THE RELATIONSHIP BETWEEN MUSCULOSKELETAL STRENGTH, PHYSIOLOGICAL CHARACTERISTICS, AND KNEE KINESTHESIA FOLLOWING FATIGUING EXERCISE

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Fatiguing exercise may result in impaired functional joint stability and increased risk of unintentional injury. While there are several musculoskeletal and physiological characteristics related to fatigue onset, their relationship with proprioceptive changes following fatigue has not been examined. The purpose of this study was to establish the relationship between musculoskeletal and physiological characteristics and changes in proprioception, measured by threshold to detect passive motion (TTDPM), following fatiguing exercise. Twenty, physically active females participated (age: 28.65 ± 5.6 years, height: 165.6 ± 4.3 cm, weight: 61.8 ± 8.0 kg, BMI: 22.5± 2.3 kg/m^2, BF: 23.3 ± 5.4%). During Visit 1, subjects completed an exercise history and 24-hour dietary questionnaire, and body composition, TTDPM familiarization, isokinetic knee strength, and maximal oxygen uptake/lactate threshold assessments. During Visit 2, subjects completed TTDPM and isometric knee strength testing prior to and following a fatiguing exercise protocol. Wilcoxon signed rank tests determined TTDPM and isometric knee strength changes from pre- to post-fatigue. Spearman's rho correlation coefficients determined the relationship between strength and physiological variables with pre- to post-fatigue changes in TTDPM and with pre-fatigue and post-fatigue TTDPM in extension and flexion (α=0.05). No significant differences were demonstrated from pre-fatigue to post-fatigue TTDPM despite a significant decrease in

isometric knee flexion strength ($P<0.01$) and flexion/extension ratio ($P<0.05$) following fatigue. No significant correlations were observed between strength or physiological variables and changes in TTDPM from pre- to post-fatigue in extension or flexion. Flexion/extension ratio was significantly correlated with pre-fatigue TTDPM in extension ($r=-0.231$, $P<0.05$). Peak oxygen uptake was significantly correlated with pre-fatigue ($r=-0.500$, $P<0.01$) and post-fatigue ($r=-0.520$, $P<0.05$) TTDPM in extension. No significant relationships were demonstrated between musculoskeletal and physiological characteristics and changes in TTDPM following fatigue. The results suggest that highly trained individuals may have better proprioception, and that the high fitness level of subjects in this investigation may have contributed to absence of TTDPM deficits following fatigue despite reaching a high level of perceptual and physiological fatigue. Future studies should consider various subject populations, other musculoskeletal strength characteristics, and different modalities of proprioception to determine the most important contributions to proprioceptive changes following fatigue.

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PREFACE

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1.0 INTRODUCTION

The effects of fatigue on proprioception have been widely studied because decreased sensorimotor function may diminish functional joint stability, and this has been purported to increase risk of unintentional musculoskeletal injuries in athletes and trained individuals.[110, 112, 161-166, 251] As these individuals participate in repeated, intense physical activity during practice and competition, they experience a gradual decline in peripheral (muscle) and central nervous system (CNS) function that can only be alleviated after a period of rest, otherwise known as fatigue.[7, 57] Understanding the causes, mechanisms, and prevention strategies of fatigue are important in order to decrease risk of injury in athletes and trained individuals.[5, 6] Many studies have identified decrements in several sub-modalities of proprioception following fatiguing exercise, including both local and general fatigue protocols. [136, 153, 154, 171, 179, 256, 266] These studies have found that peripheral and/or central fatigue may cause a decrement in proprioceptive mechanisms and disturb neuromuscular control, which may place fatigued individuals at a higher risk of unintentional musculoskeletal injury. Several musculoskeletal and physiological characteristics may be related to the onset of fatigue as well as the preservation of sensorimotor function following fatigue. However, while it has been demonstrated that fatigue plays a role in decreasing proprioception measured by threshold to detect passive motion, there is limited research on the relationship between musculoskeletal strength of the quadriceps and hamstrings, maximal oxygen uptake, and lactate threshold with the onset of fatigue and

proprioceptive deficits following fatiguing exercise. If a relationship exists between these modifiable characteristics and changes in proprioception following fatigue, injury prevention programs may be developed in order to optimize these characteristics, diminish proprioceptive deficits following fatigue, and ultimately decrease risk of unintentional musculoskeletal injury.

1.1 FATIGUE: IMPLICATION AND MECHANISMS

1.1.1 Fatigue and Injury

The number of athletes and trained individuals participating in sporting activities has grown exponentially in recent years. With the upsurge in athletic participation, incidence of unintentional musculoskeletal injuries has also increased.[123] National Collegiate Athletic Association (NCAA) surveillance data has revealed that a majority of unintentional musculoskeletal injuries occur in the lower extremity.[123] This research has also revealed that females are at a much greater risk of incurring injury, specifically at the knee, than males. [15, 29, 100, 104] On the whole, understanding the risk factors of these injuries will allow for the creation of injury prevention programs which will help mitigate the occurrence of unintentional musculoskeletal injury. This will in turn reduce the negative implications of sustaining injury, including time lost from practice, training, and competition, decreased team or unit morale, and the financial burden of treatment and rehabilitation.

The epidemiology of sports injuries has been widely studied and authors have investigated a number of potential factors relating to injury. [6, 65, 89, 90, 181, 252] A consistent theme throughout many of these investigations is that fatigue plays an important role in the onset of

unintentional musculoskeletal injury during practices and games.[5, 89, 90] These studies have found that injuries frequently occur during preseason practices,[123] and this may be the case because athletes who often begin the season with poor conditioning are more susceptible to fatigue, and may be unaccustomed to the movement patterns of the sport. Further, these studies have revealed that many injuries occur during games, and more specifically, during the latter portion of games after fatigue has set in.[89, 90] The increased risk of injury after fatigue may be due to slower reaction time, which could be a result of diminished sensorimotor function. Since fatigue appears to be a frequently mentioned risk factor in many injury epidemiology studies, understanding the various peripheral and central mechanisms of fatigue may help better explain why fatigue during practice, training, and competition may increase risk of unintentional musculoskeletal injury.

1.1.2 Mechanisms of Fatigue

As the study of fatigue has evolved, so has its definition. It is difficult to assign a single definition to fatigue because of its widespread classification, causes, and mechanisms. A simple definition of fatigue is the inability to maintain a power output or force during repeated muscle contraction that may be attributed to either metabolic or non-metabolic peripheral factors.[75] Contributions to fatigue can be classified as either central or peripheral, with the processes inside the spinal cord and above labeled as central, and the processes in the peripheral nerve, neuromuscular junction, and muscle labeled as peripheral.[7]

Peripheral fatigue can be studied by focusing on the changes that occur inside the muscle fiber during fatiguing exercise. Muscle fiber type plays an important role in muscle fatigue, as oxidative fibers are far more fatigue resistant than fast-twitch fibers.[7] Other factors, such as

temperature, metabolic changes, and pH level within the muscle may also contribute to the onset of fatigue.[7] Since fatigue is defined as reversible decline of performance during activity,[7] it differs from muscle injury in that most recovery occurs within the first hour,[7] and there is a slow component which may take several days to reverse.[70] In contrast, muscle injury usually occurs in muscles that have been eccentrically stretched during contraction and normal function only returns very slowly.[7]

Davis and colleagues[57] classify central nervous system (CNS) fatigue as a subset of fatigue (failure to maintain the required or expected force or power output) associated with specific alterations in CNS function that cannot reasonably be explained by dysfunction within the muscle itself, suggesting that "psychological" factors are important to consider with fatigue. Central fatigue is hypothesized to be elicited by alterations in neurotransmitters, cerebral oxygen delivery, hyperthermia, and perceived exertion/homeostatic regulation.[57, 191, 192]

During practice and game situations, athletes and trained individuals likely experience a combination of peripheral and central fatigue.[58] Fatigue-related changes in the muscle may include reduced force production, decreased velocity of shortening, and slowed relaxation.[8] Impaired CNS function due to fatigue may result in delayed reaction times and impaired motor performance.[192] The implication of the negative changes elicited with the onset of fatigue is of great concern because reduced function at both the peripheral (muscle) and the CNS level may result in decreased sensorimotor function and increased risk for unintentional musculoskeletal injury.

1.2 PROPRIOCEPTION

1.2.1 Definition of Proprioception

Proprioception is a subcomponent of the sensorimotor system and is defined as the afferent information arising from the periphery of the body (both static and dynamic components) providing the central nervous system information about joint stability, postural control, and motor control.[161, 217] Conscious proprioception is subdivided into four submodalities, including posture (joint position sense), passive movement (joint kinesthesia), active movement (kinesthesia), and resistance to movement (resistance or heaviness).[161, 217] Proprioceptive information arises from peripheral afferents in the body to the CNS and plays a crucial role in mediating neuromuscular control and overall functional joint stability.

1.2.2 Proprioceptive Contributions to Functional Joint Stability

The sensorimotor system includes the sensory, motor, and central integration and processing involved in maintaining joint stability during bodily movements. Joint stability is defined as the state of remaining or promptly returning to proper alignment through the equalization of forces and moments.[161] A relationship between static (clinical/mechanical) components and dynamic (functional) stabilizers is necessary to achieve joint stability. Functional joint stability requires maintenance of functional activity and cooperation between static and dynamic stabilizers,[161, 217] including feedforward (anticipatory) and feedback (response) mechanisms. The interaction between dynamic and static stabilizers arises from proprioceptive information from the static and dynamic joint mechanoreceptors. The sensorimotor system must function at a high level during

intense physical activity to maintain and/or restore homeostasis of the joints to prevent unanticipated perturbations or forces that may lead to unintentional musculoskeletal injury.

1.2.3 Fatigue and the Sensorimotor System

The implication of injury risk due to fatigue-related proprioceptive deficits has driven researchers to examine the underlying physiological mechanisms of fatigue-induced disruption of neuromuscular control. The mechanisms that prompt the onset of fatigue in humans are purported to implicate sensorimotor system function, but the exact relationship remains unclear. Proprioceptive information arising from peripheral areas of the body is vital for efficient neuromuscular control, postural stability, and overall functional joint stability, so any disruption of peripheral afferents through muscular fatigue may ultimately lead to increased risk of injury. This notion is further evidenced by a study of microneurographic recordings in humans that found a decrease in muscle spindle afferent activity during the onset of fatigue.[170] Likewise, the onset of central fatigue may have negative implications for proprioceptive information that is conveyed to higher levels of motor control, including the cerebral cortex, spinal level, brain stem, cerebellum, and basal ganglia.[172, 217]

Researchers have attempted to draw a connection between fatigue-induced decreases in proprioception, neuromuscular control, and increased risk of injury. Studies have shown that lower extremity kinematics are altered following fatigue,[30, 45] suggesting fatigue has a negative impact on neuromuscular control. Muscular fatigue after eccentric contractions of the knee has also been cited as a source of diminished neuromuscular control and has been identified as a potential injury risk factor.[65, 194] Many researchers have studied the effects of fatigue on proprioception, and most have concluded that fatigue results in diminished proprioception.[136, 153,

[179] Some studies have found that locally applied eccentric fatigue protocols elicit deficits in several sub-modalities of proprioception, including TTDPM.[136, 153, 202, 256] Other research has found that a general load caused a significant decrease in joint position sense acuity while a local fatigue protocol did not.[179] On the whole, while the results of studies examining fatigue and proprioception have been equivocal depending on fatigue protocol and sub-modality of proprioception evaluation, it can be concluded that both peripheral and central fatigue have the capability of negatively impacting proprioception and, thereby, may potentially increase risk of unintentional musculoskeletal injury.

1.3 CHARACTERISTICS RELATED TO THE ONSET OF FATIGUE, DIMINISHED PROPRIOCEPTION, AND INJURY RISK

A multitude of intrinsic and extrinsic risk factors have been identified as potential risk factors for unintentional musculoskeletal injury, including musculoskeletal strength, and aerobic fitness/anaerobic threshold.[181] However, these characteristics may also be important to consider as modifiable risk factors that may play a role in the onset of fatigue development and the ability to maintain sensorimotor function after fatigue. Poor muscle conditioning has been cited as a potential risk factor for early onset of fatigue and related injury risk.[6, 143] Therefore, muscle strength of the quadriceps and hamstrings may be related to changes in knee proprioception following fatiguing exercise because better muscle conditioning may delay the onset of peripheral fatigue. Likewise, poor aerobic and anaerobic conditioning may play a role in early onset fatigue, as evidenced in early season and late game injury incidence attributed to fatigue.[123] Thus, maximal oxygen uptake and lactate threshold may also be related to changes in

proprioception following fatiguing exercise. Individuals with greater aerobic and anaerobic fitness have enhanced ability to resist the onset of both peripheral and central fatigue due to enhanced metabolic adaptations at both levels. On the whole, musculoskeletal strength and aerobic fitness/anaerobic threshold are modifiable risk factors, and improving these risk factors may, in turn, enhance an athlete's or trained individual's ability to become more fatigue resistant, retain sensorimotor function during practice, training, and competition, and decrease risk for unintentional musculoskeletal injury.

1.4 DEFINITION OF THE PROBLEM

Previous research has revealed fatigue as a common risk factor for injury in athletes. Other studies have linked fatigue to proprioceptive deficits, which contribute to disruption of the sensorimotor system. Yet, while numerous studies have examined musculoskeletal strength and aerobic fitness/anaerobic threshold to establish their relationship to performance and injury, no studies to the author's knowledge have assessed these characteristics and their relationship with the decrements in proprioception after fatiguing exercise. An individual who possesses sub-optimal muscular strength, aerobic fitness, or lactate buffering capacity may be at an increased risk of proprioceptive disruption following fatigue, whereas, individuals who possess adequate or optimal physiological and musculoskeletal characteristics may be more resistant to fatigue and, therefore, able to offset the proprioceptive deficits noticed after fatigue.

1.5 PURPOSE

The purpose of this dissertation is to establish the relationship between physiological and musculoskeletal characteristics related to the onset of fatigue in athletes and decrements in proprioception following fatiguing exercise. Isokinetic muscle strength of the quadriceps and hamstrings, aerobic capacity measured during a treadmill test of maximal oxygen uptake, and lactate threshold will be correlated with absolute angle difference during TTDPM of the knee from pre-fatigue to post-fatigue conditions. A general fatigue protocol will be administered to simulate a game situation and elicit both central and peripheral fatigue mechanisms.

1.6 SPECIFIC AIMS AND HYPOTHESES

Specific Aim 1: To establish the relationship between muscular strength of the quadriceps and hamstrings and changes in knee kinesthesia following fatiguing exercise.

Hypothesis 1: Isokinetic muscular strength (N*m %BW) will have a significant correlation with angle error difference from pre- to post-fatigue TTDPM, with direction indicating that higher muscular strength is correlated with a more favorable change in TTDPM following fatigue.

Specific Aim 2: To establish the relationship between flexion/extension ratio and changes in knee kinesthesia following fatiguing exercise.

Hypothesis 2: Flexion/extension ratio will have a significant correlation with angle error difference from pre- to post-fatigue TTDPM, with direction indicating that higher flexion/extension strength ratio is correlated with a more favorable change in TTDPM following fatigue.

Specific Aim 3: To establish the relationship between aerobic capacity and changes in knee kinesthesia following fatiguing exercise.

Hypothesis 3: Maximal oxygen uptake (ml/kg/min) will have a significant correlation with angle error difference from pre- to post-fatigue TTDPM, with direction indicating that higher VO_2 Max is correlated with a more favorable change in TTDPM following fatigue.

Specific Aim 4: To establish the relationship between lactate threshold and changes in knee kinesthesia following fatiguing exercise.

Hypothesis 4: Lactate threshold (% of VO_2 Max) will have a significant correlation with angle error difference from pre- to post-fatigue TTDPM, with direction indicating that higher lactate threshold is correlated with a more favorable change in TTDPM following fatigue.

1.7 STUDY SIGNIFICANCE

The outcomes of this study will be important for lower extremity injury prevention in athletes. Particularly, they will contribute knowledge to the existing research on how fatigue affects the sensorimotor system, and, specifically, which characteristics can help offset these deleterious effects. Current literature has already identified risk factors contributing to unintentional

musculoskeletal injury to the knee in females, including intrinsic factors such as anatomical, neuromuscular, and biomechanical characteristics, hormonal effects, and extrinsic factors such as playing environment and shoe-surface interaction.[114] Several of these risk factors are affected by fatigue during exercise, including pre-activation of protective muscle groups, muscle co-contraction during activity, and proprioception. If certain modifiable musculoskeletal and physiological characteristics related to the onset of fatigue, including muscular strength, aerobic capacity, and lactate (anaerobic) threshold are related to changes in proprioception following fatigue, injury prevention programs may be developed that incorporate quadriceps and hamstring strengthening exercises, and endurance/anaerobic threshold training. Therefore, if these characteristics are optimized, the components of the sensorimotor system that provide proprioceptive information during the latter stages of training, practice, and games may be better preserved, and unintentional musculoskeletal injuries may be prevented.

2.0 REVIEW OF LITERATURE

The review of the literature will first discuss the epidemiology and implication of lower extremity injury in athletic populations, including injury incidence in athletes and military personnel. Next will be a discussion on fatigue as a risk factor for unintentional musculoskeletal injuries, followed by a dissemination of the mechanisms of muscular and central fatigue and the implication of fatigue on the sensorimotor system. The musculoskeletal and physiological characteristics purported in this study to be related to the onset of fatigue and the preservation of proprioception following fatigue will be highlighted in detail. Finally, the methodology of this study will be considered.

2.1 LOWER EXTREMITY INJURY EPIDEMIOLOGY

The number of young adults participating in interscholastic and intercollegiate athletics has drastically increased in the recent decades.[15, 91] Rising injury rates in both the athletic and military populations are cause for concern because of time lost as well as fiscal implications. A review of lower extremity risk factors in athletics[181] reported that the annual cost of sports injuries world-wide is approximately $1 billion,[71] and that annual injury occurrence among competitive and recreational athletes is 3-5 million.[145] A study of injury epidemiology among all military branches showed that roughly 1,000,000 service members suffered nonfatal, non-battle

injuries, and injuries accounted for about 17% of all hospitalizations.[134] Authors also found that for every traumatic death in 2006, there were 11 hospitalizations and 715 injuries treated in outpatient settings,[134] and when taking into account both acute and chronic/overuse injuries, there were over 1500 outpatient visits for injury for every death.[134] This statistic led authors to conclude that nonfatal injuries are largely the biggest health problem of the military.[134] Therefore, research surrounding injury etiology, risk factors, and prevention is paramount in order to suppress the detrimental effect of unintentional musculoskeletal injuries.

Epidemiological studies of athletic and military related injuries have found that the majority of unintentional musculoskeletal injuries occur in the lower extremity. NCAA injury surveillance data over 16 years across 15 sports revealed that more than 50% of all injuries were to the lower extremity, and that knee and ankle injuries were the most commonly injured sites.[123] When reported as a percent of all injuries reported, ankle ligament sprains accounted for 14.9%, and anterior cruciate ligament injuries accounted for 2.6% of injuries.[123] While the rate of ACL knee injury was relatively low, 88% of these injuries accounted for 10-plus days of time lost,[123] which has tremendous financial and psychological effects on the athlete, team, and institution. Further, ACL injury rate has increased on average 1.3% per year,[123] which warrants further attention to research on the etiology and prevention strategies for such injuries.

In a study of risk factors for training-related injuries in basic combat training, results showed that the five most common injury sites for men (% of total injuries) were the knee (21%), ankle (16%), foot (14%), low back (11%), and shin (8%), and for women were ankle (20%), foot (20%), knee (19%), shin (10%) and low back (7%).[144] Overall, for men, 83% of all injuries involved the lower body and back, and 75% of male injuries and 78% of female injuries were classified as overuse injuries.[144] In a study examining injuries in weight-bearing collegiate

athletics in females at a Division III college,[143] 40% of the sample studied had suffered one or more injuries, of which 80% were lower extremity injuries. Overall, 29% of injuries consisted of muscle strains, while 27% consisted of knee and ankle sprains.[143]

Gender may play a role in increased risk of injury, as epidemiological evidence has revealed an increased rate of injury in female athletes. With the rise of Title IX, there has been a marked increase in female athletic participation. According to the NCAA Participation Study: 1989-90 to 1992-93, there was a 9% increase in female participation in all NCAA athletic programs from 1989 to 1992, and the number of NCAA institutions sponsoring varsity women's soccer programs has increased by 48% during the same time period.[123] Concurrent with the rise in female sports participation has been an increase in lower extremity injuries in females. Considerable attention has been given to gender differences in injury occurrence. Evidence has shown a 2.3-9.7 time higher risk of anterior cruciate ligament (ACL) rupture in women than men.[15, 29, 100, 104] Thus, much research has been devoted to the examination of lower extremity risk factors of female athletes and exploring potential biomechanical and hormonal differences that create a higher risk in females compared to males.[2, 111, 112, 115, 182, 230, 231] Further research is needed to examine other musculoskeletal and physiological characteristics related to onset of fatigue, diminished sensorimotor function, and injury risk in females.

2.2 LOWER EXTREMITY INJURY RISK FACTORS

2.2.1 Extrinsic and Intrinsic Risk Factors for Lower Extremity Injury

Many risk factors have been identified as key contributions to lower extremity injury. These have been classified as extrinsic and intrinsic, with extrinsic factors defined as factors outside the body, and intrinsic as those inside the body.[181] Risk factors may also be classified as modifiable versus non modifiable, and those considered modifiable are often characteristics targeted for enhancement through injury prevention programs and interventions. Murphy et al[181] has revealed level of competition, skill level, shoe type, use of prophylactics or tape, and playing surface as extrinsic risk factors, and age, sex, previous injury/inadequate rehabilitation, aerobic fitness, body size, limb dominance, flexibility, limb girth, muscle strength, imbalance/reaction time, postural stability, anatomical alignment, and foot morphology as intrinsic risk factors. Although there have been numerous identified risk factors for injury, for the purpose of this literature review, fatigue will be highlighted as an implication for injury risk in athletes.

2.2.2 Fatigue as a Risk Factor for Lower Extremity Injury

Several studies identifying risk factors for unintentional musculoskeletal injury have found that fatigue may contribute to injury during training and competition. Many of these studies have found that injuries occur in early stages of the season and at the end of matches. NCAA injury surveillance data revealed that the rate of injuries sustained during games was 3.5 times higher than the rate of practice injuries,[123] and these injuries may have in part been due to late game fatigue. The NCAA data also showed that for injuries sustained during practices, preseason

practices accounted for the highest injury rate (6.6 per 1000 athlete exposures), and were 3 times higher than in-season practices and 5.5 times higher than postseason practice rates.[123] Early season fatigue has been identified as a potential factor in the increased rate of injury reported during preseason practices and games in NCAA women's basketball athletes,[6] and authors noted that coaches must recognize that fatigue may compromise performance and raise the risk of injury in tired players because performance is compromised in tired players and fatigue may raise the risk of injury.[254] Early season injury was noted in another study of injury incidence of sports,[247] and authors suggested that decreased activity level prior to the season likely contributed to this finding, which may indicate that early onset fatigue due to lack of conditioning may have resulted in injury incidence.

A study of injuries in amateur rugby players found that injuries were often sustained in the latter stages of the season and during half of matches, and therefore, fatigue may contribute to injuries.[89, 90] Perhaps the explanation for fatigue during latter stages of the season is because players participating in physically demanding activity for a sustained time reach a level of fatigue later in the season, which predisposes them to a higher risk of injury. Authors of this study mentioned that head and neck injuries were more likely to occur in fatigued players (National Health and Medical Research Council, 1994), and that decreased level of skill and physical fitness may have contributed to the high incidence of head and neck injury.[77, 233] In an epidemiological study of injuries in ice hockey players, authors stated that fatigue may influence the speed of players' reactions, and that a slow reaction time may predispose a player to sports injuries.[180, 252] A study of gymnastic injuries found a positive correlation between frequency of practice and injury rate, and defined a high risk gymnast as someone practicing more than 20

hours per week.[206] The increased risk of injury in this study may have been due to fatigue caused by the high frequency of participation in high intensity activity.

In summary, fatigue during early season and late in games is a known risk factor for unintentional musculoskeletal injury. Understanding the potential mechanisms contributing to central and peripheral fatigue during exercise is fundamental in order to formulate injury prevention strategies to prolong the onset of fatigue during practice and games. Several of these mechanisms relate to characteristics of muscle fibers themselves, as well as both central and peripheral metabolic characteristics.

2.3 MECHANISMS OF MUSCULAR FATIGUE

2.3.1 Muscle Contraction under Normal Conditions

Understanding muscle function under normal conditions is important in order to comprehend the many proposed mechanisms that may disrupt normal muscle contraction. Skeletal muscle is innervated by the somatic nervous system and contains long, cylindrical muscle fibers.[126] The functional unit of a skeletal muscle fiber is a sarcomere,[174] which contains the myofibrillar proteins myosin (thick filament) and actin (thin filament). Muscle contraction is based upon the interaction of the myosin and actin filaments; more specifically, the heavy chains contain the myosin heads that interact with the actin to allow muscle contraction.[208] The head region of the myosin contains adenosine triphosphate (ATP) binding site, and this region also serves as the enzyme adenosinetriphosphatase (ATPase) for hydrolyzing ATP into adenosine diphosphate (ADP) and inorganic phosphate (P1).[174]

The sliding filament model is the most widely accepted model of muscle contraction, [126, 209] and describes the series of events that lead to a muscle contraction.[127] At rest, tropomyosin inhibits the actin-myosin binding and calcium is stored in the sarcoplasmic reticulum.[126] During contraction, neural stimulation causes the sarcoplasmic reticulum to release calcium, which binds to troponin and removes the inhibitory effect of tropomyosin and actin-myosin bind.[126] Specifically, an electrical impulse passes down a motor neuron, and releases acetylcholine (ACH) when it reaches the end bulb, or end of the neuron. This occurs at the neuromuscular junction, or where the motor neuron and muscle fiber meet. The ACH is released into a synapse, which is the small gap between the motor neuron and muscle fiber, and binds to a receptor site on a motor end plate.[126] This initiates an action potential (AP) if sufficient ACH binds to the receptors which then spread along the sarcolemma. The AP travel down the transverse tubules (t-tubules), which are extensions of the sarcolemma that allow the AP to move from the outside of the fiber to the inside of the fiber, where contraction occurs.[126] Once the AP reaches the sarcoplasmic reticulum (SR), calcium is released into the sarcoplasm. The shape of tropomyosin after calcium binds to it changes so that it uncovers the binding sites on the actin molecule, allowing the myosin cross-bridge (myosin head) to be free to bind with the binding site on the actin molecule by swiveling and pulling the actin and Z-lines.[126] The availability of adenosine triphosphate (ATP) and adenosine diphosphate (ADP) and inorganic phosphate (Pi) are important for muscle contraction because the breakdown of ATP supplies large amounts of energy.[126] Fresh ATP binds to the myosin cross-bridges, leading to cross bridge recycling. Finally, neural stimulation ends and relaxation occurs, because calcium no longer binds to the troponin molecule and it returns to its inhibitory shape.[126]

There are a multitude of mechanisms that have the potential to influence normal muscle function and create peripheral fatigue in humans during intense activity. These mechanisms include muscle fiber composition, muscle temperature, alterations in muscle excitability, and metabolic changes within the muscle, including increased inorganic phosphate, lactic acid accumulation, and decreased muscle glycogen.[7] Understanding these mechanisms is crucial in preventing fatigue-related changes in proprioception, because impaired muscle function may disrupt the proprioceptive information arising from peripheral afferents, which may result in impaired sensorimotor function. Many of the mechanisms contributing to muscle fatigue can be mitigated by enhancing musculoskeletal and physiological characteristics through strength training, aerobic conditioning, and increasing lactate threshold. Injury prevention programs may consider these characteristics as modifiable risk factors that protect against early onset fatigue and injuries that are attributed to fatigue-related sensorimotor deficits.

2.3.2 Muscle Fiber Composition

An individual's muscle fiber composition may play a role in their susceptibility to fatigue during intense physical activity. Skeletal muscle fiber types have varying fatigue resistance, as well as speed of contraction, intracellular Ca^{2+} handling, glycolytic versus oxidative capacity.[8] There have been several proposed nomenclature classifications in the literature throughout the years. Dubowitz and Brooke[64] classified red, slow twitch fibers as Type I, and white, fast twitch fibers as Type IIa and Type IIb. Smerdu et al[240] classified red, slow twitch fibers as Beta/slow, and white, fast twitch fibers as Type IIa and Type IIx. Peter et al[205] classified red, slow twitch fibers as slow oxidative (SO), and white fast twitch fibers as fast, oxidative, glycolytic (FOG) and fast glycolytic (FG). According to Allen and colleagues,[7] in mammals, fiber type is classified by the

expression of myosin heavy chain (MHC) isoforms, including Type I, Type IIa, and Type IIx in humans. Type I fibers are slow twitch, oxidative fibers with large amounts of myoglobin, mitochondria, and blood capillaries, and are highly resistant to fatigue. Type IIa fibers are fast oxidative fibers that also have large amounts of myoglobin, mitochondria, and blood capillaries, but unlike Type I, have a high capacity for splitting and generating ATP. Likewise, Type IIa fibers are not as resistant to fatigue as Type I. Type IIx are fast glycolytic fibers that have low myoglobin content, mitochondria, and few blood capillaries, and large amount of glycogen. These fibers split ATP quickly, and therefore, fatigue easily. Skeletal muscle fiber composition is largely genetic, but can also be modified with training. Simoneau and colleagues[235] reported that about 45% of muscle fiber composition is related to inherited factors and about 40% can be attributed to environmental factors, while about 15% of the variance may be due to sampling error and technique variance.

Ivy et al[128] examined muscle respiratory capacity and fiber type as determinants of lactate threshold. Muscle biopsies were obtained from the vastus lateralis muscle prior to undergoing physiological analysis, where maximal oxygen uptake and lactate threshold was determined during an incremental cycling test.[128] Muscle respiratory capacity was found to be significantly related to VO_{2max} (r=0.83), and was also found to be significantly related to the relative lactate threshold (r=0.83), percent of slow twitch fibers (r=0.73), and percent relative area of slow twitch fibers (r=0.70).[128] The percent of slow twitch fibers as well as percent relative area of slow twitch fibers was found to be significantly related to both relative (r=0.70, r=0.62) and absolute (r=0.74, r=0.73) lactate threshold.[128]

Characteristics Related to Muscle Fiber Type and Fatigue

Muscle fiber composition is important when considering susceptibility to early onset of fatigue, as Type I (oxidative) fibers are the most resistant to fatigue. Since characteristics of muscle fiber types are largely modifiable,[228] training programs may be developed that increase slow-twitch fiber capacity, and, may increase oxidative function during exercise to exhaustion. Training to improve oxidative capacity may result in increased endurance, and this physiological characteristic can be quantified by an individual's maximal oxygen uptake level.[36] Although researchers have found that individual's VO_{2max} is more dependent on the cardiovascular system's ability to deliver oxygen to the muscles more than it is to muscle respiratory capacity,[72] increased mitochondrial content of muscle may contribute to the improvement of VO_{2max} after training, as evidenced by an increase in arteriovenous O_2 difference.[72, 121, 122] Overall, improving aerobic capacity via muscle fiber adaptations may help mitigate early onset fatigue and decrease risk of unintentional musculoskeletal injury.

2.3.3 Muscle Temperature

Temperature may affect several of the mechanisms that contribute to fatigue, such as the effects of intracellular pH and Pi on contractile proteins, reactive oxygen species production.[7] Factors that may affect muscle temperature include activity, blood flow, core temperature, closeness to body surface, and environmental temperature,[7] and performance may decline due to muscle temperature, core temperature, and increased competition for blood flow to the muscle.[63]

Gonzalez-Alonso and colleagues[93] investigated the influence of body temperature on the development of fatigue during prolonged exercise in the heat. The study was based on the premise that heat stress reduces stroke volume and increases heart rate, and, subsequently,

reduces cardiac output during moderately intense exercise.[225] Although the subjects in the study started exercising with different initial temperatures, subjects fatigued at the same level of hyperthermia (esophogeal temperature=40.1-40.2°C, muscle temperature=40.7-40.9°C, skin temperature=37.0-37.2°C) and cardiovascular strain (heart rate=196-198 beats/min, cardiac output 19.9-20.8 l/min). Researchers concluded that highly trained athletes may become fatigued due to high internal body temperature during prolonged exercise in hot environments and rate of heat storage may have an inverse relationship with time to exhaustion.[93]

Characteristics Related to Muscle Temperature and Fatigue

Several physiological processes may be related to temperature regulation during exhaustive exercise. With endurance training, cardiovascular adaptations occur within the body, including increased capillarization of the muscles for more efficient blood redistribution as well as overall enhanced cardiac and pulmonary function.[36] Therefore, endurance training may enhance an individual's ability to regulate body temperature and intracellular pH during exercise. Since an individual's VO_{2max} is a measure of aerobic capacity, it may also lend insight to an individual's ability to mediate temperature related onset of fatigue.

2.3.4 Metabolic Changes

Inorganic Phosphate

Muscle activation during most types of muscle activity are activated with repeated short bursts of APs.[7] Allen and colleagues[7] propose three phases in which this occurs. First, there is a fast decline of titanic force along with an increase in titanic $[Ca^{2+}]$, then a phase of constant titanic force, followed by a decline of titanic force and $[Ca^{2+}]$.[7] The length of phase 2 may be affected by the oxidative capacity of the muscle fibers, as evidenced by studies showing a shortened

phase 2 with mitochondrial inhibition with cyanide in mice [152, 262] or with decreased oxygen pressure.[245] Slow-twitch fibers and motor units are typically more resistant to fatigue caused by repeated short tetani. [7, 42, 43, 94, 147]

Increased levels of inorganic phosphate have been purported to be a cause of impaired muscle function.[7] During the reaction of PCr + ADP + H+ → Cr + ATP, the ATP concentration remains somewhat constant while CrP breaks down into Cr and Pi, and Pi may cause a decrease of myofibrillar force production and Ca^{2+} sensitivity and SR Ca^{2+} release.[7] Research examining Pi and cross-bridge force production is limited to experimental models with genetically modified mice.[246] From this research, Allen and colleagues concluded that increased myoplasmic Pi can inhibit force production by action on cross-bridge function, and that this is a probable mechanism for the decrease in titanic force occurring early during fatigue in fast twitch fibers.[7] They also surmised that an increase in Pi due to fatigue may reduce myofibrillar Ca^{2+} sensitivity, which may impact force production in later stages of fatigue where titanic [Ca^{2+}] decreases.[246] During early fatigue, an operating CK system and Pi accumulation are required for the early increase in titanic [Ca^{2+}] during but further research is needed to determine the exact mechanism(s) involved.[7] Likewise, in late fatigue, while increased Pi can cause a decrease in titanic [Ca^{2+}], further research is needed to determine the exact process.[7]

Lactic Acid and H+

Muscle fatigue has been attributed to lactic acid accumulation in exercising muscles for some time.[7, 81] During exercise, the intracellular lactate level in humans has been found to reach 30 mM or greater and intracellular pH decreases by ~0.5 pH units.[7, 227] Similarly, decreased muscle force has been related with an increase in intracellular H^+.[7] However, literature surrounding these theories is controversial. In studies looking at skinned muscle fibers, lactate concentrations

of up to 50 mM did not have significant effects on force production or Ca^{2+} sensitivity.[12, 46, 67, 210] In animal studies involving muscle twitch and titanic force at acid pH levels (~6.5), there was little to no reduction in titanic force.[3, 7, 213, 263] Further, while low pH reduces the direct activation of the Ca^{2+} release channel to stimulation by Ca^{2+} and caffeine, [155, 168, 265] the voltage-sensor activation of Ca^{2+}[150, 151] release is not noticeably inhibited at pH 6.2 or the activation of the sensors themselves.[7, 17] Reduced pH lowers the Ca^{2+} sensitivity of the contractile apparatus,[62, 78] likely because of the H+ competing with Ca^{2+} binding to troponin C,[7] which is thought to have detrimental effects on muscle performance. Overall, low pH does not result in the large inhibition of the activation of the contractile apparatus and Ca^{2+}. Instead, while the affinity of troponin C for Ca^{2+} may be reduced under acidic conditions, the total amount of Ca^{2+} binding to the TnC may not be affected.[7] In all, the effect of pH on the Ca^{2+} within the sarcoplasmic reticulum may actually favor force development.[7] While the previously discussed studies did not show evidence for deficits in muscle performance during lactate accumulation, a decrease in blood pH during exercise may negatively affect blood oxygen saturation and oxygen unloading, cardiac, and local vascular function, central nervous system drive, among other processes.[7]

Muscle Glycogen

Glycogen, the stored glucose in skeletal muscle, is a source of energy during exercise and is correlated to time to fatigue during moderately intense exercise.[31, 109] Fatigue is often attributed to muscle glycogen depletion, as carbohydrate is an important substrate for contracting muscle during intense exercise.[52] Muscle glycogen stores are also important because manipulating the level of pre-exercise glycogen stores often dictates the body's dependency on other fuel sources during exercise.[99] A study by Coyle and colleagues[54] examined whether a

carbohydrate feeding prior to prolonged exercise would delay the onset of fatigue. In this crossover study, cyclists ingested a placebo or glucose polymer solution during exercise at ~70% of their maximal oxygen consumption. During the placebo condition, subjects fatigued on average one hour earlier than during the glucose feeding condition, and when fed carbohydrate, their plasma glucose concentration remained higher (4.2-5.2 mM vs 2.5 ± 0.5 mM).[54] However, the mechanism for the relationship between muscle glycogen and fatigue onset is unclear. One theory is that depletion of glycogen causes a reduction in the ATP regeneration rate and muscle force is reduced because of lack of motor drive.[99] Nonetheless, other studies looking at ATP concentration at fatigue show little change in ATP concentration even when glycogen stores are low, suggesting that other factors may cause fatigue in low glycogen states.[99] In a study of a single muscle fiber fatigued by repeated tetani, fiber bundles fatigued more quickly during a subsequent fatigue run in a glycogen depleted state.[47] The decreases in titanic force during fatigue were associated with reduced Ca^{2+} transients.[47] Allen and colleagues concluded that depleted glycogen during prolonged exercise may contribute to fatigue by diminishing sarcoplasmic reticulum Ca^{2+} release, but the mechanism between these factors is not clear.[7, 8]

Characteristics Related to Metabolic Changes and Fatigue

An individual's strength, aerobic, and anaerobic conditioning may influence metabolic characteristics and function during exhaustive exercise. Since increased levels of inorganic phosphate are purported to cause early onset muscle fatigue, enhancing muscle conditioning via strength training may help to mitigate suboptimal Cr/ATP cycling during activities of high intensity. Noakes[188] proposed that sustained, intense training may directly alter muscle contractility, which would likely enhance contractile properties of trained skeletal muscle.[106] Researchers have proposed that percent of peak VO_2 is inversely related to the amount of blood

lactate accumulation in the working muscle.[50, 53, 79, 149, 236, 237] Although the research surrounding increased lactate accumulation and fatigue is equivocal, improving anaerobic/lactate threshold may help to buffer and clear lactic acid build-up in the muscle during intense exercise, thereby increasing blood pH during exercise and mitigating the proposed negative effects of lactic acid accumulation. Finally, an adaptation that occurs with aerobic conditioning is the sparing of glycogen during exercise in favor of fat oxidation. Thus, if the body is trained to utilize fat as the preferred substrate, muscle glycogen stores may stay intact longer during exhaustive exercise, and the onset of fatigue may be delayed. A study by Hawley and colleagues[106] found that cyclists were able to sustain higher work rates during a time-trial ride. Authors stated that this may have been due to decreased reliance on carbohydrate as a fuel source, which was evidenced by the fact that carbohydrate oxidation was significantly decreased and fat oxidation was increased during sub-maximal rides following a training program.[106] On the whole, improving musculoskeletal and physiological characteristics may help to mitigate several mechanisms of fatigue, and, subsequently, may decrease risk of unintentional musculoskeletal injury.

2.4 MECHANISMS OF CENTRAL FATIGUE

2.4.1 Central Nervous System Function following Fatigue

According to Davis and colleagues,[57] central nervous system (CNS) fatigue is a subset of fatigue, or failure to maintain the required or expected force or power output, associated with specific alterations in CNS function that cannot reasonably be explained by dysfunction within the

muscle itself. The two theories behind a reduction in CNS drive to motor neurons are either a reduction in the corticospinal (descending) impulses reaching the motoneurons and/or an inhibition of motoneuron excitability by neurally mediated afferent feedback from the muscle.[57] Bigland-Ritchie et al[33] proposed that inhibition of motor neuron firing rates may be a result of a reflex involving feedback from mechanoreceptors or even group III or IV free nerve endings known to be sensitive to muscle metabolites that accumulate during fatigue.[57] A study performed in human subjects utilized transcranial magnetic stimulation to assess central nervous system excitability from the motor cortex to the alpha-motoneuron.[41] They found that the magnitude of the motor responses in the muscle elicited by transcranial magnetic stimulation decreased after fatiguing exercise, and postulated that the decreased central drive may have been attributed to the accumulation and depletion of neurotransmitters in the CNS pathway located upstream from the corticospinal neurons.[41]

There has been significant interest on the possible role of neurotransmitters in exercise fatigue. Newsholme et al[185] proposed that serotonin (5-hydroxytryptamine, 5-HT) may be a mediator of CNS fatigue. The mechanisms surrounding the control of brain serotonin synthesis and turnover implicate 5-HT as a potential mediator of CNS fatigue during prolonged exercise,[57] and increases in 5-HT have been found to impact arousal, lethargy, sleepiness, and mood that may contribute to altered perceptions of effort and muscular fatigue.[41] The Central Fatigue Hypothesis implies that a diminished sport and exercise performance may be a result of impaired CNS function caused by increased concentrations of brain 5-HT.[185]

The onset of central fatigue may negatively affect higher levels of motor control. Proprioceptive information arises from peripheral afferents and is transmitted to the CNS. The information is conveyed to three levels of motor control, including the cerebral cortex, spinal

level, and brain stem, as well as two associative levels, including the cerebellum and basal ganglia. In the event that central fatigue impairs CNS function and proprioceptive information at the higher level, it may affect the way the somatosensory cortex processes proprioceptive information to provide information about conscious awareness of joint position sense, joint motion, sense of tension, and sense of velocity. The cerebellum operates at a subconscious level and plays a role in motor control and postural maintenance, so the onset of central fatigue due of inadequate cerebral oxygen delivery or insufficient homeostatic regulation may disrupt optimal cerebellum contributions to motor control and functional joint stability.

There are several musculoskeletal and physiological characteristics that may impact mechanisms of central fatigue, including perceived exertion, homeostatic regulation and cerebral oxygen delivery.[57, 58] If these characteristics are optimized, the onset of central fatigue may be delayed or offset during strenuous physical activity, and retain optimal sensorimotor function. This will, ultimately, lead to an overall decrease in risk of unintentional, musculoskeletal injury during training and competition.

2.4.2 Perceived Exertion and Homeostatic Regulation

In Davis and colleagues'[59] definition of central fatigue, they specify fatigue as a failure to meet required or "expected" force output. They formulated this definition in the argument that psychological factors such as motivation and perception are likely important factors in fatigue.[57] These "psychological/physiological" processes should be included as possible fatigue mechanisms because impaired motor performance is usually associated with increased perceived effort and failure to produce the necessary force.[76]

Literature has brought light to the homeostatic regulation model to explain why fatigue occurs despite a lack of peripheral failure.[187] Noakes and colleagues[187] hypothesized that the primary determinant of homoeostatic regulation is the CNS, by continuously altering the number of motor units that are recruited during exercise and regulating the total metabolic demand. Research has found that skeletal muscle ATP concentrations do not reduce to less than 50% of resting value during exercise, including maximal exercise even in people with reduced capacity to generate ATP oxidatively or glycolytically or in muscles that are ischemic after application of a tourniquet and forced to contract until exhaustion by external stimulation.[186] Thus, the hypothesis that peripheral "limitations" or "catastrophe" models require that all available motor units are recruited at exhaustion is challenged by the fact that a majority of available motor units are inactive at the point of exhaustion.[186, 187] The central governor model[244] suggests that the brain does not recruit additional motor units during prolonged exercise because recruiting additional motor units may cause the body to be unable to maintain homeostasis, which is thought to lead to stopping exercise early in order to prevent against worse conditions, such as organ damage, organ failure, or death.[187]

Characteristics Related to Perceived Exertion, Autonomic Regulation, and Fatigue

Enhancing musculoskeletal and physiological characteristics may aid in decreasing an individual's perceived exertion during fatiguing exercise. Since there is a psychological component involved with homeostatic regulation, training programs may help to decrease an athlete's perceived exertion during the same intensity of exercise. If their training results in increased muscle strength, increased aerobic capacity, and increased lactate threshold, they will become more metabolically efficient at the same submaximal intensities, and therefore, potentially be able to mitigate early onset fatigue.

2.4.3 Cerebral Oxygen Delivery

As evidenced above, homeostatic disturbances may greatly impact the onset of fatigue during strenuous exercise. Nybo and Rasmussen[192] explored the effect of physiological factors that may impact these homesostatic disturbances. They hypothesized that fatigue may be elicited by inadequate oxygen delivery to the brain, and thus, low cerebral capillary and mitochondrial oxygen tension (PO_2).[192] Further, the reduction in oxygen delivery may affect the ability to maintain motor activation due to the influence of reduced oxygen on the function of neurons and astrocytes.[192] During exercise, cerebral blood flow is blunted due to hyperventilation-induced reductions of the arterial carbon dioxide tension.[192] This blunted effect may fail to compensate for lower arterial oxygen content, and the anecdotal evidence of athletes fainting following maximal exercise may support this idea.[192] It is difficult to distinguish whether performance declines as an effect of the low PO_2 in active brain regions or from feedback from the muscles and from increased cardiorespiratory stress.[192] However, afferent feedback does not appear to be of importance during severe hypoxia because when the inspired oxygen fraction is lowered to ~10%, epidural anesthesia (blocking or reducing feedback from group 3 and 4 muscle afferents) has no effect on performance or perceived exertion during maximal exercise.[141] In another study that looked at varying levels of cerebral oxygen delivery and motor performance evaluated by maximal handgrip strength, the handgrip strength decreased simultaneously with an increase in lactate spillover from the brain when oxygen delivery was reduced by more than 15% below control levels.[214] This happened as a separate effect of either hyperventilation-induced reduction in cerebral blood flow (CBF) or inhalation of air with a low PO_2, perhaps indicating that cerebral oxygen levels became inadequate to support optimal aerobic metabolism.[214] Since the mechanism behind brief, intense muscle contraction is anaerobic metabolism (net ATP and

creatine phosphate degradation), the impaired motor performance noticed by Rasmussen et al[214] was likely due to central fatigue caused by inadequate oxygen to the brain.[192] During exercise performed at a moderate intensity, that does not exceed the ventilatory threshold, CBF will increase to various regions of the brain linearly with the exercise intensity.[135, 255] Regional CBF will decline as exercise intensity increases despite neuronal activity and metabolic needs increase in motor areas.[192] The uncoupling of metabolism and flow will result in a reduction in the mitochondrial PO_2 in the activated motor areas.[92, 214]

Characteristics Related to Cerebral Oxygen Delivery and Fatigue

Aerobic and anaerobic conditioning may counteract the motor performance impairment and early onset fatigue experienced due to inadequate oxygen delivery to the brain. Cardiovascular adaptations with aerobic conditioning include more efficient blood redistribution, increased capillarization, and enhanced blood viscosity, which favor increased cerebral oxygen delivery.[36] Anaerobic conditioning aimed to improve lactate threshold may help to mitigate the detrimental effects of lactate spillover in situations of oxygen deficit in the brain. Fundamentally, individuals with higher aerobic/anaerobic conditioning will likely have better cerebral oxygen delivery in fatiguing conditions, and improving these characteristics through training may help mitigate fatigue and help to prevent unintentional musculoskeletal injury during practice, training, and competition.

2.5 FATIGUE AND THE SENSORIMOTOR SYSTEM

2.5.1 The Sensorimotor System

The sensorimotor system consists of the sensory, motor and central integration and processing components involved in maintaining joint homeostasis during bodily movements, otherwise known as functional joint stability.[217] Joint stability is defined as the state of remaining or promptly returning to proper alignment through the equalization of forces and moments.[161] The ability to maintain joint stability and overall postural control is dependent on the somatosensory system, and combines sensory input from somatosensory, visual, and vestibular information within the central nervous system.[218] Maintenance of postural control is obtained through strategies elicited from the central nervous system and carried out through efferent (motor) commands to the joints throughout the kinetic chain,[218] including muscle synergies, movement patterns, joint torques, and contact forces.[125] Research has found that distinct contractile patterns and strategies occur,[183] and studies have proposed that a limited number of muscles are used during corrective mechanisms.[66, 203, 219] Functional joint stability is maintained through the static and dynamic components of a joint working in concert to prevent or restore disruption in joint homeostasis. The anticipatory mechanisms utilized prior to a disruption are feedforward mechanisms, whereas, the corrective responses are known as feedback controls.[217]

The characteristics of the static and dynamic components of a joint play an important role in functional joint stability. The static components include ligaments, joint capsule, cartilage, friction, and bony geometry; in other words, the non-contractile elements of the joint articulation.[217] The dynamic restraints of the joint are mediated by feedforward and feedback information, and this may be influenced by characteristics of the muscles surrounding the joint,

including muscle strength, endurance, and range of motion.[217] Proprioceptive information arises from joint mechanoreceptors in the muscles, tendons, fascia, ligaments, joint capsule, and skin.[217] Specific receptors can be found in the static and dynamic restraints of the body. Ruffini endings, pacinian corpuscles, and Golgi tendon-like organs are found in the static restraints, while Golgi tendon organs (GTO) and muscle spindles are found in the dynamic components. Ruffini receptors are thought to act as both static and dynamic receptors because they are low-threshold and slow-adapting, while the low-threshold, rapidly adapting Pacinian corpuscles are thought of as dynamic receptors. The GTO are found within the muscle tissue along the musculotendinous junction and the muscle spindles and provide the CNS with feedback about active muscle tension.[130] Intrafusal muscle spindles are afferent nerve endings that are wrapped around modified muscle fibers, and are sensitive to changes in muscle length and rate of change in muscle length.[96, 176] Gamma motor neurons (γ-MN) innervate the intrafusal muscle fiber peripherally, and activation of these peripheral contractile elements stretches the central regions containing the sensory receptors from both ends, which increases firing rates of the sensory endings and increases the sensitivity of the muscle spindle to length changes.[96] Essentially, input from peripheral sensory receptors, including skin, articular, and chemoreceptors all act to influence the activity of the γ-MN system[13, 131, 202] and, in turn, afferent information provided by the muscle spindle.[217]

The onset of both peripheral and central fatigue may negatively impact various components of the sensorimotor system, including impaired integration of proprioception at the muscle and CNS level. Diminished proprioception due to the onset of fatigue may decrease functional joint stability and increase risk for unintentional musculoskeletal injury. For this reason, a considerable amount of attention has focused on the effects of fatigue on

proprioception and neuromuscular control, which is mediated by proprioceptive input to the CNS.

2.5.2 Proprioception and Injury

The implication of decreased proprioception following fatigue is important in fully understanding proprioception as a risk factor for unintentional musculoskeletal injury. Proprioceptive feedback helps to mediate neuromuscular control;[100] thus, impaired sensorimotor function may disrupt functional joint stability, and therefore, create an environment more susceptible for injury occurrence. In situations where an individual experiences central or peripheral fatigue, proprioception may be compromised, and the risk for injury may increase.

The body of literature surrounding proprioception and injury is dominated with research on proprioception deficits following injury rather than looking at it prospectively as a risk factor. Many of these studies have found that proprioception is diminished in ACL-deficient knees,[25, 40, 44, 80, 84, 88, 162, 169, 196, 215, 221, 258] while others have found no differences in proprioception between injured and uninjured limbs.[87, 95, 199, 215] Since rehabilitation following ACL reconstruction often involves physical training that improves the integrity of static and dynamic restraints about a joint, many studies have found proprioceptive improvements in injured limbs following surgery and subsequent rehabilitation.[26, 83, 84, 129, 215]

Studies examining proprioception as a prospective risk factor are few and varied. A literature review conducted by De Noronha and colleagues[60] looking at voluntary strength, proprioception, postural sway, and range of motion as possible risk factors for ankle sprain injury found that dorsiflexion range of motion was a strong predictor of ankle sprain, and that postural sway and possible proprioception are also predictors of injury. A study by Payne et al[200]

investigated if ankle muscular strength, flexibility, and proprioception were predictors of ankle injury in college basketball players. In this study, flexibility of active ankle dorsiflexion, ability to match reference joint angles in dorsiflexion-plantar flexion and eversion-inversion planes, and concentric and eccentric torque for dorsiflexion-plantar flexion and eversion-inversion at 30 degrees and 180 degrees per second were measured. Proprioception was a predictor of left ankle injury in all subjects, while ankle strength and flexibility measures were not, and there were no significant differences in ankle injury rate between males and females.

While research is warranted to further establish the prospective relationship between proprioception deficits and injury, there is a wide body of literature examining the effect of various fatigue protocols on different modes of proprioception. These studies each provide insight to the complex relationship between fatigue, sensorimotor impairment, and unintentional musculoskeletal injury risk.

2.5.3 Fatigue and Proprioception

Many studies have investigated the effect of fatigue on proprioception, and the majority of this research has utilized joint position sense (JPS) as the preferred sub-modality of proprioception. These studies have been conducted with various fatigue protocols and with both passive and active modes of JPS, and results are equivocal dependent on methodology.

Marks and colleagues[171] looked at the effects of fatiguing isokinetic quadriceps exercise on the ability of sedentary women to passively reproduce an actively generated knee angle and found a significant increase in target overshooting between the initial and final constant error measurements between the experimental and control sessions.[171] The authors concluded that

exercise-induced contractile fatigue may influence the encoding of positional information in healthy knees.[171]

Miura et al[179] examined the effect of a local and general fatigue protocol on joint position sense. They hypothesized that the difference between a local load, produced by isokinetic exercise, and general fatigue, which was designed to more practically simulate sports activity and produce both local and general fatigue, would affect the changes in knee proprioception after exercise.[179] They also aimed to determine which component in the neuromuscular control pathway may change after fatigue. Absolute angle error was determined between a passively positioned knee angle and actively reproduced knee angle during 8 consecutive trials. Local load consisted of 60 maximum concentric contractions of knee extensors and flexors, and the general load consisted of 5 minutes of running at 10 km/h on treadmill with a 10% uphill grade. No significant change in AAE resulted after local load (3.8° ± 1.1°) while a significant increase of AAE was found after general load (5.1° ± 2.1°).[179] Authors concluded that neuromuscular training, including central motor programming, is essential in the prevention of fatigue-induced proprioceptive decline.[179]

Ju and colleagues[136] aimed to study the effect of repetitive active movement versus repetitive passive movements on JPS. The JPS protocol passively produced an angle in which the subject had to actively reproduce and relative error and absolute error were determined. The repetitive active movement included 60 repetitions of isokinetic concentric and eccentric contraction of the quadriceps at 120°/second, while the repetitive passive movements included continuous passive motion of the knee joint at 120°/second for 60 repetitions. Joint position sense (absolute angle error) was significantly worse following repetitive active movement, while

an improvement was following repetitive passive movement, indicating that passive movement may help to improve JPS.

Lattanzio et al[153] examined the effects of muscular fatigue on JPS in a standing, closed-kinetic position. An electrogoniometer and strain gauges were used to actively flex the subject's knee to a starting angle of 35°. The subject was then asked to either extend or flex the knees to a predetermined test angle and then back to the start angle of 35°. Absolute angle error was the absolute difference between the actual and perceived test angle. The first of three fatigue protocols administered was a ramp test on a cycle ergometer. Maximal oxygen uptake was also determined and utilized to determine workloads for the other two fatigue protocols, the continuous test and the interval test. The continuous test required subjects to cycle at 80% of their VO_{2max} to maximal exhaustion, and the intermittent protocol required the subject to cycle at alternating 30s workloads equal to 120% VO_{2max} and 40% VO_{2max} until exhaustion. In male subjects, there was a statistically significant increase in AAE after the ramp test (1.0 ± 0.66°, $p<0.01$), the continuous test (0.70 ± 0.66°, $p<0.03$), and the intermittent test (1.24 ± 0.79°, $p<0.01$).[153] In female subjects, there was a statistically significant increase in AAE after the continuous test (0.73 ± 0.73°, $p<0.03$), and the intermittent test (1.1 ± 0.89°, $p<0.01$).[153] Authors concluded that while there was a statistically significant decrease in proprioception following fatiguing exercise, more work is needed to determine the clinical significance.[153]

Rozzi et al[226] studied the effect of muscular fatigue on knee joint laxity and neuromuscular characteristics of male and female athletes. Fatigue in this study was induced by performing maximal concentric contraction repetitions. While EMG data showed significantly increased onset of hamstring firing after fatigue, there were no significant changes to anterior tibial translation, lower extremity balance, or TTDPM in the flexion direction. However,

TTDPM in the extension direction significantly increased following fatigue ($F_{1,49}$ = 6.50, P = 0.014).[226] Authors noted that there may be other mechanisms to explain the significant decrease in knee kinesthesia in the extension direction because these changes occurred despite no significant changes in knee laxity following fatiguing exercise.

A recent study evaluated the effects of exercise-induced quadriceps muscle damage on knee proprioception, including JPS, force sense, and TTDPM, in young, healthy men.[256] Muscle soreness (visual analog scale (VAS)), proprioception, and plasma creatine kinase (CK) were measured prior to and one, 24, 48, 72, and 96 hours following the fatigue protocol. The fatigue protocol in this study consisted of sets of thirty eccentric quadriceps contractions at a target of 60% of maximal concentric peak torque, and termination occurred when the subject could not complete two sets, and results demonstrated that eccentric muscle damage was achieved as evidenced by biomarkers of muscle damage and significantly increased muscle soreness.[256] Joint position sense was significantly decreased after fatigue up to 48 hours.[256] Force sense decreased significantly one hour after exercise and stayed decreased until 48 hours.[256] Threshold to detect passive motion showed significant changes at 30 degrees of flexion and 70 degrees of flexion at one hour and up to 24 hours post fatigue, but the changes were significantly different between the two angles at 24 hours post.[256] Authors reported that the muscle damage elicited form eccentric exercise disrupted joint proprioception, and that there may be impairment of the intrafusal fibers of muscle spindles and in the tendon organs.[256]

Research surrounding fatigue and proprioception has equivocal results depending on mode of fatigue induction and mode of proprioception tested. Several conclusions may be gathered by this data. First, when applying a local fatigue protocol, eccentric isokinetic contractions are more successful in inducing proprioceptive changes than concentric

contractions.[136, 256] Also, based on the varying results of the studies detailed above, the speed and number of contractions may influence proprioceptive changes. Others have suggested that local fatigue is not enough to induce proprioceptive changes, and rather central mechanisms of fatigue play a greater role in diminished sensorimotor function.[179]

2.5.4 Fatigue and Neuromuscular Control

A number of research studies have investigated the effect of fatigue on different aspects of neuromuscular control. Several studies have examined the effect of fatigue on kinematic and kinetic characteristics of athletes during functional sport movements, such as stop-jumps and drop-landings. Chappell and colleagues[45] investigated the effect of lower extremity fatigue on knee kinetics and kinematics during stop-jump tasks in the forward, vertical, and backward direction. The fatigue protocol consisted of unlimited repetitions of vertical jumps and 30-m sprints until volitional exhaustion, and 5 vertical jumps were performed after each post-fatigue stop-jump in order to maintain a high level of fatigue.[45] Results revealed significantly increased peak proximal tibial anterior shear forces, increased valgus moments, and decreased knee flexion angles in both male and female subjects, but peak knee extension moment was not significantly affected by fatigue induction.[45] A study by Nyland et al[194] sought to determine if kinematic and kinetic changes occurred at the knee, ankle, and subtalar joints during the plant-and-cut phase of a crossover cut following quadriceps and/or hamstring fatigue. Eccentric hamstring fatigue caused decreased peak impact knee flexion moments, increased internal tibial rotation at peak knee flexion, and decreased peak ankle dorsiflexion, while eccentric quadriceps fatigue cause increased peak ankle dorsiflexion moments, decreased peak posterior braking forces, decreased peak knee extension moments, delayed peak knee flexion, delayed peak propulsive forces, and

delayed subtalar peak inversion moments.[194] A study by McClean and colleagues[175] aimed to evaluate the effects of fatigue on lower-limb kinematics and kinetics during the landing phase of a drop-jump task, and to further examine gender specificity in these effects by studying ten male and ten female NCAA athletes. Subjects completed ten drop jumps prior to and following a fatigue protocol that was designed to simulate game play, and consisted of continuous drills, including step-up and down movements and plyometric bounding movements.[175] The fatigue protocol increased initial and peak knee abduction and internal rotation motion and peak knee internal rotation, adduction, and abduction moments, and these increased moments were more pronounced in females.[175] Benjaminse et al[30] studied kinematic characteristics of the hip and knee during single-leg stop-jumps prior to and following fatiguing exercise consisting of an incremental treadmill exercise test. During the post-fatigue stop-jumps, male and female subjects had significantly less knee valgus and decreased knee flexion at initial contact, but no differences were identified at the hip from pre- to post-fatigue, and no gender effects were revealed.[30]

Research has also examined muscle activation following lower extremity fatigue. Another investigation by Nyland et al[193] examined the effects of fatigue after eccentric quadriceps femoris work on muscle activation prior to crossover cut landing heel strike. In this study, twenty recreationally active women participated in crossover cut training prior to undergoing testing of fatigue effects after three different conditions and one control condition. Compared to control, eccentric quadriceps fatigue resulted in delayed vastus medialis, rectus femoris, and vastus lateralis activation onsets.[193] However, these results were not significant when compared with hamstring fatigue, and neither hamstring nor quadriceps femoris fatigue produced differences in medial hamstring or biceps femoris activation onsets compared to

control.[193] Earlier gastrocnemius activation occurred following eccentric fatigue of the quadriceps femoris compared to the control, but not hamstring fatigue.[193]

Based on these findings, it is apparent that fatigue impairs neuromuscular control, and the contribution of proprioception to neuromuscular control is likely effected by fatigue-induced disruption to the muscle and/or CNS. Since several modifiable musculoskeletal and physiological characteristics that may contribute to the onset of fatigue have been previously identified, these characteristics may be optimized through injury prevention programs in order to mitigate the detrimental effects of fatigue on the sensorimotor system and decrease risk of unintentional musculoskeletal injury.

2.6 CHARACTERISTICS RELATED TO FATIGUE ONSET, PROPRIOCEPTION FOLLOWING FATIGUE, AND INJURY RISK

2.6.1 Muscular Strength

Muscle strength has been identified as a potential modifiable characteristic related to the onset of fatigue. Enhancing muscle strength may mitigate inadequate metabolic and physiological functions within the muscle that predispose an individual to early onset peripheral fatigue. Likewise, for the above mentioned reasons, muscle strength has been cited as a risk factor for injury in many epidemiological studies, and some of these studies have linked sub-optimal muscle strength to early onset fatigue.

In research examining muscle strength as a risk factor for injury, inadequate muscle strength has been identified as a risk factor for lower extremity injury in a majority of studies. In

a study of NCAA male soccer injuries, Agel et al[5] noted that poor muscle conditioning and repetitive explosive movements during preseason practice following a period of lower activity levels may cause many noncontact thigh and hip muscle injuries. Authors recommended that during the summer months prior to season, graduated muscle conditioning programs focusing on general muscle endurance but also explosive motions of the hip and thigh should be implemented to minimize noncontact muscle injuries.[5] This statement implies that the premature onset of fatigue in deconditioned athletes may contribute to increased injury risk, and that increasing muscular endurance and strength may help to prevent unintentional musculoskeletal injury. In the study identifying risk factors for injury during basic combat training, fewer push-ups were associated with higher injury risk in both men and women, and a lower number of sit-ups was associated with higher injury risk in men.[144] This suggests that poor upper body and core muscle endurance is a risk factor for unintentional musculoskeletal injury during a period of intense physical training, and that enhancing these characteristics may lead to better attrition and outcomes for Soldiers during basic training or athletes participating in intense physical training programs. However, while these studies found a significant relationship between general muscle endurance and injury risk, a study measuring isokinetic muscle strength of the quadriceps and hamstring at 60 and 180 degrees per second found no difference in strength between injured and uninjured groups.[197] Researchers proposed that isokinetic strength may not have been a risk factor for injury since it has little to no correlation to muscle function,[11, 164] and that perhaps eccentric strength may have been more advantageous to test because eccentric strength decreases landing forces through plyometric training.[116] Additionally, eccentric muscle fatigue in athletes has been related to fatigue related injuries, and fatigue from eccentric quadriceps femoris exercise but not hamstring exercise has been shown to decrease onset of muscle firing during

crossover cutting training.[195] Increased anterior tibial translation has been demonstrated following fatiguing exercise as well as a delay in intermediate- and voluntary-level EMG activity. Since research is limited surrounding isokinetic strength measurements as a predictor of injury, further research is warranted in this area.

In addition to inadequate muscular strength, research has shown that knee flexor/extensor agonist/antagonist ratios and side-to-side muscle imbalances may also pose risk of lower extremity musculoskeletal injury. In a prospective study looking at risk factors for injuries during a soccer season in females, a higher concentric H/Q ratio (90 degrees/sec) was non-significantly related to a higher risk of overuse injuries (OR=1.13, P=0.004).[241] These findings agreed with a study by Knapik et al[143] that investigated isokinetic strength and flexibility imbalances in female collegiate athletes. This study found that athletes with a knee flexor/knee extensor ratio of less than 75% had a greater incidence of lower extremity injuries.[143] However, this study was performed at an isokinetic speed at 180 and 30 degrees/sec, and only measurements at 180 degrees/sec were found to be significant,[143] which suggests that strength differences at higher velocities might better translate to strength imbalances during functional activity at similar speeds. This study also found that athletes with a right leg stronger than the left leg by 15% or more were 2.6 times more likely to get injured than athletes with imbalances less than 15%, and authors implied that this was due to a strong force generated by the right leg that may have resulted in damage to the left leg because the weaker hamstring muscle group was unable to absorb or properly transfer the force.[143]

On the whole, it is apparent that sub-optimal muscular strength as well as bilateral and agonist/antagonist imbalance may pose an increased risk for unintentional musculoskeletal injury. Research is needed to establish the relationship between muscular strength and changes

in proprioception following fatigue, including concentric strength characteristics of the quadriceps and hamstrings. This research is especially important since inadequate muscle conditioning and muscle strength may predispose an athlete to early onset fatigue, and therefore potentially lead to decreased sensorimotor function during training, practice, and competition.

2.6.2 Aerobic Fitness/Anaerobic Threshold

Aerobic and anaerobic fitness, quantified by maximal oxygen uptake and lactate threshold, have also been identified as modifiable injury risk factors that are related to the onset of both peripheral and central fatigue. Many epidemiological studies have cited aerobic fitness or endurance capacity as a risk factor for unintentional musculoskeletal injury, but research is lacking related to lactate/anaerobic threshold and injury risk.

Inadequate aerobic fitness has been identified as a characteristic linked to unintentional musculoskeletal injury occurrence in prospective injury prevention research. In an attempt to define the relationship between aerobic fitness and injury, Murphy et al[181] discussed the conclusions drawn from several studies about the relationship between fitness level and injury occurrence. Murphy concluded that fatigue resulting from diminished aerobic fitness may lead to a reduction in the protective effect of musculature on skeletal structures, but the studies related to the matter had used different methods to quantify aerobic fitness so comparing their findings is difficult.[181] However, in five out of the seven studies examined, there was an association between measures of aerobic fitness and injury.[28, 48, 124, 133, 144] In the study looking at risk factors for injuries during basic combat training, slower 3.2-km run times were associated with higher injury risk in both men and women, and lower peak oxygen uptake was associated with higher risk of injury.[144] Further, lower exercise or sports frequency in the previous month was

associated with injury in men,[144] implying that individuals starting physical training programs at a lower level of fitness are at greater risk for unintentional musculoskeletal injury. Comparable results have been found in similar research of physical fitness and injury outcome during physical readiness training,[108, 132, 133] including a study that found that slower 2-mile run time was associated with a higher incidence of musculoskeletal injuries, and that soldiers in the slowest quartile were 1.6 times more likely than subjects in the fastest quartile.[142] In contrast, a study examining aerobic capacity measured during a continuous multistage fitness test found no difference between the injured and uninjured group.[197]

The majority of research looking at aerobic fitness as a risk factor for unintentional musculoskeletal injury has used run times as the fitness variable, as run times have been positively correlated with maximal oxygen uptake.[51] Research is limited regarding lactate threshold as a prospective injury risk. There is evidence that ability to buffer and clear lactic acid may help mitigate the onset of fatigue. [50, 53, 79, 149, 236, 237] Studies are needed to analyze both aerobic fitness and lactate threshold as they relate to the onset of fatigue and as contributions to injury risk.

2.7 METHODOLOGICAL CONSIDERATIONS

In this section, the rationales behind the testing methodologies chosen will be described. The specific protocols will be further detailed in chapter 3.

2.7.1 Isokinetic Strength Assessment

Isokinetic strength is a common measure of quantifying muscle performance of the sensorimotor system.[204, 218] With this measurement, the angular speed of the moving limb is held constant throughout a range of motion, which happens independently of magnitude and velocity of muscle contraction.[74, 118, 120, 204] Isokinetic strength is important to assess because of the implication of the agonist/antagonist torque ratio and co-contraction on the maintenance of joint stability.[18, 38, 119, 198, 242, 243]

In this study, isokinetic concentric strength of the quadriceps femoris and hamstrings was evaluated using a Biodex isokinetic dynamometer. Test-retest reliability of reciprocal concentric-concentric quadriceps/hamstrings contractions at 60 degrees/second have been demonstrated in our lab with ICCs of 0.809-0.9112 and SEM of 0.07-0.15 %BW.[2]

2.7.2 Aerobic Capacity/Lactate Threshold Assessment

Aerobic capacity can be evaluated in the field as well as the laboratory. Examples of field measurements include multistage fitness tests[157] and timed runs, where total distance achieved correlates with maximal oxygen uptake.[51] Laboratory measurements involve metabolic assessment, and valid tests have been established utilizing numerous protocols,[137] techniques, and equipment utilized across various modes of exercise. Maximal oxygen uptake is reliable and predictive for evaluating differences in aerobic fitness across populations,[232] and provides a more objective and controlled measurement than field testing of aerobic capacity. For this study, an incremental treadmill protocol will be utilized based on a variation of the protocol designed by Astrand.[55, 137, 229] The graded exercise protocol utilized in this investigation was chosen because

it closely imitates the type of running an athlete or trained individual would perform during a training run, and similar graded treadmill exercise protocols have been utilized in studies on athletes and trained individuals.[1, 144, 178, 229] Research has demonstrated that cross-country skiers, rowers, and cyclists achieved significantly higher VO2max values during testing protocols that are more sport specific in comparison to general incline protocols,[249] and that, in general, trained individuals perform better with a test modality resembling their typical training.[85, 137, 201, 242] The ParvoMedics TrueOne 2400 (TrueOne2400, Utah) will be utilized to collect VO_{2max} data. At various work rates during cycling, the TrueOne2400 has been shown to have similar between-day reliability when compared with the gold standard Douglas Bag method (CV 4.7-5.7% versus 5.3-6.0%, respectively).[56] The TrueOne2400 has also shown accuracy when compared to the Douglas Bag, as Crouter et al[56] did not find significant differences between the devices for VE, VO_2, or VCO_2 at any work rate ($P > 0.05$).

Because research surrounding lactate and induction of fatigue is equivocal, lactate levels during incremental treadmill exercise and lactate threshold are valuable variables to consider in relation to proprioceptive changes after fatigue. Lactate assessment during incremental exercise tests are widely used in the literature and are considered a valid and reliable estimate of endurance performance.[9, 34, 35, 79, 82, 107, 148, 158, 236] In this study, lactate threshold will be measured by taking a blood sample during the last minute of each stage of the incremental treadmill protocol for analysis with a Lactate Pro® Analyzer. This method has been previously utilized in our laboratory.[55, 229] The Lactate Pro® Analyzer has been shown to have good accuracy, with limits of agreement with the reference method, EBIO plus®, of -1.3 to +1.5 mMol. It also had good reliability at different lactate concentrations (coefficient of variation between 2.8 and 5.0%), and had good reliability for intra-, inter-analyzers and between test strips (ICC r=0.999).[16]

2.7.3 Threshold to Detect Passive Motion

Threshold to Detect Passive Motion (TTDPM) is a common measurement of kinesthesia. It has been found to be more beneficial than JPS to detect differences between groups, particularly between patients with knee injury and/or disease.[86, 215] Previous research has examined kinesthesia utilizing TTDPM in healthy subjects and athletes, and has established the validity and test-retest reliability of the measurement using several techniques.[4, 37]

While TTDPM is not a direct measure of functional joint stability, it is an objective measure of passive joint proprioception that eliminates accessory sensory cues arising from visual, auditory, vestibular, and cutaneous receptors. In selecting this test, we will be able to more directly elucidate the relationship between the selected musculoskeletal and physiological characteristics with knee proprioception following fatigue. Once these relationships are established, further research can evaluate the relationship between these characteristics and measures of functional joint stability, such as single-leg balance. A study by Lee and colleagues[156] sought to correlate quadriceps and hamstring muscle strength, knee laxity, passive-repositioning proprioception (PRP), and TTDPM with dynamic standing balance of the injured limb in patients with chronic anterior cruciate ligament deficiency. Of all variables, only TTDPM had a significant positive correlation ($p<0.05$) with dynamic single-limb stance balance,[156] suggesting that training to improve TTDPM in injured individuals may help restore functional joint stability.

Lephart and colleagues[159] assessed passive joint motion in the flexion direction in female gymnastic athletes compared with healthy controls starting in 45 degrees of knee flexion. The TTDPM test used in this study emulate principles previously established by Barrack et al[20-24] and Skinner,[238, 239] which included use of a sitting position with a starting angle of 45 degrees knee

flexion, and accounting for external sensory cues by utilizing a blindfold, white noise, and a pneumatic sleeve. The leg was passively flexed during five repetitions at 0.5 degrees/second, and he/she stopped the machine using a hand-held switch when motion was detected. Methods comparable to those utilized in the Lephart study will also be implemented in this study, and a similar TTDPM protocol has shown test-retest reliability of r=0.92.[162, 251]

2.7.4 Fatigue Protocol

Fatigue may be induced by exercise of varying intensities and durations. Typically, these characteristics and the metabolic pathways utilized during the activity will implicate the level of recovery from fatigue. When a muscle is continuously stimulated at a high frequency close to maximal force, the force production often rapidly declines, but recovery is also very rapid and occurs in about one to two seconds.[8, 32] The rapid decline in force is attributed to a loss of muscle circulation, which often occurs at ~50% of maximal effort exertion.[19] Central fatigue is likely induced from repeated or sustained maximal contractions, rather than a single brief voluntary contraction (MVC).[192]

Given that equivocal results were found following various local and general fatigue protocols in the section detailing fatigue and proprioception, the fatigue protocol chosen for this study included components that elicit both peripheral (local) and general (central) fatigue and simulate fatiguing motions likely experienced during a game situation. Therefore, a protocol utilized by Wilkins and colleagues[264] was selected, which includes seven different stages of various fitness components (i.e. sprinting, stepping, pushups, sit-ups). In order to confirm that fatigue has been produced, rating of perceived exertion scales were utilized,[39] heart rate was monitored, and lactate measurements were taken.[189]

3.0 METHODOLOGY

3.1 EXPERIMENTAL DESIGN

This study utilized a cross-sectional, correlational design. A correlational design was chosen to determine the strength and direction of the relationship between the variables outlined in the specific aims. However, this study design will not provide evidence for causality between the predictor and outcome variables, so results were interpreted with caution.

3.2 SUBJECT RECRUITMENT

The study was approved by the Institutional Review Board at the University of Pittsburgh prior to implementation of all research procedures. Subjects were recruited from the communities surrounding the University of Pittsburgh. Study flyers were posted and distributed, and interested participants called the NMRL for additional details.

3.3 SUBJECT CHARACTERISTICS

3.3.1 Inclusion Criteria

Subjects were included for this study if female, aged 18-40, physically active under the definition that they work out at least five days per week for at least 50 minutes per session, and that they had been working out at this frequency for at least six months.

Females were chosen for inclusion in this study because research has shown that there are proprioceptive differences between genders,[153, 202] females are at greater risk of knee injury than males, [15, 29, 100, 104] females may have reduced O_2 carrying capacity compared to males,[167] and that females may be more fatigue resistant than males.[117, 173, 177, 261] Because of the potentially large baseline differences in anthropometric, musculoskeletal, and physiological characteristics between sexes, female only inclusion allowed for a more homogenous sample for data collection and analysis.

3.3.2 Exclusion Criteria

Subjects were excluded if they were male and did not meet the above exercise requirements. They were also excluded if they exhibited lower extremity injury symptoms within the previous months, had lower extremity injury within the past year, or had lower extremity surgery within the past 5 years. Since subjects engaged in intense exercise as part of the testing protocol, they were excluded if they had a medical condition that contraindicated participation, such as a cardiovascular, pulmonary, vestibular, neurological, or vascular condition. Questions found in the Physical Activity Readiness Questionnaire (PAR-Q,

http://www.csep.ca/CMFiles/publications/parq/par-q.pdf) were included in the phone screen and were used to exclude a subject with potential contraindication to participation in maximal exercise. These questions were designed to exclude individuals with potential cardiac issues and exclude those who were on certain medications, such as beta-blockers.

3.4 POWER ANALYSIS

To the author's knowledge, there were no previous studies examining the correlational relationship of the independent and dependent variables outlined in this study Using a PASS11(NCSS, LLC., Kaysville, Utah) sample size calculator, a sample size of 20 subjects would achieve 81.2% power to detect a difference of -0.40 between the null hypothesis correlation of 0.40 and the alternative hypothesis correlation of 0.80 using a two-sided hypothesis test with a significance level of 0.05.[98, 103, 267] To account for 30% attrition, a total of N=26 subjects were needed for enrollment into the study,

3.5 INSTRUMENTATION

3.5.1 BODPOD Body Composition System

The BODPOD Body Composition System (Cosmed, Chicago IL) was utilized in order to measure % body fat as part of demographic data collection. The BODPOD has been shown to be reliable in a large, heterogenous sample,[190] and has been shown to be valid compared to

hydrostatic weighing and dual x-ray absorptiometry in a population of female collegiate track athletes.[260] Our laboratory has also demonstrated reliability and validity of the instrument (ICC=0.98, SEM=0.47% BF).

3.5.2 Biodex System 3 Multi-Joint Testing and Rehabilitation System

The Biodex System 3 Multi-Joint Testing and Rehabilitation System (Biodex Medical Inc, Shirley, New York) is an isokinetic dynamometer with capabilities to measure strength at the shoulder, elbow, wrist, hip, knee, and ankle in passive, eccentric, isokinetic, and isometric modes. The Biodex System 3 was used to measure TTDPM of the knee as well as to measure isokinetic and isometric strength of the quadriceps and hamstring.

3.5.3 PresSsion Gradient Sequential Compression Unit

A PresSsion gradient sequential compression unit and compression sleeve (Chattanooga group, Hixson, TN) were utilized during TTDPM in order to mitigate feedback from tactile sense. The pneumatic sleeve was inflated around the lower leg to a constant pressure (40 mm Hg) during the test so that equal sensation was felt over the entire limb.

3.5.4 ParvoMedics Metabolic Unit

The ParvoMedics TrueOne 2400 (TrueOne4200, Utah) was utilized to measure metabolic variables. The TrueOne 2400, which is a non-breath-by-breath system that uses a mixing

chamber, has been previously established as an accurate device for measuring gas exchange,[27] and provides accurate and reliable results when compared to the gold standard Douglas bag.[56]

3.5.5 OMNI Rating of Perceived Exertion (RPE) Scale

The OMNI RPE scale was utilized during the maximal oxygen uptake test and fatigue protocol in order to quantify perceived exertion. While the OMNI scale was originally designed for children and adolescents, a version has been created for adults.[223] The OMNI scale for adults displays the numbers 0-10 on a chart with pictorial descriptors which correspond with effort experienced during a stage of exercise, with 0 meaning "extremely easy" and 10 being "extremely hard."[39, 223] The OMNI scale has been shown to have high reliability in female adolescents performing graded treadmill exercise (r=0.91-0.95) and was shown to have better reproducibility than the Borg scale (r=0.64-0.78).[207, 223] The OMNI scale has been validated against criterion measures such as heart rate (HR) and VO_2, and has been validated in adults (M, F) and children (C) performing cycle ergometer exercise[223, 224] (HR: F, r=0.94; M, r=0.92; C=0.93; VO_2: F, r=0.93; M, r=0.94; C, r=0.94), and female adolescents performing graded treadmill exercise[207, 223] (HR: r=0.82, VO_2: r=0.88) (all $P<0.05$). Similar RPE scales have been correlated with other physiological measurements relating to effort and exertion, including blood lactate concentration.

3.5.6 Lactate Pro® Lactate Measurement System

The Lactate Pro® Analyzer was utilized to measure blood lactate concentration during the incremental treadmill test for maximal oxygen uptake as well as during the administration of the

fatigue protocol. The Lactate Pro® Analyzer has been shown to be easy-to-use, accurate, reliable, and shows high levels of agreement with the ABL 700 Series Acid-Base analyser, the Accusport Lactate Meter, and the YSI 2300 Stat lactate analyser.[212]

3.6 TESTING PROCEDURES

3.6.1 Informed Consent, Exercise History Questionnaire, Dietary Recall

Subjects were given the informed consent document prior to engaging in any research activities. The principal investigator explained the contents of the consent and allowed the potential participant to ask any questions regarding the study. Once subject gave informed consent, inclusion/exclusion criteria were reconfirmed prior to study enrollment.

All research procedures took place at the Neuromuscular Research Laboratory (NMRL) within the Department of Sports Medicine and Nutrition at the University of Pittsburgh. Subjects reported for two testing sessions. The first session consisted of administration of an exercise history and dietary recall questionnaire, a TTDPM familiarization session, where subjects underwent a full practice session of TTDPM in both the extension and flexion directions. Then, subjects performed a test of muscular strength utilizing the Biodex System 3 and a test of VO_{2max} and lactate threshold. During the second session, subjects performed a test of TTDPM, participated in a fatigue protocol, and then performed a follow-up test of TTDPM.

Prior to reporting for each test session, subjects were instructed not to participate in strenuous exercise within 24-hours of the session to mitigate residual fatigue as a confounding variable. They were also instructed not to consume a meal within 2 hours of each test session.

3.6.2 Exercise History Questionnaire and ASA 24-hour Dietary Recall

After verbally stating that they understood the study and signed the informed consent, subjects were administered an Exercise History Questionnaire. The questionnaire was modified and designed in order to quantify participation in different areas of fitness as well as to assess perceived fitness level in those areas. A copy of the questionnaire is found in Appendix A.

Subjects were also given a 24-hour dietary recall questionnaire. This questionnaire is an automated, self-administered 24-hour dietary recall called ASA24 developed by the National Cancer Institute. The ASA 24 has multi-level food probes to accurately assess food types and amounts, and uses a triple-pass system to cue users to include items often overlooked, such as beverages and condiments. The questionnaire also includes pictures to help the user choose the correct portion size of food consumed. The information was analyzed through the program software using the USDA's most current Food and Nutrient Database for Dietary Studies database.

3.6.3 Body Composition Measurement

The BODPOD Body Composition System was utilized in order to measure body composition (fat mass and fat-free mass). The system utilizes air displacement plethysmography in order to measure body volume and calculate body density. Prior to testing, the system underwent a standardized calibration with a 50.683 L calibration cylinder in addition to a separate two-point calibration prior to each test. The subject wore a spandex outfit or swimsuit as well as a cloth swim cap prior to entering the BODPOD. They also removed any metal jewelry. Body volume

was measured until two tests met criteria for consistent tests. Lung volume was predicted and percent body fat was calculated using an appropriate densitometry equation.

3.6.4 Threshold to Detect Passive Motion

Threshold to detect passive motion was measured during both test sessions. A TTDPM familiarization session was performed at the beginning session 1. Then, during session 2, TTDPM was measured before and after the fatigue protocol.

Prior to TTDPM testing, the Biodex System 3 was calibrated according to factory recommendations. The limb tested was the dominant leg, defined as the leg used to kick a ball as hard as possible. Subject set-up included setting the chair of the device to the subject by lining the lateral condyle of the femur with the center of the dynamometer and raising the chair height and fore/aft until proper alignment was achieved. A cotton tube sock was placed on the lower leg before being placed inside the pneumatic sleeve, which was inflated to 40 mmHg so that the subject felt equal sensation along and around the lower limb. Range of motion was set by extending the knee and jig arm of the dynamometer to set the "away" limit, and flexing the knee and jig arm to set the "toward" limit. The subject was placed at a starting position of approximately 20 degrees of knee flexion, and knee position was confirmed with a goniometer measuring along the line of the lateral malleolus and lateral condyle. Software set-up included setting the "go-to" button to record the degree of starting position, and the value was typed into the "get-position" box. Isometric mode was selected and starting position was synchronized before passive mode selection and zeroing the speed values. The researcher manually selected the randomized direction of motion (clockwise or counterclockwise) and set the speed of movement to 0.25 degrees per second. The subject was instructed to hit the remote button when

they were able to detect both motion and direction of motion in either knee extension or flexion. Prior to the start of the test, subjects were outfitted to eliminate visual and auditory sensory cues by being blindfolded and wearing ear plugs as well as headphones with white noise. The researcher recorded the degrees from the start position until the subject hits the remote button, as well as the direction of the movement. A total of 10 repetitions were performed, with 5 in the flexion direction and 5 in the extension direction. Direction of movement was recorded, and a trial was counted even if direction was incorrectly identified.

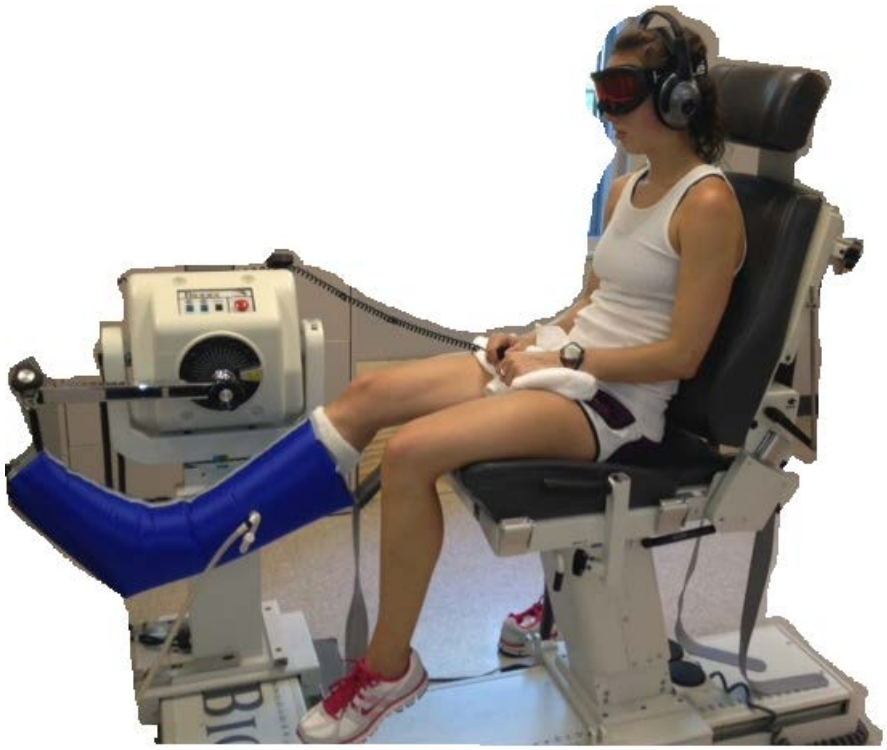

Figure 1. Threshold to Detect Passive Motion Set-up

3.6.5 Muscular Strength

Isokinetic muscular strength of the quadriceps and hamstring was assessed on Day 1 following TTDPM familiarization (con/con, 60 degrees/second). The Biodex System 3 was set up and calibrated according to factory recommendations. Then, subject set-up was initiated, consisting of setting the subject's knee joint center with the axis of the dynamometer. Chair height and fore/aft was adjusted so that there was a two-finger width space between the edge of the chair and the popliteal fossa behind the knee joint. The calf pad of the jig arm was adjusted so that the bottom edge of the pad was two-finger-widths above the calcaneus. The subject was secured to the chair using padded straps across the shoulders, lap, thigh of testing leg, and lower leg to the calf pad. Subjects were instructed to place their hands on the handlebars but not to use them as leverage. Prior to strength assessment, range-of-motion/safety stop limits were set by extending the knee and jig arm to full extension for the "away" limit, and then brought to just under 90 degrees of flexion for the "toward" limit. Limb weight was taken into account for the force of gravity at full extension, and then neutral knee angle was set. Subjects first performed three practice repetitions of knee flexion and extension at 50% maximal effort, then three practice repetitions at 100% maximal effort followed by one minute of rest. During the actual test, subjects performed five maximal effort repetitions of knee flexion and extension. Verbal cues were given during the test to "kick away as hard and as fast as you can" and "pull back as hard and as fast as you can." The results report generated over the five maximal effort repetitions reported peak torque produced during knee flexion and extension normalized to body weight.

3.6.6 Maximal Oxygen Uptake

Maximal oxygen uptake was assessed on Day 1 following strength testing during a graded exercise treadmill test utilizing the ParvoMedics TrueOne2400 metabolic unit. Prior to subject testing, the metabolic unit was warmed up and calibrated according to factory recommendations. Subject set-up included acquisition of height and weight using a calibrated wall stadiometer and electronic scale, and being outfitted with a Polar heart rate monitor strap worn just below the chest level. Then, after being equipped with the face mask, subjects were instructed to perform a five minute warm-up on the Woodway treadmill at a pace corresponding with 60% of their maximal effort, then begin the graded exercise test, which is an adapted Astrand protocol.[137] Subject pre-selected a speed that they predicted they would be able to maintain for a moderately long distance run. The selected speed remained constant through the entire test, and incline was increased by 2% every three minutes of testing. Subjects continued the protocol until volitional exhaustion. To encourage completion of a maximal effort test, RPE will be collected with an OMNI RPEscale[39] at the end of each three-minute stage. [189] The OMNI scale was used to measure perceived exertion of overall body (RPE-O), limbs (RPE-L and RPE-A), and chest (RPE-C). The subject was given a standardized set of instructions for perceived exertion, with the adult definition being "What is the subjective intensity of effort, strain, discomfort, or fatigue that I feel during exercise"?[223] An example of an OMNI scale and verbal instructions are found in Appendix A. Prior to using the scale, anchor points were established with the subject using a memory procedure. The subject was asked to think of a time when she had exerted herself at a level corresponding with the pictures on the OMNI scale at the bottom and top (low and high anchor points).[223] These anchor points were used to estimate levels of exertion during exercise,

and, for instance, if the subject felt they were working at 50% of their maximal exertion, their RPE would fall at 5 or 6 on the OMNI scale.[223] A maximal effort was verified by at least two of the following criteria: maximum heart rate during the test achieving within 10 bpm of age-predicted heart rate maximum; a plateau of oxygen uptake values with increasing intensity; RER greater than or equal to 1.1; blood lactate concentration of greater than or equal to 8 mmol/L.

3.6.7 Lactate Threshold

Lactate threshold was measured during the graded exercise test described above. During the last minute of each three-minute stage, the subject received a small finger stick with a lancet needle. Prior to receiving the finger stick, the tester sanitized and protected her own hands with non-latex gloves, then sanitized the surface of the subject's skin with an alcohol swab, and blotted the area with a sterile gauze pad. After the finger stick, the initial drop of blood was wiped from the finger, so that the second drop of blood was able to be collected on the lactate strip for analysis in the Lactate Pro® analyzer. The Lactate Pro® analyzer gave a digital reading of blood lactate level one minute after the test strip received the drop of blood.

3.6.8 Fatigue Protocol

Day 2 consisted of pre- and post-fatigue TTDPM assessment. The fatigue protocol utilized a circuit design and was performed in the Neuromuscular Research Laboratory. The seven stations in the fatigue protocol consisted of:

Station 1: 5-min run at 95% VO_2 pace

Station 2: 3-min run at 110% VO_2 pace

Station 3: 2-min of push-ups (modified)

Station 4: 2-min of sit-ups (YMCA partial curl-up)

Station 5: 3-min of 12-in step-ups

Station 6: 3-min run at 110% VO_2 pace

Station 7: 2-min run at 115% VO_2 pace

While the original circuit proposed by Wilkins et al[264] utilized a gymnasium floor to perform the running exercises, each running exercise was replicated on the Woodway treadmill within the laboratory using speeds corresponding to 95% (jogging) 110% (sprinting), and 115% (maximal run, Station 7) of the speed utilized during maximal oxygen uptake. The push-ups were performed in the modified position on the subject's knees. The sit-ups were modified to use the YMCA partial curl-up protocol, where the subject began with knees bent at a 30 degree angle and feet placed flat on the ground. Subjects curled up with arms extended until their fingertips reached their knees before returning to the start position. Subjects were encouraged to complete as many modified push-ups, curl-ups, and step-ups as possible during stations 3, 4, and 5 and were encouraged to continue movement throughout the duration of each station. OMNI RPE (RPE-A, RPE-L, RPE-C, RPE-O), heart rate, and lactate levels were measured at the conclusion of each station during a 1-minute break.

If at the end of Station 7 the subject was not volitionally fatigued, the station continued by increasing the incline by 1% each minute until volitional exhaustion. Following Station 7, maximal effort was verified with perceptual (OMNI RPE criteria), and at least one of two physiological (lactate level equal to or above 8.0 mmol/L, or heart rate within 10 bpm of previously determined heart rate max) criteria.

3.7 DATA REDUCTION

Threshold to detect passive motion results were calculated by averaging the first three correctly identified angle error measures in the flexion and extension direction for each test. For the pre- to post-fatigue TTDPM assessments, the average angle error for each direction (flexion and extension) were calculated between pre- and post-fatigue. Isokinetic strength of the quadriceps and hamstrings normalized to body weight (%BW, kg) was determined from a print-out obtained from the Biodex System 3 Dynamometer following strength assessment. Flexion/extension ratios were calculated by dividing the average normalized peak flexion torque by the average normalized peak extension torque. Post-test analysis determined VO_2 max by applying a 15-second filter to the breath-by-breath data and exporting the file to Microsoft Excel. Then, oxygen uptake values were plotted to determine the minute of data with the four highest consecutive points. These points were then averaged to determine VO_2 max normalized to body weight (ml/kg/min). Post-test analysis determined the stage at which lactate threshold occurred by plotting each lactate value in a line graph. Lactate threshold was determined using two methods: the lactate level occurring prior to a greater than 1 mmol/L increase with increasing intensity and by best visual determination of best fit inflection point on the line graph plotted. Then, the minute-average oxygen uptake at the end of the corresponding stage was calculated and divided into VO_2 max in order to quantify lactate threshold (% of VO_{2max}).

3.8 DATA ANALYSIS

Data was first assessed for normality. Descriptive data was reported as mean ± standard deviation (SD) if normality was assumed and as median and interquartile range if assumptions were violated. If assumptions of normality were met, Pearson correlation coefficients were calculated for each relationship described in the Specific Aims. If assumptions of normality were violated, Spearman's Rho correlation coefficients were calculated instead. Baseline musculoskeletal and physiological characteristics were also correlated with pre-fatigue TTDPM. Additional analyses were conducted in order to assess significant changes from pre- to post-fatigue TTDPM in each direction, as well as significant changes in isometric quadriceps strength, hamstring strength, and quadriceps/hamstring ratio from pre- to post-fatigue (T-test if normality assumed, Mann Whitney-U or Wilcoxon Signed Rank test if normality violated).

4.0 RESULTS

The purpose of this study was to investigate the relationship between baseline measures of isokinetic knee strength and physiological characteristics with threshold to detect passive motion (TTDPM) of the knee following a fatiguing exercise protocol.

4.1 SUBJECTS

4.1.1 Demographic Data

A total of 25 female subjects expressed interest in study participation, and 22 met all eligibility criteria outlined in the initial phone screen. Twenty female subjects enrolled in the study and completed data collection and two did not enroll due to scheduling conflicts. Power analysis for the significant correlations described above revealed that 20 subjects would be needed to complete data collection, and a total of 20 females meeting all eligibility criteria participated in all study activities.

Subject demographics are presented in Table 1. The age range of study participants was 20-36 years old. Of the twenty participants, 17 fell within the BMI category for normal weight, and three subjects fell within the overweight category.[97] Of the 20 participants, six fell in the "Well Above Average" classification for Body Fat% according to age and gender as outlined by

the American College of Sports Medicine,[68] four were "Above Average," four were "Average," four were "Below Average," and two were "Well Below Average." For reference, with the body fat classification, "Above Average" indicates the subject had a lower body fat, while "Below Average" indicates a subject had higher body fat. All subjects were right leg dominant, defined as the leg used to kick a ball as hard as possible, so all strength and proprioception data were collected on the right leg.

Table 1. Demographic Data

	Mean		SD	Median	LQ	UQ
Age	28.7	±	5.6	28.5	23.5	28.5
Height (cm)	165.6	±	4.3	165.5	161.7	166.7
Weight (kg)	61.8	±	8.0	60.4	56.5	63.6
BMI (kg/m2)	22.5	±	2.3	22.1	20.9	23.3
Body Fat (%)	23.3	±	5.4	22.4	21.7	27.7

LQ = Lower Quartile
UQ = Upper Quartile

4.1.2 Exercise History and Dietary Recall

Exercise history was collected in order to quantify the type of training subjects participated in. Dietary recall was collected in order to obtain a sample of total intake and macronutrient distribution. Individual results of the exercise history questionnaire and ASA24 Dietary Recall are presented in Appendix A. Data presented below represent mean ± standard deviation.

Exercise History Questionnaire

Results of the exercise history questionnaire revealed that the subjects participate in a wide range of activities. Seventeen of the 20 subject participated in high school athletics and 4 participated in collegiate athletics. On a 1-5 scale, with 1 being lowest and 5 being highest, subjects rated their overall athletic ability as 3.8±0.6, competitiveness as 3.6±1.1, cardiovascular fitness as 3.8±0.8, muscular strength as 3.7±0.7, and flexibility as 3.1±0.8.

Nineteen out of 20 subjects reported participating in endurance activities 5.3±1.0 days per week for 46.7±12.1 minutes per session at an exertion level of 3.7±0.6 on a 1-5 scale. Sixteen out of 20 subjects reported participating in strength training 4.1±1.5 days per week for 36.7±15.0 minutes per session at an exertion level of 3.7±0.8 on a 1-5 scale.

Dietary Recall

Subjects consumed 1913.1±738.3 kcal for total daily intake, with approximately 17.0±5.4% of daily intake from protein, 30.5±9.4% from fat, and 50.6±14.0 from carbohydrate. Subjects consumed 79.1±38.1 g (1.3±0.6g/kg) of protein, 62.9±27.3 g (1.0±0.4 g/kg) of fat, and 246.7±123.882 g (4.1±2.0 g/kg) carbohydrate.

4.2 MUSCULOSKELETAL STENGTH AND PHYSIOLOGICAL CHARACTERISTICS

4.2.1 Isokinetic Strength Data

Baseline isokinetic strength assessment results are presented in Table 2. Peak isokinetic knee extension and knee flexion strength are reported as the average peak torque produced across five

trials of reciprocal concentric contractions at 60°/second in absolute terms and normalized to body weight (kg).

Table 2. Isokinetic Strength Data

	Mean		SD	Median	LQ	UQ
Quad Strength (Nm)	134.7	±	22.8	140.8	110.6	146.1
Quad Strength (%BW)	219.3	±	31.6	223.8	178.5	238.1
Ham Strength (Nm)	67.4	±	13.7	65.2	54.5	69.1
Ham Strength (%BW)	109.8	±	19.7	112.4	92.4	115.5
Flex/Ext Ratio	0.50	±	0.06	0.52	0.46	0.52

LQ = Lower Quartile
UQ = Upper Quartile
Quad Strength = Average peak torque produced over 5 trials
Ham Strength = Average peak torque produced over 5 trials

4.2.2 Aerobic Capacity and Lactate Threshold Data

Results of aerobic capacity and lactate threshold assessment are presented in Table 3. Peak oxygen uptake (VO_2 Peak) was reported instead of maximal oxygen uptake because not all subjects met the physiological criteria for a maximum test. Peak oxygen uptake was defined as the highest, 15-second interval of VO_2 data collected during the test. According to normative maximal anaerobic power data by age and gender,[97] 16 subjects fell within the 90th percentile, two within the 80th percentile, one within the 70th percentile, and one within the 60th percentile. Lactate threshold values, calculated by both the point before a 1mmol increase and by the point of noticeable inflection point, were reported as a percent of VO_2 Peak.

Table 3. Physiological Characteristics

	Mean		SD	Median	LQ	UQ
VO2 Peak (ml/kg/min)	47.1	±	4.6	48.2	43.4	49.7
HR Peak (bpm)	187.8	±	11.1	185.0	179.0	200.5
Lactate Peak (mmol)	8.8	±	2.0	8.8	7.4	10.0
RPE-L at end stage	8.0	±	1.8	8.5	7.5	9.0
RPE-A at end stage	6.2	±	2.2	6.5	5.0	8.0
RPE-C at end stage	8.5	±	1.2	9.0	8.0	9.0
RPE-O at end stage	8.7	±	0.8	9.0	8.5	9.0
Lactate at LT, 1 mmol (mmol)	3.2	±	0.9	3.0	2.5	3.5
VO2 at LT, 1 mmol (ml/kg/min)	38.0	±	5.6	38.3	33.9	41.5
LT, 1 mmol (%VO2peak)	80.4	±	7.1	81.2	77.5	83.5
HR at LT, 1 mmol (bpm)	173.0	±	14.4	173.3	163.8	186.9
Lactate at LT, inflecion (mmol)	4.1	±	0.8	4.1	3.7	4.5
VO2 at LT, inflection (ml/kg/min)	40.3	±	5.3	39.8	36.3	44.4
LT, inflection (%VO2peak)	85.4	±	4.8	85.5	84.1	87.9
HR at LT, inflecion (bpm)	176.9	±	11.8	175.6	170.7	188.8
Test Speed (mph)	6.5	±	0.6	6.5	6.3	6.7
End Time (m.s)	12.6	±	2.3	13.0	12.3	14.8

LQ = Lower Quartile
UQ = Upper Quartile
VO2 Peak = Peak Oxygen Uptake (15-second interval)
HR Peak = Peak Heart Rate (15-second interval)
RPE-L = OMNI Rating of Perceived Exertion, Legs
RPE-A = OMNI Rating of Perceived Exertion, Arms
RPE-C = OMNI Rating of Perceived Exertion, Chest
RPE-O = OMNI Rating of Perceived Exertion, Overall Body
VO2 at LT = Oxygen Uptake at Lactate Threshold
LT, 1 mmol = Lactate Threshold determined before 1 mmol increase in blood lactate
HR at LT = Heart Rate at Lactate Threshold
LT, inflection = Lactate Threshold determined at point of visible threshold

4.3 PRE- TO POST-FATIGUE TTDPM AND ISOMETRIC STRENGTH

4.3.1 Fatigue Protocol Results

Results of the fatigue protocol are displayed in Table 4. Fatigue was quantified by perceptual and physiological assessments following each station. As a group, subjects reached near-maximal perceived exertion in their legs, chest, and overall, reached above maximal criteria for blood lactate (>8.0 mmol), and reached within 10 bpm of age-predicted heart rate max.

Table 4. Fatigue Protocol Results

	Station 1 Run		Station 2 Run		Station 3 Push-ups		Station 4 Sit-ups		Station 5 Step-ups		Station 6 Run		Station 7 Run	
	Mean	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**	**Mean**	**SD**
Time (min)	5.0	± 0.0	3.0	± 0.0	2.0	± 0.0	2.0	± 0.0	3.0	± 0.0	3.0	± 0.0	4.9	± 1.8
Speed (mph)	6.2	± 0.6	7.2	± 0.7	--	--	--	--	--	--	7.2	± 0.7	7.5	± 0.7
Performance (#)	--	--	--	--	59.6	± 15.5	71.0	± 11.2	108.8	± 18.8	--	--	--	--
Lactate (mmol)	2.9	± 1.6	3.7	± 1.3	5.6	± 1.4	6.2	± 1.3	6.8	± 1.9	7.1	± 2.3	8.3	± 2.4
Heart Rate (bpm)	151.8	± 12.1	168.9	± 11.8	133.7	± 17.5	120.7	± 25.0	169.4	± 15.8	174.8	± 12.3	181.8	± 11.3
RPE-L	2.9	± 1.2	4.2	± 1.3	3.2	± 1.5	3.1	± 1.8	6.8	± 1.4	6.7	± 1.4	8.4	± 1.5
RPE-A	2.0	± 1.0	3.0	± 1.3	7.4	± 1.0	4.8	± 1.9	4.4	± 2.2	5.1	± 2.0	7.1	± 2.2
RPE-C	3.1	± 1.0	4.5	± 1.1	5.4	± 2.1	5.3	± 1.4	6.7	± 1.4	7.1	± 1.2	9.4	± 0.5
RPE-O	2.9	± 1.2	4.5	± 0.9	6.2	± 1.3	5.7	± 1.3	6.8	± 1.5	7.0	± 1.2	9.1	± 0.8

Station 1 = 95% VO2max pace

Station 2 = 110% VO2max pace

Station 6 = 110% VO2max pace

Station 7 = 115% VO2max pace, 1% incline each additional minute beyond 2 minutes

RPE-L = OMNI Rating of Perceived Exertion, Legs

RPE-A = OMNI Rating of Perceived Exertion, Arms

RPE-C = OMNI Rating of Perceived Exertion, Chest

RPE-O = OMNI Rating of Perceived Exertion, Overall Body

4.3.2 Threshold to Detect Passive Motion

Threshold to detect passive motion (TTDPM) was measured during Visit 2 prior to and immediately following the fatiguing exercise protocol. Ten trials were collected, with five trials each randomized into extension and flexion. The first three trials in extension and flexion with correctly identified direction averaged for analysis. Results from pre- and post-fatigue TTDPM are presented in Table 5. Pre- to post-fatigue TTDPM differences in extension and flexion violated the assumptions of normality when assessed with a Shapiro-Wilk test, so nonparametric analyses were utilized to determine significant differences between pre- to post-fatigue TTDPM scores. No significant differences were demonstrated between pre- and post-fatigue average angle error difference during TTDPM into either extension of flexion. Mean and median results are presented as the error from starting position, with all extension results being positive, and all flexion results being negative.

Table 5. Pre- to Post-Fatigue TTDPM Changes

	Pre-Fatigue					Post-Fatigue					Pre-Post
	Mean	**SD**	**Median**	**LQ**	**UQ**	**Mean**	**SD**	**Median**	**LQ**	**UQ**	**p-value**
TTDPM Ext (°)	1.54	± 0.96	1.33	0.76	2.02	1.54	± 0.77	1.53	0.90	1.90	0.65
TTDPM Flex (°)	-1.52	± 1.09	-1.05	-1.82	-0.94	-1.51	± 1.51	-2.27	-2.02	-0.83	0.48

Wilcoxon Signed Rank Test utilized to determine significant differences from pre- to post-fatigue

TTDPM Ext (°) = Average of first three correct trials in extension

TTDPM Flex (°) = Average of first three correct trials in flexion

4.3.3 Pre- to Post-Fatigue Isometric Strength Characteristics

Isometric strength of the quadriceps and hamstrings was measured in order to demonstrate fatigue of the knee musculature following the fatigue protocol. Isometric strength was measured at 45° knee flexion as was measured in a reciprocal extension/flexion format, where subjects maximally extended and maximally flexed their knee for 5 seconds over 3 trials, with a 5-second break between each direction and each trial. Data are reported as the average peak torque produced across the three trials in each direction normalized to body weight (kg). Pre- to post-fatigue isometric extension strength, flexion strength, and flexion/extension strength ratio differences violated the assumptions of normality when assessed with a Shapiro-Wilk test, so nonparametric analyses were utilized to detect significant differences between strength measures from pre-fatigue to post-fatigue. Isometric quadriceps strength was not significantly different after the fatigue protocol, while isometric hamstring strength and flexion/extension ratio significantly decreased following the fatigue protocol. Results are displayed in Table 6.

Table 6. Pre- to Post-Fatigue Isometric Strength

	Pre-Fatigue					Post-Fatigue					Pre-Post
	Mean	SD	Median	LQ	UQ	Mean	SD	Median	LQ	UQ	p-value
Quad Strength (%BW)	217.3	± 47.7	213.5	178.4	249.6	214.1	± 42.4	200.3	180.3	256.1	0.681
Ham Strength (%BW)	116.9	± 25.3	115.2	106.2	128.0	105.5	± 24.4	109.2	88.4	128.5	0.004**
Flex/Ext Ratio	0.55	± 0.11	0.54	0.49	0.60	0.50	± 0.10	0.50	0.41	0.58	0.012*

Wilcoxon Signed Rank Test utilized to determine significant differences from pre- to post-fatigue

Quad Strength = Average peak isometric strength over 3, 5-second trials

Ham Strength = Average peak isometric strength over 3, 5-second trials

**Significantly different at the P<0.01 level *Significantly different at the P<0.05 level

4.4 RELATIONSHIP BETWEEN MUSCULOSKELETAL STRENGTH, PHYSIOLOGICAL CHARACTERISTICS, AND TTDPM

All variables in the correlation analyses were tested for normality utilizing a Shapiro-Wilk test. The following variables violated assumptions of normality: lactate threshold calculated at the point before 1mmol lactate increase, pre-fatigue TTDPM in extension, pre-fatigue TTDPM in flexion, post-fatigue TTDPM in flexion, pre- to post-fatigue TTDPM difference in extension and flexion, and percent change from pre- to post-fatigue TTDPM in extension and flexion. Therefore, Spearman's Rho correlation coefficients were calculated for all correlations analyses. Although post-fatigue TTDPM in the extension direction was normally distributed, results of Pearson correlation coefficient agree with the Spearman's Rho correlation in both significance and direction, so Spearman's Rho correlations are reported for all variables to maintain consistency.

4.4.1 Isokinetic Strength and TTDPM Correlation Analysis

A Spearman's Rho test was utilized to calculate correlation coefficients between isokinetic strength measured during Visit 1 and pre- to post-fatigue TTDPM differences (ΔTTDPM) assessed during Visit 2. Results of this correlation analysis are presented in Table 7. No significant correlations were observed between isokinetic knee extension strength, flexion strength, or flexion/extension ratio with ΔTTDPM from pre- to post-fatigue in extension or flexion.

Table 7. Isokinetic Strength (%BW) and ΔTTDPM (°) Correlation Analysis

	Pre- to Post- Fatigue TTDPM			
	Extension		Flexion	
	r	p-value	r	p-value
Quad Strength (%BW)	0.019	0.937	-0.162	0.496
Ham Strength (%BW)	0.065	0.784	-0.005	0.982
Flex/Ext Ratio	0.236	0.316	0.202	0.394

Quad Strength = Average peak torque produced over 5 trials
Ham Strength = Average peak torque produced over 5 trials

Correlation coefficients were also calculated to determine the relationship between isokinetic strength variables and pre-fatigue and post-fatigue TTDPM values in extension and flexion. No significant correlations were observed between isokinetic knee extension strength, flexion strength, or flexion/extension ratio with pre-fatigue or post-fatigue TTDPM values in extension or flexion, with the exception of a significant, negative correlation between knee flexion/extension ratio and pre-fatigue TTDPM in extension. Results of these analyses are presented in Tables 8 and 9.

Table 8. Isokinetic Strength (%BW) and Pre-Fatigue TTDPM (°) Correlation Analysis

	Pre-Fatigue TTDPM			
	Extension		Flexion	
	r	p-value	r	p-value
Quad Strength (%BW)	-0.194	0.412	0.069	0.774
Ham Strength (%BW)	-0.199	0.401	0.017	0.942
Flex/Ext Ratio	-0.231	0.024*	0.024	0.920

Quad Strength = Average peak torque produced over 5 trials
Ham Strength = Average peak torque produced over 5 trials
*Significant correlation at the P<0.05 level

Table 9. Isokinetic Strength (%BW) and Post-Fatigue TTDPM (°) Correlation Analysis

	Post-Fatigue TTDPM			
	Extension		Flexion	
	r	p-value	r	p-value
Quad Strength (%BW)	-0.138	0.561	-0.003	0.990
Ham Strength (%BW)	-0.138	0.561	-0.082	0.731
Flex/Ext Ratio	-0.152	0.523	0.016	0.947

Quad Strength = Average peak torque produced over 5 trials
Ham Strength = Average peak torque produced over 5 trials

4.4.2 Physiological Characteristics and TTDPM Correlation Analysis

A Spearman's Rho test was utilized to calculate correlation coefficients between VO_2 Peak (ml/kg/min), lactate threshold calculated using the 1mmol increase (% VO_2 Peak) criteria, and lactate threshold calculated using the noticeable inflection (% VO_2 Peak) criteria measured

during Visit 1 and TTDPM (°) measured prior to and following the fatigue protocol during Visit 2. Results of the physiological characteristics and pre- to post-fatigue ΔTTDPM correlation analysis are found in Table 8. No significant correlations were observed between VO_2 Peak and change in TTDPM from pre- to post-fatigue in in extension or flexion.

Lactate threshold calculated at the point prior to a 1 mmol increase in lactate concentration was not significantly correlated with absolute pre- to post-fatigue TTDPM difference in extension or flexion. No significant correlations were found between lactate threshold calculated by noticeable inflection point and change in TTDPM post-fatigue.

Table 10. Physiological Characteristics and ΔTTDPM (°) Correlation Analysis

	Pre- to Post- Fatigue TTDPM			
	Extension		Flexion	
	r	p-value	r	p-value
VO2 Peak (ml/kg/min)	0.281	0.230	0.256	0.276
LT, 1mmol (%VO2peak)	0.344	0.137	-0.357	0.123
LT, inf (%VO2peak)	0.152	0.523	-0.153	0.520

VO2 Peak = Peak Oxygen Uptake (15-second interval)
LT, 1mmol = Lactate Threshold determined before 1 mmol increase in blood lactate
LT, inf = Lactate Threshold determined at point of visible threshold
*Significant correlation at the P<0.05 level

Physiological characteristics were also correlated with pre-fatigue and post-fatigue TTDPM values in extension and flexion. A significant correlation was observed between VO_2 Peak and both pre-fatigue and post-fatigue TTDPM in the extension direction, indicating that subjects with higher aerobic capacity had better TTDPM in the extension direction prior to and following the fatigue protocol. No significant correlations were found between VO_2 Peak and

pre-fatigue or post-fatigue TTDPM in the flexion direction. No significant correlations were found between lactate threshold calculated at 1mmol increase or calculated by noticeable inflection point for pre-fatigue TTDPM, post-fatigue TTDPM. Results of these analyses are presented in Tables 11 and 12.

Table 11. Physiological Characteristics and Pre-Fatigue TTDPM (°) Correlation Analysis

	Pre-Fatigue TTDPM			
	Extension		Flexion	
	r	p-value	r	p-value
VO2 Peak (ml/kg/min)	-0.500	0.005**	0.172	0.467
LT, 1mmol (%VO2peak)	-0.087	0.717	0.077	0.748
LT, inf (%VO2peak)	-0.084	0.726	0.102	0.667

VO2 Peak = Peak Oxygen Uptake (15-second interval)
LT, 1mmol = Lactate Threshold determined before 1 mmol increase in blood lactate
LT, inf = Lactate Threshold determined at point of visible threshold
**Significant correlation at the P<0.01 level

Table 12. Physiological Characteristics and Post-Fatigue TTDPM (°) Correlation Analysis

	Post-Fatigue TTDPM			
	Extension		Flexion	
	r	p-value	r	p-value
VO2 Peak (ml/kg/min)	-0.520	0.019*	0.279	0.233
LT, 1mmol (%VO2peak)	0.118	0.620	-0.205	0.385
LT, inf (%VO2peak)	-0.028	0.907	-0.084	0.726

VO2 Peak = Peak Oxygen Uptake (15-second interval)

LT, 1mmol = Lactate Threshold determined before 1 mmol increase in blood lactate

LT, inf = Lactate Threshold determined at point of visible threshold

*Significant correlation at the P<0.05 level

5.0 DISCUSSION

The purpose of this study was to investigate the relationship between musculoskeletal strength and physiological characteristics with changes in TTDPM following fatiguing exercise. Physically active females participated in isokinetic knee strength testing, aerobic capacity, and lactate threshold assessments during Visit 1 and underwent TTDPM assessment prior to and immediately following a fatiguing exercise protocol during Visit 2. A correlation analysis was performed to examine the relationships between isokinetic strength, aerobic capacity, and lactate threshold with changes in TTDPM following the fatigue protocol.

It was hypothesized that isokinetic knee extension strength, isokinetic knee flexion strength, maximal oxygen uptake, and lactate threshold would have a significant, negative correlation with changes in TTDPM in extension and flexion following fatiguing exercise, meaning subjects with higher levels of strength, aerobic capacity, and lactate threshold would see less deficits in TTDPM following fatiguing exercise. Our hypotheses were rejected, as there were no statistically significant correlations between any strength or physiological variables and changes in TTDPM from pre- to post-fatigue. Subject characteristics, independent and dependent variables, research hypotheses, other analyses, limitations, and future directions are discussed in the sections below.

5.1 QUESTIONNAIRES

5.1.1 Exercise History Questionnaire

An Exercise History Questionnaire was administered in order to identify the type and quantity of training subjects participated in. Most subjects reported regular participation in strength and endurance exercise. Some subjects were primarily endurance athletes, while others were primarily anaerobic/strength athletes. Overall, based on the Exercise History Questionnaire, the sample was a good representation of a highly physically active group of females, which was the intent of subject recruitment.

5.1.2 ASA24 Dietary Recall

A 24-hour dietary recall was administered in order to obtain an example of the typical diet of the subjects and to determine macronutrient and total energy intake of the subjects. A deficit in total energy intake and suboptimal macronutrient intake and distribution has been shown to adversely affect performance[52] and may contribute to early onset fatigue. Results showed that total caloric intake and macronutrient distribution was varied among subjects, and many subjects under-consumed total energy and carbohydrates during the 24 hours prior to data collection. Previous work has recommended a total daily intake of 45-50 kcal per body weight for female athletes participating in 90 minutes of training per day.[69] Although some subjects in this investigation reported working out less than 90 minutes per session, the average kcal per body weight consumed was 31.1 kcal/kg (range 16.5 – 58.5 g/kg), which is much lower than the recommendation. In the American College of Sports Medicine's position stand on the female

athlete triad,[184] adverse effects of under-consuming energy typically occurs when consumption is less than 30 kcal per kg of fat free mass (FFM). In our investigation, average kcal per kg FFM was 41.0 kcal/kgFFM (range 21.3 – 83.0 kcal/kgFFM), so while most subjects met the minimum recommendation, there were a few consuming a risky low level of kcals per FFM. This did not appear to affect fatigue protocol performance, as reported energy intake had no significant linear relationship with time to fatigue when assessed with Spearman's Rho correlation calculation (r=-0.289, P=0.217).

Previous research on optimal nutrition of athletes suggests that carbohydrate intake of athletes should be approximately 8 to 10 g/kg bodyweight or 60 to 70% of total energy intake.[52] Results of this study revealed that subjects consumed an average of ~4.1 g/kg carbohydrate (range of 0.8 – 7.8 g/kg) which accounted for ~50.6% total intake (range of 18.2% - 73.3%), indicating that subjects did not meet the suggested consumption for athletes, and that many subjects had a drastically low carbohydrate intake. However, carbohydrate intake did not appear to affect fatigue protocol performance, as reported carbohydrate per kg intake had no significant linear relationship with time to fatigue when assessed with Spearman's Rho correlation calculation (r=-0.252, P=0.284). Further, researchers recommend that healthy adults[146] and athletes with large energy needs[69] should consume approximately 30% of their daily intake from fat, and the average percent of total daily intake of fat in this investigation was 30.5% (range 17.2% - 41.9%), and variance of fat intake level would not likely have a significant impact performance on the fatigue protocol.

5.2 MUSCULOSKELETAL STRENGTH AND PHYSIOLOGICAL CHARACTERISTICS

5.2.1 Isokinetic Strength

Knee extension strength, flexion strength, and flexion/extension ratio were evaluated with an isokinetic dynamometer in order to evaluate the relationship between knee strength characteristics and the effect of fatigue of TTDPM. Isokinetic knee flexion and extension strength were collected on the dominant limb at 60°/s, demonstrating peak knee extension strength of 219.3 ± 31.6 %BW and peak knee flexion strength of 109.8 ± 19.7 % BW. The strength data of the current subjects was higher when compared to strength data collected on 101st Airborne (Air Assault) female Soldiers utilizing the same protocol (right peak knee extension: 191.30 ± 37.16 %BW, left peak knee extension: 178.18 ± 38.19 %BW; right peak knee flexion: 92.98 ± 21.05 BW%, left peak knee flexion: 88.82 ± 20.80 %BW), but comparable data to triathletes tested using the same methodology, who likely have a more similar training history to our subjects (right peak knee extension: 216.53 ± 21.68 %BW, left peak knee extension: 213.38 ± 34.71 %BW; right peak knee flexion: 115.47 ± 15.44 BW%, left peak knee extension: 113.96 ± 14.88 %BW).[229] Results of the current study were also similar to female data from a study examining gender differences in strength in Division I athletes utilizing the five isokinetic concentric knee flexion and extension repetitions at 60°/s on the dominant limb (peak knee extension: 222.93 ± 30.86 %BW, peak knee flexion: 113.74± 23.66 %BW) .[160] Since the strength data collected in this study are reasonably similar to previous research in physically active and highly trained females and these methods have been demonstrated to be reliable, we

can conclude that the results of strength testing on the current group of subjects are representative of their strength within the context of the current testing protocol.

5.2.2 Aerobic Capacity and Lactate Threshold

In order to investigate the relationship between aerobic capacity and changes in TTDPM following fatiguing exercise, oxygen uptake was assessed during a graded treadmill running test while inspired and expired gases were measured via a mask connected to metabolic equipment. Because few subjects in this investigation reached true, physiological VO_2 max based on the outlined maximal criteria (meeting two of the following three criteria: final lactate at or above 8.0 mmol, RER at or above 1.08, heart rate within 10 bpm of age predicted maximum), VO_2 Peak was reported instead, defined as the highest VO_2 value achieved during a 15-second interval of data collection. Mean VO_2 Peak of our subjects was 47.1 ± 4.6 ml/kg/min. Our data revealed higher results compared to VO_2 data collected utilizing the same methodology on female 101st Airborne (Air Assault) Soldiers (VO_2 max: 40.29 ± 5.37 ml/kg/min) and lower data when compared to elite female triathletes (61.15 ± 5.44 ml/kg/min).[229] Mean VO_2 Peak achieved in this investigation is comparable to results from a study examining VO_2 max in Division I female Lacrosse players utilizing a Bruce protocol (VO_2 max: 45.7 ± 4.9 ml/kg/min)[73] and results from a study examining pre- and post-season VO_2 Peak in Division I women's soccer (42 and 50 ml/kg/min pre- to post-season, respectively).[49] Since our data are reasonably comparable to other data examining aerobic capacity in athletes and highly trained individuals and our methods have been demonstrated to be reliable, we can conclude that the VO_2 Peak results of the current group of subjects are representative of their aerobic capacity within the context of the current testing protocol.

Lactate threshold was assessed by collecting small drops of blood via finger stick during the final 30 seconds of each 3-minute stage of the graded treadmill exercise test. These values were plotted against the VO_2 values obtained during the final minute of each stage. Lactate threshold is a highly debated concept, and many methods have been established to determine lactate threshold.[250] Since the calculation is often variable amongst individuals, we decided to calculate lactate threshold by using two different methods: 1) the final stage prior to a greater than 1.0 mmol increase in blood lactate and 2) the stage at which a visible inflection point was noticed on the plotted lactate curve. Results revealed a lactate threshold of 80.4 ± 7.1 %VO_2 Peak and 85.4 ± 4.8 %VO_2 Peak when calculated by the two methods, respectively, which is comparable to previous findings calculated by the noticeable inflection point in female 101st Airborne (Air Assault) Soldiers (82.16 ± 13.97 % VO_2 max) and elite female triathletes (88.38 ± 6.57 % VO_2 max).[229] Since our data are reasonably comparable to other data examining lactate threshold in athletes and highly trained individuals and our methods have been demonstrated to be reliable, we can conclude that the results of lactate threshold testing on the current group of subjects are representative of their lactate threshold within the context of the current testing protocol.

5.3 PRE- TO POST-FATIGUE TTDPM

Threshold to detect passive motion was assessed prior to and immediately following a fatiguing exercise protocol. For this assessment, 10 trials were performed with 5 randomized into extension and 5 into the flexion direction. Threshold to detect passive motion and direction was utilized because the ability to detect direction as well as motion is a more specific measurement

of knee proprioception.[20, 23, 162, 218] If direction was incorrectly identified by the subject, the trial was thrown out and the direction repeated. The first three correctly identified trials in each direction were averaged for analysis, which is consistent with methods utilized in previous research.[159, 226] No significant differences were demonstrated in changes in TTDPM from pre- to post-fatigue in either extension or flexion.

The fatigue protocol utilized in this study was chosen because it simulated fatigue mechanisms that would have been experienced in a game or practice situation. The design of the protocol included stations involving aerobic activity, upper body and core strength and endurance, and isolated fatigue of the major muscles of the lower extremity. We quantified fatigue production by assessing levels of perceived exertion in the legs, arms, chest, and overall body following each station, as well as quantifying performance, heart rate, and lactate levels following each station. Subjects experienced near maximum levels of perceived exertion (7-10 on OMNI RPE) and reached maximal physiological criteria (>8.0 mmol blood lactate concentration and within 10 bpm of age-predicted heart rate max) during the protocol. In order to quantify muscular fatigue following the fatigue protocol, isometric strength of the quadriceps and hamstrings was measured in reciprocal format during three maximal trials of extension and flexion following pre-fatigue and post-fatigue TTDPM assessment. Results demonstrated a significant decrease in isometric flexion strength and flexion/extension ratio, indicating that the hamstring musculature strength decreased as a result of the fatigue protocol.

Results of our study are consistent with results from a study by Skinner et al[238] which also found no significant differences in knee kinesthesia following fatigue. Skinner et al[238] also utilized a homogenous, highly trained group for testing, and used a fatigue protocol consisting of a series of running intervals, beginning with a 2-mile warm-up and continuing with alternating 1-

mile and ¼ mile intervals with a 90-s rest. Then, subjects ran on a treadmill at 7 mph at 15% incline. The protocol utilized by Skinner et al[238] had similar aspects of our fatigue protocol, but did not specifically fatigue the upper body or core. In order to determine level of fatigue, Skinner et al[238] tested isokinetic strength prior to and following the fatigue protocol, and if subjects did not exceed 10% decrement in work output, they were given additional treadmill exercise. Their TTDPM measurement was conducted at 0.5°/s angular velocity, which is faster than our speed of 0.25°/s, but still aimed to target the slow-adapting mechanoreceptors (Ruffini endings or Golgi-type organs)[165] found within the ligamentous and capsular tissues of the knee.[217] Results demonstrated a decreased ability to reproduce a joint angle, but no significant differences were demonstrated in TTDPM following fatigue. Additionally, post-fatigue TTDPM angle error was less than before fatigue, suggesting improved TTDPM following fatigue. In agreement with results from our study, Skinner et al[238] suggested that the absence of decreased TTDPM and non-significant improvement in TTDPM may have occurred because capsular receptors may become more strongly stimulated due to decreased muscular receptor function following fatigue.[238, 248] Authors also suggested that there is an increased response rate of capsular receptors when the capsule is maximally stressed, which may actually lower the threshold for detection of passive motion.[101, 102, 238]

Our results are partially consistent with results from a study by Rozzi and colleagues[226] which demonstrated no significant changes in proprioception in the flexion direction but significant changes in the extension direction following fatigue. The investigation by Rozzi et al[226] utilized isolated concentric contractions of the quadriceps and hamstring, which may have resulted in decreased proprioception in the extension direction due to the cyclic compressive forces to the knee joint during the isokinetic fatigue protocol. Like Skinner et al,[238] Rozzi et al[226]

moved the knee at a constant angular velocity of 0.5°/s during TTDPM. Since changes to capsuloligamentous structures of the knee following fatigue would likely induce impaired TTDPM, Rozzi et al[226] also measured joint laxity changes following fatigue. However, the decrease in TTDPM in extension occurred despite no changes in joint laxity following fatigue. Authors concluded that a mechanism other than joint laxity was responsible for the decrements in TTDPM,[226] and that isokinetic fatigue did not induce fatigue that would closely simulate joint forces experienced during sport activities.[140] Unlike Rozzi et al,[226] we did not quantify changes in joint laxity from pre- to post-fatigue, so we are, unfortunately, unable to discuss to what extent joint laxity affected our results. Rozzi et al[226] also demonstrated significantly increased onset of contraction time for the medial hamstring muscle and lateral gastrocnemius muscle following fatigue.[226] Although we did not assess muscle activation as part of this study, our results showed significant decreases in isometric knee flexion strength and flexion/extension ratio which parallels the decreased activation of the hamstring musculature following fatigue demonstrated by Rozzi et al.[226] The decreased hamstring strength and flexion/extension ratio following fatigue in our investigation also suggests a similar implication for decreased ability of the hamstring musculature to control anterior tibial translation in a fatigued state, which was also implied by Rozzi et al.[226]

In recent work by Torres and colleagues[256] investigating TTDPM prior to and following exercise at 30 and 70 degrees of knee flexion, no significant differences were found at a 30 degree starting angle one hour after exercise, while TTDPM was altered at the 70 degree starting position one hour post exercise and up to 24 hours post exercise. The investigation by Torres[256] utilized reciprocal eccentric contractions of the knee musculature to induce fatigue. Repeated eccentric contractions likely induced a degree of muscle damage and delayed onset muscle

soreness,[14] which may explain why deficits in TTDPM at the 70 degree starting position were noticed up to 24 hours post-exercise. Additionally, the deficits were only noticed when the starting position was closer to mid-range than end-range of knee flexion, suggesting that TTDPM deficits may be more pronounced when starting at mid-range, where sensitivity of detecting passive motion may be decreased in comparison to end range. Likewise, the starting angle used in our study was 20 degrees of knee flexion, which is near end-range. Previous work demonstrated that TTDPM was more sensitive at a 15 degree starting angle than 45 degrees in the extension direction,[40, 163] and this may be explained by the fact that a 15 degree starting angle is closer to end range of motion where greater tensile stress is placed on the static restraints of the knee. Thus, our results may have shown significant changes in TTDPM had we utilized a starting position closer to mid-range of knee flexion rather than near end-range because the sensitivity of TTDPM may have been too high closer to end-range.

5.3.1 Isokinetic Strength and TTDPM

Isokinetic knee extension strength, knee flexion strength, and flexion/extension ratio were measured to assess the relationship between baseline knee strength and changes in knee proprioception following fatiguing exercise. No significant correlations were found between knee extension strength, knee flexion strength, or flexion/extension ratio and changes in TTDPM in extension or flexion following the fatiguing exercise protocol. Additionally, no significant correlations were revealed between strength measures and pre-fatigue TTDPM or post-fatigue TTDPM.

While previous research has investigated both muscular strength and proprioception with regard to injury prevention and rehabilitation,[105, 220, 257, 259] no study to the author's knowledge has correlated baseline strength measurements to proprioception changes following fatigue. One explanation for the absence of correlation between isokinetic strength variables and changes in TTDPM following fatigue may be because there were no significant changes in TTDPM following fatigue, which may have been due to the overall high strength values demonstrated by our subjects. Previous work has suggested that subjects with better muscle development may also have a better awareness of joint position and motion.[20, 159] Therefore, it is possible that subjects in this investigation had an overall enhanced ability to detect passive motion both before and after fatigue, which may explain why there were no changes in TTDPM following fatigue. This idea is further evidenced by the fact that knee flexion/extension strength ratio had a significant, low,[61] negative correlation with pre-fatigue TTDPM in extension, indicating that subjects with a better flexion/extension ratio also had better pre-fatigue TTDPM.

Another possibility is that another measurement of muscle strength or endurance may have a stronger relationship with changes in proprioception following fatigue. In our investigation, changes in isometric hamstring strength from pre- to post-fatigue were significantly correlated with changes in pre- to post-fatigue TTDPM in extension ($r=-0.403$, $p=0.039$) and flexion ($r=-0.616$, $p=0.002$), and changes in isometric flexion/extension strength ratio were significantly correlated with changes in pre- to post-fatigue TTDPM in flexion ($r=-0.439$, $p=0.026$). As evidenced by these findings, perhaps baseline strength measures are not as important as the ability to retain strength and maintain an optimal flexion/extension strength ratio in a fatigued state.

Another explanation for the lack of significant correlation may be that the mode of proprioception utilized was a passive measurement, which attempted to target the mechanoreceptors not located in the musculotendinous tissues of the knee joint.[217] Perhaps isokinetic strength performance would more strongly correlate with changes in an active mode of proprioception measurement following fatigue because strength and muscle force production would have a greater influence on the mechanoreceptors located within the musculotendinous tissues as well as on the muscle length/rate of length change information within the muscle spindle.[217] Further, as mentioned previously, it is possible that fatigue induced a decrease in muscular receptor function, which may have resulted in capsular receptors becoming more strongly stimulated[238, 248] and that when the capsule is maximally stressed, there may be an increased response rate of capsular receptors.[101, 102, 238] Therefore, fatigue of the knee musculature may have actually enhanced the sensitivity of the mechanoreceptors within the capsule-ligamentous structures of the knee.

5.3.2 Aerobic Capacity, Lactate Threshold, and TTDPM

Aerobic capacity and lactate threshold were measured to examine their relationship with proprioceptive changes following fatiguing exercise. We hypothesized that VO_2 Peak and lactate threshold would have a significant correlation with pre- to post-fatigue TTDPM difference in both the extension and flexion directions. It was hypothesized that VO_2 Peak would have a relationship with changes in TTDPM following fatigue because it is a measure of cardiovascular fitness, and previous research has demonstrated that general fatigue negatively affects motor control by the central nervous system and results in decreased proprioception.[179] Since lactate accumulation may be related to the onset of peripheral fatigue, it was hypothesized that lactate

threshold would also be significantly related to changes in proprioception following fatigue. Our hypotheses were not supported as no significant correlations were found between VO_2 Peak or lactate threshold and changes in TTDPM following fatigue. Statistically, this was likely due to the fact that no changes in TTDPM were observed across the group following the fatigue protocol. Although we established maximal effort via perceptual and physiological measures, it is possible that the fatigue protocol may have not induced enough dysfunction to the central pathways contributing to motor control that would cause deficits in the proprioception modality measured in the current study. It is also possible that lactate accumulation may have had more of an impact on receptors within the musculotendinous tissues, and not as much influence on receptors within the joint capsule.

The overall high fitness level of our subjects may in part explain why we did not find any significant differences between pre- and post-fatigue TTDPM, and subsequently, no significant correlations between VO_2 Peak or lactate threshold and changes in TTDPM in either direction. The range of VO_2 Peak values from this investigation was 37.5 ml/kg/min – 53.4 ml/kg/min, and all but four subjects fell above the 90th percentile for maximal aerobic power stratified by age and gender.[97] If untrained or recreationally active subjects had participated in the study, they may have demonstrated decreased ability to detect passive motion compared to the highly trained subjects, and may have had more pronounced deficits in TTDPM following fatigue. Further, VO_2 Peak had a significant, moderate,[61] negative correlation with pre-fatigue and post-fatigue TTDPM in the extension direction. The direction of this relationship indicated that the higher the subject's aerobic capacity, the better their TTDPM score, with a lower score (i.e. angle error) meaning better performance. This finding agrees with previous work demonstrating that highly trained individuals possess better ability to detect passive motion than less fit individuals,[159] and

results from this study provide evidence that trained individuals have increased ability to detect passive motion following fatigue, further explaining why no TTDPM changes occurred from pre- to post-fatigue. The fact that VO_2 Peak was only significantly correlated with TTDPM in the extension direction may potentially be explained by previous research that has suggested that individuals may possess greater proprioceptive sensitivity during TTDPM when moving in the extension direction.[40]

5.4 LIMITATIONS

This investigation has several limitations worth mentioning. Instructions were given to participants in order to eliminate potential confounding variables that would affect fatigue protocol performance. Prior to reporting for each test session, subjects were instructed to not eat a large meal for at least two hours. Despite efforts to enforce and monitor adherence to these instructions, lack of strict adherence to the instructions unbeknownst to the investigators may have confounded the results of the study. A higher carbohydrate consumption prior to performing the fatigue protocol may have impacted fatigue protocol performance because dietary carbohydrate concentration has been shown to have a positive relationship with muscle glycogen concentration[222, 234] and endurance exercise performance.[31, 139] Additionally, subjects were instructed to refrain from any strenuous exercise prior to each test session so that residual fatigue or soreness would not confound the study results. Strenuous exercise performed prior to data collection may have resulted in a decrement in exercise performance because muscles groups recently exercised to exhaustion may have higher levels of blood lactate and/or blood H+ concentration.[138] However, our study aimed to fatigue subjects to the same degree of perceptual

and physiological fatigue, so it can be assumed that potential effects of these confounding variables were negated and did not substantially affect conclusions drawn about the core hypotheses of the investigation.

We also aimed to examine the typical diet of the subjects to quantify total energy intake and macronutrient intake in order to evaluate the implication of under-consuming total energy and carbohydrates on fatigue protocol performance via self-reported 24-hour dietary recall. A potential limitation of any questionnaire or self-report is misreporting or under-reporting of data. Research has shown that women often under-report on self-reported nutrition surveys, so this may have been the case in the current study.[216] Therefore, the conclusions gathered from this data may be confounded by the validity of the self-reported answers. This data, however, does not affect the conclusions made about the core hypotheses of the investigation.

Although we controlled the study for gender differences in musculoskeletal strength, physiological characteristics, and neuromuscular characteristics by only including females in the study, we did not control for phase of menstrual cycle during testing, oral contraceptive use, or other steroidal contraceptive use. Previous research has revealed differences in neuromuscular characteristics during various phases of the menstrual cycle and during different levels of sex hormone fluctuation, including significant differences in proprioception[211] and strength.[10, 113, 160] However, research conducted previously in our laboratory demonstrated no significant differences between phases of the menstrual cycle for fine motor coordination, postural stability, hamstring-quadriceps strength ratio at 60°/s or 180°/s, knee flexion excursion, knee valgus excursion, peak proximal tibial anterior shear force, flexion moment at peak proximal tibial anterior shear force, or valgus moment at peak proximal tibial anterior shear force.[2] While the phase of menstrual cycle and use of contraceptives may have potentially impacted both fatigue

protocol performance and proprioception assessment, we did not collect the necessary data to support or refute these changes because controlling testing for phase of menstrual cycle and use of contraceptive would have been cumbersome and previous research surrounding the topic is equivocal. Additionally, when generalizing results from our study to real-life training or game situations, one cannot control for phase of menstrual cycle or contraceptive use to negate their potential impact on performance and sensorimotor control, so it may not be practical to do so in laboratory protocols. Overall, despite the potential effect of hormonal variance on fatigue protocol performance, subjects were still fatigued to a similar perceptual and physiological level, so the core hypotheses of this investigation were likely not substantially impacted.

Several limitations may have impacted aerobic capacity assessment and the fact that subjects did not achieve a true, physiological maximum test. First, subjects self-selected a test pace based off of a pace they perceived they would be able to maintain during a moderately long distance run. While the subjects participating in this study were highly physically active, some were primarily anaerobic athletes, and thus were not as confident at estimating an endurance run pace. Additionally, some subjects may have over- or under-estimated their test pace, and they may have chosen a slower or faster speed if they were to repeat the test. In a few of these cases, subjects may have warmed up at too aggressive of a pace prior to beginning the graded exercise test. In an ideal situation, it may have been beneficial for our subjects to perform a familiarization session for maximal oxygen uptake testing to become acquainted to running with the mask on. Many subjects reported that they terminated the test because they could not breathe in quickly enough or that they were uncomfortably sweaty while wearing the mask. Additionally, many subjects reported that they think they could have gone another stage or partial stage further than when they actually self-terminated the test. However, adding a familiarization session for

aerobic capacity assessment would have potentially added another study visit to the protocol and may have compromised study compliance/attrition. Despite the fact that we reported VO_2 Peak instead of VO_2 max as a result of these potential limitations, the results of our core research question were likely not impacted, as the VO_2 Peak of our subjects was adequately representative of their true aerobic capacity given the comparison of results with other studies assessing aerobic capacity in athletes and highly trained individuals.

A limitation of the lactate threshold protocol is that a more direct blood lactate measurement, such as intravenous sampling, would have been optimal. Further, a more valid measurement of true lactate threshold assessment involves determining the maximal lactate at steady state, which involves multiple testing sessions at a range of intensities.[250, 253] This methodology would not have been feasible given the time constrains of the current study, so we utilized a well-established method of lactate threshold assessment by using specific criteria to determine lactate threshold[250] that would adequately answer the core research questions of this investigation.

While we aimed to fatigue the subjects to a similar degree of perceptual and physiological fatigue, a potential limitation of the fatigue protocol is that individuals with higher fitness levels may have also ran at faster speeds, performed more push-ups, sit-ups, and step-ups, and potentially ran longer during the final station than subjects with a lower fitness, and results of the fatigue protocol would be more relative to the individual's own fitness level rather than standardized across all subjects. Although VO_2 Peak was significantly correlated to Station 1 run speed ($r=0.713$, $p=0.000$), VO_2 Peak, lactate threshold calculated at the 1mmol increase (LT 1mmol) and lactate threshold calculated at the noticeable inflection point (LT inf) did not demonstrate a significant linear relationship (calculated with Spearman's Rho correlation

coefficients) with pushups performed (VO_2 Peak: r=0.298, P=0.202; LT 1mmol: r=0.38, P=0.312; LT inf: r=0.003, P=0.990); sit-ups performed (VO_2 Peak: r=0.264, p=0.261; LT 1mmol: r=0.366, P=0.112; LT inf: r=0.334, P=0.150); step-ups performed (VO_2 Peak: r=0.255, P=0.277; LT 1mmol: r=-0.27, P=0.909; LT inf: r=-0.046, P=0.847); or time to fatigue during Station 7 (VO_2 peak: r=0.205, P=0.386; LT 1mmol: r=0.242, P=0.304; LT inf: r=0.260, P=0.268). This suggests that subjects with various levels of aerobic capacity and lactate threshold performed similarly during the fatigue protocol, and that all subjects were likely fatigued to a similar degree. Further, these findings indicate the core results of the study were not impacted by the potential limitation of the fatigue protocol.

Another potential limitation of the study is the quantification of fatigue following the fatigue protocol. We measured isometric strength following the pre- and post-fatigue TTDPM assessments in order to quantify fatigue to the musculature surrounding the knee. We did not continue to measure the other physiological variables collected during the fatigue protocol, such as heart rate, blood lactate, and ratings of perceived exertion. It may have been useful to quantify these other measures of fatigue recovery that may have implicated post-fatigue TTDPM performance because some subjects may have recovered perceived exertion, heart rate, and blood lactate at different rates than others. These measurements may not have been practical, as measuring a multitude of variables during TTDPM testing may have been cumbersome and may have potentially interrupted TTDPM assessment results. However, decreased isometric hamstring strength and flexion/extension strength ratio following the post-fatigue TTDPM measurement adequately demonstrated that subjects possessed a level of fatigue during the post-fatigue TTDPM assessment.

5.5 STUDY SIGNIFICANCE

Although our core hypotheses were rejected as a result of this study, the results contribute useful information to the current fatigue and proprioception knowledge base. To the author's knowledge, no study has investigated the relationship between musculoskeletal and physiological characteristics with changes in proprioception following fatigue. This study may provide a foundation for future research in the area of fatigue and proprioception, and this research may be generalizable to athletes and other trained individuals, including military personnel. Changes may be made in future research protocols to enhance and refine the research questions and methodologies based upon findings from this study, including different subject populations, modes of fatigue induction, various musculoskeletal and physiological assessments, and alternate modes of proprioception assessment. Specific changes in future research are described below.

5.6 FUTURE DIRECTIONS

Future research examining fatigue and proprioception can explore many variations of the current study. First, different groups of subjects can be utilized in future studies. The age range of the subjects in the current study aimed to be generalizable to a young, healthy, active population. Since age may potentially act as a confounding variable, as previous work has found that neuromuscular characteristics, namely proprioception, decline with age,[239] future studies can examine different age groups with regard to characteristics related to change in proprioception following fatigue. Additionally, since it has been evidenced that highly trained individuals may

have better proprioception compared to those with lower aerobic capacity or level of training level,[159] a broad range of athletes, recreationally active individuals, and sedentary individuals can be tested in the future. Further, gender comparisons may be made, since there are gender differences in musculoskeletal strength, physiological characteristics, and proprioception. The hypotheses from this study may also be tested across different age groups or different post-injury or post-surgery groups. In future studies, sample size can be increased in order to establish predictors of changes in proprioception following fatigue.

The fatigue protocol can also be altered in future studies. The protocol used in this study was designed to fatigue each subject to the same level of perceptual and physiological fatigue by utilizing running speeds relative to their fitness ability and encouraging subjects to perform repetitions of pushups, sit-ups, and step-ups relative to their maximal ability within a time constraint. It may be interesting to investigate changes in proprioception prior to and following a fatigue protocol that exercises each subject at the same intensity during a fixed amount of time in a group of subjects of differing fitness levels. It may also be valuable to assess the relationship between musculoskeletal and physiological characteristics with changes in proprioception following a local versus a general fatigue protocol since previous research has demonstrated difference in proprioception following a local versus general fatigue protocol.[179]

Future studies may test other musculoskeletal characteristics that may potentially relate to proprioception and changes in proprioception following fatigue. Our strength protocol aimed to objectively quantify strength of the musculature surrounding the knee in order to assess the relationship with changes in TTDPM following fatigue, and isokinetic strength testing has the ability to isolate muscle groups and objectively quantify peak torque produced.[204] A potential limitation of isokinetic strength testing that it is non-weight-bearing and is an open-chain

assessment,[204] which is not directly translatable to functional strength assessments performed in an actual game or field setting. While isokinetic extension strength, flexion strength, and flexion/extension ratio had no significant relationship with pre- or post-fatigue TTDPM, previous research has implied that individuals with better muscle development may also have a better awareness of joint position and motion.[20, 159] Further, as evidenced by our study, decreases in isometric hamstring strength and flexion/extension ratio following fatigue were significantly correlated with changes in TTDPM following fatigue. Based on the evidence above, other strength variables to consider in the future studies examining the relationship between musculoskeletal characteristics and changes in TTDPM following fatigue include time to peak torque, muscular endurance, and torque production decrement following fatigue.

Additionally, the current study can be replicated and performed using various proprioception assessment methods. The current study may be redesigned to investigate changes in TTDPM at a starting angle closer to mid-range of knee flexion since measuring close to end-range may have been too sensitive in detecting passive motion. Also, the current investigation hypothesized that a combination of muscular and cardiovascular fatigue would result in significant changes in passive proprioception from pre- to post-fatigue, but no changes were demonstrated. Since previous research has suggested that the mechanoreceptors found within the capsuloligamentous structures of the knee may actually become enhanced as a result of muscular fatigue,[238, 248] future research can look at the effect of fatigue on active joint position sense measures such as active joint repositioning, path of motion replication, and force sense.

5.7 CONCLUSIONS

The purpose of this study was to investigate the relationship between musculoskeletal strength and physiological characteristics with changes in proprioception following fatiguing exercise. Our hypotheses were not supported, as results did not demonstrate a significant relationship between the chosen modifiable musculoskeletal and physiological characteristics and changes in proprioception following fatigue. However, there was a significant correlation between VO_2 peak and TTDPM in extension both pre- and post-fatigue, indicating a linear relationship between individuals with higher aerobic capacity and proprioception. Overall, this study provides a foundation for other work to be conducted in the area of fatigue and proprioception. Future research can explore other musculoskeletal and physiological characteristics in different populations to determine the best predictors of changes in proprioception experienced after fatiguing exercise.

APPENDIX A

QUESTIONNAIRES AND OMNI RPE SCALE

A.1 Exercise History Questionnaire and Results

A.1.1 Exercise History Questionnaire

Subject ID_____ Date: _____

Please fill out this form as completely as possible.

1. Please rate your exercise level on a scale of 1 to 5 (5 indicating very strenuous) for each age range through your present age

   15-20 _____ 21-30 _____ 31-40 _____ 41-50 _____

2. Were you a high school and/or College athlete?

   □ Yes If yes, please specify _____

   □ No

3. Rate yourself on a scale of 1 to 5 (1 indicating lowest value and 5 the highest). *Circle the number that best applies.*

   Characterize your present athletic ability?

   1 2 3 4 5

   When you exercise, how important is competition?

   1 2 3 4 5

   Characterize your present cardiovascular capacity.

   1 2 3 4 5

   Characterize your present muscular capacity.

   1 2 3 4 5

   Characterize your present flexibility capacity.

   1 2 3 4 5

4. Are you currently involved in regular endurance (cardiovascular) exercise?

   ☐ Yes ☐ No

   If yes, specify the type of exercise(s) _____

   _____ minutes/day _____ days/week

   Rate your perception of the exertion of your exercise program (circle the number):

   (1) Light (2) Fairly Light (3) Somewhat hard (4) Hard (5) Very Hard

5. How long have you been endurance exercising regularly?

   _____ months _____ years

6. Are you currently involved in regular strength training (weight lifting, calisthenics) exercise?

   ☐ Yes ☐ No

   If yes, specify the type of exercise(s) _____

   _____ minutes/day _____ days/week

   Rate your perception of the exertion of your exercise program (circle the number):

   (1) Light (2) Fairly Light (3) Somewhat hard (4) Hard (5) Very Hard

7. How long have you been strength training regularly?

   _____ months _____ years

8. What other exercise, sports or recreational activities have you participated in?

   In the past 6 months? _____

   In the past 5 years? _____

9. Have you ever participated in a balance training program (i.e. training for lower body balance on one leg during static exercise/functional exercise/yoga or meditation)?

    □ Yes If yes, please specify_____

    □ No

10. If you were to run on a treadmill for one hour, what pace do you think you would be able to maintain? (please select one)

    _ 10:00/mile _ 9:30/mile

    _ 9:00/mile _ 8:30/mile

    _ 8:00/mile _ 7:30/mile

    _ 7:00/mile _ 6:30/mile

    _ 6:00/mile _ Other: _____

A.1.2 Exercise History Questionnaire Results

Table 13. Activity Level at Various Age Groups

	Exercise Level		
Subject	15-20 yrs	21-30 yrs	31-40 yrs
FP1	5	4	-
FP2	4	5	-
FP3	4	-	-
FP4	3	3	-
FP5	5	4	-
FP6	5	5	-
FP7	5	5	-
FP8	5	4	-
FP9	4	3	5
FP10	-	-	-
FP11	3	3	-
FP12	4	2	4
FP13	3	5	-
FP14	4	3	4
FP15	1	5	4
FP16	4	4	-
FP17	5	4	-
FP18	2	3	5
FP19	5	5	-
FP20	3	5	-

Exercise level based on 1-5 scale, with 1 being the lowest and 5 being the highest level of exercise

*FP10 did not answer question correctly, so no data has been reported

Table 14. High School and College Athletic Participation

Subject	High School	Sports	College	Sports
FP1	Y	cross country/track	N	-
FP2	Y	basketball/ softball	N	-
FP3	Y	swimming, softball, tennis	N	-
FP4	Y	softball, volleyball	N	-
FP5	Y	cross country, track, soccer	N	-
FP6	Y	track, basketball, cross country	Y	travel basketball
FP7	Y	basketball, dance	N	-
FP8	Y	basketball, track, cross country	N	-
FP9	Y	track, cross country	N	-
FP10	Y	track, softball, basketball	N	-
FP11	N	-	N	-
FP12	Y	volleyball, track	N	-
FP13	Y	dance	N	-
FP14	Y	track and field, dance, cheerleading	N	-
FP15	N	-	N	-
FP16	Y	swimming, running	Y	DII rowing, Ultimate Frisbee® (club)
FP17	Y	track	Y	track
FP18	N	-	N	-
FP19	Y	track	Y	track
FP20	Y	softball, soccer	N	-

Table 15. Perceived Fitness Rating

Subject	Perceived Fitness Rating (1-5 Scale)				
	Athletic Ability	Competitive-ness	Cardiovascular Fitness	Muscular Strength	Flexibility
FP1	4	3	5	3	4
FP2	5	5	5	4	4
FP3	3	2	3	4	3
FP4	3	2	3	3	1
FP5	4	2	4	3	3
FP6	4	3	3	5	3
FP7	4	3	4	4	3
FP8	3	2	3	3	2
FP9	4	5	4	3	3
FP10	4	4	4	4	4
FP11	3	4	4	3	4
FP12	3	4	4	3	2
FP13	4	4	4	4	4
FP14	3	5	3	4	3
FP15	4	3	3	4	2
FP16	4	3	4	4	4
FP17	4	3	4	3	3
FP18	4	5	5	5	3
FP19	4	4	2	3	4
FP20	4	5	4	4	3

Exercise level based on 1-5 scale, with 1 being the lowest and 5 being the highest perceived fitness rating

Table 16. Endurance Exercise Participation

Endurance Exercise Participation						
Subject	Y/N	Type	Min/Day	Days/Week	Exertion (1-5)	Months/Years
FP1	Y	running, kickboxing	60	4	4	14 years
FP2	Y	Cross Fit®, running	30	5	4	2 years
FP3	Y	running	40	5	4	6 months/5 years
FP4	N	-	-	-	-	-
FP5	Y	running, swimming	30-60	5	3	5 years
FP6	Y	Cross Fit®	10-20	5-6	4	varies depending on activity
FP7	Y	running, cross training	40	6	3	10 years
FP8	Y	running	50-75	6	4	9 years
FP9	Y	Cross Fit®, running, biking, rowing	60-90	5-6	4	20 years
FP10	Y	running, Cross Fit®, lifting	60+	5	4	2 years
FP11	Y	running	30-60	3	4	1.5 years
FP12	Y	running,Cross Fit®, rowing, biking	60-90	6	4	8 years
FP13	Y	Cross Fit®, running	30-60	6	5	3 years
FP14	Y	running, rowing, spinning, Cross Fit®, yoga	60+	5	4	20 years
FP15	Y	eliptical, arch, stairmaster	45+	7	3	12 years
FP16	Y	running	30-120	3-5	3	12 years
FP17	Y	running	50	5 or 6	4	about 10 years
FP18	Y	sprinting, plyometrics, running, spinning	20-30	5	4	10 years
FP19	Y	running/ sprinting	60	6	3	8 years
FP20	Y	running, biking	45-90	4-5	4	4 years

Table 17. Strength Training Participation

Strength Training Participation						
Subject	Y/N	Type	Min/Day	Days/Week	Exertion (1-5)	Months/Years
FP1	Y	boot camp/body sculpt	60	2	4	3 months
FP2	Y	squating, olympic lifts	20	3	4	1 year
FP3	Y	body pump, weight lifting	30	5	4	3 years
FP4	N	-	-	-	-	-
FP5	Y	weight trainig	30	2	3	5 years
FP6	Y	Cross Fit®	30	5-6	4	1 year
FP7	Y	weight lifting	20	6	3	10 years
FP8	Y	push-ups, squats, lunges, or machine lifts	15-20	2	2	9 years
FP9	Y	olympic and power lifting	30	5	5	2 years
FP10	Y	Cross Fit®, all lifting	30	5	4	2 years
FP11	Y	weights, plyos, calisthenics	30-60	3-4	4	4 months
FP12	Y	weight lifting	30	2-3	3	7 years
FP13	Y	Cross Fit® (olympic weight lifting/ power lifting)	30-60	6	4	3 years
FP14	Y	weight lifting, yoga, rowing, crossfit	60	5	4	12 years
FP15	Y	total body weight machines/ free weights	30+	3	3	12 years
FP16	N	-	-	-	-	-
FP17	N	-	-	-	-	-
FP18	Y	weights, interval training, body weight exercises	40	5	4	3 years
FP19	N	body weight exercises	-	-	3	4 years
FP20	Y	Cross Fit®	60	2-3	5	3 years

Table 18. Miscellaneous Sport and Balance Training

Subject	Miscellaneous Sport Participation		Balance Training Participation	
	6 Months	5 Years	Y/N	Type
FP1	spinning, step class	-	Y	yoga
FP2	-	softball, basketball	Y	yoga
FP3	weight lifting, cardio (treadmill, bike, eliptical)	swimming, skiing, softball, tennis, weight lifting, cardio (treadmill, bike, eliptical)	Y	balance on yoga ball or leg
FP4	kayaking, biking, running, yoga, rock climbing	walking/ running, machines at the gym	Y	yoga
FP5	3 half marathons	6 half marathons, 2 full marathons	Y	yoga
FP6	Cross Fit®, basketball (rec league)	crossfit, basketball (rec league), half marathon training	Y	yoga
FP7	dance	dance	Y	-
FP8	basketball, tennis	basketball, swimming, road races (half, full marathon)	Y	yoga
FP9	-	rock climbing, kayaking	Y	yoga
FP10	Cross Fit®, 5K races, kayaking	Cross Fit®, 5K races, kayaking	Y	yoga
FP11	running races	running races	N	-
FP12	softball, volleyball	softball, volleyball	Y	yoga
FP13	marathon, Cross Fit® competition	marathon, 3K, crossfit competition	Y	dance
FP14	-	Dragon Boating®	Y	yoga
FP15	5K, rowing, spinning	Dragon Boating®, spinning (Race to any Place®), 5K's	Y	P90X2® tapes
FP16	running, marathon training, Ultimate Frisbee®	running, Ultimate Frisbee®, rowing	N	-
FP17	softball, spin class	softball	Y	-
FP18	yoga	-	Y	yoga, Bosu® exercises
FP19	-	-	Y	ankle strengthening exercises
FP20	obstacle racing, dodgeball, Ultimate Frisbee®	-	N	-

A.2 ASA24 Dietary Recall

Table 19. ASA24 Dietary Recall Results

Subject	Total Energy (kcal)	% of Total Energy			Total Consumption (g)			Total Consumption (g/kg)		
		Protein	Fat	Carb	Protein	Fat	Carb	Protein	Fat	Carb
FP1	1248.1	20.0	24.6	56.8	62.4	34.1	177.1	1.2	0.7	3.4
FP2	1403.5	15.4	39.4	49.7	54.0	61.4	174.3	0.9	1.0	2.9
FP3	2171.3	11.6	27.9	66.3	62.7	67.3	359.8	1.2	1.3	6.8
FP4	2967.7	13.9	34.5	54.2	103.0	113.7	402.4	1.7	1.9	6.6
FP5	1470.3	17.9	28.5	56.8	65.7	46.6	208.8	1.0	0.7	3.3
FP6	1495.5	19.0	47.2	35.4	70.9	78.4	132.5	0.8	0.9	1.5
FP7	1545.9	13.6	16.7	73.3	52.6	28.6	283.1	1.0	0.5	5.2
FP8	2694.9	15.0	37.1	49.9	100.9	111.0	336.1	1.7	1.9	5.8
FP9	1972.3	20.7	21.8	27.6	102.0	47.7	136.1	1.6	0.7	2.1
FP10	975.9	20.8	48.8	18.2	50.6	52.9	44.5	0.9	0.9	0.8
FP11	1866.8	11.1	27.3	63.3	51.8	56.7	295.6	0.8	0.9	4.7
FP12	1912.9	6.8	17.2	50.7	32.6	36.5	242.5	0.6	0.6	4.2
FP13	1025.0	25.5	38.0	41.4	65.3	43.3	106.1	1.0	0.7	1.6
FP14	1773.0	16.8	41.9	42.9	74.5	82.6	190.2	1.1	1.2	2.8
FP15	4381.0	18.0	24.3	53.6	197.4	118.1	587.3	2.6	1.6	7.8
FP16	2341.0	10.3	29.5	56.2	60.2	76.7	329.1	1.0	1.3	5.5
FP17	1199.6	13.5	26.4	62.9	40.6	35.2	188.5	0.7	0.6	3.2
FP18	2241.7	22.9	29.5	41.8	128.5	73.5	234.1	2.4	1.4	4.3
FP19	1937.5	18.0	16.7	70.6	87.4	36.0	341.7	1.6	0.7	6.3
FP20	1637.8	29.2	31.8	40.1	119.6	57.9	164.0	1.8	0.9	2.5

A.3 OMNI Rating of Perceived Exertion

A.3.1 OMNI Rating of Perceived Exertion Scale (Adult Running)

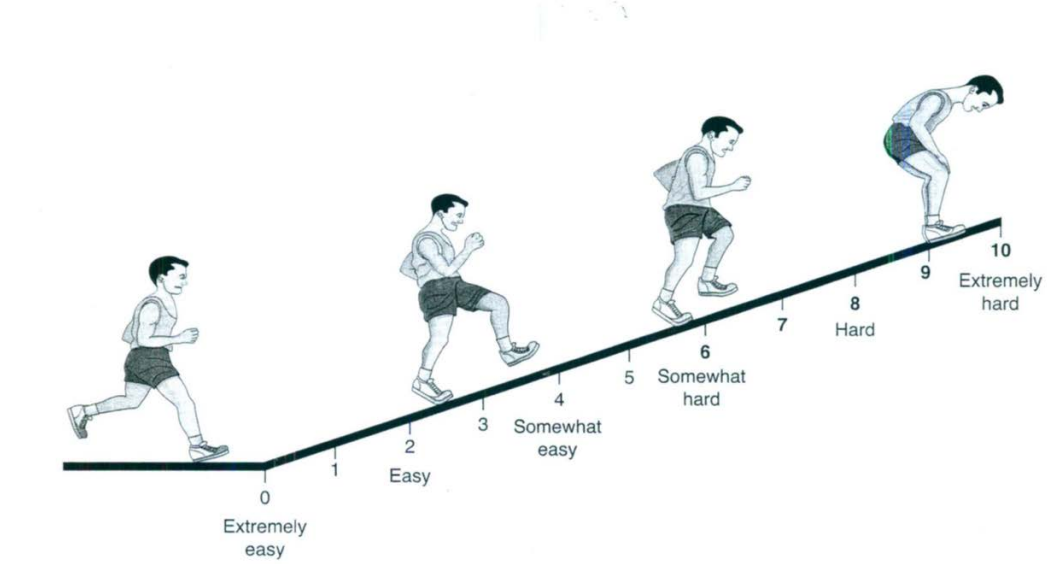

Figure 2. OMNI Rating of Perceived Exertion Scale (Adult Running)

A.3.2 Verbal Instructions for OMNI RPE Scale during Maximal Oxygen Uptake

"You are about to undergo a treadmill exercise test. Please look at the person at the bottom of the scale who is performing low-intensity running. If you feel like this person when you are running, the exertion will be *extremely easy*. When I ask you how you feel, you should respond with the number 0 (zero). Now, look at the person at the top of the scale who is barely able to continue running. If you feel like this person looks while you are running, the exertion will be *extremely hard*. When I ask you how you feel, you should respond with the number 10 (ten). If you feel your effort is somewhere between *extremely easy (0)* and *extremely hard (10)*, the respond with a number between 0 and 10. I will ask that you give a number that describes how your active muscles feel, including your legs and your arms. I am also going to ask for a number that represents how your breathing feels, then how your overall body feels. There are no right or wrong numbers. The numbers you choose may change as you continue to run. Use both the pictures and the words to help you select the numbers. Use any of the numbers to describe how you feel when running."

A.3.3 Verbal Instructions for OMNI RPE Scale during Fatigue Protocol

"You are about to undergo a maximal fatigue protocol. During this protocol, you will be performing a series of exercises, including treadmill running, push-ups, sit-ups, and step-ups. Please look at the person at the bottom of the scale who is performing low-intensity running. If you feel like this person at the end of a station, the exertion will be *extremely easy*. When I ask you how you feel, you should respond with the number 0 (zero). Now, look at the person at the top of the scale who is barely able to continue running. If you feel like this person at the end of a station, the exertion will be *extremely hard*. When I ask you how you feel, you should respond with the number 10 (ten). If you feel your effort is somewhere between *extremely easy (0)* and *extremely hard (10)*, the respond with a number between 0 and 10. I will ask that you give a number that describes how your active muscles feel, including your legs and your arms. I am also going to ask for a number that represents how your breathing feels, and then how your overall body feels. There are no right or wrong numbers. The numbers you choose may change as you continue through the stations. Use both the pictures and the words to help you select the numbers. Use any of the numbers to describe how you feel at the end of each station."

APPENDIX B

INDIVIDUAL RESULTS AND SCATTERPLOTS

A.2 INDIVIDUAL RESULTS

A.2.1 Demographics

Table 20. Individual Demographic Data

Subject	Visit 1 Date	Visit 2 Date	Age	Height (cm)	Weight (kg)	BMI (kg/m^2)	BF%
FP1	6/6/2012	6/8/2012	26	162.0	52.2	19.9	22.4
FP2	6/8/2012	6/11/2012	29	161.4	60.9	23.4	21.3
FP3	6/11/2012	6/13/2012	20	161.0	52.9	20.4	29.9
FP4	6/12/2012	6/15/2012	22	167.0	61.3	22.0	29.6
FP5	6/13/2012	6/27/2012	28	166.0	64.0	23.2	24.6
FP6	6/13/2012	6/15/2012	25	172.5	85.7	28.8	25.7
FP7	6/14/2012	6/27/2012	27	162.0	54.6	20.8	15.1
FP8	6/14/2012	6/22/2012	23	166.4	58.4	21.1	22.0
FP9	6/15/2012	6/29/2012	35	171.0	65.2	22.3	18.9
FP10	6/15/2012	6/21/2012	34	164.4	59.0	21.8	22.4
FP11	6/18/2012	6/20/2012	24	158.5	63.3	25.2	32.2
FP12	6/20/2012	6/23/2012	38	163.0	58.2	21.9	26.3
FP13	6/22/2012	6/27/2012	29	168.0	65.1	23.1	18.3
FP14	6/22/2012	6/30/2012	37	163.0	67.1	25.2	23.4
FP15	6/23/2012	6/30/2012	36	175.3	74.9	24.4	29.5
FP16	6/25/2012	6/27/2012	25	168.0	60.0	21.2	21.2
FP17	6/25/2012	6/27/2012	29	161.0	58.8	22.7	32.3
FP18	6/26/2012	6/29/2012	35	168.0	54.0	19.1	17.6
FP19	6/26/2012	6/28/2012	21	168.0	54.0	19.1	15.9
FP20	6/26/2012	6/28/2012	30	165.0	65.7	24.1	17.3

BMI = Body Mass Index

BF = Body Fat

A.2.2 Isokinetic Strength

Table 21. Individual Isokinetic Strength Data

Subject	Quad Strength (Nm)	Ham Strength (Nm)	Quad Strength (%BW)	Ham Strength (%BW)	Flex/Ext Ratio
FP1	112.7	60.6	215.9	116.0	0.54
FP2	152.2	68.9	250.2	113.3	0.45
FP3	104.7	51.5	198.7	97.7	0.49
FP4	111.7	45.2	182.2	73.7	0.40
FP5	109.4	57.4	170.9	89.7	0.52
FP6	149.9	81.6	174.7	95.1	0.54
FP7	95.2	44.3	174.8	81.4	0.47
FP8	136.6	69.2	235.1	119.1	0.51
FP9	162.3	75.4	249.9	116.2	0.46
FP10	142.2	67.9	241.0	115.0	0.48
FP11	135.8	61.6	215.1	98.1	0.46
FP12	139.4	73.3	239.9	126.2	0.53
FP13	155.6	81.5	239.6	125.6	0.52
FP14	160.3	85.3	240.2	127.8	0.53
FP15	157.6	62.2	210.3	83.0	0.39
FP16	161.8	90.9	269.9	151.7	0.56
FP17	107.8	62.4	184.1	106.6	0.58
FP18	104.0	58.8	194.1	109.8	0.57
FP19	143.1	59.7	267.1	111.4	0.42
FP20	151.5	90.6	231.7	138.5	0.60

Quad Strength = Average peak torque produced over 5 trials

Ham Strength = Average peak torque produced over 5 trials

A.2.3 Physiological Characteristics

Table 22. Individual Physiological Data

Subject	VO2Peak (ml/kg/min)	HR Max (bpm)	RER Max	Lactate Max (mmol)	Test Time (m.s)	WarmUp Speed (mph)	Test Speed (mph)
FP1	44.8	179	0.99	9.7	14.5	5.5	6.3
FP2	49.3	179	0.96	8.2	8.5	6.0	7.5
FP3	47.3	211	1.05	10.3	15.0	5.0	6.5
FP4	37.6	198	1.03	9.4	14.0	3.5	4.7
FP5	44.3	203	1.10	9.7	13.0	5.2	6.0
FP6	40.4	195	1.00	11.3	11.5	6.5	6.5
FP7	50.2	188	0.98	4.8	14.5	6.2	6.7
FP8	50.1	205	0.97	6.9	15.6	6.2	6.7
FP9	49.2	170	0.91	7.4	12.5	6.2	6.7
FP10	53.4	179	0.94	7.4	15.3	6.2	6.7
FP11	42.6	184	1.00	10.9	12.0	5.5	6.3
FP12	46.1	180	0.98	7.8	9.0	5.0	6.7
FP13	42.4	186	0.96	8.7	13.5	5.0	6.3
FP14	44.3	179	0.99	7.4	13.0	5.0	6.3
FP15	41.7	190	0.98	11.6	12.0	4.7	6.0
FP16	50.6	198	0.99	10.4	15.1	5.0	6.3
FP17	52.8	195	1.02	11.8	9.0	6.0	8.0
FP18	52.0	178	0.96	5.4	12.0	6.0	7.0
FP19	50.1	182	0.98	7.8	13.0	5.0	6.3
FP20	51.9	176	0.99	8.8	9.0	6.0	7.0

VO2 Peak = Peak Oxygen Uptake (15-second interval)
HR Max = highest heart rate achieved during test
RER Max = highest respiratory exchange ratio achieved during test

Table 23. Individual Lactate Threshold Data

Subject	LT Determined at 1mmol increase				LT Determined at Noticeable Inflection			
	Lactate @ LT (mmol)	VO2 @ LT (ml/kg/min)	LT (%VO2peak)	HR @ LT (bpm)	Lactate @ LT (mmol)	VO2 @ LT (ml/kg/min)	LT (%VO2peak)	HR @ LT (bpm)
FP1	3.0	35.1	78.3	162.5	4.3	38.5	86.1	170.6
FP2	2.6	42.1	85.4	164.4	2.6	42.1	85.4	164.4
FP3	3.7	36.2	76.6	196.5	3.7	36.2	76.6	196.5
FP4	2.9	29.8	79.4	179.5	4.1	32.1	85.3	185.0
FP5	3.2	38.3	86.5	192.5	3.2	38.3	86.5	192.5
FP6	5.7	30.2	74.7	181.3	5.7	30.2	74.7	181.3
FP7	2.1	40.9	81.5	173.3	3.6	46.6	92.8	180.3
FP8	2.2	44.7	89.2	194.0	4.6	47.8	95.4	197.5
FP9	2.4	33.4	67.9	149.0	3.9	40.8	83.0	161.0
FP10	2.7	43.5	81.4	163.3	4.0	47.7	89.3	170.8
FP11	3.7	34.5	81.0	169.5	5.7	36.4	85.5	177.8
FP12	3.1	36.9	80.1	173.4	5.0	39.5	85.6	174.3
FP13	3.6	35.4	83.5	177.0	3.6	35.4	83.5	177.0
FP14	3.0	38.3	86.5	164.8	3.0	38.3	86.5	164.8
FP15	2.7	24.8	59.5	147.1	4.6	34.5	82.7	157.4
FP16	4.1	40.2	79.5	181.8	4.1	40.2	79.5	181.8
FP17	4.4	46.5	88.0	194.3	4.4	46.5	88.0	194.3
FP18	3.0	40.7	78.2	162.0	4.1	44.4	85.4	169.8
FP19	3.9	43.8	87.5	173.5	3.9	43.8	87.5	173.5
FP20	2.2	43.7	84.2	160.4	3.9	46.2	88.9	168.0

LT = Lactate Threshold

VO2 at LT = Oxygen Uptake at Lactate Threshold

HR at LT = Heart Rate at Lactate Threshold

Table 24. Individual RPE Data

Subject	RPE Legs	RPE Arms	RPE Chest	RPE Overall
FP1	10.0	8.0	9.0	9.0
FP2	7.0	6.0	7.0	7.0
FP3	10.0	9.0	9.0	10.0
FP4	9.0	8.0	8.0	9.0
FP5	8.0	2.0	10.0	9.0
FP6	9.0	5.0	9.0	9.0
FP7	7.0	6.0	9.0	8.0
FP8	8.0	8.0	9.0	9.0
FP9	4.0	5.0	5.0	8.0
FP10	9.0	7.0	9.0	9.0
FP11	9.0	3.0	8.0	9.0
FP12	9.0	9.0	9.0	9.0
FP13	9.0	8.5	10.0	9.5
FP14	8.0	7.0	9.0	10.0
FP15	6.0	3.0	6.0	8.0
FP16	9.0	7.0	9.0	9.0
FP17	8.0	9.0	9.0	8.0
FP18	10.0	5.0	8.0	8.0
FP19	6.0	4.0	9.0	9.0
FP20	4.0	4.0	8.0	7.0

RPE=Rating of Perceived Exertion with OMNI 0-10 scale at final stage of incremental treadmill test

A.2.4 Fatigue Protocol

Table 25. Fatigue Protocol – Station 1 Individual Data

Subject	Speed (mph)	Lactate (mmol)	Heart Rate (bpm)	RPE Legs	RPE Arms	RPE Chest	RPE Overall
FP1	5.9	2.2	145	5.0	3.0	4.0	4.0
FP2	6.8	8.6	147	4.0	3.0	3.0	3.0
FP3	6.2	3.0	157	1.0	0.0	1.0	0.0
FP4	4.5	2.4	148	5.0	4.0	5.0	5.0
FP5	5.7	2.4	165	3.0	2.0	4.0	4.0
FP6	6.2	0.9	163	2.0	1.0	3.0	2.0
FP7	6.4	1.8	158	2.0	2.0	3.0	2.0
FP8	6.4	1.1	165	2.0	2.0	2.0	2.0
FP9	6.4	2.1	130	1.0	0.0	2.0	2.0
FP10	6.4	2.1	134	3.0	1.0	3.0	3.0
FP11	6.0	4.1	163	3.0	2.0	3.0	3.0
FP12	6.4	3.1	157	4.0	2.0	3.0	3.0
FP13	6.0	2.6	157	3.0	2.0	4.0	3.0
FP14	6.0	2.7	151	2.0	3.0	3.0	3.0
FP15	5.7	4.1	156	3.0	2.0	3.0	3.0
FP16	6.0	3.7	142	3.0	2.0	3.0	3.0
FP17	7.6	4.0	170	3.0	2.0	2.0	2.0
FP18	6.7	2.1	125	4.0	2.0	4.0	4.0
FP19	6.0	1.9	151	3.0	3.0	5.0	5.0
FP20	6.7	3.1	151	1.0	1.0	2.0	1.0

RPE = Rating of perceived exertion using the OMNI 0-10 scale

Table 26. Fatigue Protocol - Station 2 Individual Data

Subject	Speed (mph)	Lactate (mmol)	Heart Rate (bpm)	RPE Legs	RPE Arms	RPE Chest	RPE Overall
FP1	6.9	3.2	160	6.0	4.0	5.0	5.0
FP2	7.9	5.2	164	7.0	4.0	6.0	6.0
FP3	7.2	4.1	190	2.0	1.0	2.0	3.5
FP4	5.2	2.4	176	4.0	5.0	5.0	5.0
FP5	6.6	3.3	176	5.0	3.0	4.0	5.0
FP6	7.2	4.9	174	3.0	1.0	3.0	3.0
FP7	7.4	4.6	168	3.0	3.0	4.0	3.5
FP8	7.4	1.3	182	4.0	4.0	4.0	4.0
FP9	7.4	3.0	144	3.0	1.0	4.0	4.0
FP10	7.4	2.4	151	4.0	2.0	3.0	4.0
FP11	6.9	5.8	176	5.0	2.0	5.0	4.0
FP12	7.4	3.8	171	4.0	4.0	5.0	4.0
FP13	6.9	2.9	171	5.0	4.0	5.0	5.0
FP14	6.9	3.6	159	3.0	3.0	4.0	4.0
FP15	6.6	4.7	163	4.0	3.0	4.0	4.0
FP16	6.9	4.6	178	6.0	2.0	5.0	5.0
FP17	8.8	6.4	189	5.0	5.0	5.0	5.0
FP18	7.7	2.6	157	5.0	3.0	6.0	6.0
FP19	6.9	2.3	164	4.0	4.0	7.0	6.0
FP20	7.7	2.2	164	2.0	2.0	4.0	3.0

RPE = Rating of perceived exertion using the OMNI 0-10 scale

Table 27. Fatigue Protocol - Station 3 Individual Data

Subject	Pushups (#)	Lactate (mmol)	Heart Rate (bpm)	RPE Legs	RPE Arms	RPE Chest	RPE Overall
FP1	41	5.1	120	5.0	8.0	8.0	7.0
FP2	56	2.9	135	4.0	8.0	6.0	7.0
FP3	74	7.0	165	2.0	6.0	2.0	4.0
FP4	34	4.3	130	5.0	8.0	4.0	8.0
FP5	45	5.1	114	4.0	6.0	5.0	5.0
FP6	51	7.0	142	1.0	9.0	7.0	7.0
FP7	51	4.4	121	3.0	8.0	8.0	7.0
FP8	49	4.0	169	3.0	8.0	6.0	7.0
FP9	63	5.6	133	0.0	6.0	0.0	5.0
FP10	61	3.9	89	4.0	6.0	4.0	4.0
FP11	65	7.1	133	3.0	8.0	6.0	5.0
FP12	65	5.8	128	4.0	7.0	4.0	5.0
FP13	60	7.9	125	1.0	8.0	7.0	8.0
FP14	90	5.7	140	3.0	8.0	9.0	8.0
FP15	50	6.4	149	4.0	5.0	4.0	5.0
FP16	48	7.2	148	4.0	7.0	6.0	6.0
FP17	58	7.7	131	4.0	8.0	4.0	5.0
FP18	64	4.2	135	4.0	8.0	5.0	7.0
FP19	99	5.3	125	5.0	8.0	5.0	7.0
FP20	68	5.7	142	1.0	8.0	7.0	7.0

RPE = Rating of perceived exertion using the OMNI 0-10 scale

Table 28. Fatigue Protocol - Station 4 Individual Data

Subject	Situps (#)	Lactate (mmol)	Heart Rate (bpm)	RPE Legs	RPE Arms	RPE Chest	RPE Overall
FP1	44	4.9	111	7.0	7.0	7.0	7.0
FP2	69	6.9	124	5.0	6.0	7.0	7.0
FP3	69	7.2	148	3.0	5.0	5.0	5.0
FP4	66	7.1	120	4.0	8.0	7.0	8.0
FP5	66	5.4	95	3.0	7.0	5.0	5.0
FP6	74	7.8	128	1.0	3.0	7.0	5.0
FP7	95	3.3	104	2.0	3.0	5.0	5.0
FP8	80	4.8	135	3.0	6.0	5.0	6.0
FP9	64		113	0.0	1.0	3.0	5.0
FP10	69	4.3	84	4.0	3.0	4.0	5.0
FP11	82	6.8	118	4.0	4.0	4.0	6.0
FP12	66	6.0	118	3.0	5.0	4.0	4.0
FP13	76	7.2	119	0.0	5.0	4.0	5.0
FP14	70	5.9	117	4.0	6.0	8.0	8.0
FP15	59	7.1	210	4.0	4.0	4.0	5.0
FP16	60	7.6	124	5.0	7.0	7.0	7.0
FP17	81	7.0	104	4.0	5.0	4.0	4.0
FP18	86	4.9	113	2.0	4.0	5.0	6.0
FP19	79	7.1	118	2.0	5.0	6.0	7.0
FP20	64	5.9	111	1.0	1.0	5.0	4.0

RPE = Rating of perceived exertion using the OMNI 0-10 scale

Table 29. Fatigue Protocol - Station 5 Individual Data

Subject	Step-Ups (#)	Lactate (mmol)	Heart Rate (bpm)	RPE Legs	RPE Arms	RPE Chest	RPE Overall
FP1	100	6.6	164	8.0	6.0	7.0	7.0
FP2	72	5.6	154	7.0	3.0	6.0	6.0
FP3	147	9.6	202	6.0	6.0	6.0	7.0
FP4	80	6.3	182	8.0	7.0	8.0	8.0
FP5	88	4.8	170	6.0	4.0	6.0	5.0
FP6	97	7.4	174	8.0	2.0	7.0	7.0
FP7	129	8.0	173	8.0	4.0	9.0	8.0
FP8	121	4.8	196	7.5	7.0	7.0	7.5
FP9	108	5.4	149	3.0	1.0	6.0	6.0
FP10	94	3.1	129	5.0	2.0	3.0	4.0
FP11	90	7.7	166	6.0	3.0	6.0	6.0
FP12	104	6.3	169	7.0	7.0	7.0	7.0
FP13	137	10.2	179	9.0	8.0	9.0	10.0
FP14	121	8.1	168	9.0	4.0	8.0	9.0
FP15	112	8.2	175	6.0	4.0	5.0	6.0
FP16	115	9.8	182	7.0	6.0	8.0	8.0
FP17	120	8.7	163	6.0	5.0	5.0	5.0
FP18	121	5.1	168	8.0	4.0	7.0	7.0
FP19	110	5.9	161	6.0	5.0	7.0	7.0
FP20	109	4.8	163	6.0	0.0	7.0	5.0

RPE = Rating of perceived exertion using the OMNI 0-10 scale

Table 30. Fatigue Protocol - Station 6 Individual Data

Subject	Speed (mph)	Lactate (mmol)	Heart Rate (bpm)	RPE Legs	RPE Arms	RPE Chest	RPE Overall
FP1	6.9	5.9	165	8.0	6.0	7.0	8.0
FP2	7.9	8.4	170	8.0	7.0	8.0	8.0
FP3	7.2	9.7	200	8.0	7.0	8.0	8.5
FP4	5.2	6.2	187	8.0	8.0	9.0	9.0
FP5	6.6	5.2	182	7.0	5.0	6.0	6.0
FP6	7.2	9.2	177	8.0	2.0	8.0	7.0
FP7	7.4		172	5.0	5.0	7.0	6.0
FP8	7.4	4.4	193	6.0	6.0	6.0	6.0
FP9	7.4	5.4	153	4.0	1.0	5.0	5.0
FP10	7.4	2.9	151	5.0	2.0	4.0	5.0
FP11	6.9	9.4	177	7.0	4.0	7.0	7.0
FP12	7.4	7.1	173	8.0	7.0	7.0	7.0
FP13	6.9	11.0	173	8.0	8.0	9.0	9.0
FP14	7.2	7.3	167	4.0	4.0	7.0	7.0
FP15	6.6	10.0	176	6.0	4.0	6.0	6.0
FP16	6.9	8.4	181	8.0	7.0	8.0	8.0
FP17	8.8	9.2	192	6.0	6.0	7.0	6.0
FP18	7.7	4.9	168	6.0	4.0	7.0	7.0
FP19	6.9	4.8	166	7.0	5.0	8.0	8.0
FP20	7.7	5.7	172	6.0	4.0	7.0	6.0

RPE = Rating of perceived exertion using the OMNI 0-10 scale

Table 31. Fatigue Protocol - Station 7 Individual Data

Subject	Speed (mph)	Lactate (mmol)	Heart Rate (bpm)	RPE Legs	RPE Arms	RPE Chest	RPE Overall	Station Time (min)
FP1	7.2	11.3	179	9.0	9.0	9.0	9.0	7.0
FP2	8.3	7.4	176	10.0	8.0	10.0	10.0	3.0
FP3	7.5	9.0	200	10.0	9.0	9.5	10.0	5.0
FP4	5.4	5.4	187	6.0	7.0	9.0	8.0	3.0
FP5	6.9	9.7	194	9.0	8.0	9.0	10.0	6.0
FP6	7.5	10.2	184	9.0	3.0	10.0	9.0	4.0
FP7	7.7	3.0	182	7.0	7.0	9.5	9.0	5.0
FP8	7.7	6.1	204	9.0	9.0	9.0	9.0	7.0
FP9	7.7	10.3	170	6.0	3.0	9.0	9.0	7.0
FP10	7.7	7.8	173	9.0	7.0	9.0	9.5	8.0
FP11	7.2	10.3	183	9.0	4.0	9.0	9.0	4.0
FP12	7.7	8.9	177	9.0	10.0	10.0	10.0	4.0
FP13	7.2	11.7	186	10.0	10.0	10.0	10.0	7.0
FP14	7.2	8.0	177	6.0	7.0	9.0	8.0	5.0
FP15	6.9	9.7	155	7.0	4.0	9.0	8.0	2.0
FP16	7.2	7.1	180	10.0	9.0	10.0	10.0	4.0
FP17	9.2	11.4	198	8.0	8.0	9.0	8.0	3.0
FP18	8.1	5.3	174	10.0	6.0	9.0	9.0	4.0
FP19	7.2	7.2	182	9.0	9.0	10.0	10.0	7.0
FP20	8.1	5.4	174	6.0	5.0	9.0	8.0	3.0

RPE = Rating of perceived exertion using the OMNI 0-10 scale

A.2.5 Threshold to Detect Passive Motion

Table 32. Threshold to Detect Passive Motion Individual Data

	Pre-Fatigue TTDPM (°)		Post-Fatigue TTDPM (°)		Post-Pre TTDPM (°)		%Change TTDPM (°)	
Subject	**Extension**	**Flexion**	**Extension**	**Flexion**	**Extension**	**Flexion**	**Extension**	**Flexion**
FP1	2.23	-1.03	2.23	-1.50	0.00	-0.47	0.0	45.2
FP2	1.63	-1.83	2.27	-2.57	0.63	-0.73	38.8	40.0
FP3	0.83	-1.13	0.83	-0.67	0.00	0.47	0.0	-41.2
FP4	3.93	-3.67	2.43	-4.43	-1.50	-0.77	-38.1	20.9
FP5	1.50	-0.93	1.60	-1.33	0.10	-0.40	6.7	42.9
FP6	1.33	-1.03	1.47	-0.87	0.13	0.17	10.0	-16.1
FP7	1.70	-1.67	1.90	-1.47	0.20	0.20	11.8	-12.0
FP8	0.43	-0.43	0.60	-0.83	0.17	-0.40	38.5	92.3
FP9	0.60	-1.00	0.70	-0.77	0.10	0.23	16.7	-23.3
FP10	0.73	-0.70	0.57	-0.73	-0.17	-0.03	-22.7	4.8
FP11	1.30	-1.00	1.80	-1.27	0.50	-0.27	38.5	26.7
FP12	1.23	-1.07	1.00	-1.07	-0.23	0.00	-18.9	0.0
FP13	2.07	-2.70	1.90	-2.47	-0.17	0.23	-8.1	-8.6
FP14	3.63	-1.77	3.77	-2.53	0.13	-0.77	3.7	43.4
FP15	2.40	-0.97	1.67	-0.83	-0.73	0.13	-30.6	-13.8
FP16	0.73	-0.50	1.17	-0.93	0.43	-0.43	59.1	86.7
FP17	0.43	-0.50	1.10	-0.70	0.67	-0.20	153.8	40.0
FP18	0.90	-3.13	0.87	-1.77	-0.03	1.37	-3.7	-43.6
FP19	1.33	-1.13	1.20	-1.27	-0.13	-0.13	-10.0	11.8
FP20	1.87	-4.27	1.77	-2.10	-0.10	2.17	-5.4	-50.8

TTDPM = Threshold to Detect Passive Motion, average of first three trials with correctly identified direction

Table 33. Individual Isometric Strength Data

Subject	Pre-Fatigue Strength			Post-Fatigue Strength			Post-Pre Strength			%Change Strength		
	Quad (%BW)	Ham (%BW)	Flex/Ext Ratio	Quad (%BW)	Ham (%BW)	Flex/Ext Ratio	Quad (%BW)	Ham (%BW)	Flex/Ext Ratio	Quad (%BW)	Ham (%BW)	Flex/Ext Ratio
FP1	178.5	113.6	0.64	171.4	95.4	0.56	-7.1	-18.2	-0.08	-4.0	-16.0	-12.5
FP2	241.2	142.1	0.59	272.3	132.4	0.49	31.1	-9.7	-0.10	12.9	-6.8	-17.5
FP3	226.7	114.5	0.51	190.9	109.2	0.57	-35.8	-5.3	0.07	-15.8	-4.6	13.3
FP4	149.6	73.6	0.49	141.0	60.1	0.43	-8.6	-13.5	-0.07	-5.7	-18.3	-13.4
FP5	193.4	105.4	0.54	199.5	82.5	0.41	6.1	-22.9	-0.13	3.2	-21.7	-24.1
FP6	152.5	115.3	0.76	176.8	95.3	0.54	24.3	-20.0	-0.22	15.9	-17.3	-28.7
FP7	167.9	64.2	0.38	160.1	56.9	0.36	-7.8	-7.3	-0.03	-4.6	-11.4	-7.1
FP8	232.2	115.0	0.50	261.0	86.1	0.33	28.8	-28.9	-0.17	12.4	-25.1	-33.4
FP9	178.3	105.7	0.59	198.8	123.8	0.62	20.5	18.1	0.03	11.5	17.1	5.0
FP10	198.1	107.6	0.54	198.6	97.9	0.49	0.5	-9.7	-0.05	0.3	-9.0	-9.2
FP11	200.3	116.0	0.58	193.4	101.4	0.52	-6.9	-14.6	-0.05	-3.4	-12.6	-9.5
FP12	279.0	117.2	0.42	272.5	111.0	0.41	-6.5	-6.2	-0.01	-2.3	-5.3	-3.0
FP13	248.5	126.6	0.51	254.6	115.5	0.45	6.1	-11.1	-0.06	2.5	-8.8	-11.0
FP14	264.5	139.7	0.53	256.6	130.0	0.51	-7.9	-9.7	-0.02	-3.0	-6.9	-4.1
FP15	229.2	85.6	0.37	214.3	80.3	0.37	-14.9	-5.3	0.00	-6.5	-6.2	0.3
FP16	315.4	176.0	0.56	223.1	132.5	0.59	-92.3	-43.5	0.04	-29.3	-24.7	6.4
FP17	161.7	128.4	0.79	163.7	109.6	0.67	2.0	-18.8	-0.12	1.2	-14.6	-15.7
FP18	189.5	113.9	0.60	201.1	131.8	0.66	11.6	17.9	0.05	6.1	15.7	9.0
FP19	289.2	125.2	0.43	279.1	109.2	0.39	-10.1	-16.0	-0.04	-3.5	-12.8	-9.6
FP20	250.0	152.3	0.61	252.8	148.4	0.59	2.8	-3.9	-0.02	1.1	-2.6	-3.6

Quad/Ham Strength = Isometric strength, average peak torque of three reciprocal trials of knee extension and flexion

A.3.1 Scatterplots of Pre- to Post-Fatigue TTDPM Differences and Musculoskeletal Strength Variables

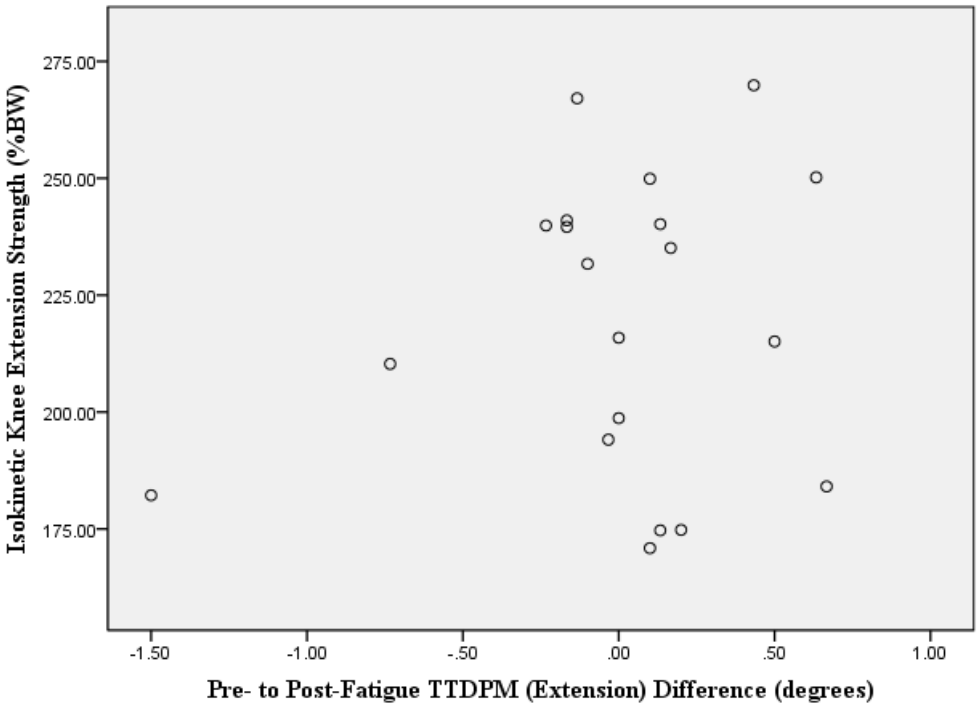

Figure 3. Pre- to Post-Fatigue TTDPM (Extension) and Isokinetic Knee Extension Strength

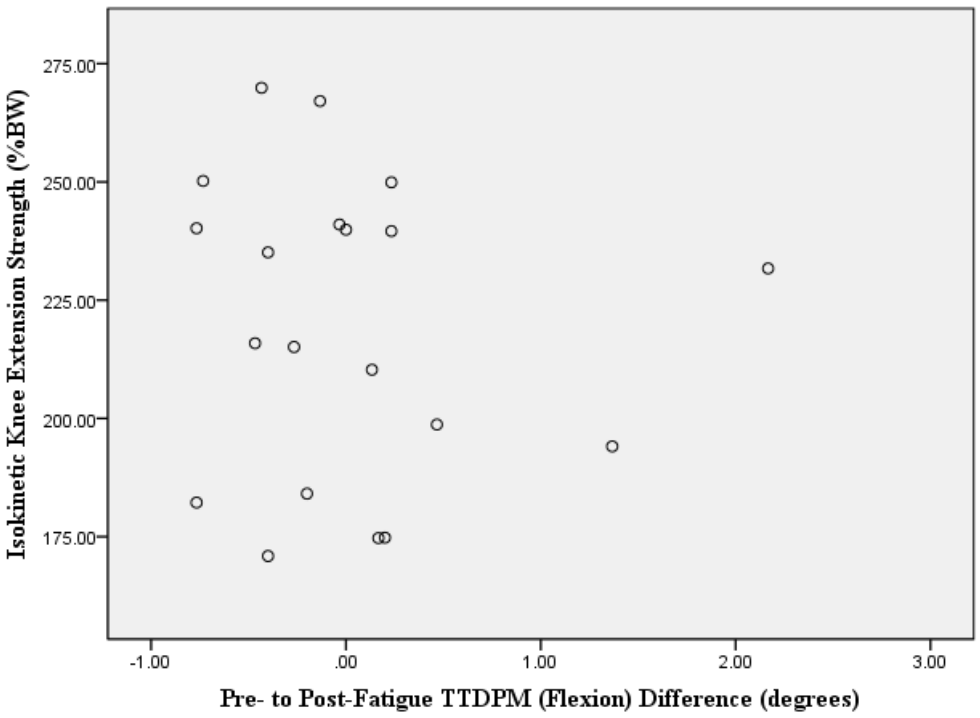

Figure 4. Pre- to Post-Fatigue TTDPM (Flexion) and Isokinetic Knee Extension Strength

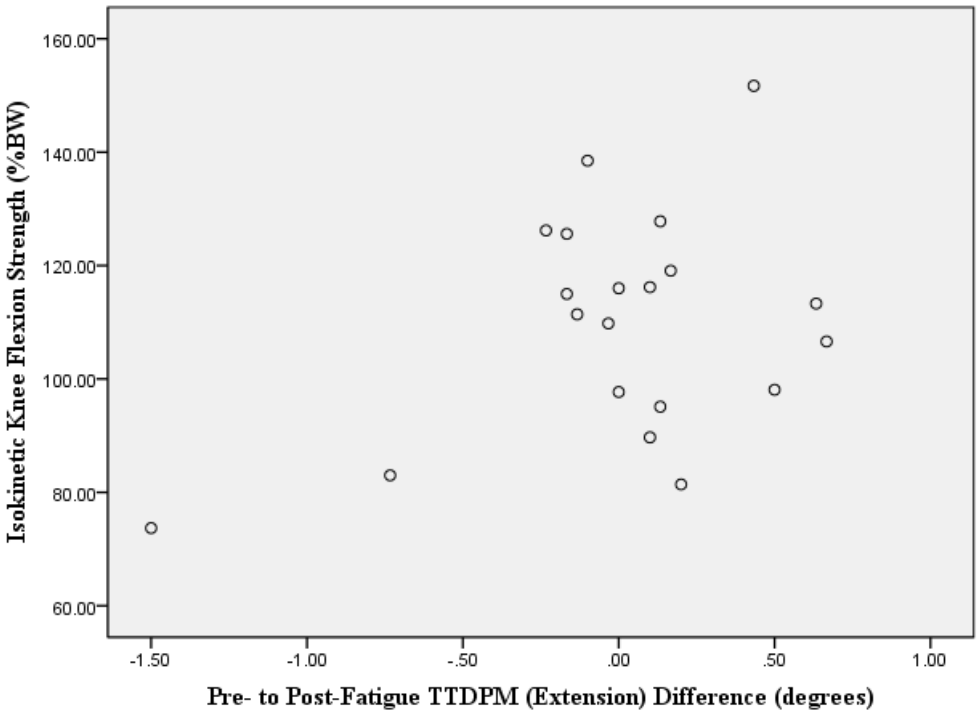

Figure 5. Pre- to Post-Fatigue TTDPM (Extension) and Isokinetic Knee Flexion Strength

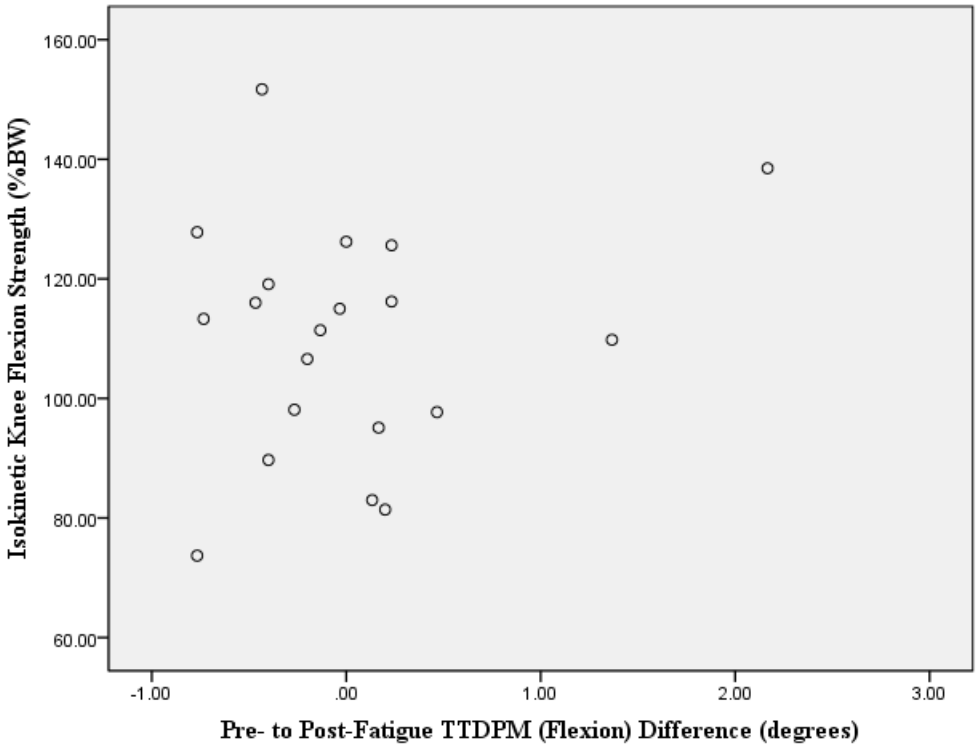

Figure 6. Pre- to Post-Fatigue TTDPM (Flexion) and Isokinetic Knee Flexion Strength

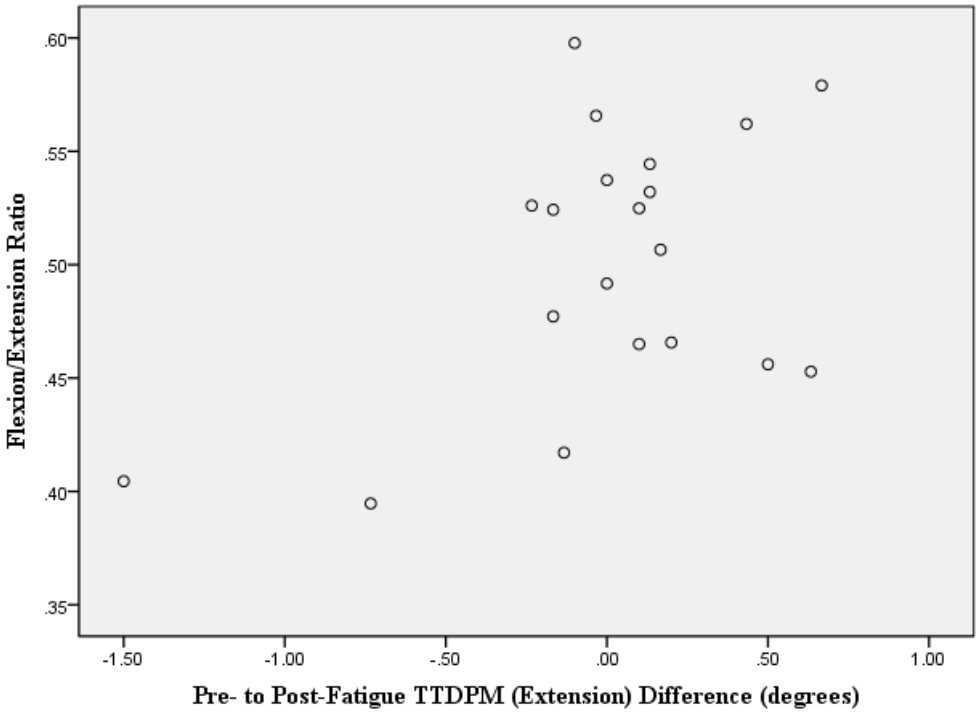

Figure 7. Pre- to Post-Fatigue TTDPM (Extension) and Flexion/Extension Ratio

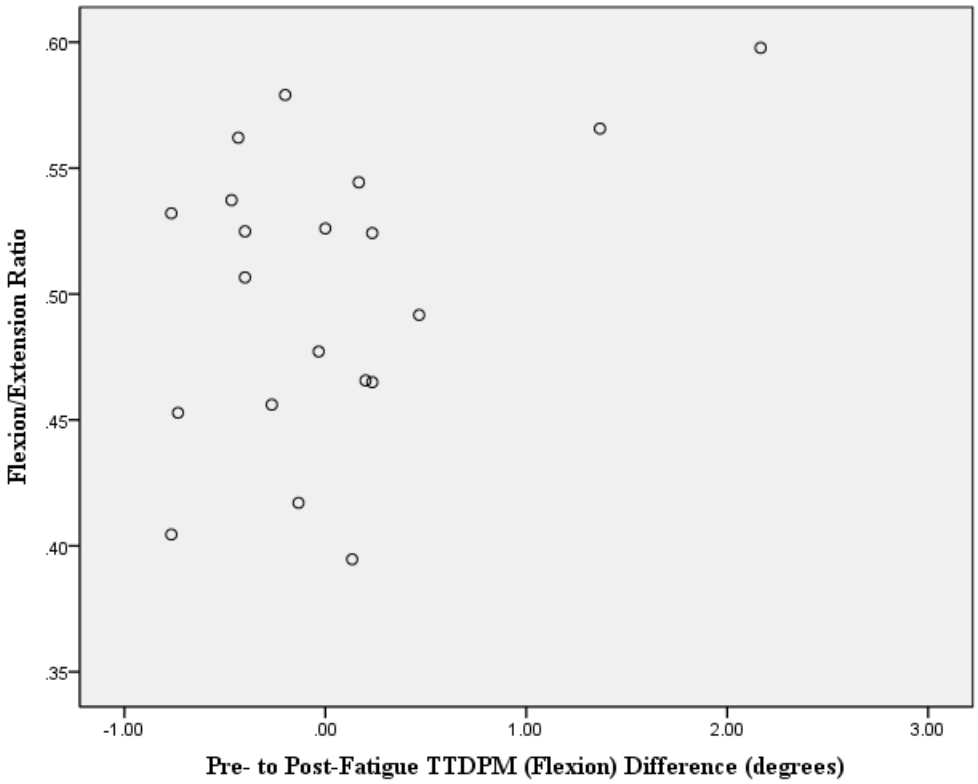

Figure 8. Pre- to Post-Fatigue TTDPM (Flexion) and Flexion/Extension Ratio

A.3.2 Scatterplots of Physiological Variables and Pre- to Post-Fatigue TTDPM Differences

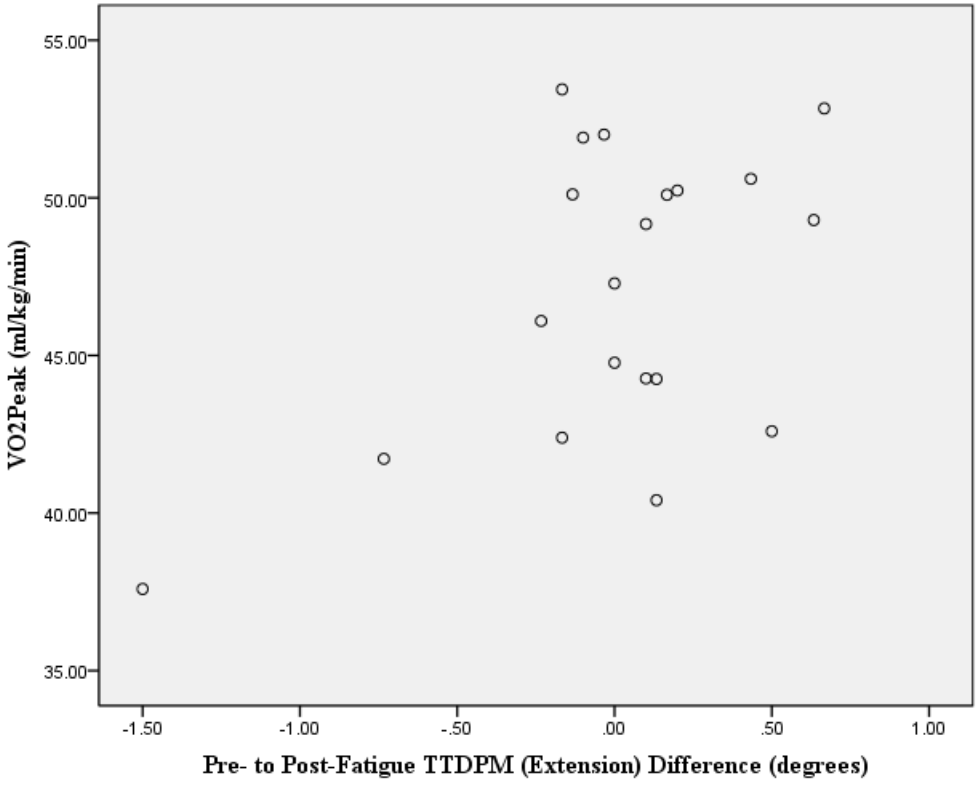

Figure 9. Pre- to Post-Fatigue TTDPM (Extension) and VO2 Peak

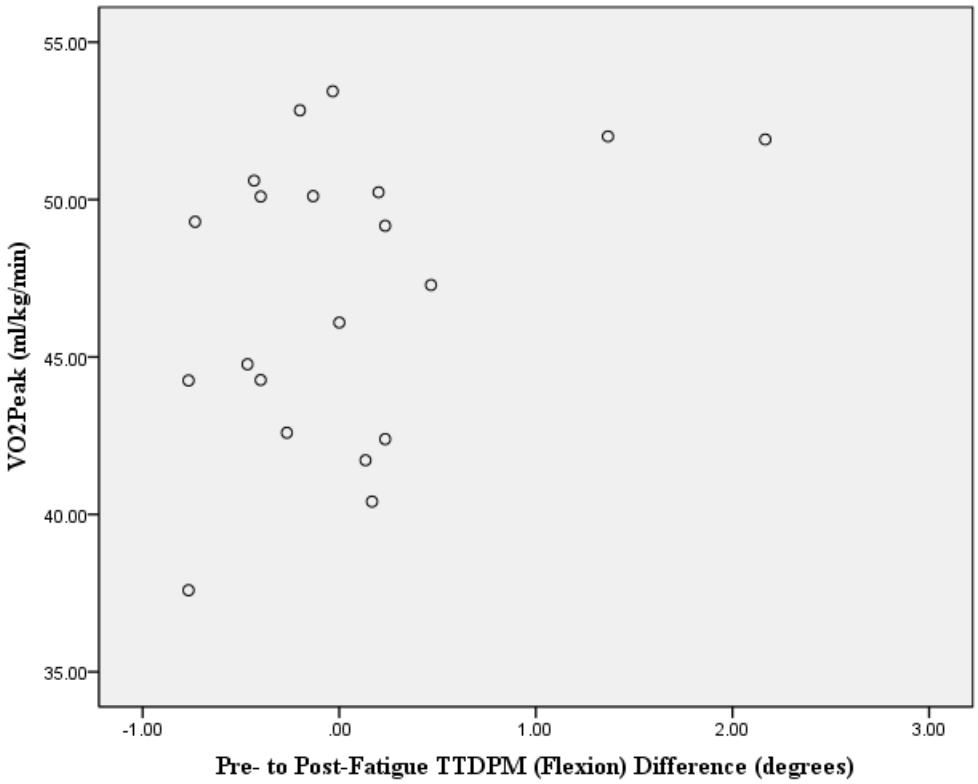

Figure 10. Pre- to Post-Fatigue TTDPM (Flexion) and VO2 Peak

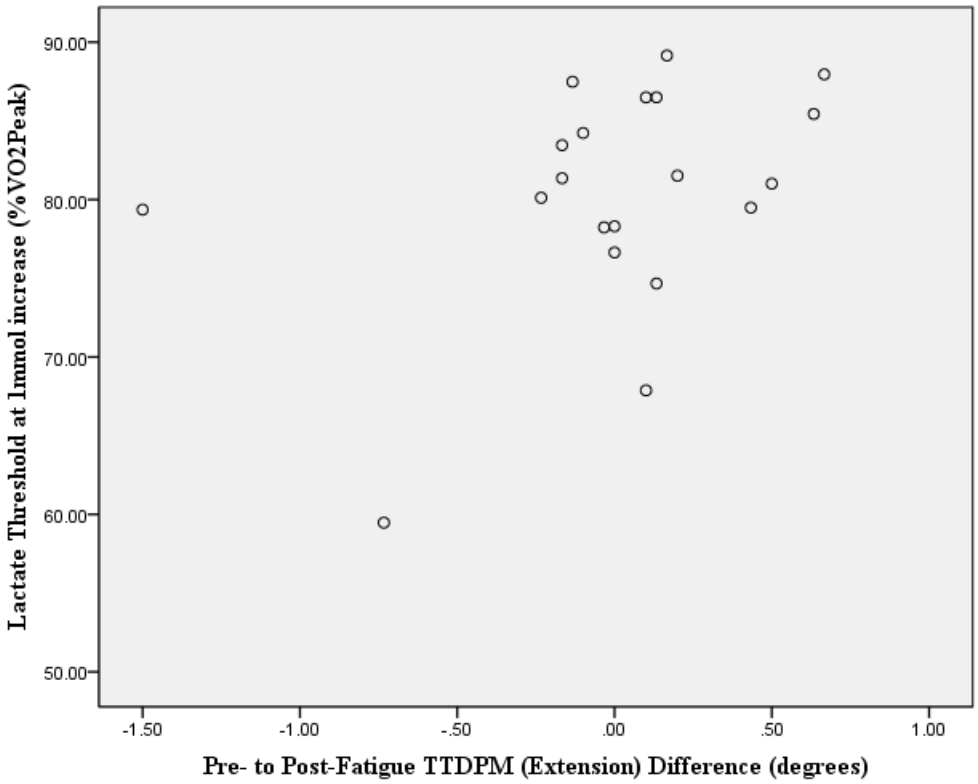

Figure 11. Pre- to Post-Fatigue TTDPM (Extension) and Lactate Threshold at 1mmol increase

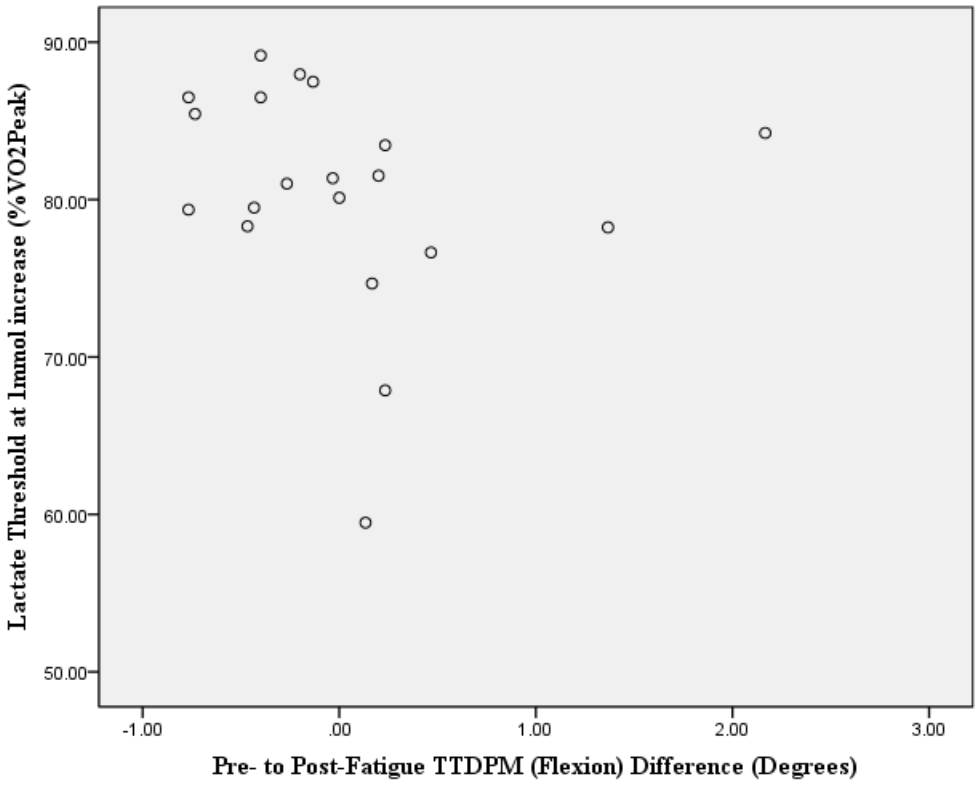

Figure 12. Pre- to Post-Fatigue TTDPM (Flexion) and Lactate Threshold at 1mmol increase

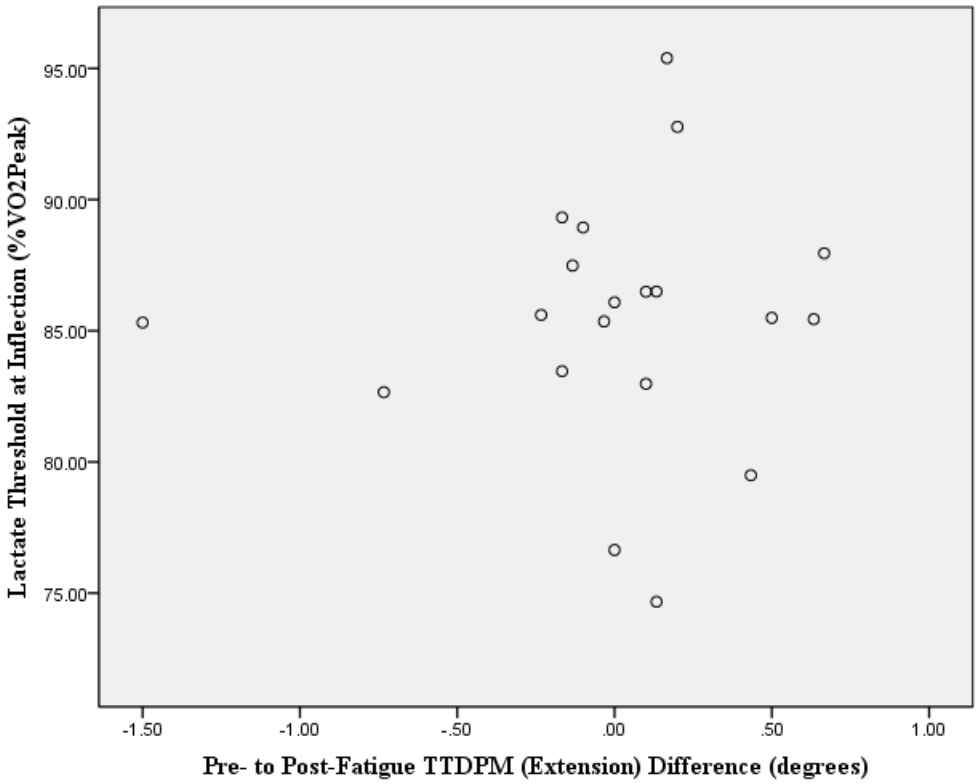

Figure 13. Pre- to Post-Fatigue TTDPM (Extension) and Lactate Threshold at Inflection

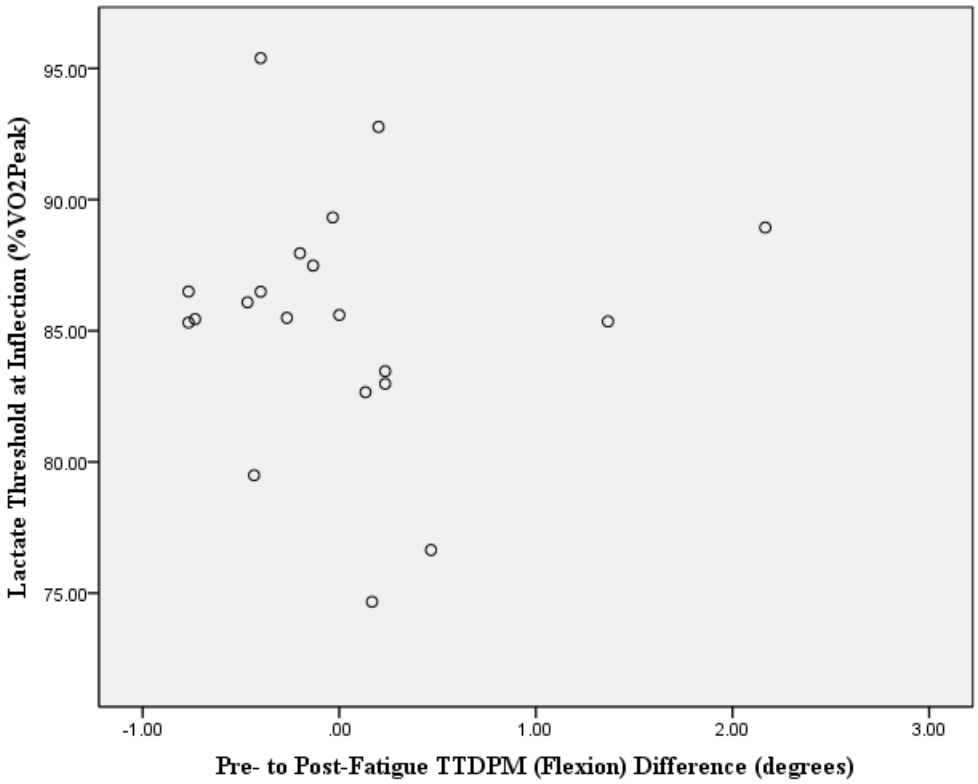

Figure 14. Pre- to Post-Fatigue TTDPM (Flexion) and Lactate Threshold at Inflection

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