Physical activity and age-related mechanical risk factors for knee osteoarthritis

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PHYSICAL ACTIVITY AND AGE-RELATED MECHANICAL RISK FACTORS FOR KNEE OSTEOARTHRITIS

A Dissertation Presented

by

JOCELYN F. HAFER

Submitted to the Graduate School of the University of Massachusetts Amherst in partial fulfillment of the requirements for the degree of

DOCTOR OF PHILOSOPHY

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PHYSICAL ACTIVITY AND AGE-RELATED MECHANICAL RISK FACTORS FOR KNEE OSTEOARTHRITIS

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Knee osteoarthritis is an age-related disease which will affect nearly 50% of individuals in their lifetime. Because there are currently no treatments to substantially slow the progression of this disease, it is important to identify mechanisms to reduce the risk of osteoarthritis initiation. Osteoarthritis is a disease which is at least partially mediated by mechanical factors which may result from age-related changes in gait. The extent to which habitual physical activity can modify the impact of age on gait, knee mechanics, and thus cartilage loading is unknown. The aim of this dissertation was to examine the effects of age and habitual physical activity level on biomechanical risk factors for knee osteoarthritis including knee mechanics during gait, knee extensor muscle function, neuromuscular control, coordination, and the physiological and biomechanical response to a bout of exercise. Three groups of 20 healthy individuals each were recruited: young adults, highly active older adults, and less active older adults. Overground gait mechanics and knee extensor muscle torque and power were collected.
before and after a 30 minute treadmill walk designed to allow for observation of changes in gait and muscle function in response to muscle fatigue. At baseline, both older adult cohorts displayed decreased concentric knee extensor power compared to young adults. Older adults, especially in the less active group, had more femoral anterior translation relative to the tibia during the stance phase of gait, a measure that has previously been linked to osteoarthritis risk, incidence, and progression. Movement coordination was more affected by age than physical activity level as older adults from both physical activity cohorts displayed differences in coordination and its variability, particularly in movement coordination about the hip and ankle during periods of single-support. When comparing males and females across different age and physical activity cohorts, sex was identified as a determinant of hip and knee mechanics, and baseline knee extensor muscle function. The results of this dissertation provide evidence that, even in relatively young, high-functioning older adults, age and low physical activity levels are associated with a shift towards markers of increased knee osteoarthritis risk.
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CHAPTER I
INTRODUCTION

Knee osteoarthritis (OA) is a mobility-limiting disease that affects millions of older adults in the U.S.\textsuperscript{1,2} The world population is aging and older adults (age 65+ years) are projected to make up 19\% of the U.S. population by 2030.\textsuperscript{3} As age itself is a primary risk factor for the initiation of knee OA this aging of the population, along with an estimated lifetime risk of knee OA of 44\% in adults over age 45,\textsuperscript{4} could result in 36 million Americans with knee OA in the coming decades. The main symptoms of knee OA are pain and joint stiffness, and as a result there are decreases in mobility resulting in lower levels of physical activity,\textsuperscript{5} poorer cardiometabolic health, and large medical costs from a combination of OA symptoms and co-morbid conditions.\textsuperscript{6} As there are currently no treatments that substantially slow OA progression and the only way to “cure” this disease is a total joint replacement, identification of mediators of knee OA risk is critical to reduce the risks for OA initiation in the first place. OA is a disease mediated at least in part by mechanical factors which may result from changes in gait with age. Initiation of knee OA in the aged has been suggested to result from age related alterations in knee mechanics that shift the loading patterns on the cartilage.\textsuperscript{7} These changes in knee mechanics are likely a manifestation of systemic deterioration of the motor system, especially in aspects of muscle and neural function. If high levels of habitual physical activity mediate age-related deterioration of the musculoskeletal and neuromuscular systems, highly active older adults may display fewer biomechanical risk factors for knee OA initiation.
Knee OA is characterized by degradation of tibiofemoral cartilage, osteophyte formation, and joint inflammation. The morphology of healthy knee joint cartilage results from the loads applied to the knee during gait over the course of development. Changes in the magnitude, location, or frequency of this cartilage loading can result in detrimental changes in cartilage morphology. Studies of individuals after anterior cruciate ligament (ACL) rupture demonstrate that an acute change in knee mechanics alters the regions of cartilage that bear load during gait and that this shift in loading pattern corresponds to rapid regional cartilage degradation. If a similar mechanism causes idiopathic knee OA, cartilage degeneration could be initiated by changes in knee mechanics due to age-related phenomena such as muscle weakness, increased fatigability, and altered neuromuscular control.

Changes in gait mechanics, including knee mechanics, appear to be an inevitable consequence of aging. Gross changes in gait mechanics include decreased step length and increased walking cadence, increased double-support time, decreased sagittal ankle range of motion during gait, and a proximal shift in joint support moments. Specifically at the knee, older adults display altered (increased or decreased) average knee flexion during stance as well as changes in moments and powers at the knee when compared to young adults. When placed along a spectrum, knee mechanics appear to progress with age such that the knee mechanics of older adults appear to be shifting towards those seen with knee OA. With increasing age, adults also demonstrate reductions in neuromuscular control. Older adults display altered coordination patterns during complex tasks such as gait, performing movements in a manner that is less complex and potentially less flexible in response to perturbations. Neuromuscular
control of the timing of muscle activations may also deteriorate with age, with older adults displaying greater co-contraction between the knee extensors and flexors during gait compared with young adults.²⁶⁻²⁸

When combined with altered neuromuscular control, decreased knee extensor function could both contribute to and exacerbate age-related changes in knee mechanics and thus cartilage health.²⁹ Reduced function of the knee extensors could play a large role in the observed changes in knee mechanics with age. This reduction in muscle function begins during the 5ᵗʰ or 6ᵗʰ decade,³⁰, ³¹ coinciding with the onset of previously reported age-related changes in gait mechanics and the average age of knee OA diagnosis.⁴ Older adults demonstrate decreased knee extensor strength and power, especially during high-velocity contractions.³⁰⁻³⁵ Additionally, older adults are less resistant to muscle fatigue induced by submaximal dynamic contractions,³⁶⁻³⁹ such as those that occur during gait. While walking does not require the full capacity of the knee extensors,⁴⁰ a gradual reduction in available muscle power combined with reduced neuromuscular control could subtly alter loads at the knee, resulting in progressive deterioration of knee joint cartilage.

The confluence of changes in knee mechanics, knee extensor muscle function, and neuromuscular control with age likely combine to alter the mechanical loading environment of the knee. While their prevalence in the literature makes altered knee mechanics and neuromuscular function seem inevitable, these changes may at least partially be the result of age-related behavioral changes. Age and knee OA incidence and progression are both associated with decreased physical activity.⁴¹⁻⁴³ As physical activity plays a strong role in the function of myriad body systems, its influence likely remains important with age. Habitual physical activity is strongly associated with knee extensor
strength and overall physical function and thus may also be a predictor of gait mechanics. Older runners demonstrate maintenance of knee extensor power as compared to their sedentary counterparts.\textsuperscript{44, 45} Middle-aged and older walkers appear to display fewer age-related changes in gait mechanics when compared to less active peers.\textsuperscript{46} High levels of physical activity may also preserve neuromuscular control with age, as motor unit numbers appear to be preserved in the lower extremity muscles of older runners as compared to sedentary older adults.\textsuperscript{47}

While physical activity seems to be a likely mediator of the factors that contribute to knee joint health, the majority of older adults do not participate in an adequate amount of physical activity. Physical activity participation decreases across the lifespan, with older adults reporting a third less habitual physical activity compared to young adults.\textsuperscript{41, 43} The correspondence between changes that occur in the musculoskeletal system with the population-wide withdrawal from physical activity in older age present a potential explanation for at least a portion of the age-related deterioration of knee function and, ultimately, knee joint health. While there is a wealth of literature examining the impact of age on gait mechanics, muscle function, and neuromuscular control, there is a lack of data which can be used to examine the impact of physical activity on these factors.

While physical activity likely impacts age-related factors related to knee joint health, the impact of physical activity may not be equal between males and females. Males are at significantly lower risk of knee OA compared to females,\textsuperscript{48} suggesting that there may be critical differences in the age related changes in gait mechanics, neuromuscular control or muscle function for males and females. This differential knee OA risk by sex may be the result of differences in gait mechanics by sex in young\textsuperscript{49} and
older adults in combination with a tendency for females to experience a greater loss of knee extensor function with age as compared to males. Knee extensor strength is a predictor of knee OA progression in females only and differences in gait are apparent between males and females with knee OA. The higher incidence of knee OA in females may be due to larger age-related decrements in knee mechanics and knee extensor function in females than males.

The aim of this dissertation was to determine if habitual participation in vigorous physical activity decreases the age-related changes in knee mechanics, knee extensor function, and neuromuscular control that have been observed in studies of older adults. An investigation of the impact of habitual physical activity, independent of age, on factors that could affect knee joint loading is needed to advance our understanding of the role of physical activity in joint health. Additionally, this project examined the roles of habitual physical activity and age in mediating or amplifying the perturbing effect of a bout of activity. Previous studies of age-related changes in gait, muscle function, and neuromuscular control have not controlled for or adequately characterized the physical activity levels of their participants. This makes it difficult, if not impossible, to determine what reported decrements are a result of aging itself, as opposed to a casualty of the tendency to be less active in older age. Finally, this project explored the possibility that males and females do not receive the same protection from age-related changes in knee mechanics, knee extensor function, and neuromuscular control in response to regular moderate to vigorous habitual physical activity. The knowledge gained from this project may bolster the importance of maintenance of physical activity in older age and the potential for this maintenance to mediate mechanical risk factors for knee OA initiation.
This cross-sectional study examined the independent effects of habitual physical activity level (PA) and age on knee mechanics, knee extensor function, and neuromuscular control. All studies included three participant groups: young moderately active adults (21-35 years), highly active older adults, and less active older adults (both groups 55-70 years). The young adult and highly active older adult groups were matched by weekly moderate to vigorous physical activity (as assessed by accelerometry). The highly active and less active older adult groups were matched by age. All studies included knee mechanics collected during overground gait, knee extensor muscle function as assessed by isokinetic dynamometry, and neuromuscular control during treadmill gait. Knee mechanics were characterized by knee flexion, knee adduction, knee internal rotation, and anterior position of the femur relative to the tibia at heel strike and during loading response, as well as by peak external knee extension, flexion and adduction moments, surrogate measures for the magnitude and distribution of loading on the knee. Knee extensor function was characterized by peak knee joint extensor torque measured isometrically and at concentric and eccentric contraction velocities of 90 and 270°·s⁻¹. Neuromuscular control was assessed through the coordination and variability in the coordination of motion that contributes to knee flexion and internal rotation angles between the thigh and shank, and shank and rearfoot, as well as by co-activation between the knee extensors and knee flexors during treadmill gait.

Study 1 used a cross sectional design to quantify the impact of both PA and age on knee mechanics, knee extensor muscle function, and neuromuscular control. We compared knee function across the three participant groups to determine if PA or age result in characteristic differences in key measures of knee mechanics during walking.
gait. Coordination and coordination variability as well as muscle co-activation were compared across groups to determine if PA or age affect neuromuscular control. Finally, differences in knee extensor function by PA or age were examined through comparison of peak isometric strength and concentric and eccentric power.

Study 2 examined the perturbing effect of a standard bout of activity across PA and age groups. This provided a within-subjects model to test for the effect of an acute deterioration in muscle function similar to what may occur longitudinally, and provided a tool for amplifying between-group differences as knee extensor fatigue resistance is expected to differ by PA status and age. All participants completed a standard 30 minute treadmill walk (30MTW) at preferred walking speed, and the magnitude of change (pre vs. post 30MTW) in knee mechanics, knee extensor muscle function, and neuromuscular control was compared between groups.

Finally, an exploratory study examined the potential that age-related changes in knee mechanics, knee extensor function, and neuromuscular control, as well as the protective effect of habitual PA with age are different by sex. Recent studies suggest that the impact of age on muscle function diverges between males and females and our preliminary data hinted at a potential differential response to PA between older males and older females. This exploratory study probed for potential interactions between PA and sex in the measures collected in studies 1 and 2.
Specific Aims

**Study 1: Age and habitual physical activity as determinants of knee function**

The overall aim of this study was to quantify the impact of habitual physical activity on age-related decrements in knee mechanics, neuromuscular control, and knee extensor function that may increase risks for knee OA.

**Aim 1:** To examine the impact of PA and age on knee joint mechanics and neuromuscular control.

**Hypothesis 1.1:** High levels of habitual PA will be protective against age-related shifts in knee mechanics. Knee mechanics of less active older adults will differ from those of highly active older and young adults.

**Hypothesis 1.2:** High levels of habitual PA will be protective against age-related decrements in neuromuscular control. Co-activation between the knee extensors and knee flexors as well as coordination of less active older adults will differ from that of highly active older adults and young adults. Coordination variability of less active older adults will be less than that of highly active older and young adults.

**Aim 2:** To examine knee extensor function and its relationship with sagittal plane knee joint mechanics across age and PA level.

**Hypothesis 2.1:** High levels of habitual PA will be protective against age-related decline in knee extensor function. Knee extensor function of less active older adults will be less than that of highly active older and young adults.
Hypothesis 2.2: Maximal concentric knee extensor power at 270°·s⁻¹ will explain the variance in sagittal plane knee mechanics at heel strike (flexion angle and anterior femur displacement) across all participant groups.

Hypothesis 2.3: Maximal eccentric knee extensor power at 270°·s⁻¹ will explain the variance in sagittal plane knee mechanics during loading response (peak flexion angle and moment, peak anterior femur displacement) across all participant groups.

**Study 2: Muscle function as the mechanism through which age and habitual physical activity affect knee mechanics**

The overall aim of this study is to examine the role of knee extensor function in determining knee mechanics.

**Aim 1:** To determine if the motor system response to a 30MTW differs by age and habitual PA status.

**Hypothesis 1.1:** In response to a 30MTW, less active older adults will display a larger change in knee mechanics than highly active older and young adults.

**Hypothesis 1.2:** In response to a 30MTW, less active older adults will display a larger change in coordination and a larger decrease in coordination variability than highly active older and young adults.

**Aim 2:** To determine if the change in knee extensor muscle function in response to a 30MTW differs by age and habitual PA status.

**Hypothesis 2.1:** High levels of habitual PA will be protective against dynamically-induced knee extensor fatigue. In response to a 30MTW, less active
older adults will display a larger decrease in knee extensor function than highly
active older and young adults.

Hypothesis 2.2: High levels of habitual PA will be protective against activity-
induced changes in knee extensor/flexor co-activation. In response to a 30MTW, 
less active older adults will display a larger change in co-activation than highly 
active older and young adults.

**Exploratory Study: Examination of a sex-specific response to habitual physical
activity across age**

**Aim:** To determine if there is a sex-specific effect of age or habitual PA on knee 
mechanics and knee extensor function.

**Hypothesis E.1:** There will be a sex by group interaction across the three 
participant groups in gait mechanics and knee extensor function, and response to a 
30MTW.
Figure 1.1. Proposed mechanisms by which age leads to increased knee osteoarthritis (OA) risk. Black solid arrows depict mechanisms for which there is supporting evidence. Black dashed arrows depict proposed mechanisms. Green physical activity (PA) overlays depict known (solid box) or proposed (dashed box) paths by which high levels of physical activity may mitigate the effects of age on factors that lead to increased knee OA risk.
CHAPTER II
LITERATURE REVIEW

Idiopathic knee osteoarthritis (OA) is an age-related disease, with reports of prevalence in adults over age 45 ranging from 19.2–27.8%\textsuperscript{1,2} and the lifetime risk of knee OA estimated at 44%.\textsuperscript{4} The number of Americans affected by knee OA is expected to increase substantially in the coming years, as older adults are projected to make up 19.3% of the population by 2030.\textsuperscript{3} Considering the huge national costs associated with the treatment of arthritis\textsuperscript{6} and the current lack of disease modifying agents, it is imperative that we understand the mechanisms affecting the initiation of knee OA and identify any preventative measures individuals can take to decrease their risk of knee OA.

While age is known to be a risk factor for knee OA, maintenance of physical activity across the lifespan may mediate this risk. Age and knee OA are both often associated with altered gait, decreased knee extensor strength, and reduced levels of physical activity, while regular participation in physical activity is associated with maintenance of mobility and knee extensor strength. Historically, the scientific and lay perspectives held that high levels of physical activity contributed to increased “wear and tear” on knee cartilage and thus increased the risk of knee OA.\textsuperscript{55,56} Some cross-sectional epidemiological studies have indicated increased rates of knee OA in current or former athletes, including runners,\textsuperscript{57-59} and especially in females.\textsuperscript{55,59} Longitudinal epidemiological research on this topic, however, does not support this perspective and may actually support high levels of physical activity as protective against knee OA.\textsuperscript{60-63} In studies with follow-ups ranging from 5 to 8 years, older runners demonstrated rates of knee OA incidence equal to\textsuperscript{64} or less than\textsuperscript{65} inactive older controls.
Females are known to be at greater risk for knee OA than males, however, the reasons for this sex-specific difference in risk are not clear. Greater knee extensor strength is protective against knee OA incidence in males and females, however, low knee extensor strength appears to only be a predictor of knee OA incidence and progression in females. There may be other factors, such as gait mechanics, which differ between males and females throughout life or in older age that alter knee joint cartilage loading and lead to a higher incidence of knee OA in females as compared to males.

Interactions between age and habitual physical activity as they relate to knee joint function and, ultimately, cartilage health, are poorly understood. This review will outline the state of the literature in regards to potential risk factors for knee osteoarthritis. Topics will include the impact of the mechanical environment on knee joint cartilage; age-related biomechanical, physiological, and neuromuscular changes that could alter the mechanical environment of this cartilage; and the potential impact of habitual physical activity in mitigating these yet to be discovered age-related changes.

**Knee joint loading and cartilage health**

Knee OA is characterized by cartilage degeneration, osteophyte formation, and inflammation of the synovial lining. The initiation of knee OA is hypothesized to be caused partially by mechanical factors, whereby changes in knee mechanics result in altered cartilage loading and, ultimately, cartilage degradation. Several changes that could affect the loading environment in the knee occur with increasing age including altered knee mechanics, decreased knee extensor strength, and altered neuromuscular function. As these changes have independently been identified in healthy aging and in
individuals with symptomatic knee OA, accumulation of age-related decrements in knee mechanics, knee extensor strength, and neuromuscular function are likely to contribute to the initiation of knee OA.

Healthy cartilage is structured in a way which is adapted to the forces acting on it. *In vitro*\(^71, 72\) and modeling\(^73\) studies have demonstrated that cartilage thickens and displays increased protein synthesis in response to higher magnitudes of load or hydrostatic pressure. In the knee, MRI studies have found that articular cartilage is thickest in regions that regularly experience high loads during gait and thinner in regions that are not frequently loaded.\(^9-11\) In contrast, chronic unloading of the knee in patients on bedrest or with spinal cord injuries results in thinning of the tibial or femoral cartilage.\(^74, 75\) While these findings demonstrate the ability of mature cartilage to adapt to increases or decreases in loading, this ability is limited. Cartilage remodeling in response to a change in loading is relatively slow, largely because cartilage is mostly avascular and so cell signaling and metabolic activity depend on the movement of extracellular fluid. Changes in knee joint cartilage loading due to age-related changes in knee mechanics may outpace the remodeling ability of chondrocytes. Additionally, loads may be shifted to cartilage locations that were not developed to withstand a particular type of stress (e.g., perpendicular vs. tangential stress).

In the knee, cartilage is adapted not only to the location of loading but also to the stresses experienced over the course of development. This results in some regions of cartilage that are well-adapted to absorbing loads applied in a perpendicular direction (e.g., regions of the central tibial plateau) while other regions of cartilage are well-adapted to absorbing tangential or shear stresses (e.g., peripheral regions of the tibial
plateau). At the periphery of the tibial plateau, cartilage resides under the meniscus and is characterized by high concentrations of evenly distributed but non-uniformly oriented collagen fibers, as well as a small concentration of proteoglycan. In the central tibial plateau, cartilage is directly exposed to mechanical loading from femoral cartilage and the tissue is characterized by high proteoglycan content and less collagen, which is generally organized into parallel clusters.\textsuperscript{76} While this specialized arrangement of cartilage morphology is excellent for distributing and absorbing typical loading patterns of the knee joint, it also results in articular cartilage anatomy that cannot adapt to changes in this loading pattern. This is especially evident in the case of rupture of the anterior cruciate ligament (ACL), where loss of this ligament results in altered knee mechanics, an abrupt change in the spatial loading of the knee cartilage, and subsequent degeneration of cartilage that is loaded in a way to which it was not adapted.\textsuperscript{12,13} If aging is associated with a change in knee mechanics, this altered loading environment could lead to degradation of articular cartilage and ultimately to the initiation of knee OA.

Studies of ACL-deficient individuals provide strong support for the role of knee mechanics, and especially a change in knee mechanics, in the initiation of OA. ACL-deficient and ACL-reconstructed knees demonstrate differences in kinematics and kinetics in comparison to both healthy control knees and individuals’ own contralateral, uninjured knees. These differences include increases in tibial internal rotation\textsuperscript{77-79} and anterior position relative to the femur\textsuperscript{79, 80} and have been shown to alter the loading of the tibiofemoral cartilage\textsuperscript{81} and to correspond with subsequent changes in cartilage.\textsuperscript{12,13} Altered loading through altered mechanics of ACL-deficient knees provides a plausible mechanism and explanation for the high rates of post-traumatic OA seen in otherwise
healthy young adults. Presumably, age-related changes in gait would happen over a longer time course than changes brought about by a traumatic injury, but this shift in knee mechanics could initiate idiopathic OA in the same manner as post-traumatic OA (Figure 2.1).

Figure 2.1. Proposed mechanisms for the shift from healthy articular cartilage to the vicious cycle of cartilage degradation. Adapted from Andriacchi et al., 2009.

**Aging and gait mechanics**

Changes in lower extremity gait mechanics with age are well documented. The correspondence in the timing of initial changes in gait with the substantial increase in the prevalence of knee OA (both around age 45) begs the question of the role of an altered loading environment at the knee in idiopathic OA initiation. As compared to young adults, older adults display decrements in several variables: step/stride length, peak hip extension, dorsiflexion at heel strike, and peak ankle plantar flexion. Additionally, older adults often display a distal-to-proximal shift in joint kinetics, such that peak moments and powers are decreased at the ankle and increased at the hip in comparison to young adults.
When compared to changes in ankle and hip mechanics, the effect of aging on knee mechanics is less clear. As compared to young adults, older adults have been shown to have decreased\textsuperscript{18} or increased\textsuperscript{19-21} average knee flexion during stance as well as decreased\textsuperscript{18} or increased\textsuperscript{19, 21, 22} powers and moments at the knee. While these alterations have not been observed in a large number of studies, they suggest that the loading environment at the knee changes with age. As adults age, physiological or neurological deterioration may result in some change in knee mechanics away from an individual’s normal pattern of motion. These initial changes away from normal motion could regionally alter the mechanical loads placed on chondrocytes, resulting in altered cartilage metabolism and, eventually, a predictable alteration in gait mechanics in response to the initiation of knee OA symptoms. As compared to young and age-matched adults, older adults with knee OA have increased knee flexion angle at heel strike, decreased knee flexion range of motion and decreased knee flexion moment, as well as increased peak knee adduction angle and moment.\textsuperscript{20, 90-95} A recent study examining sagittal plane knee mechanics across age and knee OA status suggests that knee mechanics follow a progression from young healthy adults to older healthy adults and finally to older adults with knee OA.\textsuperscript{20} These results suggest that the identification of age-related changes in gait and knee mechanics could indicate the beginning of a detrimental slide into knee OA initiation.

Maybe it’s not just age

Assuming that changes in knee mechanics are a mechanism by which OA is initiated, the overall scarcity of evidence for changes in knee mechanics with age (especially considering the number of studies indicating changes in ankle and hip
mechanics) is surprising. This lack of evidence may partially be a result of technological limitations in older studies (e.g., camera resolution, marker sets capable of minimizing skin motion artifact[90]), where investigators largely focused on sagittal plane gait mechanics due to low confidence in measurements of knee rotation, adduction, and translation. Another potential reason for a lack of reported changes in knee mechanics with age is that gait studies examining aging are often cross-sectional in nature and older adult participants (and sometimes the young adults to whom they are compared) are heterogeneous both within and between studies. Studies often report that participants were “healthy” adults, but this selection criteria may not be sufficient to detect the effects of age independent of factors such as body mass, history of injury or pathology, and habitual physical activity.

The heterogeneity of older adults in various studies likely means that many studies of aging gait include individuals that vary across a spectrum of physiological factors that are themselves determinants of gait and knee mechanics. Older adults with knee OA have reduced knee extensor strength,97 and older adults with weaker knee extensors appear to be more prone to knee OA.69 If healthy older adults describe a range on the spectrum between healthy young adults and older adults with knee OA, older healthy adults with weaker knee extensors could be at greater risk of knee OA if knee extensor function is a determinant of knee mechanics and therefore cartilage loading.

**Potential physiological determinants of knee mechanics**

Function of the knee extensor muscles may play a large role in knee mechanics. Modeling studies have shown that the knee extensors, along with the gluteal muscles, are responsible for controlling the support phase of gait,98 indicating that declines in knee
extensor function could result in altered control of knee motion during stance. Further support is given to the hypothesis that muscle function directly affects knee mechanics in studies that examined both gait mechanics and strength measures. Lower extremity strength correlates with both preferred and maximal walking speed in older adults\textsuperscript{99-104} and this correlation is stronger than that between age and walking speed\textsuperscript{105}. Moderate correlations between strength and walking speed have been found for the hip flexors, hip abductors, knee extensors, ankle dorsiflexors, and ankle plantar flexors, with strength of the knee extensors and ankle plantar flexors having the strongest relationships with speed\textsuperscript{99-104}.

Older adults have increased oxygen demand at gait speeds matched to young adults\textsuperscript{106,107} with older adults expending up to a third more energy to walk\textsuperscript{108}. This increased cost of locomotion may be due to several factors including increased coactivation\textsuperscript{108,109} and overall muscle deterioration with age (see subsequent sections for detail), requiring a larger relative effort from any given muscle to produce the same amount of force. During typical gait, the torque needed to generate joint kinetics may approach the limits of older adults’ force-generating potential. Studies comparing the demand on the knee extensors during gait by age have compared joint moments during high-velocity motion to isometric\textsuperscript{40} or low-velocity isokinetic\textsuperscript{110} joint torques. Older adults display decreases in knee extensor strength, especially at high contraction velocities, which is especially problematic for tasks requiring knee extensor torque generation during high-velocity knee motion. Due to changes in strength with age and the well-documented force-velocity characteristics of skeletal muscle, the literature on knee extensor demand may actually underestimate both the magnitude of difference between
young and old and the true demand placed on the knee extensors during gait. As most studies compare young and older adults in a rested state, the reported differences in knee extensor demand may underestimate the true difference during day-to-day activity. Understanding the demand placed on lower extremity muscles during gait is important for determining if older adults are truly at risk of exceeding their capacity to control joint motion, especially throughout daily activity or exercise when they may accumulate muscular fatigue.

Direct correlations between strength and joint kinematics and kinetics have been found in a few promising studies. Knee extensor strength correlates with knee mechanics including early stance knee power absorption, late stance knee power generation, and knee flexion moment. In individuals who have undergone ACL reconstruction surgery, those with knee extensor strength deficits display reductions in peak knee flexion angles and moments. As knee extensor strength and power are strongly tied to performance of daily activities as well as risk of osteoarthritis initiation and progression, further investigation of the relationship between knee extensor function and knee mechanics in older adults is needed. Recently, a study on adults with knee OA found correlations between knee flexion angles and knee extensor strength and power, supporting knee extensor function as a determinant of knee mechanics across the age and health spectrum. Additionally, the established link between knee extensor strength and habitual physical activity provides a potential mechanism through which age-related deterioration of knee mechanics may be mediated.
Neuromuscular control and age

Age-related changes in neural control are well-documented and are likely due to deterioration of myriad sensory components including muscle spindles, golgi tendon organs, cutaneous sensation (including sensation of pressure and vibration), and the vestibular and visual systems. In studies of general neuromuscular function, older adults have been shown to have slower reaction times, decreased balance, and poorer joint proprioception when compared to young adults. While these declines may not directly affect gait function, they may be indicators of overall motor decline that could impact locomotion. When examining more complex movements, including locomotion, studies of coordination and movement complexity provide insight into how adults may alter the organization of their movement patterns as they age.

Older adults are generally considered to perform tasks in a manner which is less complex, more random, and therefore less flexible in response to perturbations, as compared to young adults. During balance tasks, older adults display decreased use of the available degrees of freedom during postural tasks as well as a decreased ability to control these degrees of freedom in response to a perturbation. Analyses of motor control during gait, especially with regards to movement coordination and variability, may provide information about the control of gait that is not apparent when examining joint kinematics and kinetics.

During walking gait, older adults display more random stride-to-stride intervals and may have altered inter-joint coordination as compared to young adults. During running, older females have decreased segment coordination variability as compared to their young counterparts. Changes in the coordination of movement may be a result of
altered muscle activity, and older adults display higher levels of antagonist coactivation during gait.\textsuperscript{26-28} Increased coactivation and changes in the coordination of movement could alter the loads across knee joint cartilage,\textsuperscript{29} potentially increasing the risk of knee OA initiation. In fact, older adults with knee OA display increased coactivation as compared to healthy older adults, especially between lateral knee extensors and flexors.\textsuperscript{125, 126} These findings of altered motor control with age support the hypothesis that there are physiological mechanisms driving age-related changes in gait mechanics and that these mechanisms could influence the risk of knee OA in older adults.

**Muscle function and age**

In general, muscle function declines as adults age. Lower extremity muscle strength generally peaks in the 3\textsuperscript{rd} decade of life and is preserved until declines become evident in the 5\textsuperscript{th} or 6\textsuperscript{th} decade.\textsuperscript{30, 31} The timing of declines in muscle strength parallels decreases in walking speed,\textsuperscript{99} initial changes in gait mechanics,\textsuperscript{46} and a rise in the prevalence of knee OA.\textsuperscript{67} Function of the knee extensors is particularly relevant to gait and overall physical function as knee extensor function has been shown to be related to walking speed and performance of daily tasks such as rising from a chair.\textsuperscript{100, 113} Additionally, reduced knee extensor function has been tied to initiation,\textsuperscript{127, 128} progression,\textsuperscript{70} and overall function\textsuperscript{115} in individuals with post-traumatic or idiopathic knee OA.

**Whole muscle function decrements with age**

Knee extensor strength (isometric strength) and power (isokinetic strength) have been shown to decline with increasing age in both cross-sectional and longitudinal studies.\textsuperscript{30-35} Across all ages, cross-sectional area or mass of the knee extensors correlates
with strength and/or power. The age-related decline in muscle function has been partially attributed to the well-documented decline in muscle size (mass, cross-sectional area, volume) that accelerates around age 50. However, this age-related decrease in muscle strength is not wholly explained by decreased muscle mass. Differences between young and older adults’ strength are still apparent when strength is expressed relative to quantity of muscle tissue, indicating a potential decline in muscle quality.

In addition to decreases in strength with age, knee extensor muscles demonstrate a decreased ability to produce power with increasing age. The deviation in knee extensor strength between young and older adults increases at higher contraction velocities such that older adults display larger impairments in torque at higher velocities and an overall decreased ability to produce knee extensor power. Older adults display decreased peak knee extensor contraction velocity in voluntary contractions, have longer time to peak tension and greater relaxation times in stimulated contractions, and reach maximum force production at lower stimulation frequencies in response to stimulated tetani. These alterations in whole muscle strength, power, and velocity were initially suggested to be due to an inability to fully recruit motor units, however, central activation has been found to be equal between young and healthy older adults or only slightly decreased in older adults, suggesting that older adults’ ability to fully recruit motor units is not impaired.

**Muscle fiber property changes with age**

Changes in strength and function at the whole-muscle level may be partially the result of fiber-level changes. Age-related decline in knee extensor muscle mass has been
attributed to a decline in the number and size of muscle fibers. Type II (fast, glycolytic) muscle fibers may atrophy to a greater extent than type I (slow, oxidative) muscle fibers and this preferential atrophy may be partially responsible for an overall loss of muscle strength. While this decreased muscle mass explains a large portion of declines in muscle strength, several studies have demonstrated that this atrophy does not explain all of the age-related decline in strength. Declines in the strength of whole muscles may be a result of changes in the ability of muscle fibers to produce force relative to their size (specific force), reducing whole muscle and fiber force-generating capacity beyond the effects of isolated atrophy. One explanation for this reduction in specific force is an increase in co-expression of myosin heavy chain isoforms (e.g., I/IIA and IIA/IIX vs. I, IIA, or IIX), in the muscle fibers of older as compared to young adults. This co-expression could contribute to an overall decrease in the maximum force and shortening velocity of a muscle if fibers begin to co-express isoforms that are of a slower type than their initial isoform.

Atrophy of muscle fibers as well as shifts in myosin heavy chain isoform expression may result from changes in motor neuron innervation with age. As adults age, the number of motor neurons exiting the spinal cord decreases and the proportion of type I motor neurons in the remaining pool increases. This phenomenon results in a decrease in the number of motor units in a muscle and, together with re-innervation of denervated type II muscle fibers by low-threshold, type I motor neurons, may result in a larger proportion of a muscle’s fibers being in type I motor units. These cellular and motor-unit level changes in lower extremity skeletal muscle may also contribute to the well-documented drop in maximal contraction velocity with age. Both single muscle
fiber\textsuperscript{135, 143, 149} and intact human studies\textsuperscript{135, 137} have documented a decrease in maximal contraction velocity. Along with changes in fiber type and motor neuron innervation, this decrease in maximal contraction velocity may also be a result of slowed cross-bridge kinetics (e.g., slowed release of bound myosin heads from actin)\textsuperscript{51} as well as changes in mitochondrial properties.\textsuperscript{150}

**Muscle fatigue and age**

Along with decreased baseline strength and power, suggestions that older adults operate near the limits of their knee extensor strength during gait raise concerns about the potential impact of fatigue on knee mechanics. If an individual’s knee extensor strength and power only slightly exceed the torque necessary to produce their gait mechanics, any decrement in knee extensor function could put them below this threshold and result in an obligatory change in knee mechanics. Historically, older adults have been described as more or equally fatigue resistant as young adults. However, studies reporting no increased fatigue with age typically used sustained or repeated isometric contractions or low-speed dynamic contractions to induce fatigue,\textsuperscript{151-153} contraction modes which do not replicate activities of daily living such as walking. When high-speed dynamic fatigue protocols are implemented, older adults display less fatigue resistance than young adults\textsuperscript{37, 38, 138} and have been shown to sustain a drop in knee extensor isokinetic torque production as high as 30\%\textsuperscript{39}.

A drop in knee extensor power in response to high-velocity dynamic contractions in older adults suggests that older adults could fatigue during daily bouts of walking. Gait involves repeated high-velocity contractions of the knee extensors, both concentrically during the unloaded swing phase and eccentrically to resist knee flexion during weight
acceptance. A recently developed treadmill walking protocol demonstrated that older women display a loss of knee extensor power in response to a 32 minute bout of walking, supporting the hypothesis that daily activity induces measurable muscle fatigue in older adults.\textsuperscript{37} As the exercise guidelines for older adults recommend 30 minutes of exercise per day\textsuperscript{154} and this duration of activity could also be accumulated throughout a day, older adults may sustain measurable knee extensor fatigue each day. If this fatigue caused the knee extensors to exceed their functional demand during gait, fatigue-induced changes in gait mechanics may result. In young adults, fatigue of the knee extensors results in changes in knee mechanics that are similar to differences typically observed between young and older adults: increased knee flexion at heel strike and decreased peak knee flexion moments.\textsuperscript{155-157} To date, the impact of muscle fatigue on knee mechanics in older adults has not been examined.

**Physical activity as a mediator of muscle function**

If muscle function is indeed a mediator of knee mechanics in older adults, a means of maintaining strength and power during aging is needed. Physical activity and exercise have long been known to have a direct impact on muscle strength and power. Whole-body muscle strength correlates with physical activity throughout the lifespan\textsuperscript{158} and single muscle fiber studies demonstrate that older adults who habitually participate in endurance or resistance training preserve specific tension and maximum fiber velocity.\textsuperscript{149} Age-related loss of motor units may also be mediated by activity level as studies have shown that older runners have motor unit numbers equal to young adults and greater than older controls in lower extremity\textsuperscript{159} but not upper extremity\textsuperscript{47} muscles. In studies of older adults who are habitually highly active, delays in age-related concentric knee extensor
strength loss⁴⁴ and a maintenance of concentric and eccentric knee extensor power over time⁴⁵ have been demonstrated.

Correlations between physical activity, strength, and maintenance of muscle function in highly active older adults suggest that at least a portion of observed muscle function loss with age is dependent on physical activity. Participation in physical activity decreases each decade of life and older adults participate in up to a third less physical activity as compared to young adults.⁴¹,⁴³ When this comparison is expanded past healthy adults, older adults with knee OA are seen to participate in even less physical activity than their age-matched peers.⁴²,⁴³ The relationship between muscle function and physical activity together with parallel age-related declines in physical activity and muscle structure and function strongly suggest that physical activity needs to be included as an independent factor in studies of muscle function and age.

**Knee OA risk factors: males vs. females**

While physical activity may counteract the age-related increase in knee OA risk, this benefit may not be equal between the sexes. Muscle strength and power decrease with age in both sexes, however, this decrease may be more pronounced in females.⁵¹,⁵⁴,⁵⁰ Additionally, the tendency for older adults to participate in less physical activity than young adults is also more pronounced in older females, with older females participating in significantly less moderate-to-vigorous physical activity than their male counterparts.⁴¹ Even if older females participated in as much exercise as older males, they may not receive the same benefits. Both resistance⁶⁰,⁶¹ and endurance⁶² training studies have demonstrated significantly larger muscle function gains in older males as compared to older females. These differences in muscle and physical activity may contribute to or
compound altered knee joint cartilage loading when combined with altered gait mechanics. Few differences in gait mechanics by sex have been observed in young or older adults, however, this may be an inherent limitation of gait studies that do not control for participants’ physical activity status (especially in studies of older adults). Inclusion of sex-specific comparisons of age-related factors that affect knee mechanics and ultimately cartilage loading could provide insight into the reasons for higher knee OA incidence in females.

**Physical activity and gait mechanics**

In studies investigating objectively-measured physical activity (i.e., collected via accelerometer or pedometer) and measures of gait mechanics, physical activity level has been shown to be positively correlated to walking speed and to minimize some of the differences in joint kinematics and kinetics observed between young adults and older sedentary adults. Interestingly, in studies comparing the gait mechanics of groups of adults stratified by age and subjectively-measured physical activity (i.e., collected via questionnaire), few to no differences have been found between less active and more active older adults. These disparate findings demarcated by physical activity assessment methodology highlight the difficulty in determining the effect of physical activity in mediating age-related gait deterioration and inherent risk of knee OA from historical data.

Physical activity intensity may be more important than quantity in affecting change in gait function. Preliminary findings that improvements in or maintenance of muscle strength in older age mediate deterioration of walking speed and gait mechanics, suggest that physical activity of an intensity that would impact muscle
function may mediate age-related deterioration of gait mechanics. The few studies directly addressing the relationship between physical activity and gait mechanics, the differing methodologies of these studies, and the lack of inclusion of objectively assessed physical activity and lower extremity strength make this an area ripe for further research.

**Summary**

Gait mechanics are known to change with age, and the increased prevalence of knee OA with age may be due in part to age-related shifts in knee mechanics. These changes may very well be the result of deteriorations in knee extensor function and neuromuscular control that have long been known to occur with age. As a known mediator of muscle function, physical activity may provide an avenue through which knee mechanics, and therefore knee OA risk, can be moderated. We propose that physical activity may act as a mediator of the mechanical risk factors for knee OA through its impact on knee extensor function and neuromuscular control.
CHAPTER III

METHODS

This was a cross-sectional investigation of differences in knee mechanics, knee extensor muscle function, and neuromuscular control with age and habitual PA status. Three participant groups of 20 individuals (10 males, 10 females) each were recruited: young adults, less active older adults, and highly active older adults. All individuals were screened for physical activity level, medical contraindications, and injury history. Participants completed 2 lab visits. The first visit included: completion of consent documentation, screening questionnaires, activity monitor assignment, a 400 meter walk, and familiarization with the testing protocol. At the second lab visit (7-10 days after visit 1) participants returned activity monitors and completed the following testing protocols: baseline gait testing and knee extensor function testing, a 30 minute treadmill walk (30MTW), and post-30MTW gait and knee extensor testing. All procedures including recruitment, study protocol, and data storage were carried out in accordance with IRB regulations.

Participants

Young and older adults were defined as adults 21-35 and 55-70 years. The young age range was selected to provide a comparison cohort which is not yet affected by age-related impairments. The older age range was selected based on when decreases in function (including gait mechanics and muscle torque and power), decreases in physical activity, and an increased incidence of idiopathic knee OA are typically observed. All participants had no history of lower extremity traumatic joint injury or surgery, no chronic body pain, were free of neurological, musculoskeletal,
cardiovascular, and metabolic diseases, and had no other major condition affecting daily activity. All participants had BMI < 30 kg·m⁻² to control for the confounding effect of excessive body weight on muscle and gait function.

Participants were recruited from the community via word of mouth, flyers, and community electronic message boards, as well as from recruitment databases from previous Department of Kinesiology research studies. Individuals were screened for health status, age, self-reported PA level and ability to complete testing procedures (see Medical and Physical Activity History Screening in Appendix A). Highly active older adults ran ≥15 miles/week regularly for at least the last 2 years. Less active older adults reported PA participation of no more than three 30-minute bouts of exercise per week. Young adults were matched to highly active older adults for activity level as assessed by accelerometry.

Visit 1

General health documentation

Participants underwent medical screening (Medical and Physical Activity History Screening, see Appendix A) and physical activity history was verified to ensure they met inclusion criteria and to determine if there were any contraindications to completing the study protocol. If screening indicated physician clearance was needed, individuals were required to obtain a physician’s consent to complete visit 1 and participate in visit 2 of the study (see Appendix C for physician consent letter).

30MTW speed determination

Participants walked 400 meters (20 lengths of a 20 meter long runway) at their preferred, normal walking pace. The time taken to walk this distance was used to
calculate preferred walking speed. This speed was used as the treadmill speed for the 30MTW during visit 2.

**Familiarization to testing protocol**

All participants completed a practice session of strength testing to ensure that the goal of the testing was clear for visit 2. During this practice session, participants completed one set of 3 maximal repetitions for each testing condition (isometric; concentric and eccentric isokinetic testing at 90 and 270°·s⁻¹). Participants also were familiarized to walking on the treadmill.

**Physical activity monitoring**

Participants were issued Actigraph GT3X triaxial accelerometers and wore them at the hip for 7-10 days. Activity monitors were collected at visit 2. Total daily activity counts as well as average daily minutes spent in moderate-to-vigorous PA for at least 5 valid days of wear were calculated using established thresholds.¹⁶⁷

**Visit 2**

To control for the effects of activity completed before the study visit, all participants were asked to refrain from exercise in the 24 hours before visit 2.

![Figure 3.1. Summary of experimental procedures for Visit 2.](image)

**Gait analysis methods**

An 11 camera motion analysis system with 5 forceplates was used to collect motion and force data during gait. Data was captured at 3 speeds: preferred, prescribed (1.4 ms⁻¹), and fast (“walking to catch the bus”). Preferred and prescribed gait speeds provide data on individuals’ typical knee mechanics, as well as data on mechanics at a
speed which was standard across individuals as kinematics and kinetics are known to change with gait speed. The fast gait speed provides a frame of reference for knee mechanics at a more challenging speed and may identify some speed-dependent limitations. Speed was monitored using a set of photogates placed 6 meters apart on the walkway. Gait mechanics were calculated from 5 acceptable stride cycles for the right leg for each speed. Acceptable strides were of consistent speed (all trials within 5% of each other for a given speed condition) and included the right foot landing on a force plate. Gait analysis was performed before (Gait 1) and after (Gait 2) the 30MTW. During Gait 2, participants walked continuously at preferred speed between captured stride cycles to prevent recovery from any fatigue induced by the 30MTW. In order to standardize the amount of time participants walked, total walking time for Gait 2 was standardized to 15-18 minutes.

Thigh and shank segments were modeled using the Point Cluster Technique (PCT). PCT is a marker configuration and algorithm optimized for calculation of the three rotations (flexion/extension, abduction/adduction, internal/external rotation) and three translations (anterior/posterior, medial/lateral, compression/distraction) at the knee joint using clusters of markers on the thigh (10 markers) and shank (7 markers). Pelvis, thigh, shank and foot local coordinate systems are established during a static trial from anatomic markers (anterior and posterior iliac spine, iliac crest, greater trochanter, medial and lateral femoral epicondyles, medial and lateral tibial plateau, and medial and lateral malleoli, calcaneus and 5th metatarsal) and cluster markers. Foot and pelvis anatomic markers were also tracked in walking to model these segments. Correlation of PCT calculations with segment motion measured by bone-mounted markers has previously
Joint moments were calculated using inverse dynamics with a link model of the segments assuming the inertial properties of each segment are at its center of mass.\textsuperscript{168}

**Strength measures**

Isometric torque (Nm) as well as concentric and eccentric isokinetic knee extensor torque (Nm) and power (W) measured at 90 and 270°·s\textsuperscript{-1} were collected before Gait 1 and after Gait 2 (Figure 3.1). Testing at 270°·s\textsuperscript{-1} provides an indication of the power available for knee extension during the swing phase of gait (concentric muscle action) and to resist knee flexion during the loading response of gait (eccentric muscle action). Testing at 0 and 90°·s\textsuperscript{-1} provides additional data on the potential for habitual PA to modify the effects of age on isometric and slow-velocity torque production.

The order of strength testing was block randomized by mode (isometric, concentric & eccentric), and participants followed the same order at Strength 1 and Strength 2 (Figure 3.1). Concentric and eccentric testing was collected in a single motion to ensure full muscle activation at the beginning of eccentric contractions. Before beginning strength testing, participants were reminded of the strength testing procedure, refreshed on the instructions given during testing, and encouraged to perform all tests to their maximal capacity. Isometric strength was collected with the knee flexed 60° relative to neutral. Isokinetic power was collected across 70° of knee motion. At Strength 1, participants completed 1 set of 3 practice contractions, followed by 2 sets of 3 contractions at each speed for each mode. Two minutes of rest were given between each set to prevent fatigue during baseline testing. Isometric contractions consisted of five seconds of contraction followed by five seconds of rest. At Strength 2, 1 set of 3
contractions at each speed and mode were collected without rest between sets to prevent recovery from fatigue induced by the 30MTW. Peak strength and power values for Strength 1 and Strength 2 testing time points were extracted, along with the position, velocity, and torque at peak power for isokinetic trials. The % change in knee extensor strength and power from Strength 1 to Strength 2 quantified the fatigue induced by the 30MTW (see “30MTW protocol”). The primary outcomes for strength measures were peak torque generated during concentric and eccentric isokinetic contractions at 270° s⁻¹.

Coordination analyses
A custom MATLAB program was used to calculate phase (coordination) angles between the foot and shank, shank and thigh, and thigh and pelvis segments. Coupling angles (θ) were derived as the angle with respect to the right horizontal formed by a vector drawn between two adjacent time points on an angle-angle plot in each of the three planes of movement (Figure 3.2). Coupling angles were calculated as:

\[ \theta_{i,j} = \tan^{-1}\left[\frac{(y_{i,j+1} - y_{i,j})}{(x_{i,j+1} - x_{i,j})}\right] \]

(Equation 1)

where 0 ≤ θ ≤ 360 degrees and j is a percent of the ith gait cycle. For each participant, the coupling angles were calculated from 10 consecutive strides from the first and last minute of the 30MTW. As these are directional data, circular statistics were used to calculate the mean and standard deviation across trials. The standard deviation at each time-point for each participant forms the coordination variability pattern.
Figure 3.2. Determination of coupling angles and coordination variability (CV). CV is calculated as the standard deviation in the coupling angle at each percent of the gait cycle across multiple strides of data.

Muscle co-activation analyses

Co-activation between knee extensors and flexors as well as the change in co-activation in response to the 30MTW was assessed using directed co-contraction ratios (DCCRs). Electromyography (EMG) was collected during the second and last minutes of the 30MTW. Electrodes (Trigno, Delsys, Inc., Natick MA) were placed over the rectus femoris, vastus lateralis, vastus medialis, biceps femoris, semitendinosus, lateral gastrocnemius, and medial gastrocnemius according to Surface Electromyography for the Non-Invasive Assessment of Muscles (SENIAM) guidelines. EMG were bandpass filtered at 20-500 Hz. Following data filtering, all signals were full-wave rectified and lowpass filtered at 20 Hz to produce a linear envelope. The linear envelope for each muscle was expressed as a percentage of the average signal obtained during the stance phase of 10 consecutive strides during the second minute of the 30MTW.

DCCRs for the quadriceps vs. knee flexors (rectus femoris and vasti vs. biceps femoris, semitendinosus, and gastrocnemii) as well as the quadriceps vs. hamstrings
(rectus femoris and vasti vs. biceps femoris and semitendinosus) were calculated. To calculate these ratios, first, the group (i.e., quadriceps, flexors, or hamstrings) activation was determined at each data point for each stride as the average of the linear envelopes for each of the included muscles. Next, the DCCR was calculated at each data point for each stride using one of two equations.

For the quadriceps vs. flexors ratio, if quadriceps activity is greater than flexor activity:

\[
DCCR = 1 - \frac{\text{flexor mean linear envelope}}{\text{quadriceps mean linear envelope}}
\]

Else

\[
DCCR = \frac{\text{quadriceps mean linear envelope}}{\text{flexor mean linear envelope}} - 1
\]

(Equation 2)

The same procedure was followed for the quadriceps vs. hamstrings DCCR with the hamstrings mean linear envelope replacing the flexor mean linear envelope. This method results in DCCR values that fall between 1 and -1. A value closer to 1 indicates greater activation of the quadriceps, while a value closer to -1 indicates greater activation of the flexors or hamstrings. Values close to 0 indicate relatively similar activation levels of opposing muscle groups. DCCRs were calculated during terminal swing (last 15% of swing), loading response (first third of stance, 20% of gait cycle), mid-stance (second third of stance, 20% of gait cycle), and terminal stance (last third of stance, 20% of gait cycle). For both quadriceps vs. flexor and quadriceps vs. hamstrings, DCCRs from each gait cycle phase of interest were averaged over 10 consecutive strides.

**30MTW protocol**

Participants walked on a treadmill for 30 minutes with intermittent “challenge” periods to simulate an extended walk one might complete during daily activity. The
protocol began on a level treadmill with the speed set at a participant’s pre-determined 30MTW speed (see above). Challenge periods occurred at minutes 7, 17, and 27, when treadmill grade was increased to 3% for 1 minute. This challenge is meant to simulate changes in incline an individual would encounter in the real world. At the end of each challenge, grade was returned to level. Rating of perceived exertion (RPE) was collected every 2 minutes during the 30MTW.

After the walking stimulus protocol, participants walked overground at preferred speed for 2 minutes to re-acclimate to overground walking. Immediately following this, participants underwent Gait 2, followed by a standardized 2-minute break for participant transfer and equipment setup, followed by Strength 2 (Figure 3.1).

**Outcome variables**

**Knee mechanics:** Knee mechanics were calculated from motion capture data collected during overground walking before and after a 30MTW (Gait 1 and Gait 2, Figure 3.1). Kinematics were calculated using the PCT. Externally-referenced kinetics were calculated using inverse dynamics and were normalized to participants’ height and body weight. Knee mechanics variables included knee flexion, knee adduction, knee internal rotation (each in °), and anterior position of the femur relative to the tibia (mm) at heel strike and during loading response, as well as peak external knee extension, flexion, and adduction moments (% BW·Ht). Outcome variables were the mean of 5 acceptable right-sided trials for each participant at preferred, prescribed (1.4 m/s), and fast walking speeds. For Study 2, the primary knee mechanics outcomes were the change in each variable in response to the 30MTW (Gait 2 – Gait 1).
**Knee extensor function:** Peak torque (Nm) from isometric knee extensor trials as well as peak torque and power (W) from periods of constant, target velocity during concentric and eccentric knee extensor trials at 90 and 270°·s⁻¹ were collected before and after gait data collection and the 30MTW (Strength 1 and Strength 2, Figure 3.1). Knee extensor function outcomes for study 1 were peak torque and power from Strength 1. The percent change in peak torque and power in response to the 30MTW ([Strength 2 – Strength 1]/[Strength 1] × 100%) was the knee extensor function outcome for study 2.

**Neuromuscular control:** Segment coordination and variability of segment coordination were calculated from motion capture data collected during the first and last minute of level treadmill walking of the 30MTW. Globally-referenced pelvis, thigh, shank, and rearfoot segment angles were calculated using the PCT and rigid-body assumptions. A modified vector coding method was used to calculate phase angles for the following couples: thigh sagittal plane vs. shank sagittal plane, thigh sagittal plane vs. shank transverse plane, and shank transverse plane vs. rearfoot frontal plane. The standard deviation in each phase angle over 10 right-sided strides represented the variability in segment coordination. Coordination and its variability was averaged for each participant over terminal swing and early, mid, and late stance. Coordination and its variability calculated from the first minute of the 30MTW were neuromuscular control outcome variables for study 1. The difference in coordination and its variability within each gait phase between the last and first minute of the 30MTW were neuromuscular control outcome variables for study 2.

Directed co-contraction ratios (DCCRs) between the knee extensors and knee flexors as well as between the quadriceps and hamstrings were calculated for terminal
swing and early, mid, and late stance from 10 right-sided strides during the second and last minutes of the 30MTW. DCCRs at minute two were neuromuscular control outcome variables for study 1 and the difference in DCCRs between the last and second minute were neuromuscular control outcome variables for study 2.

**Sample size estimates**

Appropriate number of subjects per group was determined using the values of expected differences in primary variables between groups (Table 1). Power calculations were carried out in GPower software using an unpaired t-test protocol with $\alpha$ set at 0.05 and $\beta$ set at 0.8. Expected mean differences and standard deviations were based on literature values or preliminary data where available and represent a meaningful difference in the variable of interest. Based on these power calculations, we expected that 20 participants per group would be sufficient to detect between-group differences.
**Table 3.1.** Outcome variables and sample size estimates. All units in sample size estimates are the same as those listed for the outcome variable except where noted. *- moment values in units of Nm. ^- knee extensor torque at 270°·s⁻¹ in Nm. $- % change from baseline (Foulis 2013).

<table>
<thead>
<tr>
<th>Variable Hierarchy</th>
<th>Expected baseline difference</th>
<th>Within group SD</th>
<th>n needed per group</th>
<th>Expected post-pre 30MTW difference between groups</th>
<th>Within group SD</th>
<th>n needed per group</th>
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<tr>
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<td>Knee internal rotation angle (°)</td>
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<td>Peak knee adduction moment (%BW*ht)</td>
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<td>17$</td>
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<td>Concentric knee extensor power, 90°/sec (W)</td>
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<td>Late Stance</td>
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<td>Directed co-contraction ratio (DCCR)</td>
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<td>DCCR, early stance</td>
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<td>DCCR, mid stance</td>
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<td>DCCR, late stance</td>
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<td>Quadriceps vs. Hamstrings</td>
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</table>
Data analysis plan

Hypotheses for studies 1 and 2 (with the exception of study 1, hypotheses 2.2 and 2.3) were tested with one-way ANOVAs, with separate tests for each outcome variable. Significance was set at $p \leq 0.05$. Coordination and coordination variability measures were tested with 2-way ANOVAs for group and time. Where significant main effects of group were found, post-hoc pairwise comparisons were made using Tukey’s honest significant difference test. For study 1, hypotheses 2.2 and 2.3, linear regression was used to test for significant associations between measures of power and sagittal plane knee mechanics using data from all participants. If a significant ($p \leq 0.05$) association was found, the magnitude of Pearson correlation coefficients was examined to determine the amount of variance in knee mechanics explained by knee extensor function.

The exploratory study examined the same variables as studies 1 and 2, adding in the factor of sex. Outcome variables were examined using two-way ANOVAs, specifically to test for a significant interaction between group (age or PA level) and sex. Where significant interactions were found, post-hoc pairwise comparisons were made using Tukey’s honest significant difference test.

Limitations/Alternative strategies

While age and PA are expected to account for much of the variance in outcome variables, these are not the only factors at play in the decline of knee mechanics, knee extensor function, and neuromuscular control with age. We documented demographic information that may impact knee joint health including occupational status and history and prior exercise history which may act as covariates in this study (see Appendix B for Intake Questionnaire).
CHAPTER IV

PHYSICAL ACTIVITY AND AGE-RELATED BIOMECHANICAL RISK FACTORS FOR KNEE OSTEOARTHRITIS

Introduction

Knee osteoarthritis (OA) is a mobility-limiting, age-related disease for which there is a 44% lifetime risk in American adults. As there are currently no widely available disease modifying treatments for OA, there is a need to identify modifiable risk factors for preventing OA initiation. OA is in part a mechanically mediated disease, and characteristics of daily loading are thought to contribute to the initiation and progression of OA. Maintenance of physical activity throughout the lifespan may mediate several OA risk factors that are also associated with aging, including gait mechanics, knee extensor muscle weakness, and altered muscle activation. However, interactions between physical activity and age-related changes in gait are not well characterized and it is not clear if regular participation in physical activity can modify age-related biomechanical risk factors for knee OA.

Cartilage thinning indicative of OA may be initiated and accelerated by altered loading patterns due to injury- or age-related gait changes. Articular cartilage develops in response to its loading environment and healthy articular cartilage tends to be thickest where exposed to the highest mechanical loads. While a positive relationship between joint load and cartilage morphology exists in healthy joints, this relationship changes in individuals at high risk for OA and in those with symptomatic OA. In the post-traumatic knee OA model of anterior cruciate ligament (ACL) rupture, typical magnitude but altered spatial distribution of loading is associated with cartilage thinning.
deficient or reconstructed knees display altered tibial rotation and anterior femoral translation during gait. These altered mechanics result in changes in tibiofemoral cartilage loading and have been associated with a rapid onset of cartilage degeneration. Idiopathic OA could be initiated in the same manner as post-traumatic OA by a gradual age-related shift in knee mechanics. Healthy older adults appear to have less knee flexion at heel strike and a smaller range of motion at the knee compared to young adults along with greater anterior translation of the femur relative to the tibia during gait. These differences in knee mechanics are found to a greater extent in individuals with knee OA, suggesting that there may be a gradual age-related progression towards knee mechanics that are associated with OA.

Around the age where increased prevalence of knee OA occurs, adults display marked decreases in knee extensor torque and power and increased knee extensor fatigue following repeated contractions. Modeling studies demonstrate that the knee extensors are one of the primary muscle groups responsible for controlling center of mass motion during gait, particularly during the first half of stance, and knee extensor function has been correlated with knee power absorption, generation, and flexion moments during gait in healthy adults. Changes in knee mechanics are also apparent during gait in individuals who have knee extensor strength deficits after ACL reconstruction, and decreased knee extensor strength has been associated with OA initiation as well as knee flexion angles during gait in individuals with OA. Additionally, older adults and adults with knee OA display increased co-activation of the muscles around the knee, which could alter knee joint loading. The findings linking both decreased knee extensor function and changes in knee mechanics to altered
cartilage loading and knee OA suggest a causal link between a decline in knee extensor strength or power, altered knee mechanics, and incidence of idiopathic knee OA.

If a decline in knee extensor function promotes age-related changes in knee mechanics and subsequent knee OA initiation, then we would expect deviations in knee mechanics in older adults with lower as compared to greater knee extensor function. Physical activity level could be a discriminating factor in the maintenance of knee mechanics with age as knee extensor strength and power are associated with habitual physical activity level in older adults. Healthy older adults participate in up to a third less physical activity than younger adults. Few studies have examined the role of habitual physical activity in age-related changes in gait. Of the few studies that have compared gait in more and less active older adults, even fewer have characterized the connection from physical activity and its impact on muscle function and muscle co-activation to alterations in gait mechanics.

The primary aim of the current study was to determine if knee extensor muscle function (torque and power), co-activation of muscles that cross the knee during gait, and knee mechanics differ by age or physical activity level. We hypothesized that less active older adults would be weaker, have altered muscle co-activation across the knee, and display different knee mechanics compared to both highly active older and young adults. As a secondary aim, we sought to directly test the impact of a decline in knee extensor torque or power on knee mechanics. Because older adults fatigue in response to high-velocity dynamic contractions (such as those that would occur during daily walking), they may accumulate enough knee extensor fatigue during daily activity to substantially alter their knee motion. For our secondary aim, we hypothesized that less active older
adults would display greater knee extensor fatigue in response to a bout of walking, and that they would have correspondingly greater changes in knee mechanics and co-activation across the knee compared to both highly active older adults and young adults.

**Methods**

**Participant selection**

Three groups of individuals were recruited for this study: highly active older adults (OHI; 55-70 years, running ≥15 miles per week), less active older adults (OLO; 55-70 years, participating in no more than three 30 minute bouts of moderate exercise per week), and young adults (Y; 21-35 years). The 55-70 year age range for this study was selected because adults in this age range are at the greatest risk of incidence of knee OA. Power calculations based on literature values and preliminary data indicated that 12-19 participants per group were needed to detect meaningful group differences with a β level of 0.8 and α level of 0.05. Equal numbers of males and females were recruited for each group. All participants had BMI < 30 kg·m⁻², were free of significant musculoskeletal injury history, cardiovascular or neurological pathology, and chronic pain. Prior to completion of any study procedures, all participants completed informed consent documentation as approved by the institutional review board.

**Study protocol**

Participants completed two study visits at least 7 days apart. The first study visit consisted of a timed 400 meter walk at preferred walking speed to determine the treadmill speed for the second visit (see 30 minute treadmill walk, below), an acclimation strength testing session, and assignment of a physical activity monitor. The second visit consisted of overground gait analysis, knee extensor muscle testing, and a 30 minute treadmill walk.
(Figure 4.1). Knee muscle co-activation was captured via electromyography (EMG) during the treadmill walk.

**Physical activity monitoring** All participants wore triaxial accelerometers (GT3X, Actigraph, Pensacola, FL) at the hip for 7 days. Accelerometer wear was considered acceptable if participants wore the device ≥10 hours on ≥4 days, including at least one weekend day. Accelerometer data were used to calculate average weekly time spent in moderate-to-vigorous physical activity\(^{167}\) and average weekly activity counts.

**Gait analysis** Overground gait was captured before and after the 30 minute treadmill walk (Figure 4.1). Kinematics and kinetics of each participant’s right leg were captured using an 11 camera motion analysis system (Oqus, Qualisys, Göteborg, Sweden) with 2 forceplates (AMTI, Watertown, MA). Kinematic data were captured at 200 Hz, kinetic data were captured at 2000 Hz, and marker and force data were low-pass filtered at 8 and 15 Hz, respectively. Five acceptable trials were captured at each of 2 speeds: preferred and set (1.4 m·s\(^{-1}\)). Speed was monitored using a set of photogates placed 6 meters apart on the walkway. An acceptable trial consisted of the participant cleanly hitting a forceplate with their right foot while walking at a speed which was within 5% of the other trials for that condition (preferred or prescribed).

Thigh and shank segments were modeled using the Point Cluster Technique (PCT).\(^{96}\) PCT is a marker configuration and algorithm optimized for calculation of the three rotations (flexion/extension, abduction/adduction, internal/external rotation) and three translations (anterior/posterior, medial/lateral, compression/distraction) at the knee.
joint using clusters of markers on the thigh (10 markers) and shank (7 markers). Pelvis, thigh, shank and foot local coordinate systems were established during a static trial from anatomic markers (anterior and posterior iliac spine, iliac crest, greater trochanter, medial and lateral femoral epicondyles, medial and lateral tibial plateau, and medial and lateral malleoli, calcaneus and 5th metatarsal) and cluster markers. Foot and pelvis anatomic markers were used to track and model these segments. Externally-referenced joint moments were calculated using inverse dynamics.

Primary gait outcome variables were measures of knee mechanics as differences in knee mechanics by age could indicate differences in cartilage loading. Measures of knee kinematics were flexion angle at heel strike, peak midstance flexion angle, flexion range of motion, peak adduction angle during loading response, average rotation angle during stance, and the anterior translation of the femur relative to the tibia at the time of the first vertical ground reaction force peak. Measures of knee kinetics were the first peak extension moment, peak flexion moment, and the first peak adduction moment. For descriptive purposes, sagittal hip and ankle ranges of motion during stance and peak flexion and/or extension moments were also reported.

**Knee extensor function testing** Maximal isometric torque (Nm·kg⁻¹) as well as peak concentric and eccentric isokinetic knee extensor power (W·kg⁻¹) at 90 and 270°·s⁻¹ were collected before and after the 30 minute treadmill walk (Figure 4.1). Alternating participants performed either the isometric or the dynamic (concentric and eccentric) tests first. Concentric and eccentric power were collected in a single motion to ensure full muscle activation at the beginning of eccentric contractions. At baseline, two sets of three repetitions were performed for each test with 30 seconds of rest between sets and two
minutes of rest between tests. Isometric repetitions consisted of 5 seconds of contraction followed by 5 seconds of rest. At the final strength testing time point one set of each test was collected with 15 seconds of rest between tests. Isometric torque was collected with the knee flexed 60° relative to neutral and isokinetic power was collected across 70° of knee motion. Maximal torque and power values were extracted from all repetitions of each test. Primary outcome measures from strength testing were peak isometric torque and peak concentric and eccentric power at 270°·s⁻¹.

**30 minute treadmill walk (30MTW)** After initial gait and strength testing, all participants performed the 30MTW (Figure 4.1). Treadmill speed was set to each participant’s preferred walking speed as determined by the 400 meter walk in the first visit. If a participant indicated that they were not comfortable at this speed, treadmill speed was adjusted in increments of 0.1 mph until the participant indicated the speed felt “normal.” During the 30MTW, treadmill incline was increased to 3% at minutes 7, 17, and 27 for a single minute and then returned to 0% grade. This protocol was designed to mimic a 30 minute bout of walking exercise an individual may complete during a typical day and has been shown to cause knee extensor fatigue in older women.³⁷

**Knee muscle co-activation** Co-activation was calculated using EMG collected at 2000 Hz. Electrodes (Trigno, Delsys, Natick, MA) were placed on the rectus femoris, vastus lateralis, vastus medialis, biceps femoris, semitendinosus, and lateral and medial gastrocnemii according to SENIAM guidelines.¹⁷² Ten consecutive strides of data were extracted from the second and last minutes of the 30 minute treadmill walk. Each signal had the mean offset removed and then was band-pass filtered at 20-500 Hz, rectified, and lowpass filtered at 20 Hz to produce a linear envelope. The signal for each muscle was
then normalized to the average stance phase activation for that muscle over the 10 strides during the second minute of the 30MTW.

Directed co-contraction ratios (DCCRs) were calculated to examine the relative activation levels of muscles crossing the knee.\textsuperscript{171} These ratios were used to compare activity of the quadriceps (rectus femoris and vasti) to the flexors (biceps femoris, semitendinosus, and gastrocnemii) as well as the quadriceps to the hamstrings (biceps femoris and semitendinosus). The DCCR was calculated at each data point $t$ for each stride $s$ using the following equations:

For the quadriceps vs. flexors ratio, if quadriceps activation was greater than flexor activation:

$$DCCR_{t,s} = 1 - \frac{\text{average of flexor linear envelopes}_{t,s}}{\text{average of quadriceps linear envelopes}_{t,s}}$$

Else

$$DCCR_{t,s} = \frac{\text{average of quadriceps linear envelopes}_{t,s}}{\text{average of flexor linear envelopes}_{t,s} - 1}$$

The same procedure was followed for the quadriceps vs. hamstrings ratio with hamstrings replacing flexors in the above equations. This procedure results in a value for each data point between 1 and -1 where values closer to 1 indicate higher relative activation of the first muscle group (quadriceps) and values closer to -1 indicate higher relative activation of the second muscle group (flexors or hamstrings). Values close to 0 indicate relatively equal activation of the two muscle groups. DCCRs were averaged across the 10 strides from the second and last minute of the 30MTW and then over specific phases of the gait cycle: terminal (last 15% of) swing, and early, mid, and late (thirds of) stance.

**Statistics** Prior to performing statistical tests, data were examined for normality to determine if non-parametric tests were warranted. As the data appeared normally
distributed, primary outcome variables were compared between groups using one-way ANOVAs with significance set at p≤0.05. For the primary aim, outcome variables were from baseline gait and strength testing and the second minute of the 30MTW. For the secondary aim, outcome variables were the change in outcomes from the baseline gait, strength, and second minute of the 30MTW to the final testing time points (i.e., post-30MTW minus pre-30MTW). Note that with this convention, for kinetic outcomes that are reported as negative values (hip flexion, knee extension, knee adduction, and ankle dorsiflexion moments), a negative change indicates an increase, while a positive change indicates a decrease in this variable. Where significant main effects were found, Tukey’s post-hoc tests were performed. Baseline and post-30MTW knee extensor strength was compared using paired t-tests to test for the presence of knee extensor muscle fatigue.

**Results**

Group characteristics are shown in Table 4.1. Due to intermittent technical issues with EMG collection, the muscle co-activation data from the second minute of the 30MTW include 58 participants (N = 18 for OLO) and the muscle co-activation data from the final minute of the 30MTW include 54 participants (n = 18, 19, and 17 for Y, OHI, and OLO, respectively). OLO participated in fewer minutes of moderate-to-vigorous physical activity compared to young adults and OHI, and all groups were significantly different in terms of weekly physical activity counts (Table 4.1).

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (years)</th>
<th>Height (m)</th>
<th>Mass (kg)</th>
<th>Preferred walking speed (m·s⁻¹)</th>
<th>Treadmill walking speed (m·s⁻¹)</th>
<th>Weekly MVPA minutes</th>
<th>Weekly counts (x10³)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Y</td>
<td>27.8 (3.5)</td>
<td>1.72 (0.09)</td>
<td>69.8 (11.8)</td>
<td>1.40 (0.15)</td>
<td>1.39 (0.14)</td>
<td>393.5 (162.0)</td>
<td>2509 (783)</td>
</tr>
<tr>
<td>OHI</td>
<td>61.9 (4.0)</td>
<td>1.68 (0.11)</td>
<td>64.4 (12.9)</td>
<td>1.35 (0.12)</td>
<td>1.35 (0.12)</td>
<td>473.5 (216.5)</td>
<td>3340 (1152) *</td>
</tr>
<tr>
<td>OLO</td>
<td>62.9 (3.9)</td>
<td>1.71 (0.11)</td>
<td>69.9 (11.7)</td>
<td>1.35 (0.12)</td>
<td>1.35 (0.12)</td>
<td>147.7 (110.1) *+</td>
<td>1504 (633) *+</td>
</tr>
</tbody>
</table>

Table 4.1. Participant characteristics reported as Mean (SD). MVPA: moderate to vigorous physical activity. OHI: highly active older adults. OLO: less active older adults. *: value significantly different from young; + value significantly different from OHI.
Baseline comparison

Baseline Knee Extensor Torque and Power

Figure 4.2. Baseline knee extensor torque and power. Mean ± SE. ^ indicates OLO different from Y; * indicates OHI and OLO different from Y.

At baseline, knee extensor torque and power were lower in OLO compared to Y during concentric contractions at 90°·s⁻¹ (post-hoc p = 0.01) and in both OHI and OLO compared to Y at 270°·s⁻¹ (p = 0.006 for Y vs. OHI and OLO; Figure 4.2). During the second minute of the 30MTW there was a significant difference in the quadriceps vs. hamstrings DCCR during midstance where OLO displayed greater quadriceps:hamstrings
co-activation compared to Y, who had greater hamstrings activation (post-hoc p = 0.04; OLO DCCR = -0.01, Y DCCR = -0.22, Figure 4.3). There were no differences in net muscle activation between any groups for any comparisons.

When comparing knee mechanics between groups at baseline, results were similar whether participants walked at their preferred speed or the set speed of 1.4 m·s\(^{-1}\). However, larger inter-individual variance in the preferred walking speed vs. 1.4 m·s\(^{-1}\) condition resulted in fewer differences between groups. Therefore, the set speed results are presented here (Table 4.2), with the preferred speed results presented in supplementary tables. Differences were found between the young and older groups in measures of femoral anterior displacement (Figure 4.4), with Y having a more posterior position of the femur relative to the tibia compared to OLO at the time of the first peak of the vertical ground reaction force and at the point of peak anterior femur position. No differences were found between groups for knee joint angles (Figure 4.4). For knee kinetics, Y had a greater knee extension moment in early stance compared to both OHI and OLO, and there was a trend towards OHI having larger knee flexion and first peak adduction moments than Y and OLO (Table 4.2).
Table 4.2. Baseline knee kinematics and kinetics. KF: knee flexion; KA: knee adduction; KER: knee external rotation; FAD: femoral anterior displacement; KE: knee extension; HF: hip flexion; HE: hip extension; ADF: ankle dorsiflexion. Where significant group effects were found, post-hoc p-values are reported. * indicates young different from less active, ^ indicates young different from highly active.

<table>
<thead>
<tr>
<th></th>
<th>Young Mean</th>
<th>SD</th>
<th>Older Highly Active Mean</th>
<th>SD</th>
<th>Older Less Active Mean</th>
<th>SD</th>
<th>p-value</th>
<th>post-hoc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stride length (m)</td>
<td>1.49</td>
<td>0.06</td>
<td>1.45</td>
<td>0.10</td>
<td>1.47</td>
<td>0.08</td>
<td>0.22</td>
<td>na</td>
</tr>
<tr>
<td>KF Heel strike (°)</td>
<td>5.3</td>
<td>4.6</td>
<td>4.9</td>
<td>4.5</td>
<td>6.1</td>
<td>5.6</td>
<td>0.77</td>
<td>na</td>
</tr>
<tr>
<td>KF Midstance (°)</td>
<td>20.1</td>
<td>5.2</td>
<td>22.8</td>
<td>6.0</td>
<td>22.8</td>
<td>5.2</td>
<td>0.2</td>
<td>na</td>
</tr>
<tr>
<td>KF ROM (°)</td>
<td>38.9</td>
<td>3.5</td>
<td>38.6</td>
<td>4.1</td>
<td>40.4</td>
<td>3.8</td>
<td>0.28</td>
<td>na</td>
</tr>
<tr>
<td>KA Midstance (°)</td>
<td>2.0</td>
<td>2.7</td>
<td>1.3</td>
<td>3.4</td>
<td>1.2</td>
<td>3.4</td>
<td>0.74</td>
<td>na</td>
</tr>
<tr>
<td>KER Stance average (°)</td>
<td>0.8</td>
<td>3.8</td>
<td>0.3</td>
<td>4.2</td>
<td>-0.2</td>
<td>3.0</td>
<td>0.68</td>
<td>na</td>
</tr>
<tr>
<td>FAD Heel strike (mm)</td>
<td>-9.0</td>
<td>7.1</td>
<td>-6.0</td>
<td>7.5</td>
<td>-5.2</td>
<td>7.0</td>
<td>0.23</td>
<td>na</td>
</tr>
<tr>
<td>FAD GRF1 (mm)</td>
<td>0.2</td>
<td>5.6</td>
<td>3.9</td>
<td>4.9</td>
<td>6.0</td>
<td>5.8</td>
<td>0.005</td>
<td>*0.004</td>
</tr>
<tr>
<td>FAD Stance average (mm)</td>
<td>2.7</td>
<td>4.0</td>
<td>5.8</td>
<td>4.5</td>
<td>6.1</td>
<td>5.3</td>
<td>0.04</td>
<td>na</td>
</tr>
<tr>
<td>FAD Max stance (mm)</td>
<td>4.4</td>
<td>6.8</td>
<td>8.4</td>
<td>7.2</td>
<td>11.3</td>
<td>7.8</td>
<td>0.02</td>
<td>*0.01</td>
</tr>
<tr>
<td>KE Moment (%BW*Ht)</td>
<td>-1.9</td>
<td>0.4</td>
<td>-1.5</td>
<td>0.6</td>
<td>-1.5</td>
<td>0.5</td>
<td>0.02</td>
<td>*0.03, *0.04</td>
</tr>
<tr>
<td>KF Moment (%BW*Ht)</td>
<td>2.6</td>
<td>1.3</td>
<td>3.5</td>
<td>1.4</td>
<td>2.8</td>
<td>1.0</td>
<td>0.08</td>
<td>na</td>
</tr>
<tr>
<td>KA Moment (%BW*Ht)</td>
<td>-2.9</td>
<td>0.7</td>
<td>-3.4</td>
<td>0.6</td>
<td>-3.1</td>
<td>0.8</td>
<td>0.07</td>
<td>na</td>
</tr>
<tr>
<td>Hip ROM (°)</td>
<td>42.9</td>
<td>5.1</td>
<td>44.5</td>
<td>4.2</td>
<td>45.4</td>
<td>5.5</td>
<td>0.27</td>
<td>na</td>
</tr>
<tr>
<td>Ankle ROM (°)</td>
<td>26.1</td>
<td>4.0</td>
<td>26.1</td>
<td>3.9</td>
<td>28.3</td>
<td>4.7</td>
<td>0.2</td>
<td>na</td>
</tr>
<tr>
<td>HF Moment (%BW*Ht)</td>
<td>-3.8</td>
<td>0.7</td>
<td>-4.3</td>
<td>0.9</td>
<td>-4.0</td>
<td>1.3</td>
<td>0.26</td>
<td>na</td>
</tr>
<tr>
<td>HE Moment (%BW*Ht)</td>
<td>4.5</td>
<td>1.0</td>
<td>4.5</td>
<td>1.1</td>
<td>4.0</td>
<td>1.3</td>
<td>0.25</td>
<td>na</td>
</tr>
<tr>
<td>ADF Moment (%BW*Ht)</td>
<td>-9.3</td>
<td>0.7</td>
<td>-9.1</td>
<td>0.7</td>
<td>-8.9</td>
<td>1.3</td>
<td>0.40</td>
<td>na</td>
</tr>
</tbody>
</table>

Figure 4.4. Group mean knee kinematics and kinetics of interest. Arrows indicate discrete variables of interest. P-values noted where main comparison of group indicated p≤0.05.
Response to 30MTW

The 30MTW elicited knee extensor fatigue as defined by a significant drop in muscle torque or power from baseline (Figure 4.5). OLO fatigued in all modes and speeds except concentric contractions at 90°·s⁻¹ (all p<0.02), OHI only fatigued in eccentric contractions at 270°·s⁻¹ (p = 0.03), and Y fatigued across all contraction modes and speeds (all p<0.05, Figure 4.5). OLO fatigued more than OHI in concentric contractions at 270°·s⁻¹ (post-hoc p = 0.004, Figure 4.5). During terminal swing, OHI displayed a decrease in quadriceps:hamstrings activation, while OLO displayed the opposite change (post-hoc p = 0.05, Figure 4.6).

During terminal swing, OLO had decreased net quadriceps and flexor activation that was ~3-10x larger than that of OHI and Y (post-hoc p<0.01 for both comparisons).
and during early stance OLO had decreased net quadriceps and flexor activity that was ~3x greater than OHI (post-hoc p = 0.03).

Changes in knee kinematics in response to the 30MTW were not different between groups (Table 4.3). All kinematic changes within groups were <1.5° or <1 mm. Knee flexion moment changed differently between groups (Table 4.3) with OHI displaying a small decrease and Y displaying a small increase in response to the 30MTW (post-hoc p = 0.03).

Table 4.3. Changes in knee kinematics and kinetics in response to the 30MTW. KF: knee flexion; KA: knee adduction; KER: knee external rotation; FAD: femoral anterior displacement; KE: knee extension; HF: hip flexion; HE: hip extension; ADF: ankle dorsiflexion. Where significant group effects were found, post-hoc p-values are reported. * indicates young different from highly active.

<table>
<thead>
<tr>
<th></th>
<th>Young Mean</th>
<th>Young SD</th>
<th>Older Highly Active Mean</th>
<th>Older Highly Active SD</th>
<th>Older Less Active Mean</th>
<th>Older Less Active SD</th>
<th>p-value</th>
<th>post-hoc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stride length (m)</td>
<td>0.00</td>
<td>0.04</td>
<td>0.00</td>
<td>0.02</td>
<td>0.01</td>
<td>0.04</td>
<td>0.34</td>
<td>na</td>
</tr>
<tr>
<td>KF Heel strike (°)</td>
<td>0.2</td>
<td>2.5</td>
<td>1.1</td>
<td>1.9</td>
<td>1.1</td>
<td>1.7</td>
<td>0.31</td>
<td>na</td>
</tr>
<tr>
<td>KF Midstance (°)</td>
<td>0.0</td>
<td>1.9</td>
<td>0.0</td>
<td>2.0</td>
<td>0.5</td>
<td>1.7</td>
<td>0.61</td>
<td>na</td>
</tr>
<tr>
<td>KP ROM (°)</td>
<td>-0.4</td>
<td>1.5</td>
<td>-1.4</td>
<td>2.7</td>
<td>-1.1</td>
<td>1.8</td>
<td>0.29</td>
<td>na</td>
</tr>
<tr>
<td>KA Midstance (°)</td>
<td>-0.3</td>
<td>1.0</td>
<td>-0.4</td>
<td>1.3</td>
<td>-0.5</td>
<td>1.3</td>
<td>0.9</td>
<td>na</td>
</tr>
<tr>
<td>KER Stance average (°)</td>
<td>0.5</td>
<td>2.8</td>
<td>0.8</td>
<td>2.5</td>
<td>0.8</td>
<td>3.2</td>
<td>0.94</td>
<td>na</td>
</tr>
<tr>
<td>FAD Heel strike (mm)</td>
<td>-0.8</td>
<td>3.8</td>
<td>0.4</td>
<td>4.0</td>
<td>-0.3</td>
<td>5.0</td>
<td>0.69</td>
<td>na</td>
</tr>
<tr>
<td>FAD GRF1 (mm)</td>
<td>-0.6</td>
<td>3.7</td>
<td>0.0</td>
<td>4.2</td>
<td>-0.3</td>
<td>4.7</td>
<td>0.88</td>
<td>na</td>
</tr>
<tr>
<td>FAD Stance average (mm)</td>
<td>-0.7</td>
<td>3.7</td>
<td>-0.4</td>
<td>3.8</td>
<td>0.1</td>
<td>3.9</td>
<td>0.83</td>
<td>na</td>
</tr>
<tr>
<td>FAD Max stance (mm)</td>
<td>-0.1</td>
<td>3.9</td>
<td>0.2</td>
<td>4.4</td>
<td>0.3</td>
<td>3.8</td>
<td>0.64</td>
<td>na</td>
</tr>
<tr>
<td>KE Moment (%BW*Ht)</td>
<td>-0.2</td>
<td>0.3</td>
<td>0.0</td>
<td>0.4</td>
<td>-0.1</td>
<td>0.2</td>
<td>0.39</td>
<td>na</td>
</tr>
<tr>
<td>KP Moment (%BW*Ht)</td>
<td>0.2</td>
<td>0.4</td>
<td>-0.1</td>
<td>0.3</td>
<td>0.0</td>
<td>0.5</td>
<td>0.03</td>
<td>*0.03</td>
</tr>
<tr>
<td>KA Moment (%BW*Ht)</td>
<td>-0.1</td>
<td>0.2</td>
<td>-0.1</td>
<td>0.3</td>
<td>-0.1</td>
<td>0.3</td>
<td>0.64</td>
<td>na</td>
</tr>
<tr>
<td>Hip ROM (°)</td>
<td>1.0</td>
<td>1.9</td>
<td>0.7</td>
<td>1.2</td>
<td>0.9</td>
<td>1.6</td>
<td>0.82</td>
<td>na</td>
</tr>
<tr>
<td>Ankle ROM (°)</td>
<td>0.5</td>
<td>1.7</td>
<td>0.1</td>
<td>1.7</td>
<td>0.3</td>
<td>1.7</td>
<td>0.74</td>
<td>na</td>
</tr>
<tr>
<td>HF Moment (%BW*Ht)</td>
<td>-0.1</td>
<td>0.5</td>
<td>0.0</td>
<td>0.6</td>
<td>-0.1</td>
<td>0.5</td>
<td>0.86</td>
<td>na</td>
</tr>
<tr>
<td>HE Moment (%BW*Ht)</td>
<td>0.1</td>
<td>0.4</td>
<td>-0.1</td>
<td>0.6</td>
<td>-0.2</td>
<td>0.2</td>
<td>0.06</td>
<td>na</td>
</tr>
<tr>
<td>ADF Moment (%BW*Ht)</td>
<td>0.0</td>
<td>0.3</td>
<td>0.2</td>
<td>0.3</td>
<td>0.2</td>
<td>0.4</td>
<td>0.19</td>
<td>na</td>
</tr>
</tbody>
</table>
Discussion

The aim of the current study was to determine if high levels of physical activity can minimize differences in knee function between young and older adults. Specifically, we sought to examine the separate effects of age and physical activity on knee extensor muscle function, knee muscle co-activation, and knee mechanics during gait, as well as the response of these measures to a bout of moderate intensity exercise. We hypothesized that less active older adults would differ from highly active older adults and young adults in magnitude of changes in knee extensor muscle function, knee muscle co-activation, and knee mechanics in response to a bout of exercise. The results of the study indicate that there is a benefit of physical activity in older age for mechanical risk factors for knee OA, particularly anterior femoral translation, muscle co-activation during midstance, and knee extensor fatigue.

Both groups of older adults were weaker during concentric knee extension compared to young adults at baseline. This difference was most pronounced at the highest contraction velocity ($270^\circ \cdot s^{-1}$) which agrees with previous findings that older adults have the largest age-related declines in muscle power at high velocities. The lack of difference in eccentric power between the study groups agrees with a previous work that identified a preservation of eccentric relative to concentric muscle function with age. The current study indicated that the less active older adults had greater quadriceps:hamstrings activation during midstance compared to the other study groups at baseline. This pattern may imply that the less active older adults activate both the quadriceps and hamstrings to control sagittal knee position while the young and highly active older adults predominantly activate their hamstrings. While this difference
between groups was only identified during midstance, previous studies have also identified increased co-activation across the knee in older compared to young adults.\textsuperscript{26-28} Greater co-activation could lead to higher compressive loads in the knee during midstance in the less active older adults compared to the young and highly active older adults, especially if combined with greater joint moments. As the joint loading implied from external joint moments does not include the forces contributed by muscle activity, the combination of trends toward age-related differences in peak knee moments and greater co-activation could increase contact forces in the knee in less active older adults.

Also at baseline, less active older adults had greater anterior displacement of the femur relative to the tibia compared to young adults (but not highly active older adults). Greater anterior femoral displacement has been associated with increased thinning of posterior tibial cartilage in individuals post-ACL rupture, suggesting that the offloading of habitually loaded cartilage is detrimental.\textsuperscript{84} In studies of healthy young and older adults as well as older adults with varying degrees of knee OA, anterior femoral displacement appeared to increase in a stepwise fashion from young asymptomatic adults to older asymptomatic adults and older adults with knee OA.\textsuperscript{20,176} Together with these previous findings, the current study suggests that less active older adults may be progressing along a trajectory towards knee OA initiation. Other measures of knee mechanics were largely similar between groups both at baseline and after the 30MTW, in agreement with our recent meta-analysis, which demonstrated that there is not yet a consensus on how knee mechanics differ between young and older adults.\textsuperscript{175}

In contrast to its impact on gait mechanics, the 30MTW did induce knee extensor fatigue in the less active older and young adult groups (Figure 4.5). However, this fatigue
did not correspond to group-wise differences in the gait response to the bout of exercise. Individuals in this study may have enough knee extensor power functional reserve that the magnitude of fatigue induced was not enough to affect walking mechanics. Based on limited literature, older adults may use ~25% of the maximal capacity of their knee extensor power during gait. Assuming the older adults in the current study had the same relative effort as those in the literature, the ~20% decrease in power for the less active older adults would still leave a ~55% reserve of knee extensor function for maintaining gait. Older adults who are less functional than the current cohort likely would not have the same baseline functional reserve and could therefore surpass a relative effort threshold where knee mechanics become altered in response to daily physical activity.

The current study has some limitations. While our less active older adults participated in significantly less physical activity compared to the highly active older and young adults and would be classified as not meeting physical activity guidelines, they were still quite high-functioning. As the focus of the current study was to examine the impact of age and physical activity on knee outcomes, we chose to strictly control for BMI, health conditions, history of musculoskeletal injury, and joint pain as these are known risk factors or indicators of knee OA. Average older adults would likely present with multiple risk factors that could increase both mechanical and biological risk factors for knee OA.

The less active older adults in this study may present a “best case scenario” for biomechanical knee OA risk factors as they were selected based on only possessing the risk factors of age and below-recommended physical activity levels. The results of this
study present a model of age-related mechanical knee OA risk factors that may occur independent of systemic comorbidities. Adding common comorbidities such as higher BMI, metabolic pathology, or heart disease on top of age and low physical activity levels would be expected to exacerbate the greater baseline anterior femoral translation and increased knee extensor fatigue observed in our less active older adults. The current findings suggest that age and low physical activity have a small but measureable impact on biomechanical risk factors for knee OA, independent of typical age-related comorbidities.

**Conclusions**

This study demonstrates that age and, in some cases, physical activity level can affect variables that may be indicative of the local cartilage loading environment in the knee joint (e.g., anterior displacement of the femur relative to the tibia and knee extension moment in early stance). Physical activity was protective against knee extensor fatigue in older adults, however, physical activity was not protective against lower knee extensor concentric high-velocity power at baseline. The highly-controlled participant cohorts in this study allow for discrimination of factors that could alter the loading environment for knee joint cartilage based on age or decreased physical activity alone, independent of the many age-related comorbidities that additionally alter cartilage health.
**Supplementary Table 4.1.** Baseline knee kinematics and kinetics at preferred walking speed. KF: knee flexion; KA: knee adduction; KER: knee external rotation; FAD: femoral anterior displacement; KE: knee extension; HF: hip flexion; HE: hip extension; ADF: ankle dorsiflexion. Where significant group effects were found, post-hoc p-values are reported. * indicates young different from less active, ^ indicates young different from highly active.

<table>
<thead>
<tr>
<th></th>
<th>Young Mean (SD)</th>
<th>Older Highly Active Mean (SD)</th>
<th>Older Less Active Mean (SD)</th>
<th>p-value</th>
<th>post-hoc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gait Speed (m/s)</td>
<td>1.55 (0.15)</td>
<td>1.51 (0.16)</td>
<td>1.53 (0.11)</td>
<td>0.57</td>
<td>na</td>
</tr>
<tr>
<td>Stride length (m)</td>
<td>1.57 (0.13)</td>
<td>1.78 (0.11)</td>
<td>1.53 (0.08)</td>
<td><strong>0.02</strong></td>
<td>^0.007</td>
</tr>
<tr>
<td>KF Heel strike (°)</td>
<td>5.9 (4.6)</td>
<td>5.1 (4.6)</td>
<td>6.3 (6.0)</td>
<td>0.74</td>
<td>na</td>
</tr>
<tr>
<td>KF Midstance (°)</td>
<td>21.8 (6.4)</td>
<td>23.3 (5.8)</td>
<td>23.3 (5.2)</td>
<td>0.64</td>
<td>na</td>
</tr>
<tr>
<td>KF ROM (°)</td>
<td>38.8 (3.8)</td>
<td>38.9 (4.1)</td>
<td>40.5 (3.1)</td>
<td>0.28</td>
<td>na</td>
</tr>
<tr>
<td>KA Midstance (°)</td>
<td>1.5 (2.7)</td>
<td>1.6 (3.3)</td>
<td>1.0 (3.2)</td>
<td>0.8</td>
<td>na</td>
</tr>
<tr>
<td>KER Stance average (°)</td>
<td>0.8 (3.7)</td>
<td>0.2 (4.1)</td>
<td>0.2 (3.2)</td>
<td>0.82</td>
<td>na</td>
</tr>
<tr>
<td>FAD Heel strike (mm)</td>
<td>-10.1 (6.4)</td>
<td>-5.9 (7.5)</td>
<td>-5.6 (7.1)</td>
<td>0.08</td>
<td>na</td>
</tr>
<tr>
<td>FAD GRF1 (mm)</td>
<td>0.8 (6.9)</td>
<td>4.4 (4.8)</td>
<td>5.2 (5.7)</td>
<td><strong>0.05</strong></td>
<td>*0.05</td>
</tr>
<tr>
<td>FAD Stance average (mm)</td>
<td>2.5 (4.0)</td>
<td>6.0 (4.3)</td>
<td>5.6 (5.0)</td>
<td><strong>0.03</strong></td>
<td>^0.04</td>
</tr>
<tr>
<td>FAD Max stance (mm)</td>
<td>3.8 (5.9)</td>
<td>8.4 (6.9)</td>
<td>10.3 (7.3)</td>
<td><strong>0.01</strong></td>
<td>*0.01</td>
</tr>
<tr>
<td>KE Moment (%BW*Ht)</td>
<td>-1.9 (0.6)</td>
<td>-1.5 (0.5)</td>
<td>-1.6 (0.4)</td>
<td>0.06</td>
<td>na</td>
</tr>
<tr>
<td>KA Moment (%BW*Ht)</td>
<td>3.3 (1.8)</td>
<td>3.9 (1.5)</td>
<td>3.3 (1.0)</td>
<td>0.34</td>
<td>na</td>
</tr>
<tr>
<td>Hip ROM (°)</td>
<td>44.2 (5.4)</td>
<td>45.0 (4.5)</td>
<td>46.5 (4.0)</td>
<td>0.32</td>
<td>na</td>
</tr>
<tr>
<td>Ankle ROM (°)</td>
<td>26.9 (3.8)</td>
<td>26.2 (4.3)</td>
<td>28.3 (4.7)</td>
<td>0.28</td>
<td>na</td>
</tr>
<tr>
<td>HF Moment (%BW*Ht)</td>
<td>-4.3 (0.7)</td>
<td>-4.7 (1.1)</td>
<td>-4.3 (1.1)</td>
<td>0.46</td>
<td>na</td>
</tr>
<tr>
<td>HE Moment (%BW*Ht)</td>
<td>5.0 (0.8)</td>
<td>4.8 (1.4)</td>
<td>4.3 (1.5)</td>
<td>0.22</td>
<td>na</td>
</tr>
<tr>
<td>ADF Moment (%BW*Ht)</td>
<td>-9.8 (0.7)</td>
<td>-9.3 (0.8)</td>
<td>-9.2 (1.4)</td>
<td>0.12</td>
<td>na</td>
</tr>
</tbody>
</table>
### Supplementary Table 4.2.

Changes in preferred speed knee kinematics and kinetics in response to the 30MTW. KF: knee flexion; KA: knee adduction; KER: knee external rotation; FAD: femoral anterior displacement; KE: knee extension; HF: hip flexion; HE: hip extension; ADF: ankle dorsiflexion. Where significant group effects were found, post-hoc p-values are reported. ^ indicates young different from highly active.

<table>
<thead>
<tr>
<th></th>
<th>Young Mean</th>
<th>SD</th>
<th>Older Highly Active Mean</th>
<th>SD</th>
<th>Older Less Active Mean</th>
<th>SD</th>
<th>p-value</th>
<th>post-hoc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gait Speed (m/s)</td>
<td>0.00</td>
<td>0.06</td>
<td>-0.01</td>
<td>0.05</td>
<td>0.01</td>
<td>0.09</td>
<td>0.53</td>
<td>na</td>
</tr>
<tr>
<td>Stride length (m)</td>
<td>0.01</td>
<td>0.05</td>
<td>0.01</td>
<td>0.02</td>
<td>0.03</td>
<td>0.05</td>
<td>0.23</td>
<td>na</td>
</tr>
<tr>
<td>KF Heel strike (°)</td>
<td>0.5</td>
<td>1.3</td>
<td>1.2</td>
<td>1.5</td>
<td>1.7</td>
<td>0.21</td>
<td>na</td>
<td></td>
</tr>
<tr>
<td>KF Midstance (°)</td>
<td>-0.3</td>
<td>2.1</td>
<td>-0.1</td>
<td>2.0</td>
<td>1.0</td>
<td>1.8</td>
<td>0.09</td>
<td>na</td>
</tr>
<tr>
<td>KF ROM (°)</td>
<td>-0.5</td>
<td>1.8</td>
<td>-0.8</td>
<td>2.5</td>
<td>-1.3</td>
<td>2.0</td>
<td>0.52</td>
<td>na</td>
</tr>
<tr>
<td>KA Midstance (°)</td>
<td>-0.2</td>
<td>1.4</td>
<td>-0.7</td>
<td>1.3</td>
<td>-0.4</td>
<td>1.2</td>
<td>0.58</td>
<td>na</td>
</tr>
<tr>
<td>KER Stance average (°)</td>
<td>0.7</td>
<td>3.0</td>
<td>1.1</td>
<td>2.5</td>
<td>0.5</td>
<td>3.5</td>
<td>0.77</td>
<td>na</td>
</tr>
<tr>
<td>FAD Heel strike (mm)</td>
<td>-0.3</td>
<td>5.2</td>
<td>0.1</td>
<td>3.7</td>
<td>0.4</td>
<td>4.6</td>
<td>0.89</td>
<td>na</td>
</tr>
<tr>
<td>FAD GRF1 (mm)</td>
<td>-1.9</td>
<td>4.4</td>
<td>-0.4</td>
<td>4.0</td>
<td>0.1</td>
<td>4.5</td>
<td>0.32</td>
<td>na</td>
</tr>
<tr>
<td>FAD Stance average (mm)</td>
<td>-0.9</td>
<td>3.9</td>
<td>-0.8</td>
<td>3.5</td>
<td>0.3</td>
<td>4.0</td>
<td>0.54</td>
<td>na</td>
</tr>
<tr>
<td>FAD Max stance (mm)</td>
<td>-1.2</td>
<td>4.3</td>
<td>0.0</td>
<td>3.3</td>
<td>0.3</td>
<td>4.4</td>
<td>0.46</td>
<td>na</td>
</tr>
<tr>
<td>KE Moment (%BW*Ht)</td>
<td>-0.1</td>
<td>0.5</td>
<td>-0.1</td>
<td>0.3</td>
<td>-0.1</td>
<td>0.5</td>
<td>0.95</td>
<td>na</td>
</tr>
<tr>
<td>KA Moment (%BW*Ht)</td>
<td>0.1</td>
<td>0.5</td>
<td>-0.2</td>
<td>0.4</td>
<td>0.1</td>
<td>0.5</td>
<td>0.05</td>
<td>na</td>
</tr>
<tr>
<td>KA Moment (%BW*Ht)</td>
<td>-0.1</td>
<td>0.3</td>
<td>-0.1</td>
<td>0.3</td>
<td>-0.1</td>
<td>0.4</td>
<td>0.92</td>
<td>na</td>
</tr>
<tr>
<td>Hip ROM (°)</td>
<td>1.8</td>
<td>2.5</td>
<td>0.7</td>
<td>1.0</td>
<td>2.0</td>
<td>1.9</td>
<td>0.09</td>
<td>na</td>
</tr>
<tr>
<td>Ankle ROM (°)</td>
<td>0.6</td>
<td>1.9</td>
<td>0.4</td>
<td>1.5</td>
<td>0.2</td>
<td>1.8</td>
<td>0.71</td>
<td>na</td>
</tr>
<tr>
<td>HF Moment (%BW*Ht)</td>
<td>-0.1</td>
<td>0.7</td>
<td>-0.1</td>
<td>0.5</td>
<td>-0.4</td>
<td>0.8</td>
<td>0.44</td>
<td>na</td>
</tr>
<tr>
<td>HE Moment (%BW*Ht)</td>
<td>0.2</td>
<td>0.4</td>
<td>-0.1</td>
<td>0.6</td>
<td>-0.1</td>
<td>0.4</td>
<td>0.07</td>
<td>na</td>
</tr>
<tr>
<td>ADF Moment (%BW*Ht)</td>
<td>-0.1</td>
<td>0.4</td>
<td>0.1</td>
<td>0.4</td>
<td>0.0</td>
<td>0.4</td>
<td>0.31</td>
<td>na</td>
</tr>
</tbody>
</table>
CHAPTER V
AGE RELATED DIFFERENCES IN SEGMENT COORDINATION AND ITS VARIABILITY DURING GAIT

Introduction

Declining mobility is a hallmark of aging and is often associated with age-related differences in gait mechanics.\textsuperscript{175} Differences in gait mechanics between young and older adults occur in parallel with differences in muscle function,\textsuperscript{35} sensory function,\textsuperscript{117} and musculoskeletal health,\textsuperscript{91} however, the mechanisms linking these factors are unclear. Comparing movement coordination and its variability during gait in older and young adults could elucidate the mechanisms by which systemic physiological changes ultimately affect resultant gait mechanics. Thus, determining the extent to which movement coordination differs with age, both in terms of magnitude and site of difference, may provide a window into the mechanisms behind age-related changes in gait.

Coordination patterns provide information about both the timing and magnitude of movements and represent the organization of multiple degrees of freedom into a simpler control strategy.\textsuperscript{177,178} Segment coordination encompasses both the timing and magnitude of rotations of adjacent limb segments. As a variety of positions of adjacent segments can produce the same joint angle, different individuals or cohorts could have similar joint kinematics but different segment coordination. In addition to indicating a potential change in central nervous system control, a change in segment coordination could result in altered loading of musculoskeletal tissues. Altered segment orientations, both with respect to gravity and to other segments, would require altered muscle activity...
and could cause altered joint loading. As altered joint loading is associated with age-related pathologies such as knee osteoarthritis, changes in segment coordination with age could play a role in the incidence of this disease.

In addition to the potential consequences of altered segment coordination, altered variability of segment coordination may have implications for older adult mobility and musculoskeletal health. As with other measures of coordination variability, segment coordination variability is a surrogate measure of the flexibility of the motor system. As kinematic patterns of walking can be produced with a variety of different patterns of segment motion, a reduction in segment coordination variability represents the use of a smaller variety of coordination patterns. A reduction in coordination variability could put older adults at greater risk of falls as a smaller variety of movement patterns could limit solutions to a perturbation such as an obstacle or a trip. Additionally, decreased coordination variability could result in a concentration of chronic loads in a small area of tissue which, in combination with an age-related change in segment coordination, could concentrate loads on tissues which were not adapted to this environment earlier in life.

The impact of healthy aging on movement coordination is not well described. Much of the existing literature on coordination has focused on differences in coordination due to distinct demarcations such as injured vs. uninjured runners, older adults who fall vs. those who do not, or preferred vs. imposed gait conditions. A few studies have described differences in movement coordination between older and young adults during level gait and have shown that older adult gait is less complex and potentially less flexible in response to perturbations compared to young adult gait. While
these studies suggest there is a change in coordination with age, the factors that contribute to altered coordination in older adults are not clear. There remains a need to describe the differences in movement coordination between young and older adults and to determine if age-related changes in coordination could be minimized through behavioral interventions, such as physical activity.

While older adults may have altered segment coordination and coordination variability in comparison to young adults, this difference may be exacerbated by muscle fatigue. Older adults are more susceptible to muscle fatigue than young adults, especially in high-velocity dynamic contractions such as those that occur during walking. Muscle fatigue imposes new constraints on the motor system and therefore provides an additional tool with which to test motor control adaptability and movement variability in aging. Changes in lower extremity coordination and coordination variability have been found in response to muscle fatigue in young adults. It is not known if fatigue affects coordination in a similar manner in older adults. Understanding the impact of age on coordination as well as the possibility that older adults’ increased susceptibility to muscle fatigue could further alter coordination may provide targets for fitness or rehabilitation protocols.

If there is an age-related shift in segment coordination and its variability, this manifestation of altered motor control could have negative implications for musculoskeletal and joint health. In addition to understanding if there is a relationship between age and segment coordination, it is important to determine if this relationship differs by physical activity level as this would provide a target for exercise or lifestyle interventions. Therefore, the primary aim of the current study was to determine if there is
a difference in segment coordination and its variability between young adults, highly active older adults, and less active older adults. We hypothesized that less active older adults would display different segment coordination and decreased coordination variability in comparison to young adults and highly active older adults. To determine if older adults’ increased susceptibility to muscle fatigue could result in additional changes in coordination, the secondary aim of this study was to examine the effect of a bout of exercise on lower extremity muscle fatigue and coordination. For this secondary aim, we hypothesized that there would be an effect of a bout of exercise on segment coordination and coordination variability for less active older adults but not for young adults and highly active older adults.

**Methods**

**Participants**

Three groups of participants were recruited for this study: young adults (age 21-35, recreationally active), highly active older adults (age 55-70, running ≥ 15 miles/week), and less active older adults (age 55-70, participating in ≤ three 30 minute bouts of moderate exercise/week). Prior to any study procedures being performed, all participants completed informed consent documentation. All participants were free of major musculoskeletal injury or surgical history, reported no lower extremity arthritis or joint pain, had no cardiovascular or neurological pathology, and had BMI < 30 kg/m². Physical activity was quantified using triaxial accelerometers (GT3X, Actigraph, Pensacola FL) worn at the hip for at least 5 days.
Data collection

Three dimensional gait kinematics were captured as individuals walked on a treadmill at preferred walking speed. Preferred walking speed was determined at an earlier separate visit by having participants walk 400 meters overground. If, upon treadmill speed being set to a participant’s overground walking speed, the participant indicated that this speed was uncomfortable, treadmill speed was incrementally adjusted until the participant indicated that they felt they were walking at their preferred speed. Once participants reported that the treadmill speed felt like their preferred speed, they were given a brief accommodation period to treadmill walking, and then 30 seconds of motion capture data were collected.

Kinematic data were collected at 200 Hz using an 8 camera motion capture system (Oqus, Qualisys, Göteborg, Sweden). Pelvis and right thigh, shank, and rearfoot/foot coordinate systems were calculated from a static trial using markers on the anterior and posterior superior iliac spines, greater trochanter, medial and lateral femoral epicondyles, medial and lateral malleoli, calcaneus, and 5th metatarsal. The pelvis was tracked using its anatomic markers and the thigh, shank, and rearfoot/foot were tracked with clusters of markers under rigid body assumptions. Ten consecutive strides of data were extracted and analyzed.187

After the initial 30 second data trial, participants continued to walk on the treadmill for 30 minutes. At minutes 7, 17, and 27 of the walk, treadmill grade was increased to 3% for one minute and then returned to level. This treadmill walk was meant to simulate a bout of exercise an individual may complete on a typical day. This protocol has previously been shown to induce significant knee extensor muscle fatigue in older
women.\(^{37}\) At the end of the treadmill walk, 30 seconds of kinematic data were again captured and ten consecutive strides of these data were extracted and analyzed.

**Data processing**

Kinematic data were processed using Visual 3D software (C-Motion, Germantown, MD). Segment angles for the pelvis and right thigh, shank, and rearfoot/foot were calculated with respect to the global (lab) coordinate system, lowpass filtered at 8 Hz, and normalized to 101 points for each of 10 individual strides. To extract individual strides, heel strikes were determined as minima in the vertical position of a calcaneal marker and toe-offs were determined as maxima in the vertical velocity of a calcaneal marker (similar to \(^{188}\)).

Segment coordination was calculated using a custom MATLAB vector coding program implementing functions from the CircStat circular statistics toolbox.\(^{189}\) Angle-angle plots were created for the following segment angle couples: sagittal pelvis vs. sagittal thigh, sagittal thigh vs. sagittal shank, sagittal thigh vs. transverse shank, sagittal shank vs. sagittal foot, and transverse shank vs. frontal rearfoot. Phase angles were calculated as the angle of a vector connecting consecutive data points in each angle-angle plot with respect to the right horizontal using the below equation, where \(0 \leq \theta \leq 360\) degrees and \(j\) is a percent of the ith stride.

\[
\theta_{i,j} = \tan^{-1}\left([y_{i,j+1} - y_{i,j}]/(x_{i,j+1} - x_{i,j})\right) \tag{Equation 1}
\]

Phase angles represent the segment coordination pattern, while the standard deviation represents the segment coordination variability. Phase angles describe the rotation (clockwise vs. counterclockwise) of segments relative to each other and are categorized into one of four coordination patterns: in-phase \((22.5^\circ \leq \theta < 67.5^\circ, 202.5^\circ \leq \theta\)
< 247.5°), anti-phase (112.5° ≤ θ < 157.5°, 292.5° ≤ θ < 337.5°), distal segment phase (67.5° ≤ θ < 112.5°, 247.5° ≤ θ < 292.5°), or proximal segment phase (0° ≤ θ < 22.5°, 157.5° ≤ θ < 202.5°, 337.5° ≤ θ ≤ 360°). In-phase motion represents segments of interest rotating the same direction (e.g., thigh and shank both rotating clockwise about the knee in the sagittal plane or thigh rotating clockwise about the knee in the sagittal plane while the shank rotates externally in the transverse plane). Anti-phase motion represents segments of interest rotating in opposite directions. Distal and proximal phases represent one segment rotating while the other segment is relatively stationary.

As vector coding data are directional, circular statistics were used to calculate mean phase angles as well as the standard deviation of the mean for each segment angle couple for the 10 strides from the beginning and from the end of the 30 minute treadmill walk. Segment coordination and segment coordination variability were examined during four phases of the gait cycle: terminal swing (last 15% of swing), and early, mid, and late (thirds of) stance. Segment coordination and segment coordination variability outcomes were calculated as the mean phase angle and average variability in each gait cycle phase of interest.

**Statistics**

As the measures of mean phase angles within separate phases of the gait cycle are circular data (i.e., 0° and 360° are synonymous and do not average to 180°), statistical comparisons of segment coordination were carried out with the circular equivalent of a traditional 2-way ANOVA. Mean phase angles within each gait cycle phase of interest and for each segment couple of interest were compared between groups and for a group by time interaction using a Harrison-Kanji test implemented in MATLAB using the
circ_hktest function.\cite{189} Measures of segment coordination variability are not circular data and so could be analyzed using linear statistics. Average segment coordination variability within each gait cycle of interest and for each segment couple of interest were compared between groups and for a group by time interaction using 2-way ANOVAs (SPSS version 22, IBM, Armonk, NY). Significance was set at $p<0.05$ for all comparisons.

**Results**

Participants included 19 young adults, 13 highly active older adults, and 16 less active older adults. Groups were roughly equally split between males and females. Participant characteristics, self-selected treadmill speed, and physical activity counts from accelerometry are detailed in Table 5.1. Self-selected treadmill walking speed was not significantly different between groups.

<table>
<thead>
<tr>
<th>Group</th>
<th>N (# male)</th>
<th>Age (years)</th>
<th>Height (m)</th>
<th>Mass (kg)</th>
<th>Treadmill speed (m/s)</th>
<th>Average weekly counts $(x10^3)$</th>
</tr>
</thead>
<tbody>
<tr>
<td>Young</td>
<td>19 (10)</td>
<td>27.9 (3.5)</td>
<td>1.72 (0.09)</td>
<td>70.47 (11.79)</td>
<td>1.38 (0.14)</td>
<td>2495 (802)</td>
</tr>
<tr>
<td>Older highly active</td>
<td>13 (6)</td>
<td>62.1 (3.9)</td>
<td>1.68 (0.09)</td>
<td>64.37 (11.85)</td>
<td>1.37 (0.13)</td>
<td>3356 (1274)</td>
</tr>
<tr>
<td>Older less active</td>
<td>16 (8)</td>
<td>62.5 (3.3)</td>
<td>1.70 (0.11)</td>
<td>70.24 (12.70)</td>
<td>1.31 (0.13)</td>
<td>1649 (600)</td>
</tr>
</tbody>
</table>

**Differences in segment coordination and its variability between groups**

Differences in segment coordination (Table 5.2) and coordination variability (Table 5.3) between the three groups were small and mainly occurred during terminal swing and midstance. Across the hip, there were differences between groups in the sagittal pelvis vs. sagittal thigh couple during terminal swing and midstance. During terminal swing, highly active older adults displayed an anti-phase coordination pattern while young adults and less active older adults displayed thigh-phase coordination patterns. Young adults displayed greater segment coordination variability in this couple.
compared to both older adult groups during terminal swing and compared to the highly active older adults only during midstance.

Across the knee, both sagittal thigh vs. sagittal shank and sagittal thigh vs. transverse shank couples displayed between-group differences in coordination and its variability. During midstance in the sagittal thigh vs. sagittal shank couple, highly active older adults displayed thigh-phase coordination while young adults and less active older adults displayed in-phase coordination patterns. Also for the sagittal thigh vs. sagittal shank couple, young adults displayed greater coordination variability than the highly active older adults during terminal swing. Despite significantly different mean phase angles in the sagittal thigh vs. transverse shank couple during midstance, all groups displayed thigh phase coordination patterns. Coordination variability was different for this couple during midstance, with greater variability in the young adults compared to the highly active older adults. There was a significant main effect of group for sagittal thigh vs. transverse shank coordination variability during midstance, but no inter-group post-hoc comparisons reached significance.

For the sagittal shank vs. sagittal foot and transverse shank vs. frontal rearfoot couples across the ankle, differences were seen in all gait cycle phases of interest. Groups displayed significant differences in mean phase angle during every phase of the gait cycle for the sagittal shank vs. sagittal foot couple but these differences were small and did not result in groups having different coordination patterns except during midstance. During midstance, young adults displayed shank phase motion while both older adult groups displayed in-phase motion and highly active older adults displayed greater coordination variability than both less active older adults and young adults. Also for the sagittal shank
vs. sagittal foot couple, young adults displayed greater segment coordination variability than older adults during terminal swing. For the transverse shank vs. frontal rearfoot couple young adults displayed in-phase motion while both older adult groups displayed shank phase motion during midstance and young adults displayed greater coordination variability than the less active older adults during terminal swing.

**Differential effect of a bout of exercise on coordination across groups**

There were no group by time interactions or overall effect of time on segment coordination or segment coordination variability for any gait cycle phase within any segment couple.

**Discussion**

Previous work in the fields of biomechanics and motor control suggests that there are age-related differences in coordination and coordination variability during walking gait. The aim of the current study was to determine if part of this aging effect may be due to decreased physical activity with age. To explore this aim, we analyzed segment coordination and its variability in three groups: young adults, highly active older adults, and less active older adults. Additionally, we sought to determine if less active older adults’ coordination is sensitive to bouts of exercise which may induce fatigue. The results of the current study suggest that segment coordination and segment coordination variability differ between young adults and older adults during terminal swing and midstance, regardless of older adults’ physical activity levels. Our results also suggest that segment coordination and its variability are stable across a bout of exercise, regardless of age or physical activity level.
Our results agree with previous studies which found altered movement coordination and generally less flexible movement patterns in older compared to young adults. The current findings using a vector coding technique provide measures that are directly relatable to joint kinematics, while also having a similar interpretation as previous studies employing absolute relative phase, continuous relative phase, detrended fluctuation analysis, and other nonlinear analyses. The concentration of age-related differences in terminal swing and midstance gait cycle phases suggest that older and young adults have different gait strategies during single limb support. Older adults may alter their control strategy during periods of single limb support in an attempt to preserve stability or because they have limited muscle power to control the motion of the body over one limb.

Many of the observed differences between young adults and the older adult groups occurred in pelvis vs. thigh and shank vs. foot couples, indicating that coordination about the hip and ankle differ by age. The anti-phase sagittal pelvis vs. thigh coordination observed during terminal swing observed in the highly active older adults but not young adults could result in increased hip flexion at heel strike and potentially increased hip range of motion, patterns that have previously been observed in older compared to young adults (Figure 5.1). The in-phase sagittal
shank vs. foot coordination during midstance in older adults while young adults displayed shank phase coordination could result in decreased stance phase sagittal ankle range of motion in older compared to young adults (Figure 5.2). These results add support to current hypotheses suggesting that adults increase reliance on the hip and decrease reliance on the ankle with age.\textsuperscript{18, 175} In addition to the findings of altered segment coordination in these couples and gait cycle phases, older adults displayed coinciding decreased coordination variability about the hip and ankle. In combination with altered segment coordination, these results suggest a shift in the control or coordination of movement about the hip and ankle with age.

Overall, high levels of physical activity did not appear to provide a protective effect in age-related differences in segment coordination. Of the differences in coordination or variability between groups, highly active older adults were different from young adults more frequently than were less active older adults and were responsible for the only group differences in coordination that were observed about the hip and knee.

These coordination differences may suggest that the highly active older adults in this study used a more hip dominant strategy than the young and less active older adults to position their swing limb prior to foot contact, and to control or take advantage of midstance knee flexion range of motion. Despite these apparent disadvantageous

\textbf{Figure 5.2.} Illustration of different midstance sagittal shank vs. sagittal foot coordination strategies. The young adult strategy could provide more ankle range of motion during midstance, while the older adult strategy suggests a locking of the ankle joint during this period.
differences in highly active older adults, being highly active appeared to be advantageous for coordination about the ankle during midstance. While both older adult groups displayed ankle segment coordination patterns that would suggest they were “locking” their ankle during midstance, only highly active older adults displayed greater coordination variability at this time point. This finding suggests that high levels of physical activity may allow older adults to modify some age-related changes in coordination.

Contrary to our expectations, we found no effect of a bout of exercise on segment coordination or coordination variability in any of our groups. While we expected that muscle fatigue induced by the 30 minute walking bout would alter coordination, especially in the less active older adults, this is not what we observed. In a larger study of which the current cohort is a subset, less active older adults did display greater decrements in isokinetic knee extensor power in response to this walking protocol compared to young and highly active older adults (Hafer Dissertation Chapter IV). However, this fatigue did not result in changes in coordination or coordination variability. The findings of no group x time interactions and no effect of time on coordination and coordination variability suggest that the motor system is able to maintain coordination patterns throughout bouts of exercise. Individuals generally display a preferred movement pattern during repetitive movements\textsuperscript{190} and our results suggest that the nervous system may seek to preserve this preferred pattern despite fatigue.

The results of this study provide modest evidence that movement coordination during gait changes with age. Older adults in the current study are relatively young (mean age around 62 years) and thus, compared to adults aged 70 years and over, we may
expect fewer age-related changes in gait mechanics, neuromuscular function, and mobility to have accumulated in this cohort. However, the older participants in the current study are at an age where there are rapid increases in the incidence of health conditions including osteoarthritis, as well as decreases in habitual physical activity. Examining coordination in older middle-aged adults may help determine how early we may expect mobility issues to appear and at what point in the lifespan interventions need to be targeted.

This study is one of the first to examine differences in coordination during gait by age using a vector coding analysis of segment coordination and coordination variability. This methodological approach provides a metric which is readily relatable to gait kinematics, as the inputs for segment coordination are the global segment positions which determine joint kinematics. The current results suggest coordination mechanisms by which older adults may achieve the hip and ankle kinematics that are often observed to be different from young adults. Expansion of the use of vector coding analyses across populations may help identify motor control mechanisms which coincide with or drive altered gait mechanics.

**Conclusions**

Older adults display altered segment coordination and segment coordination variability during gait as compared to young adults, regardless of habitual physical activity level. These differences in coordination and its variability appear most often during the terminal swing and midstance phases of the gait cycle. These results may suggest that older adults alter their control strategy during single-limb stance periods, either to preserve balance or out of necessity due to muscular limitations.
Table 5.2. Segment coordination phase angles in degrees. Bold p-values indicate significant difference. Post-hoc symbols: ^ indicates young different from older highly active, * indicates young different from older less active, + indicates older highly active different from older less active.

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Table 5.3. Segment coordination variability in degrees. Bold p-values indicate significant difference. Post-hoc symbols: ^ indicates young different from older highly active, * indicates young different from older less active, + indicates older highly active different from older less active.

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<td>0.43</td>
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<td>13.0 ± 7.5</td>
<td>12.6 ± 4.6</td>
<td>10.3 ± 2.0</td>
<td>9.0 ± 2.8</td>
<td>11.3 ± 4.5</td>
<td>9.7 ± 4.4</td>
<td>0.03 ^</td>
<td>0.28</td>
<td>0.89</td>
</tr>
<tr>
<td>Sagittal thigh vs. sagittal shank</td>
<td>7.6 ± 3.9</td>
<td>7.1 ± 2.5</td>
<td>6.1 ± 1.8</td>
<td>7.3 ± 4.3</td>
<td>7.5 ± 2.5</td>
<td>7.6 ± 3.3</td>
<td>0.59</td>
<td>0.70</td>
<td>0.60</td>
</tr>
<tr>
<td>Early Stance</td>
<td>5.1 ± 2.7</td>
<td>4.7 ± 2.3</td>
<td>4.0 ± 1.2</td>
<td>4.3 ± 1.4</td>
<td>4.7 ± 1.2</td>
<td>4.6 ± 1.2</td>
<td>0.29</td>
<td>0.87</td>
<td>0.84</td>
</tr>
<tr>
<td>Mid Stance</td>
<td>4.9 ± 3.2</td>
<td>3.8 ± 1.1</td>
<td>3.7 ± 0.8</td>
<td>3.8 ± 1.0</td>
<td>4.8 ± 1.6</td>
<td>4.0 ± 1.4</td>
<td>0.31</td>
<td>0.14</td>
<td>0.42</td>
</tr>
<tr>
<td>Late Stance</td>
<td>27.4 ± 10.5</td>
<td>26.9 ± 8.9</td>
<td>25.6 ± 3.4</td>
<td>23.0 ± 6.1</td>
<td>24.3 ± 8.3</td>
<td>22.2 ± 7.5</td>
<td>0.12</td>
<td>0.32</td>
<td>0.86</td>
</tr>
<tr>
<td>Sagittal thigh vs. transverse shank</td>
<td>15.1 ± 4.8</td>
<td>14.5 ± 4.5</td>
<td>16.9 ± 4.3</td>
<td>16.7 ± 4.7</td>
<td>16.3 ± 4.9</td>
<td>15.3 ± 4.7</td>
<td>0.24</td>
<td>0.52</td>
<td>0.94</td>
</tr>
<tr>
<td>Early Stance</td>
<td>8.5 ± 5.1</td>
<td>8.7 ± 4.2</td>
<td>5.9 ± 1.2</td>
<td>6.6 ± 1.8</td>
<td>8.0 ± 2.3</td>
<td>7.8 ± 2.4</td>
<td>0.03 ^</td>
<td>0.75</td>
<td>0.88</td>
</tr>
<tr>
<td>Mid Stance</td>
<td>16.6 ± 6.7</td>
<td>14.1 ± 4.3</td>
<td>13.0 ± 3.9</td>
<td>13.4 ± 3.7</td>
<td>14.7 ± 3.7</td>
<td>12.6 ± 3.9</td>
<td>0.14</td>
<td>0.15</td>
<td>0.43</td>
</tr>
<tr>
<td>Late Stance</td>
<td>13.2 ± 6.8</td>
<td>13.4 ± 5.0</td>
<td>10.6 ± 4.8</td>
<td>10.0 ± 4.0</td>
<td>10.9 ± 4.3</td>
<td>9.0 ± 4.0</td>
<td>0.01 **</td>
<td>0.50</td>
<td>0.70</td>
</tr>
<tr>
<td>Sagittal shank vs. sagittal foot</td>
<td>8.1 ± 4.4</td>
<td>7.4 ± 3.9</td>
<td>7.4 ± 4.3</td>
<td>8.7 ± 6.6</td>
<td>6.6 ± 3.1</td>
<td>7.0 ± 5.2</td>
<td>0.55</td>
<td>0.74</td>
<td>0.68</td>
</tr>
<tr>
<td>Early Stance</td>
<td>11.1 ± 5.9</td>
<td>11.3 ± 5.5</td>
<td>16.1 ± 8.6</td>
<td>14.6 ± 6.7</td>
<td>9.6 ± 4.9</td>
<td>8.7 ± 4.8</td>
<td>0.001 ^+</td>
<td>0.57</td>
<td>0.84</td>
</tr>
<tr>
<td>Mid Stance</td>
<td>4.8 ± 4.2</td>
<td>3.7 ± 1.3</td>
<td>3.5 ± 1.2</td>
<td>3.6 ± 1.6</td>
<td>3.4 ± 0.9</td>
<td>2.9 ± 0.9</td>
<td>0.09</td>
<td>0.28</td>
<td>0.51</td>
</tr>
<tr>
<td>Late Stance</td>
<td>34.0 ± 11.4</td>
<td>36.3 ± 12.4</td>
<td>30.5 ± 9.1</td>
<td>29.8 ± 9.1</td>
<td>31.2 ± 10.5</td>
<td>26.7 ± 9.2</td>
<td>0.04 *</td>
<td>0.67</td>
<td>0.42</td>
</tr>
<tr>
<td>Transverse shank vs. frontal rearfoot</td>
<td>24.1 ± 8.2</td>
<td>23.8 ± 7.9</td>
<td>27.6 ± 5.4</td>
<td>25.8 ± 5.9</td>
<td>27.5 ± 10.7</td>
<td>24.7 ± 8.5</td>
<td>0.35</td>
<td>0.32</td>
<td>0.81</td>
</tr>
<tr>
<td>Early Stance</td>
<td>34.7 ± 8.4</td>
<td>32.4 ± 9.1</td>
<td>35.8 ± 10.6</td>
<td>34.3 ± 12.3</td>
<td>37.4 ± 13.1</td>
<td>35.6 ± 14.5</td>
<td>0.55</td>
<td>0.43</td>
<td>0.99</td>
</tr>
<tr>
<td>Mid Stance</td>
<td>21.5 ± 7.9</td>
<td>21.2 ± 4.8</td>
<td>19.5 ± 7.4</td>
<td>20.5 ± 6.2</td>
<td>19.8 ± 6.9</td>
<td>18.1 ± 6.3</td>
<td>0.33</td>
<td>0.80</td>
<td>0.72</td>
</tr>
</tbody>
</table>
CHAPTER VI

DO AGE AND PHYSICAL ACTIVITY IMPACT GAIT AND MUSCLE FUNCTION SIMILARLY IN MALES AND FEMALES?

Introduction

Aging is associated with deteriorations in muscle physiology and neuromuscular function which may ultimately result in age-related changes in locomotion or mobility. There are well documented decrements in older compared with young adults in muscle torque and power,\textsuperscript{30} muscle fatigue in response to dynamic muscle contractions,\textsuperscript{38} and muscle activation patterns during functional activities.\textsuperscript{26} There is significant interest in understanding these physiological and neuromuscular alterations as they may contribute to age-related changes in gait, mobility, and of chronic musculoskeletal pathology, such as osteoarthritis (OA). Further, there is preliminary evidence to suggest that age-related changes in muscle physiology\textsuperscript{51,191} and gait mechanics\textsuperscript{50} differ in males and females. Sex-specific differences in aging could help explain differences in musculoskeletal pathology, including the higher rates of knee OA in older females compared to their male counterparts.\textsuperscript{4} As changes in gait mechanics may be a risk factor for OA, differing OA incidence by sex may be due to sex-specific differences in the impact of age on muscle function and gait mechanics.

Differences in muscle function between the sexes have been reported in both young and older adults. Previous work has demonstrated negligible\textsuperscript{140,192} to significant\textsuperscript{30,51,193-195} differences in muscle function between males and females in both young and older adults, often demarcated by the muscle group being examined. In particular, the function of muscles which are responsible for propulsion during locomotion\textsuperscript{98} may
decline in a sex-specific fashion as knee extensor strength and power declines appear to be more pronounced in females as compared to males.\textsuperscript{38, 51, 54, 150} Given the evidence of sex differences in changes in muscle torque and power with age, sex may also differentially impact the previously documented age related increase in high-velocity muscle fatigue.\textsuperscript{138}

Older adults of both sexes display greater muscle fatigue during high-velocity contractions than young adults.\textsuperscript{38, 138} However, some studies suggest that older females are more susceptible to high-velocity muscle fatigue,\textsuperscript{39} while others suggest that there is no difference in high-velocity fatigue between older males and females.\textsuperscript{196} The limited number of studies on this topic that have compared the sexes\textsuperscript{197} makes it difficult to draw conclusions about a definite sex-specific difference in high-velocity muscle fatigue. In addition, comparisons of aging muscle function may be confounded by a differential effect of physical activity or sedentary behavior in males and females.\textsuperscript{198}

Females may have larger declines in muscle function due to lower moderate to vigorous physical activity participation compared to older males.\textsuperscript{41} Alternatively, older females may not realize the same benefits as older males from resistance\textsuperscript{160, 161} or endurance\textsuperscript{162} training or may be more sensitive to the effects of reduced physical activity.\textsuperscript{54} The potential disadvantage of female sex on muscle function and the physiological response of muscle to exercise training could help explain the increased incidence of OA in older females as reduced knee extensor strength is a risk factor for knee OA.\textsuperscript{52} Additionally, knee OA risk could be affected by sex-specific interactions between age and physical activity in muscle torque, power, and fatigue as these may
affect older adults’ gait function and joint mechanics, as well as the sensitivity of gait to fluctuations in daily activity.

Older adults display altered gait mechanics compared to young adults, especially at the hip and ankle. Few studies have compared gait mechanics between males and females within an age group but there may be sex-specific differences in both young and older adults. Differences in gait between males and females could be affected by physical activity levels, particularly if there is a sex-specific impact of physical activity on muscle function across the lifespan. If there are interactions between age, sex, and physical activity level in gait mechanics, this may help explain the higher incidence of knee OA in females compared to males. Understanding these interactions is important for determining if different recommendations are needed for males and females to maintain mobility and joint health throughout the lifespan.

The aim of the current study was to explore the effects of age and physical activity on gait mechanics and knee extensor muscle torque, power, and fatigue in males and females. To test for a sex-specific effect of physical activity on gait and knee extensor function, we compared highly active and less active older adults. In a separate analysis, we examined the sex-specific effects of age on gait and knee extensor function by comparing young and older adults who were matched for physical activity level. We hypothesized that there would be differences by sex as well as interactions between sex and either physical activity or age in gait and knee extensor function outcomes.
Methods

Participants

Highly active older adults (55-70 years, running at least an average of 15 miles/week), less active older adults (55-70 years, participating in no more than three 30 minute bouts of moderate exercise per week), and young adults (21-35 years, recreationally active) were recruited for this study. All groups included 10 male and 10 female participants. Additional inclusion criteria were BMI < 30 kg·m⁻² and no history of significant musculoskeletal injury, cardiovascular or neurological pathology, or chronic pain. All participants completed informed consent procedures as approved by the institutional review board before completing any study procedures.

The first analysis included the highly and less active older adults to examine the sex-specific impact of physical activity independent of age. The second analysis included the young adults and a physical activity matched older cohort to examine the sex-specific impact of age independent of physical activity. For the second analysis, the physical activity matched older cohort was created by pooling all older adults and selecting 20 older participants (10 female, 10 male) who were closest to the average physical activity levels of the young females and males.

Study design

All participants completed two study visits at least 7 days apart. At the first study visit, participants were assigned activity monitors, completed a 400 meter walk to determine preferred walking speed, and performed a strength testing habituation session. The second visit included overground gait analysis and knee extensor torque and power testing before and after a 30 minute treadmill walk (30MTW, Figure 6.1).
Physical activity assessment

All participants wore accelerometers (GT3X, Actigraph, Pensacola, FL) at the hip for at least 5 days (including at least one weekend day). Weekly time spent in moderate-to-vigorous physical activity\textsuperscript{167} and activity counts were determined for all participants.

Gait analysis

Gait analysis was completed as participants walked overground at 1.4 m·s\textsuperscript{-1}. Joint kinematics and kinetics of each participant’s right leg were calculated from at least 3 acceptable trials. A trial was considered acceptable if the participant walked at the set speed (+/- 5%) and struck a force plate cleanly with their right foot without visible evidence of targeting. Kinematic data were collected at 200 Hz using an 11-camera motion capture system (Oqus, Qualisys, Goteborg, Sweden). Kinetic data were collected at 2000 Hz by a force plate mounted flush with the walkway (AMTI, Watertown, MA).

Thigh and shank segments were modeled using the Point Cluster Technique\textsuperscript{96} and were tracked using clusters of 10 and 7 markers, respectively. Anatomic markers on the medial and lateral femoral epicondyles and tibial plateau were used to define the knee joint center and markers on the medial and lateral malleoli were used to define the ankle joint center. The hip joint center was defined using a regression equation based on the positions of anatomic markers on the anterior and posterior superior iliac spines and iliac crests, and the pelvis was tracked using these same markers. The foot was tracked using two heel markers and a marker on the 5\textsuperscript{th} metatarsal head. Before calculating gait kinematics and kinetics, marker data were filtered with an 8 Hz low-pass Butterworth
filter and force data were filtered with a 15 Hz low-pass Butterworth filter. Externally-referenced joint moments were calculated using inverse dynamics. Kinematic and kinetic outcome variables included sagittal plane hip, knee, and ankle mechanics. Kinematics included angles at heel strike, select peak angles, and joint ranges of motion. Kinetics included peak joint moments.

**Strength testing**

Isometric torque (Nm·kg⁻¹) as well as high-velocity concentric and eccentric isokinetic knee extensor power (W·kg⁻¹) at 270°·s⁻¹ were collected before and after the 30 minute treadmill walk (Figure 6.1). Order of strength testing was randomized such that some participants completed isometric testing first while others completed dynamic testing first. Concentric and eccentric power were collected in a single motion to ensure full muscle activation during eccentric contractions. Isometric repetitions consisted of 5 seconds of contraction followed by 5 seconds of rest. Isometric strength was collected with the knee flexed 60° relative to neutral and isokinetic power was collected across 70° of knee motion (90-20° knee flexion relative to neutral). Outcome measures from strength testing were peak isometric torque and peak concentric and eccentric power.

**30 minute treadmill walk**

After initial gait and strength testing, all participants performed the 30MTW. Walking speed was initially set as the speed at which participants completed the 400 meter walk during visit 1. If a participant indicated that this speed did not feel like their preferred speed on the treadmill, speed was adjusted in increments of 0.1 mph until the participant indicated the speed felt “normal.” During the 30MTW, treadmill incline was increased to 3% at minutes 7, 17, and 27 for a single minute and then returned to 0%
grade. This protocol was designed to mimic a 30 minute bout of walking exercise an individual may complete during a typical day and has previously been shown to induce knee extensor fatigue in older women.37

Statistics

Two-way ANOVAs were used to test for the effects of sex and physical activity (Analysis 1) or sex and age (Analysis 2) with significance set at p≤0.05. Primary outcome variables included gait kinematics and kinetics as well as knee extensor strength and power at baseline. Additionally, we examined the change in the primary outcome variables (post-30MTW – pre-30MTW) in response to the 30MTW. Note that for kinematic and kinetic variables that have a negative convention (ankle plantar flexion angle; hip flexion, knee extension, and ankle dorsiflexion moments), a negative change indicates an increase in this variable, while a positive change indicates a decrease.

Results

Group characteristics are displayed in Table 6.1. Groups for each analysis were well matched in factors that could confound the results of the analyses (e.g., preferred walking speed, age within Analysis 1, physical activity level within Analysis 2) with the exceptions that males were taller and had greater body mass than females and older highly active females had lower body mass than older less active females.
Table 6.1. Group characteristics, Mean (SD). PWS: preferred walking speed, PA: physical activity, MVPA: average weekly moderate-to-vigorous PA. Counts: average weekly physical activity counts. Older highly and less active cohorts were used in Analysis 1, Young and Older PA-matched cohorts were used in Analysis 2. * indicates value different from other cohort of same sex within analysis group. There were no differences in physical activity variables between age- or PA-matched cohorts within analysis groups.

<table>
<thead>
<tr>
<th></th>
<th>Older highly active</th>
<th>Older less active</th>
<th>Young</th>
<th>Older PA-matched</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
<td>Female</td>
</tr>
<tr>
<td>Age (years)</td>
<td>62.9 (4.0)</td>
<td>60.8 (4.0)</td>
<td>63.9 (3.3)</td>
<td>61.8 (3.1)</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.8 (0.1)</td>
<td>1.6 (0.1)</td>
<td>1.8 (0.1)</td>
<td>1.6 (0.1)</td>
</tr>
<tr>
<td>Mass (kg)</td>
<td>74.1 (8.2)</td>
<td>54.1 (7.7) *</td>
<td>77.0 (11.0)</td>
<td>62.8 (7.3) *</td>
</tr>
<tr>
<td>PWS (m/s)</td>
<td>1.39 (0.13)</td>
<td>1.32 (0.11)</td>
<td>1.35 (0.15)</td>
<td>1.34 (0.10)</td>
</tr>
<tr>
<td>MVPA (min)</td>
<td>383 (117) *</td>
<td>555 (257) *</td>
<td>161 (103) *</td>
<td>135 (121) *</td>
</tr>
<tr>
<td>Counts x10^3</td>
<td>2916 (753) *</td>
<td>3722 (1345) *</td>
<td>1552 (570) *</td>
<td>1457 (719) *</td>
</tr>
</tbody>
</table>

Analysis 1: Sex and physical activity level in older adults

There were very few differences in gait mechanics either at baseline or in response to the 30MTW between older males and females with lower and high activity levels. At baseline, males displayed longer stride lengths (1.50 vs. 1.41 m), greater sagittal plane knee range of motion during stance (41.3 vs. 37.7°) as well as smaller hip extension moments (3.7 vs. 4.7 %BW·Ht) compared to females (Table 6.2). There was also a PA by sex interaction in hip extension moments (Figure 6.2A, Table 6.2) where less active males had lower moments compared to less active females while more active males and females were not different. After the 30MTW there was a significant PA by sex interaction in the change in sagittal knee range of motion where highly active males and less active females displayed decreases in ROM while highly active females and less active males did not (Figure 6.2C, Supplementary Table 6.1).
Table 6.2. Baseline gait kinematics for Analysis 1, Mean (SD). Bold p-values indicate significant difference. HF: hip flexion, KF: knee flexion, ADF: ankle dorsiflexion, PF: plantar flexion, HE: hip extension, KE: knee extension.

<table>
<thead>
<tr>
<th></th>
<th>Older highly active</th>
<th>Older less active</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Stride length (m)</td>
<td>1.50 (0.08)</td>
<td>1.39 (0.08)</td>
<td>1.50 (0.07)</td>
</tr>
<tr>
<td>HF heel strike (°)</td>
<td>34.4 (5.1)</td>
<td>37.8 (5.4)</td>
<td>36.2 (5.2)</td>
</tr>
<tr>
<td>Hip ROM (°)</td>
<td>43.8 (4.3)</td>
<td>45.2 (4.1)</td>
<td>43.3 (3.6)</td>
</tr>
<tr>
<td>KF heel strike (°)</td>
<td>4.4 (4.1)</td>
<td>5.5 (5.1)</td>
<td>6.0 (5.6)</td>
</tr>
<tr>
<td>KF peak stance (°)</td>
<td>23.7 (6.0)</td>
<td>21.9 (6.2)</td>
<td>23.9 (4.7)</td>
</tr>
<tr>
<td>Knee ROM (°)</td>
<td>41.3 (2.9)</td>
<td>36.0 (3.3)</td>
<td>41.4 (3.2)</td>
</tr>
<tr>
<td>ADF heel strike (°)</td>
<td>5.2 (2.2)</td>
<td>2.2 (3.4)</td>
<td>4.0 (4.3)</td>
</tr>
<tr>
<td>Ankle peak PF (°)</td>
<td>-15.9 (2.2)</td>
<td>-20.0 (7.3)</td>
<td>-18.9 (6.7)</td>
</tr>
<tr>
<td>Ankle ROM (°)</td>
<td>25.6 (3.3)</td>
<td>26.6 (4.6)</td>
<td>28.1 (5.5)</td>
</tr>
<tr>
<td>HF moment (%BW·Ht)</td>
<td>-4.3 (1.0)</td>
<td>-4.2 (0.9)</td>
<td>-4.3 (1.6)</td>
</tr>
<tr>
<td>HE moment (%BW·Ht)</td>
<td>4.4 (0.9)</td>
<td>4.5 (1.4)</td>
<td>3.0 (0.8)</td>
</tr>
<tr>
<td>KE moment (%BW·Ht)</td>
<td>-1.7 (0.5)</td>
<td>-1.3 (0.6)</td>
<td>-1.6 (0.5)</td>
</tr>
<tr>
<td>KF moment (%BW·Ht)</td>
<td>3.7 (1.7)</td>
<td>3.3 (1.1)</td>
<td>2.9 (1.0)</td>
</tr>
<tr>
<td>ADF moment (%BW·Ht)</td>
<td>-8.9 (0.7)</td>
<td>-9.3 (0.7)</td>
<td>-8.5 (1.6)</td>
</tr>
</tbody>
</table>

Knee extensor muscle function at baseline did not differ by physical activity level or by sex. However, there was a PA by sex interaction in knee extensor power during concentric contractions at 270°·s⁻¹ (Figure 6.2B, Table 6.3), where less active males produced more power relative to body mass than less active females but highly active males and females were not different. After the 30MTW, highly active adults showed a preservation while less active adults displayed a decrease in concentric knee extensor power (-0.7% vs. -20.7% change in power for highly vs. less active older adults). Additionally, there was a PA by sex interaction in the change in isometric torque (Figure 6.2D, Table 6.3) where less active males showed a larger decline than less active females but highly active males and females showed no difference in decline in torque.
Table 6.3. Analysis 1 baseline and % change values for knee extensor isometric torque and power at 270 °s⁻¹. Mean (SD). Bold p-values indicate significant difference.

<table>
<thead>
<tr>
<th></th>
<th>Older highly active</th>
<th>Older less active</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Isometric torque (Nm/kg)</td>
<td>0.26 (0.07)</td>
<td>0.26 (0.06)</td>
<td>0.27 (0.04)</td>
</tr>
<tr>
<td>Concentric power (W/kg)</td>
<td>0.45 (0.18)</td>
<td>0.48 (0.11)</td>
<td>0.55 (0.14)</td>
</tr>
<tr>
<td>Eccentric power (W/kg)</td>
<td>1.50 (0.41)</td>
<td>1.30 (0.43)</td>
<td>1.40 (0.31)</td>
</tr>
<tr>
<td>Isometric torque (%Δ)</td>
<td>0.4 (15.0)</td>
<td>-4.5 (5.8)</td>
<td>-10.7 (7.6)</td>
</tr>
<tr>
<td>Concentric power (%Δ)</td>
<td>2.6 (23.8)</td>
<td>-4.0 (18.8)</td>
<td>-22.3 (9.3)</td>
</tr>
<tr>
<td>Eccentric power (%Δ)</td>
<td>-4.9 (11.4)</td>
<td>-3.3 (25.3)</td>
<td>-14.2 (11.2)</td>
</tr>
</tbody>
</table>

Analysis 2: Sex and age in adults matched for PA level

At baseline for both ages, males had longer stride lengths and also displayed some differences in hip and knee mechanics compared to females (Table 6.4). Females were more flexed at the hip at heel strike compared to males (38.9 vs. 33.5° in females vs. males) and had a smaller stance phase knee range of motion compared to males (37.0 vs. 40.7°). Additionally, females had smaller knee extension moments compared to males...
There was an age by sex interaction in knee flexion angle at heel strike (Figure 6.3A, Table 6.4), where young females were more flexed than young males but older males and females did not differ. There was also an age by sex interaction in the peak hip extension moment (Figure 6.3B, Table 6.4), where young males and older females displayed larger moments than their opposite-sex peers. Finally, there were age differences in knee moments with older adults displaying smaller extension moments (-1.4 vs. -1.9 %BW·Ht) and larger knee flexion moments (3.6 vs. 2.9 %BW·Ht) compared to young adults.

In response to the 30MTW, males displayed a small decrease in knee flexion range of motion while females did not (-1.4 vs. -0.2°). Also, older adults displayed a small decrease in knee flexion moments (-0.1 %BW·Ht) and ankle dorsiflexion moments (+0.2 %BW·Ht) while young adults displayed a small increase in knee flexion moments (+0.2 %BW·Ht) and no change in ankle dorsiflexion moments (+0.0 %BW·Ht) in response to the 30MTW (Supplementary Table 6.2).

<table>
<thead>
<tr>
<th></th>
<th>Young Male</th>
<th>Young Female</th>
<th>Older Male</th>
<th>Older Female</th>
<th>p-values</th>
<th>Age</th>
<th>Sex</th>
<th>Age x Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stride length (m)</td>
<td>1.51 (0.06)</td>
<td>1.47 (0.06)</td>
<td>1.49 (0.08)</td>
<td>1.42 (0.08)</td>
<td>0.09</td>
<td>0.02</td>
<td>0.42</td>
<td></td>
</tr>
<tr>
<td>HF heel strike (°)</td>
<td>32.8 (3.3)</td>
<td>40.6 (7.1)</td>
<td>34.2 (4.5)</td>
<td>37.2 (5.5)</td>
<td>0.55</td>
<td>0.003</td>
<td>0.16</td>
<td></td>
</tr>
<tr>
<td>Hip ROM (°)</td>
<td>42.2 (4.6)</td>
<td>43.5 (5.7)</td>
<td>43.9 (4.3)</td>
<td>46.5 (4.7)</td>
<td>0.14</td>
<td>0.20</td>
<td>0.67</td>
<td></td>
</tr>
<tr>
<td>KF heel strike (°)</td>
<td>2.7 (3.7)</td>
<td>7.9 (4.0)</td>
<td>6.0 (3.7)</td>
<td>5.6 (5.0)</td>
<td>0.74</td>
<td>0.08</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>KF peak stance (°)</td>
<td>19.5 (3.7)</td>
<td>20.6 (6.5)</td>
<td>24.1 (6.2)</td>
<td>22.2 (6.4)</td>
<td>0.10</td>
<td>0.83</td>
<td>0.42</td>
<td></td>
</tr>
<tr>
<td>Knee ROM (°)</td>
<td>40.5 (3.6)</td>
<td>37.4 (2.8)</td>
<td>40.9 (3.1)</td>
<td>36.5 (3.2)</td>
<td>0.84</td>
<td>0.001</td>
<td>0.52</td>
<td></td>
</tr>
<tr>
<td>ADF heel strike (°)</td>
<td>4.5 (2.6)</td>
<td>6.4 (3.7)</td>
<td>4.9 (2.8)</td>
<td>3.0 (3.5)</td>
<td>0.15</td>
<td>1.00</td>
<td>0.06</td>
<td></td>
</tr>
<tr>
<td>Ankle peak PF (°)</td>
<td>-18.4 (4.0)</td>
<td>-18.3 (6.5)</td>
<td>-15.6 (36.0)</td>
<td>-21.1 (7.7)</td>
<td>0.94</td>
<td>0.16</td>
<td>0.14</td>
<td></td>
</tr>
<tr>
<td>Ankle ROM (°)</td>
<td>25.9 (3.3)</td>
<td>26.3 (4.8)</td>
<td>25.3 (3.1)</td>
<td>28.4 (4.0)</td>
<td>0.56</td>
<td>0.16</td>
<td>0.28</td>
<td></td>
</tr>
<tr>
<td>HF moment (%BW·Ht)</td>
<td>-4.0 (0.7)</td>
<td>-3.6 (0.7)</td>
<td>-4.1 (1.2)</td>
<td>-4.0 (0.7)</td>
<td>0.36</td>
<td>0.37</td>
<td>0.61</td>
<td></td>
</tr>
<tr>
<td>HE moment (%BW·Ht)</td>
<td>5.0 (0.9)</td>
<td>4.0 (0.9)</td>
<td>4.0 (1.1)</td>
<td>4.7 (1.4)</td>
<td>0.57</td>
<td>0.72</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>KE moment (%BW·Ht)</td>
<td>-2.1 (0.5)</td>
<td>-1.7 (0.2)</td>
<td>-1.6 (0.5)</td>
<td>-1.2 (0.5)</td>
<td>0.001</td>
<td>0.007</td>
<td>0.90</td>
<td></td>
</tr>
<tr>
<td>KF moment (%BW·Ht)</td>
<td>2.9 (1.3)</td>
<td>2.4 (1.4)</td>
<td>3.4 (1.7)</td>
<td>3.7 (0.9)</td>
<td>0.04</td>
<td>0.86</td>
<td>0.32</td>
<td></td>
</tr>
<tr>
<td>ADF moment (%BW·Ht)</td>
<td>-9.4 (0.7)</td>
<td>-9.2 (0.7)</td>
<td>-8.6 (1.5)</td>
<td>-9.4 (0.8)</td>
<td>0.31</td>
<td>0.29</td>
<td>0.10</td>
<td></td>
</tr>
</tbody>
</table>

Despite being matched for physical activity level, at baseline, females displayed lower muscle torque and power relative to body mass compared to males (Table 6.5).

Additionally, older adults displayed lower concentric knee extensor power compared to young adults. Despite baseline differences, males and females in both groups responded similarly to the 30MTW, with no significant age, sex, or interaction effects in change in knee extensor torque or power.

Table 6.5. Analysis 2 baseline and % change values for knee extensor isometric torque and power at 270 °*s⁻¹, Mean (SD). Bold p-values indicate significant difference.

<table>
<thead>
<tr>
<th></th>
<th>Young Male</th>
<th>Young Female</th>
<th>Older Male</th>
<th>Older Female</th>
<th>p-values</th>
<th>Age</th>
<th>Sex</th>
<th>Age x Sex</th>
</tr>
</thead>
<tbody>
<tr>
<td>Isometric torque (Nm/kg)</td>
<td>0.31 (0.04)</td>
<td>0.24 (0.04)</td>
<td>0.28 (0.06)</td>
<td>0.24 (0.06)</td>
<td>0.33</td>
<td>0.003</td>
<td>0.43</td>
<td></td>
</tr>
<tr>
<td>Concentric power (W/kg)</td>
<td>0.78 (0.15)</td>
<td>0.53 (0.21)</td>
<td>0.53 (0.16)</td>
<td>0.46 (0.15)</td>
<td>0.005</td>
<td>0.006</td>
<td>0.09</td>
<td></td>
</tr>
<tr>
<td>Eccentric power (W/kg)</td>
<td>1.44 (0.43)</td>
<td>1.18 (0.22)</td>
<td>1.58 (0.37)</td>
<td>1.29 (0.28)</td>
<td>0.25</td>
<td>0.02</td>
<td>0.87</td>
<td></td>
</tr>
<tr>
<td>Isometric torque (%Δ)</td>
<td>-7.4 (14.3)</td>
<td>-4.0 (8.2)</td>
<td>-4.5 (14.2)</td>
<td>-2.9 (7.0)</td>
<td>0.57</td>
<td>0.50</td>
<td>0.80</td>
<td></td>
</tr>
<tr>
<td>Concentric power (%Δ)</td>
<td>-11.1 (8.0)</td>
<td>-8.2 (28.7)</td>
<td>-6.2 (22.5)</td>
<td>-10.1 (19.7)</td>
<td>0.82</td>
<td>0.94</td>
<td>0.62</td>
<td></td>
</tr>
<tr>
<td>Eccentric power (%Δ)</td>
<td>1.5 (39.5)</td>
<td>-12.9 (19.2)</td>
<td>-9.3 (14.9)</td>
<td>-8.6 (9.9)</td>
<td>0.67</td>
<td>0.67</td>
<td>0.32</td>
<td></td>
</tr>
</tbody>
</table>
Discussion

This study explored the independent effects of age and habitual physical activity on sex-specific differences in gait mechanics and knee extensor function before and after a moderate bout of walking. In the first analysis, older males and females of differing physical activity levels (highly vs. less active) were compared. In the second analysis, males and females of matched physical activity levels but of differing ages (young vs. older) were compared. In both analyses it was hypothesized that there would be sex-specific differences in gait mechanics and muscle function and that there would be additional interactions with physical activity level or age. The results of these analyses indicated that sex-specific differences as well as interaction effects were most apparent in hip and knee mechanics. These analyses also identified physical activity level and response to exercise as factors that could provide additional information about typical aging gait changes at the hip and ankle.

In the analysis of sex and physical activity (Analysis 1), differences between older males and females were found in sagittal plane knee and hip kinematics and kinetics. Older females displayed larger hip extension moments compared to older males and a significant interaction effect indicated that this male vs. female difference was largely driven by the less active older adults (Table 6.3). Larger hip extension moments in females have previously been reported in the literature and in general, older adults are expected to have larger hip moments compared to young adults. However, the older participants in the current study are younger than most in the literature. The observed interaction between physical activity level and sex in these relatively young older adults may suggest that females display a shift in hip moments at a younger age.
than males, and that females may be able to slow this change by participating in high levels of physical activity.

![Figure 6.4](image)

**Figure 6.4.** Differences found between older and young adults in support or propulsive moments. Curved arrows represent external joint moments, with a larger arrow demonstrating one group (older, yellow vs. young, green) having a larger moment than the other. For dorsiflexion moment (white arrow), groups were not different at baseline but older adults displayed a decrease in response to the 30MTW while young adults showed no change on average.

An interaction effect for hip extension moments was again observed in the comparison of young and older adults of matched physical activity (Analysis 2). For this age by sex interaction, older females displayed larger moments than older males (similar to in Analysis 1), while young females displayed smaller moments than younger males.

While there are few studies on sex-specific differences in gait, previous studies comparing gait in young males and females have not reported differences in hip extension moments. Even when matched for physical activity, our study found that males also had a more extended hip at heel strike compared to females which agrees with previous findings in young adults and may be a result of increased anterior pelvic tilt in young females. Sex-specific differences or age by sex interactions in knee flexion angle at heel strike and knee extension moment in early stance were also present in the comparison of young and older adults but not in the older-adult only analysis. This difference in sex-specific findings based on age cohort may suggest that age-related alterations in early stance sagittal plane knee mechanics differ by sex. As changes in knee
mechanics may alter the distribution of loads on knee joint cartilage, these age-related differences in knee mechanics may be important considerations for understanding the higher incidence of knee osteoarthritis in females compared to males.

There was an effect of age on the change in joint kinetics in response to the 30MTW. Older adults displayed decreases in knee flexion and ankle dorsiflexion moments (-0.1 and +0.2 %BW·Ht changes, Supplementary Table 6.2) while young adults displayed increases in knee flexion moments and no change in ankle dorsiflexion moments (+0.2 and +0.0 %BW·Ht changes, Supplementary Table 6.2). Both older adult cohorts in Analysis 1 demonstrated a similar decrease in dorsiflexion moments in response to the 30MTW (Supplementary Table 6.1), indicating that older adults may lose distal joint torque production capability in response to moderate exercise. Older adults are expected to rely more on proximal vs. distal joints for torque production during gait\(^\text{18}\)\(^\text{,175}\) and while there was not an effect of age on baseline hip or ankle moments in Analysis 2, a loss of propulsive ankle torque following exercise may indicate that these older adults have some deficiency in ankle function. In contrast to gait kinetics, a general interaction between physical activity level or age and sex was not apparent in the response of gait kinematics to the 30MTW. Qualitatively, most kinematic changes in response to the 30MTW were small (e.g., changes in kinematics generally less than 2°), suggesting that walking kinematics are stable in response to modest muscle fatigue.

Knee extensor muscle torque and power were lower in females than males when comparing cohorts matched for physical activity but not age (Analysis 2), but this sex-specific difference was not apparent in cohorts matched for age but not physical activity (Analysis 1). This discrepant finding appeared to be mainly due to highly active older
females being more similar to highly active males while less active older females had lower torque and power values compared to their male counterparts. High levels of physical activity appear to provide a protective benefit for knee extensor function in older females. This benefit of physical activity extended to muscle fatigue where highly active older males and females displayed smaller decreases in high-velocity concentric knee extensor power compared to their less active counterparts. These results are meaningful for supporting the importance of habitual physical activity for older females in particular as decreased knee extensor muscle function has been identified as a stronger predictor of knee OA risk in females than males.70

The results of the study suggest that sex is a larger determinant of gait mechanics than physical activity in older adults and that sex imparts additional differences above the effects of age on gait mechanics and knee extensor muscle function. The older participants in these analyses are relatively young (mean age ~62 years) and high functioning and differences found here may evolve with increasing age. As the rates of musculoskeletal pathology differ between the sexes, determining if gait mechanics of older males and females are different and if modifiable factors such as physical activity level or muscle fatigue further discriminate between the sexes may provide meaningful information for interventions focused on maintaining mobility throughout the lifespan. This exploratory study provides initial evidence that male and female gait differs across age and physical activity level. As the sex-specific differences found here were isolated to hip and knee mechanics, these results may suggest that there are different mechanisms driving mobility issues in males vs. females.
**Supplementary Table 6.1.** Change in gait kinematics in response to the 30MTW for Analysis 1, Mean (SD). Bold p-values indicate significant difference. HF: hip flexion, KF: knee flexion, ADF: ankle dorsiflexion, PF: plantar flexion, HE: hip extension, KE: knee extension.

<table>
<thead>
<tr>
<th></th>
<th>Older highly active</th>
<th>Older less active</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Stride length (m)</td>
<td>0.01 (0.02)</td>
<td>0.00 (0.02)</td>
<td>0.02 (0.02)</td>
</tr>
<tr>
<td>HF heel strike (°)</td>
<td>0.4 (1.4)</td>
<td>0.8 (1.7)</td>
<td>-0.3 (1.6)</td>
</tr>
<tr>
<td>Hip ROM (°)</td>
<td>0.9 (1.4)</td>
<td>0.5 (1.0)</td>
<td>0.8 (1.0)</td>
</tr>
<tr>
<td>KF heel strike (°)</td>
<td>0.7 (1.4)</td>
<td>1.5 (2.3)</td>
<td>0.4 (1.2)</td>
</tr>
<tr>
<td>KF peak stance (°)</td>
<td>0.1 (1.6)</td>
<td>-0.1 (2.4)</td>
<td>0.8 (1.5)</td>
</tr>
<tr>
<td>Knee ROM (°)</td>
<td>-0.3 (1.6)</td>
<td>1.3 (2.7)</td>
<td>-0.2 (1.9)</td>
</tr>
<tr>
<td>Ankle peak PF (°)</td>
<td>-0.5 (2.7)</td>
<td>-0.1 (2.7)</td>
<td>0.7 (2.7)</td>
</tr>
<tr>
<td>Ankle ROM (°)</td>
<td>-0.2 (2.4)</td>
<td>0.8 (1.4)</td>
<td>-0.1 (2.4)</td>
</tr>
<tr>
<td>HF moment (%BW·Ht)</td>
<td>-0.2 (0.4)</td>
<td>0.0 (0.6)</td>
<td>-0.2 (0.4)</td>
</tr>
<tr>
<td>HE moment (%BW·Ht)</td>
<td>-0.2 (0.2)</td>
<td>0.0 (0.5)</td>
<td>-0.2 (0.2)</td>
</tr>
<tr>
<td>KE moment (%BW·Ht)</td>
<td>0.1 (0.3)</td>
<td>-0.1 (0.4)</td>
<td>0.0 (0.2)</td>
</tr>
<tr>
<td>KF moment (%BW·Ht)</td>
<td>-0.1 (0.4)</td>
<td>-0.2 (0.3)</td>
<td>0.0 (0.4)</td>
</tr>
<tr>
<td>ADF moment (%BW·Ht)</td>
<td>0.2 (0.4)</td>
<td>0.1 (0.3)</td>
<td>0.1 (0.4)</td>
</tr>
</tbody>
</table>

**Supplementary Table 6.2.** Change in gait kinematics in response to the 30MTW for Analysis 2, Mean (SD). Bold p-values indicate significant difference. HF: hip flexion, KF: knee flexion, ADF: ankle dorsiflexion, PF: plantar flexion, HE: hip extension, KE: knee extension.

<table>
<thead>
<tr>
<th></th>
<th>Young</th>
<th>Older</th>
<th>p-values</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Male</td>
<td>Female</td>
<td>Male</td>
</tr>
<tr>
<td>Stride length (m)</td>
<td>0.00 (0.04)</td>
<td>0.00 (0.03)</td>
<td>0.01 (0.03)</td>
</tr>
<tr>
<td>HF heel strike (°)</td>
<td>0.8 (3.5)</td>
<td>-0.6 (2.3)</td>
<td>0.4 (1.2)</td>
</tr>
<tr>
<td>Hip ROM (°)</td>
<td>1.5 (1.1)</td>
<td>0.6 (2.5)</td>
<td>1.0 (1.4)</td>
</tr>
<tr>
<td>KF heel strike (°)</td>
<td>1.1 (1.4)</td>
<td>-0.7 (3.0)</td>
<td>0.8 (1.5)</td>
</tr>
<tr>
<td>KF peak stance (°)</td>
<td>0.7 (1.8)</td>
<td>-0.8 (1.8)</td>
<td>-0.1 (1.5)</td>
</tr>
<tr>
<td>Knee ROM (°)</td>
<td>-0.8 (1.4)</td>
<td>0.0 (1.6)</td>
<td>-2.0 (2.1)</td>
</tr>
<tr>
<td>ADF heel strike (°)</td>
<td>0.9 (1.8)</td>
<td>-0.2 (3.2)</td>
<td>-0.5 (2.3)</td>
</tr>
<tr>
<td>Ankle peak PF (°)</td>
<td>-0.4 (1.9)</td>
<td>-0.6 (3.5)</td>
<td>-1.5 (2.8)</td>
</tr>
<tr>
<td>Ankle ROM (°)</td>
<td>0.9 (0.9)</td>
<td>0.1 (2.2)</td>
<td>0.4 (1.2)</td>
</tr>
<tr>
<td>HF moment (%BW·Ht)</td>
<td>-0.2 (0.2)</td>
<td>0.1 (0.6)</td>
<td>-0.2 (0.6)</td>
</tr>
<tr>
<td>HE moment (%BW·Ht)</td>
<td>0.1 (0.4)</td>
<td>0.2 (0.3)</td>
<td>0.0 (0.5)</td>
</tr>
<tr>
<td>KE moment (%BW·Ht)</td>
<td>-0.2 (0.4)</td>
<td>-0.1 (0.2)</td>
<td>0.1 (0.2)</td>
</tr>
<tr>
<td>KF moment (%BW·Ht)</td>
<td>0.3 (0.4)</td>
<td>0.1 (0.4)</td>
<td>0.0 (0.4)</td>
</tr>
<tr>
<td>ADF moment (%BW·Ht)</td>
<td>0.1 (0.3)</td>
<td>-0.1 (0.4)</td>
<td>0.2 (0.4)</td>
</tr>
</tbody>
</table>
CHAPTER VII

SUMMARY

The primary aim of this dissertation was to investigate the effects of age and physical activity level on measures of knee mechanics and knee extensor muscle function that have been associated with knee osteoarthritis (OA) risk. In addition to variables that have previously been associated with knee OA, factors that could alter the mechanical loading environment in the knee, including muscle activation and movement coordination about the knee, were compared between groups differing by age or physical activity level. To test the sensitivity of these proposed knee OA risk factors to daily activity or fatigue, changes in all outcome variables in response to a 30 minute treadmill walk were compared between groups. An exploratory study was also carried out to determine if gait mechanics and muscle function differ in a sex-specific fashion, and if this sex-specific difference is additionally affected by age or physical activity level.

The initial study of this dissertation demonstrated that age and, in some cases, physical activity level affect variables that may be indicative of the local cartilage loading environment in the knee joint (e.g., anterior displacement of the femur relative to the tibia, knee extension moment in early stance, knee muscle co-activation during midstance). Concentric knee extensor power was lower in older compared to young adults (especially at the highest contraction velocity), but there were no differences in baseline knee extensor torque or power by physical activity level. The highly active older adults were less susceptible to knee extensor fatigue in response to the 30 minute treadmill walk compared to young adults and less active older adults. Despite significant fatigue, knee mechanics were unchanged in response to the 30 minute treadmill walk.
The highly-controlled, purposefully healthy participant cohorts in this study allowed for discrimination of factors that could alter the knee joint cartilage loading environment based on age or decreased physical activity alone, independent of the many age-related comorbidities that additionally alter cartilage health.

When comparing movement coordination between the study cohorts, age, rather than physical activity level, appeared to be the primary factor driving differences in coordination. Both older adult cohorts displayed different coordination or coordination variability compared to young adults at some couples or time points, while differences were only apparent between the highly or less active older adults and the young adults in other segment couples or gait cycle phases. Additionally, most differences in coordination and its variability were found in couples about the hip and ankle while fewer coordination differences were identified in segment couples about the knee. Differences in coordination and its variability appeared most often during phases of the gait cycle when an individual was in single support: terminal swing and midstance phases of the gait cycle. These results suggest that older adults may alter control of the hip and ankle during single-limb stance periods, either to preserve balance or out of necessity due to muscular limitations.

In the final study of sex-specific effects of age or physical activity, results suggested that sex imparts additional differences above the effects of age on gait mechanics and knee extensor muscle function. It also appeared that older females could mitigate some sex-specific aging effects, especially reductions in knee extensor muscle function and shifts in hip moments during gait, by being highly physically active. In addition to the above-mentioned sex-specific findings, this analysis identified decreases
in ankle dorsiflexion moments in all older adult cohorts but not in the young adults in response to the 30 minute treadmill walk. Despite there being no baseline difference in ankle mechanics, this finding suggests that the older adults in this study have some deficits in ankle function when perturbed, a common finding in aging gait literature.

This dissertation identified biomechanical risk factors for knee OA that appear to be sensitive to age and low physical activity in otherwise healthy adults. While the differences in knee mechanics and knee extensor muscle function appear small, their measureable presence in the absence of a multitude of typical age-related risk factors for knee OA provides support for a role of physical activity in knee OA risk reduction. Additionally, differences found by age or sex in gait mechanics and movement coordination about the hip or ankle at baseline or in response to a bout of walking may suggest targets for interventions aiming to preserve overall gait function or mobility with age.
APPENDIX A

MEDICAL AND PHYSICAL ACTIVITY HISTORY SCREENING

Medical and Physical Activity History Screening (to be completed via phone or email at initial screening and confirmed after consent):
For all potential participants:
Please indicate your:
Age:____
Height:____
Weight:____
BMI must be <30

If female:
1. To your knowledge, are you or could you be pregnant? Yes/No If yes, individual is excluded

Do you have any history of:
1. Arthritis in any joint? Yes/No
   - If yes, what joint(s)? __________________________ If lower extremity joint, individual is excluded
2. Major injury to your legs or feet? Yes/No
   - If yes, what was the injury? __________________________ If injury was ACL rupture, meniscal tear, or required major reconstructive surgery (e.g. more than a pin to set a fracture), individual is excluded
3. Major surgery in your legs or feet? Yes/No Yes generally indicates exclusion
   - If yes, what was the surgery? __________________________
4. Diagnosis of heart problems, high blood pressure, or high cholesterol? Yes/No
   - If yes for heart problems, physician consent required
   - If yes for HBP or cholesterol, what medication are you on - __________________________.
   - Is your condition considered controlled by your physician? Yes/No Individuals will be excluded if on beta blockers. If unsure of control of HBP or cholesterol, physician consent required.
5. Pulmonary disease (e.g. asthma, dyspnea, COPD) that limits daily activity? Yes/No If yes, individual is excluded
6. Diagnosis of Parkinson’s disease, MS, or other neurological disease? Yes/No If yes, individual is excluded
7. Do you experience dizziness or vertigo? Yes/No If yes, individual is excluded

8. Stroke? Yes/No If yes, individual is excluded

9. Loss of sensation in legs or peripheral vascular disease? Yes/No If yes, individual is excluded

10. Any other chronic condition (e.g. diabetes, cancer)? Yes/No If yes, physician consent required
    - If yes, document condition______________________________.
    - If diabetes, Is your diabetes properly controlled? Yes/No If no, individual is excluded

11. Do you currently have pain when you walk? Yes/No If yes, individual is excluded

12. Do you have pain when you climbing stairs or stand up from a sitting position? Yes/No If yes, individual is excluded

13. Are you able to walk for 40 minutes without an assistive device? Yes/No If no, individual is excluded

14. Are you able to participate in resistance exercise/strength testing? Yes/No If no, individual is excluded

15. Have you ever been told to limit your exercise or that you need physician clearance before beginning an exercise program? Yes/No If yes, physician consent required

Medication:
1. Are you currently on any medication for a chronic condition? Yes/No
   - If yes, what medications_____________________________
   - Exclusion medications: beta blockers, sedatives, tranquilizers. If there is a question about a medication, physician consent will be required

PA History:
1. How often do you exercise: 5 or more days per week, 2-4 days per week, or 1 or fewer days per week?

2. When you exercise, how long do you exercise for: more than 30 minutes, less than 30 minutes?
   Sedentary older individuals must be < 2 30 minute structured bouts of exercise per week. Young adults must be recreationally active (e.g., jog twice a week, coach kid’s soccer on weekends, play basketball on a regular basis. NO DAILY RUNNING.)
3. What types of exercise do you participate in? (walking, biking, running, golf, lifting weights, etc.) - ________________________________________________________

Sedentary individuals must not participate in substantial amounts of vigorous activity

4. Do you have adverse effects when you exercise (e.g. dizziness, light-headedness, pain, cramping)? Yes/No If yes, individual is excluded

For older runners:
1. How many years have you been running?_____________________________________

2. How many miles do you currently run each week?_______________________________ Must be >=15 miles/week. How many months/years have you been running your current mileage? _______________________

3. Are you currently injured? Yes/No If yes, participant in excluded

4. Have you experienced a running injury in the last year and had to take more than 1 week off of running? Yes/No
   If yes, what was this injury and how was it treated? ________________________________

5. Are you training for any races currently? Yes/No If yes, schedule visits appropriately to avoid race-induced fatigue/soreness
APPENDIX B

INTAKE QUESTIONNAIRE

Intake Questionnaire
Participant ID:__________ Date:____________ Group:__________

Occupational History:
1. What is your current employment status? (circle one)
   Employed full-time
   Employed part-time
   Unemployed
   Retired

2. Have you ever worked in a job requiring heavy lifting, extended kneeling, or strenuous work? (circle one)
   Yes / No
   If yes,
   describe:__________________________________________________________
   _______________________________________________________________
   _______________________________________________________________
   _______________________________________________________________

Physical Activity History:
5. How often do you regularly exercise? (circle one)
   5 or more days per week
   2-4 days per week
   1 or fewer days per week

6. When you exercise, how long do you exercise for? (circle one)
   0-15 minutes
   15-30 minutes
   More than 30 minutes

7. What types of exercise do you regularly participate in? (walking, biking, running, golf, lifting weights, etc.)

8. How long have you been following this pattern of physical activity? (circle one)
   Less than 1 year
   1-2 years
   2-5 years
   More than 5 years
9. Have you ever had a drastically different pattern of physical activity? (circle one)
   Yes / No
   If yes, describe:
   _____________________________________________________________
   _____________________________________________________________
   _____________________________________________________________

10. Have you ever had a body weight significantly different from your current weight? (circle one)
    Yes / No

For runners:
   6. How many years have you been running? _________________

   7. How many miles do you currently run each week?
      ______________________________

   8. How many months/years have you been running your current mileage?
      ______________________________

   9. Have you experienced a running injury in the last year? (circle one)
      Yes / No
      If yes, what was this injury and how was it treated?
      _____________________________________________________________
Re: UMass study: “Physical activity and age-related mechanical risk factors for knee osteoarthritis”

Dear Dr. ____________.

Researchers in the Biomechanics and Muscle Physiology Laboratories in the Department of Kinesiology at the University of Massachusetts Amherst are conducting a study of the effects of age and physical activity habits on gait mechanics and fatigue in response to walking. We are recruiting generally healthy adults between the ages of 55-70 years. The principal investigator on this study is Dr. Katherine Boyer. We are requesting a physician’s clearance for participants in this study.

All prospective participants are screened for medical and physical activity history and sign an informed consent document. The study protocol will require volunteers to perform a series of maximal knee extension (quadriceps) muscle contractions while in a seated position. Participants will also complete a treadmill walking protocol in which they will walk at a self-selected constant pace for 30 minutes.

Our exclusion criteria include the following: lower extremity osteoarthritis, rheumatoid arthritis, history of lower extremity joint surgery, neurological (including peripheral neuropathy) or metabolic (including uncontrolled diabetes) disease, pulmonary disease which limits activity, or significant heart conditions. Healthy individuals on antihypertensive (with the exception of beta-blockers) and anticholesterol (i.e. statin) medications will NOT be excluded for those medications.

The individual named below has indicated an interest in participating in this study. If you have examined this individual within the last 12 months and believe it appropriate, we ask that you provide clearance for this person for entry into this study. If you have any questions, please contact Katherine Boyer, Ph.D. at 413-545-1717.

I, ______________________________, give permission to my physician to approve/disapprove my participation in this study.

____________________________________               ________________
(Signature)                                          (Date)

As a result of my examination of ____________________,

(Participant’s Name)

I (circle one) approve disapprove of his/her participation in the study.

____________________________________               ________________
(Physician’s Signature)                              (Date)

Please return to Jocelyn Hafer, 110 Totman Building, 30 Eastman Lane, Amherst, MA 01003
REFERENCES


