AGE AND SEX-RELATED NORMATIVE JOINT KINEMATIC AND KINETIC WALKING STRATEGIES IN A HEALTHY ADULT POPULATION

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LAY ABSTRACT

Since variability in healthy walking gait strategies may provide evidence for early mobility decline, this thesis aimed to identify the primary walking gait strategies in a healthy adult population. This work is distinct from previous work in that it comprehensively investigates the influence of sex and age on walking gait features and simultaneously defines primary walking gait strategies in healthy adults. The results indicate an overall difference in walking strategy between healthy male and female adults but no significant differences with age, indicating that age-matching for gait studies using adult controls is not as critical as sex considerations. Additionally, the results suggest that gait differences within healthy adults are concentrated in the patterns of their gait mechanics. Understanding how these strategies may link to susceptibility of injury and disease may provide important insight into age-related mobility limitations and help improve mobility longevity in the aging population.

ABSTRACT

A comprehensive understanding of sex-specific gait patterns throughout the lifespan is important considering differences between males and females that can manifest biomechanically, and epidemiological evidence of female sex being a risk factor for some age-related pathologies such as osteoarthritis. This thesis aimed to, 1) characterize the differences in lower extremity joint kinematics and kinetics during gait between healthy women and men in different age groups, and 2) define salient inter-joint kinematic coordination strategies in healthy adult gait. Gait data from 154 asymptomatic adult participants was analyzed. Waveform principal component analysis (PCA) was applied to hip, knee and ankle joint angles and net external moments to extract major patterns of variability. Using a two-factor ANOVA, PC scores were examined for significant sex, age and interaction effects. A second series of PCA models were also developed with the PC scores of the kinematic features of each joint to model the inter-joint kinematic coordination. Demographics, anthropometrics and root mean square (RMS) of EMG waveforms for the high and low groups (85^{th} and 15^{th} percentile) of the retained kinematic strategies were statistically compared using a one-way ANOVA analysis. 13 PC features differed between healthy male and female gait patterns and were independent of age category. No PC features significantly differed between the age groups, and there was no significant sex by age interactions. Four different kinematic gait coordination strategies were identified, one with a significant sex-effect. Therefore, both analyses supported sex-differences in gait biomechanics and the importance of using sex-specific normative data in clinical gait studies. Additionally, the results suggest underlying kinematic differences within asymptomatic adults are concentrated in the patterns of their gait mechanics. Understanding how these strategies may link to susceptibility of injury and disease has important implications for patient-centered care and may provide important insight into age-related pathology and disease.

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Any successes I have had would not have been possible without the incredible support system I am blessed to have in my family and close friends. Thank you to my Mom, Dad, and brothers, Nathan and Dawson, for always providing an open ear and open arms when I needed it and seeing my potential even when I couldn't see it myself. To my grandpas, who provided support both financially, as well as in the form of two furry friends (my kittens Bella and Oliver), throughout my university education – our conversations about my papers, and this research, are something I will always hold close to my heart. To Ryan, thank you for providing the utmost love and support even from afar. Your encouragement and understanding contributed to my success more than you will probably ever know. And last, but certainly not least, I'd like to thank my "COVID bubble" (aka. my King St. roommates) – thank you for keeping me grounded and sane during the last year and a half, I would not have made it through everything in half as good of spirits without you!

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LIST OF ABBREVIATIONS AND SYMBOLS USED

DOHM	Dynamics of Human Motion
3D	Three-dimensional
GRF	Ground Reaction Force
PCA	Principal Component Analysis
PC	Principal Component
ROM	Range of Motion
PW-FL	Pelvis Width to Femur Length Ratio
DPCA	Double Principal Component Analysis
DPC	Double Principal Component
RF	Rectus Femoris
GL	Gastrocnemius Lateralis
EMG	Electromyography
VL	Vastus Lateralis
VM	Vastus Medialis
LH	Lateral Hamstring
MH	Medial Hamstring
LG	Lateral Gastrocnemius
MG	Medial Gastrocnemius
BMI	Body Mass Index
SD	Standard Deviation

DECLARATION OF ACADEMIC ACHIEVEMENT

This thesis would not have been possible without the data collected over the last number of years at the Dynamics of Human Motion (DOHM) lab at Dalhousie University. While I was not personally involved in the recruitment or collection of this dataset, I took the lead on the data analysis, funding application submissions (MIRA, OGS, CGS) and writing for this thesis project. Data collection of complementary gait data was originally planned for summer 2020 at McMaster Innovation Park; however, due to the COVID-19 pandemic, and the nature of the older adult cohort, this was unable to commence. Considering that I was unable to collect data for my own project due to circumstances that were out of my control, I contributed to the gait system setup and patient data collections at the Charlton St. site of St. Joseph's Hospital in Hamilton for another gait analysis study. This allowed me to gain the hands-on experience that I was missing and contribute to Dr. Wilson's research program throughout my time in the Biomedical Engineering program.

CHAPTER 1 INTRODUCTION

1.1 Introduction

Walking is one of the most common and fundamental of human movements and is crucial for human mobility. As we age, the prevalence of cognitive decline and pathology, and thus the likelihood of experiencing walking gait impairments, increases [1]. This can lead to social isolation, decreased physical activity and accompanying health co-morbidities [2,3] that can significantly impact the independence and quality of life of older adults. Mobility limitations are associated with many age-related pathologies and disorders, including osteoarthritis and other musculoskeletal diseases [4,5]. Since age-related differences in mobility are frequently accompanied by changes in walking gait patterns, variability in walking gait strategies may provide evidence for early mobility decline, as well as knowledge for targeted strategies to improve mobility longevity with age.

To date most biomechanics research on human gait has been limited to comparing the mechanics of those diagnosed with clinical conditions to those without [6–8], and thus normative gait data has not been comprehensively investigated on its own. Consequently, there is a dearth of comprehensive data on walking kinematics and kinetics for healthy aging across the lifespan and our current mechanistic understanding of normal gait coordination, as well as the dimensionality of person-to-person variability, is limited. It is necessary to address this gap in the literature as deviations from asymptomatic, or normative data may be used to better understand pathology and inform patient-specific clinical decisions. Considering this important role that demographic-

specific normative data has, it is critical to understand healthy gait coordination throughout the lifespan to define normative strategies for both research and clinical applications.

Understanding the differences in the effect of aging on coordination between men and women is also critical, as previous research has shown significant differences in walking biomechanics between men and women [9–13]. Currently, only a handful of studies have investigated sex differences in joint mechanics during healthy walking gait, resulting in few consistent descriptions of normative sex differences in gait kinematics and kinetics [9,12–15]. Recent evidence that certain sex differences in gait kinematics may be age-dependent [11], as well as epidemiological evidence of higher incidence rates of osteoarthritis and other orthopedic diseases in females [16], highlights the need to more comprehensively investigate sex-specific gait patterns and strategies throughout the lifespan in order to better understand clinical pathology differences that differ between women and men.

Mechanistic information is critical for providing a comprehensive understanding of age- and sex-related changes in gait coordination strategies and can be used for the development and testing of targeted therapies and interventions. Most aging research that incorporates measurements of mobility and function focusses on summary metrics such as walking speed, symmetry, or functional tasks such as timed up and go, six-minute walk tests, etc. While these metrics and tasks can provide valuable information to detect deterioration and changes, they are not specific enough to joint-level mechanics and muscle activity to provide any diagnostic information. Of the few studies describing joint kinematics and kinetics with age, variables are most often selected from resultant waveforms at select points of the gait cycle such as peak maximum or

minimum values [6,17–19]. While these discrete metrics provide more mechanistic information than spatiotemporal metrics alone, they are limited by their dependence on the investigator's variable selection, which is subjective and often overlooks temporal information, such as joint range of motion (ROM) or the relative magnitude of angles/moments at different points of the gait cycle, that may be present in the waveform shape. There is much clinical value in this temporal information, highlighting the importance and utility of considering the entire waveform shape when interpreting gait data.

Despite considerable growth in our understanding of walking gait biomechanics, there is not yet conclusive evidence on normative temporal gait kinematic and kinetic patterns with aging nor how inter-joint coordination strategies for ambulation change with age. Considering that men and women demonstrate differences in walking biomechanics [9,10,12,13,20], as well as differences in disease incidence rates [5,16], there is significant value in understanding sex-specific differences throughout aging. Due to limitations of the few past studies investigating sex and age differences in gait biomechanics, it remains unclear: a) how age and sex interact to contribute to kinematic and kinetic gait performance in healthy adults; b) the importance of age considerations for matching of control participants in adult clinical gait investigations that explore kinematic and kinetic gait outcomes; and c) how inter-joint kinematic coordination strategies change with age and the neuromuscular control associated with these coordination strategies. Therefore, the objectives of this thesis project aim to improve the mechanistic understanding of healthy male and female gait coordination strategies throughout the aging process. The output of this research is a hoped for improved understanding of the inter-relationships in normative joint-level biomechanics and neuromuscular control during walking

gait with age, that could be used to identify specific deviations and inform translational activities. This is a timely topic considering the importance of mobility to overall health and the rapid aging population in Canada. Such models and knowledge may help inform earlier diagnoses and patient-targeted treatments as well as improve mobility longevity for older adults.

1.2 Objectives

1.2.1 Objective 1: Salient Joint-Level Features of Healthy Human Gait

Objective 1 aims to identify salient joint biomechanics features of asymptomatic human gait and compare these magnitude and temporal features between young and older male and female adults to understand differences in the effect of aging on gait kinematics and kinetics between men and women.

1.2.2 Objective 1 Hypotheses

i) There will be significant sex-specific differences in hip and knee joint kinematic and kinetic features during gait.

ii) Age-specific kinematic and kinetic differences will primarily occur at the hip and ankle joints.

1.2.3 Objective 2: Inter-Joint Kinematic Coordination Strategies in Healthy Adults

Objective 2 aims to investigate the correlation structure among the salient kinematic gait variables from Objective 1 to define and interpret prominent inter-joint kinematic coordination strategies in healthy adult gait. A sub-objective includes to examine significant differences in demographics, anthropometrics and neuromuscular activation of lower extremity muscles during

walking for those healthy adults who weigh high and low on the identified salient coordination strategies.

1.2.4 Objective 2 Hypotheses

i) Salient inter-joint lower extremity kinematic features of healthy gait patterns can be defined and interpreted

ii) There will be a significant sex effect on salient inter-joint kinematic features during gait.

1.3 Structure of Thesis

The chapters of this thesis are organized in the following manner: Chapter 2 provides background information related to healthy human gait, including in-depth reviews of the current literature available for both age and sex-specific walking gait. Chapter 3 describes the general methodology utilized in this thesis, specifically the data collection protocol used by the Dynamics of Human Motion (DOHM) laboratory at Dalhousie University, and the details of the Principal Component Analysis (PCA) and Double PCA (DPCA) analyses. Chapters 4 and 5 each address *Objective 1* and *Objective 2* respectively. It should be noted that Chapter 4 was recently published in 'Gait and Posture' [21] and is included in full in this thesis with permission from the journal. As first author of this peer-reviewed manuscript, I contributed to the formal analysis, writing and visualization of this project. Finally, Chapter 6 concludes the thesis by summarizing the findings and implications of this research, as well as addressing limitations and providing suggestions for future directions.

CHAPTER 2 BACKGROUND

2.1 The Human Gait Cycle

In healthy humans, walking is assumed to be a repetitive, cyclic and symmetric process and therefore can be represented by a single cycle referred to as the "gait cycle". A single gait cycle encompasses the time from initial foot contact with the ground to the time that same foot returns to the ground and can be divided into two phases: stance phase and swing phase. Stance phase encompasses the time when the foot is in contact with the ground starting from initial foot contact and ending at toe off. It can be further divided into the loading response (until approx. 20% of gait cycle), mid-stance (20-30% of gait cycle), terminal stance (30-50% of gait cycle) and pre-swing (50-60% of gait cycle). Swing phase begins at toe-off and encompasses the time when the foot is above the ground and the body is propelled forward. It can also be further divided into initial swing (60-80% of gait cycle), mid-swing (80-90% of gait cycle) and terminal swing (90-100% of gait cycle).

Gait is a term used to describe the individualized manner of walking that results from each person's unique anatomical features and mechanical patterns. The degrees of freedom in the lower extremity joints create redundancy in the possible walking joint configurations and as a result, there is natural variance in the kinematics and kinetics of the lower extremity among individuals. Additionally, individualized gait patterns are continually changing and adapting throughout the lifespan [22,23] resulting in natural variance in the lower extremity gait patterns within the same person as well.

On the surface, gait is visually quite simple; however like other voluntary human movements, smooth and efficient walking is a complex behaviour that requires a great deal of both cognitive and motor coordination [24]. In order to successfully accomplish upright human walking, each leg must be able to support the weight of the body without collapsing, balance must be maintained during single leg stance, the swinging leg must be able to advance to a position where it can take over the supporting role and sufficient power must be provided to advance the trunk forwards. Pathology or injury often challenges 'normal' walking gait and thus it has been suggested that changes in gait coordination and balance control may provide early evidence of cognitive decline and disease development prior to clinical diagnoses [25–27].

2.2 Gait Analysis and Demographic-specific Mechanics

Gait analysis is a valuable tool to objectively measure joint function during walking, and one that provides a more comprehensive mechanical and functional assessment than spatiotemporal metrics (ex., walking speed) or performance-based measures (ex., sit-to-stand tasks) alone. A typical modern gait analysis system consists of a synchronized optoelectronic motion capture and force platform system that is most commonly used for the acquisition of three-dimensional (3D) motion and ground reaction force data for biomechanical modelling of the musculoskeletal system [28]. Electromyography (EMG) data is at times collected simultaneously with the motion and force data [29]. 3D joint angles are most often calculated using Cardan-Euler rotations [30] while an inverse dynamics approach is frequently used to calculate the net resultant external joint moments [31]. The data included in this thesis was collected at the Dynamics of Human Motion (DOHM) laboratory at Dalhousie University using a protocol that is outlined in *Chapter 3* and

has been shown to have high day-to-day repeatability and reliability for kinematic, kinetic and EMG data [32,33].

2.2.1 Gait Variables: Spatiotemporal Metrics

Spatiotemporal metrics, such as gait velocity and time spent in stance, offer a general description of the outward appearance of gait, but lack the specificity of joint-level kinematic and kinetic changes that are more diagnostic and reflective of age-related changes in neuromuscular strategies. However, they can provide valuable summary metrics of function and recovery and can be quite useful for comparisons among participant cohorts. For example, walking speed is an important, and frequently reported, measure of mobility and gait function. Slower walking speeds are associated with age [34,35], higher risk of falls [36] and even a higher risk of mortality [37]. In a recent review, Telfer et al. also reported that of all the moderating variables they investigated, walking speed had the largest influence on the knee adduction moment [38], a feature that has been reported to increase with knee osteoarthritis (OA) severity [7,39,40] and predict OA progression [41]. Since individuals with pathologies tend to walk at a slower speed than healthy individuals, it is important to consider the contributions of spatiotemporal factors on normative gait strategies, as they may provide insight into early signs of orthopedic disease and mobility decline for different populations.

2.2.2 Gait Variables: Kinematics and Kinetics

2.2.2.1 Age-specific Changes in Gait Mechanics

There is evidence that the evaluation of certain gait parameters may be valuable in the assessment of health status [42], fall risk [43] and risk of cognitive decline [44] in older

adults. However, in order to be able to clinically recognize abnormal gait indicative of pathology, clinicians must be able to understand and define 'normal' healthy gait. As mentioned previously, most of the current aging research that incorporates measurements of mobility and function focuses on spatiotemporal metrics or functional tasks and thus there is not currently a strong consensus on which biomechanical gait parameters are most relevant for clinical applications.

Older adults, including those who are healthy, typically exhibit greater gait variability during walking compared to young adults [45,46]. Gait variability describes the fluctuations in gait characteristics from one step to the next [47] and is highly correlated with fall risk in older adults [43,48]. As such, it is considered an important indicator of mobility in the aging population and is frequently investigated. However, despite much research on mobility and balance with aging, the cause of this age-related variance remains unclear. Many studies have reported that older adults tend to walk at slower gait speeds than younger adults [34,35,49,50] and thus, it has been proposed that the increased gait variability in older adults may be attributed to this difference in gait speed; however, conflicting studies have found no walking speed differences between younger and older adults [46] suggesting that there may be other factors involved.

Another suggested explanation for the gait changes accompanying aging is that the alterations may be part of a strategy used by older adults to compensate for age-related changes in muscle strength and activation, or to maximize stability [35,51]. There is convincing evidence in the literature that the age-related changes in variability are not dependent on walking speed, but instead on other age-related factors such as decreased muscle strength and ROM [46] that can

impact the walking mechanics at the level of the joint itself. In support of this idea, older adults often walk with altered joint kinematics and kinetics that persist independent of gait speed [35,51,52]. For example, increased hip extension torque [35,51], decreased hip flexion torque [51] and decreased plantarflexion at toe off [50] have all been reported in older adults; however, what remains unclear is how age and sex interact to contribute to gait performance in asymptomatic adults, and the importance of age considerations for matching of control participants in adult clinical gait investigations that explore kinematic and kinetic gait outcomes.

2.2.2.2 Sex-specific Changes in Gait Mechanics

Only a handful of studies have investigated sex differences in joint mechanics during walking gait in an asymptomatic population and most have looked at a small age range. Thus, even though it is widely acknowledged that men and women walk differently in general, there are few consistent descriptions of normative sex differences in gait kinematics with age reported across current studies. While some studies report that females walk with greater hip flexion ROM [9,13,15] throughout the gait cycle, others report that they walk with less hip flexion ROM compared to their male counterparts [10]. Additionally, females have been reported to walk with significantly greater hip adduction [12,13] and internal rotation [13] throughout the gait cycle, as well as with significantly greater ankle flexion ROM [9,10,12], compared to their male counterparts. With respect to the knee, some studies have shown that females have significantly greater knee valgus motion throughout the gait cycle [13] as well as a greater peak knee flexion angle [9], while conflicting results have reported that males walk with larger knee flexion ROM compared to females [15] particularly during stance phase [53]. While biological and anthropometric differences may contribute to these sex-differences, recent evidence that

normative sex-differences in range of motion (ROM) at the ankle, pelvis and torso persist when controlling for body size and gait speed suggests that biomechanical differences between males and females may be more inherent and pervasive than previously thought [54].

To this end, biomechanical sex-differences also propagate into musculoskeletal pathology. Epidemiological evidence of higher incidence rates of osteoarthritis and other orthopedic diseases in females [16], as well as evidence of different OA manifestations in females compared to males, highlights the prevalence of sex-differences in pathological populations as well. McKean et al., previously reported that females with moderate OA walk with smaller knee flexion moments, a smaller knee flexion ROM and a smaller early stance external knee rotation moment (KRM) during stance phase compared to asymptomatic females but these differences were not observed between OA and asymptomatic males [55]. Other studies have reported lower mid-stance internal rotation angles, larger overall stance flexion moments and larger external rotation moments in females with OA compared to symptomatic males, as well as sex-differences in response to interventions such as joint replacement surgery [20]. Therefore, it is evident that sex significantly influences gait and mobility; however, the specific underlying mechanism and explanation for the biomechanical and epidemiological differences between males and females remains unclear.

2.2.3 Gait Variables: Neuromuscular

Evidence of differences in neuromuscular activation patterns with sex [55–58] and age [35,51,52] motivated the inclusion of synchronous surface electromyography (EMG) data in this thesis. Previous studies using surface EMG have reported higher magnitudes of stance phase

medial gastrocnemius (MG) activity pre- and post-knee surgery in females compared to males [20] as well as increased gastrocnemius activity in healthy female adolescents from early to mid-stance during a running and cross-cutting maneuver [59]. Bailey et al. also recently reported that asymptomatic men have higher rectus femoris (RF) activation at mid-swing whereas asymptomatic females have higher gastrocnemius lateralis (GL) activation. Further, with age, men have lower variability of EMG signals at loading, whereas females have higher variability at terminal stance [58]. As mentioned previously, there is evidence in the literature that age-related factors such as decreased muscle strength and ROM may impact walking mechanics at the level of the joint itself [46]. It has been proposed that older adults compensate for decreased use of the ankle plantarflexors by adopting a gait strategy that increases the use of the proximal hip extensors [51]. This distal-to-proximal shift in neuromuscular control with healthy aging is supported by previous findings of proximal/distal muscle activity differences among age-groups [9,60,61] and appears to be even more pronounced at faster gait speeds [52]. Considering that proximal joints have previously been shown to have a larger role in balance control during walking compared to distal joints [62], this proposed aging mechanism would make sense as a potential balance compensatory strategy. Schloemer et al. also recently reported that while healthy older and young adults utilize similar muscles during walking gait, the magnitude and timing of muscle activity differs among age-groups [35]. Specifically, the peak gastrocnemius activity during propulsion in older adults occurs at the ipsilateral heel strike and slightly after heel strike in young adults. Older adults also produced a later peak, and more sustained, tibialis anterior force during weight acceptance compared to the young adults [35].

2.2.4 Gait Variables: Coordination

With respect to this thesis, inter-joint coordination refers to the correlation between features of joint movement in one lower extremity joint to another lower extremity joint during walking. This can provide valuable information for neuromuscular control and adaptability; however, research examining the inter-joint kinematic coordination during gait in an asymptomatic population is currently quite limited. Of the few studies that have investigated normative inter-joint coordination, there is evidence that young and older adults walk with different neuromuscular control strategies at different walking speeds. Specifically, older adults maintain similar patterns in hip–knee coordination when walking at different speeds, whereas younger adults have more variable hip-knee coordination at different speeds [63]. This indicates that walking speed may elicit different motor control patterns in young and older adults and suggests that older adults may struggle to adopt different coordination patterns in response to changes in motor task. In support of this, Wang et al. (2021), recently reported no significant correlation between walking speed and the inter-segmental coordination patterns in healthy older adults at both the thigh-shank and shank-foot; however for patients with knee OA, walking speed was highly correlated to the inter-segmental coordination patterns, suggesting that adaptations at the hip and ankle may be used to compensate for the limited motion or pain at the knee joint [64]. To this point, there is also evidence that inter-joint coordination of gait kinematics and kinetics is altered before and after hip replacement surgery, suggesting that hip OA patients have compromised kinematic coordination that persists even after surgery [65]. Considering that these studies are limited by small sample sizes and focus primarily on the hip-knee coordination, there are currently limited conclusive findings on the inter-joint coordination strategies of the entire

lower limb during healthy gait with age. Similarly, no one has investigated sex-specific coordination during walking gait in a healthy adult population. One study recently looked at the effect of speed on intersegmental coordination of the lower limb and reported that coordination does scale with speed but does not meaningfully differ between healthy males and females [66]. Considering how difficult it is to simultaneously interpret multiple biomechanics differences, and the important role that these strategies can play in informing clinical interventions and therapies, there is a lot of value in more comprehensively understanding the correlation structure that exists among kinematic gait variables to shed light on lower extremity kinematic coordination strategies in healthy adults.

2.3 Methodological Considerations

Biomechanical data is multivariate by nature, with many simultaneous and often correlated, biomechanical changes occurring over time. As a result, 3D gait analysis produces high dimensional and highly variable biomechanical data that often requires data reduction prior to interpretation. A common data reduction practice is to select parameters of interest, usually peak maximum or minimum values, from the resultant kinematic and kinetic waveforms at particular times during the gait cycle [6,17–19]. While this is relatively easy to implement and has some clinical value, these discrete metrics are limited in that they do not consider the overall shape characteristics of the waveforms and thus, do not capture valuable magnitude and temporal information present in the data. Due to the subjectivity of this discrete parameter selection method, it is possible that the selected parameters may not best characterize a specific biomechanical feature or may even fail to capture the same parameter between individual waveforms. Multivariate statistical techniques can be used to address these limitations and

examine the total dimensionality of gait biomechanics. Principal component analysis (PCA) is one example of a multivariate statistical technique that has gained popularity in this area over the last number of years. PCA is a technique that captures the variability and correlation structure within a highly dimensional dataset and presents this information as a single score for each participant, simplifying the complexity in a large dataset. PCA was selected for use in this thesis due to its past utility and success when applied to gait data [67,68].

CHAPTER 3 METHODS

3.1 General Methodology

3.1.1 Participants & Recruitment

This was a secondary analysis of data from 154 healthy adult participants between the ages of 20-75 years (94 females, 60 males). Participants were recruited on a voluntary basis and were eligible if they were in good general health and able to ambulate without the use of walking aids, walk a city block, jog for 5 meters and ascend/descend stairs. Exclusion criteria included any diagnosed musculoskeletal disease, osteoarthritis or rheumatoid arthritis, lower extremity joint injury or surgery in the past year, permanent lower extremity implants, neurological or neuromuscular disorders affecting gait, and uncontrolled heart disease. Informed consent was obtained from all participants in accordance with the institutional ethics board.

3.1.2 Gait Analysis Procedure

Three-dimensional (3D) motion data was collected at the DOHM laboratory using a 12 camera Optotrak optoelectric motion capture system (Northern Digital, Incorporated, Waterloo, ON, CA). At each visit to the lab, infrared light emitting diode (IRED) markers were securely taped on a randomly selected limb. Accurately tracking the locations of specific anatomical landmarks as the participant walks is necessary to model movement kinematics, so anatomical landmarks were identified as precisely as possible through palpation. Based on standardized protocols to measure segment motion and define the joint coordinate system, individual diodes were attached to the shoulder, greater trochanter, lateral epicondyle of the femur and lateral

malleolus of the tibia. Rigid tracking cluster triads, each consisting of three non-collinear IREDs, were also fixed to the pelvis, thigh, shank and foot (Figure 3.1). A marker digitizing probe was used to identify virtual anatomical markers for the right and left anterior superior iliac spine, medial epicondyle, fibular head, tibial tuberosity, medial malleoli, second metatarsal and heel of the selected limb during quiet standing. Both the virtual markers and the single diodes were used to define the anatomical coordinate system in the standing trials.

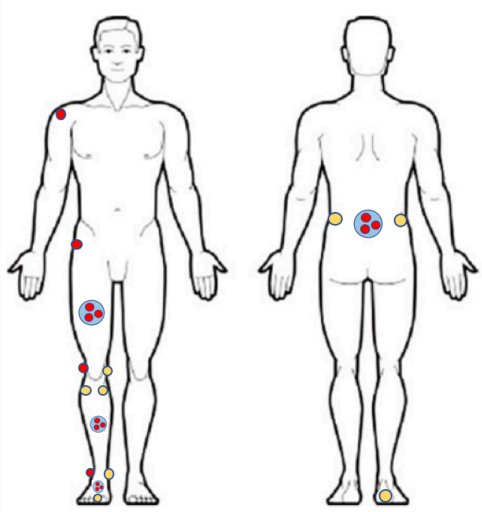

Figure 3.1: Marker set diagram used in the DOHM data collection protocol. Red = individual diodes, yellow = virtual markers created by the digitizing probe and blue = rigid cluster triad.

Once the markers were securely attached, the participant stood in a neutral position with their feet shoulder width apart to complete a static calibration trial. Then, the participant walked at their self-selected speed across the 6m walkway while the 3D IRED marker position data was captured at 100Hz. External ground reaction forces (GRF) were also measured at 1000Hz using an AMTI force platform (Advanced Mechanical Technology, Incorporation, Watertown, MA, USA). A minimum of five trials for each participant were collected and averaged.

A second order bi-directional Butterworth filter was used to filter the data with cut off frequencies of 8Hz and 60Hz for 3D kinematic data and force kinetic data, respectively. 3D joint angles were calculated using Cardan-Euler rotations and described according to the recommended joint coordinate system [69]. 3D motion and GRF data were then input to an inverse dynamic model [31] developed using a custom Matlab (The Mathworks Inc., Natick, MA, USA) code to calculate the joint resultant moments. The magnitudes for all moment waveforms were normalized to body mass and gait events (foot contact and toe off) were determined using a GRF threshold of 5N.

All kinematic gait waveforms were time normalized to one complete gait cycle from 0% (foot contact) to 100% (second foot contact). Exceptions included the frontal and transverse plane knee angles which, like the kinetic waveforms, were time normalized to stance phase of the gait cycle from 0% (foot contact) to 100% (toe off). The average, time normalized data waveforms for each participant were then written as an n x p data matrix in Matlab, where n is the number of participants, and p is the number of variables representing each participant (n=154, p=101). Anthropometric data was used in combination with the data matrices to divide participants into groups based on sex (male, female) and age (20-40 years, 41-50 years, 51-59 years and 60+ years) in order to investigate sex- and age-specific gait strategies. Once the data was divided based on sex and age, the individual waveforms for these groups were plotted to be visually compared. The mean of each group was also calculated in Matlab and plotted to visualize average trends and make general comparisons between the groups.

3.2 Statistical Methods

3.2.1 Principal Component Analysis (PCA)

Principal Component Analysis (PCA) was used in this thesis because of its ability to capture the variability and correlation structure within a high dimensional dataset, something that is particularly important within the present dataset due to the natural variance that exists among healthy individuals. In this thesis, PCA was used to summarize temporal and magnitude information over the entire gait waveform and present this information as a single score for each participant. This method simplifies the complexity in the large dataset by reducing the dimensionality of the data and presenting only the most salient information.

In this thesis, PCA was applied to individual gait kinematic and kinetic waveforms separately by constructing *n* by *p* data matrices, where *n* is the total number of participants and *p* is the number of data points of the gait cycle (101). Normalized joint angle and moment waveforms for each lower limb joint (hip, knee and ankle) in each plane of movement (sagittal, frontal and transverse) resulted in 9 separate kinematic (i.e. 3D joint angles) data matrices and 9 separate kinetic (i.e. 3D joint moments) data matrices. A custom Matlab code was used to create the PCA models. First, the initial variables were standardized by subtracting the mean from each variable in the data matrix ($X = X-X_{mean}$). Then a covariance matrix was calculated to determine the pairwise correlation structure between variables. The eigenvectors (U) and eigenvalues of the covariance matrix were extracted, and orthogonal transformations were completed ($Z = U^{T}X$) for each data matrix, converting the original data variables into principal components (PCs). PCs represent the directions of the data that explain a maximal amount of variance, and act as new axes to improve the representation and visualization of magnitude and pattern features present in

the data. The resulting U matrix is thus a transformation matrix that rotates the original waveforms into this new coordinate system, where each PC loading vector then represents a specific, independent feature of the original waveform data. PCs are mutually uncorrelated and are defined in order of decreasing eigenvalues. Eigenvalues define the amount of variance carried in each PC and thus, the first principal component (PC1) explains the greatest amount of variability in the dataset with each subsequent principal component explaining less.

In order to accomplish data reduction, scree plots were used to define the number of principal components included in each PCA model. For most of the models, at least 80% of the variance in the data was explained by the first 3 principal components suggesting that there was an underlying structure to the variability in the gait data. Any additional principal components were discarded from the model, reducing the dimensionality of the remaining data. The remaining principal components were interpreted based on the shape of the loading vector [70] and the individual gait waveforms that corresponded to high and low PC scores.

Finally, principal component score (PC score) vectors for each participant were determined by reorienting the original waveform along the new principal component loading vectors. This process transforms the original data for each participant into a set of scores that measure the degree to which the shape of their original waveform corresponds to each loading vector feature. A high PC score indicates a high correlation with the pattern feature whereas a low PC score indicates the opposite. Once the PCA models were complete for each joint the group differences were tested, with respect to the PC scores, in a statistical analysis to determine if any age-related or sex-related differences existed within the models.

3.2.2 Double Principal Component Analysis (DPCA)

A second series of PCA models were developed with the PC scores of the retained features from the first PCA to determine the dimensionality of the inter-joint kinematic coordination in the original waveforms. Walking speed, stride length and the original PC scores for the hip, knee and ankle 3D angles were arranged in a 154 x 29 data matrix (154 participants x 29 variables) for the DPCA. Again, a custom MATLAB code was used to extract the first 4 double principal components (DPCs), or the major modes of variability, and reduce the dimensionality of the dataset. The retained DPCs were then interpreted based on the coefficients of the original variables that were >=50% of the maximum coefficient and the individual gait waveforms that corresponded to high and low (85^{th} and 15^{th} percentile) DPC scores.

CHAPTER 4 AGE AND SEX DIFFERENCES IN NORMATIVE GAIT PATTERNS

This chapter contains previously published material from Gait and Posture (July 2021, Volume 88, Pages 109-115). Outlined below is an accurate and detailed description of each author's diverse contributions to the work included in this chapter. Erynne Rowe: formal analysis, writing – original draft, visualization; Dr. Marla Beauchamp: writing – review & editing; Dr. Janie Astephen Wilson: conceptualization, investigation, writing – review & editing, supervision, funding acquisition.

4.1 Introduction

As we age, the likelihood of experiencing walking limitations increases[1]. This can lead to social isolation, decreased physical activity and accompanying health co-morbidities [2,3], which significantly impact the independence and quality of life of older adults. Mobility limitations are associated with many age-related pathologies and disorders, including osteoarthritis and other musculoskeletal diseases [4,5]. Therefore, there is significant interest in improving mobility longevity in the aging population. Since age-related differences in mobility are frequently accompanied by changes in walking gait patterns, investigations of gait changes with aging are at the forefront of the mobility and aging literature. Despite this, normative gait data is typically used as control data in gait pathology studies and not comprehensively investigated on its own. As a result, there is a dearth of comprehensive data on walking kinematics and kinetics for healthy aging across the lifespan. Considering the role of mechanical loading in osteoarthritis and other age-related diseases [6], it is necessary to address this gap in the literature to better understand demographic-specific pathology and disease development.

Past literature on age-related changes in gait mechanics with aging is highly focussed on spatiotemporal metrics, which offer a general description of the outward appearance of gait, but lack the specificity of joint-level kinematic and kinetic changes that are more diagnostic and

reflective of age-related changes in neuromuscular strategies. Many studies have reported that healthy older adults walk at slower speeds than younger adults [34,35,50], with shorter step length [51,61,71], and more time in the double support stance phase [34,50]. Of the few studies describing joint kinematics and kinetics, they have shown that healthy older adults walk with altered joint kinematics and kinetics that persist independent of differences in gait speed [35,51], such as smaller peak hip extension angles [71–73], decreased plantar flexion kinetics [51,61,71,73], and decreased plantarflexion at toe off [50,74]. What remains unclear is how age and sex interact to contribute to gait performance in asymptomatic adults, and the importance of age considerations for matching of control participants in adult clinical gait investigations that explore kinematic and kinetic gait outcomes.

There is an increasing recognition of the need to consider sex-specific analyses in biomedical and clinical research, and there is evidence for sex differences in gait kinematics and kinetics [10,11,13,73,75]. Past investigations of sex differences in gait have focused on a relatively small age range, leaving it unclear if the differences are consistent across the adult lifespan. Recent evidence that certain sex differences in gait kinematics are age-dependent [11], as well as epidemiological evidence of higher incidence rates of osteoarthritis and other orthopedic diseases in females [76], highlights the need to investigate sex-specific gait patterns throughout the lifespan in order to better understand clinical pathology differences that differ between women and men. Therefore, the objective of this study was to comprehensively examine and describe age and sex-specific temporal pattern differences in lower extremity gait mechanics in asymptomatic adults. Based on previous literature, we hypothesized that there would

be significant kinematic and kinetic sex-specific differences at the hip and knee joint [10,13], and age-related differences would be primarily at the hip and ankle joints [51,71,73].

4.2 Methods

4.2.1 Participants

This was a secondary analysis of data from 154 healthy adult participants between the ages of 20-75 years (94 females). Participants were recruited on a voluntary basis and were eligible if they were in good general health and able to ambulate without the use of walking aids, walk a city block, jog for 5 meters and ascend/descend stairs. A sample size calculation for a two-factor ANOVA with 8 groups (2 sex categories; 4 age levels), alpha = 0.001, power of 0.80, and medium effect size (0.50) indicated a sample of 134 would provide sufficient statistical power. Exclusion criteria included any diagnosed musculoskeletal disease, osteoarthritis or rheumatoid arthritis, lower extremity joint injury or surgery in the past year, permanent lower extremity implants, neurological or neuromuscular disorders affecting gait, and uncontrolled heart disease. Informed consent was obtained from all participants in accordance with the institutional ethics board.

4.2.2 Gait Analysis

Participants walked at their self-selected walking velocity along a 6-meter walkway at the Dalhousie University Dynamics of Human Motion (DOHM) lab. Participants were instructed to wear comfortable closed toe walking shoes to their lab visit, and in all cases complied. Three-dimensional (3D) kinematics of the lower limb and external ground reaction forces (GRF) were recorded at 100Hz and 1000Hz respectively, using a synchronized Optotrak motion capture

system (Northern Digital, Inc.), and inground force platform (AMTI, Watertown, MA). Using a protocol that has previously been shown to have high day-to-day reliability [32], rigid tracking triads (each consisting of three non-collinear infrared light emitting diodes) were fixed to the pelvis, thigh, shank and foot segments of one randomly selected limb. Individual infrared markers were also placed on the shoulder, greater trochanter, lateral epicondyle of the femur and lateral malleolus of the tibia. A marker digitizing probe was used to identify virtual markers for the right and left anterior superior iliac spine, medial epicondyle, fibular head, tibial tuberosity, medial malleoli, second metatarsal and heel of the selected limb during quiet standing. Custom Matlab programs were used to calculate 3D ankle, knee and hip angles expressed in the joint coordinate system [30]. The 3D net external moments at the ankle, knee and hip were calculated using an inverse dynamics approach [77,78], also expressed about the joint coordinate system axes, and normalized to body mass. A minimum of five walking trials for each participant were averaged and gait measures were defined with 101 data points, one for each percentage of the gait cycle (angles), or stance phase (moments).

4.2.3 Statistical Methods

4.2.3.1 Principal component analysis of gait waveforms

Waveform principal component analysis (PCA) was applied to the hip, knee and ankle 3D angles and net resultant moments separately (18 gait measures in total) [79]. Data was arranged in 18 separate 154x101 data matrices (154 participants x 101 time points). Using a scree analysis, principal components (PCs) that explained a significant portion of variability were retained. PCs were interpreted based on their pattern over the gait cycle, as well as examining high and low PC scores (95^{th}, 5^{th} percentiles). PC scores, the projection of each observation onto each PC, were

calculated, and differences in PC scores were examined with two factor (sex, age category) ANOVA models. Bonferroni post hoc tests were used to examine pair-wise group differences. A conservative statistical significance level of 0.001 was chosen to account for multiple gait variable comparisons.

4.3 Results

4.3.1 Demographics

Demographic, anthropometrics and spatiotemporal characteristics for all participants by groups are summarized in Table 4.1. The only significant difference among age categories was a greater stride length in those > 60 years as compared to those 51-59 years. Female participants had lower mass (p=<0.0001) and height (p=<0.0001) compared to male participants, and walked with significantly lower stride lengths and stance times as males. Full data for the peak and range values of each joint angle and external moment can be found in Appendix A.3-A.4.

Table 4.1: Demographic and spatiotemporal characteristics for groups based on age and sex

Parameter	20-40 years	41-50 years	51-59 years	60+ years	*p-value*
n	38	45	47	24	
Female: Male	25:13	30:15	30:17	9:15	
Age (years)	34.7 (5.9)	46.2 (2.7)	55.1 (2.6)	63.7 (3.5)	<0.0001*
Mass (kg)	76.7 (14.4)	74.4 (15.4)	75.3 (15.1)	79.0 (17.1)	0.66
Height (m)	1.72 (0.10)	1.69 (0.08)	1.68 (0.09)	1.72 (0.10)	0.12
BMI (kg/m^2)	25.9 (4.65)	26.0 (4.46)	26.6 (4.8)	26.7 (4.4)	0.81
Walking Speed (m/s)	1.37 (0.16)	1.35 (0.18)	1.30 (0.15)	1.39 (0.18)	0.14
Stride Length (m)	1.47 (0.13)	1.43 (0.13)	1.40 (0.11)	1.48 (0.15)	0.02
Stance Time (s)	0.68 (0.06)	0.67 (0.07)	0.68 (0.06)	0.68 (0.06)	0.93
Parameter	Female	Male	*p-value*		
n	94	60			
Age (years)	47.8 (10.2)	50.3 (11.2)	0.16		
Mass (kg)	70.7 (13.8)	84.2 (13.8)	<0.0001*		
Height (m)	1.65 (0.07)	1.77 (0.07)	<0.0001*		
BMI (kg/m^2)	25.9 (4.9)	26.8 (4.0)	0.26		
Walking Speed (m/s)	1.35 (0.17)	1.34 (0.17)	0.59		

Stride Length	1.40 (0.12)	1.49 (0.13)	<0.0001*		
Stance Time (s)	0.66 (0.06)	0.71 (0.06)	<0.0001*		

Data is presented in the form: mean (SD). The p-value corresponds to a two-factor ANOVA analysis comparing the demographic and spatiotemporal characteristics among the four age groups as well as between male and female participants.
* Significant difference (p <= 0.001)

4.3.2 Statistical Results

The statistically significant kinematic and kinetic PCs and interpretations for each joint are discussed below and summarized in Figure 4. Statistical results are summarized in Table 4.2 and statistically significant PC loading vectors and high low plots are available in Appendix A.1-A.2.

4.3.2.1 Sex Effects

Knee: Females had significantly less range in knee flexion to extension angles during stance than males (PC3; 8.4% variance explained, p = 0.0004; Figure 4.1A). In the transverse plane, females also had less range of knee internal/external rotation angles in early stance (PC3, 6.8% variance explained, p<0.0001; Figure 4.1B). Additionally, females walked with smaller range of flexion/extension moments during stance (PC2; 26.6% variance explained, p=0.0004; Figure 4.1C), and with a time delayed early stance knee adduction/abduction moment (PC3; 10.1% variance explained, p=<0.0001; Figure 4.1D).

Hip*:* At the hip joint, females had lower overall transverse plane hip internal rotation angle magnitudes (PC1, 68.9% variance explained, p=<0.0001, Figure 4.1E), but increased internal rotation range of motion (ROM) from initial foot contact to loading (PC3, 5.0% variance explained, p=0.0001, Figure 4.1F) compared to males. Females also walked with less change in hip ab/adduction moments from early to mid-stance (PC2; 14.2% variance explained, p=0.0005; Figure 4.1G), and with a reduced flexion moment in late stance (PC3; 8.9% variance explained, p=<0.0001; Figure 4.1H).

***Ankle**:* At the ankle, females walked with less dorsi-plantar flexion ROM during stance (PC3; 10.8% variance explained, p=0.0003, Figure 4.1I), a smaller ROM in the frontal plane during loading (PC2, 12.4% variance explained, p=0.0009) and less internal rotation going into single leg stance, followed by less external rotation during swing phase (PC2; 12.0% variance explained, p<0.0001, Figure 4.1J). Females also walked with smaller overall magnitudes of flexion moments during the majority of stance (PC1; 44.3% variance explained, p=<0.0001; Figure 4.1K) and less range of ankle internal/external rotation moment during mid to late stance (PC3; 7.7% variance explained, p=0.0007; Figure 4.1L).

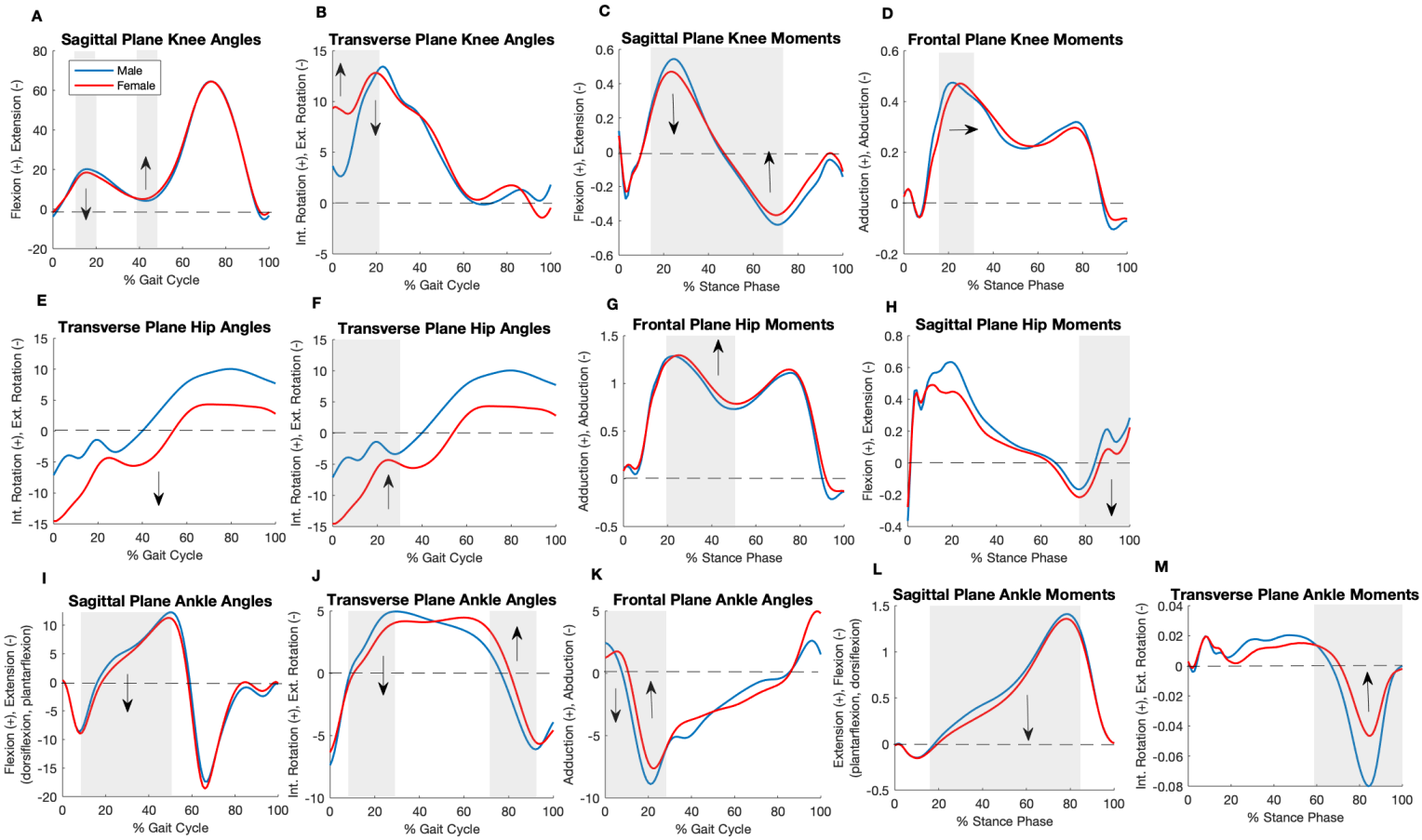

Figure 4.1: Sex-differences in kinematic waveform patterns, dashed=females (n=94, mean age=47.8 +/- 10.2 years) and solid=males (n=60, mean age=50.3 +/- 11.2 years). Shading indicates the area of the gait cycle where the % variation explained is the highest for each statistically significant PC. Direction of arrows corresponds to the direction of the female pattern compared to the male pattern.

4.3.3.2 Age Effects

There were no statistically significant PC differences among the four age groups; however, there were notable trends toward age-related differences (Figure 4.2). 20-40 year-olds trended towards smaller magnitudes of hip flexion/extension angles (PC1; p=0.02); larger hip ab/adduction ROM in early to mid-stance (PC3; p=0.03) than 51-59 year olds; and larger pre-swing hip internal rotation moments than both the 41-50 year olds and the 51-59 year olds (PC3, p=0.05). The 51-59 year-old participants also trended towards smaller range of hip flexion/extension moments in stance compared to all the other groups (PC2, p=0.02).

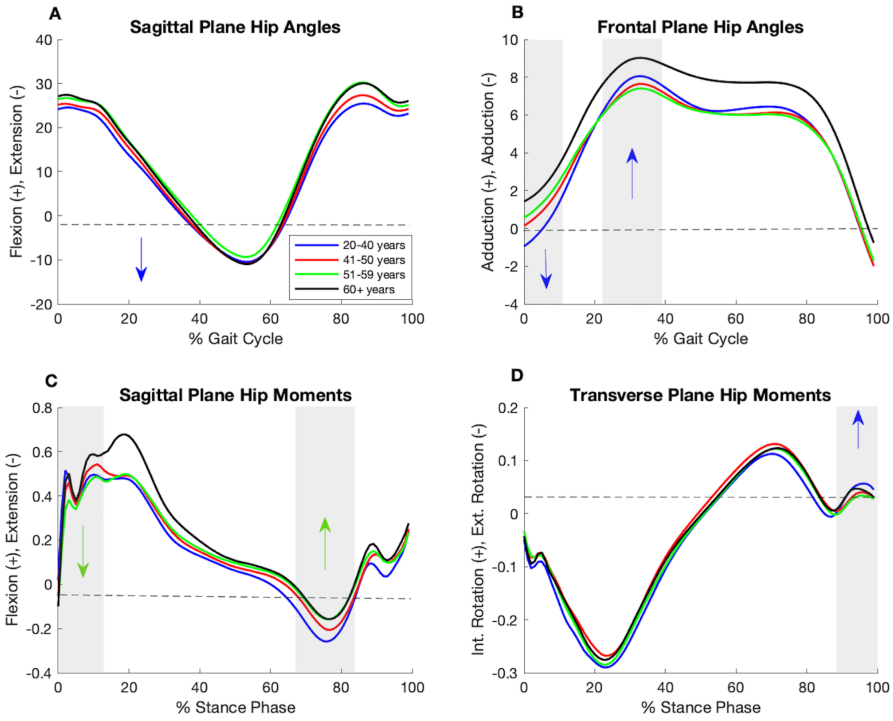

Figure 4.2: Age-related trends in kinematic and kinetic waveform patterns, dark solid=20-40 years (n=38, mean age=34.7 +/- 5.9 years), dashed=41-50 years (n=45, mean age=46.2 +/- 2.7 years), light solid =51-59 years (n=47, mean age=55.1 +/- 2.6 years) and dash-dot=60+ years (n=24, mean age=63.7 +/- 3.5 years). Grey bars indicate the area of the gait cycle where the % variation explained is the highest for each statistically significant PC. Direction of dark arrows corresponds to the direction of the 20-40 year old patterns compared to the 51-59 year old patterns and direction of light arrows corresponds to the direction of the 51-59 year old patterns compared to the rest of the age groups.

Table 4.2: Principal Component Analysis Summary

Model		PC1				PC2					PC3				
	Total Variance Explained; 3 PCs (%)	Feature	Variance explained (%)	Age Effect (p-value)	Sex Effect (p-value)	Interaction (p-value)	Feature	Variance explained (%)	Age Effect (p-value)	Sex Effect (p-value)	Interaction (p-value)	Feature	Variance explained (%)	Age Effect (p-value)	Sex Effect (p-value)	Interaction (p-value)
Knee Angles																
Flexion	**88.4**	Magnitude	66.0	0.7755	0.89	0.51	Phase shift	14.0	0.85	0.40	0.69	Stance Difference	8.4	0.77	**0.0004***	0.58
Adduction	**93.9**	Magnitude	68.7	0.48	0.91	0.75	Stance Difference	15.6	0.21	0.67	0.54	Phase Shift	9.6	0.62	0.22	0.26
Rotation	**93.6**	Magnitude	71.3	0.70	0.35	0.69	Stance Difference	15.4	0.77	0.40	0.69	Difference	6.8	0.87	**<0.0001***	0.67
Knee Moments																
Flexion	**80.7**	Magnitude	45.2	0.67	0.23	0.55	Difference	26.6	0.48	**0.0004***	0.62	Difference	8.9	0.04	0.04	0.33
Adduction	**75.4**	Magnitude	49.9	0.90	0.70	0.07	Difference	15.4	0.523	0.05	0.18	Phase Shift	10.1	0.39	**<0.0001***	0.16
Rotation	**83.5**	Difference	42.4	0.96	0.003	0.57	Magnitude	34.9	0.10	0.08	0.13	Phase Shift	6.2	0.27	0.01	0.10
Hip Angles																
Flexion	**92.8**	Magnitude	70.7	**0.02**	0.19	0.92	Difference	15.1	0.48	0.04	0.43	Phase Shift	7.0	0.63	0.40	0.0459
Adduction	**98.1**	Magnitude	84.6	0.37	0.67	0.82	Stance Difference	10.6	0.69	0.009	0.37	Stance Difference	3.0	0.03	0.09	0.16
Rotation	**94.4**	Magnitude	68.9	0.90	**<0.0001***	0.16	Stance Difference	20.6	0.15	0.33	0.48	Stance Difference	5.0	0.99	**0.0001***	0.72
Hip Moments																
Flexion	**80.7**	Magnitude	45.2	0.60	0.11	0.36	Difference	26.6	0.02	0.02	0.25	Difference	8.9	0.13	**<0.0001***	0.53
Adduction	**83.5**	Magnitude	61.5	0.40	0.33	0.86	Difference	14.2	0.71	**0.0005***	0.09	Difference	7.8	0.13	0.0021	0.06
Rotation	**86.5**	Magnitude	65.3	0.65	0.42	0.72	Difference	14.6	0.95	0.96	0.83	Difference	6.6	0.05	0.0074	0.05
Ankle Angles																
Flexion	**84.0**	Magnitude	58.7	0.91	0.61	0.15	Stance Difference	14.5	0.58	0.81	0.18	Difference	10.8	0.52	**0.0003***	0.24
Adduction	**90.5**	Magnitude	71.5	0.49	0.32	0.34	Difference	12.4	0.77	**0.0009***	0.74	Difference	6.6	0.25	0.11	0.79
Rotation	**94.6**	Magnitude	74.6	0.88	0.75	0.54	Difference	12.0	0.75	**<0.0001***	0.29	Difference	8.0	0.58	0.79	0.97
Ankle Moments																
Flexion	**79.1**	Magnitude	44.3	0.85	**<0.0001***	0.26	Difference	20.0	0.54	0.19	0.56	Phase Shift	14.8	0.28	0.65	0.10
Adduction	**89.5**	Magnitude	63.3	0.86	0.002	0.30	Difference	19.3	0.76	0.36	0.83	Foot Contact	6.9	0.78	0.77	0.91
Rotation	**87.7**	Magnitude	63.8	0.70	0.60	0.63	Difference	16.2	0.46	0.17	0.77	Difference	7.7	0.42	**0.0007***	0.56

Difference feature indicates a pattern feature describing a difference in magnitude of the signal throughout stance (moments) or gait cycle (angles), unless otherwise stated.

*** Significant difference** ($p <= 0.001$)

4.4 Discussion

Our results showed a number of sex-specific differences in kinematic and kinetic gait features at all three major lower-limb joints in asymptomatic adults of varying ages, yet no statistically significant age or interaction effects were found. Most of the significant sex-specific differences were in second or third PC features as opposed to first, which generally represent pattern differences throughout the gait cycle as opposed to magnitudes [79]. Pattern differences encompass features that describe the waveform shape and can include anything from range of motion differences to the relative magnitude of angles/moments at different temporal points of the gait cycle. Our findings therefore suggest that gait differences between asymptomatic females and males are significantly concentrated in the *pattern*s of their gait mechanics as opposed to purely magnitude differences.

While this study is not the first to investigate asymptomatic adult gait, or the influence of sex and age, it is distinct from previous efforts in that it comprehensively investigates the interaction between sex and age in lower extremity joint kinematics and kinetics. This is a logical extension of previous work that provides important normative information for both joint angles and mechanical loading. As summarized in Figure 4.3, our results showed that differences were not isolated to a single plane of motion, or to a single joint, with most differences in stance phase. Some of our results were consistent with previous studies, including the finding that females have increased internal rotation at the hip from initial foot contact through to the loading response [75], as well as smaller ankle flexion moments throughout most of stance [13]. Discrepancies between our results and those of previous studies were also revealed. For example, while previous literature has supported that females walk with greater sagittal plane

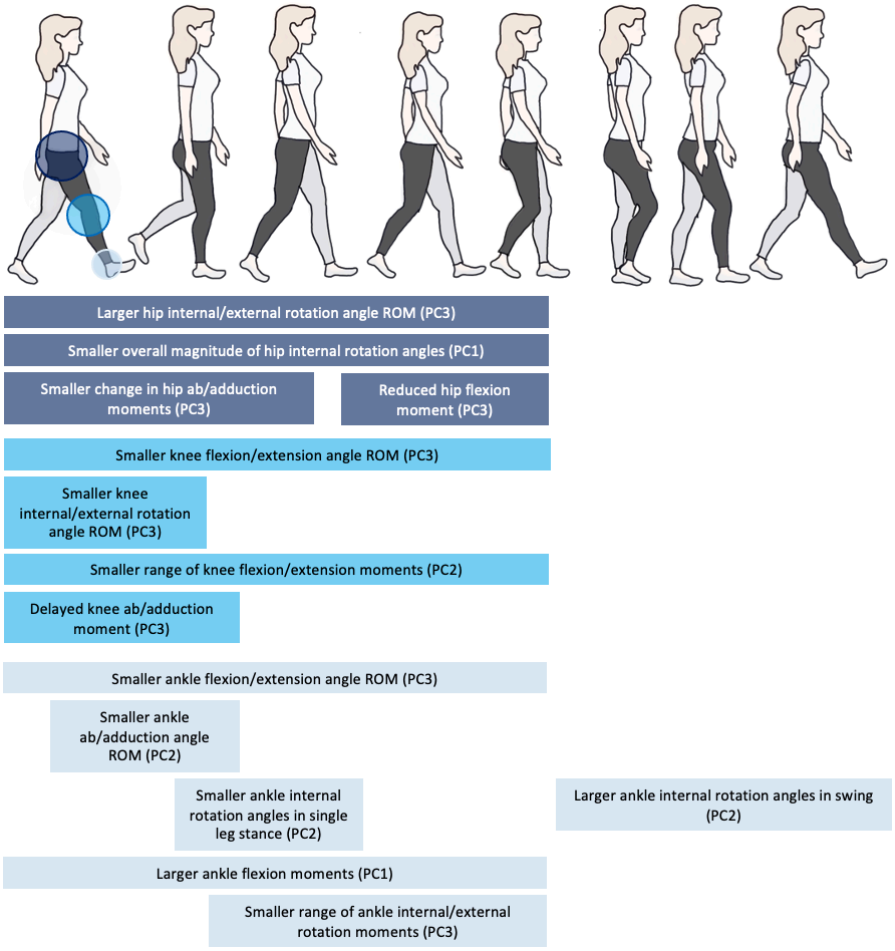

Figure 4.3: Summary of female walking gait cycle as compared to male gait cycle. Sex-related joint angle and moment features highlighted by the description bars. Dark grey=hip features, grey=knee features and light grey=ankle features. Location and length of description bar for each feature indicates the part of the gait cycle where a significant portion of variability is explained by the PC.

ankle ROM and smaller hip ROM [10], we report smaller flexion/extension ROM during stance in females compared to males and larger hip ROM in the transverse plane. This may be due to differences in participant age or to differences in gait speed, as Ko et al. only included participants above the age of 50 years old and reported slower preferred gait speeds [10]. Many others have reported discrete metrics such as larger peak knee flexion angles [73] and greater hip adduction magnitudes [13] in female gait, but we report no sex-differences in peak knee flexion or hip adduction (Appendix A.3).

Although the PC scores for many features differed between males and females, the effect size of these differences were relatively small and therefore the individual features may not represent meaningful differences between the sexes; however, when considering all of these small differences together, an overall difference in walking strategy between healthy male and female adults is evident. Differences may partially reflect sex deviations in structural anatomy. For example, females in general tend to have a larger pelvis width to femur length ratio (PW-FL) than males which may affect both frontal plane motion as well as alter the alignment of the other lower extremity joints [80]. We report that females walk with smaller hip and ankle angles as well as a reduced range of hip and knee moments in the sagittal plane, suggesting more stiffness (in a clinical sense) in female sagittal plane mechanics compared to males. Similar to previous reports [10,11,73,75], we did not find significant differences in self-selected gait speeds between females and males and thus, these differences in sagittal plane mechanics cannot be attributed to slower walking velocity. As reported in previous literature, females trended towards shorter stride lengths ($p=0.02$) suggesting they may walk with higher stride frequencies to maintain similar gait speeds to their male counterparts. This adjustment of shorter and more frequent strides to maintain gait speed may affect the mechanics at the lower extremity joints, possibly explaining the combined sagittal plane differences, and the coincident differences in transverse plane hip mechanics, exhibited by the female participants throughout stance. Additionally, there is evidence of differences in neuromuscular strategies between women and men. Bailey et al. [58] recently reported that men have higher rectus femoris (RF) activation at mid-swing whereas females have higher gastrocnemius lateralis (GL) activation. Further, there is evidence that with age, men have lower variability of electromyography (EMG) signals at loading, whereas females have higher variability at terminal stance [58]. The evidence of sex-dependent neuromuscular

strategies provides support for our results of sex-specific gait kinematic and kinetic strategies and future work should investigate these differences further using EMG.

We did not find any statistically significant age category or age by sex interaction effects for lower extremity joint kinematics and kinetics during gait. This has implications for the ability to use healthy adult controls in clinical gait studies without the need for strict age-matching. However, it should be noted that there were some trends towards age effects in hip angles and moments. Previous literature has supported reduced hip ROM during gait in older adults compared to younger adults [81], and so this particular feature may be an important consideration when interpreting aging gait patterns. Others have reported additional age-related differences in gait biomechanics including reduced plantar flexion [82] and plantar flexor kinetics [51,61,73], increased muscle co-contraction [83] and different spatiotemporal features of gait. Reduced ROM would be expected with higher muscle co-contraction; however, unlike previous studies [82], we did not find any significant age-related kinematic or kinetic differences. This may be due to the nature of this normative study and our inclusion criteria. Since it is common to develop comorbidities with age, the asymptomatic participants in the 60+ group are a selective group of individuals that may not be representative of the general population at that age. Interestingly, we also report significantly greater stride lengths in the 60+ participants compared to the 51-59 year group (Table 4.1). While this finding initially seems counterintuitive it is possible that, unlike the asymptomatic 60+ group, the 51-59 year group may currently be ‘asymptomatic’ but at risk of developing health comorbidities in the near future. This may also explain our age-related trends, all of which differentiated the 51-59 year group from the other age groups.

There are certain limitations that should be considered when interpreting our results. First, this study was limited to four discrete age groups making it difficult to draw conclusions about mechanisms and gait changes within the groups. Age groups were initially defined based on decades; however, it was difficult to recruit participants older than 65 who fit the inclusion criteria of no co-morbidities. As such, the older decades were merged to create the 60+ age group. In a recent review of mobility changes due to aging, Grimmer et al. (2019) report that most age-related decreases in self-selected walking speed, and steps per day, occurred between the ages of 60-85 providing general support for this group classification [1]. Similarly, the youngest decades were also merged to form the 20-40 year group as we did not anticipate significant age-related changes prior to this age. Further, the 60+ year group was the smallest group and had a mean age of only 64 years, which is young in terms of expected mobility decline. To examine if our categorization was limiting our ability to detect potential age effects, we additionally performed some supplementary analyses using age as a continuous variable. No significant correlations between age on a continuum and gait outcomes were identified (Appendix A.5). Further study could consider a larger prospective study with both an older and younger cohort of participants to further understand aging effects on healthy gait mechanics beyond the ages considered in this study. This study, however, provided a comprehensive picture of sex-dependent age changes in lower extremity kinematic and kinetic gait features to understand deviations in gait mechanics in healthy adult aging, dependent on sex. Our univariate approach was used to comprehensively present and describe these differences, as the literature is sparse in such demographic-specific normative data. Future research could further our understanding with more multivariate analyses and could include consideration of neuromuscular strategies with electromyography data.

In conclusion, these results support the need to consider sex-specific gait biomechanics in future gait studies. The combination of kinematic and kinetic differences identified between healthy adult male and female participants suggest an overall difference in walking gait strategy that should be interrogated further using electromyography to understand neuromuscular control differences. Major sex-specific differences represented *pattern* differences, highlighting the utility of considering the entire gait waveform shape. All of the significant sex-differences were independent of age, suggesting that these differences are relatively consistent in adult aging until approximately age 70 and strict age-matching of healthy participants in pathology and clinical studies may not be critical.

CHAPTER 5 INTER-JOINT KINEMATIC COORDINATION STRATEGIES IN HEALTHY ADULTS

5.1 Introduction

Walking is one of the most common and fundamental of human movements, and has well-established links to musculoskeletal injury, disease development and propagation, as well as balance and control. Variability in walking gait strategies may provide evidence for early mobility decline, as well as knowledge for targeted strategies to improve mobility longevity with age; however, our current mechanistic understanding of normal gait coordination, as well as the dimensionality of person-to-person variability, is limited. Considering the important role that demographic-specific normative data plays in informing patient-centered diagnoses and treatments, it is necessary to understand healthy gait coordination throughout the lifespan to define normative strategies for both research and clinical applications.

Previous research has shown significant differences in walking biomechanics [9–11,75] and neuromuscular activation patterns [55–57] between healthy men and women. Recently, Bruening et al. (2020) reported that normative sex-differences in range of motion (ROM) at the ankle, pelvis and torso persisted when controlling for body size and gait speed, suggesting that these sex-differences may be more inherent and pervasive than previously thought [54]. Biomechanical sex-differences also propagate into musculoskeletal pathology and we see sex-specific mechanistic links to osteoarthritis (OA) and other orthopedic diseases [76], as well as sex-differences in response to interventions such as joint replacement surgery [20]. Thus, while it is evident that sex significantly influences gait and mobility, the specific underlying mechanism and explanation for these biomechanical differences remains unclear and provides strong support

for investigating and characterizing sex-specific normative kinematic strategies throughout the lifespan.

Our previous work presented a comprehensive analysis of age-independent sex differences in lower extremity kinematic and kinetic gait features. Several gait features, including angles of all three lower limb joints, differed between asymptomatic male and female adults regardless of age category, suggesting that female adults utilize a different strategy when walking compared to males [21]. Because it is difficult to simultaneously interpret multiple biomechanics differences, there is value in further understanding the correlation structure among these variables to shed light on lower extremity kinematic coordination strategies in healthy adults. The aim of this current study was therefore to use a multivariate analysis to model the correlation structure among 3D joint angle magnitude and patterns at the hip, knee and ankle joints during walking in a large cohort of healthy adults to understand salient lower extremity kinematic features that may represent different gait strategies. For this study, we chose to focus on gait kinematics in order to model sex-dependent asymptomatic adult movement strategies with age. A secondary aim was to use simultaneously-captured lower extremity electromyography (EMG) data to interpret the neuromuscular activation strategies associated with the age- and sex-related salient kinematic gait features. Based on previous literature [9–11,21,75], we hypothesized that salient inter-joint lower extremity kinematic features of healthy gait patterns could be defined and that there would be significant differences between females and males in gait strategies in healthy adults.

5.2 Methods:

5.2.1 Participants

This was a secondary analysis of a previous study using walking gait data from 154 healthy adult participants between the ages of 20-75 years (94 females) [21].

5.2.2 Double Principal Component Analysis (DPCA) Model

Previously, a waveform principal component analysis (PCA) was conducted on hip, knee and ankle 3D angles during walking to extract key patterns of variability [8,21]. Principal components (PCs) that explained a significant portion of variability (%) were retained and interpreted (27 PCs total) (Appendix B.1). PC scores for each participant were calculated.

Double PCA (DPCA): A second PCA model was developed with the previously retained PC scores of the lower extremity joint angles during walking to extract salient features of inter-joint kinematics during gait. A custom MATLAB code was used: walking speed, stride length, and the hip, knee and ankle 3D angle PC scores were arranged in a 154x29 data matrix (154 participants x 29 variables) for the DPCA procedure [8]. To reduce the dimensionality of the data, the first 4 DPCs were retained for interpretation as they represented the major modes of variability. The coefficients of the original variables in each retained DPC were examined and those that were >=50% of the maximum coefficient were used in the DPC interpretation along with the individual gait waveforms that corresponded to high and low (85^{th} and 15^{th} percentile) original PC scores [84].

Differences in the DPC scores were examined with two factor (sex, age) ANOVA models. Age was included as a continuous variable and interaction effects were not included in the ANOVA model as there was no evidence of interaction in our previous univariate analyses [21].

Bonferroni post hoc tests were used to examine pair-wise group differences and a statistical significance level of 0.01 was chosen to account for multiple comparisons.

5.2.3 EMG

Synchronized electromyography (EMG) data was collected for each participant during the walking trials using an eight-channel surface EMG system (AMT-8 EMG, Bortec Inc., Calgary, Alberta). EMG collection and processing followed previously published protocols [85]. Briefly, silver/silver chloride pellet surface electrodes were attached in a bipolar configuration (20 mm centre-to-centre) over the rectus femoris (RF), vastus lateralis (VL), vastus medialis (VM), lateral hamstring (LH), medial hamstring (MH), lateral gastrocnemius (LG) and medial gastrocnemius (MG) of the same randomly selected leg used for motion capture. The raw EMG signals were digitized at 2000 Hz, using the analog data capture feature of the Optotrak motion capture system. Following the walking trials, participants completed a set of eight voluntary maximal-effort isometric contractions (MVIC) which were used to assess muscle strength and to provide a physiological reference for EMG normalization purposes [85]. Using a custom MATLAB code, the EMG waveforms for each muscle were amplitude normalized to the maximal 0.1-s amplitude that occurred during the MVIC exercises [29] and time-normalized to 100% of the gait cycle. Root mean square (RMS) of the EMG waveforms for high and low groups (85^{th} and 15^{th} percentile) for retained DPCs were then statistically compared using a one-way ANOVA analysis for an interpretation of the neuromuscular control patterns associated with salient kinematic features.

5.3 Results:

5.3.1 Participants

Demographic, anthropometric and spatiotemporal characteristics for all participants are summarized in Table 5.1. Female participants had lower mass and height compared to male participants and walked with significantly smaller stride lengths and stance times as males (p=<0.0001).

Table 5.1: Demographic and spatiotemporal characteristics

Parameter	Female	Male	*p-value*	Total
n	94	60		154
Age (years)	47.8 (10.2)	50.3 (11.2)	0.16	48.8 (10.6)
Mass (kg)	70.7 (13.8)	84.2 (13.8)	**<0.0001***	75.9 (15.3)
Height (m)	1.65 (0.07)	1.77 (0.07)	**<0.0001***	1.7 (0.09)
BMI (kg/m^2)	25.9 (4.9)	26.8 (4.0)	0.26	26.3 (4.6)
Walking Speed (m/s)	1.35 (0.17)	1.34 (0.17)	0.59	1.35 (0.17)
Stride Length	1.40 (0.12)	1.49 (0.13)	**<0.0001***	1.44 (0.13)
Stance Time (s)	0.66 (0.06)	0.71 (0.06)	**<0.0001***	0.68 (0.06)

Data is presented in the form: mean (SD). The p-value corresponds to a two-factor ANOVA analysis comparing the demographic and spatiotemporal characteristics between male and female participants.
* Significant difference (p <= 0.01)

5.3.2 Double Principal Component Analysis (DPCA) Model

The % variation explained by each DPC and statistical results for the DPCA model are summarized in Table 5.2. PC coefficients for the retained DPCs are presented in Figure 5.1. Variables with coefficients >=50% of the max (highlighted in blue) were included in the interpretation of each DPC. Interpretations of DPC1-DPC4, including the waveforms corresponding to the high (85th percentile, n=23) and low (15th percentile, n=23) PC scores (Figures 5.2-5.5) and the interpretations of the original PC features included in each model (Tables 5.3-5.6), are presented, and discussed more thoroughly below.

Table 5.2: Double PCA Statistical Summary

	Variance Explained (%)	Age Effect (p-value)	Sex Effect (p-value)	DPC Interpretation
DPC1 (speed-related strategy)	13.8	0.44	0.99	Spatiotemporal and angular pattern differences in all three planes of the knee joint, and hip and ankle. High DPC1 scores = higher speed, larger stride lengths; higher transverse plane angular ROM at the knee and hip; earlier sagittal plane extension (pre-swing) at the knee and ankle.
DPC2 (speed-independent ROM strategy)	10.0	0.47	**<0.0001***	Angular ROM and magnitude differences at different temporal points of the gait cycle in all 3 planes and at all three joints. High DPC2 scores = larger sagittal plane knee and hip ROM; larger frontal plane hip and ankle ROM; smaller transverse plane hip ROM from initial foot contact to loading; increased knee internal rotation midstance; decreased ankle adduction at foot contact; more ankle internal rotation in stance compared to more external rotation in swing.
DPC3 (lower leg strategy)	8.7	0.78	0.62	Knee and ankle strategy characterized by ROM of knee and ankle in the sagittal and transverse planes. High DPC3 scores = larger sagittal plane knee and ankle angles; larger knee, and smaller ankle angles in the transverse plane.
DPC4 (hip & frontal plane strategy)	7.3	0.08	0.36	Hip sagittal and transverse plane strategy associated with frontal plane motion at hip, knee and ankle joints. High DPC4 scores = Larger transverse and sagittal plane hip angles; smaller frontal plane angles at the hip, knee and ankle; larger transverse plane ankle angles

The p-value corresponds to a two-way ANOVA analysis (with age as a continuous variable) comparing the high and low scoring groups for the retained DPCs. * Significant difference (p <= 0.01)

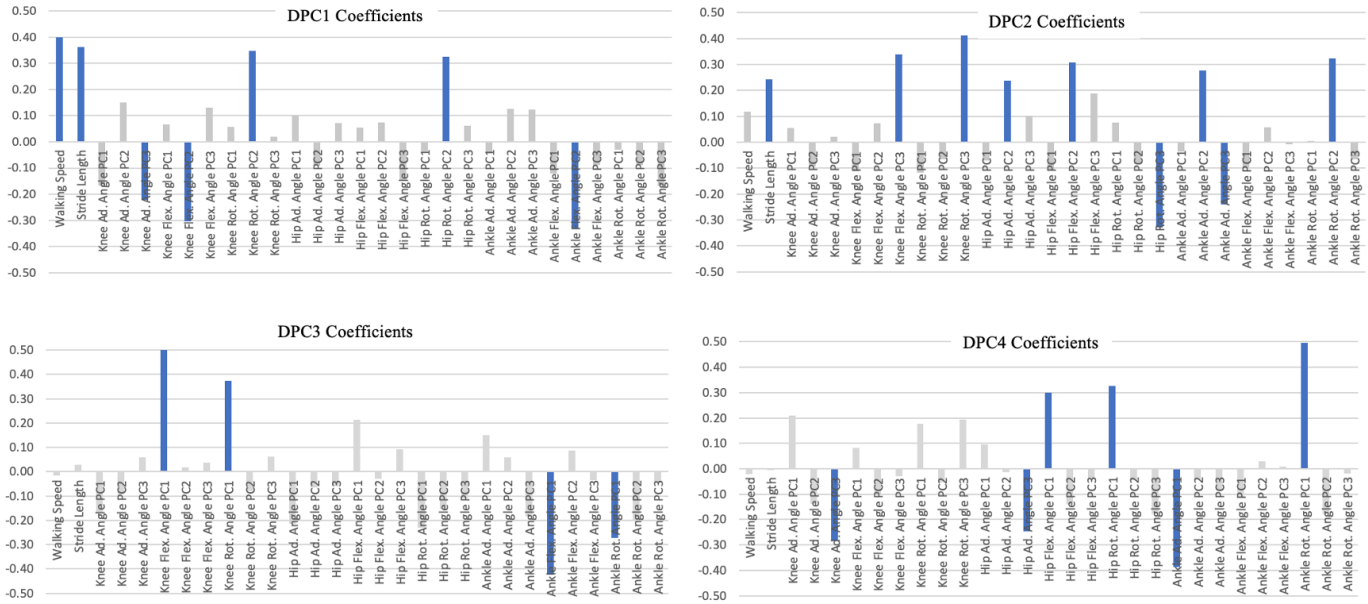

Figure 5.1: Coefficients for DPC1-DPC4. Blue bars indicate the co-efficients that are >=50% of the max co-efficient and thus included in the DPC interpretations.

5.3.2.1 Double Principal Component 1 (DPC1): Speed-Related Strategy

As shown in Table 5.3, DPC1 captures a speed-related kinematic strategy with high scoring participants (85th percentile) represented by significantly faster walking speeds (<0.0001), larger stride lengths (<0.0001), and a shorter time spent in stance (<0.0001). Participants with higher DPC1 scores walked with more knee abduction (knee adduction PC3) throughout stance and a larger transverse plane ROM at both the knee (knee rotation PC2) and hip (hip rotation PC2), throughout stance and the entire gait cycle respectively. Pre-swing, high DPC1 scoring individuals exhibited earlier knee extension (knee flexion PC2) and ankle plantarflexion (ankle flexion PC2) compared to the low DPC1 scoring (slower) individuals (Figure 5.2).

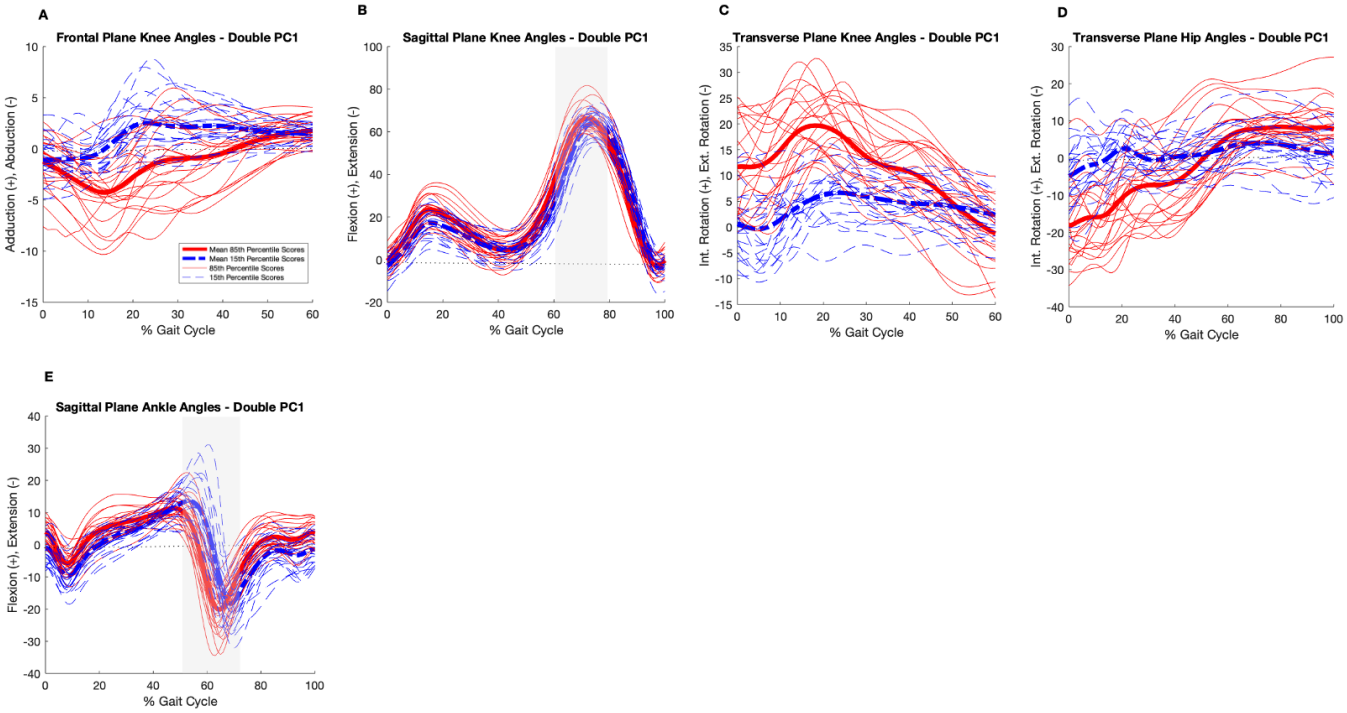

Figure 5.2: Gait waveforms associated with the high (85th percentile, Red) and low (15th percentile, Blue) DPC1 score plots. Thin lines represent the data waveforms for the participants in the 85th and 15th percentiles of DPC1 scores. Thick lines represent the average waveforms associated with these scores. Shading highlights the part of the gait cycle where the % variance explained is the highest for each statistically significant DPC.

Table 5.3: Summary of DPC1 Interpretation

Contributing Feature	Original High Score Interpretation	Double PC Co-efficient	Double PC1 High Score Interpretation
Walking Speed	n/a	0.40	Faster walking speed
Stride Length	n/a	0.36	Longer stride lengths
Knee Adduction PC3	More sustained adduction during stance	-0.22	More sustained abduction during stance
Knee Flexion PC2	Phase shift – delayed pre-swing extension	-0.30	Earlier pre-swing knee extension
Knee Rotation PC2	Difference feature – larger ROM in stance	0.35	Larger knee rotation ROM in stance
Hip Rotation PC2	Difference feature – larger ROM throughout gait cycle	0.33	Larger hip rotation ROM throughout gait cycle
Ankle Flexion PC2	Phase shift – larger and more delayed pre-swing extension	-0.33	Smaller and earlier pre-swing ankle extension

5.3.2.2 Double Principal Component 2 (DPC2): Speed-independent ROM Strategy

At the knee, participants with high DPC2 scores had more range in flexion to extension angles during stance (knee flexion PC3) as well as more range of internal/external rotation angles in early stance (knee rotation PC3). At the hip, high DPC2 scorers had a larger ROM in both the frontal and sagittal planes (hip adduction and flexion PC2) but a decreased internal rotation ROM from initial foot contact to loading (hip rotation PC3). At the ankle, participants with high DPC2 scores had a larger ROM in the frontal plane from loading to mid-swing (ankle adduction PC2) as well as smaller magnitudes of adduction at both initial and terminal foot contact (ankle adduction PC3). High DPC2 scoring participants also walked with more ankle internal rotation going into single leg stance, followed by more external rotation during swing phase (ankle rotation PC2) (Figure 5.3). Interestingly, there was a statistically significant difference in DPC2 scores between female and male participants ($p=<0.0001$), with male participants having higher scores on average than their female counterparts.

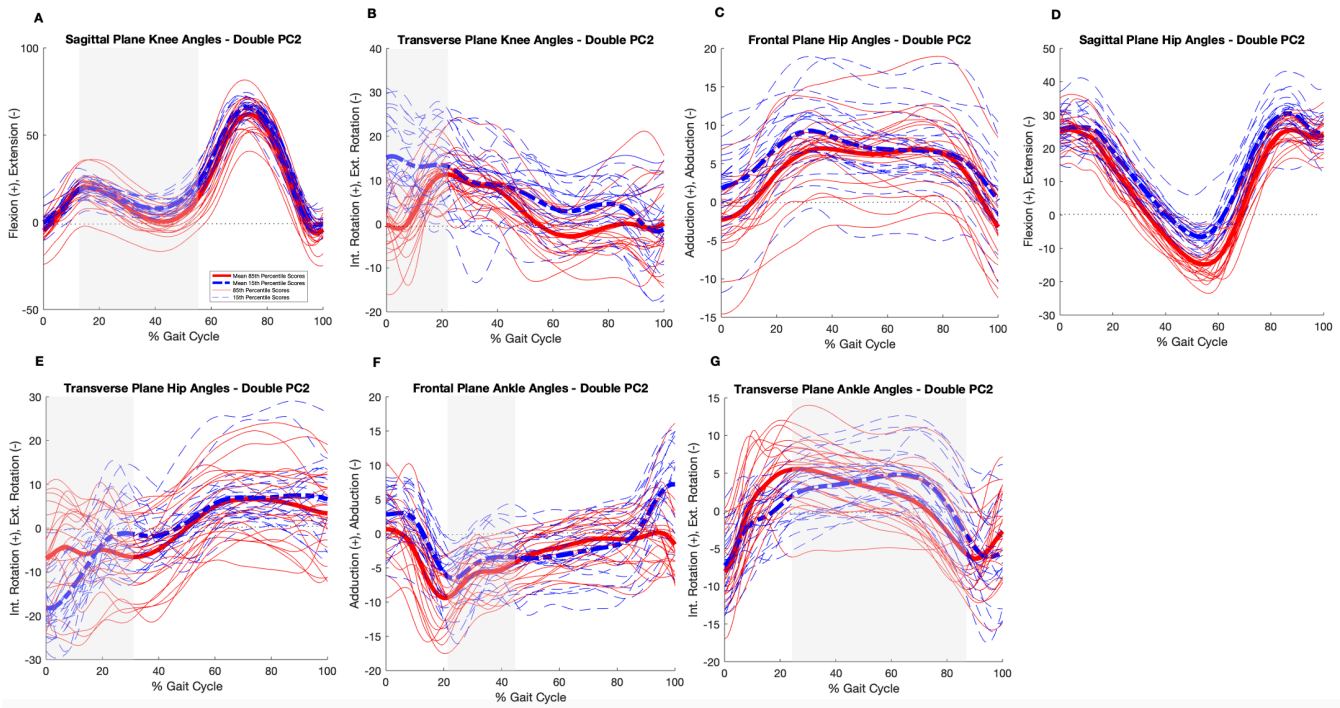

Figure 5.3: Gait waveforms associated with the high (85th percentile, Red) and low (15th percentile, Blue) DPC2 score plots. Thin lines represent the data waveforms for the participants in the 85th and 15th percentiles of DPC2 scores. Thick lines represent the average waveforms associated with these scores. Shading highlights the part of the gait cycle where the % variance explained is the highest for each statistically significant DPC.

Table 5.4: Summary of DPC2 Interpretation

Contributing Feature	Original High Score Interpretation	Double PC Co-efficient	Double PC2 High Score Interpretation
Knee Flexion PC3	Larger ROM early to midstance	0.34	Larger knee flexion ROM early to midstance
Knee Rotation PC3	Pattern Difference: Neutral early stance, into internal rotation midstance, neutral late stance	0.41	Neutral knee early stance, into internal rotation midstance, back to neutral late stance
Hip Adduction PC2	Larger ROM in stance	0.24	Larger hip adduction ROM in stance
Hip Flexion PC2	Larger ROM across gait cycle	0.31	Larger hip flexion ROM across gait cycle
Hip Rotation PC3	Larger ROM from initial foot contact to loading	-0.33	Smaller hip rotation ROM from initial foot contact to loading
Ankle Adduction PC2	Larger ROM across gait cycle	0.28	Larger ankle adduction ROM across gait cycle
Ankle Adduction PC3	Increased adduction at foot contact (beginning of stance & end of swing)	-0.24	Decreased ankle adduction at foot contact (beginning of stance & end of swing)
Ankle Rotation PC2	Pattern Difference: More internal rotation in stance compared to more external rotation in swing	0.32	More ankle internal rotation in stance compared to more external rotation in swing

5.3.2.3 Double Principal Component 3 (DPC3): Lower Leg Strategy

DPC3 captured a "lower leg strategy" characterized by angle magnitude differences at the knee and ankle joints. Participants with high DPC3 scores walked with greater flexion and internal rotation magnitudes (knee flexion and rotation PC1) at the knee and larger flexion (ankle flexion PC1) and smaller ankle internal rotation (ankle rotation PC1) magnitudes at the ankle (Figure 5.4).

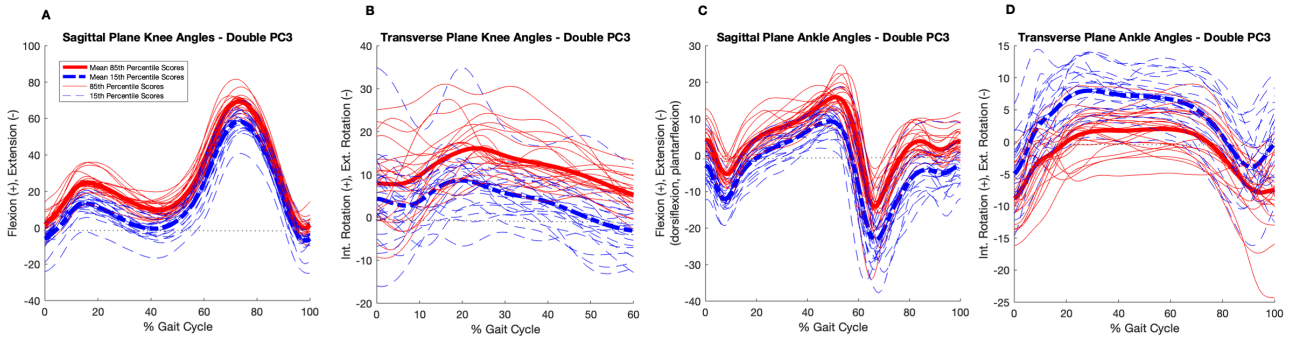

Figure 5.4: Gait waveforms associated with the high (85th percentile, Red) and low (15th percentile, Blue) DPC3 score plots. Thin lines represent the data waveforms for the participants in the 85th and 15th percentiles of DPC3 scores. Thick lines represent the average waveforms associated with these scores.

Table 5.5: Summary of DPC3 Interpretation

Contributing Feature	Original High Score Interpretation	Double PC Co-efficient	Double PC3 High Score Interpretation
Knee Flexion PC1	Larger magnitudes of flexion	0.50	Larger magnitudes of knee flexion angles
Knee Rotation PC1	Larger magnitudes of rotation	0.37	Larger magnitudes of knee rotation angles
Ankle Flexion PC1	Smaller magnitudes of flexion	-0.42	Larger magnitudes of ankle flexion angles
Ankle Rotation PC1	Larger magnitudes of rotation	-0.27	Smaller magnitudes of ankle rotation angles

5.3.2.4 Double Principal Component 4 (DPC4): Hip & Associated Frontal Plane Strategy

DPC4 also captured angle magnitude differences during walking, with an emphasis on the hip sagittal and transverse plane kinematics. Participants with high DPC4 scores walked with larger hip flexion and internal rotation magnitudes (hip flexion and rotation PC1) as well as smaller

adduction angle magnitudes at all three lower limb joints (adduction PC1) (Figure 5.5). Indicating that when walking with more "hip strategy", or more hip flexion and rotation, there is less movement in the frontal plane of the lower extremity in general.

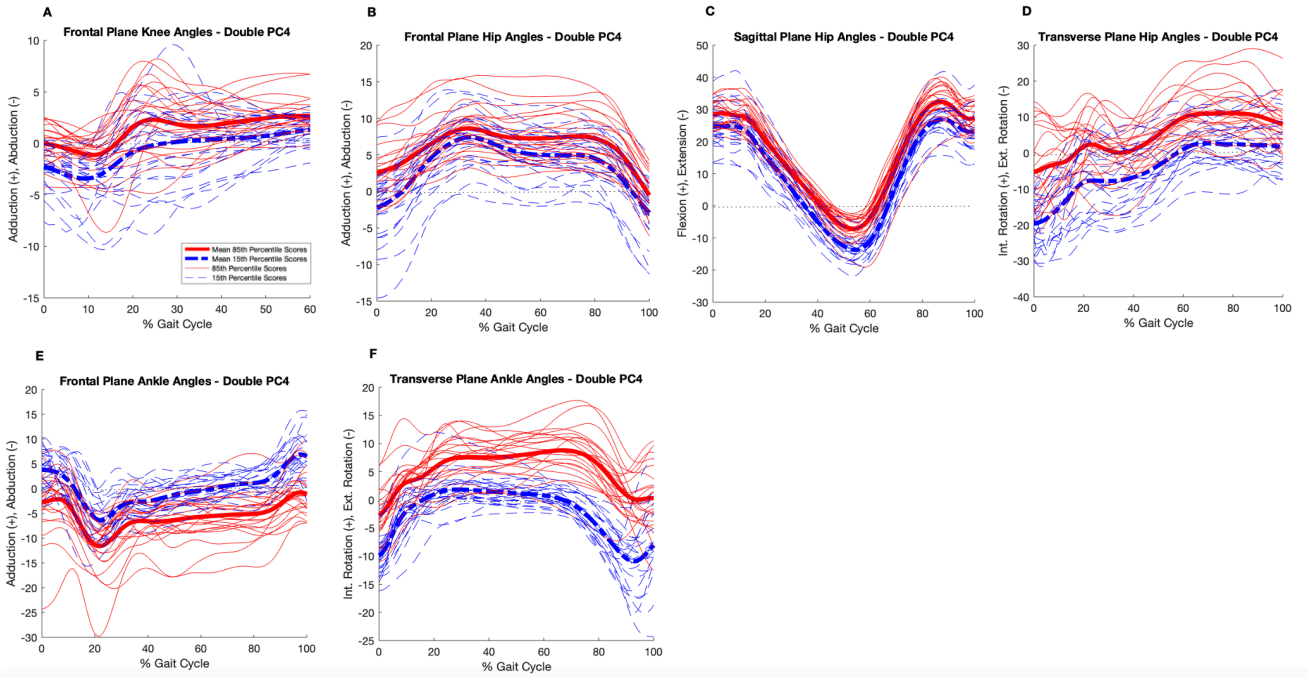

Figure 5.5: Gait waveforms associated with the high (85th percentile, Red) and low (15th percentile, Blue) DPC4 score plots. Thin lines represent the data waveforms for the participants in the 85th and 15th percentiles of DPC4 scores. Thick lines represent the average waveforms associated with these scores.

Table 5.6: Summary of DPC4 Interpretation

Contributing Feature	Original High Score Interpretation	Double PC Co-efficient	Double PC4 High Score Interpretation
Knee Adduction PC1	Larger magnitudes of adduction	-0.28	Smaller magnitudes of knee adduction angles
Hip Adduction PC1	Larger magnitudes of adduction	-0.25	Smaller magnitudes of hip adduction angles
Hip Flexion PC1	Larger magnitudes of flexion	0.30	Larger magnitudes of hip flexion angles
Hip Rotation PC1	Larger magnitudes of rotation	0.33	Larger magnitudes of hip rotation angles
Ankle Adduction PC1	Larger magnitudes of adduction	-0.39	Smaller magnitudes of ankle adduction angles
Ankle Rotation PC1	Larger magnitudes of rotation	0.49	Larger magnitudes of ankle rotation angles

Table 5.7: Demographic characteristics for PC1-PC4 based on participants in the high and low (85th and 15th percentile) score groups.

Parameter	High PC1	Low PC1	*p-value*	High PC2	Low PC2	*p-value*	High PC3	Low PC3	*p-value*	High PC4	Low PC4	*p-value*
n	23	23		23	23		23	23		23	23	
Female: Male	14:9	15:8	0.77	7:16	20:3	**<0.0001***	14:9	12:11	0.56	15:8	15:8	1
Age (years)	47.4 (10.6)	51.5 (10.4)	0.19	49 (11.6)	47.4 (11.6)	0.65	52 (12.2)	50.3 (10.5)	0.61	51.8 (9.79)	47.6 (11.0)	0.17
Mass (kg)	74.9 (11)	82.0 (18.1)	0.11	89.3 (16.7)	67.3 (11.2)	**<0.0001***	77.3 (12.7)	78.2 (16.1)	0.83	74.3 (11.4)	72.8 (13.2)	0.69
Height (m)	1.71 (0.08)	1.68 (0.08)	0.39	1.76 (0.1)	1.66 (0.06)	**0.0001***	1.7 (0.09)	1.74 (0.11)	0.22	1.69 (0.1)	1.72 (0.11)	0.30
BMI (kg/m^2)	25.7 (2.9)	28.9 (6.4)	0.03	28.9 (5.97)	24.4 (4.06)	**0.004***	26.6 (3.01)	25.8 (4.74)	0.53	26.2 (3.62)	24.6 (3.71)	0.16
Stance Time (s)	0.62 (0.05)	0.73 (0.06)	**<0.0001***	0.68 (0.19)	0.68 (0.14)	0.84	0.7 (0.18)	0.68 (0.19)	0.42	0.68 (0.16)	0.69 (0.2)	0.58

Data is presented in the form: mean (SD). The p-value corresponds to a one-way ANOVA analysis comparing the demographic characteristics between the high and low score groups for the retained DPCs.
* Significant difference (p <= 0.01)

5.3.3 EMG Results

To further interpret the kinematic strategies, neuromuscular activation patterns of seven muscle sites during gait were investigated using synchronized EMG data. EMG waveforms for participants with high and low (85th and 15th percentile) scores were included in this secondary interpretation. The individual and average EMG waveforms for these groups, are discussed below and summarized in Figures 5.6-5.9. A statistical comparison of the high and low groups for each of the seven muscle sites is also included in Table 5.8.

Table 5.8: EMG RMS ANOVA Results

Gait Cycle RMS (%MVIC)	Variable (EMG) LG	MG	VL	VM	RF	LH	MH
High PC1	25.5 (6.86)	30.5 (15.3)	12.1 (4.62)	12.4 (4.00)	8.1 (3.77)	10.6 (3.81)	11.9 (4.81)
Low PC1	19.4 (8.42)	25.7 (10.4)	12.1 (5.32)	13.1 (7.35)	7.6 (4.00)	11.5 (4.96)	11.9 (3.77)
p-value	***0.02***	0.26	0.98	0.72	0.66	0.54	0.98
High PC2	22.4 (7.52)	24.2 (9.42)	14.7 (5.24)	13.0 (5.35)	10.8 (7.12)	12.7 (7.63)	15.1 (7.70)

Low PC2	20.5 (7.38)	27.5 (7.09)	11.7 (3.74)	12.8 (6.28)	6.9 (2.13)	10.3 (3.45)	10.6 (3.28)
p-value	0.45	0.24	***0.04***	0.91	0.45	0.21	***0.02***
High PC3	21.6 (7.54)	29.1 (7.23)	13.5 (5.71)	12.2 (4.36)	8.1 (3.55)	10.1 (3.37)	10.5 (3.35)
Low PC3	19.9 (8.62)	20.9 (7.88)	11.7 (4.36)	11.4 (5.37)	7.0 (3.04)	11.0 (3.58)	10.8 (3.72)
p-value	0.55	**0.001***	0.25	0.63	0.27	0.43	0.73
High PC4	18.2 (7.74)	25.4 (9.44)	12.9 (5.42)	12.2 (6.57)	6.5 (3.04)	11.1 (5.23)	10.1 (4.54)
Low PC4	20.3 (8.32)	25.4 (7.26)	11.6 (5.07)	13.3 (8.61)	7.8 (4.02)	10.4 (4.83)	11.9 (3.19)
p-value	0.43	0.99	0.47	0.66	0.24	0.63	0.14

Data is presented in the form: mean (SD). The p-value corresponds to a one-way ANOVA analysis comparing the RMS of the EMG waveforms between the high (85th percentile) and low (5th percentile) score groups. * Significant difference (p <= 0.01)

5.3.3.1 DPC1 Neuromuscular Strategy: Speed-Related Strategy

There were no statistically significant differences between the EMG waveforms of the participants who scored high and low on DPC1; however, the statistical results revealed a trend towards significantly higher LG RMS for the high DPC1 participants compared to the low DPC1 participants (p=0.02). Both the individual and average EMG waveforms (Figure 5.6) visually show that participants in the high DPC1 group exhibit a slightly earlier shifted, and much larger, % MVIC pre-swing than the participants in the low DPC1 group providing general support for this trend.

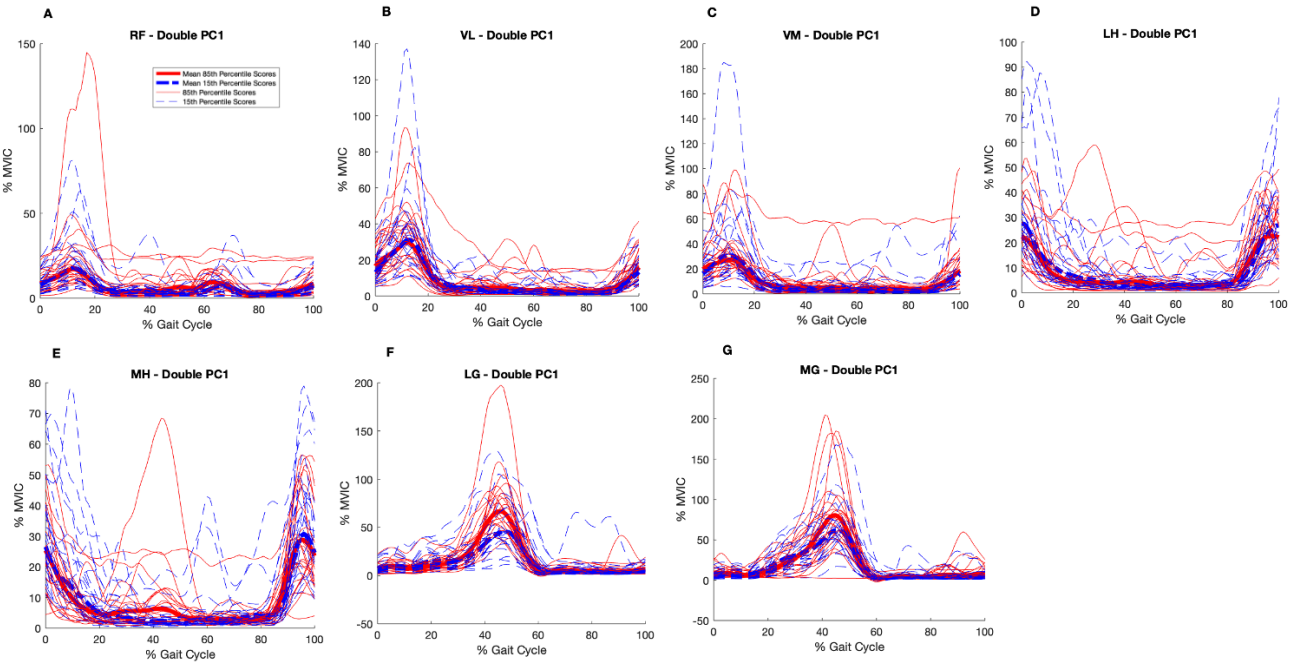

Figure 5.6: EMG waveforms of the participants with high (85th percentile, Red) and low (15th percentile, Blue) DPC1 scores. Thin lines represent individual participants and thick lines represent the high and low group average.

5.3.3.2 DPC2 Neuromuscular Strategy: Speed-independent ROM Strategy

Similar to DPC1, there were no statistically significant differences between the EMG waveforms of the high and low DPC2 scoring participants. Nonetheless, high DPC2 scoring participants trended towards higher RMS for both the VL (p=0.04) and the MH (p=0.02) compared to low DPC2 scoring participants. This trend is supported by the average EMG waveforms (Figure 5.7) that show high DPC1 scorers exhibited larger % MVIC for the VL from initial foot contact to loading, both individually and on average, as well as larger % MVIC for the MH at initial and terminal foot contact (start of stance phase and end of swing phase).

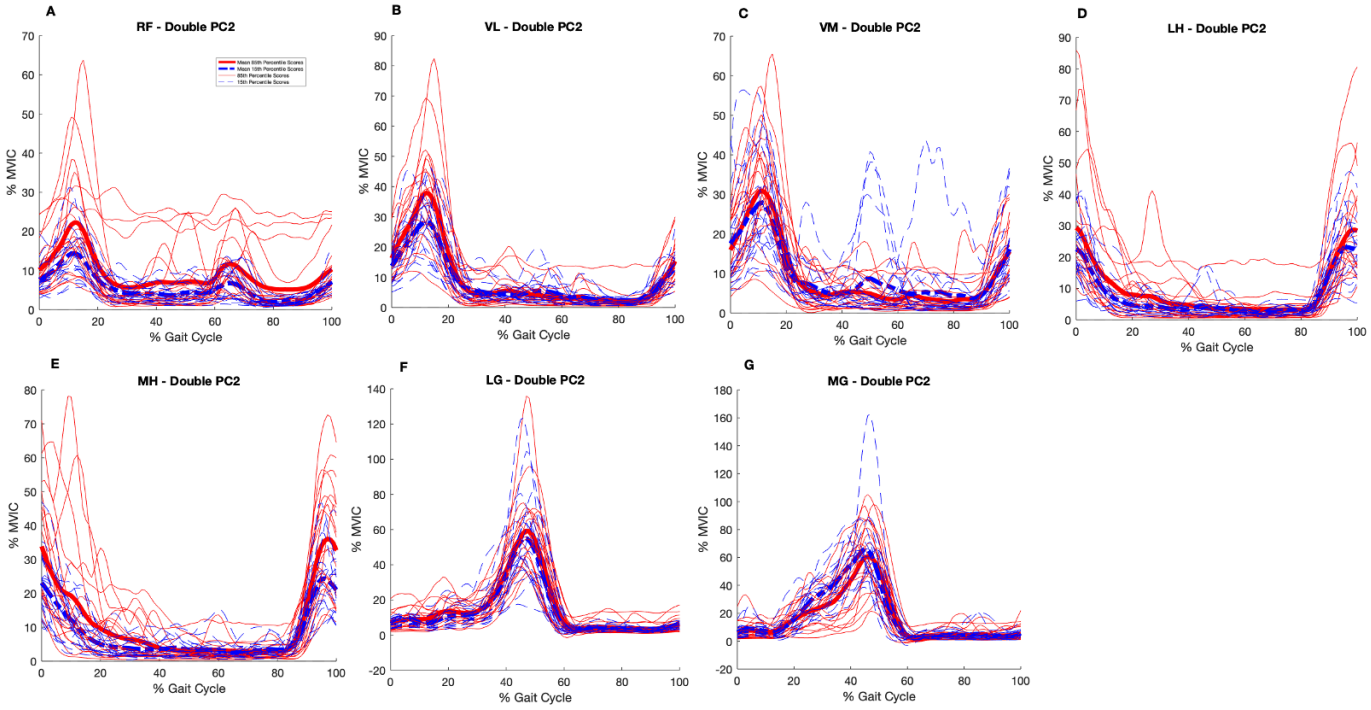

Figure 5.7: EMG waveforms of the participants with high (85th percentile, Red) and low (15th percentile, Blue) DPC2 scores. Thin lines represent individual participants and thick lines represent the high and low group average.

5.3.3.3 DPC3 Neuromuscular Strategy: Lower Leg Strategy

Participants with high DPC3 scores had statistically significantly higher RMS of the MG activity waveforms compared to participants with low DPC3 scores (p=0.001). The individual and average EMG waveforms (Figure 5.8) for the high and low DPC3 groups support this finding. This is not particularly surprising considering DPC3 captures a "lower leg" strategy, with kinematic emphasis on the knee and ankle transverse and sagittal plane mechanics, and the gastrocnemius is a lower leg muscle group responsible for knee and ankle flexion.

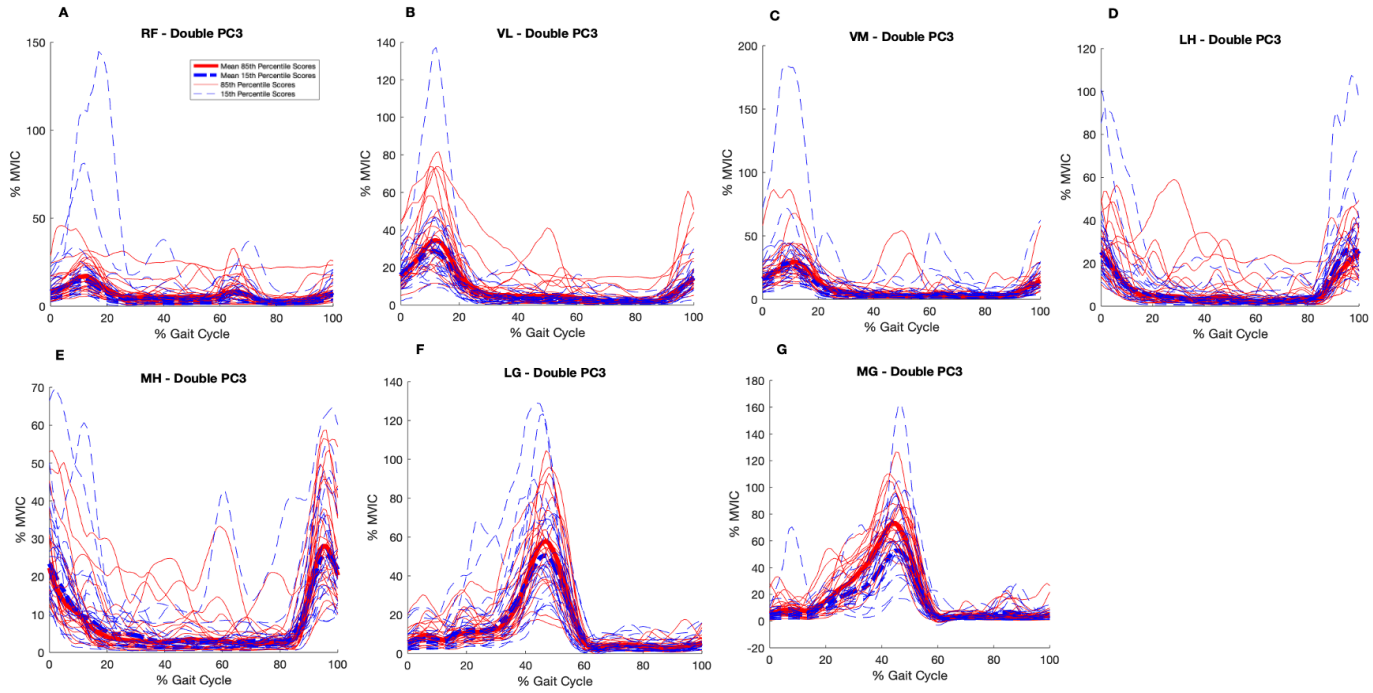

Figure 5.8: EMG waveforms of the participants with high (85th percentile, Red) and low (15th percentile, Blue) DPC3 scores. Thin lines represent individual participants and thick lines represent the high and low group average.

5.3.3.4 DPC4 Neuromuscular Strategy: Hip and Associated Frontal Plane Strategy

There were no statistically significant differences between the EMG waveforms of the high and low DPC4 scoring participants. Additionally, there were no trends towards differences among the EMG, visually (Figure 5.9) or statistically.

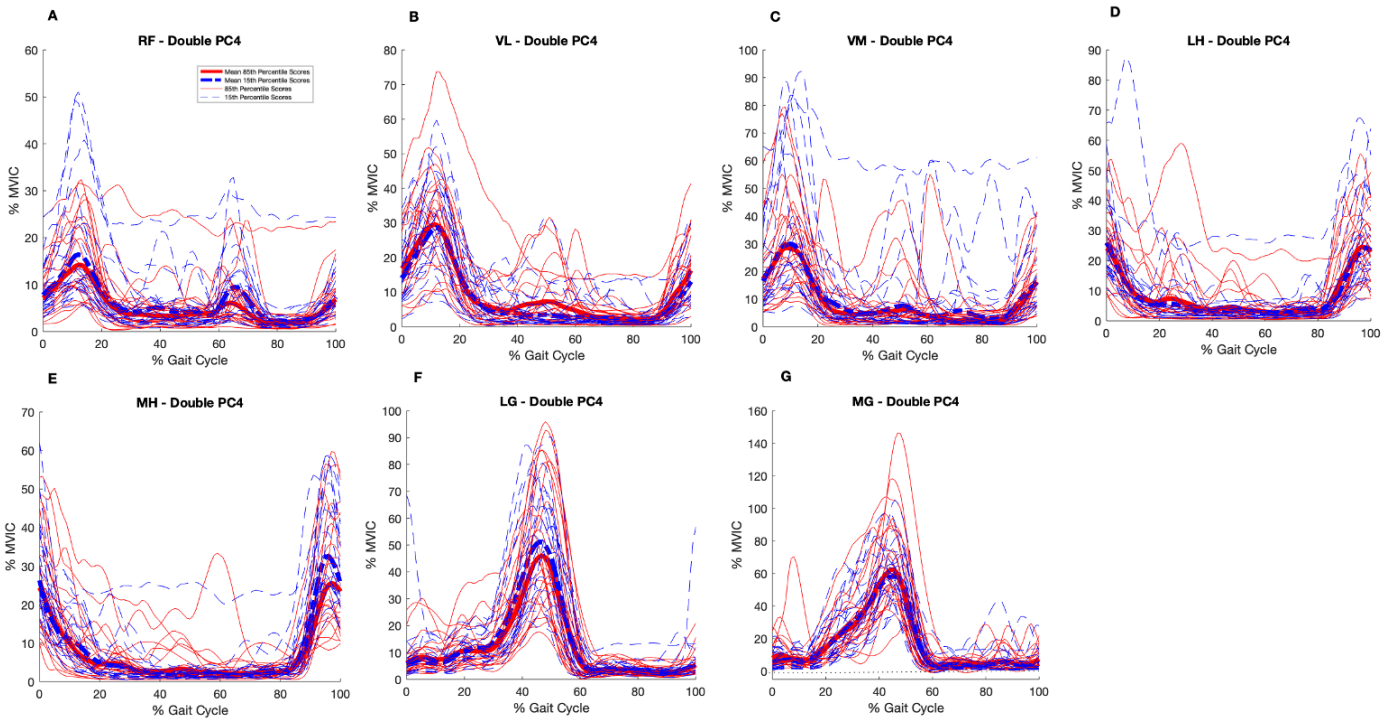

Figure 5.9: EMG waveforms of the participants with high (85th percentile, Red) and low (15th percentile, Blue) DPC4 scores. Thin lines represent individual participants and thick lines represent the high and low group average.

5.4 Discussion:

We used a multivariate analysis to identify inter-joint kinematic coordination strategies in asymptomatic adults of varying ages, highlighting the dimensionality of the kinematic relationships among the lower extremity joints in healthy adult gait. Examination of the DPC co-efficients, as well as the individual gait waveforms that corresponded to high (85th percentile, n=23) and low (15th percentile, n=23) scoring participants, for each potential strategy revealed that DPC1 captured a "speed-related strategy", DPC2 captured a "speed-independent ROM strategy" with a significant sex-effect, DPC3 captured a "lower leg strategy" (emphasis on knee and ankle kinematics) and DPC4 complementarily captured a "hip and frontal plane strategy". Interestingly, the first two DPCs capture correlated pattern features from the original data, while DPC3 and DPC4 capture only magnitude features. This suggests that in terms of kinematic coordination in an asymptomatic adult population, it is the biomechanical gait patterns that are

most variable. Although these strategies are subjectively labelled, the labels help to synthesize the meaning behind each strategy and improve the current understanding of kinematic coordination in healthy adults throughout the lifespan.

This study investigated the variability in the interactions among the lower extremity joints during walking gait in a normative population and is a logical multivariate extension of our previous work that presented a comprehensive summary of salient variability in joint angle and mechanical loading patterns based on age and sex [21]. Walking speed is known to affect gait parameters and was not controlled for in this study. As such, walking speed varied among the participants, from 0.94-1.90m/s. Therefore, it is not particularly surprising that DPC1, which explains the highest amount of underlying variability in the data, captures the correlation between variable speed and lower extremity kinematic gait features. Participants who walked faster also walked with larger stride lengths, larger knee abduction angles, a larger internal rotation ROM at both the knee and the hip, as well as earlier pre-swing knee flexion and ankle plantarflexion compared to those with low DPC1 scores (Figure 3). These high DPC1 scoring participants spent significantly less time in stance ($p=<0.0001$) than the low scoring group which likely explains the earlier onset of knee flexion and ankle plantarflexion pre-swing. Previous studies have demonstrated that sagittal plane knee and ankle motion are the primary drivers of limb clearance during walking [86,87] and thus it is not surprising that the timing of this sagittal plane propulsive motion is affected by faster gait speed when preparing for toe-off and swing phase. Interestingly, DPC1 does not capture any magnitude features in the sagittal plane motion of the knee flexion angle, something that has been previously suggested to be correlated with gait speed [88,89]. Instead, we report increased frontal plane angles at the knee joint as well as

increased internal rotation ROM at both the knee and hip joints suggesting less stiffness (in a clinical sense) in the transverse plane mechanics of those walking at a faster speed. Due to the nature of our asymptomatic adult population, the average walking speed for the low scoring (slower) DPC1 group (1.17m/s) was relatively normal in terms of average walking speed for healthy adults which may explain this discrepancy. Additionally, despite reports that healthy older adults walk at slower speeds [34,35,90] and with shorter step lengths [61,91,92] than younger adults, we report no age-effects within the high and low DPC1 groups. This again may be explained by the fact that the walking speed of the slower group was still a very normal healthy gait speed (1.17m/s) as well as the fact that there were no underlying significant differences in walking speed with age in our previous analysis ($p=0.14$) [21].

DPC2 was independent of speed and captured several correlated pattern-features among angles of all three lower limb joints. Thus, DPC2 represented a salient, underlying kinematic coordination strategy that persists despite gait speed in healthy adult walking. Pattern differences describe the waveform shape and refers to time-dependent features such as ROM differences and the relative magnitude of features at different temporal points of the gait cycle. Interestingly, female participants had statistically significantly lower DPC2 scores than males, supporting the influence of sex on kinematic gait mechanics. This aligns with our previous work that reported several individual kinematic and kinetic differences between asymptomatic female and male adults [21]. Participants with low DPC2 scores (i.e., female direction) walked with smaller knee ROM in the sagittal and transverse planes, smaller hip ROM in the frontal and sagittal planes, and larger hip ROM in the transverse plane, as well as smaller ankle ROM in the frontal plane, greater ankle adduction at foot contact and smaller ankle internal rotation in single leg stance

compared to larger ankle internal rotation in swing. Interestingly, many of the individual sex-related feature differences we previously reported [21] were correlated and captured by DPC2 further highlighting the importance of using sex-specific normative data in clinical gait studies and further supporting the value of using a multivariate analysis to synthesize multiple, correlated univariate analyses. DPC2 was also consistent with previous studies on the influence of sex on walking gait, including the finding that females walk with a smaller knee flexion and rotation ROM in stance [21], a smaller hip ROM in the sagittal plane [14] and a larger hip internal ROM from foot contact to loading [21,75] as well as a smaller ankle ROM in the frontal plane and less internal rotation at the ankle going into single leg stance followed by less ankle external rotation in swing phase [21]. On the other hand, while previous literature has supported that females walk with greater sagittal plane ankle ROM [14], DPC2 did not capture any differences in sagittal plane ankle kinematics. This may be due to the fact that while females were significantly more likely to have low DPC2 scores, low DPC2 scorers were not explicitly female and thus comparing the kinematic coordination differences between high and low scoring groups is not equivalent to a direct comparison between sexes. DPC2 also captured a stride length difference, with low DPC2 scores exhibiting significantly smaller stride lengths than high DPC2 scores. This is not particularly surprising considering that participants with low DPC2 scores were also significantly shorter than participants with high DPC2 scores. Since DPC2 was independent of gait speed, these results suggest that participants in the low DPC2 group may walk with higher stride frequencies to maintain similar gait speeds as the high DPC2 group, an adjustment that could affect the mechanics at the lower extremity joints and potentially explain the reported differences in sagittal plane mechanics. Additionally, participants with low DPC2 scores also had significantly smaller body mass index (BMI) than those with high DPC2 scores.

BMI has previously been linked to altered gait biomechanics, particularly altered knee joint loading, in both asymptomatic adults and those diagnosed with knee osteoarthritis [93]. While some studies have shown that obese individuals walk with reduced magnitudes of sagittal plane motion of the knee joint [94] and less knee flexion excursion [95] during gait, we contradictorily report that high DPC2 scoring individuals (higher BMI) exhibit larger knee flexion ROM in stance compared to low DPC2 scoring individuals (lower BMI). However, there are limitations to using BMI as a measure of "obesity", something particularly important to consider in this study due to the fact that there was also a significant sex-effect for DPC2. Some men may have higher muscle mass which could contribute to a higher BMI, particularly in an asymptomatic cohort. Additionally, this BMI discrepancy may be explained by the fact that these previous studies investigated obese populations, whereas the average BMI for the high DPC2 group was only 28.9 which is classified as "overweight" (>25) and not "obese" (>30), according to the World Health Organization (WHO).

The DPCs describe the underlying variability in the original kinematic PC features in a decreasing order (from highest contribution to lowest). DPC1 explains the highest amount of variability in the kinematic coordination and is speed dependent, which is unsurprising considering the evidence that speed influences gait kinematics and was not controlled for in this study. The next highest, DCP2, captures underlying mechanistic pattern differences that are independent of gait speed suggesting that without the variability attributed to speed differences, there are still underlying mechanistic differences within asymptomatic adults that are concentrated in the patterns of their gait mechanics. Following this, DPC3 and DPC4 both capture what appear to be complementary magnitude differences in the original kinematic PC

features. This is interesting as it suggests that within the asymptomatic population, it is the patterns of their gait mechanics that are most variable. DPC3 exclusively captures sagittal and transverse plane knee and ankle kinematics, whereas DPC4 indicates an emphasis on the hip in the same planes. High DPC3 scoring participants walk with more knee flexion and internal rotation, as well as more ankle flexion and less ankle internal rotation compared to those with low DPC3 scores. On the other hand, high DPC4 scoring participants walk with more hip flexion and internal rotation throughout the gait cycle, as well as smaller magnitudes of adduction angles at all three joints. These results are quite noteworthy as they appear to indicate two different but complementary strategies, lower leg walkers (DPC3) and hip walkers (DPC4), and suggest that healthy adults may favour one type over the other while walking at self-selected speeds. This is a critical outcome of our work, and one that has considerable potential for impact, as it suggests that adults who utilize one strategy over the other may potentially differ in pathology onset and presentation. Future investigations in pathology and aging should therefore investigate if and how these different kinematic strategies affect musculoskeletal injury and disease across the lifespan, as well as the mutual exclusivity among these different strategies.

Evidence of differences in neuromuscular activation patterns with sex [55–57] and age [35,51] motivated our inclusion of a secondary interpretation of the inter-joint kinematic coordination models using synchronous EMG data. Interestingly, we did not find any statistically significant EMG differences for DPC1, DPC2 or DPC4 and only one statistically significant difference in the EMG waveforms of the high and low scoring DPC3 participants. Specifically, participants with high DPC3 scores walked with larger midstance MG magnitudes compared to the low DPC3 scoring participants. Considering that the gastrocnemius muscles are responsible for knee

and ankle flexion it was expected that high DPC3 scoring participants who walk with more knee and ankle flexion, would have higher gastrocnemius activation than low DPC3 scoring participants. This EMG difference between the high and low DPC3 groups further supports the proposed "lower leg" strategy and the resulting kinematic coordination differences in the knee and ankle transverse and sagittal plane mechanics captured by this DPC. Conversely, we report no statistically significant EMG differences between the high and low DPC4 scoring groups. Considering that most of the muscles included in the EMG analysis were periarticular knee muscles, it is not particularly surprising that there are no differences between the high and low "hip strategy" (DPC4) groups. Anatomically the RF spans both the hip and knee and thus it could have been expected that participants with high DPC4 scores, who walk with more hip flexion and internal rotation, would exhibit more rectus femoris muscle activity than participants with low DPC4 scores; however, we do not report any significant RF activity differences between these groups, suggesting that these differences may be attributed to different hip muscles that were not included in the present study. This is something that should be considered in future work to better understand this hip strategy. It should also be noted that, although they did not reach statistical significance, there were some trends towards neuromuscular strategy differences in both DPC1 and DPC2. Participants with high DPC1 scores trended towards significantly higher % MVIC in the LG ($p=0.02$), particularly pre-swing, compared to the participants in the low DPC1 group. This dominant pre-swing peak (occurring around 40-45% into the gait cycle) has been reported to increase in magnitude as walking speed increases [96] supporting our reported EMG trend for participants in the high DPC1 (faster) group. The gastrocnemius accounts for most of the force generated during ankle plantarflexion (extension) at toe off [97] and thus this earlier and more increased pre-swing LG amplitude may also contribute

to the earlier ankle extension captured by the speed-related DPC1 model. On the other hand, participants with high DPC2 scores trended towards higher % MVIC in both the VL ($p=0.04$) and MH ($p=0.02$), during early stance and loading. Interestingly, VL recruitment prior to and during, the loading phase has previously been reported to be higher in a moderate OA population compared to asymptomatic controls [29]. This, combined with the fact that the high DPC2 group exhibited trends towards increased hamstring activity at foot contact to prepare for loading, supports a typical response that may serve to decrease medial joint loading [29]. The fact that a subset of this asymptomatic cohort is demonstrating neuromuscular trends typically observed in pathological populations is quite interesting and should be investigated further.

As always, there are some limitations to be considered with regards to this study. First, while the asymptomatic dataset used to create the double PCA models was robust ($n=154$) the distribution of adult ages represented was not particularly balanced. Most participants fell within 40-59 years of age as it was challenging to recruit participants older than 65 who fit the inclusion criteria of no diagnosed musculoskeletal disease, injury or comorbidities. With a mean age of only 49 years, further study should consider both an older and younger cohort of participants to further understand healthy biomechanical coordination strategies beyond the ages considered in this study. Additionally, this study only presented a kinematic-specific model of inter-joint coordination. While there is clinical value in this kinematic-focused model, developing joint-specific and kinetic-specific models, to represent the correlation among the joint-level features of the original variables and the inter-joint force propagation respectively, has additional value and should be explored in future work. Additionally, the EMG data included in this study primarily focused on knee muscle data, limiting our ability to fully investigate hip and ankle

neuromuscular activity. As such, it would be valuable to include hip and ankle specific muscular patterns in future work to understand the underlying neuromuscular activity more comprehensively. Finally, the fact that the first few salient features did not represent a profound amount of the variability in the original data (only 40%) suggests that while there is an underlying correlation structure to this data, there are more than 4 strategies adopted by healthy adults and we cannot assume that the strategies reported are the only ones utilized by asymptomatic adults. To this point, we did not examine the exclusivity of each strategy and thus, cannot conclude on whether the reported strategies are mutually exclusive (i.e., a person who scores high on DPC3 for instance, scores low on DPC4). Teasing out the relationship among these strategies and linking them to future development or susceptibility of injury and disease, has important implications and should most definitely be explored in future work.

In conclusion, this study provided a comprehensive model of healthy gait kinematic coordination in an asymptomatic adult population with age. Since it is challenging to simultaneously interpret multiple biomechanics differences, we utilized a double-PCA approach to capture the correlation among previously reported kinematic features and investigate the dimensionality of kinematic inter-joint coordination during healthy adult gait. This was a logical extension of our previous work that provides important insight to further understand deviations in gait kinematics in healthy adult aging, dependent on sex. Spatiotemporal metrics had significant influence on the kinematic coordination mechanics in this population, which is unsurprising considering we did not control for gait speed. There was also evidence of sex-related inter-joint kinematic coordination in this asymptomatic population, which provides further support for our previous conclusion [21] and the importance of considering sex-specific normative data in future research

and clinical applications. Additionally, DPC3 and DPC4 captured complementary magnitude-specific gait strategies, highlighting both a lower leg strategy (DPC3) and a hip strategy (DPC4). Different joint emphasis during walking could have downstream effects on joint health and mobility and as such, there is a lot of value in comprehensively understanding these different strategies to better understand pathology initiation and progression. With this in mind, our double PCA model has considerable potential for impact given the importance of mobility to overall health and the rapid aging population in Canada. There is a myriad of potential future applications, including use in research to better understand patient-specific kinematic changes over time and informing the development and validation of innovative treatment interventions to preserve mobility longevity in the aging population. Going forward, future work could expand this normative kinematic-specific model to a pathological population to investigate different strategies, opening the door to an improved understanding of age-related pathology and disease as well as better insight into early signs of orthopedic disease and mobility decline.

CHAPTER 6 GENERAL CONCLUSIONS & FUTURE DIRECTIONS

6.1 Thesis Overview

Since mobility limitations are associated with many age-related pathologies and disorders [4,5], and as we age the likelihood of experiencing walking limitations increases [1], there is significant interest in improving mobility longevity in the aging population. While both age and sex have previously been linked to kinematic and kinetic gait differences [9,12–14,61,72,74,91,92,98], it remains unclear how age and sex interact to contribute to gait performance in asymptomatic adults. The work presented in this thesis aimed to improve the mechanistic understanding of healthy male and female gait coordination strategies throughout the aging process and the output of this research is an improved understanding of the inter-relationships in normative joint-level biomechanics and neuromuscular control during walking gait with age.

The first objective of this thesis aimed to comprehensively define the salient temporal kinematic and kinetic gait features of healthy adult gait and compare them between older and younger males and females. This included investigations into how age category and sex individually influence joint-level mechanics, as well as examining how these demographic features interact to contribute to gait performance throughout the lifespan. The hypotheses for Objective 1 were partially supported by the results as significant sex-differences at the lower extremity joints during gait were reported but no significant age-specific differences at either the hip or the ankle joints were found. Most of the major sex-specific differences represented *pattern* differences, or features that describe the waveform shape (ROM, relative magnitude of angles/moments at

different temporal points of the gait cycle), indicating that gait differences between asymptomatic females and males are significantly concentrated in the patterns of their gait mechanics as opposed to purely magnitude differences. Additionally, all the sex-specific differences were independent of age, suggesting that these differences are relatively consistent in adult aging until approximately age 65. Interestingly, there were no statistically significant age or age-by-sex interactions which further suggests that consideration of strict age-matching for gait analysis studies using adult controls is not as critical as sex considerations.

While this thesis is not the first to investigate asymptomatic adult gait, or the influence of sex and age [98], it is distinct from previous efforts in that it comprehensively presents temporal kinematic and kinetic waveform features. This is a logical extension of previous work that provides important normative information for both joint angles and mechanical loading. Because it is difficult to simultaneously interpret multiple biomechanics differences, there is a lot of value in interrogating the correlation structure among individual kinematic and kinetic variables to better understand lower extremity kinematic coordination strategies in healthy adults. This thesis comprehensively quantified the interaction between sex and age as summarized by key joint-level mechanistic differences and salient kinematic coordination strategies, providing a baseline to understand demographic-specific mechanistic differences and person-to-person variability in an asymptomatic population.

The second objective of this thesis aimed to investigate the correlation structure among the salient kinematic variables from *Objective 1* to define prominent inter-joint kinematic coordination strategies in healthy adult gait. This included a Double PCA (DPCA) analysis using

the PC scores of the retained features from the first PCA to determine the dimensionality of the inter-joint kinematic coordination in the original waveforms. This was a logical extension of our previous work and one that provides important insight to further understand deviations in gait kinematics in healthy adult aging, dependent on sex. A sub-objective was to interpret salient coordination strategies by understanding demographic and muscle activity differences between those who score high and low on each strategy, to better understand the dimensionality of person-to-person variability in gait coordination strategies. Spatiotemporal metrics had significant influence on the kinematic coordination mechanics in this population (DPC1), which is unsurprising considering we did not control for gait speed. There was also evidence of speed-independent, sex-related inter-joint kinematic coordination (DPC2), further supporting the importance of considering sex-specific normative data in future research and clinical applications. Additionally, complementary magnitude-specific gait strategies revealed both a lower leg dominated strategy (DPC3) and a hip dominated strategy (DPC4), highlighting the variability and dimensionality of the kinematic relationships among the lower extremity joints in healthy adult gait. Thus, the hypothesis that inter-joint lower extremity kinematic features could be defined and interpreted, and that there would be a significant sex-effect on these features during gait, was accepted based on the results of the Objective 2 investigation.

6.2 Implications of Thesis Results

Previous research investigating healthy gait strategies may have presented salient gait features [9,10,12,13,51,98], but this was the first research to comprehensively present both normative kinematic and kinetic temporal gait patterns in an adult population across a wide age spectrum. This study is distinct from previous efforts in that it comprehensively investigates the interaction

between sex and age in lower extremity joint kinematics and kinetics and simultaneously defines the inter-joint kinematic relationships in healthy adult gait. Considering the role of mechanical loading in osteoarthritis [6], this is a logical extension of previous work that provides important normative information for both joint angles and mechanical loading as well as the correlation structure among these variables. We were motivated in *Objective* 1 by the lack of comprehensive normative data on healthy adult gait patterns in the literature and therefore first focused on a univariate approach that recognized temporal gait patterns, and the thorough presentation and representation of this data based on age and sex. Some of the key results from *Objective 1* showed that the combination of kinematic and kinetic differences identified between healthy adult male and female participants were not isolated to a single plane of motion, or to a single joint. When considering all sex differences together, an overall difference in walking strategy between healthy male and female adults is evident. Additionally, it was suggested that consideration of strict age-matching for gait analysis studies using adult controls is not as critical as sex considerations. Together, this information highlights the importance of considering sex-specific analyses in gait study design, and the use of sex-specific normative data in clinical gait studies and can have implications for the matching of control participants in adult clinical gait investigations that explore kinematic and kinetic outcomes.

Building off the results from *Objective 1*, that indicated an overall difference in walking strategy between healthy male and female adults, *Objective 2* aimed to investigate the correlation structure among the salient kinematic gait features to better understand lower extremity kinematic inter-joint coordination strategies in healthy adults and examine whether normative walking patterns can be classified into sub-groups, based on demographic and anthropometric

characteristics. Because it is difficult to simultaneously interpret multiple biomechanical differences, a multivariate double PCA approach was used to capture the correlation among previously reported kinematic features and investigate the dimensionality of kinematic inter-joint coordination during healthy adult gait. One of the main findings suggested that inter-joint pattern differences account for the most variability in the kinematic coordination utilized by this healthy adult population. The highest amount of variability in the kinematic coordination was speed dependent, and the next highest was independent of gait speed suggesting that without the variability attributed to speed differences, there are still underlying mechanistic differences within asymptomatic adults that are concentrated in the patterns of their gait mechanics. This may be intuitive, considering the evidence of individualized gait mechanics; however, this finding has broader implications for use in research to better understand patient-specific kinematic changes over time as well as to inform the development and validation of innovative treatment interventions to preserve mobility longevity in the aging population. These current findings of different inter-joint kinematic coordination strategies in an asymptomatic adult population, drives the need to further understand how different joint emphasis during walking may have downstream effects on joint health and mobility and if this is something that can be targeted by patient-specific interventions. It also promotes the idea that future work should aim to expand this normative kinematic-specific model to a pathological population, opening the door to an improved understanding of age-related pathology and disease as well as better insight into early signs of musculoskeletal or neurological disease and mobility decline.

6.3 Limitations and Considerations

There are certain limitations that should be considered in interpreting this research. First, while the asymptomatic dataset used to create the PCA models was robust (n=154), it was difficult to recruit participants older than 65 who fit the inclusion criteria of no co-morbidities and as such, the mean age of the participant cohort was only 49 years. Additionally, *Objective 1* was limited to four discrete age groups making it difficult to draw conclusions about mechanisms and gait changes within the groups. Age groups were initially defined based on decades; however, due to low numbers in some age categories, and an inability to collect additional data due to the COVID-19 pandemic, the older decades were merged to create the 60+ age group. Similarly, the youngest decades were also merged to form the 20-40 year group, as we did not anticipate significant age-related changes prior to this age. Further, the 60+ year group was the smallest group and had a mean age of only 64 years, which is young in terms of expected mobility decline [99,100]. To examine if our categorization was limiting our ability to detect potential age effects, we additionally performed some supplementary analyses using age as a continuous variable but no significant correlations between age on a continuum and gait outcomes were identified (Appendix A.5).

Objective 2 focused on a kinematic-specific model of inter-joint coordination. While there is clinical value in this kinematic-focused model, developing joint-specific and kinetic-specific models, to represent the correlation among the joint-level features of the original variables and the inter-joint force propagation respectively, has additional value and should be explored in future work. Additionally, as this thesis consisted of secondary interpretations of previously collected gait data, the EMG data included in this study primarily focused on periarticular knee muscles, which may have limited our ability to fully investigate hip and ankle neuromuscular

activity. Furthermore, the exclusivity of each kinematic coordination strategy in *Objective* 2 was not examined and therefore conclusions regarding the mutual exclusivity of the reported kinematic coordination strategies (i.e., a person who scores high on DPC3 also scores low on DPC4) was not made in the current thesis. Teasing out the relationship among these strategies has a lot of value and may be used to better understand patient-specific strategies and potential links to future development or susceptibility of injury and disease.

Lastly, I acknowledge the inherent errors associated with 3D gait analysis. Variability in anatomical landmark identification can lead to malalignment of coordinate system axes resulting in kinematic crosstalk, an error that results in the bleeding over of rotation from one plane to another [101]. This error is most prevalent at the knee joint, as the knee moves through a large ROM during walking gait. Therefore, in this thesis, the transverse and frontal plane knee angles were captured during stance phase only as they are less prone to kinematic crosstalk error. Skin motion artefact can also introduce errors during 3D gait analysis and is often increased in individuals with high adiposity [102]. To address errors resulting from marker placement, a standardized protocol was used for data collection that follows the suggested standard for expression of lower-limb joint kinematics and kinetics known as the joint coordinate system [69], and has shown good to very good reliability for the variables of interest in this study for asymptomatic participants [32]. Furthermore, the goal of this study was to present normative data and differences and to provide evidence of different gait strategies, and as such we did not put significant emphasis on or over-interpret the magnitudes of the reported differences. We chose instead to interpret them collectively as a group and look more at strategy differences between groups instead of focusing too much on each individual feature difference.

6.4 Future Work

Expanding upon the framework presented in this thesis for the development of models in pathological populations would lend itself to an improved understanding of age-related pathology and disease, as well as better insight into early signs of musculoskeletal and neurological disease and mobility decline. Considering that the first few salient features in *Objective 2* did not represent a profound amount of the variability in the original data (only 40%) suggests that while there is an underlying correlation structure to this data, there are more than 4 strategies adopted by healthy adults and we cannot assume that the strategies reported are the only ones utilized by healthy adults. Teasing out the relationship between these strategies and linking them to future development or susceptibility of injury and disease, has important implications for patient-centered care and should most definitely be explored in future work. This normative kinematic model could also be further utilized in future research investigations to better understand person-specific kinematic changes with age as well as to inform the development and validation of innovative treatment interventions to preserve mobility longevity in the aging population. In order to address the limitations of this work, future investigations should also consider both an older and younger cohort of participants to further understand healthy biomechanical coordination strategies beyond the ages considered in this study.

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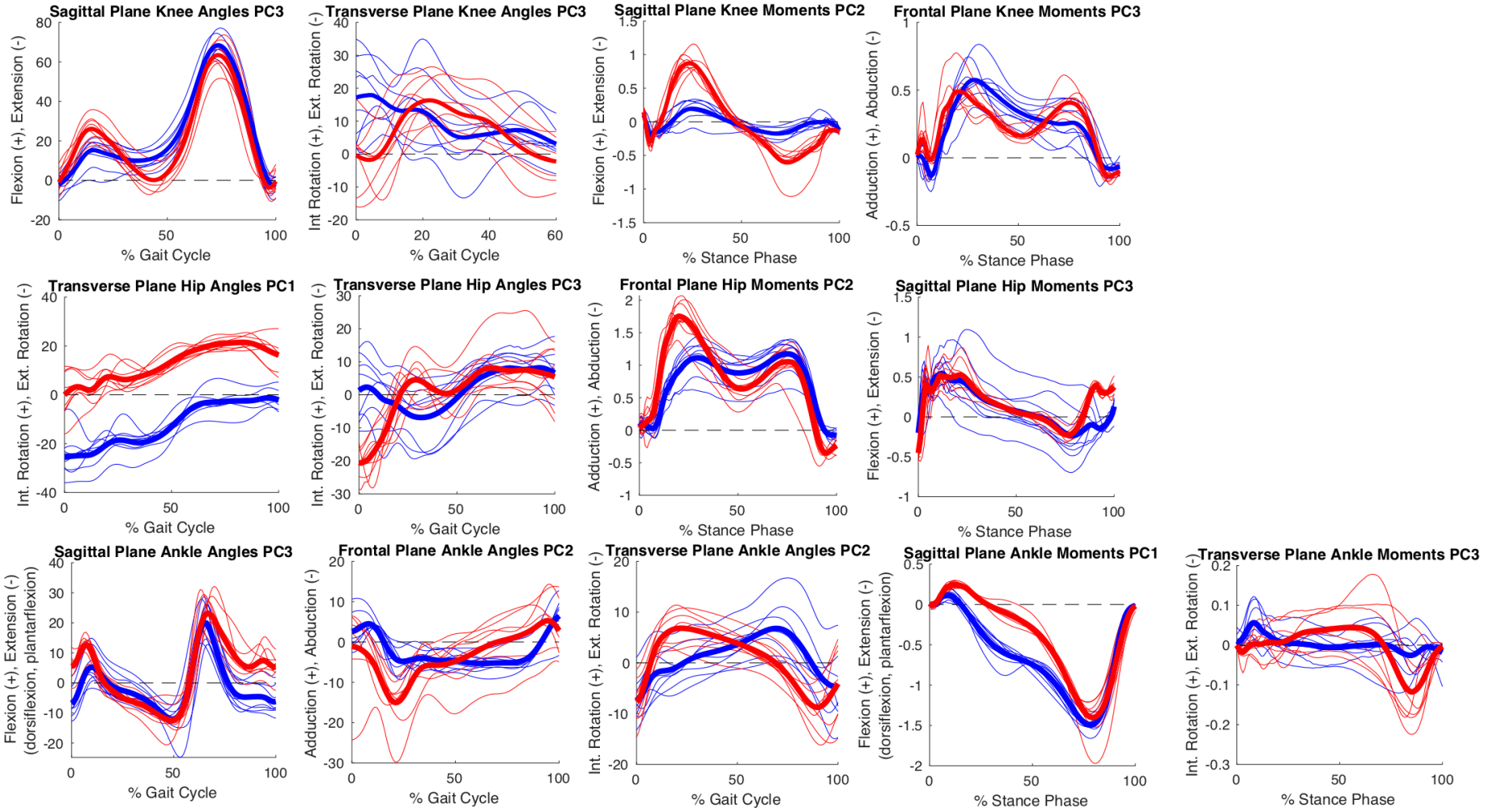
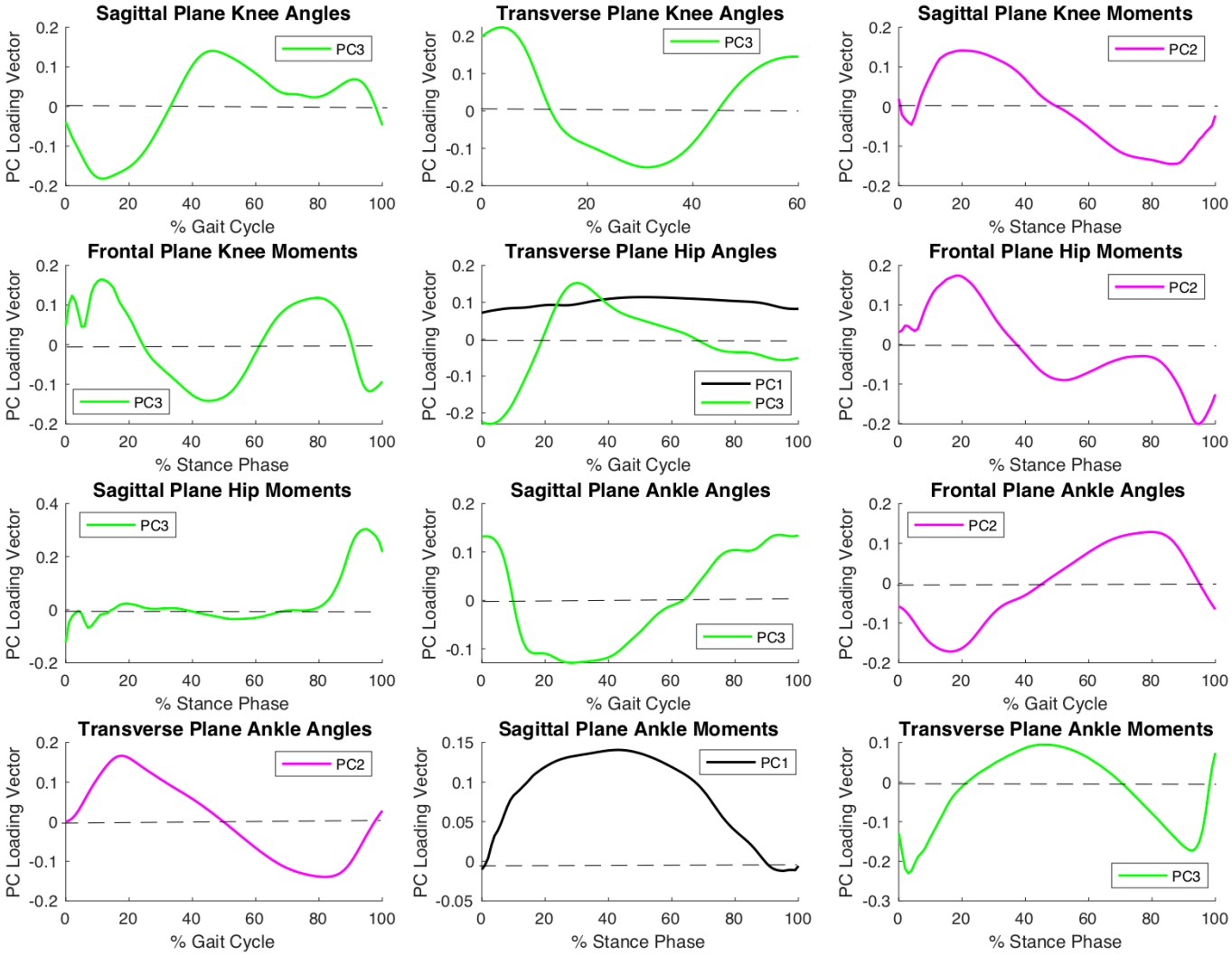
Appendix A Chapter 4 Supplementary Material

Appendix A.1 Gait waveforms associated with the high (95th percentile, Red) and low (5th percentile, Blue) PC score plots. Thin lines represent the data waveforms for the participants in the 95th and 5th percentiles of PC scores. Thich lines represent the average waveforms associated with these scores.



Appendix A.2 Loading vectors for the statistically significant PCs. Black = PC1, Pink = PC2, Green = PC3.



Appendix A.3 Mean kinematic ROM and peak values for age and sex.

	Peak Values (deg.)					ROM (deg.)				
	20-40 years	41-50 years	51-59 years	60+ years	*p value*	20-40 years	41-50 years	51-59 years	60+ years	*p value*
Sagittal Knee Angles	65.40	64.52	65.27	63.93	0.71	69.04	69.10	69.35	69.27	0.95
Frontal Knee Angles	7.00	6.72	6.58	5.37	0.45	9.85	9.86	9.04	7.93	0.32
Transverse Knee Angles	15.85	15.51	15.11	16.07	0.92	21.20	20.91	18.78	20.00	0.53
Sagittal Hip Angles	28.00	28.28	30.87	30.57	0.02	39.77	39.53	40.57	41.88	0.43
Frontal Hip Angles	8.44	8.35	7.95	9.74	0.30	11.43	10.91	9.94	11.22	0.03
Transverse Hip Angles	8.00	9.00	8.73	9.34	0.81	22.46	23.17	20.96	21.48	0.73
Sagittal Ankle Angles	21.30	18.93	18.54	20.91	0.09	33.53	30.73	31.66	33.93	0.05
Frontal Ankle Angles	6.11	5.17	5.01	6.66	0.27	15.07	14.31	13.80	14.72	0.54
Transverse Ankle Angles	5.13	5.55	5.65	6.86	0.31	12.57	13.77	13.70	15.44	0.04

	Peak Values (deg.)			ROM (deg.)		
	Males	Females	*p value*	Males	Females	*p value*
Sagittal Knee Angles	64.94	64.83	0.77	70.59	68.34	0.003
Frontal Knee Angles	6.31	6.91	0.27	9.25	9.45	0.55
Transverse Knee Angles	15.92	15.02	0.40	20.32	20.04	0.86
Sagittal Hip Angles	29.42	29.32	0.68	39.80	41.08	0.23
Frontal Hip Angles	8.57	8.31	0.45	10.38	11.53	0.006
Transverse Hip Angles	11.88	6.71	<0.0001*	23.03	21.31	0.22
Sagittal Ankle Angles	20.13	19.03	0.18	32.24	32.15	0.65
Frontal Ankle Angles	4.80	6.12	0.04	14.58	14.19	0.48
Transverse Ankle Angles	5.67	5.69	0.74	13.72	14.25	0.81

The p-value corresponds to a two-factor ANOVA analysis comparing the ROM and peak kinematic values between the four age groups as well as between male and female participants.
* Significant difference (p <= 0.001)

Appendix A.4 Mean kinetic range of moment and peak values for age and sex

	Max Values (Nm/kg)					Range (Nm/kg)				
	20-40 years	41-50 years	51-59 years	60+ years	*p-value*	20-40 years	41-50 years	51-59 years	60+ years	*p-value*
Sagittal Knee Moments	0.52	0.53	0.46	0.57	0.31	0.97	0.96	0.88	1.03	0.28
Frontal Knee Moments	0.49	0.48	0.51	0.52	0.49	0.62	0.59	0.62	0.65	0.58
Transverse Knee Moments	0.19	0.19	0.19	0.19	0.93	0.25	0.25	0.24	0.27	0.73
Sagittal Hip Moments	0.75	0.66	0.64	0.79	0.06	1.08	0.95	0.92	1.07	0.02
Frontal Hip Moments	1.31	1.38	1.37	1.34	0.70	1.50	1.57	1.57	1.60	0.73
Transverse Hip Moments	0.15	0.15	0.15	0.15	0.97	0.47	0.43	0.45	0.44	0.61
Sagittal Ankle Moments	0.16	0.16	0.15	0.16	0.65	1.57	1.57	1.51	1.54	0.22
Frontal Ankle Moments	0.27	0.25	0.24	0.29	0.59	0.31	0.30	0.28	0.34	0.44
Transverse Ankle Moments	0.06	0.06	0.04	0.05	0.30	0.14	0.14	0.12	0.13	0.63

	Max Values (Nm/kg)			Range (Nm/kg)		
	Males	Females	*p-value*	Males	Females	*p-value*
Sagittal Knee Moments	0.56	0.49	0.07	1.03	0.90	0.009
Frontal Knee Moments	0.50	0.49	0.74	0.64	0.60	0.20
Transverse Knee Moments	0.21	0.18	0.01	0.28	0.24	0.02
Sagittal Hip Moments	0.76	0.66	0.02	1.17	1.03	0.16
Frontal Hip Moments	1.35	1.36	0.92	1.60	1.53	0.26
Transverse Hip Moments	0.15	0.15	0.74	0.46	0.44	0.41
Sagittal Ankle Moments	0.16	0.16	0.61	1.57	1.53	0.06
Frontal Ankle Moments	0.28	0.24	0.07	0.32	0.29	0.16
Transverse Ankle Moments	0.05	0.05	0.57	0.14	0.13	0.09

The p-value corresponds to a two-factor ANOVA analysis comparing the ROM and peak kinematic values between the four age groups as well as between male and female participants.
* Significant difference (p <= 0.001)

Appendix A.5 Summary of supplementary statistical analysis with age as a continuous variable

Knee				
Angles	*Age*		*Gender*	
	p-value	*correlation, r*	*p-value*	*correlation, r*
Frontal Plane PC1	0.05	0.01	0.09	0.02
Frontal Plane PC2	0.35	-0.08	0.54	0.06
Frontal Plane PC3	0.62	-0.03	0.2	-0.1
Sagittal Plane PC1	0.34	-0.08	0.96	0.01
Sagittal Plane PC2	0.86	-0.008	0.49	-0.05
Sagittal Plane PC3	0.88	0.02	**0.0002***	-0.30
Transverse Plane PC1	0.63	0.03	0.57	0.04
Transverse Plane PC2	0.52	-0.06	0.41	0.07
Transverse Plane PC3	0.47	0.1	**<0.0001***	-0.40
Moments				
Frontal Plane PC1	0.44	0.06	0.9	0.003
Frontal Plane PC2	0.65	0.05	0.08	-0.15
Frontal Plane PC3	0.56	0.002	**<0.0001***	-0.40
Sagittal Plane PC1	0.92	-0.0004	0.38	0.07
Sagittal Plane PC2	0.98	0.03	**0.0004***	-0.28
Sagittal Plane PC3	0.29	-0.11	0.02	0.2
Transverse Plane PC1	0.89	0.02	0.002	-0.25
Transverse Plane PC2	0.52	0.01	0.41	-0.07
Transverse Plane PC3	0.89	-0.04	0.007	0.22
Hip				
Angles	*Age*		*Gender*	
	p-value	*correlation, r*	*p-value*	*correlation, r*
Frontal Plane PC1	0.35	0.07	0.76	0.02
Frontal Plane PC2	0.35	-0.05	0.002	-0.24
Frontal Plane PC3	0.04	-0.15	0.13	-0.10
Sagittal Plane PC1	0.007	0.21	0.2	0.08
Sagittal Plane PC2	0.69	-0.01	0.03	-0.18
Sagittal Plane PC3	0.41	-0.05	0.25	-0.09
Transverse Plane PC1	0.52	0.09	**<0.0001***	-0.41
Transverse Plane PC2	0.32	-0.07	0.39	-0.06
Transverse Plane PC3	0.71	-0.008	**<0.0001***	0.32
Moments				
Frontal Plane PC1	0.8	0.008	0.17	0.11
Frontal Plane PC2	0.78	0.05	**0.0007***	-0.27
Frontal Plane PC3	0.57	-0.07	0.005	0.23
Sagittal Plane PC1	0.17	0.13	0.06	-0.16
Sagittal Plane PC2	0.46	-0.04	0.02	-0.18
Sagittal Plane PC3	0.21	0.14	**<0.0001***	-0.40
Transverse Plane PC1	0.89	0.02	0.48	-0.06
Transverse Plane PC2	0.62	0.04	0.8	0.02
Transverse Plane PC3	0.05	-0.13	0.01	-0.18
Ankle				
Angles	*Age*		*Gender*	
	p-value	*correlation, r*	*p-value*	*correlation, r*
Frontal Plane PC1	0.82	0.01	0.54	0.05
Frontal Plane PC2	0.58	-0.01	**0.0005***	-0.27
Frontal Plane PC3	0.26	-0.11	0.07	0.15
Sagittal Plane PC1	0.78	-0.03	0.52	0.05
Sagittal Plane PC2	0.44	0.07	0.53	-0.06
Sagittal Plane PC3	0.18	-0.07	**0.0005***	-0.27
Transverse Plane PC1	0.42	0.06	0.61	0.03
Transverse Plane PC2	0.71	0.01	**<0.0001***	-0.35
Transverse Plane PC3	0.63	0.04	0.8	0.02
Moments				

Frontal Plane PC1	0.99	0.03	0.002	-0.25
Frontal Plane PC2	0.5	-0.06	0.43	0.07
Frontal Plane PC3	0.89	0.01	0.65	-0.04
Sagittal Plane PC1	0.27	0.05	**<0.0001***	0.32
Sagittal Plane PC2	0.28	-0.07	0.13	-0.11
Sagittal Plane PC3	0.77	0.02	0.91	-0.01
Transverse Plane PC1	0.56	-0.05	0.85	0.02
Transverse Plane PC2	0.52	-0.04	0.21	-0.10
Transverse Plane PC3	0.89	0.04	**0.0006***	-0.28

The p-value corresponds to a two-factor ANOVA analysis comparing the PC scores between the four age groups as well as between male and female participants, with age as a continuous variable. The r-value corresponds to Pearson's Coefficient.
* Significant difference ($p <= 0.001$)

Appendix B Chapter 5 Supplementary Material

Appendix B.1 Summary of variance explained by the retained kinematic features from original PCA

Model		PC1		PC2		PC3	
	Total Variance Explained; 3 PCs (%)	Feature	Variance explained (%)	Feature	Variance explained (%)	Feature	Variance explained (%)
Knee Angles							
Flexion	**88.4**	Magnitude	66.0	Phase shift	14.0	Stance Difference	8.4
Adduction	**93.9**	Magnitude	68.7	Stance Difference	15.6	Phase Shift	9.6
Rotation	**93.6**	Magnitude	71.3	Stance Difference	15.4	Difference	6.8
Knee Moments							
Flexion	**80.7**	Magnitude	45.2	Difference	26.6	Difference	8.9
Adduction	**75.4**	Magnitude	49.9	Difference	15.4	Phase Shift	10.1
Rotation	**83.5**	Difference	42.4	Magnitude	34.9	Phase Shift	6.2
Hip Angles							
Flexion	**92.8**	Magnitude	70.7	Difference	15.1	Phase Shift	7.0
Adduction	**98.1**	Magnitude	84.6	Stance Difference	10.6	Stance Difference	3.0
Rotation	**94.4**	Magnitude	68.9	Stance Difference	20.6	Stance Difference	5.0
Hip Moments							
Flexion	**80.7**	Magnitude	45.2	Difference	26.6	Difference	8.9
Adduction	**83.5**	Magnitude	61.5	Difference	14.2	Difference	7.8
Rotation	**86.5**	Magnitude	65.3	Difference	14.6	Difference	6.6
Ankle Angles							
Flexion	**84.0**	Magnitude	58.7	Stance Difference	14.5	Difference	10.8
Adduction	**90.5**	Magnitude	71.5	Difference	12.4	Difference	6.6
Rotation	**94.6**	Magnitude	74.6	Difference	12.0	Difference	8.0
Ankle Moments							
Flexion	**79.1**	Magnitude	44.3	Difference	20.0	Phase Shift	14.8
Adduction	**89.5**	Magnitude	63.3	Difference	19.3	Foot Contact	6.9
Rotation	**87.7**	Magnitude	63.8	Difference	16.2	Difference	7.7