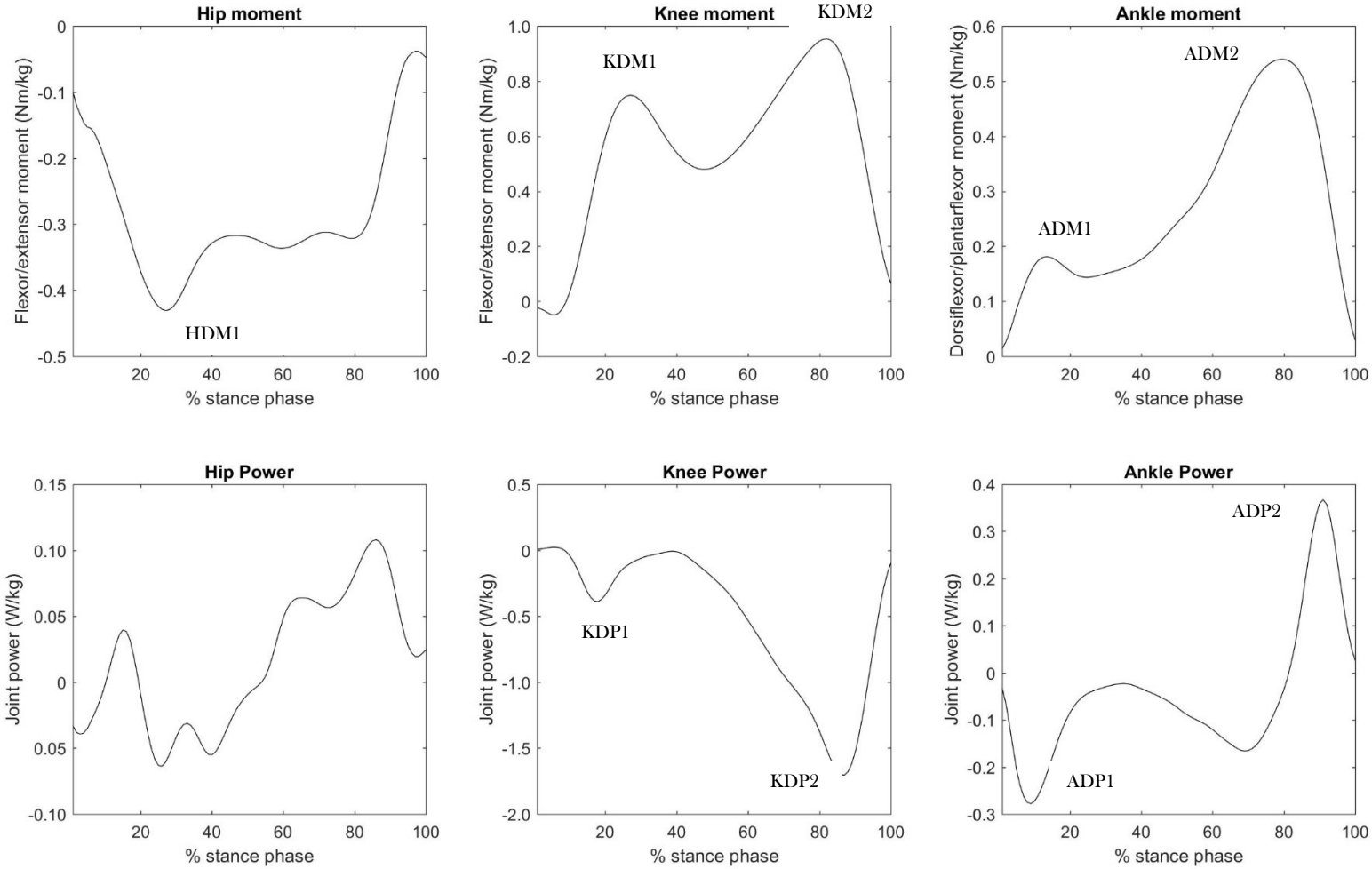


Figure 8.4. Typical joint moments and powers observed in a normal flexibility group during stair descent. Flexion (and dorsiflexion) positive, extension (and plantarflexion) negative.

8.3 Results:

All GJH and NF participants completed the stair climbing using the step-over-step method, without using the hand rails for support. One JHS participant could not perform the step-over-step method, instead using the step-by-step method. Another JHS participant was unable to perform the exercise without using the hand rails. Both participants were excluded from the analysis; the sample size for this study was 21 JHS individuals, 23 GJH individuals, and 22 NF individuals. Since a couple of participants were excluded from the analysis, the JHS group characteristics changed marginally from previous chapters. The new characteristics are displayed in Table 8.1, and differences between groups were investigated with a MANOVA test. JHS and GJH had a significantly greater Beighton Score than NF ($p<.001$ in both cases), and there was no significant difference between JHS and GJH. JHS had a significantly greater Visual Analogue Pain Score than both GJH and NF groups ($p<.001$ in both cases).

	JHS (n=21)	GJH (n=23)	NF (n=22)
Age (years)	32±9	28±6	28±5
Height (cm)	168.9±8.0	169±10	172±8
BMI	25.3±5.7	22.9±4.4	22.0±2.8
Sex (m/f)	3/18	4/19	6/16
Beighton score	7.0±2.0	6.6±1.6	0.3±0.7
Visual Analogue Pain Score	3.0±1.9	0.0±0.0	0.0±0.0

Table 8.1 Characteristics of the groups used in this study.

Stair ascent

The MANOVA test showed there was a statistically significant difference between groups in stair ascent ($p=.004$).

In all the variables measured, there were no significant differences between GJH and NF groups. The only significant differences observed, occurred between the JHS and the GJH and/or NF groups. Mean values and standard deviations are shown in Table 8.2. Joint angles, moments, and powers are shown in figures 8.5 to 8.7.

For the spatiotemporal measures, there was no significant difference between groups for stride width, however JHS had a significantly longer stance time than both GJH and NF groups ($p<.001$ in both cases).

There was little difference in mean ankle angle and ankle range of motion between groups, and this difference was not significant. JHS had a lower peak dorsiflexion moment (Figure 8.5) than both GJH and NF groups at AAM1 ($p=.020$ and .042 respectively) and AAM2 ($p=.000$ and .007 respectively).

There was a significant difference between JHS and NF in the peak knee joint flexor moment at KAM1 ($p=.002$); JHS had a greater moment than NF, with the mean GJH moment being somewhat in the middle. At the peak extensor moment KAM2, JHS had a significantly lower peak than both GJH and NF groups ($p=.032$ and $<.001$ respectively).

The only significant difference in terms of joint angles between groups was observed at the hip; JHS mean hip angle was significantly more flexed than NF ($p=.016$). Figure 8.5 shows the hip angle for the three groups; although JHS tended to exhibit greater flexion throughout stance phase, these differences were more pronounced during early stance and late stance. Similar to the pattern at the ankle and knee joints, the JHS had smaller moment peaks (at HAM1 and HAM2), however these differences were not significant.

In terms of joint powers, ankle power RMS was significantly lower in the JHS group than GJH and NF groups ($p=.001$ and .017). JHS AAP1 peak was lower than GJH and NF, but the difference was not significant. At the knee, JHS had a greater power generation peak KAP1, than both GJH and NF groups ($p=.014$ and .001 respectively). Similarly, for knee power RMS, JHS was greater than GJH and NF ($p=.027$ and $<.001$ respectively). There were no significant differences observed between groups for hip joint power parameters.

	JHS (n=21)	GJH (n=23)	NF (n=22)
Spatiotemporal			
Stride Width (cm)	31.94 ± 10.58	31.35 ± 9.29	29.43 ± 11.28
Stance Time (s)†*	**1.36 ± 0.71**	**0.89 ± 0.13**	**0.94 ± 0.1**
Velocity (cm/s)	**2.6 ± 0.9**	**3.8 ± 1.7**	**2.7 ± 1.2**
Ankle			
Ankle range-of-motion (°)	38.3 ± 8.28	40.51 ± 6.74	36.8 ± 5.86
Ankle mean angle (°)	103.25 ± 4.22	103.44 ± 3.08	101.48 ± 5.5
Ankle moment AAM1 (Nm/kg) †*	**0.72 ± 0.23**	**0.95 ± 0.31**	**0.92 ± 0.26**
Ankle moment AAM2 (Nm/kg)†*	**1.17 ± 0.23**	**1.46 ± 0.18**	**1.37 ± 0.23**
Ankle power RMS (W/kg)†*	**0.23 ± 0.10**	**0.34 ± 0.07**	**0.31 ± 0.09**
Ankle power peak AAP1 (W/kg)	1.59 ± 0.47	1.75 ± 0.37	1.73 ± 0.60
Knee			
Knee range-of-motion (°)	61.7 ± 7.17	60.48 ± 5.09	61.82 ± 5.38
Knee mean angle (°)	29.95 ± 5.49	32.78 ± 3.78	28.95 ± 6.52
Knee moment KAM1 (Nm/kg)†	**0.80 ± 0.23**	**0.67 ± 0.20**	**0.55 ± 0.24**
Knee moment KAM2 (Nm/kg)†*	**-0.39 ± 0.15**	**-0.56 ± 0.22**	**-0.66 ± 0.22**
Knee power RMS (W/kg)†*	**0.24 ± 0.09**	**0.16 ± 008**	**0.12 ± 0.12**
Knee peak KAP1 (W/kg)†*	**1.29 ± 0.66**	**0.851 ± 0.37**	**0.71 ± 0.32**
Hip			
Hip range-of-motion (°)	53.62 ± 4.56	52.02 ± 5.78	52.58 ± 3.59
Hip mean angle (°)†	**33.92 ± 6.98**	**32.15 ± 6.82**	**28.43 ± 4.35**
Hip moment HAM1 (Nm/kg)	0.63 ± 0.14	0.75 ± 0.23	0.69 ± 0.29
Hip moment HAM2 (Nm/kg)	0.12 ± 0.14	0.17 ± 0.19	0.14 ± 0.14
Hip power RMS (W/kg)	0.19 ± 0.07	0.23 ± 0.09	0.22 ± 0.11
Hip power peak HAP1 (W/kg)	0.76 ± 0.32	0.70 ± 0.24	0.62 ± 0.27

Table 8.2: Results of stair ascent movement. † = significant difference between JHS and NF groups, * = significant difference between JHS and GJH groups, ^ = significant difference between NF and GJH groups. $\alpha = 0.05$ and Bonferroni correction was used.

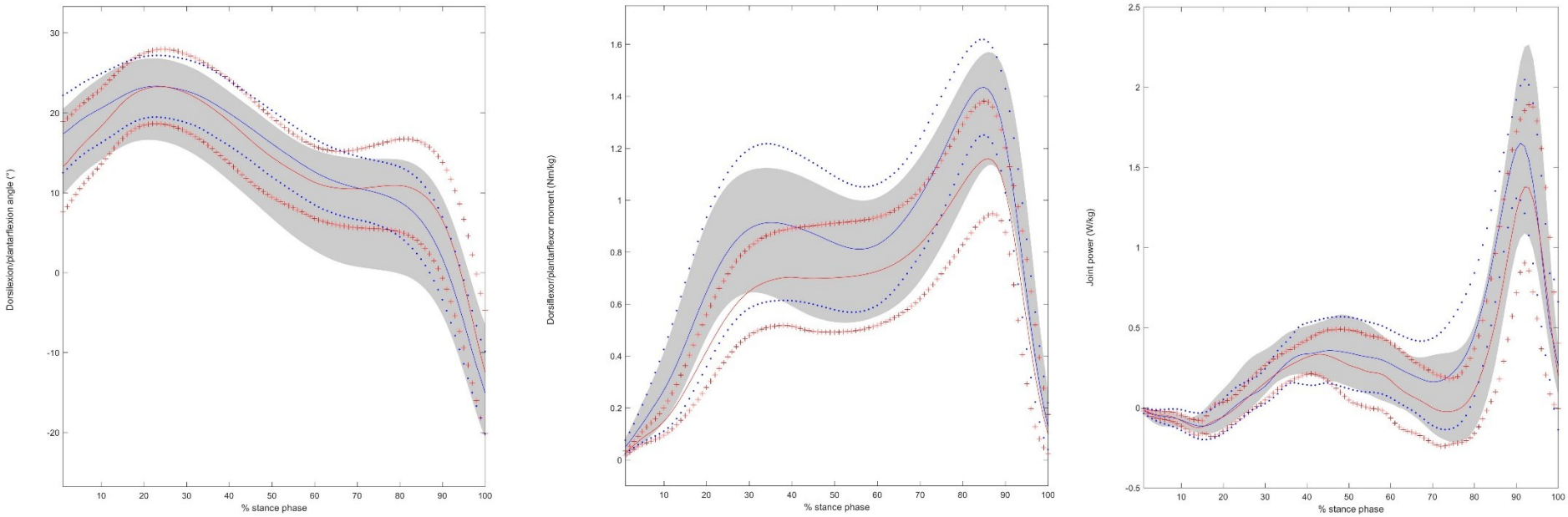


Figure 8.5: Ankle angle, moment and power during stair ascent. Plantarflexion negative, dorsiflexion positive. Grey shaded area is within 1 standard deviation of normal mean, solid red line is JHS mean ± one standard deviation (red '+' lines), solid blue line is GJH mean ± one standard deviation (blue dotted lines).

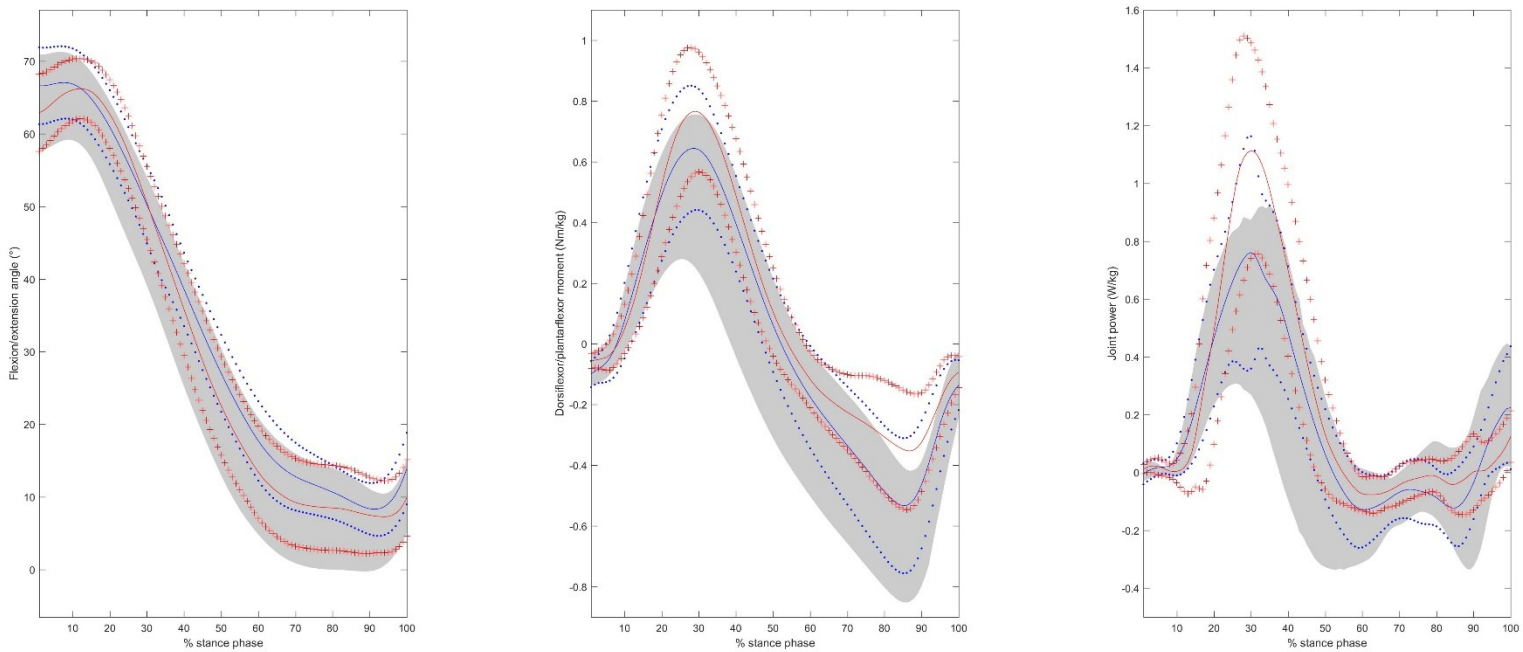


Figure 8.6: Knee angle, moment and power during stair ascent. Flexion negative, extension positive. Grey shaded area is within 1 standard deviation of normal mean, solid red line is JHS mean ± one standard deviation (red '+' lines), solid blue line is GJH mean ± one standard deviation (blue dotted lines).

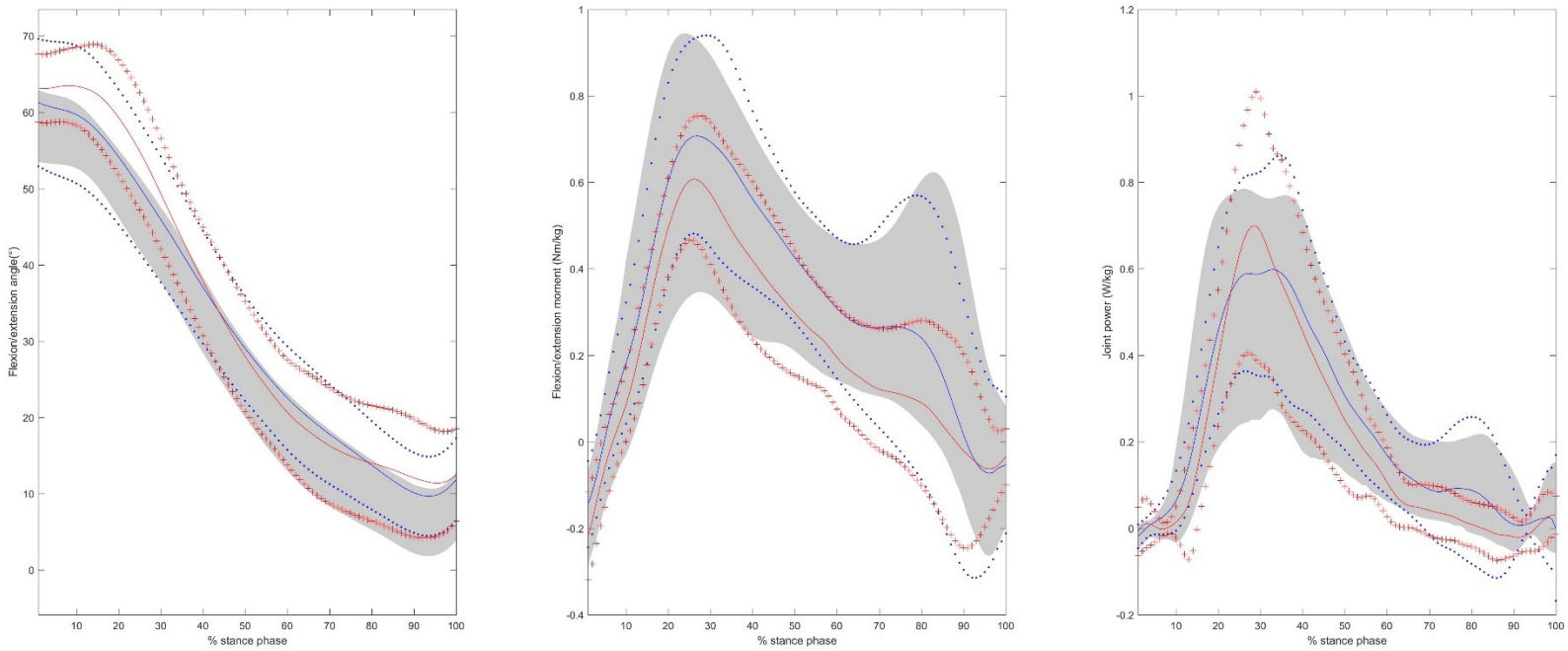


Figure 8.7: Hip angle, moment and power during stair ascent. Flexion negative, extension positive. Grey shaded area is within 1 standard deviation of normal mean, solid red line is JHS mean ± one standard deviation (red '+' lines), solid blue line is GJH mean ± one standard deviation (blue dotted lines).

Stair descent

The MANOVA test showed a significant difference in stair descent between groups (p=.007). Similar to stair ascent, there were no significant differences between GJH and NF groups in any of the variables measured. The only significant differences observed, occurred between the JHS and the GJH and/or NF groups. Mean values and standard deviations are shown in Table 8.3. Joint angles, moments, and powers are show in figures 8.8 to 8.10.

Similar to ascent, JHS had a significantly longer stance duration than GJH and NF (p<.001 in both cases). JHS had a significantly wider stride width than GJH (p=.038) but not NF. There was no significant difference between groups for velocity.

At the ankle, JHS had a significantly greater dorsiflexion peak than the NF group (p=.014). There was no significant difference between JHS and GJH, or NF and GJH. The JHS group had a greater range of motion than NF, and remained slightly more dorsiflexed during stance phase, however these differences did not reach significance. There were no significant differences in any of the joint moment parameters measured.

At the knee, there was no significant difference between groups for mean joint angle and range of motion. There was no significant difference in knee moment between any of the groups at KDM1, however the KDM2 peak was significantly larger in JHS than NF group (p=.036).

At the hip, for mean joint angle the JHS group were significantly more flexed than NF (p=.001). This difference was greatest during early and mid-stance (Figure 8.10). Hip joint moment was highly variable, however JHS had a significantly greater peak extension moment (HDM1) than both GJH and NF groups ($p < .001$ and $p = .021$ respectively).

For joint power parameters, at the ankle the only significant difference observed was at the peak ADP2, which was greater in JHS than NF (p=.036). At the knee, JHS had a smaller peak at KDP1, but this difference was not significant. At KDP2, JHS had a significantly greater peak than both GJH and NF (p=.027 and .008 respectively). There were no significant differences observed in hip power.

	JHS (n=21)	GJH (n=23)	NF (n=22)
Spatiotemporal			
Stance Time (s)†*	**1.06 ± 0.26**	**0.77 ± 0.1**	**0.82 ± 0.1**
Stride Width (cm)*	**25.71 ± 2.88**	**23.94 ± 1.56**	**25.21 ± 2**
Velocity (cm/s)	4.1 ± 2.6	3.3 ± 1.7	3.1 ± 1.8
Ankle			
Ankle range-of-motion (°)	54.4 ± 7.61	51.33 ± 7.7	49.23 ± 5.53
Ankle angle mean (°)	108.02 ± 4.28	108.26 ± 3.6	105.29 ± 5.34
Ankle moment ADM1 (Nm/kg)†	**1.25 ± 0.07**	**1.23 ± 0.07**	**1.18 ± 0.07**
Ankle moment ADM2 **(Nm/kg)**	0.28 ± 0.18	0.33 ± 0.26	0.32 ± 0.22
Ankle power min ADP1(W/kg)	-0.48 ± 0.27	-0.41 ± 0.29	-0.41 ± 0.28
Ankle power max ADP2 (W/kg)†	**0.57 ± 0.26**	**0.48 ± 0.17**	**0.40 ± 0.17**
Ankle power RMS (W/kg)	0.05 ± 0.05	0.05 ± 0.07	0.05 ± 0.06
Knee			
Knee range-of-motion (°)	85.89 ± 7.75	82.37 ± 6.56	84.15 ± 6.55
Knee angle mean (°)	34.65 ± 6.33	35.65 ± 4.75	30.45 ± 9.17
Knee moment Knee moment KDM1(Nm/kg)	0.79 ± 0.27	1.00 ± 0.34	0.82 ± 0.39
Knee moment KDM2 (Nm/kg)†	**1.25 ± 0.31**	**1.15 ± 0.28**	**1.00 ± 0.33**
Knee power KDP1 (W/kg)	-0.38 ± 0.33	-0.64 ± 0.44	-0.51 ± 0.56
Knee power KDP2(W/kg)†*	**-2.41 ± 0.64**	**-1.89 ± 0.49**	**-1.80 ± 0.70**
Knee power RMS (W/kg)	0.64 ± 0.15	0.80 ± 0.16	0.51 ± 0.18
Hip			
Hip range-of-motion (°)	17.21 ± 4.54	17.8 ± 7.59	17.49 ± 4.64
Hip angle mean (°)†	**20.88 ± 8.28**	**16.44 ± 6.75**	**12.52 ± 5.87**
Hip moment HDM1(Nm/kg)†*	**0.16 ± 0.20**	**-0.07 ± 0.16**	**0.00 ± 0.21**
Hip power RMS (W/kg)	0.02 ± 0.03	0.03 ± 0.03	0.01 ± 0.03

Table 8.3: Stair descent results. † = significant difference between JHS and NF groups, * = significant difference between JHS and GJH groups, ^ = significant difference between NF and GJH groups. $\alpha = 0.05$ and Bonferroni correction was used.

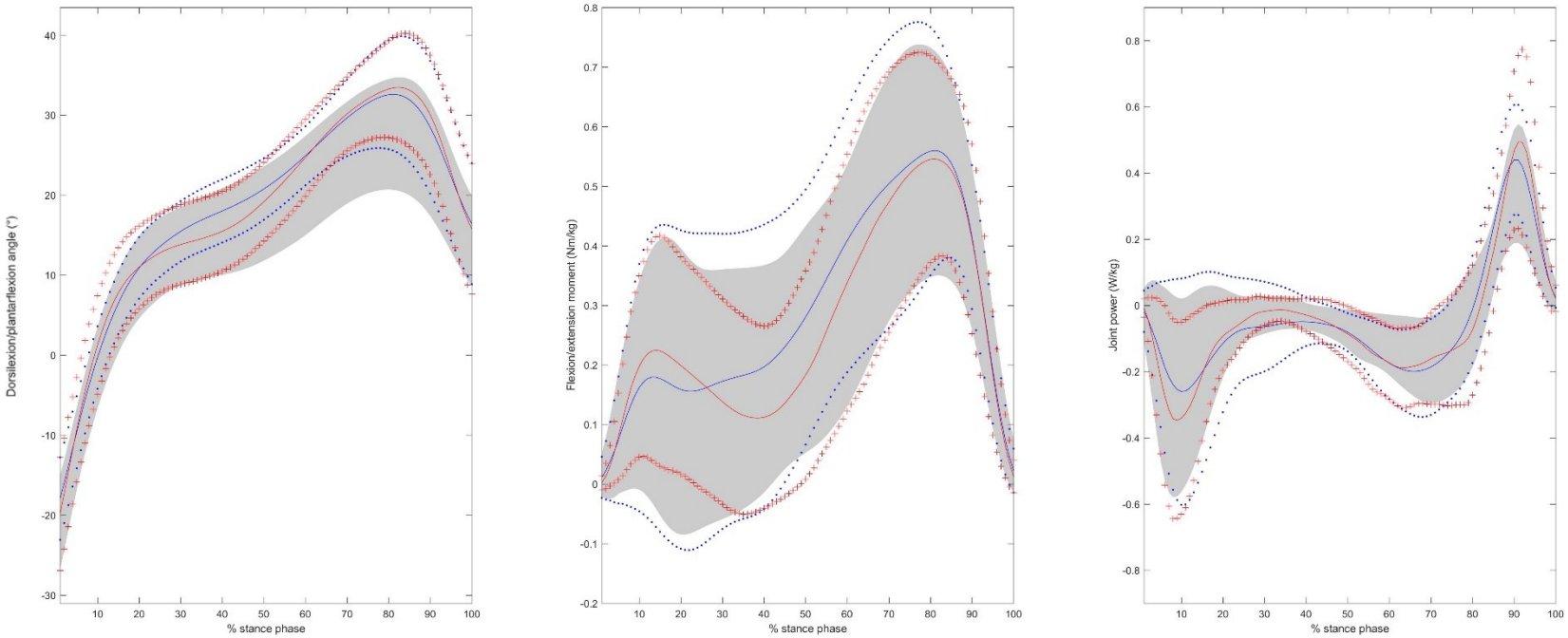


Figure 8.8: Ankle angle, moment and power during stair descent. Plantarflexion negative, dorsiflexion positive. Grey shaded area is within 1 standard deviation of normal mean, solid red line is JHS mean ± one standard deviation (red '+' lines), solid blue line is GJH mean ± one standard deviation (blue dotted lines).

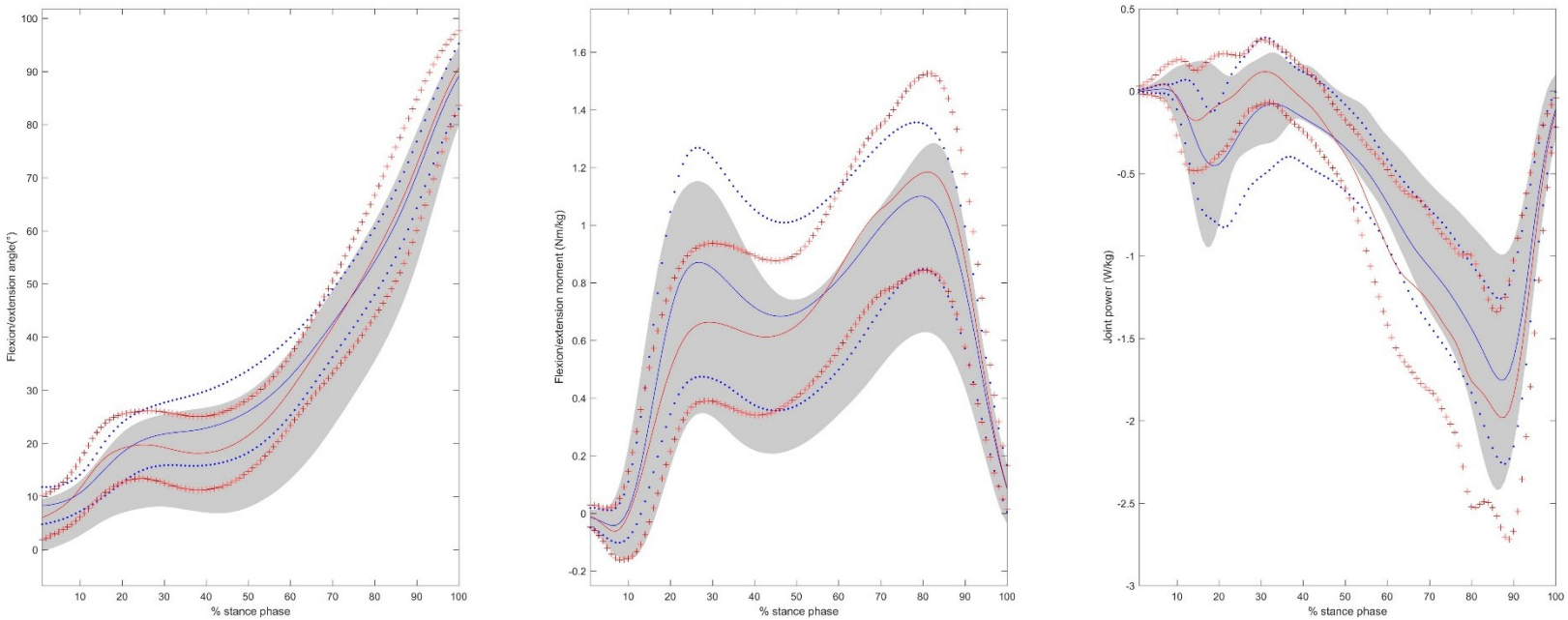


Figure 8.9: Knee angle, moment and power during stair descent. Extension negative, flexion positive. Grey shaded area is within 1 standard deviation of normal mean, solid red line is JHS mean ± one standard deviation (red '+' lines), solid blue line is GJH mean ± one standard deviation (blue dotted lines).

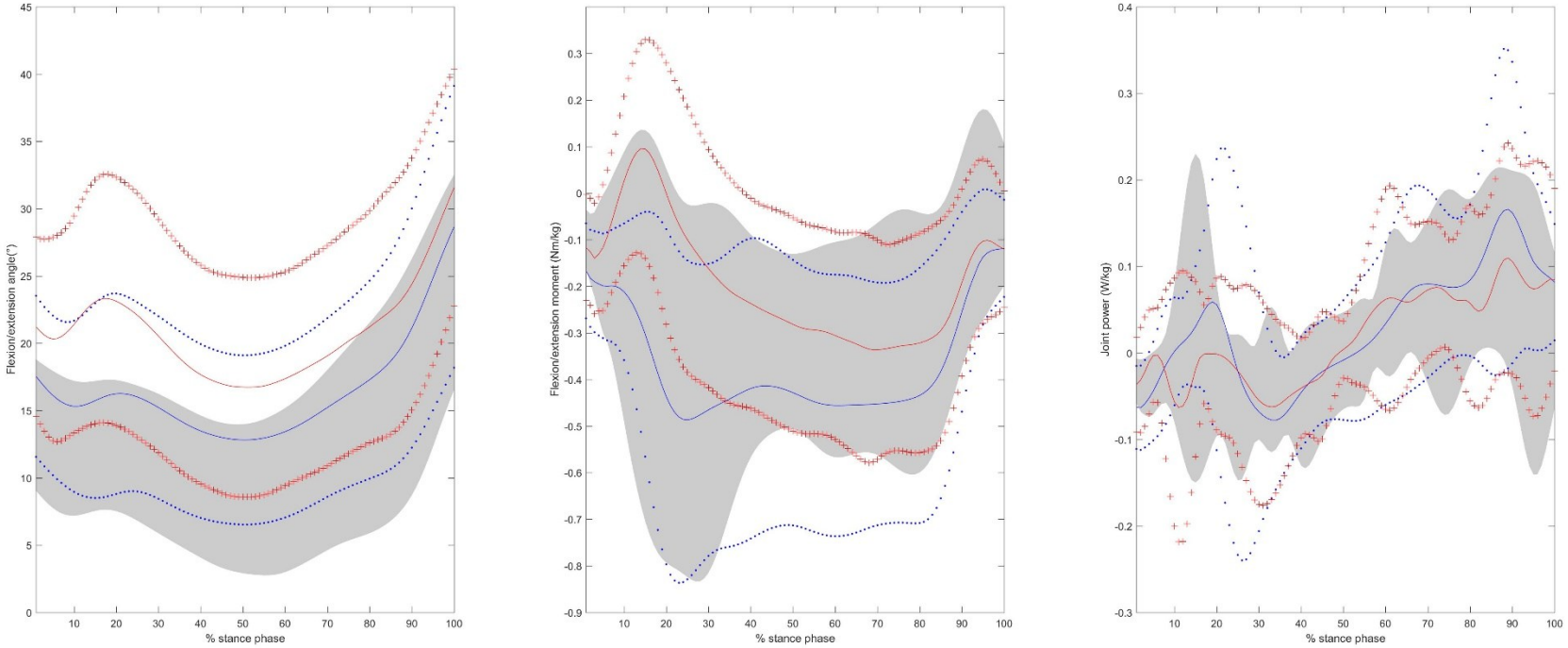


Figure 8.10: Hip angle, moment and power during stair descent. Extension negative, flexion positive. Grey shaded area is within 1 standard deviation of normal mean, solid red line is JHS mean ± one standard deviation (red '+' lines), solid blue line is GJH mean ± one standard deviation (blue dotted lines).

8.4 Discussion:

Gait speed influences the demand on muscles to decelerate and accelerate the centre of mass[218]. Muscle activity, and possibly pain, can be lessened by reducing the demand on the muscles by using a slower gait and/or a limited range of motion[218]. In both stair ascent and descent, stride time was slower in JHS than GJH and NF groups, whereas there was no significant difference between GJH and NF groups. This would suggest that the activity of stair climbing is impaired in JHS. In other conditions, such as total knee arthroplasty, decreased muscle strength was found to lower gait velocity during stair descent[219]. This is feasibly the reason here, as people with JHS do tend to have reduced muscle strength[39,64]. Although other factors such as fatigue and joint pain cannot be disregarded.

In healthy gait stair descent is typically quicker and has a shorter stance duration than ascent[214]. Although testing for differences between stair ascent and stair descent was not the purpose of this study, the same pattern was observed here; all groups had a shorter stance duration during descent than ascent.

Stair ascent

In other conditions where knee pain is a feature, such as patellofemoral pain syndrome[218] and knee osteoarthritis[216], a reduction in knee flexion during stair ascent has been observed. The fact that JHS knee flexion is not significantly different to the other groups, would suggest that this compensatory mechanism is not being used. The only significant difference observed in kinematics between groups was mean hip flexion; with the JHS group being more flexed than the NF group. An increase in hip flexion may signify a forward trunk lean, which has been observed in other cohorts with knee pain[215]. Increased hip flexion can be caused by the trunk 'thrusting' forwards, which generates torque around the hip joint and so lowers the demand on the knee extensors[231]. Unfortunately, markers were not placed on the trunk, and so trunk lean cannot be directly measured. Trunk lean can be inferred by the fact that hip flexion was increased[231]; forward lean of the trunk may rotate the pelvis anteriorly, which would have the effect of putting the hip into greater flexion. Forward trunk lean moves the vector of ground reaction force anteriorly; a mechanism that reduces the moment and joint contact forces at the knee[215]. This may be a strategy to reduce knee pain in JHS participants.

For the peak knee powers at KAP1 and KAP2, where the knee is producing positive power to accelerate the centre of mass vertically, JHS had significantly greater peaks than both GJH and NF groups. This is combined with a significantly greater RMS power generated throughout stance phase, and significantly greater knee moments at KAM1 and KAM2. In their study of joint powers generated during stair ascent, Wilken *et al.*[227] noted that although knee power is responsible for generating a significant proportion of positive power during stair ascent, the majority of power is produced while the

acceleration of the centre of mass is near zero. The authors stipulate that the ankle is used to initiate acceleration of the centre of mass, and the knee is responsible for maintaining vertical velocity of the body. It seems feasible that people with JHS are using more of a "knee-strategy" to produce the force necessary to raise the centre of mass, with a reluctance to use the ankle. This potential reluctance to use the ankle is reflected in the significantly lower peak external dorsiflexion moment the JHS group exhibited during the early stance (AAM1) and push-off phase (AAM2). The JHS group also had a significantly lower ankle power RMS than GJH and NF groups, and a lower ankle power peak, although the difference was not significant. If the knee is indeed producing relatively more force than normal, then the increased hip flexion (and inferred trunk lean), may be a compensatory strategy to limit the extra forces at the knee; i.e. impairments in the distal lower limb joints being adapted for by more proximal joints.

The fact that there were no significant differences between GJH and NF groups, for joint angle, moment, or power parameters, would indicate that people with asymptomatic joint hypermobility are able to use the 'normal' ankle strategy to provide vertical acceleration during stair ascent.

This would seem to contrast the findings of Luder *et al.*[104], who found during stair ascent women with GJH had a reduced peak activity of Vastus Medialis, and attribute this to them being unwilling to produce force at the knee joint. It should be noted however, that joint kinematics and kinetics were not measured as part of the study, and so the reduced force and mechanism was inferred. Furthermore, Luder *et al.*[104] did not observe any significant difference in peak EMG in the Vastus Lateralis muscle, and the Rectus Femoris muscle was not measured. Both muscles are involved with knee extension and are active during stair ascent. In addition, Luder *et al.*[104] state that the peak activity of Vastus medialis in the NF group was 110%, which would indicate that the maximum voluntary contraction normalisation methods used in the study were not successful, and may account for the differences they observed.

Descent:

In terms of kinematics during stair descent, there were no significant differences between groups in ankle and knee range-of-motion and mean value. The only significant differences observed were in peak dorsiflexion, and mean hip angle, with the JHS group having a greater peak dorsiflexion at the ankle and more flexion at the hip than the NF group. Like stair ascent, increased hip flexion may be associated with forward trunk lean; a mechanism described previously to reduce moment and contact force at the knee. This forward trunk lean corresponds to a significant difference in hip moment at (HDM1). Interestingly this coincided with a peak flexor moment in the JHS group, whilst all of the GJH participants stayed in an extension moment for the entire stance phase, and there was huge

variability in NF participants (figure 8.10). Hip moments during stair climbing can be highly variable between individuals, due to the variety of trunk positions assumed[134].

As can be seen in figure 8.10, the greatest difference in hip flexion is in early stance, where JHS also show a lower peak of negative power at the knee in early stance (KDP1). Although the difference was not significant, the results may allude to a compensatory movement strategy such as forward trunk lean.

In contrast to stair ascent, peak ankle power (ADP2) was significantly greater in the JHS group than the NF group. This would contrast the lower ankle powers and moments observed in stair ascent, however it should be noted that the peak power at ADP2 is approximately 50% of the peaks generated through stair ascent. ADP2 occurs towards the end of stance phase, close to lift-off. As JHS individuals may be showing more forward trunk lean, which has the effect of reducing knee extensor moment, it may be that the ankle is required to provide the force to propel the supporting limb into swing phase; the forward trunk lean inhibiting power generation at the knee. The peak ankle power corresponds to a negative knee power peak KDP2, where JHS had significantly more power absorption than GJH and NF, and the knee moment peak at KDM2, where JHS had a greater flexor moment than NF. The increased ankle power could be an adaptation to overcome these differences at the knee joint.

8.5 Conclusion

The results of this study show that stair climbing is impaired in people with JHS, which is perhaps expected given the survey results by Palmer *et al.*[19], where stair-climbing was listed as a potential activity that people with JHS found difficult. There are several deficits and symptoms of JHS that could contribute to the differences observed, and it is still not clear how these interplay to cause the differences observed in the current study. The results of this study indicate a switch in JHS participants, from generating force at the ankle, to generating force at the knee during stair ascent. During stair descent, similar differences between JHS and NF /GJH groups can be observed; forward trunk lean may be reducing knee moments and powers, and the ankle works harder to compensate. The differences in lower limb joint kinematics and kinetics observed in this study could be used to develop treatment strategies to address these changes; testing if physical therapy could normalise stair climbing, with a focus on strengthening ankle muscles so they can generate the force during stair ascent and focus on quadriceps strength to reduce the load through the ankle during stair descent. Further detail of future work is given in the following chapter.

Chapter 9. Discussion, conclusion, and future work.

9.1. Classifying JHS

At the time of performing and writing this study, the Brighton criteria were the most commonly used classification criteria for JHS[2]. The details of the Brighton criteria were discussed in Chapter 1. To recap, the Brighton criteria incorporates the Beighton Score, a method of classifying people as hypermobile. There has been some criticism of the Beighton Score as it only incorporates specific joints[2]. For example, it does not consider hypermobility in the shoulders, neck, and ankles. Hypothetically, someone with hypermobility in these joints, but not in the joints measured in the Beighton Score, would score negatively for hypermobility and be placed in the same category as someone with normal flexibility. Whilst this thesis has investigated whether, and how, movement differs between groups JHS, GJH, and NF, the comparisons of movement are only as valid as the underlying classification criteria. Despite the shortcomings of the Beighton Score, a recent systematic review of methods of classifying hypermobility recommended the Beighton Score as the most valid and reliable method[232]. Additionally, the fact that differences were observed in this thesis between GJH and JHS groups, suggests that the Brighton criteria were effective in separating individuals into their respective cohorts. Despite this, in many of the movements analysed the GJH group results were between the NF and JHS values. For example, in cumulative angle during perturbations, sway during prolonged standing, and many joint angle parameters during gait and stair climbing. There are several potential reasons for this. Firstly, it may be that the classification criteria lack the nuances of the underlying condition, particularly if JHS is considered a spectrum disorder[233]; some people with GJH may have JHS characteristics. Secondly, the criteria and/or the researcher giving the criteria may incorrectly label someone as GJH/JHS, causing the groups to become more similar. Thirdly, that the criteria are accurate, the JHS and GJH are clinically distinct, and movement of JHS and GJH truly does differ less than between JHS and NF. All of these factors may contribute, however, given the reliability and validity of the Beighton Score and Brighton Criteria have been well established[7,8], it seems most likely that GJH and JHS are clinically distinct, and the reason there are fewer differences in between JHS and GJH than JHS and NF, could be due to the common factor of hypermobility.

The problems relating to classification are well known[25,233], and in 2016, the Ehlers-Danlos Society met with the objective of revising the classification of GJH, EDS, and JHS. One of their suggestions is that the classification for EDS hypermobility type and the more severely presenting JHS individuals with more severe symptoms, be tightened and unified under the term hypermobile EDS (hEDS)[18]. Since this study was started and the testing of participants completed before the new terminology had been suggested, the original terms have been used in this thesis. The classification has also introduced various other terms; “Localised Joint Hypermobility” for when joint hypermobility is

present if only a few joints, "Peripheral Joint Hypermobility" for when joint hypermobility is present in the hands/feet only, "Historical Joint Hypermobility" to describe someone who has lost their hypermobility through ageing, and "Generalised Joint Hypermobility" where hypermobility is present in multiple joints (usually five or more)[18]. The meeting of the Ehlers Danlos Society proposed that classification should fit into three broad categories: 1) People with asymptomatic joint hypermobility; either localised, peripheral, or general hypermobility types. 2) People who meet the new, more stringent diagnostic criteria be classified as hEDS (Table 9.1). 3) People who do not have hEDS but do exhibit some symptoms. In this case, they propose the term hypermobility spectrum disorder (HSD). The hope is that this new and tightened criterion for hEDS leads to greater homogeneity so that research can be better targeted. When considering the new criteria, the JHS group recruited for the studies within this thesis are likely to be a mix of people now classified as hEDS and HSD. Therefore, it is interesting to note that differences were still demonstrated between cohorts without the potential benefit of using the new tighter classification.

9.2. Summary of aims

This PhD aimed to improve the understanding of how people with JHS move compared to two groups of people; people who are hypermobile, but do not have symptoms (GJH), and people with normal flexibility (NF). People with JHS find many activities of daily living painful, and the cause of pain in JHS is not fully understood. Physiotherapy is the mainstay of treatment, but it is not always effective. The relationship between pain and movement in JHS is not understood, and there has been little research about how people with JHS move compared to others. Quantifying movement in JHS may improve the understanding of pain aetiology, and provide information on differences and impairments that physiotherapists may be able to target. This study sought to answer two questions.

3) What is currently known about how people with JHS move?
4) Do people with JHS move differently to people with GJH and NF?

Criteria	Details
Criterion 1. Patient MUST have:	A Beighton Score of ≥6 for children (pre-puberty), ≥5 for ages under 50, ≥4 for over 50 years. OR 1 point below the above AND a positive 5 point questionnaire score.
Criterion 2. Patient MUST have at least two of the following features (e.g. A&B, A&C, B&C, A&B&C):	
Feature A, At least 5 of the following:	- Unusually soft or velvety skin - Mild skin hyperexstensibility - Unexplained skin striae (without a significant gain/loss of body fat) - Bilateral piezogenic papules - Recurrent or multiple abdominal hernia(s) - Atrophic scarring of at least two sites and without the formation of truly papyraceous and or hemoisderic scars, - Pelvic floor, rectal, and/or uterine prolapse in children, men or nulliparous women without a history of morbid obesity or other known predisposing medical condition. - Dental crowding and/or a narrow palate - Arachnodactyly - Arm span to height ratio ≥1.05 - Mitral valve prolapse, mild or greater based on strict echocardiographic criteria - Aortic root dilation with Z-Score <+2
Feature B:	A positive family history, with one or more first-degree relatives meeting the criteria for hEDS.

Feature C, At least one of the following:	- Musculoskeletal pain in two or more limbs, recurring daily for at least 3 months
	- Chronic widespread pain for ≥3 months
	- Recurrent joint dislocations or frank instability:
	  o Three or more atraumatic dislocations in the same joint or two or more in two different joints occurring at different times
	  o Medical confirmation of joint instability at two or more sites not related to trauma

Criterion 3, All the following must be met:	- Absence of unusual skin fragility - Exclusion of other heritable and acquired connective tissue disorders - Exclusion of alternative diagnoses that may also include joint hypermobility by means of hypotonia and/or connective tissue laxity.

Table 9.1. The recently established criteria for hEDS, reproduced from Malfait *et al.*[233] All three criterion must be met for a positive classification of hEDS.

9.3. Study findings

The empirical findings are specific to each research question and/or each individual activity, the results of which have been discussed in Chapter 2, and Chapters 5 - 8. In this conclusion chapter, the specific findings of each chapter are integrated to answer each research question, and future work is suggested.

1) What do we currently know about how people with JHS move?

Chapter 2 contains the specific results regarding the systematic review of movement in hypermobile cohorts. It was the first time studies relating to movement in JHS had been collated in a systematic way, and a paper based on the chapter was published in Gait & Posture[82]. The review identified a lack of knowledge about how people with JHS move compared to people with asymptomatic GJH and people with NF. The only studies of movement in JHS that could be related to activities of daily living, were concerning gait and standing balance. Of the balance studies, all had investigated quiet standing for short periods, and how JHS responded to dynamic perturbations was unknown. Gait was the most commonly investigated activity, but there was no consensus to exactly how JHS and NF differed. GJH and NF participants had been compared during stair climbing[104], but stair climbing of a JHS group had not been investigated.

In addition to a lack of investigation into activities of daily living, none of the studies had directly compared people with JHS to both GJH, and NF groups, within the same study. It was therefore impossible to conclude whether it was hypermobility that was causing differences in movement in JHS individuals, or some other factor of the syndrome. Furthermore, although EMG had been used to measure gait, stair climbing, and standing in GJH cohorts, no research had been performed using EMG to measure muscle activity during activities of daily living in JHS.

The systematic review also identified that most of the studies reviewed did not perform a power calculation. Part of the problem was that the reliability of 3D movement analysis of hypermobile people had not been established; skin hyperextensibility and extra joint range-of-motion might affect the

reliability of measurements[109]. This gap in knowledge was addressed by performing a reliability study (Chapter 3), which compared the reliability of 3D movement analysis of hypermobile gait with normal flexibility gait, this was also published in Gait & Posture[191].

The results of the review and reliability study were combined with information from experienced physiotherapists, and the work by Palmer *et al.*[19] in measuring the impact of JHS, to inform a decision to investigate four activities; balance reactions to perturbation, prolonged standing, gait, and stair climbing.

2) Do people with JHS move differently to people with GJH and NF?

The specific differences between cohorts for each activity are discussed in Chapters 5 to 8. Rather than repeat and summarise the findings for each activity, this section will discuss how the results of this study generally apply to movement of JHS individuals.

Over 100 outcome measures were used in the process of investigating the 4 activities. Of all these measures, there was only one significant difference observed between the GJH and NF groups; GJH had a greater mean stride length during gait. In comparison, there were many more differences between JHS and NF movement; 48 significant differences across the 4 activities. There were 32 significant differences between the JHS and GJH groups. In conclusion, taking these broad trends, movement of JHS individuals does differ from NF and GJH in the activities investigated, whereas there is very little to no difference in movement between GJH and NF groups. The fact that there were fewer significant differences between JHS and GJH, than between JHS and NF, would suggest that for some movement parameters the GJH group are between the NF and JHS groups. This would also suggest that although GJH have hypermobility, their movements are more similar to NF, whereas JHS show a departure from normal. Many of the symptoms and features of JHS could contribute to this difference and have been discussed in this thesis; pain, muscle weakness, proprioception and balance deficits, and anxiety issues such as fear of falling. A reason for this is that people with GJH may be better at 'normalising' their movements, i.e. their hypermobility does not affect their day to day movement during activities of daily living. In contrast, JHS movement does differ from normal, and so a potential treatment would be for physiotherapy to address the differences, and shift JHS movement to be more similar to NF/GJH.

Sticking with broad trends, JHS movement parameters tended to be more variable than NF and GJH; JHS had greater cumulative angle in the perturbation activity, and greater anterioposterior sway during prolonged standing. During gait, JHS joint angle variability was significantly greater than NF at the ankle and hip, and significantly greater than GJH at the knee and hip. Gait variability can be taken as a measure of stability[234], and so these results support the research and consensus that people with JHS

have joint instability[1]. In contrast, there was little difference between cohorts in peak angle and range-of-motion parameters; during gait, only peak hip extension was significantly different between JHS and NF groups. During stair climbing, there were no significant differences between any of the groups in these parameters. The lack of a significant difference between groups indicates that although both JHS and GJH groups have a greater range-of-motion available than NF, they do not use the extra range-of-motion during the activities investigated here. One of the theories of the cause of pain in JHS is that people with JHS are more likely to enter hyperextension and cause more wear and tear on the joints. This behaviour was not observed in this study, and so the results do not support this mechanism of pain causation.

If a common difference may be picked out of the results for each activity, it would be in ankle joint parameters. During the postural tasks of perturbations and prolonged standing (Chapters 5 & 6) the JHS group showed impaired ankle joint parameters when compared to GJH and NF groups. After a forward perturbation, the main control mechanism employed to control the centre of mass is an ankle strategy using the plantarflexors/dorsiflexors, which control the excursion of the centre of mass over the base of support[131]. JHS not only took longer to reach peak EMG intensity in the tibialis anterior, which is the main muscle use to arrest a forward perturbation, but had a greater cumulative angle in all joints than the other groups following the perturbation (i.e. they were wobblier), indicating that they are less able to control perturbations. The results from the prolonged standing activity complement these results; the JHS group had significantly greater anterioposterior (AP) sway than the NF group. Sway in the AP direction is again controlled by an ankle dorsiflexion/plantarflexion mechanism[140,168].

During gait, differences were also observed in ankle joint parameters. During gait, JHS had a significantly lower peak ankle power generated during push-off, where the plantarflexors provide power to accelerate the limb forward. The JHS group also had more variability in ankle dorsiflexion/plantarflexion angle. Interestingly, there is evidence from other studies comparing JHS and NF gait that this is consistent. Of the 4 studies which compared gait using 3D movement analysis[96,98,100,102] (Chapter 2), all reported significant differences in at least one kinematic ankle joint kinematic parameter, whereas findings were not as consistent for the other lower-limb joints. The JHS group also spent significantly longer in Tibialis Anterior and Gastrocnemius co-contraction than NF.

Turning to stair climbing there were more significant differences between JHS and the other groups than during gait. Both stair ascent and descent generate greater forces in the joints than gait, as the muscles/joints must generate force to raise the weight of the body during ascent, and conversely decelerate the centre of mass during descent. In stair climbing significant differences in the ankle are more pronounced, with a smaller moment and power peaks during ascent, showing that JHS were reluctant to use the ankle to generate power. This was combined with an increase in knee moment, indicating that JHS were perhaps using the knee extensors to generate lift of the COM rather than an ankle strategy. Interesting in descent this trend is not apparent; JHS actually had a significantly greater

peak moment at the peak following initial contact, although the difference was small and may not be clinically meaningful. Significant differences between cohorts were not solely limited to ankle parameters. In both stair ascent and descent, the JHS group mean hip angle was significantly more flexed than in the NF group. It is feasible that an increase in hip flexion could be associated with an increase in forward trunk lean; leaning forward at the trunk would tilt the pelvis anteriorly, causing flexion of the hip joint. Although markers were not placed on the trunk in this study, so trunk lean cannot be directly measured, observation of the JHS individuals during the study did seem to reveal that they were performing this behaviour. In postural activities, forward trunk lean is thought to increase the stiffness of the ankle, possibly by lengthening the connective tissue, which stiffens as it is stretched[235,236]. Therefore, the increased mean hip flexion observed might be an adaptation to address an ankle joint impairment.

It should be noted that most outcome measures used in this study related to flexion/extension joint angles. Therefore, it may be expected that differences would be observed in the AP direction, since in the activities investigated flexion/extension of the lower limb joints generally act in the AP plane. Nonetheless, the combined results of the four activities support the fact that people with JHS have impaired ankle joint movement parameters.

9.4 Where these results fit with current research.

Researchers have suggested that improving strength, instability, proprioception, and correcting badly adapted posture/movements will improve symptoms of JHS[63]. One of the reasons given in Chapter 1 for investigating movement in JHS, was that by exposing differences in movement, information may be gained that could help physiotherapists improve treatment. This thesis has found that the JHS group had differences in movement and impairments in each of the activities investigated. Given these differences and impairments, there is now more information about how JHS people move that may be of use in physiotherapy treatment. It is therefore pertinent to discuss the results of this study in the context of current physiotherapy practice of treatment of JHS.

In their systematic review, Palmer *et al.*[3] found that there was no conclusive evidence as to what type of physiotherapy was most effective; generalised exercise was not better than specific exercises targeting specific joints, and knee exercises were not more effective than control programmes. This finding was echoed by another systematic review of physiotherapy as a treatment for JHS by Smith *et al.*[237] and a survey of physiotherapists by Rombaut *et al.*[4]. They also state that although exercise is prescribed and there are benefits of exercise-based interventions, the evidence is not clear. A potential reason why specific interventions have not shown a benefit over general exercise approaches, is that the specific intervention was not targeting the correct joint. To date, none of the studies investigating the

efficacy of physiotherapy as a treatment for JHS have specifically targeted the ankle joint. Instead, either general exercise programmes have been trialled, or the focus had been on the knee joint[32,43].

Two studies have aimed to improve symptoms by addressing proprioception; Sahin *et al.*[43] and Ferrell *et al.*[32] Both measured knee joint proprioception, before and after a physiotherapy programme which aimed to improve proprioception. In both studies, the motivation of focusing on knee joint proprioception as an outcome measure is not given in the papers; possibly it is because the knee is a common site of pain in JHS[28], that knee extensor/flexor strength has been found to be weaker in JHS[144], and/or that knee hyperextension is one of the tests in the Beighton Score, so is immediately noticeable to those administering the test. Alternatively, the studies may be using knee joint proprioception as a surrogate for proprioception in general (or at least proprioception in the lower limb joints).

The only study to specifically state muscle strength and range-of-motion in the ankle is Kemp *et al.*[59], who found that both targeted and general physiotherapy interventions improved children's symptoms. Although muscle strength was taken prior to the treatment, it was not an outcome measure and was not measured after the treatment, so it is unknown whether ankle strength and range-of-motion also improved.

More recently, in a pilot study for a randomised control study, participants rated physiotherapy very positively[238]. The specific details of the physiotherapy treatment are not given, so it is not possible to say whether it was a general exercise or targeting specific joints.

Another trial; the BENDY trial[239], compared a multidisciplinary treatment approach with standard care, in the treatment of children with JHS. The conclusion was that although symptoms of hypermobility syndrome were improved in both treatment avenues, there was no evidence to suggest that one was more effective than the other. To date, the details of the trial have been published in conference proceedings, and no details of any physiotherapy treatment was included for either the multidisciplinary approach or the standard care. For this reason, no comment can be made about how the results of the trial relate to physiotherapy. The authors conclude that "The findings emphasise the benefit of informed diagnosis and management according to clinical need, but highlight the difficulty in demonstrating subtle benefit from specific interventions without better tools for case definition and outcomes assessment."[239]

Turning now to framing this study in a biopsychosocial context. JHS is a condition that has a wide range of symptoms, which are affected by biological and psychosocial influences. This thesis has focused on the 'bio' part of the syndrome; it has measured kinematics, kinetics, and EMG. As was discussed in the introduction, there are a huge combination of factors, both biological (e.g. example muscle weakness, instability) and psychological (e.g. anxiety, depression, fear of falling) that could contribute to the differences observed in each activity. It is not possible to tease apart the cause-effect relationship for differences in movement between JHS and the control groups using the results of the

current study. However, the current study was the first to use a GJH group as a control group when investigating movement. Since almost no differences were observed between GJH and NF groups, it alludes that hypermobility alone does not cause the pain. Therefore this study brings the current understanding incrementally closer to defining the relationship between JHS and pain. In the wider context, there is a lack of awareness and confidence about treating JHS among physiotherapists[4,60], and this study will improve the current understanding by showing that there is no difference in movement in activities of daily living between GJH and NF groups, and highlighted where JHS movement differs.

9.5 Limitations

The design of the current study means that it is not possible to determine how the factors and symptoms of JHS contribute to the observed differences between the JHS group and the GJH and NF groups in the four activities measured. As has been discussed in the individual chapters concerning each activity, the multifactorial nature of JHS means that there are many confounding factors that could affect movement. Most prominent of these confounding factors is pain, which is the main presenting feature of JHS[28]. Other confounding factors include fear of falling, muscle weakness, proprioception, nervous system differences, balance and instability – how these factors interplay to affect movement in JHS is unknown.

Another limitation is the EMG aspects of the current study. Unfortunately, as the JHS group were unable to generate MVCs during the EMG procedure (discussed in Chapter 7), EMG could not be normalised and so magnitude-based outcome measures could not be used. It should be stated that the co-contraction method employed in the Gait activity is rather a blunt instrument.

This study tested 23 people with JHS. JHS is a under-recognised condition, and it is common for people to go many years without diagnosis. Almost all of these participants were recruited through the Hypermobility Syndromes Association and Ehlers Danlos Support UK. In recruiting mainly from these sources, only JHS participants who had received a diagnosis and had been more 'active' in joining a support group were included in the current study. It is possible that their characteristics, both in physical symptoms and psychosocial factors to seeking treatment and participating in research are different to the underlying JHS population. In addition, participation in the study required participants to undergo balance perturbations, stand, walk, and ascend and descend stairs. It is possible that some potential participants, for example those with very severe and limiting symptoms, avoided the study if they could not complete these activities.

It was not possible to blind the researcher at the data collection stage, as it was necessary to perform the Brighton Criteria and Beighton Score on each participant by the researcher. In theory data could be anonymised at the data processing stage, however it was still obvious when processing data in the motion analysis software whether a participant had JHS due to how they moved.

9.6 Future work

In the perturbation study (Chapter 5), we found that people with JHS had significantly different timings in some EMG parameters compared to NF. We could measure these EMG parameters as there was a 'rest' period where the participant was standing still immediately prior to the perturbation, which meant we could use this period as a base line to measure muscle activity during the perturbation. For the other activities, there was no such baseline, and so a nuanced analysis of EMG would rely on normalisation by maximum voluntary contraction[141,157].

The fact that JHS participants were unable to produce an MVC may be an interesting result in itself, in that it is not clear whether JHS participants could not produce an MVC due to pain, reduced proprioception, muscle weakness, or poor muscle activation through the nervous system. Although pain may have been a limiting factor in producing MVCs, anecdotally participants reported that they did not feel pain during the attempted MVC, and future work would benefit in measuring peak EMG amplitude and force by evoking responses using transcranial magnetic stimulation or electrical stimulation of peripheral nerves, to see if people with JHS have deficiencies in producing maximal voluntary contractions. A reliable MVC could then be used to expand on the results from this study. For example, here JHS participants had a different knee/ankle strategy during stair ascent, with greater moments and powers generated at the knee, and reduced moments and powers at the ankle, when compared to NF participants. From this result, it is not clear whether the adaption is due to pain in the ankle, and JHS compensating at the knee, or that the ankle plantarflexors are weak. EMG may be able to clarify this; if %MVC is low in ankle plantarflexors, it would hint that JHS participants are actively avoiding using the ankle, and alternatively if %MVC is high, it would indicate that JHS are trying to generate power using the plantarflexors, but muscle weakness is limiting the effectiveness.

Since the current study has found that the majority of differences between JHS and NF movement act around the ankle, one avenue for further work is a study to see if physiotherapy that includes specifically targeting increasing strength and proprioception around the ankle joint normalises movement and ameliorates pain during lower limb activities more broadly in JHS. Given the multifactorial nature of JHS, it seems pertinent to point out that this is unlikely to be a 'magic bullet' of treatment, but may be a contributory aspect of a multidisciplinary approach using the biopsychosocial model of health. Furthermore, since this study has determined the minimal detectable change in 3D movement analysis of hypermobile gait, 3D motion analysis could be used as an outcome measure to confirm whether the physiotherapy treatment was effective in normalising JHS movement. If the movement was normalised and pain persists, it would imply that the differences in movement were not the cause of pain.

9.7 Summary and Conclusions

In the current study a systematic review identified that there was a lack of knowledge about JHS movement. Only gait had been investigated in a JHS cohort, EMG had not been used as an outcome measure in any studies concerning JHS movement, and perhaps most importantly, no study had compared JHS, GJH and NF groups within the same study. This meant that the confounding factor of GJH had not been addressed.

From there, this thesis revealed that the reliability of 3D motion analysis measurement was not influenced by GJH. The minimal detectable change of kinematic parameters measurable using 3D movement analysis was defined, which may be useful if 3D movement analysis is to be used as a monitor of physiotherapy in future work. The reliability study was used to inform a sample size for a study comparing JHS, GJH, and NF groups.

For the four activities investigated; postural response to perturbations, prolonged standing, gait, and stair-climbing, differences were observed in each task between JHS and both GJH and NF groups, but only one significant difference was found between GJH and NF group across the four tasks. This shows that the JHS group represents a distinct population, and a benefit of future work would be to see if physiotherapy could normalise JHS movement and alleviate symptoms. This study found that there were differences in a range of tasks with different functional goals. In the perturbation task possible muscular control deficits were identified, which although the JHS group were able to normalise compared to GJH and NF groups, this did not result in a normalisation in task performance. In the prolonged standing task, JHS individuals had increased AP sway, which may indicate balance impairments found in JHS are prevalent in their natural standing behaviour. During gait people with JHS walked more slowly and generally had reduced joint power. There was a general trend for their joint angles to be more variable, which is indicative of joint instability. In both stair-ascent and stair-descent differences were observed between JHS and GJH/NF groups, particularly in joint moment and power parameters. The overall trend was that JHS participants favoured an ankle strategy during stair climbing rather than a knee strategy which the GJH and NF used. Some results were surprising, for example the fact that JHS generated significantly more power at the knee, and less power at the ankle, than GJH and NF groups during stair ascent. It is surprising as people with JHS have been found to have quadriceps weakness, and the knee is the most common site of pain. With this in mind it might be expected that people with JHS would generate *less* power at the knee. The fact that the opposite is occurring is testament to how complex JHS is, with multiple biopsychosocial factors that contribute to symptoms and differences in movement. It also highlights the value of analysing how people with JHS move during activities, as the information gleaned may help direct future research and ideas for therapy.

The results of this thesis have important implications for the management and understanding of JHS. Given the balance deficits shown in the perturbation activity, and the increased sway observed during prolonged standing, balance training should be considered in future interventions. The differences in joint powers observed during gait and stair climbing show differences that can be targeted with physiotherapy. Whether improving balance and addressing differences in movement improves the symptoms of JHS needs to be investigated in future research.

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Appendix A:

Individual Downs and Black scoring sheets for the reviewed studies in Chapter 2. UtD = Unable to determine.

Fatoye *et al.* (2011). Gait kinematics and passive knee joint range of motion in children with hypermobility syndrome.		
Item	**Score**	**Comments**
1. Is the hypothesis/aim/objective of the study clearly described?	Yes (1) ✓ No (0)	
2. Are the main outcomes to be measure clearly described in the Introduction or Methods section	Yes (1) No (0) ✓	Describe outcome measures of knee kinematics and passive range of motion. What specific factors of knee kinematics are not described (e.g. overall difference, difference in peaks, differences at specific points in the gait cycle).
3. Are the characteristics of the patients included in the study clearly described	Yes (1) ✓ No (0)	Age, gender, mass and where recruited from are described.
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?	Yes (2) Partially (1) No (0) ✓	No mention of knee pain
6. Are the main findings of the study clearly described?	Yes (1) No (0) ✓	Figures show the mean joint angle of each group, specific values for points in the gait cycle where significant differences are reported are not given. Figure for ankle kinematics is shown but is not referred to in the text (not known if there are significant differences in ankle kinematics).
7. Does the study provide estimates of the random variability in the data for the main outcomes?	Yes (1) ✓ No (0)	Standard deviations are shown on figures and reported in tables.
8. Have all important adverse events that may be a consequence of the intervention been reported?	Yes (1) No (0) ✓	No adverse effects described.
10. Have actual probability values been reported (e.g.0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	Yes (1) ✓ No (0)	
11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes (1) ✓ No (0) UtD (0)	
12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Yes (1) ✓ No (0) UtD (0)	
15. Was an attempt made to blind those measuring the main outcomes of the intervention?	Yes (1) No (0) UtD (0) ✓	
16. If any of the results of the study were based on "data dredging", was this made clear?	Yes (1) No (0) ✓ UtD (0)	Since specific outcome measures were not listed it is difficult to determine. In Abstract discuss evaluating gait, in introduction solely the knee, ankle results are included.
18. Were the statistical tests used to assess the main outcomes appropriate?	Yes (1) ✓ No (0) UtD (0)	
20. Were the main outcome measures used accurate (valid and reliable)?	Yes (1) ✓ No (0) UtD (0)	
22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Yes (1) ✓ No (0) UtD (0)	
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	Yes (1) No (0) ✓ UtD (0)	For the JHS group the more painful knee was used in the analysis. Do not know if differences observed are due to pain or JHS.
27. Was a power calculation of sample size calculation provided?	Yes (1) No (0) ✓	

Galli *et al.* (2011). Gait strategy in patients with Ehlers–Danlos syndrome hypermobility type: A kinematic and kinetic evaluation using 3D gait analysis.		
Item	**Score**	**Comments**
1. Is the hypothesis/aim/objective of the study clearly described?	Yes (1) ✓ No (0)	Aim is to 'quantify gait', no hypothesis as such.
2. Are the main outcomes to be measure clearly described in the Introduction or Methods section	Yes (1) No (0) ✓	Some outcomes (PT-ROM and AMSw) are not defined until the results section.
3. Are the characteristics of the patients included in the study clearly described	Yes (1) ✓ No (0)	
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?	Yes (2) Partially (1) No (0) ✓	No mention of knee pain.
6. Are the main findings of the study clearly described?	Yes (1) No (0) ✓	Some outcomes (PT-ROM and AMSw) are not defined.
7. Does the study provide estimates of the random variability in the data for the main outcomes?	Yes (1) ✓ No (0)	Standard deviations are listed
8. Have all important adverse events that may be a consequence of the intervention been reported?	Yes (1) No (0) ✓	No mention of any adverse events
10. Have actual probability values been reported (e.g.0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	Yes (1) No (0) ✓	
11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	Selection criteria was over 30yrs of age for JHS patients. No indication of where subjects were recruited from.
12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	Participants were selected from 40 patients; no details of patient group given.
15. Was an attempt made to blind those measuring the main outcomes of the intervention?	Yes (1) No (0) UtD (0) ✓	
16. If any of the results of the study were based on "data dredging", was this made clear?	Yes (1) No (0) UtD (0) ✓	Given that some outcomes (PT-ROM and AMSw) are not defined until results section data-dredging cannot be eliminated.
18. Were the statistical tests used to assess the main outcomes appropriate?	Yes (1) ✓ No (0) UtD (0)	
20. Were the main outcome measures used accurate (valid and reliable)?	Yes (1) ✓ No (0) UtD (0)	
22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Yes (1) No (0) UtD (0) ✓	Mentions participants from a 'clinical genetics outpatients clinic', no details of where/name of clinic. No details given of where/when CG was recruited.
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	Yes (1) No (0) ✓ UtD (0)	Subjects were recruited from a clinic so presumably had symptoms – no mention of any symptoms (i.e. pain).
27. Was a power calculation of sample size calculation provided?	Yes (1) No (0) ✓	

Simonsen *et al.* (2012). Gait analysis of adults with generalised joint hypermobility		
Item	**Score**	**Comments**
1. Is the hypothesis/aim/objective of the study clearly described?	Yes (1) ✓ No (0)	Hypothesis was that joint moments during walking are elevated in GJH group, although specific joint moments were not mentioned.
2. Are the main outcomes to be measure clearly described in the Introduction or Methods section	Yes (1) ✓ No (0)	
3. Are the characteristics of the patients included in the study clearly described	Yes (1) ✓ No (0)	
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?	Yes (2) ✓ Partially (1) No (0)	Knee pain, gender and age is described.
6. Are the main findings of the study clearly described?	Yes (1) No (0) ✓	Significant results shown on figure but actual numerical results are not listed. Unclear where asterix (indicating a significant result) refers to on figures. Vague description of results, e.g. describe hip angle in frontal plane as lower for "most of stance phase".
7. Does the study provide estimates of the random variability in the data for the main outcomes?	Yes (1) No (0) ✓	No standard deviations etc. are given.
8. Have all important adverse events that may be a consequence of the intervention been reported?	Yes (1) No (0) ✓	No mention of adverse effects in the paper.
10. Have actual probability values been reported (e.g.0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	Yes (1) ✓ No (0)	
11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes (1) ✓ No (0) UtD (0)	Subjects were randomly selected.
12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	
15. Was an attempt made to blind those measuring the main outcomes of the intervention?	Yes (1) No (0) UtD (0) ✓	
16. If any of the results of the study were based on "data dredging", was this made clear?	Yes (1) No (0) UtD (0) ✓	Report results that were not mentioned in hypothesis/outcomes – see comment above.
18. Were the statistical tests used to assess the main outcomes appropriate?	Yes (1) ✓ No (0) UtD (0)	
20. Were the main outcome measures used accurate (valid and reliable)?	Yes (1) ✓ No (0) UtD (0)	
22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Yes (1) ✓ No (0) UtD (0)	
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	Yes (1) No (0) ✓ UtD (0)	53% fo the GJH group reported knee pain, no adjustment in the analysis.
27. Was a power calculation of sample size calculation provided?	Yes (1) No (0) ✓	

Rigoldi *et al.* (2012). Gait strategy in patients with Ehlers-Danlos syndrome hypermobility type and Down syndrome.		
Item	**Score**	**Comments**
1. Is the hypothesis/aim/objective of the study clearly described?	Yes (1) ✓ No (0)	
2. Are the main outcomes to be measure clearly described in the Introduction or Methods section	Yes (1) ✓ No (0)	
3. Are the characteristics of the patients included in the study clearly described	Yes (1) No (0) ✓	No beighton score, no information on how diagnosed. Info on hypermobility of lower limb joints should be included in studies of gait? CG mean age is described differently in table vs. text.
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?	Yes (2) Partially (1) No (0) ✓	Pain not described
6. Are the main findings of the study clearly described?	Yes (1) No (0) ✓	Anterior Step Length is calculated incorrectly
7. Does the study provide estimates of the random variability in the data for the main outcomes?	Yes (1) ✓ No (0)	Standard deviations are given in results
8. Have all important adverse events that may be a consequence of the intervention been reported?	Yes (1) No (0) ✓	No mention of any adverse effects
10. Have actual probability values been reported (e.g.0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	Yes (1) No (0) ✓	
11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	No details of what the source population is
12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	
15. Was an attempt made to blind those measuring the main outcomes of the intervention?	Yes (1) No (0) UtD (0) ✓	
16. If any of the results of the study were based on "data dredging", was this made clear?	Yes (1) No (0) UtD (0) ✓	Wording of the first paragraph of *Data analysis* section of 'Methods' is unclear. Did they compute graphs and then decide at which points to test for significance based on the graphs?
18. Were the statistical tests used to assess the main outcomes appropriate?	Yes (1) ✓ No (0) UtD (0)	
20. Were the main outcome measures used accurate (valid and reliable)?	Yes (1) ✓ No (0) UtD (0)	
22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Yes (1) No (0) UtD (0) ✓	
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	Yes (1) No (0) ✓ UtD (0)	
27. Was a power calculation of sample size calculation provided?	Yes (1) No (0) ✓	

(5) Celletti *et al.* (2013). Use of the Gait Profile Score for the evaluation of patients with joint hypermobility syndrome/Ehlers–Danlos syndrome hypermobility type.		
Item	**Score**	**Comments**
1. Is the hypothesis/aim/objective of the study clearly described?	Yes (1) ✓ No (0)	Aim is described at the end of Introduction section.
2. Are the main outcomes to be measure clearly described in the Introduction or Methods section	Yes (1) ✓ No (0)	
3. Are the characteristics of the patients included in the study clearly described	Yes (1) ✓ No (0)	
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?	Yes (2) Partially (1) No (0) ✓	No mention of knee pain.
6. Are the main findings of the study clearly described?	Yes (1) No (0) ✓	Results are reported in a bar chart (the Movement analysis Profile), however actual results/numbers are not reported. Interpretation is difficult without kinematic graphs.
7. Does the study provide estimates of the random variability in the data for the main outcomes?	Yes (1) No (0) ✓	Standard deviations are shown in figure but are not listed.
8. Have all important adverse events that may be a consequence of the intervention been reported?	Yes (1) No (0) ✓	
10. Have actual probability values been reported (e.g.0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	Yes (1) No (0) ✓	
11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	Population is not defined in the paper.
12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	Where they are recruited from is not described.
15. Was an attempt made to blind those measuring the main outcomes of the intervention?	Yes (1) No (0) UtD (0) ✓	
16. If any of the results of the study were based on "data dredging", was this made clear?	Yes (1) ✓ No (0) UtD (0)	
18. Were the statistical tests used to assess the main outcomes appropriate?	Yes (1) ✓ No (0) UtD (0)	
20. Were the main outcome measures used accurate (valid and reliable)?	Yes (1) ✓ No (0) UtD (0)	
22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Yes (1) No (0) ✓ UtD (0)	Likely that the control group was tested at an earlier time (control group has same characteristics as those from Galli *et al.* (2011) and Rigoldi *et al.* (2012)).
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	Yes (1) No (0) ✓ UtD (0)	
27. Was a power calculation of sample size calculation provided?	Yes (1) ✓ No (0)	

(6) Nikolajsen *et al.* (2013). Gait pattern in 9-11-year-old children with generalized joint hypermobility compared with controls; a cross-sectional study		
Item	**Score**	**Comments**
1. Is the hypothesis/aim/objective of the study clearly described?	Yes (1) ✓ No (0)	Aim was 'to study gait differences'.
2. Are the main outcomes to be measure clearly described in the Introduction or Methods section	Yes (1) ✓ No (0)	
3. Are the characteristics of the patients included in the study clearly described	Yes (1) ✓ No (0)	
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?	Yes (2) Partially (1) ✓ No (0)	Inclusion criteria for NGJH group was no pain in the previous week, suggesting that GJH group experienced pain. No description of pain as a confounding factor. Questionnaire aimed to address physical activity as a confounding factor.
6. Are the main findings of the study clearly described?	Yes (1) No (0) ✓	Results of joint moments reported in tables do not match those reported in figures.
7. Does the study provide estimates of the random variability in the data for the main outcomes?	Yes (1) ✓ No (0)	
8. Have all important adverse events that may be a consequence of the intervention been reported?	Yes (1) No (0) ✓	No mention of adverse effects
10. Have actual probability values been reported (e.g.0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	Yes (1) ✓ No (0)	
11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	
12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	
15. Was an attempt made to blind those measuring the main outcomes of the intervention?	Yes (1) No (0) UtD (0) ✓	
16. If any of the results of the study were based on "data dredging", was this made clear?	Yes (1) ✓ No (0) UtD (0)	
18. Were the statistical tests used to assess the main outcomes appropriate?	Yes (1) ✓ No (0) UtD (0)	
20. Were the main outcome measures used accurate (valid and reliable)?	Yes (1) ✓ No (0) UtD (0)	
22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Yes (1) ✓ No (0) UtD (0)	
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	Yes (1) No (0) ✓ UtD (0)	
27. Was a power calculation of sample size calculation provided?	Yes (1) No (0) ✓	

(7) Cimolin *et al.* (2011) Gait pattern in two rare genetic conditions characterized be muscular hypotonia: Ehlers-Danlos and Prader-Willi syndrome.		
Item	**Score**	**Comments**
1. Is the hypothesis/aim/objective of the study clearly described?	Yes (1) ✓ No (0)	"...identify, quantify and compare... gait in EDS and PWS adults."
2. Are the main outcomes to be measure clearly described in the Introduction or Methods section	Yes (1) ✓ No (0)	All outcome measures are described in Methods section.
3. Are the characteristics of the patients included in the study clearly described	Yes (1) ✓ No (0)	
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?	Yes (2) Partially (1) ✓ No (0)	Pain was not quantified or assessed. Hypermobility was not measured in the PWS group.
6. Are the main findings of the study clearly described?	Yes (1) ✓ No (0)	Although not sure what "EDS and PWS presented a physiological position" means.
7. Does the study provide estimates of the random variability in the data for the main outcomes?	Yes (1) ✓ No (0)	Standard deviation for all parameters are listed
8. Have all important adverse events that may be a consequence of the intervention been reported?	Yes (1) No (0) ✓	There is no mention of adverse events
10. Have actual probability values been reported (e.g.0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	Yes (1) No (0) ✓	P values are reported for most parameters, but not for 'stiffness' parameters.
11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	
12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	Not clear how limiting PWS participants by score of 24 and over on Mini Mental State Examination.
15. Was an attempt made to blind those measuring the main outcomes of the intervention?	Yes (1) No (0) ✓ UtD (0)	
16. If any of the results of the study were based on "data dredging", was this made clear?	Yes (1) ✓ No (0) UtD (0)	
18. Were the statistical tests used to assess the main outcomes appropriate?	Yes (1) No (0) ✓ UtD (0)	There was no adjustment for multiple comparisons.
20. Were the main outcome measures used accurate (valid and reliable)?	Yes (1) ✓ No (0) UtD (0)	
22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Yes (1) No (0) UtD (0) ✓	
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	Yes (1) No (0) ✓ UtD (0)	Pain and mental retardation were not discussed.
27. Was a power calculation of sample size calculation provided?	Yes (1) No (0) ✓	

(8) Luder *et al.* (2015). Stair Climbing – An insight and comparison between women with and without joint hypermobility: A descriptive study.		
Item	**Score**	**Comments**
1. Is the hypothesis/aim/objective of the study clearly described?	Yes (1) ✓ No (0)	To compare GRF and muscle activity.
2. Are the main outcomes to be measure clearly described in the Introduction or Methods section	Yes (1) ✓ No (0)	Parameters are clearly described in the methods section.
3. Are the characteristics of the patients included in the study clearly described	Yes (1) ✓ No (0)	
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?	Yes (2) ✓ Partially (1) No (0)	Participants had no acute pain or clinically relevant problems in the legs or back.
6. Are the main findings of the study clearly described?	Yes (1) ✓ No (0)	Although only selected sig results are shown in the tables.
7. Does the study provide estimates of the random variability in the data for the main outcomes?	Yes (1) ✓ No (0)	
8. Have all important adverse events that may be a consequence of the intervention been reported?	Yes (1) No (0) ✓	
10. Have actual probability values been reported (e.g.0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	Yes (1) ✓ No (0)	
11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	
12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	
15. Was an attempt made to blind those measuring the main outcomes of the intervention?	Yes (1) ✓ No (0) UtD (0)	Testing performed in a separate room to the researcher who assessed hypermobility.
16. If any of the results of the study were based on "data dredging", was this made clear?	Yes (1) No (0) ✓ UtD (0)	Parameters were not defined in the methods.
18. Were the statistical tests used to assess the main outcomes appropriate?	Yes (1) ✓ No (0) UtD (0)	
20. Were the main outcome measures used accurate (valid and reliable)?	Yes (1) ✓ No (0) UtD (0)	
22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Yes (1) No (0) UtD (0) ✓	
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	Yes (1) ✓ No (0) UtD (0)	
27. Was a power calculation of sample size calculation provided?	Yes (1) No (0) ✓	

(9) Celletti *et al.* (2012) Relationship between fatigue and gait abnormality in Joint Hypermboility Syndrome/Ehlers-Danlos Syndrome Hypermobility Type		
Item	**Score**	**Comments**
1. Is the hypothesis/aim/objective of the study clearly described?	Yes (1) ✓ No (0)	
2. Are the main outcomes to be measure clearly described in the Introduction or Methods section	Yes (1) No (0) ✓	Outcome measures are listed as "some parameters", however specific details are not given.
3. Are the characteristics of the patients included in the study clearly described	Yes (1) No (0) ✓	Participants were required to meet Beighton or Villefranche criteria, actual scores are not listed however.
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?	Yes (2) Partially (1) ✓ No (0)	Hypermobility scores are not stated in the results. Not clear if control group included people with hypermobility.
6. Are the main findings of the study clearly described?	Yes (1) No (0) ✓	
7. Does the study provide estimates of the random variability in the data for the main outcomes?	Yes (1) No (0) ✓	No results reported apart from in one figure.
8. Have all important adverse events that may be a consequence of the intervention been reported?	Yes (1) No (0) ✓	
10. Have actual probability values been reported (e.g.0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	Yes (1) No (0) ✓	Some results are unreported
11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	
12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	
15. Was an attempt made to blind those measuring the main outcomes of the intervention?	Yes (1) No (0) ✓ UtD (0)	
16. If any of the results of the study were based on "data dredging", was this made clear?	Yes (1) No (0) UtD (0) ✓	Outcome defined in methods as "some parameters..."
18. Were the statistical tests used to assess the main outcomes appropriate?	Yes (1) No (0) UtD (0) ✓	Since they do not list all the results.
20. Were the main outcome measures used accurate (valid and reliable)?	Yes (1) No (0) UtD (0) ✓	
22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Yes (1) No (0) UtD (0) ✓	Seems unlikely given that there are multiple papers reporting the same cohort.
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	Yes (1) No (0) UtD (0) ✓	
27. Was a power calculation of sample size calculation provided?	Yes (1) No (0) ✓	

(10) Rombaut *et al.* (2011) Balance, Gait, Falls and Fear of Falling in Women with the Hypermobility Type of Ehlers Danlos syndrome.		
Item	**Score**	**Comments**
1. Is the hypothesis/aim/objective of the study clearly described?	Yes (1) ✓ No (0)	Aim is clearly described in the abstract.
2. Are the main outcomes to be measure clearly described in the Introduction or Methods section	Yes (1) ✓ No (0)	
3. Are the characteristics of the patients included in the study clearly described	Yes (1) ✓ No (0)	Hypermobility, pain and lower limb surgery are all described.
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?	Yes (2) ✓ Partially (1) No (0)	
6. Are the main findings of the study clearly described?	Yes (1) ✓ No (0)	
7. Does the study provide estimates of the random variability in the data for the main outcomes?	Yes (1) ✓ No (0)	
8. Have all important adverse events that may be a consequence of the intervention been reported?	Yes (1) No (0) ✓	No mention of adverse events.
10. Have actual probability values been reported (e.g.0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	Yes (1) ✓ No (0)	
11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	
12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	
15. Was an attempt made to blind those measuring the main outcomes of the intervention?	Yes (1) No (0) UtD (0) ✓	
16. If any of the results of the study were based on "data dredging", was this made clear?	Yes (1) ✓ No (0) UtD (0)	
18. Were the statistical tests used to assess the main outcomes appropriate?	Yes (1) ✓ No (0) UtD (0)	
20. Were the main outcome measures used accurate (valid and reliable)?	Yes (1) ✓ No (0) UtD (0)	
22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Yes (1) ✓ No (0) UtD (0)	
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	Yes (1) ✓ No (0) UtD (0)	
27. Was a power calculation of sample size calculation provided?	Yes (1) No (0) ✓	

(11) Galli *et al.* (2011). Postural analysis in time and frequency domains in patients with Ehlers-Danlos Syndrome		
Item	**Score**	**Comments**
1. Is the hypothesis/aim/objective of the study clearly described?	Yes (1) ✓ No (0)	
2. Are the main outcomes to be measure clearly described in the Introduction or Methods section	Yes (1) ✓ No (0)	
3. Are the characteristics of the patients included in the study clearly described	Yes (1) No (0) ✓	No mention of how patients were classified, how hypermobile they were, or hypermobility of the control group.
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?	Yes (2) Partially (1) No (0) ✓	See above. Also there is no mention of pain or excluding participants with other confounding conditions.
6. Are the main findings of the study clearly described?	Yes (1) No (0) ✓	Acronyms are different for the table and the text of the results section – difficult to understand.
7. Does the study provide estimates of the random variability in the data for the main outcomes?	Yes (1) ✓ No (0)	
8. Have all important adverse events that may be a consequence of the intervention been reported?	Yes (1) No (0) ✓	
10. Have actual probability values been reported (e.g.0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	Yes (1) No (0) ✓	
11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	
12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	
15. Was an attempt made to blind those measuring the main outcomes of the intervention?	Yes (1) No (0) ✓ UtD (0)	
16. If any of the results of the study were based on "data dredging", was this made clear?	Yes (1) ✓ No (0) UtD (0)	
18. Were the statistical tests used to assess the main outcomes appropriate?	Yes (1) No (0) ✓ UtD (0)	Separate t-tests are used, with no correction for multiple comparisons.
20. Were the main outcome measures used accurate (valid and reliable)?	Yes (1) ✓ No (0) UtD (0)	
22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Yes (1) No (0) UtD (0) ✓	
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	Yes (1) No (0) ✓ UtD (0)	
27. Was a power calculation of sample size calculation provided?	Yes (1) No (0) ✓	

(12) Greenwood *et al.* (2011). Electromyographic activity of pelvic and lower limb muscles during postural tasks in people with benign joint hypermobility syndrome and non hypermobile people. A pilot study		
Item	**Score**	**Comments**
1. Is the hypothesis/aim/objective of the study clearly described?	Yes (1) ✓ No (0)	We hypothesised that BJHS leads to altered recruitment patterns in muscles of both the pelvis and the lower limbs
2. Are the main outcomes to be measure clearly described in the Introduction or Methods section	Yes (1) No (0) ✓	Procedures for normalising EMG are given in the methods sections, however the actual outcome measures are not described. Co-contraction is defined, but 'muscle activity' is not.
3. Are the characteristics of the patients included in the study clearly described	Yes (1) No (0) ✓	The term BJHS is used, however participants are GJH and were symptom free.
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?	Yes (2) Partially (1) ✓ No (0)	Participants were not seeing a rheumatologist, however no mention of any other factors which may affect balance; surgery, neurological conditions etc.
6. Are the main findings of the study clearly described?	Yes (1) ✓ No (0)	Reported in figures and results section
7. Does the study provide estimates of the random variability in the data for the main outcomes?	Yes (1) ✓ No (0)	Error bars shown on figures
8. Have all important adverse events that may be a consequence of the intervention been reported?	Yes (1) No (0) ✓	No mention of adverse events
10. Have actual probability values been reported (e.g.0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	Yes (1) No (0) ✓	One case where p<.05 was given, for all other results actual p numbers were.
11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes (1) No (0) ✓ UtD (0)	Since the incorrect term is used.
12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	
15. Was an attempt made to blind those measuring the main outcomes of the intervention?	Yes (1) No (0) UtD (0) ✓	
16. If any of the results of the study were based on "data dredging", was this made clear?	Yes (1) ✓ No (0) UtD (0)	
18. Were the statistical tests used to assess the main outcomes appropriate?	Yes (1) ✓ No (0) UtD (0)	Within and between ANOVA. Used a correction for multiple comparisons.
20. Were the main outcome measures used accurate (valid and reliable)?	Yes (1) ✓ No (0) UtD (0)	Co-contraction and EMG parameters well established measures.
22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Yes (1) ✓ No (0) UtD (0)	Recruitment methods are described.
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	Yes (1) ✓ No (0) UtD (0)	Limitations are described.
27. Was a power calculation of sample size calculation provided?	Yes (1) No (0) ✓	No power calculation performed.

(13) Schmid *et al.* (2013). Neuromechanical gait adaptations in women with joint hypermobility – An exploratory study.		
Item	**Score**	**Comments**
1. Is the hypothesis/aim/objective of the study clearly described?	Yes (1) ✓ No (0)	Described in abstract: to explore differences in ground reaction forces, temporal parameters and muscle activation patterns.
2. Are the main outcomes to be measure clearly described in the Introduction or Methods section	Yes (1) ✓ No (0)	Clearly described in the "Data reduction and variables of interest" section of Methods.
3. Are the characteristics of the patients included in the study clearly described	Yes (1) ✓ No (0)	Ages, heights, BMI etc. listed
5. Are the distributions of principal confounders in each group of subjects to be compared clearly described?	Yes (2) ✓ Partially (1) No (0)	
6. Are the main findings of the study clearly described?	Yes (1) ✓ No (0)	All variables listed have reported results
7. Does the study provide estimates of the random variability in the data for the main outcomes?	Yes (1) ✓ No (0)	Standard deviations are listed with results.
8. Have all important adverse events that may be a consequence of the intervention been reported?	Yes (1) No (0) ✓	There is no mention of adverse events.
10. Have actual probability values been reported (e.g.0.035 rather than <0.05) for the main outcomes except where the probability value is less than 0.001?	Yes (1) ✓ No (0)	
11. Were the subjects asked to participate in the study representative of the entire population from which they were recruited?	Yes (1) ✓ No (0) UtD (0)	
12. Were those subjects who were prepared to participate representative of the entire population from which they were recruited?	Yes (1) No (0) UtD (0) ✓	
15. Was an attempt made to blind those measuring the main outcomes of the intervention?	Yes (1) ✓ No (0) UtD (0)	Lab investigators were blinded.
16. If any of the results of the study were based on "data dredging", was this made clear?	Yes (1) ✓ No (0) UtD (0)	Outcome measures are clearly defined.
18. Were the statistical tests used to assess the main outcomes appropriate?	Yes (1) ✓ No (0) UtD (0)	
20. Were the main outcome measures used accurate (valid and reliable)?	Yes (1) ✓ No (0) UtD (0)	
22. Were study subjects in different intervention groups (trials and cohort studies) or were the cases and controls (case-control studies) recruited over the same period of time?	Yes (1) ✓ No (0) UtD (0)	
25. Was there adequate adjustment for confounding in the analyses from which the main findings were drawn?	Yes (1) ✓ No (0) UtD (0)	Limitations of the study are listed.
27. Was a power calculation of sample size calculation provided?	Yes (1) No (0) ✓	No power calculation was performed.