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The influence of patellofemoral pain on muscle coordination, segment coordination, and segment coordination variability in runners

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**THE INFLUENCE OF PATELLOFEMORAL PAIN ON MUSCLE COORDINATION,
SEGMENT COORDINATION, AND SEGMENT COORDINATION VARIABILITY IN
RUNNERS**

A Dissertation Presented

By

CARL M. JEWELL

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

DOCTOR OF PHILOSOPHY

September 2018

Department of Kinesiology

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ABSTRACT

THE INFLUENCE OF PATELLOFEMORAL PAIN ON MUSCLE COORDINATION, SEGMENT COORDINATION, AND SEGMENT COORDINATION VARIABILITY IN RUNNERS

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Management of patellofemoral pain syndrome (PFPS) remains a significant challenge in clinical practice and there is a need to understand the mechanisms for altered gait and muscular function which may lead to poor patient outcomes. The overall aim of the three studies in this dissertation was to determine if runners with current PFPS adapt their gait and muscle activation as a result of long-term, daily pain and/or in response to an acute pain flare and exertion during a moderate intensity 21-minute treadmill run compared to healthy controls. In addition, a resolved, asymptomatic PFPS group was included to investigate potential mechanisms for the frequent reoccurrence of pain experienced by those with a history of PFPS.

The lack of differences in baseline kinematic, segment coordination, and segment coordination variability measures suggest that there are no long-term gait adaptations to pain in either injury group that manifest as resultant gait patterns. Several differences were identified in baseline kinetics among all three groups for peak hip abduction and external rotation as well as ankle inversion moments. These findings indicate that: 1) runners with a history of PFPS have different loading patterns at the hip and ankle compared to healthy runners and 2) these altered loading patterns are not substantial enough to alter resultant kinematic patterns of movement. In addition to these joint moments, altered muscle coordination discriminated between all three groups. These findings have significant implications for identifying individuals at risk of re-injury and helping to improve treatment efficacy in runners with PFPS.

Movement evoked pain is a primary characteristic of PFPS, and the treadmill run used in these studies was sufficient to cause a pain response in the injured group. Changes seen in the outcome measures of the three studies at the end of the run are indicative of a response to a combination of increased pain and exertion. Greater anti-phase motion of the sagittal thigh-transverse shank in the injured group compared to controls suggests that altered movement control about the knee may be related to increased pain in those with PFPS. In addition to the decreased coordination variability observed in those with PFPS, there were also differences in coordination variability between the resolved and control groups, with the resolved group often showing increases in variability compared to controls. This suggests that abnormal movement flexibility may persist even once painful symptoms are resolved and that individuals with a history of PFPS do not return to healthy gait patterns following resolution of symptoms.

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CHAPTER 1

INTRODUCTION

Running is one of the most accessible and effective forms of cardiovascular exercise. More than 50 percent of the 30 million runners in the United States get injured each year (McCrary, Martin et al. 1999). The most common lower limb injury is patellofemoral pain syndrome (PFPS) which comprises 20 percent of all running-related injuries (Taunton, Ryan et al. 2002). Classified as an overuse injury resulting from cumulative micro-trauma, PFPS presents as diffuse pain in and around the patellofemoral joint (PFJ) (Taunton, Ryan et al. 2002) and is exacerbated by load-bearing activities involving knee flexion (Taunton, Ryan et al. 2002). Despite significant attention from researchers and clinicians over the past two decades, 91% of those who develop PFPS have pain and 36% are restricted from performing daily activities at follow-up 4 years later (Stathopulu and Baildam 2003). Additionally, the longer the pain is present, the greater the chance for continued symptomatic PFPS and reoccurrence (Collins, Crossley et al. 2010, Collins, Bierma-Zeinstra et al. 2013). This is especially concerning given recent evidence linking chronic PFPS (pain lasting > 2 months) to retropatellar cartilage damage, increased PFPS severity, PFJ osteoarthritis, and disability with old age (Utting, Davies et al. 2005, Wyndow, Collins et al. 2016).

Despite our current depth of knowledge about factors predisposing individuals to PFPS and the resulting impairments in muscle function and gait mechanics, PFPS treatment often remains ineffective, leaving runners in continued pain that worsens with activity. Thus, even though there are a plethora of conservative management strategies for PFPS, there is a need to understand the mechanism for altered gait and muscular function with PFPS in order to improve treatment efficacy and patient outcomes. One possible direction, in order to better understand how increased pain and fatigue influence the organization of movement, is to examine patterns of segment coordination variability and muscle activity throughout a prolonged run. Through the analysis of these coordinated movement patterns, we may be able to pinpoint underlying,

potentially modifiable differences in gait mechanics that are not discernable through traditional methods which can be used to build a foundation of knowledge on which future treatments can be based.

Patellofemoral pain syndrome can be a difficult condition to diagnose given interpatient variability in experienced pain severity, location, and duration of symptoms. Confirmation of symptoms by a clinician is preferred as injury history, visual inspection of the lower limb, and palpation all play a critical role in diagnosis. The typical diagnostic criteria of PFPS are: 1) retropatellar knee pain during activity, 2) no apparent structural damage to the knee and 3) pain on palpation of the medial or lateral patellar facets or femoral condyles (Boling, Padua et al. 2009). PFPS is often accompanied by stiffness, swelling, locking, and crepitus of the knee (Blond and Hansen 1998, Fulkerson 2002, Thomee, Thomee et al. 2002). The primary source of PFJ pain is believed to be cumulative microtrauma of subchondral bone (Fulkerson 2002, Draper, Besier et al. 2006), though activation of nociceptive fibers within the synovium and retinaculum have been proposed as other pain sources (Fulkerson 2002). Pain is often localized to a single location on or around the patella. Given the prevalence of PFPS in runners, this population is ideal for PFPS investigation given the repetitive loading from distance running as well as runners' otherwise good overall health.

As the magnitude, location and rate of loading of PFJ contact forces can influence the onset and progression of PFPS, the strength of the muscles around the knee and those crossing the ankle and hip are especially important. These muscles provide overall joint stability, control tracking and tilt of the patella and modify how forces are directed throughout the knee. Hip abductors and extensors are typically weakened in those suffering from PFPS (Ireland, Willson et al. 2003, Souza and Powers 2009, Finnoff, Hall et al. 2011, Lankhorst, Bierma-Zeinstra et al. 2012, Bazett-Jones, Cobb et al. 2013, Chen, Powers et al. 2014) likely contributing to altered hip and knee kinematics, specifically increased femoral internal rotation throughout weight-bearing activities (Souza and Powers 2009). This may contribute to altered PFJ kinematics and PFJ

contact stress patterns. Prospective studies have revealed that hip abductor strength declines pre- to post-injury (Finnoff, Hall et al. 2011, Herbst, Foss et al. 2015). Conversely, increased hip abductor strength and low external-to-internal hip strength ratios pre-injury have been linked to increased injury risk in adolescent athletes (Finnoff, Hall et al. 2011, Herbst, Foss et al. 2015). These conflicting findings may be due to increased recruitment of the gluteus medius muscle as both a hip abductor and an external hip rotator to compensate for other weak hip external rotator muscles (Finnoff, Hall et al. 2011). In addition to the primary hip rotator muscles, the quadriceps have also been implicated in pain onset and progression. Imaging techniques have identified quadriceps atrophy with PFPS (Giles, Webster et al. 2013). A weak vastus medialis oblique (VMO) has been shown to increase lateral pressure on the patella (Elias, Kilambi et al. 2009). Weakened quadriceps muscles, as well as the rotators at the hip, may contribute toward poor dynamic control of the femur causing increased lateral patellar subluxation (Powers, Ward et al. 2003), increased PFJ stress (Lee, Morris et al. 2003, Finnoff, Hall et al. 2011), and may potentially lead to greater pain with PFPS.

In addition to changes in muscle size and strength, a combination of structural factors both distal and proximal to the knee may contribute to PFPS onset. These factors include large Q-angles (Lankhorst, Bierma-Zeinstra et al. 2012), increased patellar tilt (Lankhorst, Bierma-Zeinstra et al. 2012), poor knee alignment (Ferber, Hreljac et al. 2009), and patellar maltracking (Dierks, Manal et al. 2008). Patellar maltracking may lead to PFPS by altering stress on the PF cartilage and the infrapatellar fat pad. One factor thought to contribute to patellar maltracking is patella alta, characterized by increased patellar height relative to the femoral condyles (Pal, Besier et al. 2013). This altered geometry may lead to increased PFJ contact area, joint stress and eventual development of PFPS (Pal, Besier et al. 2013). Patellar femoral pain syndrome is a chronic injury thought to initiate due to altered cumulative loading patterns on the retropatellar cartilage/joint. Previous work has found that patellar cartilage deforms more than twice as much following activity in healthy individuals compared to patients with PFPS (Farrokhi, Colletti et al.

2011). As a result, decreased cartilage deformation in those with PFPS during repetitive activities, such as ambulation, could potentially be a significant contributing factor to pain onset and progression through a lack of flexibility and reduction in the shock attenuation capability of the PFJ (Farrokhi, Colletti et al. 2011). Examining the underlying cartilage changes throughout a bout of activity is difficult. However, studying gait mechanics during repetitive, loading tasks such as running may play an important role in understanding PFPS onset and progression. Thus, non-invasive measures of gait may provide insight into the mechanisms leading to altered loading as a result of pain or fatigue.

Several cross-sectional studies have investigated kinematics and kinetics of the lower limb in individuals with PFPS to elucidate differences from healthy controls. These studies consist of two primary motivations: identifying gait risk factors for PFPS development and how individuals adapt their gait once they develop PFPS. Causality is difficult to determine from the design of these case-control studies but may provide the most insight into the observed persistence and reoccurrence of PFPS. Excessive frontal plane motion has been suggested as a primary cause for pain experienced on the lateral aspect of the patella (Stefanyshyn, Stergiou et al. 2006). Additionally, a systematic review investigating kinematics of the knee found studies that indicated increased knee external rotation was present at the time of the peak knee extension moment (Barton, Levinger et al. 2009). There was moderate evidence of an association between PFPS and increased peak hip adduction, internal rotation, and contralateral pelvic drop as well as weak evidence between PFPS and reduced peak hip flexion during stance (Neal, Barton et al. 2015). Proximal kinematics have long been considered to have the primary influence on mechanics at the knee; however, studies have begun to emphasize the effects of alignment and soft tissue distal to the knee on overall joint health, specifically calcaneal eversion and pronation of the foot (Rodrigues, Chang et al. 2013, Rodrigues, TenBroek et al. 2013). Despite the recent surge in investigations, strong evidence indicates no association between PFPS and increased peak rearfoot eversion (Neal, Barton et al. 2015). At the knee, decreased flexion-extension

moments during running have been found in those with PFPS, potentially as a mechanism of reducing PFJ stress or simply as a mechanism to adapt less painful gait (Besier, Fredericson et al. 2009); however, increased PFJ reaction force on the lateral patellar facet has been indicated in one study (Chen, Powers et al. 2014). In the frontal plane, knee abduction impulse has been found to be increased in runners with PFPS compared to controls (Stefanyshyn, Stergiou et al. 2006). There has been little evidence of altered joint kinetics at the ankle and hip, as the majority of studies have focused on hip isometric and dynamic strength rather than joint moment measurements in comparing groups (Rathleff, Rathleff et al. 2014).

While the altered movement patterns that have been observed in those with PFPS may alter PFJ stress and contribute to PFPS duration, the initial onset and progression of PFPS may be caused by motor system responses to pain. One recent theory posits that pain leads to a redistribution of muscle activity throughout the lower limb, causing adaptations in muscle coordination (the organization of activation intensity and timing across multiple muscles) through changes at multiple levels of the motor system (Hodges and Tucker 2011). When possible, the body appears to adapt to pain with a reorganization of muscle activity to reduce stress or loads on the affected structures (Hug, Hodges et al. 2014). Adaptive muscle coordination strategies to reduce load and joint stress may be a primary goal of pain reduction, triggering the movement pattern changes that have been observed in those with PFPS. These changes may provide short-term protection leading to decreased levels of pain but likely have negative long term consequences (Hodges and Tucker 2011).

Previous work studying surface electromyography (EMG) have attempted to capture these altered activation patterns with pain but have primarily focused on either timing, frequency, or intensity individually, not at the level of muscle coordination. One of the most frequently observed changes in EMG with PFPS is a delay in the onset of vastus medialis oblique (VMO) activation relative to the vastus lateralis (VL) at touchdown both pre- (Van Tiggelen, Cowan et al. 2009) and post-injury (Cowan, Bennell et al. 2001, Chester, Smith et al. 2008, Van Tiggelen,

Cowan et al. 2009). The delayed activation of the medial muscles about the knee may lead to excess lateral patellar tracking (Cowan, Bennell et al. 2001, Pal, Besier et al. 2012) resulting in altered PFJ dynamics and increased pain. Lateral patellar tracking may also be a result of increased co-activation from concurrent lateral hamstring activation observed in those with PFPS (Patil, Dixon et al. 2011). Quadriceps and hamstrings co-activation is a strategy for increasing knee joint stability (Besier, Fredericson et al. 2009); however, increased recruitment of muscles about the knee may also increase PFJ forces and stresses (Besier, Fredericson et al. 2009). Muscles at the hip and ankle may also play a critical role in influencing changes in gait mechanics in the presence of pain. Altered gluteus maximus and medius activation profiles and longer duration soleus activation (Esculier, Roy et al. 2015) have been found in those with PFPS (Souza and Powers 2009, Willson, Kernozek et al. 2011, Barton, Lack et al. 2012, Neal, Barton et al. 2015), potentially in an attempt to generate and maintain force in otherwise weakened muscles (Souza and Powers 2009, Willson, Kernozek et al. 2011).

The prior research discussed above has used traditional gait outcome measures, such as discrete EMG, kinematics, and kinetics, in comparing the gait patterns of healthy and injured runners. While evidence exists for altered hip and knee kinematics and knee kinetics in those with PFPS, the lack of evidence on hip and ankle kinetics suggests that further investigation into the gait mechanics of those with PFPS is warranted. In addition, despite the strong and moderate evidence for the kinematic and kinetic variables found in systematic reviews of the literature, there has been disagreement in other studies on the primary gait outcomes. For example, one study found that injured runners used a greater portion of their available rearfoot range of motion during stance relative to healthy runners despite no observed differences in peak values (Rodrigues, TenBroek et al. 2013). Another example involves kinematics proximal to the knee, as Dierks and colleagues found that runners with PFPS displayed decreased peak hip adduction relative to controls (Dierks, Manal et al. 2011), contrary to other studies as reported by Neal and colleagues (Dierks, Manal et al. 2011, Neal, Barton et al. 2015). Thus, although several studies

that have investigated runners with PFPS, there remain contradicting results on mechanics throughout the entire lower limb. One of the potential sources for these conflicting results may be the variability inherent to PFPS, as both pain severity and duration vary between patients. With varying degrees of PFPS severity, there may be a wider natural variation in movement adaptations than in the general population.

Due to the large number of degrees of freedom available in human movement (muscles, joints), there are several possible solutions for generating task-specific movement patterns. Complex, multi-joint movements such as running require the neuromuscular system to coordinate the movement of multiple segments to produce the target lower extremity postures needed for locomotion. Segment coordination is defined as the relationship between segments in terms of both relative motion and relative timing of each segment (Hamill, van Emmerik et al. 1999). One current theory for quantifying human movement patterns using a dynamical systems approach suggests that healthy humans organize their movements within a functional window of coordinative variability (Hamill, Palmer et al. 2012). Too much or too little variability outside this window is believed to lead to injury and decreased function (Hamill, Palmer et al. 2012). Segment coordination variability, or the variability in coordination between different segments from cycle-to-cycle, differs from traditional ‘end-point’ variability, or lack of consistency in the product of a movement (Hamill, Palmer et al. 2012). The latter would be lowest in healthy individuals or experts at a given task and highest in injured or novice individuals. With segment coordination variability the opposite result is expected, in that novice or injured individuals would exhibit the least variability in segment coordination to complete a task (Hamill, Palmer et al. 2012). In repetitive movements like running, segment coordination variability may be considered part of a healthy system as this variability accomplishes two goals: 1) maintains flexibility in the system to respond to perturbation; and 2) provides enough variety in movement that the same underlying tissues are not stressed to the point of injury. Vector coding (Sparrow, Donovan et al. 1987, Heiderscheit 2002, Cunningham, Mullineaux et al. 2014), continuous relative phase (CRP)

(Miller, Meardon et al. 2008), and discrete relative phase (DRP) are a few of the methods used to quantify the variability of coupling angles between segments and joints and overall coordination variability of the lower limb segments (Hamill, van Emmerik et al. 1999, Heiderscheit 2002, Miller, Meardon et al. 2008, Hamill, Palmer et al. 2012, Cunningham, Mullineaux et al. 2014), and interpretations of each should be considered independently.

Coordination has been quantified in several case-control studies using runners with ITBS, PFPS, and individuals with low back pain (Hamill, van Emmerik et al. 1999, Heiderscheit 2002, Miller, Meardon et al. 2008, Seay, Van Emmerik et al. 2011, Hamill, Palmer et al. 2012, Cunningham, Mullineaux et al. 2014). While the dynamical systems theory would suggest decreased coordination variability with injury, the results of these studies have found little change (Heiderscheit 2002), increased (Cunningham, Mullineaux et al. 2014), and decreased variability (Hamill, van Emmerik et al. 1999, Seay, Van Emmerik et al. 2011, Hamill, Palmer et al. 2012) for injured individuals. In fact, two studies have observed varied results depending on which coupling was analyzed (Heiderscheit 2002, Miller, Meardon et al. 2008). In one study investigating coordination in those with PFPS, a reduction in transverse plane variability at the knee joint was found between the affected leg of those with PFPS and controls (Heiderscheit 2002), while another indicated greater variability across nearly all analyzed couplings (Cunningham, Mullineaux et al. 2014). These results may be contradictory due to variations in pain severity and injury duration experienced by respective recruited populations. It is possible that a reduction in the number of movement strategies may lead to increased repetitive stress on the patellofemoral joint causing increased pain of longer duration. This is especially important in pathological populations such as those with PFPS as reoccurrence is a marked consequence of the injury. There is evidence that movement coordination variability may not immediately return to “normal” following a resolution of primary symptoms (pain) for individuals with chronic injuries. Individuals with low back pain, similar to PFPS due to its persistence and frequent reoccurrence, have reduced segment coordination variability during ambulation relative to controls (Seay, Van

Emmerik et al. 2011). Asymptomatic individuals do not return to the same level of variability as those with no history of low back pain, indicating that there is a residual effect of injury even when pain has been resolved (Seay, Van Emmerik et al. 2011). This failure to return to variability levels representative of a healthy population may be an important piece to understanding why certain individuals are predisposed to reoccurrence. Given the results of the low back pain study, it is reasonable to propose that runners who previously suffered from PFPS but are currently asymptomatic may not exhibit segment coordination variability similar to that of healthy runners; in fact, we believe these runners with a former diagnosis of PFPS may exhibit levels of coordination variability that fall between those of healthy runners and those with current PFPS.

In order to achieve these coordinative patterns of segment motion, appropriate muscle coordination is needed for muscles to contract at the correct times and intensities to supply the necessary forces to coordinate the limb movements. Thus, many changes that occur in muscle activity are not represented in the resultant kinematic patterns as a result of the large number of muscles acting throughout the body. In order to study muscle coordination, aside from some of the more traditional amplitude/timing measures, higher dimensional analysis techniques have been developed. Using synchronous multi-muscle analyses, changes in activation patterns associated with increases in speed, effort, and gait pathology during running have been found (von Tscharner 2002, Stirling, von Tscharner et al. 2011). These multi-muscle intensity patterns of activity have the potential to identify common underlying changes in muscle organization relating to altered kinematics and kinetics experienced with fatigue previously observed in a prolonged run in forefoot runners (Jewell, Boyer et al. 2016). Thus, utilizing these methods to study runners with PFPS may provide more insight into the relationship of each muscle with one another in generating coordinated patterns of movement.

When muscle coordination is altered, there may be an uncoupling of segment motion due to altered muscular action and stride-to-stride variability of segment coordination may be reduced. While baseline differences between healthy individuals and those with PFPS are

important, how each group responds to the demands of continued activity may be more relevant when considering overall functional health and pain. Pain increases in response to a continued bout of running in those with PFPS, peaking after approximately 18 minutes and is accompanied by an increase in perceived effort (Noehren, Pohl et al. 2012). Runners with PFPS may not be able to change their mechanics in response to fatigue as healthy runners do, leading to excessive stress on the PFJ over the course of a prolonged run (Noehren, Sanchez et al. 2012). Increased hip flexion, knee flexion (Dierks, Manal et al. 2011, Bazett-Jones, Cobb et al. 2013) and patellar tilt angles along with increased knee abduction and hip internal/external rotation moments (Bazett-Jones, Cobb et al. 2013) with fatigue have been found in those with PFPS. After fatigue onset, decreased hip strength (Bazett-Jones, Cobb et al. 2013), hip adduction (Dierks, Manal et al. 2008, Dierks, Manal et al. 2011), and peak hip internal rotation (Dierks, Manal et al. 2011) have also been observed. In runners with PFPS, perceived fatigue levels were higher than healthy runners despite a similar running bout (Noehren, Sanchez et al. 2012), indicating that fatigue perception may be influenced by accompanying pain.

Study aims

Given the gait differences observed between healthy runners and those with PFPS, there is a need to understand the mechanisms for altered gait and muscular function. The primary aim of the proposed dissertation is to quantify the differences in muscle coordination and segment coordination variability between runners with a current or former diagnosis of PFPS and healthy runners. Our hypothesis is that there will be a substantial reduction in variability and altered muscle coordination patterns as a function of the pain and fatigue experienced during activity. We believe this variability will remain low following the resolution of acute PFPS symptoms as compared to healthy runners, similar to the results seen in individuals with low back pain.

Movement evoked pain is a characteristic symptom of PFPS; therefore, we will quantify movement coordination (muscle coordination and segment coordination variability) throughout a

prolonged 21-minute treadmill run (21MTR) in three groups: healthy runners, those with a current PFPS diagnosis (PFPS), and asymptomatic runners with a previous PFPS diagnosis in which knee pain has resolved (RES). Muscle coordination will be quantified by decomposing multi-muscle EMG activation patterns using a principal component analysis. The principal components and their weightings will be used as inputs to a support vector machine (SVM) to identify discriminant muscle coordination patterns. Three studies, outlined below, are proposed to 1) investigate the differences in kinematics and kinetics; 2) quantify changes in coordination variability; and 3) muscle coordination throughout the 21MTR between the three groups. In addition, an exploratory study will be performed in an attempt to classify the RES runners into either healthy or PFPS pattern groups in hopes of finding metrics that may indicate risk of injury reoccurrence.

Study 1: The impact of patellofemoral pain on gait during a prolonged run in recreational runners

Aim: The primary aim of this study is to quantify the changes in hip internal rotation and adduction angles, as well as hip and knee adduction moments, in response to increased pain and effort during the 21MTR.

H1.1 At baseline, hip internal rotation and adduction angles will be different between the CON, PFPS, and RES groups, such that $CON < RES < PFPS$.

H1.2 At baseline, knee adduction moments will be smaller in CON and RES groups as compared to PFPS, such that $CON < RES < PFPS$, while the opposite relationship will be true for hip adduction moments.

H1.3 Between the beginning and end of the 21MTR, the hip internal rotation and adduction angles and hip and knee adduction moments outcome will not change in the CON group. These measures will change from baseline in the PFPS and RES groups, such that the magnitude of these changes will be as follows: $Con < RES < PFPS$.

Exploratory H1.4 There will be a correlation between pre-post run changes in the above gait mechanics and the changes in pain as rated on a Verbal Numeric Rating Scale (VNRS).

Study 2: Segment coordination and coordination variability throughout a prolonged run in runners with patellofemoral pain

Aim: The primary aim of this study is to quantify differences in segment coordination and coordination variability between the CON, PFPS, and RES groups at baseline and over the course of the 21MTR in the following couplings: 1) frontal pelvis vs. transverse thigh and 2) frontal pelvis and frontal thigh.

H2.1 Segment coordination variability will be lower in individuals with PFPS as compared to RES and healthy controls, such that variability differs as $PFPS < RES < CON$ at baseline of the 21MTR for the above couplings.

H2.2 Segment coordination will be different for the above couplings between CON, PFPS, and RES at the end of the 21MTR.

H2.3 Segment coordination variability will decrease in PFPS and RES but not healthy controls over the 21MTR for the above couplings such that the change in variability is $Con < RES < PFPS$.

Exploratory H2.4 There will be a progressive decrease in segment coordination variability throughout the run.

Study 3: Muscle coordination throughout a prolonged run in runners with patellofemoral pain

Aim: The primary aim of this study is to quantify changes in muscle coordination of the CON, PFPS, and RES groups of runners over the course of the 21MTR.

H3.1 Muscle coordination will be different between the beginning and end of the run for both PFPS and RES, with the largest change occurring in PFPS. There will be no change in the CON group. A change in muscle coordination will be quantified as the change in respective weight factors for each principal pattern.

Exploratory Aim: To test the ability of a machine learning algorithm to classify RES multi-muscle patterns as healthy or injured. The weight factors at the end of the run for the PFPS and CON groups will be used to train the support vector machine.

The purpose of this dissertation is to investigate the relationship of knee pain, injury status, and perceived exertion on 3D kinematics, kinetics, muscle coordination, segment coordination and segment coordination variability of trained runners. Three studies were completed to compare

these outcome measures between healthy, injured, and previously injured runners. The results of these studies will further the knowledge of the field through an improved understanding of the underlying mechanisms to development and progression of injury, as well as to help aid in focusing our efforts onto specific targets for improved rehabilitation, function, and return to activity.

CHAPTER 2

REVIEW OF THE LITERATURE

Introduction

Running is one of the most accessible effective forms of cardiovascular exercise with myriad benefits. However, each year, between 50-85% of runners will get injured (Bovens, Janssen et al. 1989, Lun, Meeuwisse et al. 2004). Injury in the previous 12 months has been cited as the main risk factor for developing subsequent injuries (Saragiotto, Yamato et al. 2014), indicating that injury prevention is of great importance. The most common lower limb injury experienced by runners is patellofemoral pain syndrome (PFPS) which comprises 20% of all running-related injuries. Classified as an overuse injury resulting from cumulative micro-trauma, PFPS presents as pain on the anterior surface of the knee, leading to diffuse pain in and around the patellofemoral joint (PFJ) that is exacerbated by load-bearing activities involving knee flexion (Taunton, Ryan et al. 2002). The primary source of PFJ pain is believed to be cumulative microtrauma in subchondral bone (Biedert and Sanchis-Alfonso 2002, Fulkerson 2002, Draper, Besier et al. 2006), though activation of nociceptive fibers within the synovium and retinaculum have been proposed as other sources of pain (Fulkerson 2002). Common criteria for injury diagnosis are: 1) Retropatellar knee pain during 2 of the following activities: walking up/down stairs, hopping/jogging, prolonged sitting, kneeling, and squatting; 2) Negative findings on examination of structural components of knee and at least one of the following: 1) Pain on palpation of medial or lateral patellar facets and/or 2) Pain on palpation of the anterior portion of the medial or lateral femoral condyles (Boling, Padua et al. 2009). Patellofemoral pain syndrome is commonly accompanied by stiffness, swelling, locking, and crepitus at the knee (Blond and Hansen 1998, Fulkerson 2002, Thomee, Thomee et al. 2002) and can greatly restrict activity.

Those with PFPS deal with both poor short and long term outcomes: 70 % of those suffering from PFPS still have pain one year after onset; long-term prognosis is just as bleak as 91% remain in pain 4-18 years post onset (Stathopulu and Baildam 2003). In this cohort of long-

term outcomes, 36% were restricted in daily activities (Stathopulu and Baildam 2003). Patellofemoral pain syndrome is considered to be periodic, often cycling between phases of diminished and increased pain, with restricted activity cycling with the ebbs and flows of pain (Blond and Hansen 1998). Poor outcomes of PFPS have been associated with the duration of pain. The longer the pain is experienced, the less likely an intervention is to be successful and the greater the chance for prolonged PFPS and reoccurrence (Collins, Crossley et al. 2010, Collins, Bierma-Zeinstra et al. 2013). PFPS has long been believed to be self-limiting (Sandow and Goodfellow 1985, Jensen and Albrektsen 1989, Arroll, Ellis-Pegler et al. 1997); however, evidence now exists that chronic pain is related to internal damage and detrimental effects on PFJ cartilage (Utting, Davies et al. 2005). Altered knee motion exhibited by those with PFPS may cause altered joint loading leading to cartilage damage that may lead to the onset of knee osteoarthritis (OA) progression (Andriacchi and Mündermann 2006). Further progression of PFPS has been linked to OA of the PFJ and further joint degeneration (Utting, Davies et al. 2005) and disability with older age (Wyndow, Collins et al. 2016). Patellofemoral pain syndrome and knee osteoarthritis combined account for upwards of \$20 billion in healthcare costs each year (Seeley, Park et al. 2013); thus there is a large economic impetus for treatment management and prevention of PFPS.

With increased progression of PFPS symptoms, activity can become limited leading to further negative health outcomes, including but not limited to obesity, diabetes, and other chronic diseases. It is necessary to understand what factors can predispose runners and other active individuals to PFPS, as well as what types of changes occur at the outset of the pain. This review will outline the current state of the literature in regards to the risk factors leading to PFPS development, the influence of PFPS on the mechanical structures within the knee, as well as the changes in gait mechanics and muscle function that occur in those suffering from PFPS. In addition, this review will discuss the potential applications of dynamical systems and

coordination analyses to the study of PFPS based on previous work that has applied these tools to running injury.

Patellofemoral alignment

Several theories have been proposed for the initial causes of PFPS injury and pain onset. Previous research indicates that a combination of the following factors are major contributors to PFPS onset: decreased muscle strength, altered alignment, and the influence of the alignment on lateral patellar maltracking, or disrupted tracking of the patella within the trochlear groove (Messier, Davis et al. 1991, Powers 2003, Dierks, Manal et al. 2008). The Q-angle is the angle formed between the force vector of the quadriceps muscles and tibia and is typically measured as the angle between the anterior superior iliac spine, the middle of the patella, and the tibial tuberosity (Horton and Hall 1989). One prospective study found increased static Q-angle and ankle dorsiflexion in recreational runners who developed PFPS (Lun, Meeuwisse et al. 2004). This was the only lower limb injury that these runners developed that was significantly associated with static alignment.

While static alignment is important, dynamic alignment may be even more critical given the greater impact of dynamic loads compared to static loads on tissue properties. There are various factors that can influence the dynamic alignment of the knee and patella. Increased dynamic valgus alignment may be caused by altered strength of muscles at the hip (Herbst, Foss et al. 2015). Patella alta, or increased patellar height relative to the femoral condyles, is thought to lead to increased patellar maltracking, decreasing PFJ contact area thus increasing joint stress at specific sites (Pal, Besier et al. 2013, Salsich and Perman 2013). Abnormal motion of the tibia and femur in transverse and frontal planes directly influence patellofemoral joint mechanics and pain; thus, alignment in all planes can play a role in joint mechanics (Powers 2003). Any change

in alignment may directly affect the interaction between the patella and underlying cartilage/bone even in the absence of muscle weakness.

Patellofemoral joint stress

Modeling the joint aids in understanding how these loads are affected by joint mechanics (Dye 2001). In order to quantify potential changes within the knee joint that result from structural differences and poor alignment, several different models have been used to estimate the individual muscle forces and stresses acting about the PFJ using both computer simulations and cadavers (Scott and Winter 1990, Besier, Gold et al. 2008, Farrokhi, Keyak et al. 2011, Chen, Powers et al. 2014, Besier, Pal et al. 2015). The onset of pain in those with PFPS is believed to occur from excessive loads and an internal shift of the load distribution where the osseous and soft tissues of the knee joint lose homeostasis causing the perception of pain. Typically in these models, cartilage stresses are depicted as complex interactions of joint kinematics, morphology, and the muscles acting about the joint (Besier, Gold et al. 2008).

Static and dynamic alignment of the lower limbs have been found to influence the stress at the PFJ. Peak patellar shear and octahedral stress have been found to increase more than 10% with a 15-degree increase in external rotation of the femur (Besier, Gold et al. 2008). With PFPS, patellar stress has been found to be either increased across several discrete knee flexion angles (Farrokhi, Keyak et al. 2011) or similar to healthy controls in magnitude but occurred earlier during stance (Brechtler and Powers 2002). In individuals where the peak stress is not higher than controls, maintenance of lower peak stress levels was achieved by a reduction in the overall joint reaction force. This was achieved through altered gait mechanics including slowed cadence and decreased knee extensor moments (Brechtler and Powers 2002, Chen, Powers et al. 2014). These findings suggest that a quadriceps avoidance strategy is used in those with PFPS to decrease peak stresses. A significant increase in PFJ reaction force on the lateral facet of the patella has been

identified in runners with PFPS (Chen, Powers et al. 2014), which is likely a main factor in the observed increased stress at the joint.

Modeling studies have estimated knee joint contact forces at up to 7.6 times body weight (Scott and Winter 1990). In one study, magnetic resonance imaging (MRI) was used to measure patellofemoral contact area, tibiofemoral rotation angle, and PFJ alignment. With PFPS, there was a reduced contact area as well as higher lateral patellar displacement than healthy controls, indicating that patellofemoral alignment may be more closely related to contact area of the patella than tibiofemoral rotation at increased knee flexion angles (Salsich and Perman 2013).

Cartilage properties

Increased joint reaction forces, especially when combined with abnormal joint loading, may lead to damage of the retropatellar cartilage. Damage to and changes in the composition of retropatellar cartilage have been proposed to cause PFPS progression and graduation to early-stage knee OA. Damage to the cartilage may also lead to damage of the subchondral bone and synovial inflammation, believed to be primary sources of pain in those with PFPS (Draper, Besier et al. 2006, Cunningham, Mullineaux et al. 2014). Cartilage is aneural and cannot be a source of pain (Biedert and Sanchis-Alfonso 2002), which holds true even in the presence of significant cartilage lesions (Joensen, Hahn et al. 2001). Inflammation or damage to underlying tissues in the bone or synovium likely activates the free nerve endings presiding in these tissues, causing pain (Biedert and Sanchis-Alfonso 2002). Cartilage health plays a significant role in the development and progression of pain in individuals with PFPS as altered cartilage profiles can contribute to inflammation and changes in bone stress leading to pain. The two main factors in cartilage health in relation to PFPS are the composition and thickness of the articular cartilage.

Several biomarkers have been used to monitor cartilage composition. One such marker of importance is T1 ρ relaxation time, which is typically measured with nuclear magnetic resonance spectroscopy (NMRS) (Duvvuri, Reddy et al. 1997). T1 ρ relaxation time is used as a surrogate

measure of proteoglycan content within the cartilage (Duvvuri, Reddy et al. 1997). Increased proteoglycan loss is marked by increased T1p transverse relaxation times (Duvvuri, Reddy et al. 1997). Osteoarthritic cartilage frequently exhibits increased water content which may be caused by a weakening of the collagen network and loss of proteoglycans in the extracellular matrix (Duvvuri, Reddy et al. 1997). Increased T1p relaxation time on the lateral facet of the patella has been observed in those suffering from PFPS, signifying proteoglycan loss at greater levels than healthy controls (Thuillier, Souza et al. 2013, van der Heijden, Oei et al. 2016), similar to individuals with osteoarthritis. Proteoglycan loss has been suggested as an etiological factor in the onset and progression of PFPS and may signify osteoarthritis development. Despite these reported increased T1p relaxation times, not all studies have found similar results in regards to proteoglycan loss and fluid content of articular cartilage. In another study, no differences in T2 (a marker related to fluid content and collagen levels within the cartilage) were found between healthy and controls, signifying water and collagen levels remained constant in the observed cartilage (Farrokhi, Colletti et al. 2011).

In addition to measures of water, proteoglycan, and collagen content, cartilage thickness measured with magnetic resonance imaging (MRI) has been used as a surrogate measure for cartilage health. As the deformation of articular cartilage plays a significant cushioning role in load-bearing activity, its thickness can be considered a direct measure of load attenuation capacity (Goodfellow, Hungerford et al. 1976, Farrokhi, Colletti et al. 2011). Baseline cartilage thickness in females with PFPS has been found to be 14 % thinner on both the lateral facet and across the total patellar cartilage compared to controls (Farrokhi, Colletti et al. 2011). In the same population, after 50 deep knee bends, healthy cartilage deformed more than twice as much as the cartilage of those with PFPS (Farrokhi, Colletti et al. 2011). The lack of cartilage deformation may be linked to increased stress in the joint and the onset of pain due to a decreased ability to attenuate reaction forces about the knee (Farrokhi, Colletti et al. 2011). In addition to the differences observed in females in baseline cartilage thickness, peak cartilage thickness in males

with PFPS has been found to be 18 % thinner than healthy controls (Draper, Besier et al. 2006). Given the observed differences in cartilage composition and thickness in those with PFPS, it is likely that altered PFJ cartilage health plays a significant role in PFPS development.

Muscle function

Alignment of the bones in the lower limb may have a distinct impact on PFJ mechanics and underlying cartilage function. However, the muscles proximal and distal to the knee also play a significant role in knee joint function, providing joint stability and controlling patellar tracking and tilt that may be disrupted by malalignment, as well as modifying how forces are directed throughout the knee. Prospective studies looking at adolescent athletes have found that greater hip abduction strength (Finnoff, Hall et al. 2011, Herbst, Foss et al. 2015) in addition to increased hip external rotator strength (Finnoff, Hall et al. 2011) predisposed athletes to develop PFPS later on; this was proposed to be a result of increased eccentric loading due to excessive valgus alignment (Herbst, Foss et al. 2015). This surprising result may be due to increased recruitment of the gluteus medius muscle as both a hip abductor and an external hip rotator to make up for other weak hip external rotator muscles (Finnoff, Hall et al. 2011). Other evidence has indicated that isometric hip strength and PFPS risk are not associated (Rathleff, Rathleff et al. 2014).

Several studies have found that musculature around the hip, especially hip abductors and extensors, are typically weakened in those suffering from PFPS (Ireland, Willson et al. 2003, Souza and Powers 2009, Finnoff, Hall et al. 2011, Lankhorst, Bierma-Zeinstra et al. 2012, Bazett-Jones, Cobb et al. 2013, Chen, Powers et al. 2014). This may lead to altered hip and knee kinematics (Souza and Powers 2009), specifically increased femoral internal rotation throughout weight-bearing activities (Souza and Powers 2009). According to a meta-analysis, strong evidence has been found that individuals with PFPS have a deficit in hip external rotation (Ireland, Willson et al. 2003, Piva, Goodnite et al. 2005, Cichanowski, Schmitt et al. 2007, Robinson and Nee 2007, Bolgla, Malone et al. 2008, Willson, Binder-Macleod et al. 2008),

abduction (Ireland, Willson et al. 2003, Piva, Goodnite et al. 2005, Cichanowski, Schmitt et al. 2007, Robinson and Nee 2007, Bolgla, Malone et al. 2008, Magalhães, Fukuda et al. 2010), and extension strength (Cichanowski, Schmitt et al. 2007, Robinson and Nee 2007, Magalhães, Fukuda et al. 2010, Lankhorst, Bierma-Zeinstra et al. 2012), with moderate evidence for a deficit in hip flexion and internal rotation strength (Prins and Van Der Wurff 2009). However, as is common in the PFPS literature, other researchers are in disagreement with the findings of decreased hip abductor strength, especially in those with early stage PFPS (Plastaras, McCormick et al. 2016). These researchers found increased hip abductor strength in those with early stage PFPS (Plastaras, McCormick et al. 2016). A reduction in knee extensor strength has also been found in individuals suffering from PFPS (Bennett and Stauber 1986, Kannus and Niittymäki 1994, Kaya, Citaker et al. 2011).

After PFPS development, hip abductors and hip external rotators decline in strength relative to their baseline measures (Ireland, Willson et al. 2003, Finnoff, Hall et al. 2011, Lankhorst, Bierma-Zeinstra et al. 2012, Herbst, Foss et al. 2015). These changes are seen in the unaffected limb of injured individuals as well, indicating a bilateral deficit compared to healthy controls (Duffey, Martin et al. 2000) which maintains symmetry between legs (Plastaras, McCormick et al. 2016). This indicates that unilateral study of the affected limb is sufficient for observing changes in gait mechanics in those with PFPS and also marks a need for PFPS treatment to be focused on both legs to restore healthy gait and overall function.

Changes found in muscle strength, reduced muscular endurance (Duffey, Martin et al. 2000) and muscle atrophy (Giles, Webster et al. 2013) of the knee extensors have also been found in those with PFPS. These muscles are of great importance to the overall stability of the knee. In fact, the vastus medialis oblique (VMO) muscle is a primary muscle involved in patellar tracking (Jan, Lin et al. 2009). One group measured muscle endurance isokinetic testing of the knee extensors at 60°s^{-1} and 240°s^{-1} using a dynamometer (Duffey, Martin et al. 2000) and found that knee extensor endurance was impaired at both velocities in the injured group compared to healthy

controls (Duffey, Martin et al. 2000). Quadriceps atrophy has been identified in studies on individuals with PFPS, but it is not understood whether the atrophy occurs as a result of PFPS or is a predisposing factor given that measurements have not been taken in prospective studies (Kaya, Citaker et al. 2011, Giles, Webster et al. 2013). Quadriceps muscle atrophy has not been discernable through girth measurements or visual inspection in those with PFPS; however, using imaging such as MRI, evidence of quadriceps atrophy has been found through smaller VMO volume (Giles, Webster et al. 2013). The quadriceps muscle atrophy was significant both between the affected limb and contralateral limb, as well as between injured and healthy controls (Giles, Webster et al. 2013). Altered VMO characteristics have been proposed to be a predisposing factor to PFPS development (Jan, Lin et al. 2009). Differences have been found in the insertion level, fiber angle, and volume of VMO; all were significantly smaller in those with PFPS (Jan, Lin et al. 2009). Given that one of the primary roles of the VMO is to provide stability of the patella, changes in VMO characteristics could affect the dynamic moment arms of the VMO and have a dramatic impact on PFJ mechanics. These results may provide a rationale for strengthening exercises of the affected limb in PFPS treatment.

Neuromuscular control

Apart from changes in baseline VMO and hip abductor characteristics and function, the relative timing of muscle activation of the quadriceps, gluteus medius and maximus, and the hamstrings is believed to play a role in tracking of the patella about the PFJ (Cowan, Bennell et al. 2001, Patil, Dixon et al. 2011, Willson, Kernozek et al. 2011, Lankhorst, Bierma-Zeinstra et al. 2012, Hug, Hodges et al. 2014, Esculier, Roy et al. 2015). Muscle activation is typically measured as surface recordings (non-invasively on the skin) of the underlying action potentials propagating through firing muscles. One of the most frequently observed changes in this surface electromyography (EMG) has been a delay in the onset of VMO relative to vastus lateralis (VL) at touchdown (Cowan, Bennell et al. 2001, Chester, Smith et al. 2008). This has been observed

prospectively in healthy men who developed PFPS (Van Tiggelen, Cowan et al. 2009). These effects are magnified in those classified as maltrackers, leading to increased patellar tilt (Pal, Besier et al. 2012). A cadaveric study found that increased VMO force led to a decrease in lateral pressure on the patella, which could reduce pressure and pain at the PFJ even with cartilage lesions present (Elias, Kilambi et al. 2009), indicating the importance of this muscle to overall knee function with pain. Excessive lateral tracking of the patella may be brought on by a difference in relative timing of the VMO relative to the VL or a reduction in force-producing capability of the VMO (Cowan, Bennell et al. 2001). This increased lateral tracking may also be a result of increased lateral hamstring activity, which has also been observed in patients with knee OA and shown to be more prevalent in females than males (Patil, Dixon et al. 2011). In addition, quadriceps avoidance (a decrease in quadriceps activity) has been found in individuals suffering from PFPS, which may influence changes in coordination of quadriceps activity (Lin, Hua et al. 2015). Throughout the literature, the influence of muscle strength and activation profiles appear as primary considerations in PFPS development.

The gluteal muscles play a significant role in hip function and PFPS development. Altered gluteus maximus and medius activation profiles have been found in individuals with PFPS (Souza and Powers 2009, Willson, Kernozek et al. 2011). The gluteus medius altered profile is characterized by delayed timing of activation relative to ground contact as well as shortened durations of activity (Willson, Kernozek et al. 2011, Barton, Lack et al. 2012, Neal, Barton et al. 2015). The gluteus maximus has been found to have increased magnitude of activation (Souza and Powers 2009). These altered profiles have been associated with greater hip adduction and internal rotation excursion (Souza and Powers 2009, Willson, Kernozek et al. 2011). It is believed that increased gluteus maximus activity occurs in an effort to increase force production from an otherwise weakened muscle to stabilize the hip (Souza and Powers 2009).

In addition to the observed changes in activation profiles of the above muscles, one characteristic of muscle activity in those with PFPS is increased activation of the antagonist

muscles about the knee. Increased co-activation between the quadriceps and hamstrings has been observed with PFPS (Besier, Fredericson et al. 2009). Co-activation of agonist and antagonist muscles frequently occurs in older and pathological populations and may be a strategy employed to aid in increased stability of the knee (Besier, Fredericson et al. 2009, Hortobágyi, Solnik et al. 2009, Peterson and Martin 2010, Hortobágyi, Finch et al. 2011, Tsai, McLean et al. 2012). This greater co-activation in PFPS patients causes increased overall muscular force applied to the joint. These increased muscle forces may generate greater joint contact forces and stresses than healthy controls and thus contribute to increased levels of pain (Besier, Fredericson et al. 2009, Tsai, McLean et al. 2012).

Muscle coordination

As seen above, several groups have studied the activation patterns of lower limb muscles in healthy and pathological populations using EMG. Differences in timing of muscle activations, amplitude of the action potentials, and frequency content of the electrical signal are used to make inferences about the control and state of the recorded muscles. Each of these components of the electromyogram are used for a different interpretation in how the motor system functions; timing relates to when these muscles are being recruited by the motor cortex, amplitude relates to the number of motor units being recruited, and frequency is often used as a surrogate measure for the type of fibers that are being recruited in addition to the conduction velocities of the measured motor unit action potentials. To date, these methods of muscle analysis have provided much-needed information about how humans generate specific movements and the differences between healthy and pathologic muscle control. However, when considering the overall organization of movement, these measures are limited. With traditional measures, one of either the timing, amplitude, or frequency must be sacrificed to study the relationship between the other two signal components. In order to study muscle coordination, the organization of activation intensity and timing across multiple muscles, more comprehensive methods must be used.

To understand the role of muscle function and activity in the development and onset of PFPS, a variety of analysis methods can be employed to quantify coordinative patterns of muscle activity. One of these techniques is centered around using a wavelet-based time/frequency analysis of EMG signals throughout an activity (von Tscharner 2000). This method allows the power spectra to be analyzed without forgoing, or dramatically adjusting, the temporal component of an activity (von Tscharner 2000). Using wavelets of a specified resolution, the power spectra of non-stationary EMG signals can exist in a physiologically relevant time domain (von Tscharner 2000). When the wavelet-transformed EMG patterns are combined with principal component analysis (PCA), the extraction of principal patterns of muscle reveals information about intra- and inter-muscular changes in the relative magnitude and timing of muscle activation events (von Tscharner 2002). It also affords the ability to perform linear statistics on higher dimensional data, using simple methods to analyze complex relationships.

This synchronous multi-muscle analysis has been used previously to study changes in activation patterns associated with increases in speed and effort during running and to classify groups between differing footwear conditions and levels of fatigue in cycling (von Tscharner 2002, von Tscharner, Goepfert et al. 2003, Stirling, von Tscharner et al. 2011). Multi-muscle patterns of activity have also been used to differentiate between ankle OA patients with a history of traumatic injury and healthy controls, and to identify the time periods in which differences in activation patterns occur (von Tscharner and Valderrabano 2010). The multi-muscle principal patterns have the potential to identify common underlying changes in muscle organization relating to altered kinematics and kinetics experienced with fatigue, and likely have a similar potential in differentiating between activity patterns in those with differing perceived levels of pain (Jewell, Boyer et al. 2017). These methods have also been paired with both machine learning linear classifiers, such as a support vector machine, and spherical classifiers to segment the multi-muscle patterns into segregable groups depending on the spread of these data (von Tscharner 2009, Stirling, von Tscharner et al. 2011, von Tscharner, Enders et al. 2013). These methods for

EMG analysis and classification lend themselves to further understanding of muscle coordination in the creation of organized movement, and towards using these changes and differences between groups to further classify muscle coordination patterns. These are especially important when considered in the context of the resultant kinematic and kinetic patterns of movement generated from the underlying muscle organization.

Gait mechanics

While all voluntary movement originates in the motor cortex and is dependent on the forces generated by individual muscles, the resultant macroscopic movement patterns like gait kinematics and kinetics have been more frequently and rigorously studied in individuals with PFPS. One of the primary difficulties in studying PFPS is that the syndrome covers a wide spectrum of both pain level and duration (Fulkerson 2002) and thus adaptations to PFPS may be highly variable. In addition, the interpretation of results from cross-sectional studies often makes it difficult to determine whether observed differences in gait mechanics between healthy controls and those with PFPS are what caused or occurred as a result of the progression of the syndrome.

Prospective studies that attempt to tease out the cause-and-effect relationships between observed differences in those with PFPS and those without typically focus on strength and alignment related measures (Hetsroni, Finestone et al. 2006, Stefanyshyn, Stergiou et al. 2006, Boling, Padua et al. 2009, Collins, Crossley et al. 2010, Finnoff, Hall et al. 2011, Rathleff, Baird et al. 2013). Increased hip adduction throughout stance relative to controls has been observed in those who go on to develop PFPS (Noehren, Scholz et al. 2010, Neal, Barton et al. 2015). There is little additional evidence of gait parameters that may lead to PFPS development given the lack of prospective studies using gait analysis methods, apart from plantar pressure measurements (Thijs, Van Tiggelen et al. 2007). However, several studies have looked retrospectively at kinematics and kinetics of those with PFPS; fewer of these studies have focused specifically on the kinematics and kinetics of gait.

Several studies have indicated changes in hip mechanics during running in those with PFPS. Given the large amount of studies that have found significant changes in hip kinematics, the hip appears to be the primary site for adaptations from or leading to development of PFPS. There is evidence of an association between PFPS and increased peak hip adduction (Souza and Powers 2009, Dierks, Manal et al. 2011, Noehren, Pohl et al. 2012, Noehren, Sanchez et al. 2012, Willy, Manal et al. 2012, Bazett-Jones, Cobb et al. 2013, Esculier, Roy et al. 2015) and hip internal rotation (Souza and Powers 2009, Dierks, Manal et al. 2011, Noehren, Pohl et al. 2012, Noehren, Sanchez et al. 2012, Willy, Manal et al. 2012, Bazett-Jones, Cobb et al. 2013, Esculier, Roy et al. 2015, Neal, Barton et al. 2015) throughout stance as well as peak contralateral pelvic drop (Noehren, Pohl et al. 2012, Willy, Manal et al. 2012, Bazett-Jones, Cobb et al. 2013, Esculier, Roy et al. 2015) and reduced stance phase peak hip flexion (Neal, Barton et al. 2015). As with much of the research regarding PFPS, there has been some disagreement in results. One study found evidence of decreased hip internal rotation with PFPS (Willson and Davis 2008). Greater hip adduction and increased internal rotation excursions have been found in those with PFPS (Willson, Kernozek et al. 2011). At toe-off, PFPS runners exhibit increased hip adduction and increased range of motion between mid-stance and toe-off (Esculier, Roy et al. 2015).

Despite the frequency of significant findings in changes in hip motion in those with PFPS, the site where the pain is experienced still deserves significant attention. Several studies have observed changes in knee kinematics and kinetics in those with PFPS. Compared with healthy females, those with PFPS had greater knee external rotation and decreased knee internal rotation excursion across a wide range of activities (Willson and Davis 2008). Runners with PFPS exhibited increased peak knee adduction during running and squatting (Willy, Manal et al. 2012), and decreased peak knee flexion (Dierks, Manal et al. 2011) and knee flexion velocity (Dierks, Manal et al. 2011) relative to controls. Changes have also been found in regards to the moments experienced about the knee.

Knee adduction moments are important when understanding PFPS considering the pain is usually experienced on the lateral aspect of the patella (Stefanyshyn, Stergiou et al. 2006). Along with the previously mentioned increased peak knee adduction angles, runners with PFPS have been found to have increased external knee adduction moments relative to healthy counterparts (Willy, Manal et al. 2012). In addition to the altered joint moments in those with PFPS, decreased vertical ground reaction forces have been identified compared to healthy controls during running (Esculier, Roy et al. 2015), though peak forces have been found to be increased during walking trials (Callaghan and Baltzopoulos 1994).

Proximal factors are thought to be more influential on knee mechanics; however, recently studies have begun to emphasize the effects of alignment and soft tissue distal to the knee on overall joint health, specifically calcaneal eversion and pronation of the foot (Rodrigues, Chang et al. 2013). Despite this recent interest in distal factors and PFPS progression, a meta-analysis has found strong evidence that no association exists between rearfoot eversion and PFPS (Neal, Barton et al. 2015), although one study has reported that individuals with anterior knee pain utilize a greater percentage of their rearfoot eversion range of motion throughout stance than their healthy counterparts (Rodrigues, TenBroek et al. 2013). This was proposed to be a greater indicator of risk of injury than peak eversion (Rodrigues, TenBroek et al. 2013). Given this finding, there may be factors below the knee that influence mechanics of those with PFPS, and thus more research may be warranted.

Kinematics and kinetics have been investigated in those with PFPS during activities other than running which may be informative to the progression of PFPS. During stair ambulation, individuals with PFPS displayed decreased knee extensor moments, which was achieved by decreased cadence, suggesting a quadriceps avoidance strategy to reduce the PFJ reaction force (Salsich, Brechter et al. 2001). During walking, a reduction in knee flexion angle (Nadeau, Gravel et al. 1997, Powers, Heino et al. 1999) has been observed at multiple points throughout the gait cycle with PFPS, along with modified knee joint moments around foot strike (Nadeau, Gravel et

al. 1997). Decreased knee flexion has been observed in those with PFP in fast walking; however, this was not accompanied by increased lower limb loading (Powers, Heino et al. 1999). This appears to have been accomplished by selecting a slower walking velocity than controls to minimize ground reaction forces (Powers, Heino et al. 1999). Given these findings, it would seem that individuals with PFPS limit movement at the knee in an attempt to minimize pain.

Pain response

How individuals respond to pain is an important factor to consider in the gait and muscle function differences observed between those with PFPS and healthy controls. There have been several theories explaining how the body adapts and responds to pain: the pain adaptation theory (Lund, Donga et al. 1991), the vicious cycle theory (Roland 1986), and the theory of muscle redistribution with pain (Hodges and Tucker 2011). These are defined, respectively, as an inhibition of the muscles that create a painful movement accompanied by the excitation of the antagonist muscles in an effort to stabilize the joint (Lund, Donga et al. 1991); a hyper sensitive condition brought on by the presence of pain (Roland 1986); and finally, a redistribution of muscle activity throughout the body in an effort to reorganize movement (Hodges and Tucker 2011, Hodges 2014).

The most recent pain response theory is the muscle redistribution theory (Hodges and Tucker 2011). It has been demonstrated recently that when possible, the body adapts to pain with a reorganization of muscle activity to reduce stress or loads on the affected tissue (Hug, Hodges et al. 2014). This theory of redistribution involves increased activation in some muscles while inhibiting others. This is believed to affect changes in the mechanical behavior of movement as a means for protection from further pain or injury. These modifications are believed to occur throughout multiple levels of the motor system and may have a short term benefit in pain reduction but bring about potential long-term consequences such as muscle weakness and reduced function (Hodges and Tucker 2011). This particular response to pain is important to consider in

the development and progression of PFPS and has been linked with changes in movement variability (Falla, Gizzi et al. 2014, Hodges 2014). The redistribution of muscle activity throughout the body may have a profound impact on gait mechanics of individuals with PFPS, as adaptive strategies to reduce load by coordinating muscle activation may be a primary goal of pain reduction. This, in turn, may trigger the resulting changes in kinematics and kinetics that have been observed.

One manner in which the effects of pain alone, apart from structural changes within a joint or muscle, has been examined in individuals has been through experimentally-induced pain. These pain models have the advantage of being able to model similar pain responses to degenerative conditions such as osteoarthritis but can be implemented in otherwise healthy individuals to test if changes in gait and muscle activity come from adaptations to pain as opposed to mechanical changes of the joint or surrounding tissues. These pain models typically use an injection of a hypertonic saline solution into the infrapatellar fat pad or muscle (Henriksen, Graven-Nielsen et al. 2010, Henriksen, Rosager et al. 2011, Seeley, Park et al. 2013, Denning, Woodland et al. 2014, Son, Kim et al. 2015). Group III and IV nociceptive afferents have been shown to be active due to hypertonic saline in animal models (Seeley, Park et al. 2013), validating these injections as an appropriate method to induce pain. This experimental pain model has been used in a number of different applications from investigating changes in muscle function to comparing pathological populations to healthy.

Differences in muscle strength and direction of force generation have been observed with experimental pain. With a saline injection into the infrapatellar fat pad, quadriceps maximal voluntary contractions are reduced by 15-34% accompanied by a 5% decline in central activation ratio (ratio of voluntary contraction force to added stimulation) (Henriksen, Rosager et al. 2011, Park and Hopkins 2013). This indicates a reduction in the voluntary ability to produce force with pain. In addition to a decline in strength, experimentally-induced pain has been shown to cause

individuals to change the direction of force generation and application during a knee extension task through a redistribution of active motor units in the quadriceps (Tucker and Hodges 2010).

In addition to changes seen in muscle function in isometric or fixed path exercises, experimental pain has been used to study the effects of localized pain on less controlled movements. In individuals with experimentally induced muscle pain of the VMO, no changes were found in VMO EMG or in the shear elastic modulus of the muscle during a unilateral task (single leg knee extension, single leg squat) (Hug, Hodges et al. 2014). However, in a bilateral squat, VMO and VL EMG amplitude, along with shear elastic modulus and force production, decreased in the painful leg while force was increased as a compensatory mechanism in the unaffected leg (Hug, Hodges et al. 2014). This suggests that reorganization of muscle activation and limb loading occurs only when there are multiple degrees of freedom available for movement and the metabolic cost and tissue loading profiles are in agreement with one another (Hug, Hodges et al. 2014).

These pain models have also been applied to gait to observe the impact of localized pain on muscle activity, kinematics, and kinetics. Single injections have been used prior to walking and running trials to induce pain, as well as continuous saline infusion being used during longer duration walking and running to maintain a constant pain response. Experimental knee pain has been associated with a decrease in peak plantarflexion moment, hip abduction moment, support moment, ground reaction force, peak plantar flexion angle and peak hip adduction angle while walking (Seeley, Park et al. 2013). With a painful running condition, involved leg VMO, VL, and gastrocnemius EMG amplitude were 5-10% less than the uninvolved leg (Denning, Woodland et al. 2014). Another group found that pain reduced sagittal and frontal plane peak moments similar to early stage OA patients (Henriksen, Rosager et al. 2011). In these experimental pain conditions, there is a redistribution of muscle activation throughout the body as an adaptation to pain in order to create new movement patterns. The acute introduction of pain appears to cause

immediate gait adaptations to mimic those of chronic pain populations which may present an interesting avenue for research moving forward.

Dynamical systems approach

Human movement is controlled by the coordination of several segments of the body. These segments span multiple muscles and joints that make up the many degrees of freedom available for movement. Given the large number of degrees of freedom available, several possible solutions for generating task-specific movement patterns exist. Complex movements such as running require the neuromuscular system to coordinate the movement of multiple segments to produce the target lower extremity postures needed for locomotion. Segment coordination is defined as the relationship between segments in terms of both relative motion and relative timing of each segment (Hamill, van Emmerik et al. 1999). One current theory for quantifying human movement patterns using a dynamical systems approach suggests that healthy humans organize their movements within a functional window of coordinative variability (Hamill, Palmer et al. 2012). Too much or too little variability outside this window is believed to lead to or describe injury and decreased function, while variability within this window provides flexibility to a system and allows it to respond to internal and external perturbations (Hamill, Palmer et al. 2012). In the context of human movement, segment coordination variability can be used to quantify the variability of particular motions and compare this flexibility in movement generation between different participants and groups.

Segment coordination variability, or the variability in coordination between different segments from cycle-to-cycle, differs from traditional ‘end-point’ variability, or lack of consistency in the product of a particular movement (Hamill, Palmer et al. 2012). The latter would be lowest in experts at a given task and highest in novice individuals. A classic example of ‘end-point’ variability, as provided by Bernstein, is the hammering of a chisel (Bernstein 1967). Expert workers are able to consistently place the head of the hammer in the same spot without

variation, while novices have a widespread area over which they make contact (Bernstein 1967). With segment coordination variability the opposite result is expected, in that novice or injured individuals would exhibit the least variability in segment coordination to complete a task (Hamill, Palmer et al. 2012). In Bernstein's example, the expert workers were able to achieve the same end-point precision despite moving their limb in several different ways while novices used the same, unvarying pattern of movement despite not achieving the same end-point precision (Bernstein 1967). This so-called “freezing” of degrees of freedom is a trait common to the learning of novel tasks. As an individual becomes more accomplished, they are able to “unlock” degrees of freedom and achieve high task accuracy while using a wider range of movement combinations (Bernstein 1967).

In repetitive movements like running, segment coordination variability may be considered part of a healthy system as this variability accomplishes two goals: 1) maintain flexibility in the system to respond to perturbation; and 2) provide enough variety in movement that the same underlying tissues are not stressed to the point of injury. Vector coding (Sparrow, Donovan et al. 1987, Heiderscheit 2002, Cunningham, Mullineaux et al. 2014), continuous relative phase (CRP) (Miller, Meardon et al. 2008), and discrete relative phase (DRP) are a few of the methods used to quantify the variability of coupling angles between segments and joints and overall coordination variability of the lower limb (Hamill, van Emmerik et al. 1999, Heiderscheit 2002, Miller, Meardon et al. 2008, Hamill, Palmer et al. 2012, Cunningham, Mullineaux et al. 2014), and interpretations of each should be considered independently. Coordination variability analysis has an advantage over previously mentioned discrete analyses as it allows for continuous analysis throughout the entire gait cycle, providing spatiotemporal information about an entire movement pattern (Hamill, McDermott et al. 2000, Heiderscheit 2002). Using dynamical systems approaches to investigate coordinative variability has led to increased knowledge on the functional organization strategies and structures for underlying movements (Hamill, Palmer et al. 2012).

Coordination has been quantified in several case-control studies using runners with ITBS, PFPS, and individuals with low back pain (Hamill, van Emmerik et al. 1999, Heiderscheit 2002, Miller, Meardon et al. 2008, Seay, Van Emmerik et al. 2011, Hamill, Palmer et al. 2012, Cunningham, Mullineaux et al. 2014). While the dynamical systems theory would suggest decreased coordination variability with injury, the results of these studies have found little change (Heiderscheit 2002), increased (Cunningham, Mullineaux et al. 2014), or decreased variability (Hamill, van Emmerik et al. 1999, Seay, Van Emmerik et al. 2011, Hamill, Palmer et al. 2012) for injured individuals. In fact, two studies have observed varied results depending on which coupling was analyzed (Heiderscheit 2002, Miller, Meardon et al. 2008). Increased stride-to-stride variability has been found in those with PFPS compared to healthy controls (Ferber, Kendall et al. 2011) as well as increased stride length variability (Heiderscheit 2002). In one study investigating coordination in those with PFPS, a reduction in transverse plane variability at the knee joint was found between the affected leg of those with PFPS and controls (Heiderscheit 2002), while another indicated greater variability across nearly all analyzed couplings (Cunningham, Mullineaux et al. 2014). In the study which found increased variability for most couplings, Cunningham and colleagues theorized this may have occurred due to a decrease in muscle control and coordination (Cunningham, Mullineaux et al. 2014).

The results from these studies may be contradictory due to the natural variations in pain severity and injury duration experienced by respective recruited populations. Despite contradictory results, it is still quite possible that a reduction in the number of movement strategies may lead to increased repetitive stress on the patellofemoral joint causing increased pain of longer duration. This is especially important in pathological populations such as those with PFPS, as reoccurrence is a marked consequence of the injury. Coordination has been studied in other pathological populations as well. A study on those with ITBS found decreased variability in tibial rotation/rearfoot coupling and rearfoot/thigh abduction/adduction coupling, but increased variability in knee flexion/extension-foot ad/abduction coupling (Miller, Meardon et al. 2008).

Changes are presumed to have occurred to avoid painful coordination patterns or patterns that were painful in the past (Miller, Meardon et al. 2008).

There is evidence that movement coordination variability may not immediately return to “normal” following a resolution of primary symptoms (pain) for individuals with chronic injuries (Seay, Van Emmerik et al. 2011). Individuals with low back pain, similar to PFPS due to its persistence and frequent reoccurrence, have reduced segment coordination variability during ambulation relative to controls (Seay, Van Emmerik et al. 2011). Asymptomatic individuals do not return to the same level of variability as those with no history of low back pain, indicating that there is a residual effect of injury even when pain has been resolved (Seay, Van Emmerik et al. 2011). This failure to return to variability levels representative of a healthy population may be an important piece in understanding why certain individuals are predisposed to reoccurrence. Thus, understanding how segment coordination variability varies within a population of individuals with PFPS, as well as healthy controls and previously injured individuals, may provide insight into the mechanisms behind PFPS progression and reoccurrence.

Fatigue

In individuals with PFPS, pain is not typically present at the outset of activity (Dierks, Manal et al. 2011). Even when pain is experienced at the beginning of activity, it often peaks after an extended bout of exercise. Thus, the role that fatigue plays in modulating the adaptations to pain in those with PFPS is crucial to understanding how gait mechanics are changed. Fatigue has been shown to have a wide range of effects throughout the running literature in terms of muscle activation, kinematics, and kinetics. One of the difficulties when studying fatigue comes from the fact that there are several different definitions of the word, whether it be central versus peripheral fatigue or fatigue centered on whole systems rather than individual muscles. One of the most common methods for investigating fatigue throughout the literature is task specific; e.g., running individuals to a point of exhaustion or high levels of exertion. Pain has been shown to influence

rating of perceived exertion (RPE) in individuals with PFPS; during a 30-minute run, at the time of first incidence of peak pain in those with PFPS, there was a higher reported level of fatigue than at the equivalent time in healthy controls (Noehren, Pohl et al. 2012).

There are only a few studies that have directly studied the effects of exertion using a prolonged run in runners with PFPS. One study had runners complete an exhaustive run until either a pain or exertion metric was achieved (Bazett-Jones, Cobb et al. 2013). Those with PFPS displayed larger increases relative to healthy controls in hip flexion and knee flexion angles increased, along with patellar tilt, knee abduction, and hip internal and external rotation moments (Bazett-Jones, Cobb et al. 2013). These changes were accompanied by a decrease in hip abductor and extensor torque output (Bazett-Jones, Cobb et al. 2013). These responses may be indicative of a combination of pain and fatigue, with the pain leading to poor muscular endurance (Bazett-Jones, Cobb et al. 2013). Dierks and colleagues also found weak hip abductor muscles and increased hip adduction by run's end in those with PFPS, as well as decreased peak knee flexion angle and velocity, peak hip adduction angle and velocity, eversion excursion, and peak hip internal rotation velocity (Dierks, Manal et al. 2008). This group also found that of the runners with PFPS, three distinct subgroups were formed based on how they responded to the prolonged run (Dierks, Manal et al. 2011). The subdivisions were formed on the basis of knee abduction, hip abduction, and typical frontal plane motion patterns (Dierks, Manal et al. 2011). The fact that multiple responses were found in the pain group speaks to the varied nature of PFPS and suggests that multiple factors come into play when determining mechanics of those with pain (Dierks, Manal et al. 2011).

Current interventions

Several exercise interventions have been used to reduce pain and allow a return to activity for individuals with PFPS. One of the most common interventions involves strengthening of the hip and thigh muscles. With improved hip and core strength, significant improvements in

pain have been achieved, accompanied by a significant reduction in the knee abduction moment during running (Dolak, Silkman et al. 2011, Earl and Hoch 2011). Improved hip abductor strength has been found to decrease pain and stride-to-stride knee-joint variability in those with PFPS (Ferber, Kendall et al. 2011).

While improvements in pain have been found with hip strengthening interventions, a vasti-targeted muscle strengthening protocol may be effective in those classified as maltrackers with PFPS, as improved muscle strength can bring about improved patellar mechanics (Pal, Besier et al. 2012). Other alternatives to muscle strengthening protocols have been pursued to improve patient outcomes. Transcutaneous electrical nerve stimulation has been found to reduce pain levels and restore quadriceps function after inhibition due to pain (Son, Kim et al. 2015). Gait retraining has been implemented to improve load symmetry between injured and contralateral limbs (Noehren, Scholz et al. 2010) and has been shown to reduce contralateral pelvic drop, hip adduction, as well as vertical ground reaction force loading rate, accompanied by an 86 % pain reduction. These improvements were maintained at retest 1-month post-intervention (Noehren, Scholz et al. 2010).

Despite several different interventions, poor outcomes have still been shown at 3- and 12-month follow-ups, with 55 % and 40 % respectively still reporting pain and decreased function (Collins, Bierma-Zeinstra et al. 2013). Mulligan taping of the knee has been shown to significantly reduce pain in a PFPS group during a single leg squat, improving gluteus medius onset time and reducing peak hip internal rotation (Hickey, Hopper et al. 2016), and potentially reducing pain (Lan, Lin et al. 2010). Pain should not be used as an indicator for surgical need (Pihlajamäki, Kuikka et al. 2010), as gentle rehabilitation, load restriction, and anti-inflammatory therapy has been proposed as the best option (Dye 2001).

If conservative treatment is ineffective, and the pain continues to worsen, certain cases may be considered for surgical treatment (Fulkerson 2002). Common surgical procedures include lateral release for patellar tilt, resection of scar tissue and other debris using arthroscopy, and

patellar realignment (Fulkerson 2002). When lesions are present and accompanied by pain, tibial tubercle transfers may be used in an attempt to alleviate pain (Fulkerson 2002). While surgical procedures may improve outcomes for certain patients, these procedures should only be considered when all other treatment options have been exhausted. Thus, information that may aid in improving non-invasive, conservative treatment of PFPS is of utmost importance in regards to patient outcomes and treatment efficacy.

Summary

Patellofemoral pain syndrome is a multi-faceted injury with primary issues of persistence and reoccurrence. Several factors are believed to play a role in the onset and progression of PFPS, including joint, limb and muscle alignment, cartilage health, and muscle function. Despite the current body of literature covering PFPS, current treatment modalities are not universally effective in resolving PFPS symptoms. We propose that underlying muscle and segment coordination may play a critical role in understanding the reasons for PFPS progression as well as elucidating the reasons for frequent reoccurrence in individuals who have resolved their primary symptoms.

CHAPTER 3

METHODS

Introduction

The purpose of this dissertation was to investigate the influence of patellofemoral syndrome (PFPS) knee pain severity and fatigue on the 3D kinematics, kinetics, muscle coordination and segment coordination variability of runners using a 21-minute treadmill run (21MTR). Three aims were proposed to explore these relationships and further understanding of the mechanisms of injury progression and reoccurrence in those with PFPS. Three groups of runners were recruited for this study: 1) healthy controls (CON); 2) runners with a current diagnosis of PFPS (PFPS); and 3) runners who were asymptomatic but formerly had patellofemoral pain (RES). The aims of this dissertation were to:

- 1. Quantify the changes in hip internal rotation and adduction angles, as well as hip and knee adduction moments, in response to increased pain and effort during the 21MTR.**
- 2. Quantify differences in segment coordination and coordination variability between the CON, PFPS, and RES groups at baseline and over the course of the 21MTR.**
- 3. Quantify differences in muscle coordination between the CON, PFPS, and RES groups at the beginning and end of the run.**

Participants

In order to address the above aims, (n=58) participants were recruited, with n=20, n=20, and n=18 recruited from the CON, PFPS, and RES groups. The participants recruited for this study were recreationally active individuals between the ages of 18-35. Age 35 was the upper

limit to avoid the possibility of structural damage that may be present in older adults with chronic PFPS. All participants were generally healthy and free of traumatic lower limb extremity injury, neurological, or cardiovascular pathology, apart from knee joint pain in the PFPS group. Every participant completed a Modified Physical Activity Readiness Questionnaire (PAR-Q, see Appendix) and signed an informed consent document approved by the University of Massachusetts Institutional Review Board in order to be eligible to take part in this study. To ensure all participants met the physical standards required for this study, they all indicated via self-report that they were capable of completing a 30-minute run treadmill run.

Participants were recruited through several media. Participants for the CON group were recruited via word of mouth, flyers posted around the area colleges, universities, and fitness facilities, as well as through contact with local athletics groups and electronic message boards. The PFPS and RES groups were recruited using the above methods in addition to posting flyers in clinics and through the assistance of local sports medicine clinicians/physicians. Injury status was determined by their respective clinicians. In cases where participants in the PFPS and RES groups were not directly referred by a clinician, a note from their own provider who diagnosed their injury was sought for appropriate group assignment.

Sample size estimation

The estimated number of participants needed per group were calculated using the values of similar outcome measures, and their standard deviations, present in the literature. These values can be viewed in Tables 1 and 2. Power calculations were conducted using GPower software (Faul, Erdfelder et al. 2007) to determine “a priori” sample size estimates for ANOVAs with an ($\alpha=0.05$) and ($\beta=0.8$). Based on these power calculations, it is expected that 20 participants per group would be sufficient to detect differences in the measures of interest.

For kinematic, kinetic, and coordination measures, the primary measures of interest were selected as those involving frontal plane hip (Souza and Powers 2009, Dierks, Manal et al. 2011,

Noehren, Pohl et al. 2012, Noehren, Sanchez et al. 2012, Willy, Manal et al. 2012, Bazett-Jones, Cobb et al. 2013, Esculier, Roy et al. 2015) and knee motion (Stathopulu and Baildam 2003, Willson and Davis 2008, Willy, Manal et al. 2012), as well as internal rotation of the femur (Souza and Powers 2009, Dierks, Manal et al. 2011, Noehren, Pohl et al. 2012, Noehren, Sanchez et al. 2012, Willy, Manal et al. 2012, Bazett-Jones, Cobb et al. 2013, Esculier, Roy et al. 2015, Neal, Barton et al. 2015). These measures were chosen based on previous differences reported in the literature as well as the expected importance of these frontal and transverse planes of motion in regards to the impact of PFPS on segment coordination and coordination variability.

Table 3.1. Expected differences and outcome variables for discrete kinematics and kinetics. Values adapted from Noehren et al., 2012 and Dierks et al., 2011.

	Expected Baseline Difference	Within group SD	n needed per group	Expected pre-post run difference	Within group SD	n needed per group
Hip						
Flexion angle						
Internal rotation angle	5	4	9	3	4	23
Adduction angle	3	3	14	4	4.5	17
Knee						
Flexion angle				4	5	25
Internal rotation angle						
Abduction angle						
Ankle						
Plantar flexion angle						
Eversion angle						
Adduction angle						

Experimental protocol

Participants underwent a phone screening prior to one in-lab testing session. During the phone screening, data were collected regarding age, height, weight, injury history, training status, and any medical contraindications to study participation. If the individual qualified for the study, they were scheduled for a lab visit lasting about two hours. When the participant first arrived at the lab, they completed an informed consent document approved by the local University of

Massachusetts Institutional Review Board (IRB), outlining the procedures and associated risks of the study, as well as a Modified Physical Activity Readiness Questionnaire (PAR-Q) and general demographics form. No participants were excluded from this study on account of the PAR-Q. In addition, the PFPS group completed two additional surveys: 1) a Functional Index Questionnaire – Knee (FIQ) as well as 2) Visual Analog Scale of 0-100 (where 0 is “no pain” and 100 is “most severe pain”) indicating the worst pain they have experienced in the previous 7 days (See Appendix). The FIQ is an instrument for the evaluation of pain and was developed specifically for PFPS (Chesworth, Culham et al. 1989) and, compared with other measurement tools, has undergone the most evaluations in patient populations (Garratt, Brealey et al. 2004). It consists of 8 questions, each related to a different activity that may cause knee pain (Chesworth, Culham et al. 1989). The VAS has been used extensively in evaluating pain in patients, and its reliability and validity has been found to be moderate in patients with PFPS (Flandry, Hunt et al. 1991, Eng and Pierrynowski 1993).

After all paperwork is complete, participants were fitted with data acquisition hardware (markers and electrodes). Once markers were placed and EMG signal quality was checked, they began to run on the treadmill at a self-selected, preferred speed. A speed determination procedure was used to find the 21MTR test speed. To ensure a comfortable, sustainable running speed for the duration of the test, the speed of the treadmill was set to the initial preferred speed at which participants ran for up to 1 minute. The participant was then asked if they believe they can sustain the speed for 30 minutes. The speed was increased or decreased based on this response. If the speed was determined to be appropriate according to their normal training speeds, this speed was selected for the run test. If not, the speed was further adjusted up or down until a new speed was

Table 3.2. Expected baseline differences in selected coordination variability measures. Early stance marks 0-33% of stance phase, mid stance marks 34-66% of stance phase, while late stance comprises the final 67-100% of stance. Values adapted from Cunningham et al., 2014 and Hafer et al., 2015.

	Expected Baseline Difference	Within group SD	n needed per group
Coordination Measures			
<u>Coordination variability (°)</u>			
<u>Early Stance</u>			
Frontal pelvis vs. transverse thigh			
Frontal pelvis vs. frontal thigh			
Sagittal thigh vs. sagittal shank	1	2	51
Frontal thigh vs. frontal shank			
Sagittal thigh vs. transverse shank	2	2	14
Transverse shank vs frontal foot			
<u>Mid Stance</u>			
Frontal pelvis vs. transverse thigh			
Frontal pelvis vs. frontal thigh			
Sagittal thigh vs. sagittal shank			
Frontal thigh vs. frontal shank			
Sagittal thigh vs. transverse shank	7	8	17
Transverse shank vs frontal foot	6	6	14
<u>Late Stance</u>			
Frontal pelvis vs. transverse thigh			
Frontal pelvis vs. frontal thigh			
Sagittal thigh vs. sagittal shank	1.2	2.5	55
Frontal thigh vs. frontal shank			
Sagittal thigh vs. transverse shank	2.5	3	19
Transverse shank vs frontal foot			

chosen. After speed determination, they will be given a rest period of up to ten minutes, after which they will begin the 21MTR. Speed determination took no more than 2-3 minutes; this did not cause a clinically significant increase in perceived pain in the PFPS group.

Kinematic, kinetic, and EMG data, in addition to Rate of Perceived Exertion (RPE) (Borg 1971), were collected for 30 seconds every 2 minutes throughout the run. Data was not collected

until the participants had been running for 1-minute to allow for treadmill acclimatization. After this 1-minute period, data were collected at minutes (1, 3, 5, 7...19, 21). For the participants in the PFPS and RES groups, a pain measurement rating was taken using an 11-point Verbal Numeric Rating Scale (VNRS, 0-10, with 0 being “no pain” and 10 being “worst possible pain”) immediately following each data collection window. No participants stopped the run early because of pain. Throughout the prolonged run, the participant was monitored closely for safety by lab personnel. The overall study workflow is presented in Figure 1.

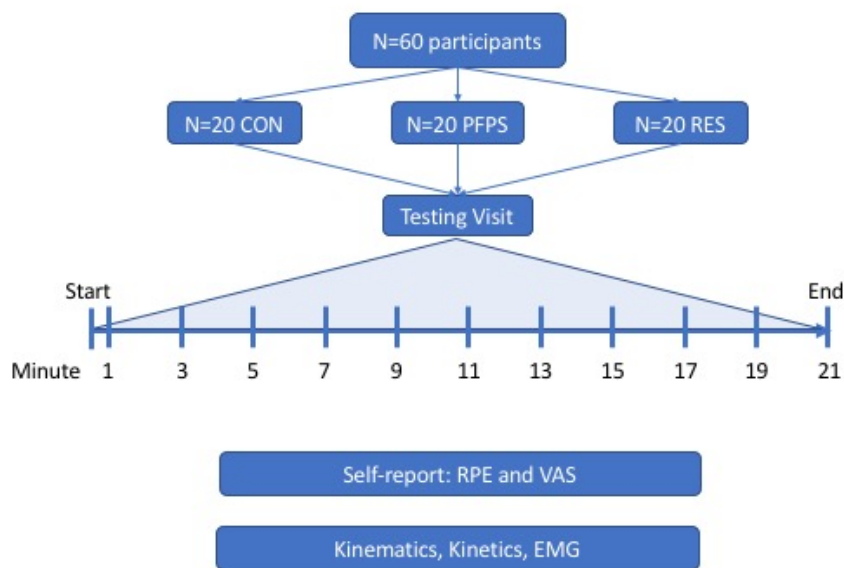


Figure 3.1. Workflow of study design, indicating run collection points and data collected.

Experimental setup

Several different measurement systems were used to collect the data necessary to complete this study. All collections were conducted in the University of Massachusetts Biomechanics Lab.

Motion capture

Fifty retro-reflective markers were placed unilaterally on each participant. For pain-free participants, the right side was used while in the PFPS group, data was collected on the affected

leg. Markers were tracked by eight infrared cameras (Oqus-5 series, Qualisys, Inc., Gothenburg, Sweden) sampling at 200 Hz. The marker setup is shown in Figures 2 and 3. The pelvic segment was demarcated by markers on the right and left anterior superior iliac spines (ASIS), posterior superior iliac spines (PSIS), iliac crests, and greater trochanters. Plates of 4 non-colinear markers were placed on the thigh and shank, and calibration markers were placed on both the lateral and medial malleoli and femoral epicondyles. The thigh segment was calibrated using greater trochanter and femoral epicondyle markers. The shank was calibrated using the femoral epicondyle and malleoli markers. The foot segment was calibrated using the malleoli markers and markers on the first and fifth metatarsal heads, using three markers placed on the heel to track foot movement.



Figure 3.2. Frontal and sagittal views of marker set up.



Figure 3.3. Posterior view of marker setup.

Instrumented treadmill

Participants completed the 21MTR on an instrumented treadmill (Athletic Republic, Park City, UT). The treadmill rests on four load cells (AMTI, Watertown, MA) and ground reaction forces were determined by summing the forces recorded by each load cell. Force data was sampled at 1000 Hz via Qualisys Track Manager (Qualisys, Inc., Gothenburg, Sweden).

Electromyography

Electromyographic data were collected over the duration of the prolonged run from 11 different muscles on the same limb that the motion capture data was collected: the tibialis anterior (TA), medial and lateral gastrocnemius (MG, LG), soleus (SOL), rectus femoris (RF), vastus lateralis (VL), vastus medialis (VM), biceps femoris (BF), semitendinosus (ST) and gluteus maximus and medius (GMAX, GMIN). The location of each electrode was determined by palpating participants' muscles and placing each sensor on a shaved and abraded site on the muscle belly to ensure an accurate, clean signal. Skin preparation and electrode placement was based on SENIAM recommendations (Hermens, Freriks et al. 1999). Tape pulls and alcohol wipes were used to remove any excess skin prior to electrode placement. Electrodes were placed as near to the muscle belly as possible to ensure the most reliable signal collection. EMG data were sampled at 2000 Hz and collected in Qualisys Track Manager. After electrode placement, each signal was viewed in Qualisys Track Manager. Participants were asked to perform activities in which the respective muscle would be activated. The signal to noise ratio was evaluated using visual inspection to confirm appropriate electrode placement and overall EMG quality. When the quality was deemed poor, the electrode was removed and the process for skin preparation and electrode placement was repeated until the desired signal quality was achieved. An external trigger, connected to the master motion capture camera, was used to begin synchronous collection of all kinematic, kinetic and EMG data in this protocol.

Data treatment

Kinematic and kinetic data were filtered using a dual-pass, low pass Butterworth filter with a cutoff frequency of 8 Hz. 3D foot, ankle, knee, and hip angles were calculated using a Cardan Xyz rotation sequence in Visual 3D (C-Motion Inc., Germantown, MD). Segment angles were calculated for the foot, shank, thigh, and pelvis relative to the lab (global) coordinate system. These data were used to calculate segment coordination variability for each time point of

the treadmill run using at least 10 strides from each data collection window (30 seconds) (Hafer and Boyer 2017). Ground reaction force data were filtered using a low pass, 4th order zero-phase lag Butterworth filter with a 30 Hz cutoff frequency. These data were interpolated and normalized to 101 data points, representing 0-100% of the stance phase for each step. The vertical ground reaction force (VGRF) data were used to determine foot contact and toe-off to establish the duration of the stance phase. Discrete outcome joint angles and moment calculations were calculated for each stance phase at each time point of the run for 10 individual strides, and then averaged together to create means for each participant/time point.

Coordination Variability

The angles calculated in the above step for 10 stance phases were used as input into a custom MATLAB (Mathworks, Inc., Natick, MA, USA) program to calculate phase angles for the forefoot, rearfoot, shank, thigh, and pelvis. From these phase angles, coupling angles were calculated between the forefoot-rearfoot, rearfoot-shank, shank-thigh, and thigh-pelvis for each third of stance (early, mid-stance, and late). These were derived from angle-angle plots generated from the phase angles. The coupling angle was defined as the angle between a vector drawn between two subsequent time points on these angle-angle plots and the right horizontal (Eq. 1, Figure 4) (Chang, Van Emmerik et al. 2008).

$$\theta_{i,j} = \tan^{-1} [(y_{i,j+1} - y_{i,j}) / (x_{i,j+1} - x_{i,j})] \quad (\text{Equation 1})$$

$$0^\circ \leq \theta \leq 360^\circ, j \text{ is \% stance of trial}$$

As these angles are directional data, it was necessary to use circular statistics to calculate the mean and standard deviation across trials. The coordination variability pattern was created by determining the standard deviation at each time point between subsequent strides.

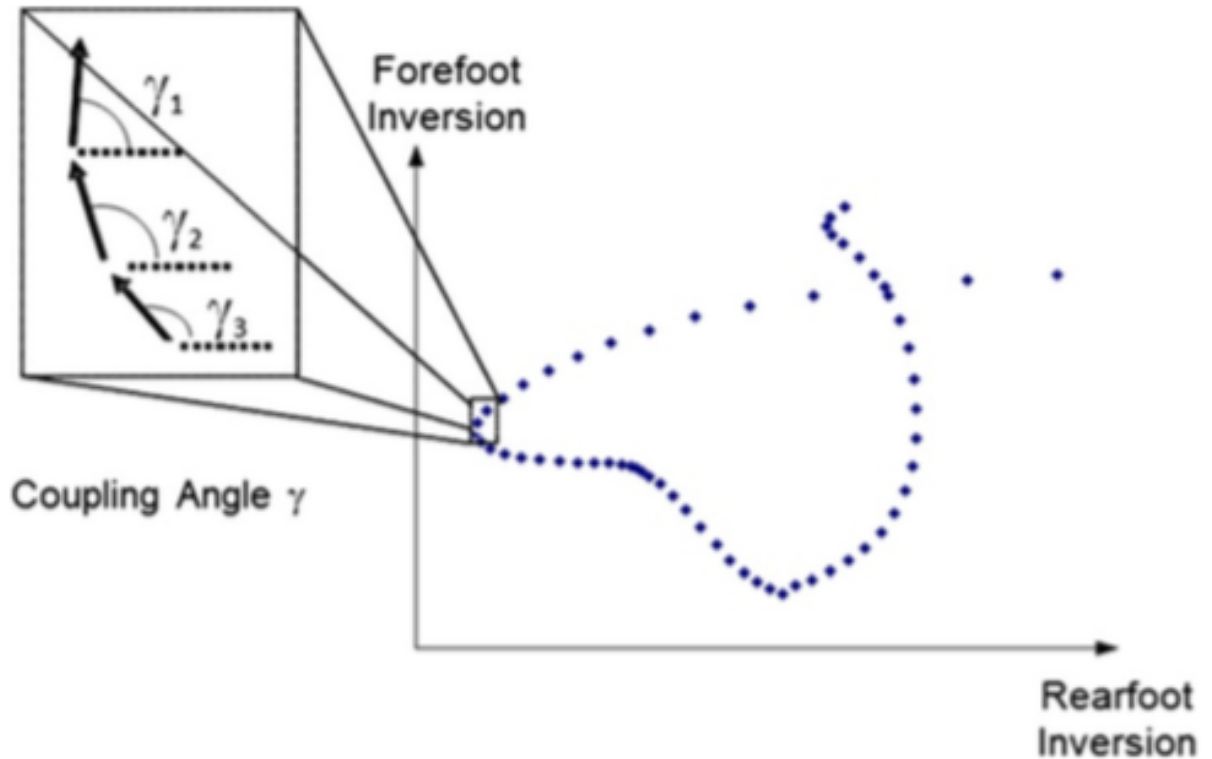


Figure 3.4. Angle-angle plot of segment angles used to quantify segment coordination. Angles are created as the angle between the line connecting two consecutive points and the right horizontal. Adapted from Hamill et al., 2012.

Muscle coordination and intensity

EMG signals were analyzed for 200 milliseconds pre- and post-foot strike as determined from vertical ground reaction forces. The EMG signals were resolved with respect to intensity of activity, time and frequency using a previously-developed wavelet analysis (von Tscharner 2000). A set of 13 non-linearly scaled wavelets was used as outlined by von Tscharner (2000) (Figure 5). A mean wavelet intensity pattern was calculated from 10 consecutive strides for each of the time points throughout the run. Wavelet filter center frequencies were defined as follows: 7, 19, 38, 62, 92, 128, 170, 218, 271, 331, 395, 466 and 542 Hz, respectively. A wavelet domain is defined as the time series of intensity for each wavelet (von Tscharner 2000). Intensity (i_{jk}) was calculated for each sample point j and wavelet domain k (Wakeling, Pascual et al. 2001). The mean global intensity (I) for each wavelet domain k over each total 400 millisecond window was calculated as

(Equation 2):

$$I_k = \sum_{j=1}^{400} i_{j,k} \text{ (Equation 2) (Wakeling, Pascual et al. 2001)}$$

The mean global intensity is equivalent to twice the square of the root mean square (RMS) value for that window. Peak intensity was calculated as the peak instantaneous intensity value for each given muscle summed across their respective wavelets. Mean and peak intensity, as well as the timing of the peak, was calculated for each muscle.

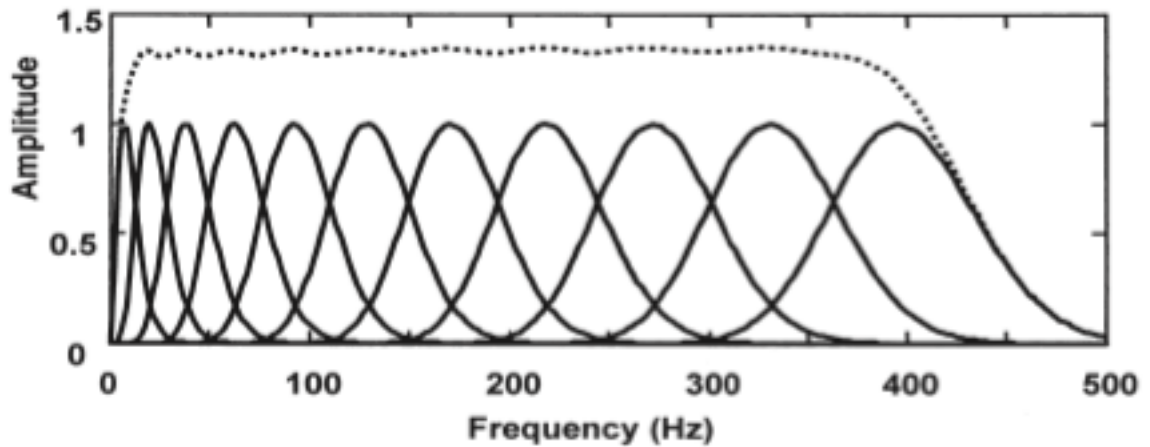


Figure 3.5. Example of wavelet filter bank used for EMG signal decomposition.

Principal component analysis (PCA)

To further process the large amount of data stored in these wavelet intensity patterns, a pattern space analysis was conducted (von Tschärner 2002) on the intensity patterns of the lower extremity muscles. For this analysis, the EMG intensity patterns for each muscle were concatenated to form a multi-muscle intensity pattern for each subject at each time point of the run. Each resulting data matrix following the wavelet transform had dimensions of (143×81) . The number of rows (143) corresponds to the 13 wavelets generated for each muscle across eleven muscles being studied (13×11) . The number of columns is representative of the time scale. This

process was then repeated for each muscle at each point in time for every subject. The data matrices generated for each time point for each subject were unwrapped into single column vectors of length $11,583$ (143×81). There were 11 vectors (each 10% of the run) generated for each participant, giving a total of 660 vectors. These column trial vectors were concatenated to create a (660×11583) input matrix for further analyses.

The principal patterns (PP) of lower extremity muscle coordination were determined by the eigenvectors of the covariance matrix of the input matrix described above where the mean was subtracted, centering the data about the origin of a multi-dimensional pattern space. These PP represent the primary directions of variance (axes) in pattern space (Figure 6). The spread of these data about each PP represents the variance explained along each axis, represented by the corresponding eigenvalues of the principal component analysis (Figure 7). Because each direction in pattern space can be visualized by a multi-muscle intensity pattern, one can inspect them and assess how their intensities contribute to the overall intensity pattern. The degree to which a pattern contributes to the overall intensity pattern is indicated by the PP **weight factors**, which are the projections of the overall intensity pattern onto the axes (Figure 8). The associated eigenvalues for each of the PP indicate the amount of variation in the multi-muscle EMG pattern explained respectively by each PP and is equal to the sum of all weight factors squared.

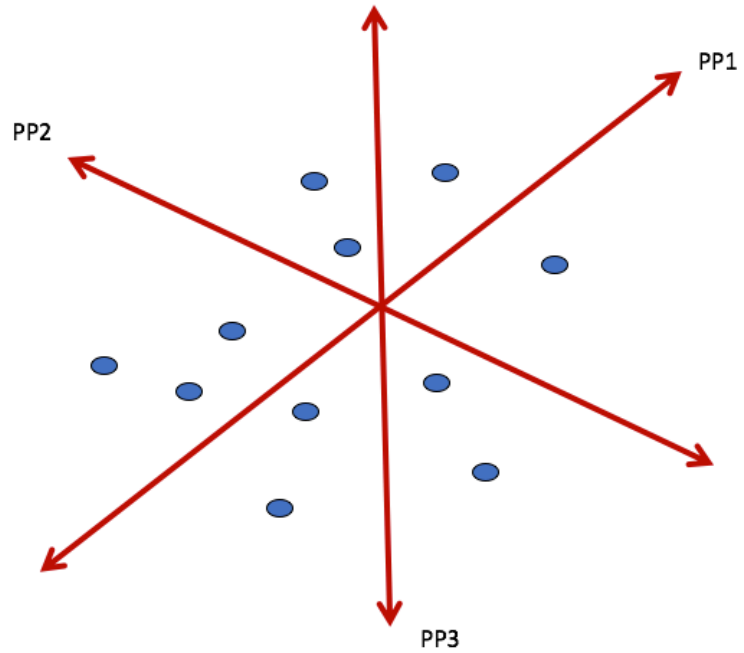


Figure 3.6. Visualization of the eigenvectors, or principal patterns, generated from principal component analysis. These represent the primary directions of variance (bolded axes) in pattern space.

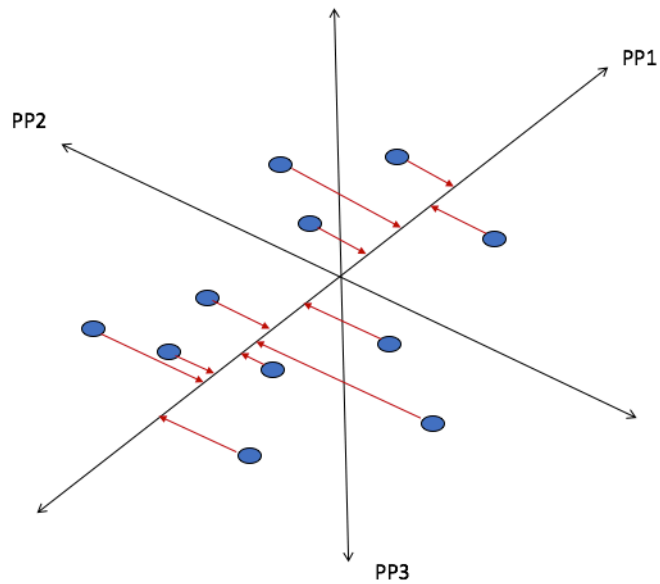


Figure 3.7. Visualization of the spread of data about principal pattern 1. This is representative of the eigenvalues for this axis as determined by principal component analysis.

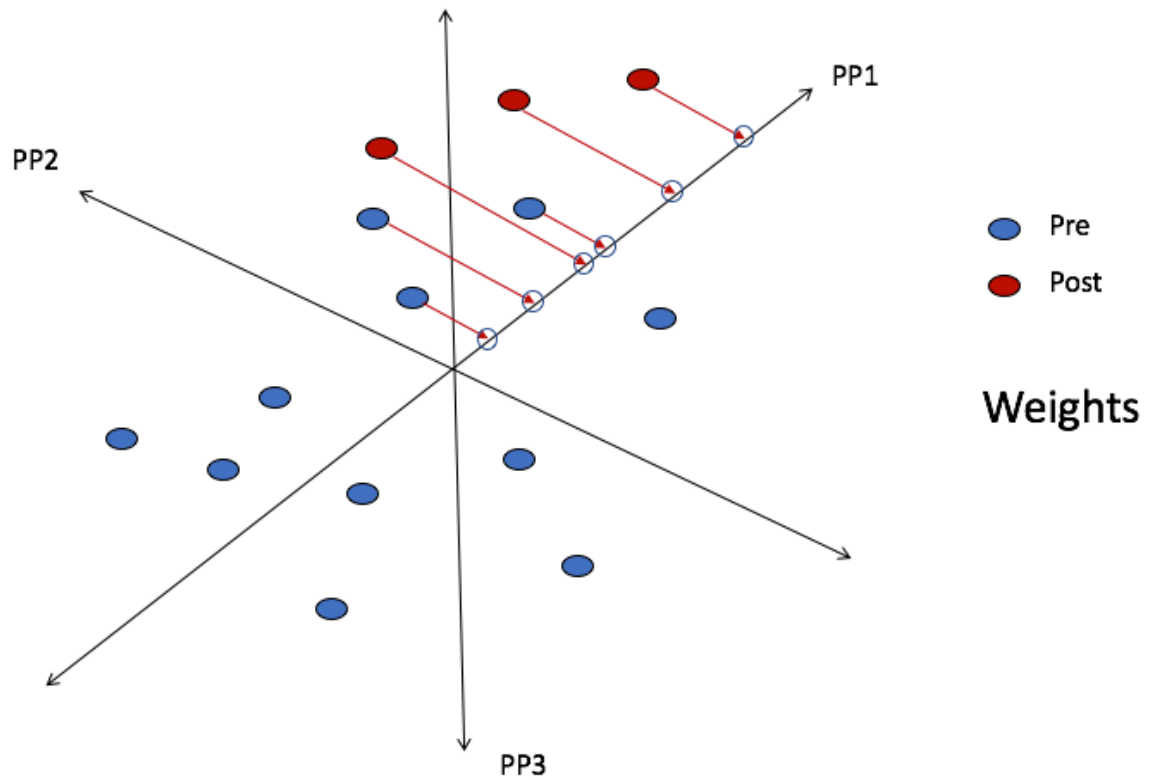


Figure 3.8. Visualization of the weight factors along principal pattern 1. These weights for each principal pattern can be treated as a weighted linear combination with all generated principal patterns and can be used to reconstruct the original signal. This figure depicts the differences for three points in the higher dimensional pattern space that change in weight factor between the beginning and end of run.

After the principal component analysis was performed, 660 of these principal patterns were created due to the mathematical construct of the analysis. The 660th pattern did not contain any information regarding the signal, and thus was removed, bringing the dimensionality to 659. In order to restore this final dimension and bring back information lost by removing the mean, a residual mean basis vector was calculated by projecting the removed mean onto the calculated PP, reconstructing the mean, and then subtracting this reconstructed mean from the original removed mean. This **residual mean** was then used to form a normalized basis vector orthogonal to the other PP, creating the 660th PP.

The trial vectors for each subject, when projected onto the orthogonal set of PP, can be represented by a p-vector pointing from the origin of the PP space to the point representing the

trial. Thus, each p-vector can be decomposed into a weighted linear combination of PP, with each weight factor indicating the contribution of that particular PP to the total multi-muscle EMG intensity patterns (Figure 9). The multi-muscle EMG intensity pattern of any trial can be recreated for any subject at any time point during the prolonged run by a weighted linear combination of PP added to the mean. Each weight factor for this analysis was treated as its contribution to the overall EMG intensity pattern. The PP used in further analyses were those that described at least 1% of the variance in the data.

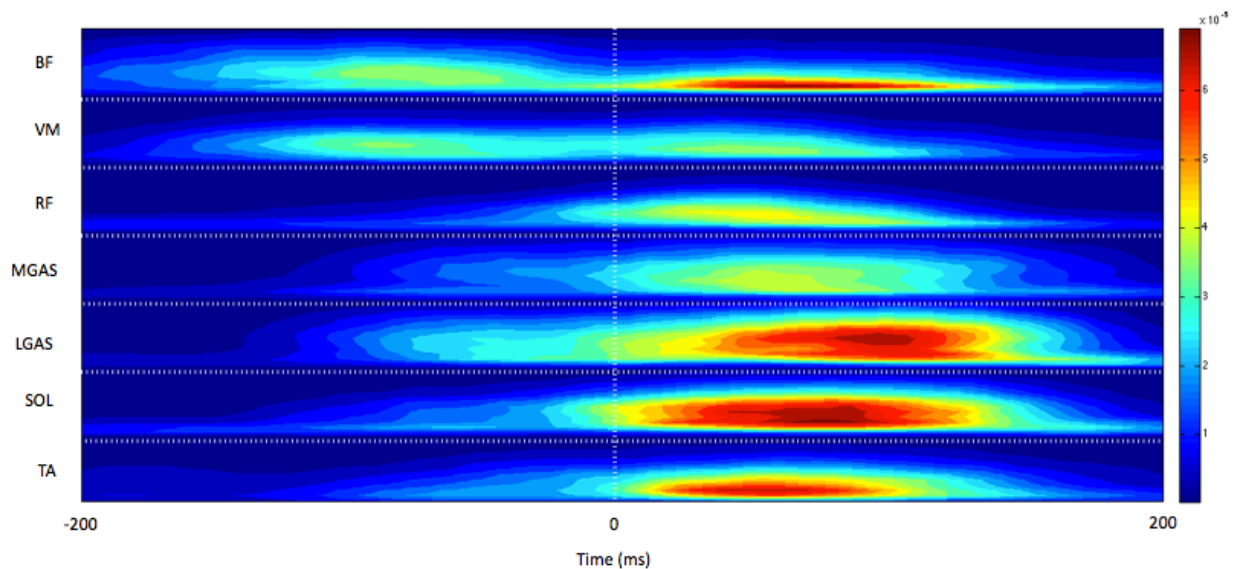


Figure 3.9. Example multi-muscle pattern of EMG activity. Wavelet frequency and muscle make up the y-axis values, while time is depicted on the x-axis. Color represents intensity of given wavelet domains, with “hotter” colors depicting greater intensity of a particular frequency band at each given time point.

Statistical analysis

Study 1: The impact of patellofemoral pain on gait during a prolonged run in recreational runners

Aim: The primary aim of this study was to quantify the changes in hip internal rotation and adduction angles, as well as hip and knee adduction moments, in response to increased pain and effort during the 21MTR.

H1.1 At baseline, hip internal rotation and adduction angles would be different between the CON, PFPS, and RES groups, such that $CON < RES < PFPS$.

H1.2 At baseline, knee adduction moments would be smaller in CON and RES groups as compared to PFPS, such that $CON < RES < PFPS$, while the opposite relationship would be true for hip adduction moments.

H1.3 Between the beginning and end of the 21MTR, the hip internal rotation and adduction angles and hip and knee adduction moments outcome would not change in the CON group. These measures would change from baseline in the PFPS and RES groups, such that the magnitude of these changes would be as follows: $Con < RES < PFPS$.

Exploratory H1.4 There would be a correlation between pre-post run changes in the above gait mechanics and the changes in pain as rated on a Verbal Numeric Rating Scale (VNRS).

Study 2: Segment coordination and coordination variability throughout a prolonged run in runners with patellofemoral pain

Aim: The primary aim of this study was to quantify differences in segment coordination and coordination variability between the CON, PFPS, and RES groups at baseline and over the course of the 21MTR in the following couplings: 1) frontal pelvis vs. transverse thigh and 2) frontal pelvis and frontal thigh.

H2.1 Segment coordination variability would be lower in individuals with PFPS as compared to RES and healthy controls, such that variability would differ as $PFPS < RES < CON$ at baseline of the 21MTR for the above couplings.

H2.2 Segment coordination would be different for the above couplings between CON, PFPS, and RES at the end of the 21MTR.

H2.3 Segment coordination variability would decrease in PFPS and RES but not healthy controls over the 21MTR for the above couplings such that the change in variability would be $Con < RES < PFPS$.

Exploratory H2.4 There would be a progressive decrease in segment coordination variability throughout the run.

Study 3: Muscle coordination throughout a prolonged run in runners with patellofemoral pain

Aim: The primary aim of this study was to quantify changes in muscle coordination of the CON, PFPS, and RES groups of runners over the course of the 21MTR.

H3.1 Muscle coordination would be different between the beginning and end of the run for both PFPS and RES, with the largest change occurring in PFPS. There would be no change in the CON group. A change in muscle coordination would be quantified as the change in respective weight factors for each principal pattern.

Exploratory Aim: To test the ability of a machine learning algorithm to classify RES multi-muscle patterns as healthy or injured. The weight factors at the end of the run for the PFPS and CON groups would be used to train the support vector machine.

The statistical analysis methods that were used for all three studies follow similar testing standards. All statistical tests used an alpha criterion level of ($\alpha=0.05$). For baseline testing, one-way Analysis of Variance (ANOVA) were used to test for differences between groups in outcome measures of interest. When significant main effects of group were found, post-hoc pairwise comparisons were made using Tukey's honest significant difference test. To test for group differences, one-way ANOVAs were used to test for differences in change over the course of the 21MTR. When significant main effects of group were found, post-hoc pairwise comparisons were made using Tukey's honest significant difference test.

Regression analyses were performed to observe the time course of the discrete kinematic and kinetic outcome measures with relation to pain and exertion as an exploratory aim. For all statistical tests involving coordination, circular statistics were used due to the circular nature of these data.

For the exploratory aim in the muscle coordination study, a support vector machine (SVM) was trained and utilized from beginning and end of run time point weight factors of the CON and PFPS groups, and used to classify patterns of the RES group as more similar to CON or PFPS. A binomial test was used to determine if the rate of classification is significantly different from random classification.

Effect sizes were calculated to determine if any differences found between trials or pre- and post-run measures were biologically meaningful. An effect size (d) greater than 0.3 indicated

a small effect, greater than 0.5 a moderate effect, and an effect size larger than 0.8 indicated a large effect (Cohen 1992).

Limitations

As this study used a case-control design, the strength of evidence is not as high as a clinical trial or cohort study. However, given the resources and outcome measures, this design was appropriate for the proposed research questions. In addition to the overall study design, there are limitations of the methods used. First, all data were collected from participants running on a treadmill as opposed to over ground in a free-living environment. This was necessary in order to collect the type, quantity, and quality of data necessary to address the proposed research questions but may have influenced recorded muscle activation and coordination patterns of movement. Second, the speed was selected as a preferred speed for each runner and thus differences in muscle activations, kinematics, and kinetics will have differences induced by speed apart from differences in injury status, pain, or exertion. Finally, the measures used to determine pain and exertion are self-report measures come with inherent limitations in relative comparisons between individual participants. Despite this, these measurements are consistent as within-participant measures.

Summary

The purpose of this dissertation was to investigate the relationship of knee pain, injury status, and perceived exertion on 3D kinematics, kinetics, muscle coordination, segment coordination and segment coordination variability of trained runners. Three studies were considered to compare these outcome measures between healthy, injured, and previously injured runners. The results of these studies will further the knowledge of the field through an improved understanding of the underlying mechanisms to development and progression of injury, as well as to help aide in

focusing our efforts onto specific targets for improved rehabilitation, function, and return to activity.

CHAPTER 4

BIOMECHANICAL RESPONSE TO ACUTE PAIN IN RUNNERS WITH PATELLOFEMORAL PAIN SYNDROME

Introduction

Patellofemoral pain syndrome (PFPS) is the most common lower limb injury in runners, comprising 20 percent of all running injuries (Taunton et al., 2002). Presenting as pain in and around the patellofemoral joint and often resulting from overuse, PFPS is characterized by its persistence and frequent reoccurrence. Up to 91% of individuals with PFPS still experience symptoms more than 4 years after initial symptoms set in and more than 36% have restricted daily activity because of this pain (Stathopulu & Baildam, 2003). Several factors are associated with increased patellofemoral joint loading, the primary mechanism for patellofemoral pain, such as impaired muscle function, abnormal lower extremity anatomy and alignment, and altered lower extremity kinematics and kinetics (Powers, Witvrouw, Davis, & Crossley, 2017). Prospective studies have associated lesser lower limb strength and poor lower limb alignment with increased risk for PFPS development (Finnoff et al., 2011; Herbst et al., 2015). However, cross-sectional, cohort design studies have identified additional differences in lower extremity mechanics for individuals with PFPS as compared to healthy but the pathological significance of these differences is not clear. Symptom severity with PFPS varies substantially depending the activity being performed and it remains unclear how acute pain symptoms influence lower extremity mechanics as opposed to long-term adaptations to pain and injury history.

Prospective studies have identified imbalanced hip musculature, poor dynamic femur control and larger knee abduction impulses as primary risk factors for PFPS development (Finnoff et al., 2011; Herbst et al., 2015; Stefanyshyn et al., 2006). However, cross sectional studies have found differences in those with PFPS compared to non-injured controls that cannot be implicated in PFPS development given the relatively weak evidence associated with these

types of studies. Individuals with PFPS often show differences from healthy controls in hip kinematics, specifically larger peak hip adduction and internal rotation but smaller peak flexion angles, and knee kinematics, such as larger peak knee adduction and smaller peak knee flexion angles (Barton et al., 2009; Neal et al., 2015). In terms of kinetics, evidence of larger internal knee abduction moments has been found in those with PFPS as well as smaller internal knee extensor moments (Neal et al., 2015). Little evidence has been found distal to the knee; however, previous work has found that injured runners may utilize a greater range of calcaneal eversion than their healthy counterparts (Rodrigues, TenBroek, et al., 2013). These biomechanical differences in runners with PFPS are not prognostic of injury development but may stem from motor system adaptations to the presence of pain and joint pathology. However, the motor system adaptation to acute pain in PFPS has not been well characterized in the literature. A proposed framework for the impact of pain on gait with PFPS can be seen in Figure 1. Neither the cause nor consequences of previously observed gait differences for injury severity and persistence have been identified. Thus, there is a need to understand the relationship between self-reported pain and gait mechanics with PFPS in order to improve treatment efficacy and patient outcomes.

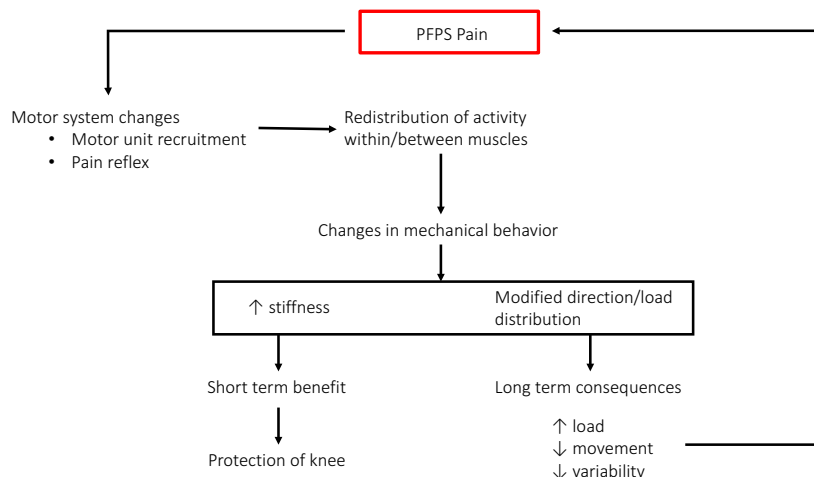


Figure 4.1. Pain model for gait adaptation in runners with patellofemoral pain syndrome. Adapted from Hodges & Tucker 2011.

A critical challenge in the management of PFPS is the frequent reoccurrence of the injury. Over 50 percent of those who experience PFPS-related pain have reoccurrence of symptoms within 6 years (Blond & Hansen, 1998). Previous work in chronic injuries, such as low back pain, has indicated that simply resolving painful symptoms does not ensure that gait will closely mimic that of non-injured runners (Seay et al., 2011). However, little is known about how or if gait patterns in individuals with PFPS differ from those without a recent history of the injury. Given the high incidence of reoccurrence in those whose primary symptoms have resolved, it is important understand how runners with resolved PFPS are different from healthy controls in order to identify why these runners may be at a greater risk for further patellofemoral pain.

There is high inter-subject variability in pain reporting and there is not strong evidence of a relationship between self-reported pain and experimentally derived pain thresholds (Edwards & Fillingim, 2007). This makes a pure case-control study design inadequate to quantify the role of PFPS pain severity in causing gait differences from healthy controls. PFPS symptoms are not constant and are typically exacerbated by dynamic knee loading. Pain experienced by those with PFPS typically peaks about 18 minutes into an easy-to-moderate effort run (Noehren, Pohl, et al., 2012). Thus, utilizing a prolonged treadmill run stimulus to induce pain in those with PFPS is an ecological model for investigating gait responses to pain. In addition, there remains a lack of consensus in the literature regarding differences in gait patterns in those with PFPS.

The aim of this study was to examine the impact of a 21-minute treadmill run (21MTR) on self-reported pain and three-dimensional (3D) hip, knee, and ankle mechanics in healthy runners (CON), runners with PFPS (PFPS), and runners who formerly had PFPS but have resolved symptoms (RES). We hypothesized the following:

H1.1 At baseline, peak and initial hip internal rotation and adduction angles would be different between the CON, PFPS, and RES groups, such that $CON < RES < PFPS$.

H1.2 At baseline, peak knee abduction moments would be smaller in CON and RES groups as compared to PFPS, such that $CON < RES < PFPS$, while the opposite relationship would be true

for hip abduction moments.

H1.3 Between the beginning and end of the 21MTR, the hip internal rotation and adduction angles and hip adduction and knee abduction moments outcome would not change in the CON group. These measures would change from baseline in the PFPS and RES groups, such that the magnitude of these changes will be as follows: CON < RES < PFPS.

H1.4 There would be a correlation between pre-post run changes in the above gait mechanics and the changes in pain as rated on a Verbal Numeric Rating Scale (VNRS) (Hjermstad et al., 2011).

Methods

Participants

Based on previous reported means in the literature (Dierks et al., 2011; Noehren, Sanchez, et al., 2012), an *a priori* sample size calculation yielded a necessary sample of n=15 per group in order to detect true differences of kinetic and kinematic variables of runners with patellofemoral pain syndrome ($\alpha=0.05$, $\beta=0.20$). Fifty-eight total participants (20 CON, 20 PFPS, 18 RES) were recruited for this study who were recreationally active runners and athletes who ran at least 24 km per week. Each group was made up of equal numbers of males and females. A heterogeneous sample was recruited to accurately represent the population; however, females are twice as likely to develop PFPS than males (M. Boling et al., 2010). Participants were excluded from the study if they had any history of cardiovascular or neurological problems or lower extremity injury or surgery within the previous year. Each participant in the PFPS or RES group had a diagnosis of PFPS confirmed by a clinician. To be included in the RES group, participants had to have experienced PFPS pain within the previous 4 years and have been asymptomatic for >1 month.

All participants underwent a phone screening prior to one in-lab testing session. During the phone screening, data were collected regarding age, height, weight, injury history, training status, and any medical contraindications to study participation. After ensuring that all

participants were cleared to participate, each was scheduled for a two-hour lab testing session at the University of Massachusetts Amherst. All participants first completed an informed consent document prior to any additional study measures that was approved by the local Institutional Review Board, outlining the procedures and associated risks of the study, as well as a Modified Physical Activity Readiness Questionnaire and general demographics form.

Experimental Setup

Participants were fitted bilaterally with 50 retro-reflective markers that were tracked by eight infrared cameras (Oqus-5 series, Qualisys, Inc., Gothenburg, Sweden) sampling at 200 Hz. The pelvis was defined by markers placed on the right and left anterior superior iliac spines (ASIS), posterior superior iliac spines (PSIS), iliac crests, and greater trochanters with a hip joint center determined by landmarks created as midpoints between the PSIS, ASIS, and greater trochanter markers. Markers on the lower limb were placed unilaterally; for pain-free participants, the right lower limb was used while in the PFPS group, data were collected on the affected leg. Movement of both feet were measured for all participants. Plates of 4 non-colinear markers were placed on the thigh and shank, with calibration markers placed on both the lateral and medial malleoli and femoral epicondyles. The foot segments were created using the malleoli markers and markers on the first and fifth metatarsal heads, using three markers placed on the heel counter of a standard laboratory shoe (Brooks T7) to track foot movement.

Protocol

Data collection took place on an instrumented treadmill (Athletic Republic, Park City, UT). The treadmill rests on four load cells (AMTI, Watertown, MA) and ground reaction forces were sampled via an analog board at 1000Hz, collected in Qualisys Track Manager synchronously with the motion capture data. After all markers were placed, a speed determination procedure was used to find the 21MTR test speed. To ensure a comfortable, sustainable running

speed for the duration of the test, the speed of the treadmill was set to the initial preferred speed of each participant at which they ran for up to one minute. The participant was then asked if they believed they can sustain the speed for 30 minutes. The speed of the treadmill was increased or decreased based on this response. If the speed was determined to be within their range of normal training speeds, this speed was used for the run. If this speed fell outside of the participants normal training range, the speed was again adjusted up or down until a new speed was selected. After speed determination, participants were given up to 5 minutes to rest prior to the initiation of the 21MTR. No pain increases were reported in any participants during this time.

Kinematic and kinetic data were collected continuously for 30 seconds at minutes 1 and 20 of the 21MTR. In addition, Rate of Perceived Exertion (RPE) was collected for each participant as well as a pain measurement rating using an 11-point Verbal Numeric Rating Scale (VNRS, 0-10, with 0 being “no pain” and 10 being “worst possible pain”). Pain was recorded at two-minute intervals through the run to ensure participant safety. After 20 minutes and 30 seconds, another 30 second collection window was taken, at which both RPE and pain were again recorded.

Data processing

Kinematic data were filtered using a dual-pass, low pass Butterworth filter with a cutoff frequency of 8 Hz. 3-dimensional ankle, knee, and hip angles were calculated using a Cardan Xyz rotation sequence in Visual 3D (C-Motion Inc., Germantown, MD). For the calculation of internal joint moments, ground reaction forces were filtered using a low pass, 4th order zero-phase lag Butterworth filter with an 8 Hz cutoff frequency. Both the kinematic and kinetic data were interpolated and normalized to 101 data points, representing 0-100% of the stance phase for each step. Vertical ground reaction force data was used to determine foot contact and toe-off to establish the duration of the stance phase with a threshold of 40 N. Discrete peak and initial joint angles and peak moments were calculated for each stance phase at each time point of the run for

10 individual strides and then averaged together to create means for each participant/time point. All moments are internally referenced.

Statistics

All statistical tests used an alpha criterion level of ($\alpha=0.05$). For baseline testing, one-way Analyses of Variance (ANOVA) were used to test for differences between groups, with partial eta² (η_p^2) used as a measure of effect size. A value of η_p^2 of 0.01 is a small effect, 0.06 a medium effect, and 0.14 a large effect (Jacob Cohen, 1988). When significant main effects of group were found, *post hoc* pairwise comparisons were made using Tukey's honest significant difference tests. For tests comparing the change from the beginning to end of run within group, the end of run values were subtracted from the beginning of run data. To test for group differences, one-way ANOVAs were used to test for differences in change over the course of the 21 MTR. Pearson's correlations were performed to test for the association of changes in pain with changes in discrete outcome measures.

Results

All results are presented as mean \pm SD. No participants stopped early due to pain or fatigue. RPE in the first minute was: 8.7 ± 1.7 and at minute 20: 12.8 ± 2.0 . The highest RPE achieved by any participant was 18. The average pain increases of the CON, PFPS, and RES groups were 0.0 ± 0.0 , 3.0 ± 2.0 , and 0.5 ± 1.0 points, respectively. Fourteen out of 20 PFPS participants showed a clinically significant (>2 points) increase in pain as did one RES participant. No significant differences were found in speed between groups; the average speed across all groups was $2.84 \pm 0.29 \text{ ms}^{-1}$.

Table 4.1. Peak joint angles for the hip, knee, and ankle at baseline and as a change over the run. Group means(SD) are given for each peak angle. Bolded results are significant. * = significant main effect for group ($p < 0.05$). Effect sizes given as η_p^2 .

Kinematics					
Baseline			Angle (°)		
Peak Angles	p_{Group}	η_p^2	CON	PFPS	RES
Hip			mean(SD)	mean(SD)	mean(SD)
Flexion	0.543	0.02	30.3(5.8)	28.2(8.1)	28.2(6.3)
Adduction	0.155	0.07	12.1(3.5)	10.0(4.2)	9.7(4.8)
Internal rotation	0.074	0.09	4.5(4.3)	4.7(4.5)	7.4(3.9)
Knee					
Flexion	0.294	0.04	46.0(4.4)	44.1(3.3)	44.4(4.3)
Abduction	0.785	0.01	3.6(2.8)	2.8(3.7)	3.1(3.2)
Internal rotation	0.919	0.00	1.8(6.3)	2.1(7.2)	2.7(5.6)
Ankle					
Dorsiflexion	0.024*	0.13	26.2(4.3)a	22.7(4.0)b	23.9(3.8)ab
Eversion	0.065	0.10	7.9(3.1)	6.7(2.2)	5.9(2.5)
Abduction	0.062	0.10	11.4(4.2)	13.7(7.0)	9.5(4.2)
Peak Angles	Group	η_p^2	CON	PFPS	RES
Hip			mean(SD)	mean(SD)	mean(SD)
Flexion	0.183	0.06	0.2(2.0)	1.2(2.1)	1.4(2.1)
Adduction	0.373	0.04	-0.3(1.3)	-0.1(1.6)	-0.8(1.6)
Internal rotation	0.170	0.06	1.0(1.3)	0.6(1.8)	0.1(0.9)
Knee					
Flexion	0.957	0.00	0.4(1.8)	0.3(2.0)	0.5(2.8)
Abduction	0.821	0.01	0.7(0.9)	0.6(1.2)	0.5(1.1)
Internal rotation	0.660	0.02	-1.3(1.3)	-0.4(5.4)	-1.1(1.6)
Ankle					
Dorsiflexion	0.973	0.00	0.5(1.0)	0.4(3.4)	1.0(2.4)
Eversion	0.234	0.05	-1.2(1.0)	-1.0(1.2)	-1.7(1.4)
Abduction	0.782	0.01	0.1(1.2)	-0.6(5.2)	-0.5(1.2)

* = significant main effect for group ($p < 0.05$). Letters represent mean separation among groups by Tukey's honest significant difference tests ($p < 0.05$).

Baseline – joint angles

No differences in peak angles were found in any plane at the hip or knee (Table 1). The peak ankle dorsiflexion angle showed a main effect for group ($p = 0.024$, $\eta_p^2 = 0.128$). *Post hoc* tests indicated that this difference was mainly due to greater dorsiflexion in the CON (26.2 ± 4.3 degrees) relative to PFPS (22.7 ± 4.0 degrees) groups ($p = 0.020$). The RES group fell in the middle (23.9 ± 3.8 degrees).

Baseline – joint moments

Several differences were found at baseline between groups in joint moments (Table 2). For peak joint moments, group differences were found in both frontal and transverse plane moments at the hip ($p < 0.001$). The CON group exhibited a larger hip abduction moment ($2.0 \pm 0.7 \text{ Nm} \cdot \text{kg}^{-1} \cdot \text{m}^{-1}$) than both the PFPS group ($0.9 \pm 1.0 \text{ Nm} \cdot \text{kg}^{-1} \cdot \text{m}^{-1}$, $p < 0.01$) and the RES group ($1.4 \pm 0.8 \text{ Nm} \cdot \text{kg}^{-1} \cdot \text{m}^{-1}$, $p = 0.025$). No differences were found between the PFPS and RES groups ($p = 0.228$). The CON group had a greater external rotation moment ($0.3 \pm 0.2 \text{ Nm} \cdot \text{kg}^{-1} \cdot \text{m}^{-1}$) relative to the PFPS group ($0.1 \pm 0.1 \text{ Nm} \cdot \text{kg}^{-1} \cdot \text{m}^{-1}$, $p < 0.001$) and the RES group has a significantly larger external rotation moment compared to the PFPS group ($p = 0.028$).

For peak moments at the knee, there was a main effect for group in the transverse plane ($p = 0.017$, $\eta_p^2 = 0.137$). Post-hoc tests found significantly larger knee internal rotation moments for the CON group ($0.5 \pm 0.2 \text{ Nm} \cdot \text{kg}^{-1} \cdot \text{m}^{-1}$) relative to the PFPS group ($0.3 \pm 0.2 \text{ Nm} \cdot \text{kg}^{-1} \cdot \text{m}^{-1}$, $p = 0.015$).

At the ankle, main effects for group were found in peak frontal ($p < 0.001$, $\eta_p^2 = 0.25$) and transverse ($p = 0.014$, $\eta_p^2 = 0.143$) plane moments. In the frontal plane, the CON group ($0.4 \pm 0.2 \text{ Nm} \cdot \text{kg}^{-1} \cdot \text{m}^{-1}$) had a significantly larger inversion moment relative to both the PFPS group ($0.2 \pm 0.2 \text{ Nm} \cdot \text{kg}^{-1} \cdot \text{m}^{-1}$, $p = 0.001$) and the RES groups ($0.2 \pm 0.2 \text{ Nm} \cdot \text{kg}^{-1} \cdot \text{m}^{-1}$, $p = 0.002$).

In the transverse plane, both the CON and RES groups had greater abduction moments relative to PFPS.

Differences between beginning and end

When comparing the mean differences between groups from the beginning to end of run, there was one significant difference found across all kinematic and kinetic variables (Tables 1& 2). There was a main effect for group in peak frontal plane knee moment in differences between the beginning and end of run ($p = 0.03$, $\eta_p^2 = 0.12$; Table 2). After post-hoc analysis, the CON group increased their knee abduction moment ($0.04 \pm 0.08 \text{ Nm} \cdot \text{kg}^{-1} \cdot \text{m}^{-1}$) while the PFPS group decreased their knee abduction moment ($-0.48 \pm 0.12 \text{ Nm} \cdot \text{kg}^{-1} \cdot \text{m}^{-1}$, $p = 0.025$) over the course of the prolonged treadmill run.

Correlation with pain

Peak knee flexion angles showed significant Pearson's correlations with increases in pain in the PFPS group. A moderate positive relationship ($r = 0.56$, $p = 0.005$) was found for peak knee flexion angle with increased pain. A weak positive relationship ($r = 0.40$, $p = 0.039$) was found for peak dorsiflexion angle with increased pain. No differences were seen in any other planes or at the hip, as well as for any joint moments.

Table 4.2. Peak joint moments for the hip, knee, and ankle at baseline and as a change over the run. Group means(SD) are given for each peak angle. Bolded results are significant. Effect sizes given as η_p^2 .

Kinetics					
Baseline			Moment (Nm*kg ⁻¹ *m ⁻¹)		
Peak Moments	p _{Group}	η_p^2	CON	PFPS	RES
Hip			mean(SD)	mean(SD)	mean(SD)
Extension	0.478	0.03	1.18(0.25)	1.10(0.39)	1.27(0.54)
Abduction	<0.001*	0.27	2.04(0.71)a	0.95(0.95)b	1.37(0.85)b
External Rotation	<0.001*	0.29	0.30(0.17)a	0.08(0.14)b	0.21(0.14)a
Knee					
Extension	0.625	0.02	2.40(0.74)	2.26(0.48)	2.44(0.40)
Abduction	0.306	0.04	0.59(0.36)	0.42(0.38)	0.57(0.32)
Internal rotation	0.017*	0.14	0.48(0.19)a	0.27(0.24)b	0.42(0.25)ab
Ankle					
Plantar flexion	0.290	0.04	2.70(0.51)	2.46(0.51)	2.54(0.45)
Inversion	<0.001*	0.25	0.45(0.22)a	0.19(0.22)b	0.20(0.18)b
Abduction	0.014*	0.14	0.21(0.12)a	0.11(0.16)b	0.21(0.10)a
Change			Moment (Nm*kg ⁻¹ *m ⁻¹)		
Peak Moments	Group	η_p^2	CON	PFPS	RES
Hip			mean(SD)	mean(SD)	mean(SD)
Extension	0.475	0.03	-0.04(0.13)	0.01(0.12)	-0.07(0.36)
Abduction	0.446	0.03	-0.04(0.12)	0.02(0.14)	0.00(0.09)
External Rotation	0.609	0.02	0.00(0.07)	0.02(0.17)	0.05(0.10)
Knee					
Extension	0.254	0.05	-0.04(0.12)	-0.12(0.20)	-0.03(0.22)
Abduction	0.030*	0.12	0.04(0.08)a	-0.05(0.12)b	0.00(0.09)ab
Internal rotation	0.740	0.01	0.02(0.04)	0.04(0.17)	0.05(0.12)
Ankle					
Plantar flexion	0.261	0.05	-0.03(0.18)	0.07(0.33)	0.13(0.39)
Inversion	0.243	0.05	0.00(0.06)	0.00(0.08)	-0.04(0.05)
Abduction	0.638	0.02	0.01(0.05)	0.03(0.14)	0.04(0.07)

* = significant main effect for group (p < 0.05). Letters represent mean separation among groups by Tukey's honest significant difference tests (p < 0.05).

Discussion

The aim of this study was to determine the influence of a prolonged treadmill run on lower limb biomechanics and pain in runners with PFPS, runners with resolved PFPS and healthy controls. The results of this study were not in support of the first hypothesis as there were no group differences at baseline for hip abduction and internal rotation angles. However, the PFPS group exhibited lower peak dorsiflexion at baseline compared to the CON group, in support of this first hypothesis. In partial support of the second hypothesis, hip abduction and external rotation and knee internal rotation moments were larger in the CON group compared with RES and PFPS at baseline. Over the course of the prolonged run, PFPS runners decreased their peak knee abduction moment while the CON group increased knee abduction moments, in opposition of our third hypothesis. The final hypothesis was partially supported by the correlations observed between pain and peak sagittal plane knee and ankle angles in the PFPS group. Together, these results indicate that acute pain flares in the PFPS lead to motor system changes when compared to CON and RES groups that are not present in their baseline state. In addition, these results provide further evidence of a lack of consensus in the literature in basic kinematic and kinetic measures and indicate that other biomechanical markers should be used to understand gait mechanics of these three groups.

Given the chronic nature of PFPS, as well as previously observed gait differences between healthy and injured runners, it was reasonable to expect that there would be baseline differences in gait mechanics among all three groups. However, given the current study findings, this was not the case at both the hip and knee joints where there were no differences observed among groups in either peak angles or angles at foot strike. This was surprising given previous reported differences between groups in the literature (Noehren, Pohl, et al., 2012); however, there are several possible explanations for the lack of these baseline differences. One of the leading theories on how pain influences movement is that pain encourages a redistribution of muscle activation and forces both within a muscle grouping and between muscle groupings for the

purpose of both changing loading behavior and lower extremity mechanics and avoiding painful movements (Hodges & Tucker, 2011). Given the care in recruiting participants with diagnosed pain, we expected to find similar differences in baseline gait between the PFPS group and the other two. However, it may be that the severity of daily, long-term pain experienced by the PFPS group was not large or regular enough to elicit long-term adaptations in gait that remain in a rested, relatively pain-free state. At baseline, the PFPS participants indicated initial pain values <2 on the VNRS, so all of the groups exhibited similar initial pain values at the beginning of the run. Another reason for the lack of differences seen at the hip and knee may be that the length of time of injury for the PFPS and RES was highly variable, with some individuals having only had pain for a month and others for several months. This may not have been long enough to see the types of long-term adaptations in gait mechanics to pain that have been previously observed.

Again in contrast to the literature, differences in ankle kinematics were found between the PFPS and CON group. The CON group had the highest peak dorsiflexion angle. Movement of the foot and at the ankle is considered to be used as a shock absorber during stance, particularly at foot strike (Dickinson, Cook, & Leinhardt, 1985). The CON group used a greater ankle range of motion which may have been to aid in attenuating impact, likely reducing the load experienced at the hip and knee. The mean dorsiflexion angle for the RES group was between that of the PFPS and CON group which suggests that the RES group may have begun to resume using movement patterns more similar to the CON group in the long-term absence of pain but may not have fully returned to a healthy state. The lower peak dorsiflexion angles achieved by both the PFPS and RES group may indicate a lesser ability to attenuate impact at the ankle, placing greater reliance on the knee and hip which may eventually lead to increased pain with activity. While there were no differences in baseline flexion moments at the ankle, there were differences observed in both the frontal and transverse planes. The CON had larger moments in both planes which potentially indicate a greater reliance on the ankle during gait and a possible preventative measure for knee joint pain.

From the results of the current study, PFPS may loading at the hip, knee, and ankle, as evidenced by the altered moments, but these changes are not sufficient to influence the resultant kinematic patterns at the hip and knee. The CON group had the largest hip abduction and external rotation moments of both groups, while the PFPS group had the smallest with the RES group falling between. A larger internal hip abduction moment will be resisting hip adduction and may indicate that the CON group has greater forces acting to keep the femur from collapsing towards the midline of the body. Paired with the larger external rotation moments, the CON group demonstrated the greatest forces around the hip that, combined, seem focused in keeping the thigh within a neutral path (i.e. not collapsing inwards or splaying outwards). In addition, there were greater internal rotation moments at the knee in the CON group compared to the PFPS group, adding support to this idea of keeping the lower extremity on a neutral movement path. These results are in agreement with previous literature regarding kinetics at the hip (Bazett-Jones et al., 2013).

Runners in the PFPS group experienced a clinically significant (>2 points) increase in pain over the course of the 21MTR. This result is in agreement with previous literature and supports the idea that movement-evoked pain is a characteristic of patellofemoral syndrome (Thomeé, Augustsson, & Karlsson, 1999). In partial agreement with our third hypothesis that pain would influence a change in joint moments throughout the run, peak frontal plane moments showed a differential change between the beginning and end of run across groups. Pain in PFPS is believed to originate from increased load and damage to subchondral bone, as well as pressure on the infrapatellar fat pad as a result of altered loading at the knee (Draper et al., 2006; Fulkerson, 2002). The CON group experienced increased knee abduction moments while the PFPS group showed the opposite. While greater knee abduction moments are often observed in individuals with PFPS during baseline or rested measurements, it's likely that both pain and exertion influenced this result in the PFPS group, causing them to decrease these frontal plane moments to alter the loading pattern at the knee. This cannot be related to pain alone, as there

were no correlations to pain increases and knee abduction moments. This was a relatively short run for these trained individuals that was designed to allow for increased pain with the least participant burden; thus, it is possible that in longer runs there would be more changes evident in the observed outcome measures.

One outcomes measure had a significant correlation with the change in pain: peak knee flexion and ankle dorsiflexion angles. Typically, knee flexion has been shown to be lower in those experiencing pain at the knee and it has been proposed as part of an avoidance strategy to limit motion at the painful knee joint. With increasing pain in this study, however, runners tended to use greater peak knee flexion during stance accompanied by increased dorsiflexion. In order to achieve greater dorsiflexion and potentially allow for the ankle to attenuate impact forces, the knee likely needs to have a greater degree of flexion to accomplish this landing position. However, it may also be that runners experienced greater pain as a result of their increased knee flexion and compensated with increased dorsiflexion.

There are several limitations that must be considered when interpreting the results of this study. While this study used an ecological running model, it was conducted on a treadmill at a constant speed. It is possible that participants would have varied their speed and gait mechanics as they experienced more pain had they been running overground. The length of the run was selected to be long enough to increase pain but not excessive; however, many runs last longer than 20 minutes and thus more changes may have been observed if the run was longer. All participants in the PFPS and RES groups were confirmed by a clinician to have patellofemoral pain syndrome; however, there still was variability in the severity of this pain and how long they had been experiencing it, as well as for how long the RES group had been without pain. These both could have affected the individual responses of each runner who participated in this study despite the efforts to have consistent group characteristics.

CONCLUSIONS

Based on these study findings, there do not appear to be significant long-term kinematic adaptations to PFPS injury in a rested state at the hip and knee. It is likely that the average pain felt on a daily basis outside activity is insufficient to elicit a motor system response to trigger gait modification from healthy controls at these joints, despite lower peak dorsiflexion observed in those with PFPS. However, while kinematic patterns appear essentially unchanged, the kinetic results found at baseline indicate changes in the loading profiles at joints within the lower extremity in those with a history of PFPS. This shift in loading throughout the lower extremity may place these runners at a greater risk for pain development. When an acute pain flare was introduced, only increased knee abduction moments in the PFPS group were found relative to the other groups. Thus, a significant increase in pain (>2 points on the VNRS) does not have a prominent effect on gait mechanics. These results indicate that runners may become injured as they are unable to sufficiently modify their gait mechanics in response to increased pain. Finally, runners who have resolved their pain symptoms do not appear to have returned to completely healthy gait which may place them at a greater risk for future patellofemoral pain syndrome reoccurrence.

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CHAPTER 5
SEGMENT COORDINATION AND COORDINATION VARIABILITY IS
DIFFERENT IN RUNNERS WITH PATELLOFEMORAL PAIN
SYNDROME

Introduction

To produce the necessary resultant lower extremity postures for complex movements like running, the neuromuscular system is required to coordinate multiple degrees of freedom (e.g., joints, segments) throughout the body. The relative movement of two segments, or segment coordination, represents the organization of movement throughout the body and provides information regarding movement control. A hypothesis based on dynamical systems theory posits that there may be an uncoupling of segment coordination and a reduction in the stride-to-stride variability of segment coordination (coordination variability) in response to joint pain (Hamill et al., 2012; Hodges & Tucker, 2011). While segment coordination refers to the control of movement, coordination variability characterizes the flexibility of the motor system and its ability to respond to both internal and external perturbations. There have been few studies related to the effects of different injuries on segment coordination and coordination variability; however, the potential benefits of this line of research may provide important insight into movement pattern deficits or changes experienced by those in pain (Cunningham et al., 2014; Hafer, Brown, & Boyer, 2017; Hamill et al., 2012; Heiderscheidt, 2002). These studies have used several different methods of looking at coordination and coordination variability, including discrete relative phase, continuous relative phase, and vector coding. While continuous relative phase may be the most sensitive to changes in coordination with gait, the data must be sinusoidal in nature and normalized to address frequency and amplitude differences (Robertson, Caldwell, Hamill, Kamen, & Whittlesey, 2013). Vector coding can be applied to nonsinusoidal data as well and does not require the same normalization, as well as being more useful in clinical applications and interpretations (Robertson et al., 2013). This makes it a primary choice for looking at injury

populations.

As many as 85 percent of the 30 million runners in the United States get injured each year (Bovens et al., 1989), and the most common lower limb injury in runners is patellofemoral pain syndrome (PFPS) (Taunton et al., 2002). Chronic PFPS can lead to cartilage damage and osteoarthritis, contributing to disability in older age (Utting et al., 2005). Despite our current depth of knowledge about factors predisposing individuals to PFPS and the resulting impairments in gait mechanics, PFPS interventions show little improvement (Esculier et al., 2018). By studying movement control and the flexibility of that movement using segment coordination and coordination variability, we may better understand how pain and injury status affect gait mechanics and be able to use this information more effectively in clinical translation than traditional kinematic measures to improve treatment efficacy.

Pain symptoms associated with PFPS are thought to originate from the infrapatellar fat pad, subchondral bone or synovial tissues within the joint in response to abnormal tissue stress patterns resulting from poor running mechanics (Draper et al., 2006). Responses and adaptations to increasing pain are believed to alter muscle and movement coordination. Quantification of segment coordination may allow for an interpretation of the factors that influence discrete kinematic and kinetic variables that have been previously reported to differ in individuals with PFPS, such as weak hip musculature and poor dynamic femur control. Weak hip musculature and poor dynamic femur control have been linked with both PFPS progression due to their propensity to increase patellar maltracking and potentially patellofemoral joint stress (Cichanowski et al., 2007). Previous work has found that individuals with overuse injuries have lower segment coordination variability when compared with healthy cohorts (Cunningham et al., 2014; Heiderscheit, 2002; Seay et al., 2011), though not across all couplings or in all populations (Cunningham et al., 2014; Hafer et al., 2017). The current interpretation is that lower coordination variability represents a smaller number of available movement patterns, or “locking” of the available degrees of freedom for movement, which may lead to repeated tissue stresses and

the inability to adapt to changing conditions thereby contributing to the persistence of PFPS. The mechanism for PFPS development is believed to be due to altered loading of the patellofemoral joint; therefore, lower coordination variability in runners with PFPS would be in support of this mechanism. Given that the hip is implicated in most of the literature as the primary cause behind PFPS development, particularly the gluteus medius, coupling of the pelvis and thigh in the frontal and transverse planes would be of primary importance.

While changes in segment coordination and coordination variability may initially be part of the motor system's response to pain, there is also evidence that altered segment coordination and coordination variability may persist even after pain has subsided. In a study looking at the effects of low back pain on coordination variability, greater in-phase segment coordination (adjacent trunk and pelvis segments moving in the same direction) and lower coordination variability were found in the injured group compared to the healthy group (Seay et al., 2011). This increased in-phase motion was thought to be an effort to minimize movement between two adjacent segments. A third group made up those individuals who had previously had low back pain, but with resolved painful symptoms, fell in between these two groups, having greater coordination variability than the injured group but not reaching the same level of coordination variability of the healthy cohort (Seay et al., 2011). These initial findings indicate that this resolved group may be important in understanding the mechanism behind the reoccurrence of chronic injuries. Therefore, investigation of an asymptomatic group of runners who formerly had PFPS is warranted. In addition, little is known about the effects of an acute pain flare on segment coordination and coordination variability in those with PFPS. Thus, using a pain flare protocol to investigate how coordination and coordination variability may change in runners with PFPS compared to their healthy and resolved counterparts may help explain why pain typically worsens with duration of activity with PFPS.

To better understand how pain influences the flexibility of movement, we examined segment coordination and coordination variability during a moderate, self-paced 21-minute

treadmill run (21MTR) in healthy runners (CON), runners with PFPS (PFPS), and runners whose pain had resolved (RES). This length of run was chosen as an ecological model to mimic the typical training conditions these runners may encounter on a daily basis. In addition, peak pain in runners with PFPS occurs about 18 minutes into a run (Noehren, Pohl, et al., 2012). Therefore, the primary aim of this study was to quantify differences in segment coordination and coordination variability between the CON, PFPS, and RES groups at baseline and over the course of the 21MTR in the following couplings that have the greatest influence on dynamic femoral control: 1) frontal pelvis vs. transverse thigh and 2) frontal pelvis and frontal thigh. We hypothesized the following:

H 1.1 There would be greater in phase coordination for the above couplings between CON, PFPS, and RES at the end of the 21MTR.

H 1.2 Segment coordination variability would be lower in individuals with PFPS as compared to RES and healthy controls, such that coordination variability differed as $PFPS < RES < CON$ at baseline of the 21MTR for the above couplings.

H 1.3 Segment coordination variability would decrease in PFPS and RES but not healthy controls over the 21MTR for the above couplings such that the change in variability was $CON < RES < PFPS$.

Secondary analyses were performed on four other couplings more distal in the lower extremity: sagittal thigh-sagittal shank, sagittal thigh-transverse shank, frontal thigh-frontal shank, and transverse shank-frontal foot, which also have been indicated as potential sites of change in runners with PFPS (Bazett-Jones et al., 2013; Dierks et al., 2011; Esculier et al., 2015; Noehren, Sanchez, et al., 2012; Souza & Powers, 2009; Willy et al., 2012).

Methods

Twenty CON (10 female, 10 male), 20 PFPS (10 female, 10 male), and 18 RES (9 female, 9 male) recreationally active runners between the ages of 18-35 were asked to complete a 21-minute moderate, self-paced treadmill run on an instrumented treadmill (Treadmetrix, Park City, UT). All participants completed the informed consent process as approved by the University Institutional Review Board. Prior to the run, retro-reflective markers were placed on anatomical landmarks of each participant to define 4 segments: pelvis, thigh, shank and foot. The pelvis was defined by markers placed on the right and left ASIS, PSIS, iliac crests, and greater trochanters. The thigh segment was defined proximally by the greater trochanters and distally by the medial and lateral femoral condyles, which also defined the proximal end of the shank. The medial and lateral malleoli defined the distal end of the shank. These segments were tracked using rigid cluster markers placed on the thigh and shank. The foot was defined by the malleoli and the first and fifth metatarsal heads and tracked by three markers placed on the heel counter.

Protocol

After all markers were placed, participants were given five minutes to warm up as necessary on the treadmill, during which their preferred running speed was determined. The instructions given were to select “a pace that you would choose to comfortably run for twenty minutes on an easy-to-moderate training run”. Once that speed was determined for each participant, speed was increased and decreased around that speed to ensure the appropriate speed was selected. A short rest was then provided prior to the start of the prolonged run. Kinematic and kinetic data were collected for 30 seconds at minutes 1 and 20 of the run, sampling at 200 and 2000 Hz, respectively. Pain was assessed every two minutes of the run using a verbal numeric rating scale (vNRS) with 0 being “no pain” and 10 being “the most severe pain you’ve experienced” in either the participants’ right leg (healthy) or the affected leg (injured). In

addition, each participant's Rating of Perceived Exertion (RPE) on a 6-20 Borg scale (Borg, 1981) was recorded at these same time intervals.

Data processing

Data were collected, tracked and labelled in Qualisys Track Manager (Qualisys, Inc, Gothenberg, Sweden). Data processing was performed using Visual 3D software (C-motion, Inc., Rockville, MD). All marker position data were low pass filtered using a dual-pass, 4th order Butterworth filter at 8 Hz . Ground reaction force data were filtered at 25 Hz and were used for gait event detection (foot strike, toe off). Global segment angles for the pelvis, thigh and shank for 10 stance phases for each participant were exported from Visual3D for each participant at the beginning and end of the run (right leg for healthy, affected leg for injured).

Coordination

To compare the segment coordination between groups the frequency of the coordination pattern (i.e. percentage of stance the coordination pattern was observed) were calculated from the angle-angle plots. The number of times a data point for each point of stance fell within one of 8 coordination bins determined a frequency spectrum for each participant. These were used to determine group differences in frequency. The 8 bins were defined as: in-phase, proximal-dominant (0-45 degrees); in-phase, distal-dominant (45-90); anti-phase, distal-dominant (90-135); anti-phase, proximal-dominant (135-180); in-phase, proximal-dominant (180-225); in-phase, distal-dominant (225-270); anti-phase, distal-dominant (270-315); and anti-phase, proximal-dominant (315-360) (Figure 1) (Needham, Naemi, & Chockalingam, 2015).

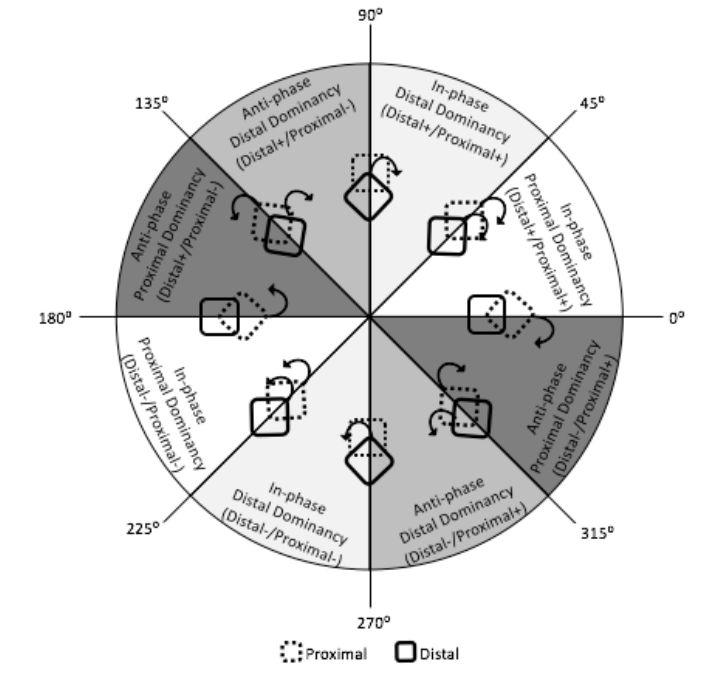


Figure 5.1. Polar plot showing the coordination pattern classification as described by Needham et al., (2015). Visual illustrations at each 45° interval of coupling angle show coordination pattern between the proximal (dashed box) and distal (solid box) segments. Figure courtesy of Dr. Gillian Weir.

Coordination variability

Segment coordination variability for each participant was calculated for 10 stance phases at the beginning and end of the run using a modified vector coding technique (Chang et al., 2008) using a Matlab (Mathworks, Inc., Natick, MA) program. The number of strides chosen for analysis has been shown to be reliable for treadmill running (Hafer & Boyer, 2017). With the modified vector coding technique, angle-angle coordination plots were created for the relative motion between adjacent segments (pelvis, thigh, shank) over stance (Figure 2). Based on the prior findings of injury mechanisms of PFPS, the following intra-limb couplings from the stance limb were examined: frontal pelvis-transverse thigh, frontal pelvis-frontal thigh, sagittal thigh-sagittal shank, sagittal thigh-transverse shank, frontal thigh-frontal shank, and transverse shank-frontal foot. Coordination variability was calculated as the standard deviation of the angle between the vector connecting corresponding consecutive time points of the angle-angle plots and

the right horizontal across trials using circular statistics (Hafer & Boyer, 2017). Coordination variability was averaged over each third of stance (i.e. weight acceptance, mid-stance, push off) to account for the differing demands of each phase.

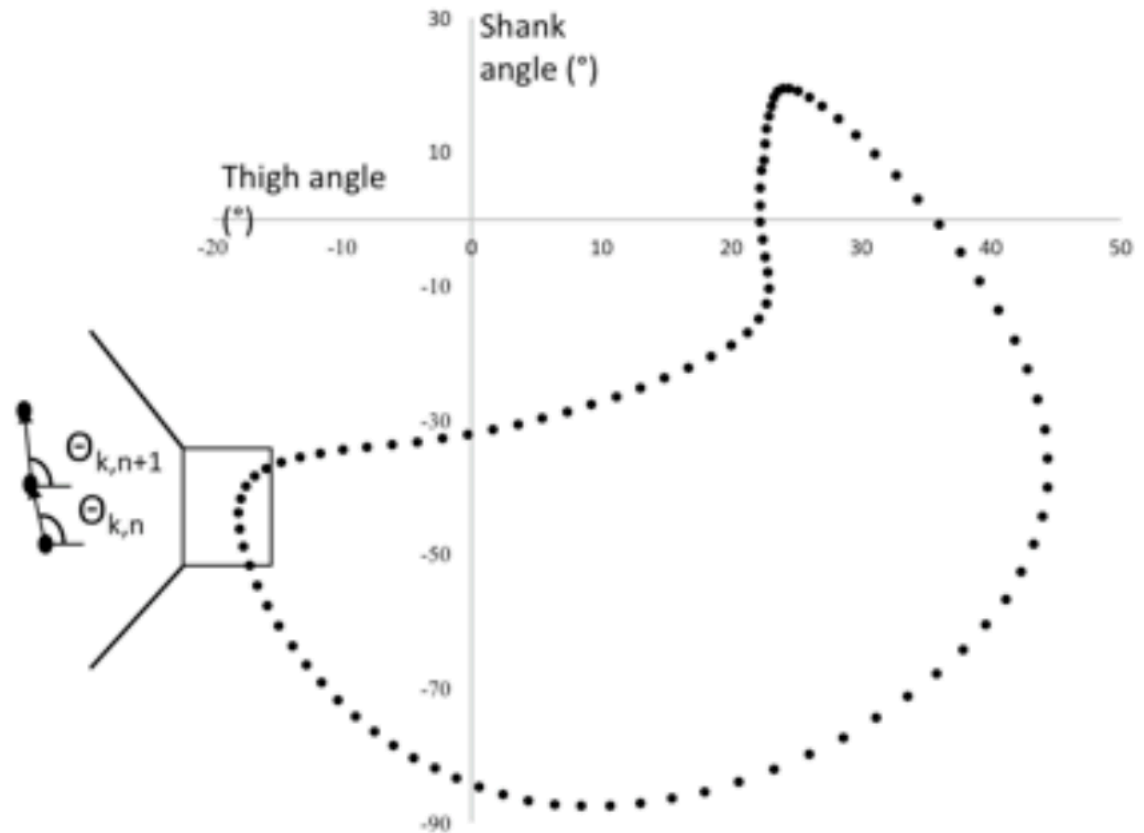


Figure 5.2. Thigh-shank angle-angle plot. A vector is drawn between successive points and the angle of that vector relative to the right horizontal defines the phase angle for that trial. Coordination is defined as the mean phase angle calculated over 10 strides using circular statistics. Coordination variability is defined as the standard deviation of the mean phase angle over multiple strides again, using circular statistics. Figure courtesy of Dr. Jocelyn Hafer.

Statistics

To test for group differences at baseline, one-way ANOVAs were performed in SPSS (IBM SPSS Statistics 22, SPSS Inc., Chicago, IL) with $\alpha = 0.05$ for each respective third of stance for each coupling with partial eta² (η_p^2) used as a measure of effect size. A value of η_p^2 of 0.01 is a small effect, 0.06 a medium effect, and 0.14 a large effect (Jacob Cohen, 1988). Tukey's

honest significant difference tests were performed *post-hoc* to test for differences when significant main effects for group were found. One-way ANOVAs were also performed to test for both differences in segment coordination at the end of the run as well as the change in coordination variability between the beginning and end of run by analysing the difference calculated by the (beginning CV – end CV). In order to test for differences in segment coordination, differences in frequency for each bin were compared between groups.

Results

All results are presented as mean \pm SD. All participants had final RPEs of $12 \leq \text{RPE} \leq 16$. The average pain increases of the CON, PFPS, and RES groups were 0.0 ± 0.0 , 3.0 ± 2.0 , and 0.5 ± 1.0 points, respectively. Fourteen out of 20 PFPS participants showed a clinically significant (>2 points) increase in pain as did one RES participant. No differences among groups in coordination of either pelvis-thigh couplings was observed (Table 1). No significant differences were found in speed between groups; the average speed across all groups was $2.84 \pm 0.29 \text{ ms}^{-1}$.

Baseline

There was a main effect for group in the anti-phase, shank dominant coordination bin (90-135 degrees) for the sagittal thigh-transverse shank coupling (Figure 3, Table 1). The PFPS group spent a greater percentage of time during stance in anti-phase, shank dominant motion ($9.65\% \pm 8.4$) than both CON ($p = 0.023$, $4.9\% \pm 2.4$) and RES ($p = 0.012$, $4.3\% \pm 3.7$).

Table 5.1. Coordination of the pelvis-thigh couplings and the sagittal thigh-transverse shank coupling. Results from ANOVA are in the “Group” column, with effect sizes given in the following column “ η_p^2 ”. Mean (SD) of the frequency of each coordination pattern are given for each group for each of the 8 possible bins of coordination.

Coordination Measures	Frequency (% stance)				
	p_{group}	η_p^2	CON	PFPS	RES
Frontal pelvis - transverse thigh			mean(SD)	mean(SD)	mean(SD)
In-phase, proximal-dominant (0-45°)	0.432	0.03	20.0(14.2)	26.3(18.0)	24.6(13.7)
In-phase, distal-dominant (45-90°)	0.291	0.04	29.8(16.4)	21.6(18.6)	23.4(16.0)
Anti-phase, distal-dominant (90-135°)	0.231	0.05	4.3(5.5)	2.5(4.4)	5.4(6.3)
Anti-phase, proximal-dominant (135-180°)	0.872	0.01	3.8(4.2)	4.0(6.2)	3.2(4.5)
In-phase, proximal-dominant (180-225°)	0.515	0.02	10.8(8.8)	10.0(10.5)	7.6(7.3)
In-phase, distal-dominant (225-270°)	0.800	0.01	15.4(10.1)	17.3(11.6)	17.4(10.6)
Anti-phase, distal-dominant (270-315°)	0.477	0.03	6.4(4.9)	8.3(6.3)	8.9(8.2)
Anti-phase, proximal-dominant (315-360°)	0.949	0.00	9.4(8.1)	10.2(8.3)	9.6(8.4)
Frontal pelvis - frontal thigh					
In-phase, proximal-dominant (0-45°)	0.850	0.01	24.5(16.5)	26.8(16.8)	27.2(14.5)
In-phase, distal-dominant (45-90°)	0.662	0.02	5.5(10.8)	3.4(4.0)	5.1(7.1)
Anti-phase, distal-dominant (90-135°)	0.359	0.04	5.9(7.7)	4.7(5.9)	3.1(3.3)
Anti-phase, proximal-dominant (135-180°)	0.942	0.00	11.7(8.3)	12.0(10.5)	12.7(8.4)
In-phase, proximal-dominant (180-225°)	0.940	0.00	13.4(8.6)	14.3(10.1)	14.3(8.7)
In-phase, distal-dominant (225-270°)	0.949	0.00	3.4(3.0)	3.2(2.9)	3.4(3.3)
Anti-phase, distal-dominant (270-315°)	0.779	0.01	3.6(5.4)	5.0(6.4)	4.2(6.3)
Anti-phase, proximal-dominant (315-360°)	0.929	0.00	32.1(18.1)	30.9(16.4)	30.1(15.1)
Sagittal thigh - transverse shank					
In-phase, proximal-dominant (0-45°)	0.27	0.046	2.5(3.5)	3.0(3.9)	4.9(6.8)
In-phase, distal-dominant (45-90°)	0.067	0.094	17.6(6.1)	12.5(7.6)	14.3(6.5)
Anti-phase, distal-dominant (90-135°)	0.007*	0.167	4.9(2.4)a	9.7(8.4)b	4.3(3.7)a
Anti-phase, proximal-dominant (135-180°)	0.513	0.024	14.0(10.5)	17.6(10.0)	16.6(9.2)
In-phase, proximal-dominant (180-225°)	0.339	0.039	58.9(10.3)	54.2(10.9)	54.8(11.1)
In-phase, distal-dominant (225-270°)	0.098	0.081	1.1(2.6)	1.0(2.5)	3.3(5.2)
Anti-phase, distal-dominant (270-315°)	0.266	0.047	0.3(0.8)	1.1(2.2)	0.5(0.9)
Anti-phase, proximal-dominant (315-360°)	0.865	0.005	0.9(3.0)	1.1(2.2)	1.3(2.3)

* = significant main effect for group ($p < 0.05$). Letters represent mean separation among groups by Tukey’s honest significant difference tests ($p < 0.05$).

Table 5.2. Coordination variability for the pelvis-thigh couplings at baseline and the change over the run. Results from ANOVA are in the “ p_{group} ” column, with effect sizes given in the following column “ η_p^2 ”. Mean(SD) of the frequency of each coordination pattern are given for each group for each of the 8 possible bins of coordination.

Coordination Variability					
Baseline	p_{Group}	η_p^2	CON	PFPS	RES
Frontal pelvis - transverse thigh			mean(SD)	mean(SD)	mean(SD)
Weight acceptance	0.493	0.025	14.92(7.41)	16.49(8.39)	18.31(10.27)
Mid-stance	0.451	0.029	17.81(7.07)	19.42(12.47)	22.58(14.59)
Pushoff	0.063	0.096	9.49(6.78)	14.81(10.65)	18.02(14.72)
Frontal pelvis - frontal thigh					
Weight acceptance	0.052	0.102	10.45(6.20)a	13.21(7.19)ab	16.96(10.41)b
Mid-stance	0.164	0.064	12.89(7.03)	19.03(11.96)	17.46(11.59)
Pushoff	0.143	0.068	7.02(4.85)	11.64(9.86)	11.72(9.67)
Change					
Frontal pelvis - transverse thigh					
Weight acceptance	0.852	0.002	-0.14(6.73)	0.17(6.42)	0.65(9.95)
Mid-stance	0.962	0.001	-1.04(6.46)	-0.81(10.06)	-0.04(16.22)
Pushoff	0.743	0.011	0.78(3.46)	-1.59(8.90)	-1.63(17.40)
Frontal pelvis - frontal thigh					
Weight acceptance	0.846	0.006	1.90(3.80)	0.83(3.96)	1.69(9.56)
Mid-stance	0.020*	0.133	4.36(6.46)a	-3.95(9.94)b	2.92(11.97)ab
Pushoff	0.264	0.047	-0.52(2.47)	-2.97(9.63)	0.81(7.54)
Sagittal thigh - transverse shank					
Weight acceptance	0.026*	0.125	-1.68(4.13)a	1.51(4.02)ab	1.88(4.98)b
Mid-stance	0.552	0.021	0.47(1.08)	-1.56(8.78)	-1.26(6.35)
Pushoff	0.719	0.012	-0.14(0.70)	-1.13(6.44)	-1.62(7.74)
Transverse shank - frontal rearfoot					
Weight acceptance	0.026*	0.124	-0.63(3.26)a	0.74(2.84)ab	2.27(3.51)b
Mid-stance	0.588	0.019	-1.36(8.40)	0.95(7.00)	-1.88(11.53)
Pushoff	0.729	0.011	-0.41(2.73)	-2.09(9.43)	-3.27(17.12)

* = significant main effect for group ($p < 0.05$). Letters represent mean separation among groups by Tukey’s honest significant difference tests ($p < 0.05$).

Change over run

A main effect for group was found for the change in frontal pelvis-frontal thigh coupling during mid-stance between the beginning and end of the run ($p = 0.02$, $\eta_p^2=0.13$, Figure 4). From post-hoc tests, the PFPS group displayed an increase in coordination variability that was significantly greater than the CON during mid-stance ($p = 0.023$). The RES group was not significantly different from either the CON ($p = 1.00$) or the PFPS group ($p = 0.081$); however, the mean variability fell in between the CON and PFPS groups. No other differences were found in beginning-end run differences for coordination variability for the pelvis-thigh coupling.

For the change in coordination variability of the sagittal thigh-transverse shank coupling, there was a main effect for group between the beginning and end of the run during weight acceptance ($p = 0.026$, $\eta_p^2=0.13$, Table 2). Post-hoc tests indicated that CON and RES groups had a different response during prolonged running ($p = 0.040$), with the CON exhibiting an increase in coordination variability (1.7 ± 4.1) and the RES a decrease (-1.9 ± 5.0). There was no significant difference between the CON and PFPS groups ($p = 0.063$).

There was a main effect for group for the change in coordination variability of the transverse shank-frontal rearfoot coupling between the beginning and end of the run during weight acceptance ($p = 0.03$, $\eta_p^2=0.12$). Post-hoc tests indicated that CON and RES groups had a different response during this phase ($p = 0.02$), with the CON exhibiting an increase in coordination variability (0.6 ± 3.3) and the RES a decrease (-2.3 ± 3.5).

Discussion

The purpose of this study was to investigate whether segment coordination would differ, coordination variability would be lower and these differences would be exacerbated at the end of a 21MTR when grouped by PFPS injury status. It was hypothesized that differences amongst groups would in part be due to the motor system response to pain and thus an exacerbation of the

groups was expected in response to an acute pain flare with running. These findings did not support our first study hypothesis regarding segment coordination, as no differences were found among groups in the pelvis-thigh couplings tested. However, differences in the sagittal thigh-transverse shank coupling at baseline were found between the PFPS and other groups. For the second and third hypotheses, there were no differences at baseline for coordination variability in any of the observed couplings; however, several differences in the change between the beginning and end of the run were found amongst groups for the frontal pelvis-frontal thigh, sagittal thigh-transverse shank, and transverse shank-frontal rearfoot couples. All of these differences were observed during either weight acceptance or mid-stance, in which the loads experienced at the knee joint are greatest. Given these findings, altered coordination about the hip does not appear to be the mechanism for previously observed gait differences at baseline in runners with PFPS compared to healthy cohorts. However, it does appear that pain and prolonged running cause a differential response in coordination variability for a number of lower limb segment couples.

No findings were in support of the first hypothesis as there were no differences amongst the three groups for the pelvis-thigh coordination couplings. This result was unexpected as much of the literature in agreement that the hip is the primary site leading to PFPS development and progression. For the frontal pelvis-frontal thigh coupling, this indicates that there was no disruption in the relationship between pelvis obliquity and femoral ab/adduction in those with PFPS, while in the frontal pelvis-transverse thigh the relationship between pelvis obliquity and femoral rotation did not differ between groups. Thus, deficits in hip musculature strength and altered hip kinematics reported in the literature in PFPS populations compared to healthy controls, injury status, pain, and exertion were not enough to affect these segment couples (Cichanowski et al., 2007; Souza & Powers, 2009). This suggests that movement control of these couples may not be a primary factor in PFPS injury.

Even though there were no observed differences in the pelvis-thigh couplings, there were differences in segment coordination for the sagittal thigh-transverse shank coupling as the PFPS group had a greater frequency of shank dominant, anti-phase behavior compared to the two other groups. This coordination pattern would tend to internally rotate the tibia (+) more while the thigh extends (-). Findings from Seay et al. (2011) indicated that both injured and resolved patients with low back pain displayed greater in phase motion of the trunk and pelvis, which they attributed to an effort to reduce the relative movement between these two segments. Although the direct cause of low back pain is unknown, their conclusion was that reducing relative segment movement was an attempt to avoid pain. However, it is possible that in this case, greater anti-phase motion observed here appears to be indicative of greater relative motion between the thigh and shank. One possible explanation for this difference is that the runners with PFPS may be unable to adjust their movement patterns to limit this anti-phase motion and place themselves at a greater risk of pain development. However, having a shank dominant coordination pattern indicates that the femur is moving less when compared to the tibia, which indicates that there may not be a lack of control over femoral movement. Previous work has found an increase in rearfoot excursion in those with anterior knee pain (Rodrigues, TenBroek, et al., 2013), which may be the source of increased tibial movement relative to the tibia.

Despite these findings, care must be taken in the interpretation of these coordination results using the binning definitions from Needham et al. (2014). These divisions of coupling angle are defined in a global sense, and are more finely divided than previous bins used (Chang et al., 2008). This may lead to an incorrect interpretation of the results, as a mean phase angle of 91 degrees using the Needham et al. divisions would be defined as anti-phase motion between two segments, while the Chang et al. (2008) divisions would be defined as in-phase motion. In order to verify the significance of these data presented, secondary analysis using the wider divisions was performed and between 0-15% of stance (during weight acceptance), the phase angle between the sagittal thigh-transverse shank coupling would still be defined as anti-phase.

No significant differences in baseline coordination variability amongst any of the three groups were in contrast to the second hypothesis. The lack differences in the baseline measures was in contrast to prior work that showed decreased coordination variability at baseline with overuse injuries (Heiderscheit, 2002; Seay et al., 2011). However, more recent work showed that chronic adaptations in coordination variability may be rare for overuse injury such as PFPS where pain is typically low during everyday activities (Hafer et al., 2017). The initial hypothesis was that these runners with current or past PFPS symptoms would have modified their gait mechanics as an adaptation to the daily pain they have experienced and therefore would have adopted a lower coordination variability in their baseline state to avoid certain painful movements. Movement evoked pain is a characteristic of PFPS (Thomeé et al., 1999), thus it is possible that runners with PFPS do not avoid using their range of movement patterns until pain is present. Given that the runners with PFPS were not in significant pain (<2 points) at the beginning of the run, it is possible that those with PFPS had no reason to alter their movement patterns. They did not have an acute pain stimulus to respond to by altering their gait to previously identified, less painful patterns which would explain the above baseline coordination variability findings.

As the run was completed, the majority of runners in the PFPS group experienced a clinically significant increase in pain, defined as >2 point increase on the vNRS. The hypothesis was that this pain would push them to limit their solutions for gait, effectively “locking” their degrees of freedom, decreasing their coordination variability. A long-term consequence of this response may be further increases in pain due to a lack of variability in how and where joint tissues are loaded. The results of this study were in support of this hypothesis as the PFPS group decreased their coordination variability throughout the run relative to the CON group in the mid-stance frontal pelvis-frontal thigh coupling. The coordination variability showed no difference in the sagittal thigh-transverse shank and the transverse shank-frontal rearfoot during weight acceptance for the PFPS group. These findings are in contrast with Cunningham et al. (2014), which found that runners with symptomatic PFPS had higher coordination variability in almost

all examined couples compared to healthy controls. While the mid-stance frontal pelvis-frontal thigh coordination variability decreased over time in the PFPS group, it increased in the CON and RES groups. This result is directly in line with the dynamical systems model of coordination variability and suggests that there may be a decrease in active degrees of freedom affecting dynamic femur control. It is possible that over time, the hip abductor muscles are no longer able to maintain their control of frontal plane movements of the pelvis and dynamic femur control in the PFPS group, whom often have weakened hip abductors (Herbst et al., 2015). This may lead to a lack of available patterns of movement in the frontal plane. The fact that the RES group fell in between the PFPS and CON groups supports this finding even more as these runners have resolved their pain but may still not have returned to normal. However, given the study design, it is not possible to make a statement regarding causality, as increased pain may lead to decreased coordination variability or vice versa.

The other two couplings that showed significant differences in how they changed over time were the sagittal thigh-transverse shank and the transverse shank-frontal rearfoot. For both of these couplings, the CON had decreased coordination variability while the RES and PFPS groups increased. It was hypothesized that the RES and PFPS group would show a decrease in coordination variability relative to the CON group. Though only the RES group was significantly different from the CON group, both the RES and PFPS did have an increase in coordination variability. These adaptations may indicate an effort to find patterns of movement that are less painful. The fact that both injury groups increased their coordination variability over the run indicates that these changes are not necessarily solely related to acute pain adaptations but may be also due to an effect of exertion. It is possible that at baseline, any long-term adaptations to injury that may have occurred in both the PFPS and RES groups are dormant; however, as exertion levels rise, these adaptations are unmasked and result in the observed changes in coordination variability.

Given that this was a relatively short run at a moderate effort level, these results may be compounded at greater training volumes and loads. In addition, given a higher effort and longer run time, more significant changes may arise. It is possible that some potential sources of change in coordination variability may have been mitigated due to the fact that this study was performed on a constant speed treadmill belt, which constrains the movement task from natural, overground distance running.

Conclusions

The findings of this study suggest that there are no long-term or acute adaptations to pain or exertion in runners with current or previous PFPS which elicit differences in pelvis-thigh coordination or coordination variability from healthy runners at baseline. However, there was greater anti-phase, shank dominant relative motion of the sagittal thigh-transverse shank coupling which may be representative of abnormal movement control at the knee in those with PFPS. Outside of a rested state, movement evoked pain from PFPS may provide a sufficient stimulus to result in alteration in coordination variability differentially over the course of a run from healthy runners, both increasing and decreasing depending on coupling. In addition, coordination variability in the resolved group changed differently over the course of the run from the control group, suggesting that these runners do not have gait patterns similar to healthy runners despite experiencing little to no pain which may indicate why PFPS has such a high rate of reoccurrence. When studying chronic injury populations, the inclusion of a resolved group is important as gait impairments may remain after even after painful symptoms have resolved.

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CHAPTER 6

MUSCLE COORDINATION PATTERNS DIFFERENTIATE INJURY STATUS IN RUNNERS WITH PATELLOFEMORAL PAIN SYNDROME

Introduction

Patellofemoral pain syndrome, characterized by retropatellar pain during or after repetitive activity, is one of the most common injuries experienced by runners each year (Taunton et al., 2002). A pathomechanical model has been proposed that suggests the etiology of PFPS is a complex interaction between biomechanical, anatomical and behavioral factors leading to abnormal loading of the patellofemoral joint (Powers et al., 2017). Clinical management of PFPS remains a significant challenge and persistence (long-term symptoms) and frequent reoccurrence (reappearance of symptoms) remain common (Collins et al., 2010). Abnormal loading of the patellofemoral joint may originate with issues of alignment (Ferber et al., 2009), strength or muscle activation deficiencies (Van Tiggelen et al., 2009) throughout the lower limb which likely affect kinematic and kinetic patterns. Poor dynamic femur control is especially important and may contribute to patellar malalignment and maltracking (Herbst et al., 2015). Voluntary movement is organized and coordinated by the activation of redundant set of lower extremity muscles. While initial evidence of muscle activation deficiencies for individual muscles in PFPS have been presented (Chester et al., 2008; Cowan et al., 2001; Esculier et al., 2015; Van Tiggelen et al., 2009), there is little knowledge of how or if muscle activation may be redistributed throughout the lower limb in response to injury and if these altered activation patterns are impacted by increasing symptom severity or resolution.

Several differences in surface electromyography (EMG) between healthy individuals and those with PFPS have been observed that may be linked to increased patellofemoral joint (PFJ) forces or altered movement of the lower limb. With PFPS, a delay in the onset of vastus medialis oblique activation relative to the vastus lateralis has been observed at touchdown while running in

runners at risk for (Van Tiggelen et al., 2009) and with symptomatic PFPS (Chester et al., 2008; Cowan et al., 2001; Van Tiggelen et al., 2009). The delayed activation of the medial muscles about the knee may lead to excess lateral patellar tracking (Cowan et al., 2001; Pal et al., 2012) resulting in altered PFJ dynamics and increased pain. Lateral patellar tracking may also be a result of increased co-activation from concurrent lateral hamstring activation observed in those with PFPS (Patil et al., 2011). Patellofemoral joint forces may also be affected by quadriceps and hamstrings co-activation. Greater quadriceps and hamstrings co-activation, a strategy for increasing knee joint stability, has been seen in those with PFPS (Besier et al., 2009); however, increased recruitment of muscles about the knee may also increase PFJ forces and stresses (Besier et al., 2009). Muscles at the hip and ankle may also play a critical role in influencing changes in gait mechanics in the presence of pain. Evidence of altered gluteus maximus and medius activation profiles (Barton et al., 2012; Esculier et al., 2015; Neal et al., 2015; Souza & Powers, 2009; Willson et al., 2011), potentially an attempt to generate and maintain force in otherwise weakened hip muscles (Souza & Powers, 2009; Willson et al., 2011) as well as longer duration soleus activation (Esculier et al., 2015), have been found in those with PFPS.

Previous work studying EMG patterns in PFPS has focused on either timing, frequency, or intensity individually, but has not quantified muscle coordination, which is the relative magnitude and timing of lower extremity muscle activations. Changes in each of these quantities (timing, frequency, intensity) have been shown in the literature to be influenced by pain or pathology (Henriksen, Alkjær, Simonsen, & Bliddal, 2008; von Tschärner & Valderrabano, 2010). One recent model posits that pain leads to a redistribution of muscle activity throughout the lower limb, causing adaptations in muscle coordination (the organization of activation intensity and timing across multiple muscles) through changes at multiple levels of the motor system (Hodges & Tucker, 2011). When possible, the body appears to adapt to pain with a reorganization of muscle activity to reduce stress or loads on the affected tissues (Hug et al., 2014). Adaptive muscle coordination strategies to reduce load and joint stress may be a primary

goal of pain reduction, triggering the movement pattern changes that have been observed in those with PFPS. These changes may provide short-term protection leading to decreased levels of pain but may have negative long term consequences such as altered gait which leads to more pain (Hodges & Tucker, 2011). While differences in EMG between PFPS and healthy controls have been found, it is not clear what, if any, of these differences are related to the presence or severity of pain symptoms. This knowledge may be critical for developing and personalizing rehabilitation strategies to improve PFPS management.

In order to study muscle coordination, aside from some of the more traditional amplitude/timing measures, higher dimensional analysis techniques have been developed (von Tscharner, 2000, 2002). Advance signal processing techniques, such as a wavelet-based time-frequency analysis, provide information about the intensity and frequency of muscle activation patterns throughout an activity while maintaining a relevant physiological time scale (von Tscharner, 2000). When the wavelet-transformed EMG are combined with principal component analysis (PCA), the extraction of principal patterns (PPs) of muscle activation may reveal information about inter- and intramuscular changes in the relative magnitude and timing of muscle activation events (von Tscharner, 2002). These methods have been used to identify disease state previously in individuals with osteoarthritis (von Tscharner & Valderrabano, 2010). The representation of multiple muscle activation patterns as a smaller set of PP also facilitates the application of vector based classification tools such as the support vector machine (Schölkopf, Platt, Shawe-Taylor, Smola, & Williamson, 2001). Several other machine learning algorithms are available to be used for classifying data into groups based on similar features in data, such as random forest models and deep neural networks; however, support vector machines allow for the establishment of a higher-dimensional hyperplane that has been used previously in biomechanics to identify different groups. The ability to discriminate “normal” from “pathological” patterns of lower extremity muscle activations would provide insight to the complex adaptation strategies

likely present with PFPS and a tool to assess if and when an injured runner returns pre- injury movement patterns.

Therefore, the first aim of this study was to investigate the potential changes in muscle activation patterns across eleven lower limb muscles in runners throughout a 21-minute treadmill run (21MTR). The second aim was to test the ability of a machine learning algorithm to classify RES multi-muscle patterns as healthy or injured. The weight factors at the end of the run for the PFPS and CON groups would be used to train the support vector machine. We hypothesized the following:

- H3.1** The change in muscle coordination between the beginning and end of the run would be different amongst the CON, PFPS, and RES groups. A change in muscle coordination would be quantified as the change in respective contribution for each principal pattern to the overall EMG signal (weight factors).
- H3.2** There would be a difference in these weight factors amongst groups for principal patterns at the end of the 21MTR.
- H3.3** A support vector machine would be able to classify data between CON and PFPS groups at a better than random rate using the extracted principal patterns.

Methods

Participants

All participants first completed an informed consent document prior to any additional study measures that was approved by the local Institutional Review Board, outlining the procedures and associated risks of the study, as well as a Modified Physical Activity Readiness Questionnaire and general demographics form.

Fifty-seven runners who ran at least 24 km per week participated in this study (19 CON - 10 males, 9 females, 20 PFPS - 10 males, 10 females, 18 RES - 9 males, 9 females). Participants

were excluded from the study if they had any history of cardiovascular or neurological problems or lower extremity injury or surgery within the previous year. The sample size was based on an *a priori* calculation and yielded a necessary sample of $n=15$ to detect true differences of kinetic and kinematic variables between healthy and injured runners ($\alpha=0.05$, $\beta=0.20$) (Laughton, Davis, & Hamill, 2003). In addition, previous surface EMG analysis in runners has achieved appropriate power with a sample of $n=13$ (Landreaneau, Watts, Heitzman, & Childers, 2014).

Experimental Set-up

Skin was prepared and electrodes were placed according to SENIAM guidelines on the right side for the following muscles: medial and lateral gastrocnemius (MGAS, LGAS), soleus (SOL), tibialis anterior (TA), rectus femoris (RF), vastus medialis (VM), vastus lateralis (VL), semitendinosus (ST) biceps femoris (BF), gluteus minimus and gluteus maximus (GMED, GMAX) (Hermens et al., 1999). A Delsys Trigno (Delsys, Inc., Natick, MA, USA) wireless EMG system was used for data collection. All runs were completed on an instrumented treadmill (Treadmetrix, Park City, UT, USA) and all participants wore a standard neutral laboratory shoe (Brooks T7). Forces and EMG were collected synchronously in Qualisys Track Manager (Qualisys, Inc., Gothenberg, Sweden).

Testing Protocol

After all sensors were placed on each participant, a speed determination procedure was used to identify an appropriate, comfortable running speed for the 21MTR. Initially, the treadmill was set to an estimated average running pace for an easy-to-moderately paced training run based off input from each participant. Participants ran at the initial speed for up to one minute and then were asked if they believed they could comfortably sustain the speed for 30 minutes. Based on this response, the speed of the treadmill was either increased or decreased. Again, the participants were asked if this was a comfortable speed. This process was repeated until a speed was selected

from both directions i.e. they reached the same speed coming from both a faster speed and a slower speed. After speed determination, participants were given up to 5 minutes of rest before beginning the 21 MTR. No pain increases were reported in any participants during this time.

Kinetic and EMG data were sampled continuously for 30 seconds every 2 minutes of the run beginning at minute 1 of the 21MTR for a total of 11 collection periods. Rate of Perceived Exertion (RPE) was collected for each participant as well as a pain measurement rating using an 11-point Verbal Numeric Rating Scale (VNRS, 0-10, with 0 being “no pain” and 10 being “worst possible pain”). Pain was recorded at two-minute intervals through the run to ensure participant safety.

Data reduction and analysis

A 40 N threshold was used to determine footstrike from the vertical ground reaction forces. EMG signals were analyzed for 200 ms pre- and post-footstrike. This 400 ms of data was down sampled by a factor of 10 for the final analysis such that each trial was 81 points in length ($0.4s * 2000 \text{ Hz} \text{ divided by } 10 = 81 \text{ points per trial}$). This window size ensured capture of terminal swing and stance phases. EMG signals were resolved with respect to intensity of activity, time and frequency using a previously-developed wavelet analysis (von Tscharner, 2000). A set of 13 non-linearly scaled wavelets were used as outlined by von Tscharner (2000). Mean wavelet intensity patterns (Figure 1) were calculated from five consecutive strides collected each of the 11 collection periods of the 21MTR. Wavelet center frequencies were as follows: 7, 19, 38, 62, 92, 128, 170, 218, 271, 331, 395, 466 and 542 Hz.

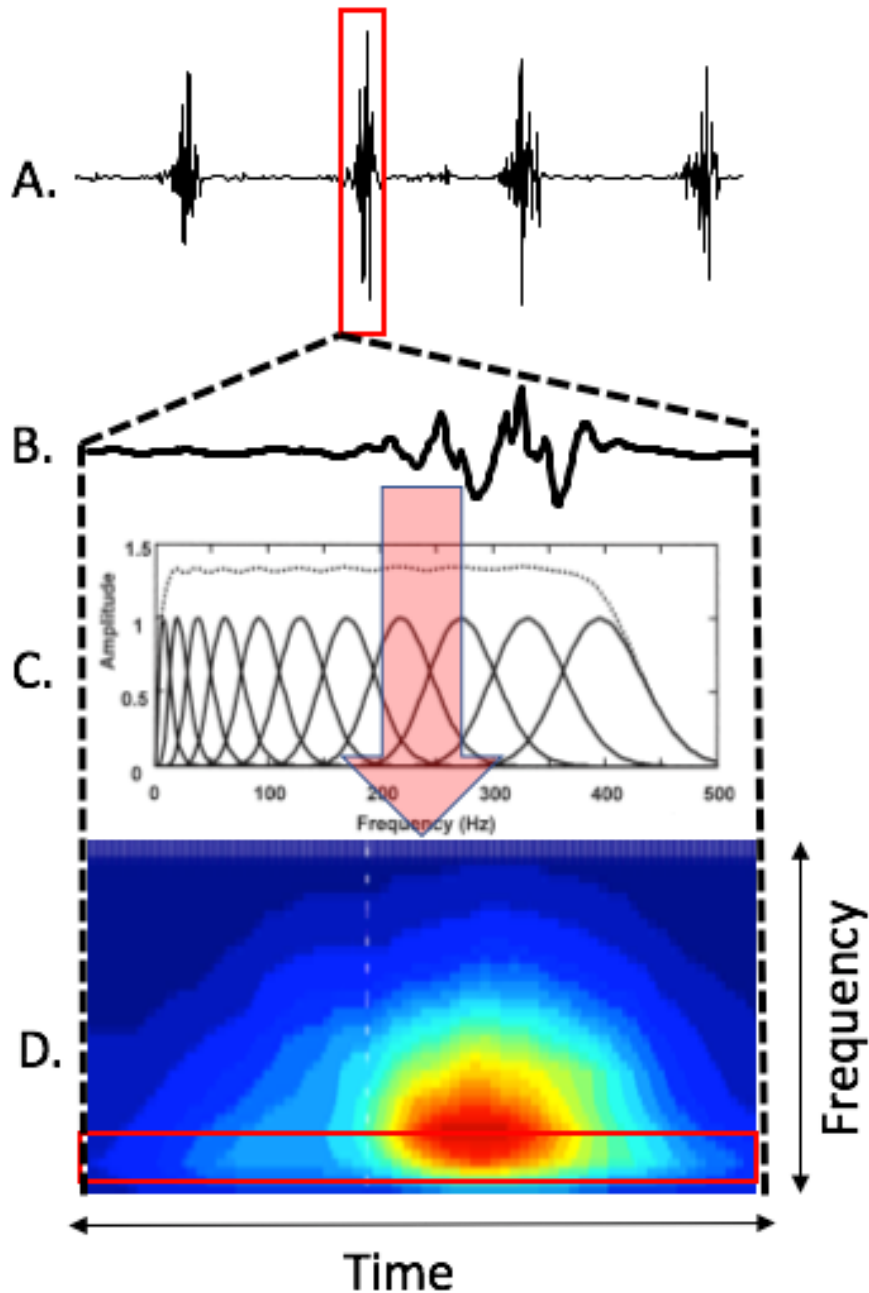


Figure 6.1. Wavelet transform workflow diagram. A. A single burst of EMG for one step is selected for analysis. B. This single burst is cut to a time window of 400 ms. C. This raw, clipped EMG signal is passed through a filter bank of 13 non-linearly scaled wavelets residing in time-frequency space. D. These wavelets are plotted together to form a single muscle pattern of EMG activation. The red box represents one of the wavelets, with time on the x-axis, frequency on the y-axis, and amplitude represented by color (red = greater amplitude). The 13 wavelets are presented vertically concatenated with the lowest frequencies on the bottom. The pattern shown in D represents the wavelet intensity pattern of one muscle. To create a multi-muscle pattern, all muscles are vertically concatenated and presented on the same time scale.

Principal component analysis

A pattern space analysis was conducted (von Tscharner, 2002) on the intensity patterns of the lower extremity muscles. For this analysis, the EMG intensity patterns for each muscle were concatenated to form a multi-muscle intensity pattern for each participant at 11 evenly-spaced collection points during the run. Each resulting data matrix had dimensions of (143×81) . The number of rows (143) corresponded to the 13 wavelets generated for each muscle across eleven muscles (13×11). The number of columns was representative of the down-sampled trial length (81). This process was then repeated for each muscle at each of the 11 evenly-spaced collection points for every participant. The data matrices generated for each collection point for each subject were unwrapped into single column vectors of length $11,583$ (143×81). There were 627 total vectors generated, with 11 vectors for each of the 57 participants. These column trial vectors were concatenated to create a $(627 \times 11,583)$ input matrix for further analyses. This organization of data in vector format is akin to representing the data each subject-collection point as a single point in higher dimensional space (Figure 2A). A PCA was then completed to identify correlated patterns of EMG signal intensity within the multi-muscle patterns activation patterns.

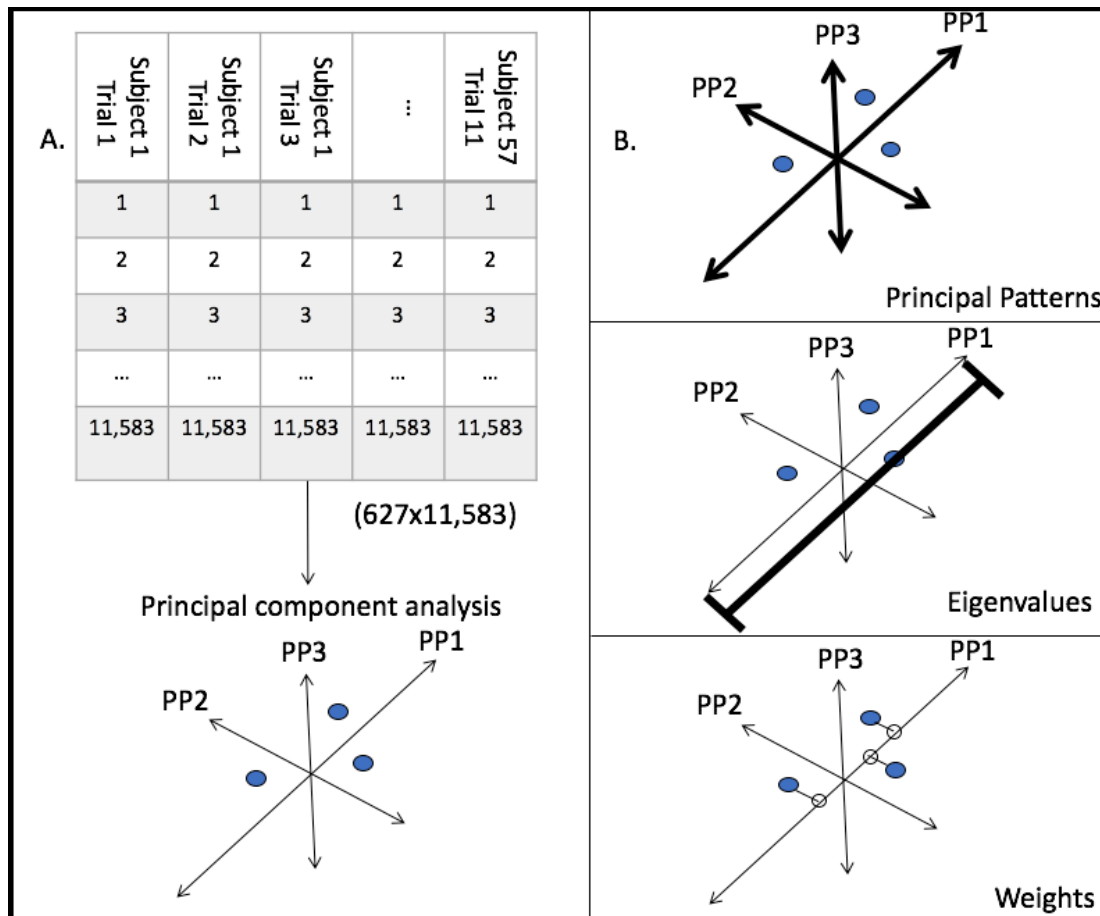


Figure 6.2. Data reduction via Principal Component Analysis. A. The (627x11,583) input matrix is prepared with each column representing a single time point for a subject. There are 11 trials per 57 subjects for a total of 627 columns. This matrix is used to generate the principal patterns, or primary axes, of a lower dimensional space (A, bottom section). Only three PPs are depicted here, but 626 patterns (number of columns of input matrix – 1) were generated. B, top panel – Depiction of PPs. B, middle panel – Eigenvalues of each PP represents the variance explained of each given PP. Each pattern multiplied by its eigenvalue and summed together with the other patterns creates a weighted linear sum, which recreates the original data. B, bottom panel – PP weight factors – the projection of individual subject/trial data (points shown in blue) onto a given PP. These weight factors represent the contribution of that PP to the individual subject/trial data.

To calculate the PP of activation, the eigenvectors of the covariance matrix of the input matrix where the mean has been subtracted, centering the data about the origin of a multi-dimensional pattern space, were determined (Figure 2B, top panel). The data were centered about this higher-dimensional space to facilitate interpretation of the results as all PP then would indicate deviations from this origin. These PP represent the primary directions (axes) in a newly defined orthogonal pattern space. As each direction in pattern space can be visualized by a multi-

muscle intensity pattern, one can inspect them and assess how their intensities contribute to the overall intensity pattern of the EMG signal (Figure 3). The associated eigenvalues for each of the PP indicate the amount of variation in the multi-muscle EMG patterns explained respectively by each PP, equal to the sum of all weight factors squared (Figure 2B, Middle Panel). After PCA, 627 PPs were extracted. The 627th pattern did not contain any signal content and was removed reducing dimensionality to 626. To restore this final dimension and bring back information lost by removing the mean to center the data, a residual mean basis vector was introduced by projecting the removed mean onto the calculated PP, reconstructing the mean, and then subtracting this reconstructed mean from the original removed mean. This **residual mean** was then used to form a normalized basis vector orthogonal to the other PP, creating the 627th PP. To simplify the analysis further, only those PP that described explained at least 1% of the variance in the original signals were retained. The original EMG multi-muscle patterns for each subject and collection point were then projected onto the set of axes defined by the PPs and residual mean vector. Each subject/trial specific patterns can then be represented by a single vector (p-vector) pointing from the origin of the PP space to the point representing the trial. The coordinates of the point representing the trial are the weight factors indication the contribution of that PP to the total multi-muscle EMG intensity patterns. (Figure 2B, Bottom Panel).

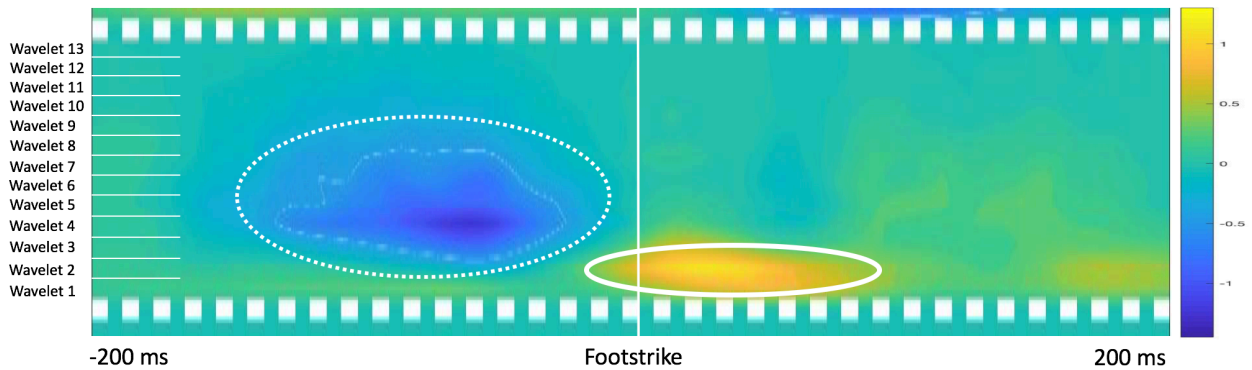


Figure 6.3. Principal pattern of activation for a single muscle; the biceps femoris. The intensity patterns described above consist of 3 axes. On the x axis, time is represented from 200 ms pre-footstrike to 200 ms post-footstrike. The y axis represents the 13 wavelets generated in the wavelet transform, with wavelet 1 having the lowest center frequency (7 Hz) and wavelet 13 having the highest (542 Hz). The third axis is defined on the right side of the figure, with color shade representing the intensity, or amplitude, of muscle activity in a given wavelet at a specific time. Two primary features have been identified for clarity. For this pattern, the dotted circle surrounds a deep blue shade, which represents a negative intensity. This means that from -125 ms to -15 ms for wavelets 2-9, there is a negative contribution of this pattern to the total biceps femoris activation. The opposite is true of the yellow shaded region from -25 ms to 90 ms from wavelets 1-3. Thus, if the weight factors for a particular group for this pattern were positive, it would contribute to the overall signal intensity as described above. This is due to the fact that all principal patterns, multiplied by their weight factors, create a weighted linear combination of the original data. If the weight factor was negative for this given pattern, then the blue area here would be a positive contribution due to a double negative, while the yellow shaded area would be a negative contribution. The multi-muscle patterns presented later consist of the same overall structure, but 11 total muscles are represented.

Statistics

Multiple one-way ANOVAs were performed to compare the difference in weight factors of the retained PP between the first and last collection time points of the run for each group, as well as a difference in weight factors between groups at the end of the run. The alpha level was set at ($\alpha=0.05$). When a significant main effect for group was found, *post hoc* Tukey's honest significant difference tests were used to test for differences between each pair of groups.

A support vector machine (SVM) was trained with the end of run weight factors (Maurer, Federolf, von Tscherner, Stirling, & Nigg, 2012) for the retained principal patterns of the CON and PFPS groups. In order to train the support vector machine, data were input along with what group they belonged to (CON, PFPS, or RES). This allows the support vector machine to create a hyperplane that best separates these known data. Then, the support vector machine was trained

and tested over 1000 iterations using half of the data set as a training set and the other half of a testing set to quantify the accuracy of the classification of multi-muscle EMG between CON and PFPS runners. The RES data was then passed through the SVM to determine if the RES multi-muscle EMG patterns are classified as more similar to CON or PFPS patterns.

Results

All results are presented as mean \pm SD. No participants stopped early due to pain or fatigue. RPE in the first minute was: 8.7 ± 1.7 and at minute 20: 12.8 ± 2.0 . The highest RPE achieved by any participant was 18. The average pain increases of the CON, PFPS, and RES were 0.0 ± 0.0 , 3.0 ± 2.0 , and 0.5 ± 1.0 points, respectively. Fourteen out of 20 PFPS participants showed a clinically significant (>2 points) increase in pain as did one RES participant. No significant differences were found in speed between groups; the average speed across all groups was $2.84 \pm 0.29 \text{ ms}^{-1}$.

Twelve PP that explained at least 1% of the variance in the data were retained for analysis. Of these 12, one that showed a significant main effect for group in the change of weight factors between the beginning and end of the run, PP12 ($p = 0.046$, $\eta^2 = 0.108$) which explained 1.2% of the variance (Table 1). There were no significant findings in *post hoc* tests for PP12.

When looking at the end of run weight factors alone, out of the 12 retained PP, 3 PP had a significant main effect for group (Table 2). *Post hoc* tests for all PP indicated there were no significant differences between the PFPS and RES groups. Several PP were significantly different between CON and PFPS and CON and RES (Table 1). The results will be given first for those that were significantly different between CON and PFPS, followed by those in which the CON group was significantly different from the RES group.

Table 6.1. Significant ANOVA results and results *post hoc* Tukey’s honest significant difference tests for each PP for change in weights over the run. Mean weights and standard deviations for each group have been multiplied by 10^3 for clarity.

Principal Pattern	Variance Explained (%)	p_{group}	η^2	CON		PFPS		RES	
				Mean	SD	Mean	SD	Mean	SD
PP1	27.50	0.410	0.03	0.38	(1.01)	1.09	(3.44)	0.23	(0.31)
PP2	26.30	0.859	0.01	-0.12	(1.05)	0.23	(3.68)	0.25	(0.33)
PP3	7.37	0.332	0.04	0.20	(0.65)	-0.01	(0.77)	0.36	(0.83)
PP4	3.89	0.321	0.04	0.38	(0.34)	0.14	(0.60)	0.32	(0.60)
PP5	3.31	0.328	0.04	0.00	(0.23)	0.47	(1.78)	0.05	(0.10)
PP6	3.15	0.165	0.07	0.13	(0.24)	-0.24	(0.96)	-0.11	(0.30)
PP7	2.62	0.280	0.05	-0.46	(0.55)	-0.31	(0.59)	-0.19	(0.33)
PP8	1.78	0.541	0.02	0.19	(0.54)	0.06	(0.54)	0.02	(0.27)
PP9	1.44	0.260	0.05	0.17	(0.48)	0.02	(0.43)	0.24	(0.35)
PP10	1.33	0.377	0.04	0.00	(0.34)	-0.15	(0.39)	-0.13	(0.33)
PP11	1.26	0.214	0.06	-0.19	(0.29)	-0.09	(0.46)	0.00	(0.09)
PP12	1.18	0.046*	0.11	0.29a	(0.50)	-0.02a	(0.40)	0.01a	(0.32)

* = significant main effect for group ($p < 0.05$). Letters represent mean separation among groups by Tukey’s honest significant difference tests ($p < 0.05$).

There were two PP that were significantly different at the end of the run between the CON and PFPS groups: PPs 9 and 11 (Table 2) which explained 1.4 and 1.3% of the variance, respectively. For PP 9 (Figure 4), the CON and PFPS group means of the weights were 3.1×10^{-4} and -7.8×10^{-6} , respectively. The opposing signs of the weight factors indicates that the contribution for the CON group was positive (additive to the overall mean muscle pattern of the group), while the contribution for the PFPS group was negative. Each PP represents correlated elements of activation within and between muscles with PP9 representing the activation intensity of the tibialis anterior, medial gastrocnemius and semitendinosus before footstrike and the gastrocnemii, vastii and semitendinosus after footstrike.

Table 6.2. Significant ANOVA results and results of *post hoc* t-tests with Tukey’s honest significant difference tests for each PP of end of run weights. Mean weights and standard deviations for each group have been multiplied by 10^3 for clarity.

Principal Pattern	Variance Explained (%)	p_{group}	$\eta p2$	CON		PFPS		RES	
				Mean	SD	Mean	SD	Mean	SD
PP1	27.50	0.489	0.03	-0.04	(1.25)	-0.44	(2.13)	0.11	(0.34)
PP2	26.30	0.450	0.03	0.16	(0.91)	0.30	(1.99)	-0.22	(0.20)
PP3	7.37	0.112	0.08	0.47	(1.20)	-0.01	(0.78)	-0.07	(0.40)
PP4	3.89	0.014*	0.15	0.40a	(0.44)	2.07ab	(0.64)	-0.15b	(0.56)
PP5	3.31	0.356	0.04	0.10	(0.23)	-0.35	(1.81)	0.07	(0.11)
PP6	3.15	0.386	0.04	-0.03	(0.24)	0.16	(0.97)	-0.11	(0.33)
PP7	2.62	0.457	0.03	-0.21	(0.93)	0.06	(0.69)	-0.10	(0.26)
PP8	1.78	0.302	0.04	0.15	(0.67)	-0.04	(0.40)	-0.07	(0.25)
PP9	1.44	0.032*	0.12	0.31a	(0.38)	-0.01b	(0.41)	0.15ab	(0.29)
PP10	1.33	0.122	0.08	0.03	(0.36)	-0.11	(0.29)	-0.18	(0.24)
PP11	1.26	0.024*	0.13	-0.16a	(0.22)	0.10b	(0.42)	-0.02ab	(0.10)
PP12	1.18	0.167	0.06	0.12	(0.51)	0.03	(0.36)	-0.12	(0.25)

* = significant main effect for group ($p < 0.05$). Letters represent mean separation among groups by Tukey’s honest significant difference tests ($p < 0.05$).

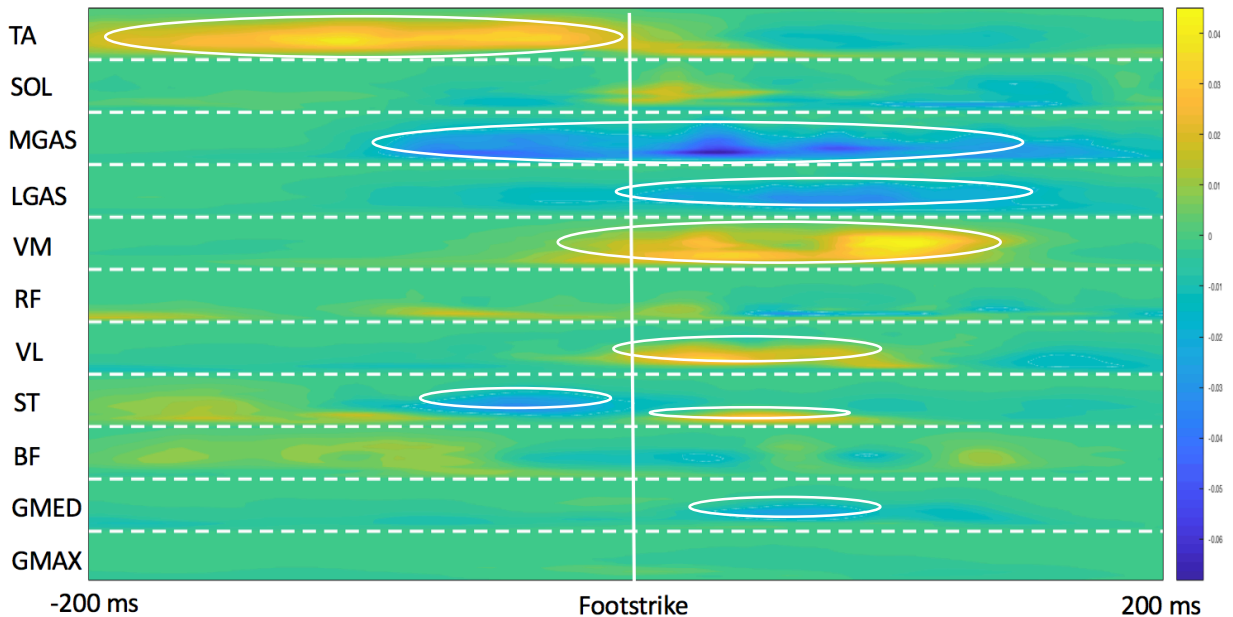


Figure 6.4. Multi-muscle intensity plot for PP 9. The contribution of this pattern to the overall signal is negative for the PFPS and positive for the CON groups, indicating a relatively greater activation intensity (dark shading) of the gastrocnemii, semitendinosus and gluteus medius and relatively less activity in the tibialis anterior before footstrike (light) and the vastii, lateralis and semitendinosus after foot strike for the PFPS group as compared to CON. Time is on the x-axis,

wavelets/muscles are represented on the y-axis. For each section representing 1 muscle (within dotted white lines) there are 13 wavelets in ascending order on the y-axis. The color scale on the right side of the figure represents the intensity shown in the plot.

The respective weights for the CON and PFPS groups for PP11 (Figure 5, Table 2)) were -1.557×10^{-4} and 1.009×10^{-4} . The notable feature for this pattern was the intensity pattern for the rectus femoris.

Principal pattern 4 (Figure 6) was the PP that was different between the CON and RES groups. The mean weight factors at the end of the run for the CON, and RES groups were 4.026×10^{-4} , and -1.488×10^{-4} (Table 2), respectively. The RES group had a negative mean weight factor for this pattern, therefore the contribution of this pattern to the overall EMG signal for the RES group is negative, while the opposite is true for the CON group. The multi-muscle intensity pattern for this PP consists of EMG intensity of the soleus, vastus medialis and lateralis prior to and at footstrike as well as the vastus medialis, rectus femoris and semi-tendinosus at approximately mid-stance (~100ms post footstrike).

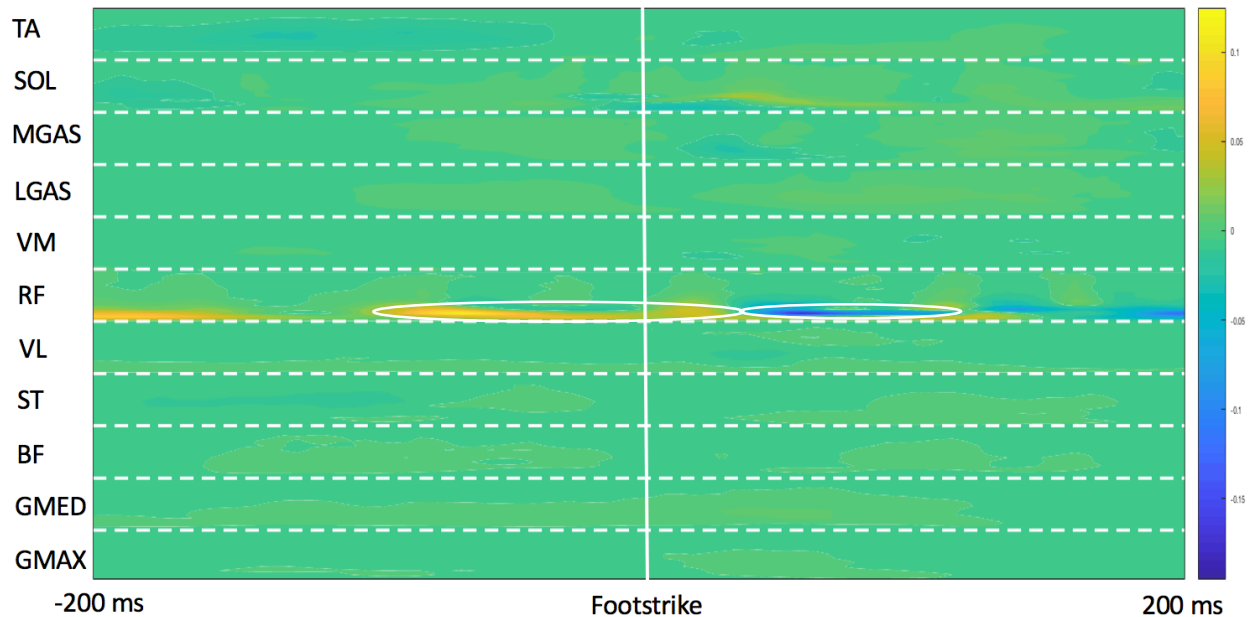


Figure 6.5. Multi-muscle intensity plot for PP 11 The contribution of this pattern to the overall signal is positive for the PFPS and negative for the CON groups and indicates greater low frequency EMG intensity for the PFPS group as compared to CON prior to and immediately following footstrike but lower EMG intensity in mid-stance. Time is on the x-axis,

wavelets/muscles are represented on the y-axis. For each section representing 1 muscle (within dotted white lines) there are 13 wavelets in ascending order on the y-axis. The color scale on the right side of the figure represents the intensity shown in the plot.

Weight factors at the end of the run for all retained PP were passed through the support vector machine. Over 1000 iterations, the average correct classification ratio of CON or PFPS was $71.6 \pm 6.4\%$, which was significantly different from random using a binomial test ($p < 0.001$). When the support vector machine was trained with all of the CON and PFPS data, and the RES participants were classified into one of these two groups, 12/18 were classified into the PFPS group with the remaining 6/18 classified as CON. This classification to PFPS was significantly different from random according to a binomial test ($p < 0.001$).

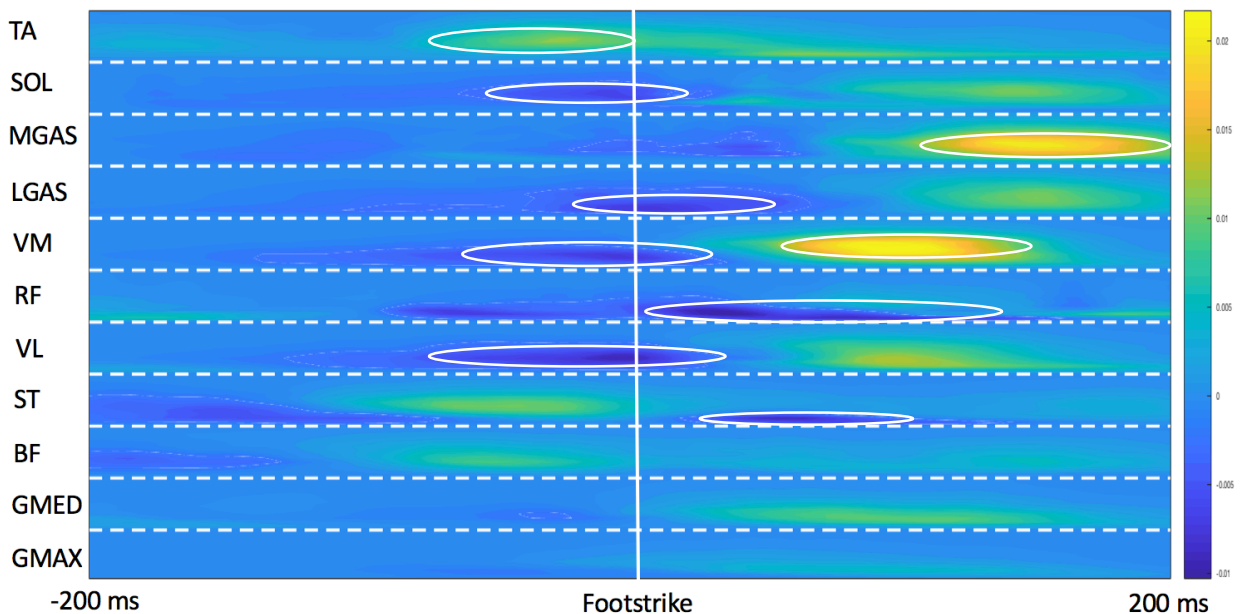


Figure 6.6. Multi-muscle intensity plot for PP 4. The contribution of this pattern to the overall signal is negative for the RES and positive for the CON groups and indicates that there is greater activity for the soleus, vastus medialis and lateralis prior to and at footstrike as well as greater activity for the rectus femoris and semitendinosus during stance for the RES group as compared to CON group. However, there is greater activity for the vastus medialis and medial gastrocnemius in mid and terminal stance for the CON group. Time is on the x-axis, wavelets/muscles are represented on the y-axis. For each section representing 1 muscle (within dotted white lines) there are 13 wavelets in ascending order on the y-axis. The color scale on the right side of the figure represents the intensity shown in the plot.

Discussion

The aim of this investigation was to quantify changes in muscle coordination over the course of a 21MTR to identify patterns of muscle activation that may discriminate runners based on injury status. The results of this study are in support of all hypotheses. In support of the first hypothesis, PP12 was found with a significant main effect for group in the change in weight factors over the course of the run; however, as there were no significant differences in *post hoc* tests, there was not enough of a differential response between any two groups to separate them. For the second hypothesis, there were 3 PPs at the end of the run with a significant main effect for group, with two being significantly different between the CON and PFPS groups, and the other between the CON and RES groups. Together the results for the first two hypothesis tests suggest that muscle coordination is different between the groups but that these differences are not directly impacted by acute variations in symptoms or effort in a moderate paced run. Finally, a support vector machine was trained that was effective at both 1) differentiating between the CON and PFPS groups better than random classification and 2) assigning the RES participants into one of the aforementioned groups better than random classification. As more than half of the RES groups were classified as PFPS this suggests that for many individuals, activation patterns adopted while injured are retained following the resolution of symptoms which may increase the risk for injury reoccurrence. While the patterns used for analysis explain relatively small amounts of variance (1-4%), the variance explained by these patterns is important to make the specific distinction of what features separate each group's data from one another.

In contrast to the study hypothesis and prior work examining the muscular response to joint pain (Denning et al., 2014; von Tscharner & Valderrabano, 2010), the changes in PP weight factors from start to end of the run were not significantly different among groups. Previous work investigating joint pain have found changes in amplitude (Denning et al., 2014) as well as timing and frequency of EMG (von Tscharner & Valderrabano, 2010). These studies were based on dynamic tasks such as running (Denning et al., 2014) and (von Tscharner & Valderrabano, 2010)

as opposed to other differences that have been observed in isometric activities (Tucker & Hodges, 2010). Given these previous findings in dynamic tasks, it was unexpected that the runners with PFPS in this study did not show any significant changes. In experimental pain work performed by Denning and colleagues (2014), the average pain increase was on a similar scale (about 25 mm on a 0-100 mm scale) as the runners with PFPS in the present study; however, the pain was constant throughout the entire run as opposed to the ramped pain response observed in the PFPS group presented here. The protocol of Denning and colleagues (2014) was also 30 minutes. Thus, the participants of this experimental pain study both experienced greater average pain from the outset of the run and experienced the pain for 9 more minutes than in the present study. It is possible that the 21MTR was too short to allow any adaptations in muscle activation to occur as peak pain did not occur until close to the end of the run. The fact that there was a main effect for group, but no significant differences in *post hoc* tests, suggests that the groups were possibly beginning to show a differential response but that those changes were not large enough yet to show significant differences among the groups in *post hoc* testing.

When comparing the multi-muscle EMG intensity patterns at the end of the run, weight factors for 3 PPs were significantly different by group. The *post hoc* analysis indicated that two of these PP (PP9 and 11) represented differences in the EMG between the PFPS and CON groups while the third PP (PP4) discriminated between the RES and CON groups. The variance explained by each of these PP was small (<4% for each pattern) suggesting that the differences represented in these PP are subtle and may be difficult to detect with more global EMG outcome metrics such as the root-mean square or net muscle activation of the muscles tested. This is an inherent strength of the higher order analysis used in this study. As a result of PCA, each PP output from PCA represents correlated elements of activation both between and within muscles. Muscle coordination in this context does not merely indicate synchronous timing or activation profiles of similar muscles. In this study, muscle coordination refers to these correlated patterns of activation intensities depicted in each PP which explain particular features within these EMG

data in intensity, timing, and frequency. Thus, all of the PP that had significantly different weight factors between two groups had a differential response (i.e. subtraction or addition of that activation pattern to the mean intensity patterns of a given group) of correlated activation pattern of multiple muscles indicating differences in the muscle coordination.

Together, PPs 9 and 11 (Figures 5-6) had several important features that both 1) differentiate between the CON and PFPS groups and 2) agree with previous reported literature. These differences were based on the weight factors at the end of the run; however, as these weight factors did not change differently over the run based on group, these findings also apply to baseline data. There were features of two primary muscle groups represented in these two patterns: the quadriceps and triceps surae. In PP9, there was greater activation in the vastii and lower gastrocnemii activation in the CON group immediately following footstrike. This indicated a strategy to reduce quadriceps activation during weight acceptance and midstance in the PFPS group, likely in an effort to reduce patellofemoral joint loading at a time when externally applied forces are greatest. There was greater rectus femoris activity prior to and immediately following footstrike in the PFPS group in PP 11; however, this was followed by a period of lower activation in late weight acceptance. All together, these features indicate lower reliance on the quadriceps muscles during loading with greater reliance on the triceps surae in the PFPS group as compared to the CON group. In addition, as the rectus femoris acts as a hip flexor in addition to a knee flexor, it may indicate greater effort to flex the hip at footstrike. This may be due to a long-term motor system adaptation that occurs as a result of continued, daily pain with activity. A similar result in quadriceps muscle amplitude reduction was observed in a previous experimental pain study, where quadriceps activation was lower in the presence of pain by 5-10% (Denning et al., 2014).

In the PFPS group in the present study, there appeared to be a distal shift in activation, a redistribution of activation between the quadriceps triceps surae, to potentially reduce joint loading at knee where pain is experienced. Although the gastrocnemii are biarticular and thus

influence knee flexion, their line of action does not cross the patella and would not have as great an influence on patellofemoral joint forces as the quadriceps. In addition to the above observed changes in PP 9, there was greater activation in the CON group in the tibialis anterior prior to footstrike and in the semitendinosus during weight acceptance. The difference in tibialis anterior activation suggests that the CON group may have greater preparatory foot control prior to footstrike, potentially allowing them to place their foot in a more advantageous position to minimize joint loading. Previous work in running and sidestepping have concluded that foot position relative to the center of mass and limb positioning may play an important role in joint loading (Besier, Lloyd, Ackland, & Cochrane, 2001), and thus having greater preparatory control of the angle of the foot may be important for lower limb loading in those with PFPS. The greater semitendinosus activation observed is indicative of greater co-activation between the hamstrings and quadriceps, which may provide a more stable knee joint than those with PFPS. However, this co-activation can also increase patellofemoral joint loading (Besier et al., 2009). Previously, work has shown that runners with PFPS display increased co-activation (Besier et al., 2009); however, these PPs suggest that greater co-activation in the CON group is a large part of the differential patterns between the CON and PFPS groups.

While individuals in the RES group had been symptom free for at least one month, differences in the weight factors for PP4 as compared to CON suggest that even when painful symptoms of PFPS have resolved, muscle coordination patterns remain different from those of healthy runners. Principal pattern 4 consisted of higher activation in the quadriceps prior to and after footstrike, as well as soleus activation pre-footstrike and lateral gastrocnemius and semitendinosus post-footstrike, for the RES group with the opposite response in the CON group. In mid-stance, there was lower activation in the vastus medialis accompanied by lower terminal stance activation of the medial gastrocnemius. The primary muscle in the literature that has shown activation and strength differences leading to PFPS development have been in the gluteus medius (Finnoff et al., 2011), which showed no difference in this study. Thus, it is difficult to

make interpretations of these findings with regard to the risk of future redevelopment of PFPS compared to previous literature. However, the differences between groups that were found in this study represent new information regarding individuals who have resolved pain from overuse injuries. To the authors' knowledge, EMG patterns in individuals with resolved chronic injuries have yet to be characterized. The results from this study indicate that the runners with resolved PFPS do not have muscle activation patterns identical to the CON group; thus, these patterns may play a role in the frequent reoccurrence of PFPS.

The high rate of reoccurrence of PFPS in runners with resolved symptoms is a primary concern with regard to patient outcomes; therefore, finding targeted and effective ways of identifying at risk runners for reoccurrence is paramount in improving rehabilitation protocols. Muscle activation patterns can be different between groups while resultant kinematics are not; thus, being able to differentiate between groups on the basis of activation patterns is a significant strength of pattern classification. Pattern classification techniques, such as a support vector machine, are able to identify reoccurring patterns in data that clearly separate groups. As these features may not be readily discernable from other analysis techniques, machine learning plays a critical role in classifications based on these features. Therefore, the positive findings of being able to differentiate between the CON and PFPS groups using a small number of PPs with 71.7% accuracy is promising when using the support vector machine trained in this study. This indicates that there are differential patterns of muscle activation between runners of known injury status, giving the authors confidence to use this classifier in the next step of analysis.

Using the support vector machine trained with the CON and PFPS data, the RES data were then classified into one of these two groups. Given the nature of PFPS and its frequent reoccurrence, the findings of the support vector machine are quite interesting as 2/3 of the RES group were classified as having weight factors more similar to the PFPS group. This result indicated that there may be potential underlying motor system difference that set these groups apart from healthy runners and place them at a greater risk for redevelopment of PFPS. Of the 12

classified into the PFPS group, 7 were female and 5 were male. In addition, the one RES participant who showed a significant increase in pain was included into this group. As females have more than twice as high an incidence of PFPS as males (M. Boling et al., 2010), it is not surprising that they may have muscle activation patterns that more closely resemble the PFPS group even when primary symptoms have resolved. While this first attempt at pattern classification in these groups is relatively crude, the findings of this study are promising. With further refinement and a greater database of participants to train the support vector machine, it is possible that this classification tool could prove invaluable in translation to clinical practice. By identifying individuals in recovery and rehabilitation from injury that have patterns more closely similar to that of injured patients, it may be possible to identify potential injury risk and improve patients' outcomes by using it as a gauge to determine recovery status and how much activity should be undertaken at a particular stage.

One of the useful aspects of higher dimensional analyses is the ability to run linear statistics on complex data sets. However, this places a great importance on the ability to qualitatively interpret the results appropriately to understand the associations between different muscle activations and frequency over time. One of the primary limitations of this study is that the interpretation is made using visual inspection. It is possible that smaller features in the patterns of EMG may be missed because of this; however, the authors took great care in conducting their analysis and were as accurate as possible. When using surface electromyography there can be movement artifact or noise from other sources, and stationarity issues are common with dynamic movements. To account for this, sensors were prepared and placed following widely accepted methods to give the best possible muscle coverage and signal given the equipment used. Sweat can also be a factor given the prolonged nature of the 21MTR; however, there was no significant accumulation of sweat between the skin-sensor interface that was noticed by the researchers. Finally, there can be differences between overground running patterns versus those on a treadmill. The speed was held constant and thus participants were unable to vary their

speed as they might during a normal training run. However, the benefits of studying these runners in a controlled environment on a treadmill outweighed these limitations.

Conclusions

The findings presented in this study have two key elements that suggest the utility of quantifying lower extremity muscle activation patterns: 1) differences were found in multi-muscle activation patterns representing coordinated patterns of lower extremity muscle activations among the three groups at the end of a 21MTR and 2) these patterns were able to successfully train a machine learning algorithm to classify individuals into different groups. No differences were observed in the change of weight factors between groups with the onset of pain; thus, the pain and exertion experienced in this study did not elicit an acute response to pain in muscle coordination. While the findings of the multi-muscle pattern analysis were in agreement with the results of the more traditional measures previously published on altered quadriceps activation, the additional observed differential features for the lower extremity muscles tested suggest these wavelet patterns were more sensitive to differences based on injury status. The results of this study are promising for using EMG-driven pattern classifiers to predict injury risk and potentially aid in prescription of empirically driven rehabilitation and training protocols.

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CHAPTER 7

SUMMARY AND FUTURE DIRECTIONS

Management of patellofemoral pain syndrome (PFPS) remains a significant challenge in clinical practice and there is a need to understand the mechanisms for altered gait and muscular function which may lead to poor patient outcomes. The overall aim of the three studies in this dissertation was to determine if runners with current PFPS adapt their gait and muscle activation as a result of long-term, daily pain and/or in response to an acute pain flare and exertion during a moderate intensity 21-minute treadmill run (21MTR) compared to healthy controls. In addition, a resolved, asymptomatic PFPS group was included to investigate potential mechanisms for the frequent reoccurrence of pain experienced by those with a history of PFPS. To test for long-term adaptations, three groups (current and resolved PFPS and healthy controls) were studied at baseline in a rested state. For the acute response to pain, changes in gait over the 21MTR were characterized to determine if pain and/or exertion lead to acute motor system adaptations. These questions were probed using three different approaches: a discrete kinematic and kinetic analysis, a dynamical systems analysis to investigate altered movement control and flexibility, and a higher-order muscular coordination analysis. These three approaches afforded the ability to look at healthy and injured gait from an upstream motor control approach to resultant and gross motor patterns.

The lack of differences in baseline kinematic, segment coordination, and segment coordination variability measures observed in these studies suggest that there are no long-term gait adaptations to pain in either injury group that manifest as resultant gait patterns. Evidence exists for differences in gait mechanics between healthy controls and runners with PFPS, particularly at the hip (Barton et al., 2009; Neal et al., 2015); however, it is possible that the variability inherent in daily pain severity in the PFPS population made it difficult to uncover any potential differences. In addition, this daily pain severity outside of activity does not appear to be

high enough to elicit any baseline kinematic changes. Despite the lack of baseline kinematic, coordination, and coordination variability differences found in this study, of which the literature is conflicted (Cunningham et al., 2014; Hafer et al., 2017; Hamill et al., 2012; Heiderscheit, 2002), several differences were identified in baseline kinetics among all three groups for peak hip abduction and external rotation as well as ankle inversion moments. These findings indicate that: 1) runners with a history of PFPS have different loading patterns at the hip and ankle compared to healthy runners and 2) these altered loading patterns are not substantial enough to alter resultant kinematic patterns of movement. In addition to these joint moments, principal patterns of lower limb muscle activation discriminated between both the CON and PFPS groups and the CON and RES groups. These differences in principal patterns and kinetics are indicative of long-term motor system adaptations in both the PFPS and RES groups that alter both muscle coordination of the lower limb and the distribution of internal and external forces about the hip and ankle. The difference in kinetics may have occurred as either an increase in muscular forces applied internally or as a result of altered external forces and the direction of force application to the body. With the nature of the present study, it is impossible to determine if these changes led to or result from injury. Nonetheless, the principal patterns proved useful in classifying runners with a history of PFPS symptoms as having muscle coordination more similar to either the PFPS or CON groups. These findings have significant implications for identifying individuals at risk of re-injury and helping to improve treatment efficacy in runners with PFPS.

Movement evoked pain is a primary characteristic of PFPS (Thomeé et al., 1999). The 21MTR was effective in producing a clinically significant increase in pain (>2 points on a VNRS) in runners in the PFPS group as well as an increase in exertion across all three groups. Changes seen in the outcome measures of the three presented studies at the end of the run are indicative of a response to a combination of increased pain and exertion. No differences were observed in muscle coordination or in the discrete kinematic outcomes. Peak knee adduction moments increased with the increased pain and exertion, in contrast to decreased moments in the control

group. This is an important finding as runners with PFPS have been reported to demonstrate greater peak knee abduction moments at baseline (Neal et al., 2015), in contrast with the findings of this dissertation. However, in the presence of pain and exertion, these differences became significant. It is possible that the sample of runners in the PFPS group did not have the same severity of long-term PFPS symptoms as those in previous studies. The reported increased pain in this study may have triggered a gait response to bring these participants more closely related to the samples used in previous literature. No differences in pelvis-coordination were present at the end of the run; however, the greater anti-phase motion of the sagittal thigh-transverse shank in the PFPS group compared to the CON group suggests that altered movement control about the knee may be related to increased pain in those with PFPS. In terms of movement flexibility, increased pain may trigger altered coordination variability for the frontal pelvis-frontal thigh coupling differentially for the PFPS group, suggesting that weak hip musculature common in those with PFPS may trigger a loss of dynamic femur control, which may lead to abnormal joint loading. In addition to the altered coordination variability observed in those with PFPS, there were also differences in coordination variability between the RES and CON groups. This suggests that abnormal movement flexibility may persist even once painful symptoms are resolved and that further investigation into this resolved group is warranted in a search for reoccurrence mechanisms of PFPS.

While these three studies have filled existing gaps in the literature, more work remains to understand how PFPS pain influences gait in runners, both long-term and acutely. While gait in those with current PFPS symptoms has been frequently studied, the work presented in this dissertation is one of the first to characterize gait and muscle activation patterns of runners with resolved PFPS pain. Given the notable differences found in coordination variability and muscle coordination patterns compared to healthy runners, further investigation may contribute to understanding the mechanism for the frequent reoccurrence common with PFPS. In addition, this was an initial attempt at using a machine learning algorithm to classify muscle activation patterns

of resolved runners as more closely related to healthy or currently injured. With more refinement, this may prove invaluable in aiding clinicians to identify those at risk for PFPS redevelopment and proactively treating these individuals to avoid the return of pain.

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