A Mechanistic View of Mental Fatigue and Motor Performance: Implications of Sex, Physical Activity and Sleep Quality

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Abstract

Sustained attention on a task leads to the development of mental fatigue, which is characterized by increases in perceived fatigue and associated with declines in submaximal exercise performance. However, the neuromuscular mechanisms underlying the relationship between mental fatigue and declines in motor performance are unclear and it is unknown if there are sex-specific responses to mental fatigue. Accordingly, the overall objective of this dissertation was to examine sex-specific differences in the impact of mental fatigue on neuromuscular function and motor performance in young adults. This objective was achieved through three studies by investigating neuromuscular function of the tibialis anterior (electrophysiological and transcranial magnetic stimulation techniques) and walking performance before and after mental fatigue, as well as evaluating the relationships between gait characteristics, postural control and fatigue, as a state variable and trait characteristic. The influence of factors such as sex, physical activity and sleep quality on the effects of mental fatigue were also examined. Chapters 2 and 3 indicated that mental fatigue did not alter maximum force production, contractile function, co-contraction, or corticospinal excitability. Motor unit firing rate declined at 20% maximum voluntary contraction and cortical silent period duration increased in males and females, however these results were not specific to mental fatigue and the absolute differences were small. Mental fatigue did not impair single or dual task gait speed and regressions models suggested sex, physical activity level and sleep quality were not associated with the development of mental fatigue (chapter 3). Regression analyses in chapter 4 revealed models which best predicted postural control included trait fatigue, trait energy and sleep quality while models which best predicted gait characteristics included state fatigue, state energy and sex. However, the variance explained by these models was low, suggesting trait and state fatigue and energy are unlikely to greatly impact gait and postural control in young adults. In summary, this dissertation suggests mental fatigue does not substantially alter neuromuscular function or motor performance in young, healthy adult males and females. However, it highlights the complex relationship between mental fatigue, sustained attention, neuromuscular function and motor performance, providing several avenues for future research.
Keywords

Mental fatigue, neuromuscular function, motor unit, EMG, force, TMS, gait, balance, sex differences.
Summary for Lay Audience

Mental fatigue occurs during or after sustained attention on a task and leads to declines in exercise performance. However, it is unknown how mental fatigue impacts the function of the brain, nerves and muscles, which may contribute to the declines in exercise performance. Further, it is unknown if males and females respond differently to a mentally fatiguing task, despite females often reporting greater fatigue than males.

Therefore, the purpose of this dissertation was to determine the effect of mental fatigue on the signals sent from the brain and nerves to a muscle in the shin important for walking, and the ability of that muscle to contract in males and females. We also determined the impact of mental fatigue on walking and balance, and examined the relationships between mental fatigue, walking, balance, and factors which influence fatigue, such as sex, physical activity and sleep quality. The results indicate that mental fatigue did not impair muscle contraction, coordination of muscles around the shin or excitability of the pathway between the brain and muscle. When contracting at 20% of maximum, the rate of signals sent from the nerve to muscle slowed and there was greater inhibition within the brain in males in females. However, these results were not specific to mental fatigue and the changes were small. Mental fatigue also did not lead to declines in walking speed in males or females. Walking characteristics were associated with sex and current feelings of fatigue, while balance was associated with sleep quality and usual feelings of fatigue. However, these associations were small, suggesting usual and current feelings of fatigue do not greatly impact walking and balance in young adults. Further, sex, physical activity level and sleep quality were not associated with the development of mental fatigue. In summary, this dissertation suggests mental fatigue does not substantially impact signals sent from the brain and nerves to muscle, the ability of muscle to contract, walking or balance in young adult males or females. However, it does highlight the complex relationship between mental fatigue, sustained attention and exercise performance, providing several avenues for future research.
Co-Authorship Statement

This thesis contains material from two published manuscripts (Chapter 2, Chapter 4) and one manuscript that is in preparation (Chapter 3). On all manuscripts, Katie Kowalski is the primary author, contributing to study design; participant recruitment; data acquisition, analysis and interpretation; and drafting and revising of all manuscripts. She is also the primary author of all chapters contained within this thesis. Dr. Anita D. Christie is a co-author of chapters 2, 3 and 4, contributing to study design, data interpretation, reviewing and revising manuscripts. Bernadette Tierney contributed to data collection and analysis on Chapter 3. Dr. Ali Boolani is a co-author of chapter 4 and contributed to study design, participant recruitment, data acquisition and revising of the manuscript.
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Chapter 1

1 Introduction

1.1 Fatigue

Fatigue is a complex construct with a multidimensional etiology. The feeling of fatigue is commonly described as tiredness, exhaustion, weariness or a lack of energy\(^1\). However, fatigue and energy are distinct, but related, constructs and not merely opposite ends of one continuum\(^1\).

Almost half of all adults in the United States experience moderate to very severe fatigue over the course of a week\(^2\). It is particularly prevalent in females aged 18-44 who are twice as likely to report feeling “very tired or exhausted” in the past three months compared to males\(^3\). Fatigue is one of the most common reasons for primary care physician visits\(^4\), resulting in greater health care utilization among those with high fatigue\(^5\). Further, high fatigue is associated with greater co-morbidity of chronic and psychosocial conditions\(^6\), lower self-reported health status\(^5\), and has been suggested to be a predictor of accelerated aging\(^7\). Therefore, it is imperative to better understand the development of fatigue and its impact on health, wellness and function. This knowledge can inform the development of targeted interventions to reduce fatigue and its burden on the healthcare system while enhancing quality of life.

1.1.1 Performance and Perceived Fatigue

The sensation of feeling fatigued arises due to the interaction between changes in the two primary attributes of fatigue – performance fatigue and perceived fatigue (Figure 1)\(^8\). Performance fatigue develops in response to muscle contractions and reduces the ability of the neuromuscular system to produce sufficient force or power necessary for the intended task\(^8,9\). It is assessed by tracking objective measures of performance, such as force or walking speed. Declines in performance measures are mediated by changes to activity within the neuromuscular pathway, such as descending drive to muscles and afferent feedback from muscles\(^8,9\). Specific neuromuscular mechanisms responsible for performance fatigue include declines in voluntary activation, alterations in muscle
activation patterns, slowing of motor neuron firing rate, neuromuscular transmission deficits and declines in twitch force⁹.

**Figure 1.1 Fatigue framework**


In contrast, perceived fatigue refers to the sensations of feeling fatigued and can arise due to prolonged or sustained attention tasks¹⁰. Perceived fatigue is regulated by changes in psychological state variables and the internal, steady state environment of the individual⁸. Prolonged or sustained attention alters psychological states through changes to executive function, mood, motivation and arousal¹⁰–¹², while the internal, steady state environment is altered through changes to cerebral oxygenation and neurotransmitters¹⁰,¹³–¹⁵. Similar to performance fatigue, perceived fatigue regulates motor performance during physical activity, in part by altering perception of effort and attentional control¹⁰,¹⁶,¹⁷. Tasks that increase perceived fatigue, such as prolonged cognitive or sustained attention tasks, lead
to declines in motor performance, including slower running and cycling speed and greater errors in accuracy-based tasks, such as soccer shooting and passing\textsuperscript{16–19}.

Declines in objective measures of motor performance due to increases in perceived fatigue suggests that perceived fatigue also leads to performance fatigue. However, the mechanisms underlying this relationship are less clear\textsuperscript{17,20}. Within the fatigue model proposed by Enoka & Duchateau\textsuperscript{8}, performance and perceived fatigue are inter-related and changes in both attributes contribute to the sensation of feeling fatigued. However, it is unclear if increases in perceived fatigue can influence factors that contribute to performance fatigue, such as muscle activation patterns or motor neuron firing behavior, or if these changes to neuromuscular function contribute to declines in motor performance in the presence of heightened perceived fatigue.

### 1.1.2 State and Trait Fatigue

Perceived fatigue can be further described as a trait characteristic or a state variable\textsuperscript{8,21}. Trait fatigue represents an individual’s predisposition to feel fatigued and is a relatively stable characteristic over time. In contrast, state fatigue represents an individual’s current feelings of fatigue, which is transient and fluctuates around the relatively stable baseline level of trait fatigue\textsuperscript{21}. Therefore, an individual’s trait fatigue level is an important determinant of their state fatigue level. As previously discussed, increases in state perceived fatigue negatively influence motor performance\textsuperscript{16,19}. However, it is unknown how trait fatigue impacts motor performance in young, healthy adults.

### 1.1.3 Mental Fatigue

Psychological state is a modulating factor contributing to the development of perceived fatigue\textsuperscript{8}. Performing a prolonged cognitive or sustained attention task changes the psychological states of arousal, executive function, mood and motivation, leading to increases in perceived fatigue\textsuperscript{10–12}. As perceived fatigue develops in response to prolonged cognitive or sustained attention tasks and involves motivation and emotion, it will be referred to here as mental fatigue.
Mental fatigue results in compromised attentional resource allocation, increases in perceptions of effort, and alterations in effort-based decision making. Further, mental fatigue leads to declines in aspects of executive function, such as cognitive flexibility, planning processes and performance monitoring. These changes are mediated in part by blood flow alterations in the anterior cingulate cortex (ACC). The ACC is an important component of the executive function system and is involved in perception of effort, effort-based decision making and allocation of attentional resources. Cognitive tasks requiring sustained attention lead to prolonged ACC activation followed by a decline in activity upon task completion. The decline in ACC activity leads to compromised attentional resources and resource allocation with increases in perception of effort. This culminates in a reduced benefit-to-cost ratio of ongoing task participation. Further, functional brain activity assessments using electroencephalography (EEG) demonstrate that mental fatigue reduces sustained and goal-directed attention. These brain blood flow and activity changes result in cognitive and motor performance alterations in response to a mentally fatiguing sustained attention task.

### 1.1.3.1 Inducing Mental Fatigue

To induce mental fatigue during laboratory investigations, researchers often use either response inhibition or sustained attention paradigms. A recent review paper identified the Incongruent Stroop task or the AX-Continuous Performance Test as common approaches to induce mental fatigue. These cognitive tasks require sustained attention and response inhibition, leading to prolonged activation of the ACC. However, when these tasks are performed for 90 minutes, it is common for study participants to have reduced motivation towards task performance with subsequent task disengagement. To counteract these declines in motivation and engagement, many laboratories increase external motivation by offering monetary or other incentives to participants. The need to facilitate external motivation could confound their results as motivation is an important component of mental fatigue.

However, alternative paradigms with shorter durations can induce mental fatigue and minimize declines in motivation. Therefore, they do not require facilitating external
motivation to maintain task engagement. The Psychomotor Vigilance Task (PVT) is a sustained attention reaction time task in which participants respond to visual stimuli appearing on a computer screen at random intervals between 2-10 seconds\textsuperscript{25,26}. When performed for 20 minutes or more, the PVT leads to mental fatigue due to prolonged activation of the ACC during the task, with subsequent reductions in ACC activity after the task\textsuperscript{14}. As a sustained attention task, the PVT reliably induces mental fatigue in a shorter duration of time than many other protocols and attenuates the confounding factors of changes in motivation and task engagement.

1.1.3.2 Measurements of Mental Fatigue

A key measure of mental fatigue is an increase in ratings of fatigue on self-reported outcome measures, such as the visual analog scale (VAS)\textsuperscript{19}. Validated questionnaires can also be used to measure current feelings of fatigue (state fatigue) or usual feelings of fatigue (trait fatigue). One such questionnaire is the Mental and Physical State and Trait Fatigue and Energy Scale, which measures both mental and physical aspects of state and trait fatigue\textsuperscript{27}.

Objective measures of mental fatigue include slowing of reaction time\textsuperscript{11,14} and a greater number of errors made during cognitive tasks\textsuperscript{11,15,28}. Indices of mental fatigue, when induced by the PVT, include increases in self-reported fatigue, slowing of reaction time and a greater number lapses (failure to respond to stimuli within 500 ms).

Mental fatigue also leads to declines in performance of a physical task, particularly submaximal endurance tasks\textsuperscript{19}. For example, inducing mental fatigue leads to slower running speeds during a three-kilometer time trial\textsuperscript{29} and reduces the time to exhaustion by 18\% during an incremental cycling exercise test\textsuperscript{17}. These declines in endurance performance occur despite no differences in common cardiovascular markers of endurance performance, such as heart rate and blood lactate, compared to the control condition\textsuperscript{16,17,19}. However, during the mental fatigue condition a common feature is a higher perception of effort, which is thought to mediate the changes in submaximal exercise performance\textsuperscript{16,17,19}. 
Not only does mental fatigue impair whole-body endurance performance, but it also negatively impacts submaximal efforts at the single-joint level. During submaximal isometric knee extensor contractions, time to exhaustion declines by 13% following performance of a mentally fatiguing task compared to watching an emotionally neutral documentary\textsuperscript{20}. However, the cognitive and neuromuscular mechanisms contributing to these declines are unclear.

Technical skill performance is also impaired in the presence of mental fatigue. For example, after inducing mental fatigue, there are declines in soccer ball passing and shooting accuracy\textsuperscript{30}. These impairments are related to declines in the ability to allocate attention and effort, slower information processing speeds with reduced error monitoring, adjusting and preparing future actions for successful task completion\textsuperscript{15,28,30,31}.

Measures of maximal exercise, however, are not impacted by mental fatigue. Whole-body maximal exercise performance, such as three minutes of “all-out” cycling and maximal countermovement jump height do not decline in response to mental fatigue\textsuperscript{20,32,33}. Therefore, it appears that mental fatigue does not impair the capacity for exercise performance.

### 1.1.3.3 Modifiers of Mental Fatigue

There are several modifiers that could influence the development of mental fatigue and subsequent alterations in neuromuscular function and motor performance. Sex is one such factor. Females, especially those with high trait fatigue\textsuperscript{34}, report higher state fatigue than males\textsuperscript{5}. This difference in baseline perceptions of fatigue could influence the likelihood of becoming mentally fatigued. Further, there are sex-specific differences in the neuromuscular response to prolonged physical\textsuperscript{35} and cognitive activity\textsuperscript{36}. However, to date, there have been very few investigations of sex differences in the neuromuscular and motor performance response to mental fatigue.

Physical activity (PA) level is another factor that could alter the development of mental fatigue. Individuals with low PA levels report higher state fatigue and lower energy than those with high PA levels\textsuperscript{37,38}. Further, high PA level is associated with adaptations in
neuromuscular function\textsuperscript{39} and cognition\textsuperscript{40}. In particular, aerobic exercise preferentially enhances the structure and function of brain regions responsible for executive function and involved in mental fatigue, such as the ACC\textsuperscript{41,42}. Indeed, highly trained male athletes are more robust to the development of mental fatigue with subsequent maintenance of cycling performance compared to recreational athletes\textsuperscript{43}. However, this study only investigated male athletes, and thus it remains unknown if highly active females demonstrate similar resistance to the development of mental fatigue.

Lifestyle factors, such as sleep quality, also influence fatigue levels. Individuals with poor sleep quality report higher state fatigue and lower energy than those with good sleep quality\textsuperscript{34}. Further, sleep deprivation reduces activity in the prefrontal and anterior cingulate cortices, brain regions responsible for attention, perception and executive function\textsuperscript{44}. Thus, individuals with poor sleep quality or low quantity may have reduced capacity for sensory integration and coordinative motor output\textsuperscript{44,45}, making them more susceptible to the development of mental fatigue.

1.2 Neuromuscular Function

1.2.1 Neuromuscular Control of Movement

The neuromuscular system is responsible for the purposeful control of movement. This system is a pathway consisting of neurons in the cerebral cortex and spinal cord, which transmit electrical signals to skeletal muscle (Figure 2). Sensory signals from the periphery then send information back to the spinal cord and cerebral cortex. This sensory information is integrated and used to refine or alter movement to successfully meet the needs of the intended task\textsuperscript{46}. 
Figure 1.2. Neuromuscular pathway

The neuromuscular pathway is depicted with electrical signal initiation in the cerebral cortex. These signals descend along the spinal cord and synapse onto alpha motor neurons located in the ventral horn of the spinal cord. The alpha motor neuron axon exits the spinal cord, travels to the periphery and synapses with skeletal muscle fibers at the neuromuscular junction. One alpha motor neuron and all skeletal muscle fibers it innervates comprises a motor unit. Once crossing the neuromuscular junction, the electrical potential travels along the sarcolemma, initiating excitation-contraction coupling for force generation. Figure reprinted (Appendix 2) from Ahmad & Roach.47

1.2.1.1 Cerebral Cortex

The generation of movement planning and preparation occurs in the premotor and supplementary motor cortices46. The prefrontal cortex further assists with the selection and generation of appropriate movements for a given internal (person) and external (environmental) context. It does so by integrating afferent signals and stored memories to generate appropriate movements for the context48. Intimately connected to the prefrontal
cortex is the ACC\textsuperscript{22}. The ACC receives afferent information from numerous cortical regions involved in evaluation of the costs and rewards of ongoing task engagement and continuously monitors task performance\textsuperscript{10}. By integrating cognitive and movement information, the ACC is closely involved with effort-based decision making and motor performance error-monitoring\textsuperscript{10,22}.

The primary motor cortex contains upper motor neurons, which are the primary source for the control of voluntary movement\textsuperscript{46}. Motor signals from the primary motor cortex and numerous cortical regions (e.g. premotor, supplementary motor and somatosensory areas) serve as the origination of the descending, efferent corticospinal tract\textsuperscript{46}. This tract transports electrical signals encoding movement from the cerebral cortex to the lower motor neuron pool in the spinal cord.

The excitability of the corticospinal tract can be measured using transcranial magnetic stimulation (TMS). In this technique, a magnetic coil is positioned on the cranium, over the contralateral motor cortex region of interest. A rapid magnetic pulse is discharged from the coil, which in turn creates an ionic current within the cortex. If the current is sufficiently strong, neuronal membranes will depolarize, leading to action potential generation within the corticospinal tract. Using surface electromyography (EMG), the muscular response to this magnetic stimulation (motor evoked potential; MEP) is recorded in the contralateral muscle of interest. The amplitude of the MEP reflects excitability of the motor cortex and corticospinal tract\textsuperscript{49}.

TMS can also be used to assess intracortical inhibition of the primary motor cortex. A single TMS pulse applied to the motor cortex during contraction leads to a period of electrical silence within the muscle of interest, termed the cortical silent period (CSP). The CSP is defined from the end of the MEP to resumption of consistent electrical activity within the muscle. The first 50-60ms of the CSP is thought to be mediated by spinal inhibition, while the remainder reflects motor cortex inhibition and influences the efferent output of the cerebral cortex\textsuperscript{49}.
1.2.1.2  Motor Unit

1.2.1.2.1  Structure and Function

The volley of efferent electrical signals descending from the cerebral cortex, along the
corticospinal tract, terminates at the lower motor neuron pool in the spinal cord. Within
this pool, alpha motor neurons are responsible for innervating extrafusal skeletal muscle
fibers to produce a contraction\(^{46,50}\). Alpha motor neurons not only receive descending
input from the corticospinal tract, but they also receive numerous excitatory and
inhibitory afferent inputs. These inputs include proprioception, nociception,
mechanoreception and chemoreception from the periphery as well as feedback from itself
via Renshaw cells. These numerous inputs are generally received at the motor neuron
dendrites and are either excitatory or inhibitory in nature\(^{50}\).

The summation of all alpha motor neuron excitatory and inhibitory afferent signals
directs the efferent output of the motor neuron. If the temporal and spatial net summation
of afferent input increases the resting membrane potential sufficiently to reach a critical
threshold for depolarization at the axon hillock, an action potential will be generated.
This action potential is then propagated along the length of the axon to the skeletal
muscle fibers it innervates. The motor neuron, its axon and all skeletal muscle fibers it
innervates is termed the motor unit\(^{50}\).

1.2.1.2.2  Recruitment

Groups of motor units work together to produce muscle force and control movement.
More force can be produced with a greater number of active motor units. Motor units are
recruited and become active based on the size of their cell body. This is known as
Henneman’s size principle\(^{51}\). Smaller neuronal cell bodies have a lower threshold for
excitation and therefore reach the critical threshold for action potential generation with
less excitatory input. These smaller motor neurons have more narrow axon diameters and
innervate fewer skeletal muscles, which are more resistant to fatigue. As the excitatory
input onto the motor neuron pool increases, motor neurons of larger diameter will be
recruited as they require greater excitatory input to reach the critical threshold for action
potential generation. These larger motor neurons have large in diameter axons and
innervate a greater number of skeletal muscle fibers, which are less resistant to fatigue\(^5^0\). Thus, through Henneman’s size principle of recruitment, force can be controlled through successively activating motor units of greater size to produce more force.

1.2.1.2.3 Rate Coding

The force produced by a muscle not only depends on the number of active motor units, but also on the rate each motor unit delivers an action potential to the muscle. This is termed rate coding. The faster the frequency of action potentials arriving at the skeletal muscle, the more force it will produce. At lower intensities of contraction, motor unit recruitment serves as the primary mechanism for increasing force. However, as force production increases, rate coding becomes the dominant means of increasing force\(^5^2,5^3\).

Motor unit firing rate can be assessed using intramuscular needle electrodes. Specifically, a quadrifilar needle is one in which the stainless-steel cannula contains four platinum-iridium wires, 50 μm in diameter. The four wires terminate at an opening within the needle cannula, 7.5 mm from the tip. The wires are configured in a square array, separated by 200 μm. This arrangement provides three distinct channels of bipolar motor unit action potential recordings, facilitating motor unit identification discrimination\(^5^4,5^5\).

1.2.1.3 Muscle

1.2.1.3.1 Excitation Contraction Coupling

When the motor unit action potential terminates at skeletal muscle, it does so at the neuromuscular junction. As the action potential reaches the axon terminal, acetylcholine is released from the terminal into the synaptic cleft between nerve and muscle. Acetylcholine binds to receptors at the motor end plate, subsequently opening sodium and potassium channels, allowing sodium and potassium ions to move down their electrochemical gradient. This ionic movement leads to a rise in resting membrane potential of the motor end plate and under normal, healthy circumstances leads to a motor end plate action potential. This action potential then travels along the skeletal muscle sarcolemma and into the t-tubules. Depolarization within the t-tubules activates dihydropyridine receptors, which in turn allow for release of calcium from the
sarcoplasmic reticulum through ryanodine receptors. It is this calcium release which allows for skeletal muscle contraction\(^{46,50}\).

To produce a contraction, calcium binds to troponin-C, a protein positioned along the actin filament. This binding leads to a conformational change in troponin, allowing tropomyosin to move away from the myosin binding site on actin. Once this site is exposed, the myosin head will bind to actin and cross-bridge cycling will occur to generate force through a process of ATP hydrolysis\(^{46,50}\).

1.2.1.3.2 Contractile Properties

To characterize the contractile properties of skeletal muscle, a single twitch contraction can be elicited using peripheral nerve electrical stimulation. This assessment allows for quantification of the peak force, time to generate peak force and rate of relaxation of skeletal muscle\(^9\). Changes to these contractile property parameters occur in response to many factors, such as the duration and magnitude of the stimulation, fiber type and temperature. However, when tracked across time they also provide insight into skeletal muscle fatigue as indicated by lower peak twitch force, longer duration to peak twitch and longer time to relax\(^9,50\).

1.2.2 Impact of Mental Fatigue on Neuromuscular Function

As previously discussed, mental fatigue leads to declines in motor performance, particularly those submaximal in nature or skill-based\(^{16,19}\). The neuromuscular mechanisms responsible for these declines in motor performance are still unclear. However, the following discussion reviews what we currently know about changes to neuromuscular function in response to mental fatigue.

1.2.2.1 Cerebral Cortex

Sustaining attention on a task leads to prolonged activation of the ACC during the task with subsequent reductions in ACC activity upon completion of the task\(^{14}\). EEG measures further demonstrate that sustained attention tasks lead to reductions in tasks regulated by the ACC and executive function systems, such as goal-directed attention, inadequate performance monitoring and adjustments following errors\(^{10,15,56}\). These alterations in
ACC function in response to mental fatigue are thought to be mediated by the neurotransmitter dopamine\textsuperscript{10,15}.

Dopamine is the primary neurotransmitter used within midbrain and cortical structures involved in reward and motivation behavior\textsuperscript{10}, action monitoring and error detection\textsuperscript{15}, and the generation of perception of effort through a cost-reward evaluation of behaviors\textsuperscript{57}. As mental fatigue leads to increases in perception of effort and declines in action monitoring and error detection, it is thought these changes are primarily moderated by alterations in dopamine concentrations\textsuperscript{10}.

1.2.2.2 Intracortical Inhibition and Cortical Excitability

There have been very few investigations into alterations in the excitability and inhibition within the corticospinal pathway in response to mental fatigue. However, one study has demonstrated there is no change in corticospinal excitability, as assessed with MEP amplitude, in response to performing a mentally fatiguing task\textsuperscript{58}. Intracortical inhibition, defined by the CSP duration, demonstrated a strong trend ($p = 0.06$) with a moderate effect size ($d = 0.56$) for a longer CSP duration after mental fatigue\textsuperscript{58}. However, this study only investigated females and to date, there have been no investigations into sex-specific differences in corticospinal excitability and intracortical inhibition changes after mental fatigue.

1.2.2.3 Maximal Contractions

Voluntary activation, as assessed with the interpolated twitch technique, in which an electrical stimulus is applied to the peripheral nerve during a maximal voluntary contraction, provides insight into the capacity of the neuromuscular system to produce force\textsuperscript{59}. Inducing mental fatigue does not lead to changes in voluntary activation in the knee extensors\textsuperscript{20,33} or anaerobic exercise performance\textsuperscript{32}. Maximum voluntary contraction, or a person’s perception of their ability to maximally contract their muscles, has demonstrated mixed results within the literature. Investigations of the knee extensors in males demonstrate MVC does not decline after a mentally fatiguing task\textsuperscript{20,33}, whereas females have demonstrated declines in dorsiflexion (DF) MVC following a mentally fatiguing task\textsuperscript{58}. Further work is required to determine if these differing results are due to
sex-specific neuromuscular responses to mental fatigue or differences in the muscles being assessed.

1.2.2.4 Submaximal Contractions

In contrast to maximal exercise, submaximal neuromuscular function does consistently change following mental fatigue. Quadriceps muscle activity is lower during cycling at 80% of peak power following 30 min of performing a mentally fatiguing task in comparison to a control task. At the single joint level, however, others have demonstrated an increase in muscle activity during a 50% MVC handgrip time to exhaustion test following a short duration (less than four min) modified Incongruent Stroop task compared to control condition. The disparate results across studies may be related to differences in the task or the muscle under investigation. However, taken together, these results suggest that while mental fatigue does not impair the capacity of the neuromuscular system, it does lead to alterations in the system during submaximal efforts. Although, it is unclear if the changes to surface EMG after mental fatigue are a result of changes to motor unit firing rate, motor unit recruitment or alterations in co-contraction.

1.2.2.5 Contractile Properties and M-wave

Neuromuscular function at or distal to the neuromuscular junction is not impacted by mental fatigue. In response to electrical stimulation, contractile properties, including peak twitch force, time to peak twitch and one-half relaxation time, do not change in response to mental fatigue. Further, mental fatigue does not alter neuromuscular transmission or skeletal muscle conduction velocity as the resultant M-wave of the electrical stimulation does not change in amplitude or duration. This suggests mental fatigue does not lead to declines in motor performance through alterations in neuromuscular function at or distal to the neuromuscular junction.
1.3 Gait and Postural Control

1.3.1 Gait

Motor control of gait is a complex system in which multimodal sensory input from the internal and external environment is integrated to create a coordinative gait pattern. The gait cycle is defined by two successive contacts of the same foot with the ground and is broadly separated into two phases: stance phase and swing phase. Stance phase accounts for approximately 60% of the gait cycle and is defined from initial contact to toe off. Within the first and last 10% of stance phase, two feet are on the ground representing double limb stance. The middle 40% of the stance phase of gait is represented by single leg stance, in which only one foot is on the ground supporting the body against gravity. Swing phase comprises the final 40% of the gait cycle and is defined from toe off to initial contact and represents the time the limb is not in contact with the ground.

Spatiotemporal parameters can be used to further describe characteristics of the gait cycle. Stride length is the distance between two successive initial contacts of the same foot while step length is the distance between two successive initial contacts of different feet. Step width represents the lateral distance between the heels of two consecutive initial contacts of different feet. Elevation of the foot during swing phase is an important spatiotemporal parameter as too low elevation leads to tripping and increases risk for falls. Further, gait speed is an important parameter as it has been suggested to be a predictor of survival in older adults.

Mechanisms contributing to these spatiotemporal parameters include the kinetics and kinematics of gait. Kinetics refers to the forces and power causing movement during gait, while kinematics are the position, angles, speeds and accelerations of body joints and limb segments. Motion capture systems have been the dominant form of assessing kinematics and spatiotemporal gait parameters, however technology has facilitated increased use of body worn movement sensors. These sensors contain tri-axial accelerometers, gyroscopes and magnetometers to measure linear and angular velocity as well as sensor orientation. Sensor systems are lower cost and require less computer...
processing than traditional motion capture systems, which increase the feasibility of use within clinical and applied settings\textsuperscript{64}.

1.3.2 Postural Control

Similar to gait, multimodal sensory input is integrated to produce motor output for maintenance of upright balance. The primary sensory inputs associated with postural control are vision, vestibular and somatosensory. These systems work in an integrative fashion to control the body’s position in space to maintain upright balance\textsuperscript{65}.

The Modified Clinical Test of Sensory Interaction and Balance is a clinically practical test used to quantify postural control while removing or altering sensory inputs. By systematically manipulating sensory input while balancing, this test allows for insight into the use of, impairments in or alterations to function of specific sensory systems\textsuperscript{66}. When performed as an instrumented task, for example with the use of body worn movement sensors, quantitative metrics can be recorded, including amplitude, velocity and jerkiness of postural sway\textsuperscript{64}. This allows for comparison of postural control across differing sensory input conditions or in response to manipulation of internal and external factors known to impact postural control, such as cognition or fatigue.

1.3.3 Cognitive Factors Influencing Gait and Postural Control

While external environmental factors, such as unstable surfaces, can impact measures of gait and postural control, so too can internal factors\textsuperscript{65,67}. As gait and postural control require input from higher cognitive centers, changes to cognitive states and function have important influences on the coordinative motor output of gait and postural control\textsuperscript{67}.

Executive function refers to a collection of high-level cognitive processes which integrate multimodal sensory information to evaluate, plan and produce effective motor output for the environmental context with appropriate allocation of attentional resources\textsuperscript{67}. Performance on tasks of executive function are associated with postural control and gait parameters\textsuperscript{68}. Further, deficits in executive function lead to insufficient or inappropriate gait control necessary for the demands of the environment leading to increased risk for
falls\textsuperscript{67}. As a specific domain of executive function, attention also impacts gait and postural control.

Attention refers to the ability to receive and process external stimuli to direct behavior. Attention has a capacity, which can grow or shrink depending on factors such as arousal, motivation and task engagement\textsuperscript{69}. All tasks, regardless of their complexity, will receive some allocation of attention which is dependent upon the demands of all ongoing tasks. Allocating sufficient attentional resources for a given task is necessary for successful task performance. When attentional capacity is reduced, insufficient attention is allocated to a task, resulting in declines in task performance\textsuperscript{69}.

A common means to investigate attentional capacity and resource allocation is with a dual-task paradigm. In this paradigm, performance of a task is evaluated when it is performed alone and compared to performance while simultaneous completing another task. The degree to which the primary task performance declines during simultaneous task performance allows for insight into the attentional capacity and resources used by the secondary task. Dual-task paradigms in young, healthy adults demonstrate that performance of a challenging cognitive task while walking leads to alterations in gait speed, double limb support time and variability in gait\textsuperscript{67}. Investigations into postural control during dual-task conditions demonstrate that the performance of a secondary cognitive task leads to a decline in postural stability\textsuperscript{65,70}. These findings suggest that changes to cognitive states and attentional resources leads to alterations in gait and postural control in young, healthy adults.

1.3.4 Mental Fatigue Influence on Gait and Postural Control

Mental fatigue leads to compromised attentional capacity and resource allocation\textsuperscript{10,12,56}. Accordingly, these changes in attention lead to alterations in gait and postural control\textsuperscript{71–73}. After a mentally fatiguing task, young adults demonstrate changes to the dynamic stability of gait\textsuperscript{71} while older adults increase the variability of gait parameters\textsuperscript{72}. Further, greater cognitive control of balance is required after performance of a mentally fatiguing task\textsuperscript{73}. However, center of pressure during unanticipated external perturbations does not change following performance of a mentally fatiguing task in young and old women\textsuperscript{74}. It
is unknown if the state of feeling fatigued has a different influence on postural control and gait than the trait characteristic of fatigue, or if this relationship is altered by demographic factors, such as sex, sleep quality and PA.

1.4 Purposes and Hypotheses

The overall objective of this dissertation was to examine sex-specific differences in the impact of mental fatigue on neuromuscular function and motor performance.

The purpose of chapter two was to determine the sex-specific influence of mental fatigue on measures of motor unit firing behavior and force variability. The hypotheses were that mental fatigue would lead to greater variability in force production and motor unit firing behavior and that this response would be greater in females than males.

The purpose of chapter three was to determine sex-specific differences in the impact of mental fatigue on properties of the central and peripheral neuromuscular system and motor performance walking tasks. We further sought to evaluate the relationship between factors which influence fatigue, such as sex, sleep quality and PA level, and the development of mental fatigue. We hypothesized that mental fatigue would negatively impact neuromuscular function and motor performance. Further, it was anticipated that the female sex, lower PA levels and poorer sleep quality would be associated with the development of mental fatigue.

The purpose of chapter four was to evaluate the relationships between postural control, gait, and perceived physical and mental fatigue and energy as state variables and trait characteristics. We also examined how these relationships are modified by sex, sleep quality and PA level. We hypothesized that high state and trait fatigue and low state and trait energy would be associated with postural control and gait characteristics indicative of unsteadiness and that these associations would be greater for females, those with poor sleep quality and low PA.
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Chapter 2

2 Force Control and Motor Unit Firing Behavior Following Mental Fatigue in Young Female and Male Adults

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2.1 Introduction

Mental fatigue is a psychophysiological state that occurs during or after prolonged periods of sustained attention or cognitive activity\(^1\) and can present subjectively or behaviorally. Subjectively, mental fatigue is characterized by increased ratings of fatigue\(^2,3\) or perceived exertion\(^4,5\). Behavioral manifestations of mental fatigue include reductions in task vigilance\(^6\) and attention\(^3,7\), slowing of reaction time\(^2,8\) and decrements in exercise performance and manual dexterity\(^4,9\). However, the neuromuscular mechanisms contributing to impaired motor performance in the presence of mental fatigue remain unclear.

With sustained attention tasks which induce mental fatigue, there are alterations in blood flow\(^2\) and brain activity\(^7,10\) in the anterior cingulate cortex (ACC). Such alterations are likely to influence the neuromuscular system, given the ACC serves as a link between cognition and motor control\(^11\). Indeed, changes to electromyographic (EMG) activity have been demonstrated during an isometric handgrip contraction\(^12\) and cycling exercise\(^13\) following a mentally fatiguing task, suggesting mental fatigue leads to changes in muscle activation strategies. While surface EMG measures following mental fatigue give insight into global muscle activity, it has not yet been determined how mental fatigue impacts motor unit (MU) firing behavior. Such information will provide better insights into changes in the neural control properties with mental fatigue, through assessment of MU firing behaviors that cannot be inferred from standard surface EMG.

Further insights about the mechanisms of mental fatigue may be gained from neuromuscular changes during the concurrent performance of a motor and cognitive task. This dual task paradigm leads to similar challenges to attentional resources\(^14\) and decrements in motor performance\(^15\) as a mentally fatiguing task. During dual-task conditions, the coefficient of variation (CV) of force during a submaximal isometric contraction increases compared with single-task\(^16,17\), suggesting greater oscillations in the common synaptic input to the motor neuron pool\(^18\) during dual tasks. This may lead to changes in force control and motor performance, however these results are limited to short-duration cognitive tasks and have not been extended to the condition of mental fatigue.
Additionally, during isometric contractions, the CV of force is higher in females than males in both upper and lower limbs\textsuperscript{19}. Relevant factors likely contributing to this sex-specific response include muscle strength and agonist-antagonist activity\textsuperscript{19}. When a cognitive task is performed concurrently during an elbow flexion isometric contraction, females have a greater increase in the CV of force and co-activation than males\textsuperscript{17}. However, this observation is less consistent in the ankle dorsiflexors\textsuperscript{20}. Females also report higher levels of mental fatigue than males\textsuperscript{21}, suggesting females may demonstrate greater mental fatigue-related declines motor performance than males. However, previous research examining the impact of mental fatigue on subsequent motor performance has not addressed sex-specific responses\textsuperscript{13,22}. Thus, it is unknown whether mental fatigue differentially impacts motor performance in males and females.

The purpose of this study was to determine if mental fatigue leads to alterations in neuromuscular function in healthy, young males and females. Specifically, we examined whether a mentally fatiguing task that requires sustained attention impacts force production of the dorsiflexors and MU firing behavior of the tibialis anterior (TA), a key muscle involved in the control of balance and walking. We also sought to determine sex-specific neuromuscular responses to mental fatigue. We hypothesized that following a mentally fatiguing task, there would be greater variability in force production and MU firing behavior compared to baseline measurements and that variability would be greater in females than males.

2.2 Methods

2.2.1 Participants

Nineteen participants (10 females, 9 males, 23.4 ± 4.4 years old) were recruited from the local university community. Sample size was estimated based on the number of participants required to detect a significant change in reaction time after the PVT, using data from Lim et al. (2010)\textsuperscript{2}, who similarly used a 20-minute PVT intervention. This analysis indicated a minimum sample size of 9 was necessary to detect a difference with $\alpha = 0.05$ and $\beta = 0.80$. As we intended to compare male and female performance, we
recruited 10 participants in each group. Due to technical difficulties, one male participant was excluded.

Study participants did not report illness associated with fatigue, use of medications which alter cognitive or neuromuscular function, a history of cognitive deficiencies including difficulty concentrating, or musculoskeletal or neurologic impairments. All participants refrained from exercise, alcohol and central nervous system stimulant and depressant pharmacological agents within 12 h of participating in this study, and had normal, or corrected to normal, vision. Each participant provided written informed consent following the procedures approved by the Human Subjects Review Board at the University of Oregon and following the standards set by the Declaration of Helsinki.

2.2.2 Experimental Protocol

Before the start of the experiment, participants completed the Pittsburgh Sleep Quality Index (PSQI), Multidimensional Fatigue Inventory (MFI) and rated their subjective feeling of tiredness on a 10-point Likert scale (1 = not tired at all, 10 = very tired). Following the mentally fatiguing task, subjects reported their feeling of tiredness on the same Likert scale.

During the single testing session, we obtained measures of dorsiflexion (DF) strength and force variability, surface EMG and indwelling MU firing patterns of the TA before, during and after a sustained attention task that induces mental fatigue (Figure 2.1). DF muscle contractile properties were also assessed at these time points to ensure no muscular fatigue occurred as a result of the experimental protocol. Baseline assessments of DF maximal voluntary contraction (MVC) force, maximal TA electrical response (M-wave) and DF muscle twitch characteristics were attained before beginning the experimental protocol. Details of these measures are provided below. Following the baseline assessments, participants performed an isometric DF contraction at 20% MVC for 10 s, rested for 6 s, then contracted at 50% MVC for 10 s. Upon relaxation, a single electrical stimulus was applied to the deep peroneal nerve to measure M-wave and muscle twitch characteristics. This series of contractions was carried out before and after completing the sustained attention task as a single-task, and within the first and final
minutes as a dual-task. Following the final series of contractions, participants performed a single 4–5 s MVC to ensure no skeletal muscle fatigue had occurred.

Figure 2.1 Experimental protocol

2.2.3 Questionnaires

As sleep quality can impact cognitive and motor functions, the PSQI self-report questionnaire was used to assess overall sleep quality. The PSQI consists of nine self-reported questions about sleeping patterns within the last month. A total score of 5 or greater is indicative of a “poor” sleeper\(^{23}\). The MFI was used to assess general fatigue. The MFI is a self-report questionnaire with 20 items related to how participants have been feeling “lately” and higher scores indicate greater fatigue\(^{24}\).

2.2.4 Sustained Attention Task

To induce mental fatigue, participants performed the Psychomotor Vigilance Task (PVT). The PVT is a sustained attention task where participants are instructed to respond to visual stimuli that occur randomly at short intervals (2–10 s) on a computer screen, by clicking a computer mouse as rapidly and accurately as possible\(^{25}\). The PVT is an objective, valid measure for assessing behavioral alertness and vigilant attention\(^{26}\). When performed for 20 min or more, a time-on-task effect is observed with a slowing of reaction time and/or decreases in task accuracy, indicating the presence of mental fatigue\(^2\). Lapses in reaction time (RT >500 ms) during this task are associated with subjective measures of physical fatigue and a decline in energy\(^{2,27}\).
A computer monitor placed 2 m from the participants was used to display the PVT. A red number appeared on a black screen and began counting up. Participants were instructed to left-click a wireless mouse they held in their dominant hand as quickly as possible when the number appeared. When the button was pressed, the number counter stopped, briefly displayed the participant’s reaction time, then the screen returned to black before the next stimulus was presented.

Participants performed the PVT for 22 min with the first and last minute as a dual task of responding to the PVT and performing the 20 and 50% MVCs. The first and final minutes of the PVT, when contractions and nerve stimulation were occurring, were not included in the assessment of PVT performance. Lapses (>500 ms response time) were counted and reaction time was calculated as an average of reaction times during minutes 1–6 (Start-PVT) and minutes 16–21 (End-PVT) of the PVT (Figure 2.1). False starts and anticipations (reaction time <100 ms) were excluded from the reaction time averages.

### 2.2.5 Force

Participants were placed in a semi-reclined position on a table with their right foot strapped to a custom-built apparatus designed to measure DF force. Because of a recent right ankle sprain, we used the left foot for one subject. The ankle was set at 20° of plantar flexion with the knee supported in a slightly bent position. An inflexible strap was placed across the dorsum of the foot to ensure contractions were isometric. The custom-built dynamometer was equipped with a load cell (SSM-AJ-250; Interface, Scottsdale, AZ, USA) from which the force signal was amplified (PM-1000; DataQ Instruments, Akron, OH, USA) and sampled at 25.6 kHz using a 16-bit A/D converter (NI USB-6251; National Instruments, Austin, TX, USA). Real-time feedback of force production was displayed to participants using DasyLab software (Data Acquisition System Laboratory, DasyTec, USA, Inc., Amherst, NH, USA).

At baseline, participants performed three MVCs each lasting 4–5 s with 1–2 min of rest between contractions. Additional trials were performed if the peak force varied by greater than 10%. The trial with the highest peak force was used as 100% MVC. Target lines were then displayed at 20 and 50% MVC on a computer monitor 2 m away. Participants
performed 10 s contractions at each intensity, separated by 6 s, before the start of the PVT (Pre-PVT), during the first (Start-PVT) and final (End-PVT) minutes of the PVT, and immediately following PVT (Post-PVT).

Using a custom-written MatLab program (Mathworks Inc., Natick, MA, USA) the force signal was down-sampled to 1,000 Hz then measures of mean force and force steadiness were calculated over a 5 s window, avoiding the ramp-up and ramp-down portions of the contraction, which were performed at a self-selected rate. Force steadiness during the 20% and 50% MVCs was quantified as the CV of mean force.

2.2.6 Intramuscular EMG

MU activity was recorded by inserting a four-wire needle electrode into the mid-belly of the TA with the position of the needle adjusted to maximize subject comfort and quality of the signal. This electrode provides three channels of MU recordings and details of its configuration have been reported previously\textsuperscript{28}. Once the needle was inserted, participants practiced performing 20 and 50% isometric MVC. The indwelling EMG signal was amplified and bandpass filtered between 1 kHz–10 kHz (P511; Grass Technologies, Warwick, RI, USA) then sampled at 25.6 kHz with a 16-bit A/D converter and DasyLab software. EMGLab software\textsuperscript{29} was used for multi-channel decomposition of the signal into single MU action potential trains. Files were manually inspected for accuracy of MU identification and firing patterns with modifications made as necessary. A custom-written MatLab program was used to calculate the mean firing rate, and CV of the interspike interval (ISI), excluding doublets (<10 ms) and long ISIs (>200 ms), avoiding the ramp-up and ramp-down portions of the contraction. MUs with fewer than 10 ISIs were excluded from the analysis. Although some MUs may have been identified in multiple contractions, MUs were not tracked across contractions.

2.2.7 Surface EMG

A wireless surface EMG electrode (Trigno Wireless EMG; Delsys Inc., Natick, MA, USA) was attached over the distal muscle belly of the TA, aligned along the assumed muscle fiber line. The EMG signal was amplified by 909, band-pass filtered at 20–450 Hz and sampled at 25.6 kHz with a 16-bit A/D converter and DasyLab software. A
custom-written MatLab program was used to down-sample the sEMG signal to 1,024 Hz and measure M-wave peak-to-peak amplitude and root mean square (RMS) amplitude. A point before and after the M-wave response was manually selected, and the maximum and minimum values within the defined window were determined automatically by the MatLab program to calculate the peak-to-peak amplitude. Mean RMS was calculated over a 5 s window, avoiding the ramp-up and ramp-down portions of the contraction, and expressed as a percent of maximum RMS during MVC trials.

2.2.8 Electrical Nerve Stimulation

With the participant at rest, the maximal electrical response of the TA was determined using a stimulating electrode secured over the deep peroneal nerve. A single, brief (200 μs) rectangular waveform stimulus was applied to the nerve (DS7A; Digitimer, Limited, Letchworth Garden City, UK) at increasing stimulus intensities until the greatest M-wave peak-to-peak amplitude was achieved. The stimulus intensity was set to 120% of this value to ensure maximal activation. Three stimuli were delivered before the experimental protocol and averaged to determine baseline M-wave amplitude. Muscle contractile properties were determined from the force response to these stimuli. A single stimulus was delivered following each 50% MVC contraction before, during and after the PVT. Twitch force characteristics were calculated using a custom-written MatLab program. Peak force was identified for each twitch and used to normalize each twitch response before calculating the time to peak force and one-half relaxation time. For peak force, the onset of the twitch was manually identified, then the peak of the force trace was automatically detected and the time between the two was calculated. For one-half relaxation time, the time it took for the force to relax from peak to one-half of the peak was automatically determined.

2.2.9 Statistical Analyses

Shapiro–Wilk tests were used to assess the normality of all outcome measures. Mauchly’s test of sphericity was performed for all variables examined with repeated measures ANOVA. Where the assumption of sphericity was violated, Greenhouse-Geisser corrections were made.
A two-way (sex, time) repeated measures ANOVA was used to evaluate PVT outcomes (reaction time, lapses, false starts, ratings of fatigue); MVC; muscle twitch characteristics; M-wave amplitude; mean force, EMG RMS and motor unit firing rate (MUFR); and the variability in force and MU ISI at each contraction intensity. When necessary, post hoc pairwise comparisons were performed using Bonferroni corrections. Independent samples t-tests were used to evaluate sex differences in participant characteristics, including age, height, weight, MFI and PSQI scores. Pearson correlation coefficients (r) were used to determine associations between changes in PVT outcomes (reaction time, lapses and fatigue rating), mean MUFR and CV of ISI and force. Effect sizes were calculated to determine the magnitude of differences in MVC and M-wave, and are reported as Hedge’s g to account for bias in small sample sizes. Interpretation of the Hedge’s g effect size uses the same criteria as Cohen’s d to determine the magnitude of the effect size. All statistical analyses were performed using SPSS (Version 24; IBM SPSS Statistics, Armonk, NY, USA). Significance was set at $p \leq 0.05$ and all data are presented as mean ± SD.

### 2.3 Results

#### 2.3.1 Participant Characteristics

Participant characteristics are presented in Table 2.1. Males and females differed only in their height ($p < 0.001$) and weight ($p = 0.002$) with males being taller and heavier than females. No sex differences were identified for age ($p = 0.78$), MVC ($p = 0.17$), BMI ($p = 0.22$), MFI ($p = 0.75$) or PSQI ($p = 0.57$).

<table>
<thead>
<tr>
<th></th>
<th>Females</th>
<th>Males</th>
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</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>23.7 ± 4.1</td>
<td>23.1 ± 4.9</td>
</tr>
<tr>
<td>Height* (cm)</td>
<td>165.4 ± 54.2</td>
<td>181.5 ± 58.4</td>
</tr>
<tr>
<td>Weight* (kg)</td>
<td>63.0 ± 11.7</td>
<td>82.3 ± 11.3</td>
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<tr>
<td>MVC (N)</td>
<td>189.4 ± 39.1</td>
<td>215.0 ± 65.0</td>
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<tr>
<td>BMI (kg/m2)</td>
<td>22.9 ± 3.2</td>
<td>25.1 ± 4.0</td>
</tr>
<tr>
<td>MFI</td>
<td>59.9 ± 4.6</td>
<td>59.3 ± 3.0</td>
</tr>
</tbody>
</table>
PSQI

<table>
<thead>
<tr>
<th></th>
<th>Start-PVT</th>
<th>End-PVT</th>
</tr>
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<tbody>
<tr>
<td>Female</td>
<td>3.7 ± 1.5</td>
<td>4.3 ± 2.9</td>
</tr>
</tbody>
</table>

Data are presented as mean ± standard deviation. * indicates significant differences between sexes.

### 2.3.2 Sustained Attention Task

PVT outcomes are presented in Table 2.2. Subjective reports of fatigue increased from an average of 3.0 ± 1.2 before the PVT to 5.0 ± 1.8 after the PVT ($p < 0.001$). However, there was no main effect of sex ($p = 0.12$) and no significant interaction between sex and time ($p = 0.88$). Reaction time significantly lengthened by 14% from the start of the PVT (276.1 ± 31.5 ms) to the end of the PVT (314.2 ± 37.7 ms; $p < 0.001$). There was no main effect of sex ($p = 0.81$) nor an interaction between sex and time ($p = 0.19$). The number of lapses increased from the beginning (0.8 ± 1.1 lapses/person) to the end of the PVT task (1.9 ± 2.5 lapses/person; $p = 0.01$). However, there was no significant difference between sexes ($p = 0.62$) and no significant interaction between sex and time ($p = 0.60$).

<table>
<thead>
<tr>
<th>Table 2.2 Psychomotor vigilance task outcomes</th>
<th>Start-PVT</th>
<th>End-PVT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Self-reported fatigue†</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>3.5 ± 1.2</td>
<td>5.4 ± 1.7</td>
</tr>
<tr>
<td>Male</td>
<td>2.4 ± 1.0</td>
<td>4.4 ± 2.0</td>
</tr>
<tr>
<td>Reaction time† (ms)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>281.3 ± 32.1</td>
<td>312.6 ± 37.3</td>
</tr>
<tr>
<td>Male</td>
<td>270.4 ± 31.8</td>
<td>315.9 ± 40.4</td>
</tr>
<tr>
<td>Lapses† (# per person)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>7 (0.7 ± 1.0)</td>
<td>16 (1.6 ± 1.6)</td>
</tr>
<tr>
<td>Male</td>
<td>8 (0.9 ± 1.4)</td>
<td>20 (2.2 ± 3.2)</td>
</tr>
<tr>
<td>False starts (# per person)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>10 (1.0 ± 1.3)</td>
<td>6 (0.6 ± 0.8)</td>
</tr>
<tr>
<td>Male</td>
<td>9 (1.0 ± 1.0)</td>
<td>12 (1.3 ± 1.4)</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD. † indicates significant main effect of time.
2.3.3 Force

There was no main effect of sex for MVC force \((p = 0.17)\), nor a significant interaction between sex and time \((p = 0.14)\). MVC did change over time \((p = 0.001)\) as participants had a 7.9% higher MVC Post-PVT \((217.4 \pm 47.2 \text{ N})\) than Pre-PVT \((201.5 \pm 53.1 \text{ N})\). However, the effect size for this difference was small \((g = 0.3)\).

Mean force values across time and contraction intensity are presented in Figure 2.2. In the 20% MVC condition, there was a significant main effect of time \((p = 0.05)\). Post hoc analysis indicates a trend for End-PVT force \((44.5 \pm 11.7 \text{ N})\) to be greater than Pre-PVT force \((43.5 \pm 10.6 \text{ N}; p = 0.06)\) by 2.5%. There was no significant main effect of sex \((p = 0.35)\) or interaction between sex and time for mean force in the 20% MVC condition \((p = 0.52)\).

![Figure 2.2 Force outcomes](image-url)

**Figure 2.2 Force outcomes**
Mean force in males (closed circles) and females (open circles) across time in the 20% maximum voluntary contraction (MVC; A) and 50% MVC (B) condition. Force steadiness quantified as the coefficient of variation (CV, %) in males and females across time in the 20% MVC (C) and 50% MVC (D) condition. †Significantly different than Pre-psychomotor vigilance task (PVT) in panel (A) and Start-PVT and End-PVT in panel (B).

In the 50% MVC condition there was a main effect of time for mean force ($p = 0.004$) with Post-PVT force (101.2 ± 26.1 N) being higher than Start-PVT (99.0 ± 25.0 N; $p = 0.009$) by 2.2% and End-PVT (99.9 ± 25.4 N; $p = 0.05$) by 1.3%. There was no significant main effect of sex ($p = 0.31$) or interaction between sex and time for mean force in the 50% MVC condition ($p = 0.62$).

CV of force across time and contraction intensity is presented in Figure 2.2. In the 20% MVC condition, CV of force was not significantly different over time ($p = 0.16$) or between sexes ($p = 0.29$), and there was no significant interaction between sex and time ($p = 0.57$). In the 50% MVC condition, CV of force was also not significantly different over time ($p = 0.29$) or between sexes ($p = 0.84$), and there was no significant interaction between sex and time ($p = 0.62$).

2.3.4 Intramuscular EMG

One-hundred and eighty-eight MUs were evaluated in the 20% MVC conditions and 198 in the 50% MVC conditions. The total number of MUs identified per contraction are presented in Table 2.3.

Mean MUFR across time and contraction intensity are presented in Figure 2.3, and in Figure 2.4 sample data from a single participant are shown. In the 20% MVC condition, there was a main effect of time ($p = 0.002$) such that mean MUFR was lower Post-PVT (12.9 ± 2.5 Hz) compared to Pre-PVT (14.8 ± 3.2 Hz, $p = 0.02$) and End-PVT (14.5 ± 2.7 Hz, $p = 0.04$). There was also a significant main effect of sex ($p = 0.02$) with a higher MUFR in females (15.5 ± 2.8 Hz) than males (12.8 ± 2.6 Hz). There was no significant interaction between sex and time for MUFR in the 20% MVC condition ($p = 0.49$).
Table 2.3 EMG and muscle twitch characteristics

<table>
<thead>
<tr>
<th></th>
<th>Pre-PVT</th>
<th>Start-PVT</th>
<th>End-PVT</th>
<th>Post-PVT</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. motor units</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20% MVC</td>
<td>58</td>
<td>43</td>
<td>47</td>
<td>40</td>
</tr>
<tr>
<td>50% MVC</td>
<td>53</td>
<td>53</td>
<td>52</td>
<td>40</td>
</tr>
<tr>
<td>RMS 20% (% MVC)†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>35.2 ± 14.3</td>
<td>35.3 ± 14.4</td>
<td>35.2 ± 14.6</td>
<td>33.6 ± 14.8</td>
</tr>
<tr>
<td>Male</td>
<td>25.7 ± 7.3</td>
<td>24.7 ± 7.8</td>
<td>25.5 ± 7.7</td>
<td>24.0 ± 7.2</td>
</tr>
<tr>
<td>RMS 50% (% MVC)*</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>57.4 ± 15.2</td>
<td>58.7 ± 14.8</td>
<td>53.6 ± 12.0</td>
<td>52.9 ± 13.9</td>
</tr>
<tr>
<td>Male</td>
<td>45.4 ± 17.6</td>
<td>41.7 ± 13.3</td>
<td>41.3 ± 13.6</td>
<td>40.3 ± 12.6</td>
</tr>
<tr>
<td>M_{Max} (mV)†</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.7 ± 0.8</td>
<td>1.7 ± 0.8</td>
<td>1.7 ± 0.8</td>
<td>1.7 ± 0.8</td>
</tr>
<tr>
<td>Male</td>
<td>2.7 ± 1.4</td>
<td>2.7 ± 1.4</td>
<td>2.8 ± 1.5</td>
<td>2.9 ± 1.5</td>
</tr>
<tr>
<td>PT (N)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>15.3 ± 5.1</td>
<td>15.3 ± 5.1</td>
<td>15.3 ± 5.1</td>
<td>15.3 ± 5.1</td>
</tr>
<tr>
<td>Male</td>
<td>17.3 ± 5.4</td>
<td>17.3 ± 5.4</td>
<td>17.2 ± 5.4</td>
<td>17.2 ± 5.4</td>
</tr>
<tr>
<td>TTP (ms)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>79.7 ± 8.8</td>
<td>80.5 ± 8.6</td>
<td>81.7 ± 9.4</td>
<td>80.9 ± 9.4</td>
</tr>
<tr>
<td>Male</td>
<td>77.2 ± 11.1</td>
<td>77.4 ± 10.1</td>
<td>77.1 ± 11.1</td>
<td>77.0 ± 11.0</td>
</tr>
<tr>
<td>½ RT (ms)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>57.1 ± 13.1</td>
<td>57.1 ± 12.4</td>
<td>56.5 ± 12.6</td>
<td>56.9 ± 12.9</td>
</tr>
<tr>
<td>Male</td>
<td>53.7 ± 27.6</td>
<td>53.6 ± 27.7</td>
<td>53.9 ± 26.7</td>
<td>54.0 ± 27.5</td>
</tr>
</tbody>
</table>

† indicates significant main effect of time. * indicates significant main effect of sex. Data are presented as mean ± SD.
Figure 2.3 Motor unit outcomes

Motor unit firing rate (MUFR) in males (closed circles) and females (open circles) across time in the 20% MVC (A) and 50% MVC (B) condition. Variability of firing rate quantified as the (CV, %) in males and females across time in the 20% MVC (C) and 50% MVC (D) conditions. *Significant difference between sexes; †significantly different from Pre-PVT and End-PVT.
At 50% MVC, there was no significant main effect of time ($p = 0.54$) or sex ($p = 0.11$) for mean MUFR. There was a significant sex by time interaction in the 50% MVC condition ($p = 0.04$). Males and females had similar mean MUFRs during the Pre- ($p = 0.92$) and Start-PVT ($p = 0.41$) trials. However, males had a lower MUFR than females during End-PVT ($p = 0.05$) and Post-PVT ($p = 0.01$).

The CV of MU ISI across time and contraction intensity is presented in Figure 2.3. In the 20% MVC condition, there was no significant change in CV ISI over time ($p = 0.37$), however, there was a significant main effect of sex with females having a higher CV ISI compared with males ($p = 0.03$). There was no significant interaction between sex and time ($p = 0.63$) in the 20% MVC condition.

In the 50% MVC condition, there was no significant main effect of time ($p = 0.65$) or sex ($p = 0.20$) for CV of MU ISI (Figure 2.3). There was also no significant time by sex interaction ($p = 0.53$) in the 50% MVC condition.
2.3.5 Surface EMG

Mean EMG RMS values across time and contraction intensity are presented in Table 2.3. In the 20% MVC condition there was a significant main effect of time ($p = 0.02$) with post hoc analysis indicating a trend for Post-PVT (29.0 ± 12.5% MVC) being lower than End-PVT (30.6 ± 12.6% MVC, $p = 0.06$). There was no main effect of sex ($p = 0.08$) nor an interaction between sex and time ($p = 0.75$). In the 50% MVC condition, the main effect of time was trending towards significance ($p = 0.06$) and the main effect of sex was significant with females having a higher EMG RMS than males ($p = 0.04$). There was no significant interaction between time and sex ($p = 0.46$).

2.3.6 M-wave and Muscle Twitch Properties

M-wave amplitude and muscle twitch characteristics are presented in Table 2.3 for a subset of participants (7F, 7M) as a stable M-wave could not be identified in some participants, due to technical difficulties. There was a significant main effect of time for M-wave peak-to-peak amplitude ($p = 0.01$), however post hoc analysis demonstrated only a trend towards Post-PVT amplitude being larger than Start-PVT amplitude ($p = 0.06$). There was no significant main effect of sex ($p = 0.10$) or interaction between sex and time ($p = 0.30$) for M-wave amplitude. Muscle twitch characteristics did not vary by time, including PT ($p = 0.07$), TTP ($p = 0.46$) or 1212RT ($p = 0.85$). There was no significant main effect of sex on PT ($p = 0.50$), TTP ($p = 0.52$) and 1212RT ($p = 0.79$). As well, there was no significant interaction between sex and time for PT ($p = 0.81$), TTP ($p = 0.30$) or ½ RT ($p = 0.56$).

2.3.7 Correlations

There were no significant correlations between the change in subjective reports of fatigue, number of lapses or reaction time and change in the CV of ISI, CV of force or mean MUFR for 20 and 50% MVC conditions ($p \geq 0.06$).

2.4 Discussion

The purpose of this study was to determine the impact of a sustained attention task on force control and MU firing behavior in young adults and identify sex-specific responses.
The results suggest that a sustained attention task induced mental fatigue, as indicated by increased subjective reports of fatigue and a slowing of reaction time on the PVT, but did not lead to changes in force steadiness or variability of MUFR. However, after the sustained attention task, mean MUFR decreased in both sexes at 20% MVC and only in males at 50% MVC, despite a slight increase in mean force in both sexes.

2.4.1 Sustained Attention Task

Sustained attention tasks have previously been shown to induce mental fatigue as indicated by increased feelings of fatigue\textsuperscript{2,3} with a slowing of reaction time\textsuperscript{2,8}. In the present study, following 22 min of performing the PVT, participants reported a 19.5% increase in subjective fatigue on a 10-point Likert scale. This increase is slightly greater than that reported by Pageaux et al. (2015) who demonstrated an increase in subjective fatigue of approximately 14% following 30 min of a modified incongruent Stroop task\textsuperscript{13}. In the current study, at the end of the PVT, reaction time was slowed by 14% and the number of lapses in reaction time more than doubled, which is consistent with others who have used 20 min of the PVT to induce mental fatigue\textsuperscript{2}. Taken together, these findings suggest we induced a level of mental fatigue that was similar to previous reports, through 22 min of the PVT as a sustained attention task.

2.4.2 Force

Despite males being 12% stronger than females, the DF MVC force was not statistically different between sexes. There are reports of males having significantly greater TA strength than females\textsuperscript{32}, however, the experimental set up could influence MVC strength due to sex differences in the TA length-tension relationship. The optimal joint position for TA MVC force is 25° of plantarflexion for females and 10° of plantarflexion in males\textsuperscript{32}. While others who have demonstrated significant sex differences in TA MVC force have used an experimental set up at 0° of plantarflexion\textsuperscript{20,33}, we used 20° of plantarflexion, which could have biased females towards being closer to an optimal position for MVC strength than males.

We also saw a small, but significant, increase in MVC Post-PVT compared with Pre-PVT. The 8% increase in MVC force was within the margin of error (10%) we used
during baseline assessment to establish participant’s MVC. The effect size for the
difference in MVC force was small ($g = 0.31$), and therefore it is unlikely that this slight
increase in MVC impacted the results of this study. No decline in MVC, combined with a
lack of change in contractile properties, suggests that our protocol did not induce
peripheral fatigue in the DF muscles and thus any changes in motor output are not a result
of peripheral fatigue. These results provide further evidence that mental fatigue does not
impair maximal force production$^{13,34}$.

Despite setting 20 and 50% MVC target lines, the mean absolute force was significantly
different over time. In the 20% MVC condition, the mean force increased by 2.5% during
End-PVT compared to Pre-PVT. In the 50% MVC condition, the mean force increased
during Post-PVT compared to Start-PVT by 2.2% and End-PVT by 1.3%. While these
changes in mean force were small, it is interesting to note that all significant changes in
mean force occurred at the end or after the mentally fatiguing task. Perhaps the presence
of mental fatigue makes it more challenging to accurately produce force at a given target
level. Indeed, others have demonstrated that mental fatigue leads to reductions in more
complex movements such as arm pointing tasks$^{35}$ and sport-specific tasks such as soccer
passing$^{36}$. Due to its extensive connections with the primary motor cortex and prefrontal
cortex, prolonged activation of the ACC during sustained attention and mentally fatiguing
tasks is thought to lead to impairments in motor control$^{11}$. Twenty minutes of PVT
performance leads to an increase in blood flow to the ACC during the PVT, followed by
a reduction in blood flow after the PVT$^2$. Prolonged activation of the ACC during our
experimental protocol could have contributed to the observed changes in mean force after
PVT performance. Additionally, the ACC serves as an error-monitoring system$^{37}$, and
thus with the decline in ACC activity after the PVT, possibly our participants had a
reduced ability to recognize they were not hitting the target lines and make appropriate
corrections. Further investigations involving more complex contractions are warranted to
determine the role of mental fatigue in impairing motor control.

Variability in force about a given value is thought to be due to variability in common
drive to the motor neuron pool$^{38}$. In the present study, DF force steadiness did not change
as a result of performing a mentally fatiguing task. While this finding is contrary to our
hypothesis, it is in agreement with Shortz and Mehta (2017) who demonstrated no change in force steadiness during an intermittent handgrip exercise to voluntary exhaustion after a cognitively fatiguing task in young and older women. The lack of identified changes in force steadiness suggests mental fatigue does not lead to changes in the variability in common drive to the motor neuron pool, despite possible alterations to cortical regions responsible for the control of movement.

We also found no difference in force steadiness between the single and dual-task portions of this study. Previous studies have demonstrated that adding a challenging cognitive task while performing an isometric contraction decreases force steadiness in the elbow flexors and first dorsal interosseus muscle. Our observed lack of change in force steadiness under dual-task conditions is consistent with other investigations of the dorsiflexor muscle group where force steadiness did not change during dual-task conditions with low to moderate DF contractions in young adults. It is also possible the PVT does not provide a sufficient challenge to cognitive resources to lead to declines in force steadiness during the dual-task condition. Nonetheless, our results suggest that the performance of a mentally fatiguing task did not lead to changes in force steadiness for short duration isometric DF contractions during single or dual-task conditions.

Additionally, we did not observe a sex difference for the variability of force production. Previous work has shown that young females have less steady force production than males. However, it was noted that force steadiness had a strong negative correlation with absolute strength, such that the stronger males were steadier than the less-strong females. In the current study, there were no sex differences in DF strength which may explain our observed lack of sex differences in DF force steadiness. Yoon et al. (2014) have also demonstrated no significant difference in DF force steadiness between males and females during a single-task isometric contraction, which was attributed to similar levels of brain activation during the isometric contractions. Our results extend these previous findings to suggest that a mentally fatiguing task does not differentially impact force steadiness in males and females.
2.4.3 EMG

Mean MUFR was significantly lower Post-PVT compared to Pre- and End-PVT in the 20% MVC condition for both sexes and only in males in the 50% MVC condition. It is an unlikely slowing of MUFR was a result of muscular fatigue as the Post-PVT MVC and contractile properties do not demonstrate muscular fatigue. In the 20% condition, EMG RMS amplitude was also reduced Post-PVT, while there was a trend for EMG RMS to decline at End-PVT compared to Start-PVT in the 50% condition. The reduction in MUFR and EMG RMS amplitude occurred despite a small, but significant, increase in absolute force at both contraction intensities. These results suggest that the presence of mental fatigue altered neural activation strategies, which could be due to prolonged activation of the ACC and its extensive connections with motor planning regions of the brain such as the prefrontal cortex and supplementary motor areas\(^{11,37,41}\). Possibly the activation of synergistic muscle groups or changes to co-contraction contributed to the observed changes in surface and indwelling EMG, as has been noted in dual-task paradigms\(^{17}\). Additional MUs could also have been recruited to maintain force, which would maintain EMG RMS amplitude while MUFR decreased. However, the exact source cannot be determined from the results of this study and future investigation is warranted.

In the current study, females had higher MUFRs than males throughout the 20% MVC condition and during End- and Post-PVT contractions in the 50% MVC condition, with higher EMG RMS throughout the 50% MVC condition than males. Previous research investigating the neuromuscular mechanisms leading to performance decrements following mental fatigue has not addressed sex-specific responses\(^{13,22}\). However, sex differences have been noted in examinations of neuromuscular function during a concurrent cognitive and motor task. Pereira et al. (2015) demonstrated sex-specific muscle activation patterns, with females using more co-contraction to maintain an isometric contraction than males during a dual-task condition\(^{17}\). While the level of co-contraction cannot be determined from the current investigation, our results suggest potential sex differences in the neural control response to mental fatigue and further work is necessary in this area to better understand sex-specific responses to mental fatigue.
Our results also suggest that the performance of a mentally fatiguing task does not impact the variability of MUFR during DF contractions as we found no changes in the variability of MUFR over time in either the 20 or 50% MVC conditions. During a concurrent arithmetic task and wrist extension isometric contraction, Bensoussan et al. (2012) have demonstrated a decline in the variability of MUFR which was accompanied by an increase in MUFR. It is, therefore, possible there are different cognitive and motor responses to a stressful mental arithmetic task and a task designed to induce mental fatigue. However, to our knowledge, the current study is the first to examine MU firing behavior during mental fatigue.

We observed a main effect of sex on the variability in MUFR, such that females had greater variability in their MUFR than males in the 20% MVC condition, though this was not observed in the 50% MVC condition. Similarly, at very low contraction intensities and using high-density surface EMG, Pereira et al. (2019) demonstrated females have greater oscillations in the common synaptic input than males during single- and dual-task conditions. There is a general paucity of data on sex differences in variability of MUFR at different contraction intensities, thus making the intensity-dependent sex difference observed here a novel observation that should be explored further.

2.4.4 M-wave and Muscle Twitch Properties

In this study we found that a sustained attention task that induced mental fatigue had no effect on muscle twitch properties as a single or dual task, indicating our contraction protocol did not induce muscular fatigue. This finding is also consistent with previous investigations in which inducing mental fatigue did not change muscle contractile properties of the knee extensors. There was a significant main effect of time for M-wave amplitude, however, given post hoc analysis did not demonstrate significant change over time, this difference is likely not significant. No change in M-wave amplitude after a mentally fatiguing task is consistent with the findings of others. These results suggest that exercise performance decrements after a mentally fatiguing task are not likely due to impaired contractile properties, and thus more central processes are contributing.
2.4.5 Limitations

While this study provides further insight into neuromuscular function changes following mental fatigue, there are some limitations. Employing a control day may provide added support to our interpretation of the impact of mental fatigue on neuromuscular properties. However, previous work has demonstrated that watching a documentary did not change neurophysiological measures, providing the support that the observed changes in our study were indeed due to the effects of mental fatigue.

Although our participants were generally recreationally active, we did not collect physical activity data. Some reports suggest that highly trained athletes are more resistant to the negative motor performance repercussions of mental fatigue. Future research is therefore warranted to delineate the role of physical activity in modulating the relationship between mental fatigue and neuromuscular function.

2.4.6 Conclusions

The performance of a mentally fatiguing task did not lead to changes in the variability of force or MUFR. However, surface and indwelling EMG results suggest there are alterations in neural activation strategies, including a decline in MUFR in both sexes during low force contractions, and only in men during moderate-intensity contractions. Our results indicate possible sex and contraction intensity-specific changes in neuromuscular activation patterns in the presence of mental fatigue. Further investigation is required to fully explore neuromuscular function changes in the presence of mental fatigue and determine if these changes contribute to impaired motor performance in the presence of mental fatigue.
2.4.7 References


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Chapter 3

3 Neuromuscular function and motor performance following mental fatigue in young adult males and females

To be submitted for publication
3.1 Introduction

Mental fatigue occurs during or after prolonged periods of cognitive activity or sustained attention on a task. It is characterized by increases in perceived fatigue and exertion with declines in cognitive task performance. Aspects of cognition particularly influenced by mental fatigue include executive function, information processing speed and attention.

These cognitive changes contribute to declines in motor performance in the presence of mental fatigue. For example, after a mentally fatiguing task, submaximal endurance performance is impaired, including slower running and cycling speeds. Accuracy-based task performance also declines in the presence of mental fatigue. Further, as mental fatigue alters attentional allocation, it may limit the ability to perform two simultaneous tasks, leading to greater declines in motor performance. However, little is known about how mental fatigue impacts submaximal walking performance as a single or dual task in young, healthy adults.

The neuromuscular mechanisms leading to impaired motor performance in the presence of mental fatigue are not well-understood. While mental fatigue does not impair voluntary muscle activation during maximal contractions, motor output to muscles may be altered during submaximal exercise. During submaximal isometric contractions, muscle activation levels, including surface electromyography (EMG) and intramuscular motor unit firing rates, decline after mental fatigue, despite no change in force. This finding suggests mental fatigue may alter muscle activation patterns, such as co-contraction. Further, previous work suggests mental fatigue leads to increases in intracortical inhibition, which may contribute to declines in motor performance.

The impact of mental fatigue on motor performance and neuromuscular function may be influenced by sex. Females report greater perceptions of fatigue than males and there are sex-specific differences in the neuromuscular response to prolonged physical activity. However, there have been few investigations characterizing sex-specific differences in the neuromuscular and motor performance response to mental fatigue.
In addition to sex\textsuperscript{11,13}, there are several factors which could influence the development of mental fatigue, including physical activity (PA) level\textsuperscript{16} and sleep quality\textsuperscript{17}. People with low PA levels report higher fatigue than those with high PA levels\textsuperscript{18,19}. Additionally, aerobic exercise preferentially enhances the structure and function of brain regions involved in the development of mental fatigue, such as the anterior cingulate cortex (ACC)\textsuperscript{20,21}. Indeed, highly trained male athletes are more resistant to the development of mental fatigue compared to recreational athletes\textsuperscript{16}, though it is not known if highly trained females have a similar response. Additionally, people with poor sleep quality report higher fatigue and lower energy than those with good sleep quality\textsuperscript{17}, which may make them more susceptible to the development of mental fatigue. However, it is not known how sex, PA level and sleep quality interact to influence the development of mental fatigue.

The purpose of this study was to investigate sex-based differences in the impact of mental fatigue on neuromuscular function and motor performance. A secondary aim was to examine the relationship between factors which may influence the development of mental fatigue, such as sex, PA level and sleep quality. We hypothesized that mental fatigue would lead to declines in motor performance during a submaximal walking test and that these changes would be greater in a dual-task condition than single-task. Further, we hypothesized that mental fatigue would impair neuromuscular function, including greater corticospinal inhibition, declines in motor unit firing rate and surface EMG amplitude. We also expected females, those with lower moderate-vigorous PA levels and poorer sleep quality would have a greater response to the mentally fatiguing task.

\section{Methods}

\subsection{Participants}

Thirty participants (15 females, 15 males; Table 3.1) were recruited from the local university community. Sample size was estimated based on the number of participants required to detect a significant change in perceived fatigue after the PVT, using combined male and female data from chapter 2. Using conventional standards of $\alpha = 0.05$ and $\beta = 0.80$, this analysis indicated a minimum total sample size of twelve participants. To allow
for sex comparisons while retaining sufficient power, we recruited 15 males and 15 females. Exclusion criteria included: medical history of illness associated with fatigue; sleep disorder; neurological, cardiovascular or pulmonary disease; diabetes; current smoker; cognitive deficiencies including difficulty concentrating; substance abuse; neuromusculoskeletal impairment affecting the lower extremities; contraindication to the use of TMS\textsuperscript{22} and use of medications that alter cognitive or neuromuscular function. All participants reported usual sleep the night before testing and refrained from exercise, alcohol, caffeine and drugs for 12 hours prior to testing. Each participant provided written informed consent of the following procedures approved by the Research Ethics Board at Western University (Project ID: 113108).

3.2.2 Experimental Protocol

Before starting the experimental protocol, participants completed the Multidimensional Fatigue Inventory (MFI) and Pittsburgh Sleep Quality Index (PSQI) questionnaires. Participants were provided with a PA monitor for the duration of the study and instructed on wear guidelines. Participants were then familiarized with all testing procedures and Likert scales encountered during the experimental protocol. The protocol consisted of experimental (mental fatigue) and control testing days. Testing days were randomized and counterbalanced across participants, separated by at least 48 hours but no more than seven days apart, and occurred at approximately the same time of day.

At the beginning of each testing day participants performed two motor performance tasks: dual-task walking and the 6-Minute Walk (6MW) test. Participants were then positioned comfortably in a chair to obtain measures of neuromuscular function. Details of these measures can be found below but, in brief, we obtained: dorsiflexion (DF) strength; muscle activity of the DFs and plantar flexors (PF); intramuscular motor unit firing rate of the tibialis anterior; and corticospinal excitability and inhibition. Participants then performed a mentally fatiguing sustained attention task (experimental day) or viewed a documentary (control day) for 30 min. The neuromuscular function measurements were then immediately repeated, followed by the motor performance tasks (Figure 3.1).
**Figure 3.1 Experimental protocol.**

Solid up arrow = electrical stimulation at deep peroneal nerve. Dashed up arrow = TMS pulse. DF, dorsiflexion; DT, dual task; PF, Plantar flexion; PVT, Psychomotor Vigilance Task; RPE = Rating of perceived exertion.

### 3.2.3 Questionnaires

As sleep quality can impact motor and cognitive function\(^{23,24}\), the PSQI was used to measure sleep quality over the last month. This nine-item questionnaire is a reliable and valid measure of sleep quality in young, healthy adults compared to other subjective measures of sleep quality\(^{25}\). Scores range from 0-21 and a score greater than five is indicative of a poor sleeper\(^{26}\).

The MFI was used to quantify participant’s perceived overall fatigue. The MFI is a 20-item questionnaire which measures how fatigued participants have been feeling “lately” in the domains of: general fatigue, physical fatigue, mental fatigue, reduced activity and reduced motivation. This questionnaire is reliable and valid in a young, healthy adult population and a higher score indicates greater fatigue\(^{27}\).

Motivation towards the motor performance tasks was assessed using the motivation subscale of the Dundee Stress State Questionnaire\(^{28}\). This subscale measures overall motivation using a 5-point Likert Scale (0 = not at all, 4 = extremely), where higher scores indicate greater motivation. This questionnaire is reliable and valid in a young, healthy adult population\(^{28}\). The questionnaire was completed twice each day: before the
first motor performance tasks (pre) and immediately after the second motor performance tasks (post).

Perceived fatigue was measured using a 10-item Likert scale, ranging from 1 (not tired at all) to 10 (very tired). Perceived fatigue was assessed before and after the motor performance tasks as well as before and after the mental fatigue and control tasks.

### 3.2.4 Physical Activity

Habitual PA was measured using a wrist-worn tri-axial accelerometer (Actigraph CentrePoint Insight Watch, Pensacola, FL). Participants wore the watch on their non-dominant wrist for a minimum of 12 hours per day for five days, including two weekend days, in accordance with best practice guidelines for measuring PA in adults. Additionally, participants completed an activity log for the corresponding five days of activity monitor wear to verify accelerometer data. A custom-written MATLAB program was used to determine PA counts and the number of minutes spent in light (800-1951 counts), moderate (1952-5724 counts) and vigorous (>5725 counts) PA per day, averaged across days.

### 3.2.5 Motor Performance Tasks

Participants began the motor performance tasks with one minute of dual-task walking in which they walked as quickly as possible while performing serial seven subtraction from a random three-digit number. The distance walked in one minute was measured and serial sevens subtraction performance was defined as the percent correct responses. Next, participants performed the 6MW test, a sub-maximal exercise test used to assess aerobic capacity and endurance, providing insight into an individual’s functional capacity. This test took place in a quiet hallway where participants were instructed to walk as quickly as possible for six minutes between two markers placed on the floor, 30 m apart. The distance walked during the 6MW test was used as a marker of physical performance in the presence and absence of mental fatigue. Rating of perceived exertion (RPE) was measured at minutes one and six of the 6MW test, on a scale from 6-20. Before and after the motor performance tasks, perceived fatigue and motivation towards the tasks were assessed.
3.2.6  Neuromuscular Function

3.2.6.1  Force

With participants sitting in 90° of hip and knee flexion, their right foot was strapped into an isometric dynamometer at 20° of plantarflexion using an inflexible strap to ensure isometric contractions. To prevent extraneous lower extremity movement, the participant’s right knee was secured within the dynamometer. The custom-built dynamometer was equipped with a load cell (FR5-300-B000; Tovey Engineering, Phoenix, AZ), from which the force signal was amplified (PM-1000; DataQ Instruments, Akron, OH) and sampled at 12.5 kHz using a 16-bit A/D converter (USB-6343; National Instruments, Austin, TX). Real-time feedback of force production was displayed to participants using DasyLab software (Data Acquisition System Laboratory, Measurement Computing Corp, Norton, MA). Before analysis, force was down-sampled to 1000 Hz using a custom-written MATLAB program (Mathworks Inc., Natick, MA).

Participants first performed three PF maximum voluntary contractions (MVC), each lasting 4-5 sec with 1-2 min of rest between contractions. Next, participants performed three, 4-5 sec DF MVCs with 1-2 min of rest between contractions. Additional trials were completed if the peak PF or DF force varied between contractions by greater than 5%. The trial with the highest peak force was used as the MVC.

Once MVC was determined, participants practiced performing 10 sec isometric DF contractions at 10, 20 and 50% MVC using real-time feedback of force production on a computer monitor placed 1.5 m away. Once comfortable with this task, participants performed two sets of 10 sec isometric DF contractions at 10, 20 and 50% MVC with 10 sec of rest in between. The order of these trials was randomized for each participant. Mean force was calculated over a five sec window during the force plateau, avoiding the force ramp-up and ramp-down, of each 10 sec isometric contraction using a custom-written MATLAB program. One additional DF MVC was performed at the end of neuromuscular function testing both before and after the mental fatigue or control task to ensure no peripheral fatigue occurred as a result of the neuromuscular function assessment.
3.2.6.2 Intramuscular EMG

Motor unit firing rate was recorded with a four-wire needle electrode inserted into the mid-belly of the TA. The position of the needle was adjusted to maximize signal quality and participant comfort. This needle electrode provides three channels of motor unit recordings and its configuration details have been previously described. The intramuscular EMG signal was amplified and bandpass filtered between 1 kHz – 10 kHz (P511; Grass Technologies, Warwick, RI), sampled at 12.5 kHz with a 16-bit A/D converter and acquired with DasyLab. EMGlab software was used to decompose the multi-channel signal into single motor unit action potential trains. Files were manually inspected for accuracy of motor unit identification with modifications made as necessary. A custom-written MATLAB program was used to calculate mean firing rate, excluding doublets and long interspike intervals (<10 ms and >200 ms, respectively), during the force plateau of each sub-maximum contraction. Motor units with fewer than 10 interspike intervals were excluded from analysis. While in some cases the same motor unit(s) may have been recorded in multiple contractions, individual motor units were not tracked across contractions.

3.2.6.3 Surface EMG

Muscle activity of the tibialis anterior (TA) and medial gastrocnemius (MG) was measured using surface EMG. Electrodes (Bagnoli-4 EMG System; Delsys Inc., Natick, MA) were placed over the TA and MG, according to SENIAM Guidelines. The EMG signal was amplified by 1000, band-pass filtered at 20-450 Hz, sampled at 12.5 kHz with a 16-AD converter and acquired with DasyLab software. A custom written MATLAB program was used to down-sample the EMG signal to 1000 Hz. The average root mean square (RMS) of TA and MG EMG amplitude was calculated over the same 5 second window defined to determine mean force. The maximum RMS of surface EMG for TA was determined by averaging the peak EMG activity over one second during the DF MVC trials, while MG peak EMG activity was determined using the same procedure from the PF MVC trials. The average RMS of surface EMG for TA and MG was then expressed as a percent of maximum RMS. Co-contraction during the sub-maximal DF
contractions was calculated as MG RMS relative to TA RMS and expressed as a percent of TA muscle activity.

### 3.2.6.4 Transcranial Magnetic Stimulation

Single-pulse transcranial magnetic stimulation (TMS) was used to assess corticospinal excitability and cortical inhibition. A 110 mm double cone coil (D110; Magstim, Eden Prairie, MN) was placed over the optimal site of the left motor cortex to elicit a motor evoked potential (MEP) in the right TA. The optimal site was defined as the coil position that consistently produced the largest MEP at 60% of stimulator output. The coil was then secured in place and an outline of the coil position was drawn on a cap worn by participants to ensure the optimal coil position was maintained. Next, the resting motor threshold (RMT) was determined as the lowest stimulator intensity required to elicit a response of at least 50 μV in at least five out of ten trials. Resting periods of at least five seconds between stimuli were provided. The stimulator intensity was then set to 120% RMT for the duration of the experiment. A single TMS stimulus was delivered during each of five, 3-4 second DF contractions at 50% MVC with 10 seconds rest in between. Corticospinal excitability was defined as the active MEP peak-to-peak amplitude averaged across all five trials. Cortical inhibition was defined as the cortical silent period (CSP) duration, as measured from the end of the MEP to resumption of voluntary EMG activity, averaged across all five trials. All trials were analyzed using custom-written MATLAB programs.

### 3.2.6.5 Electrical Nerve Stimulation

The maximal electrical response (M-wave) of the TA was determined to normalize the MEP response from TMS. This was done by securing a stimulating electrode over the deep peroneal nerve. A single stimulus (D180A; Digitimer, Ltd., Fort Lauderdale, FL) was applied to the nerve at increasing stimulus intensities until the greatest M-wave peak-to-peak amplitude was achieved. The stimulus intensity was then increased by 20% to ensure maximal activation. Three stimulations were delivered and averaged to determine maximum M-wave peak-to-peak amplitude, analyzed using a custom-written MATLAB program.
3.2.7 Mental Fatigue Task

To induce mental fatigue during the experimental condition, participants performed the Psychomotor Vigilance Task (PVT) for 30 min while wearing noise cancelling headphones to reduce the possibly of auditory distractions\(^{37,38}\). The PVT is a sustained attention reaction time task in which participants respond to visual stimuli appearing on a computer screen at random intervals between 2-10 sec, by clicking a computer mouse as rapidly and accurately as possible. When performed for 20 min or more, the sustained attention leads to a slowing of reaction time and/or decreases in task accuracy, indicating the presence of mental fatigue\(^2\). Lapses in reaction time (>500 ms) during the PVT are associated with subjective measures of physical fatigue and declines in energy\(^{39,40}\).

3.2.8 Control Task

During the control condition, participants watched the first 30 minutes of *Earth*, a documentary about the migration paths of four animal families\(^{41}\). This documentary has previously been used as an emotionally neutral, yet engaging, control task in studies of mental fatigue\(^8\). The documentary was displayed to participants on the same computer used to display the PVT with audio transmitted through noise-cancelling headphones.

3.2.9 Statistical Analysis

Shapiro-Wilk and Levene’s tests were used to assess normality and homogeneity of variance for all outcome measures. Descriptive characteristics of males and females were evaluated using independent samples t-tests, including age, height, weight, BMI, MFI, PSQI, PA level, DF and PF MVC. A two-way (pre-post, sex) repeated measures ANOVA was used to evaluate PVT outcomes (reaction time, lapses, ratings of fatigue). A three-way (day, pre-post, sex) repeated measures ANOVA was used to evaluate motor performance outcomes (dual-task distance walked, serial seven subtraction performance, 6MW distance, motivation, self-reported fatigue) and neuromuscular function outcomes (MVC, submaximal force, surface EMG RMS, motor unit firing rate, MEP amplitude, CSP duration). During the 6MW test, a four-way repeated measures ANOVA was used to evaluate RPE (day, pre-post, 6MW minute, sex) and self-reported fatigue (day, pre-post, start-end, sex). A two-way (day, sex) repeated measures ANOVA was used to evaluate
M-wave amplitude. As appropriate, post hoc pairwise comparisons were performed using Bonferroni corrections. Effect sizes were calculated for all main effects and interactions as partial eta squared ($\eta^2_p$) and interpreted as small ($\eta^2_p = 0.01$), medium ($\eta^2_p = 0.06$) and large ($\eta^2_p = 0.14$)\(^2\). Due to technical issues, sample size for MVC at pre-post testing and TMS measures includes 14 males and 14 females while MG RMS includes 15 males and 13 females.

For regression analyses, Mahalanobis distance was used to check for multivariate outliers in moderate-vigorous PA, PSQI and sex. Backward stepwise multivariate multiple linear regression models were used to evaluate the relationships between moderate-vigorous PA min/day, sleep quality and sex and changes in PVT outcome variables (subjective reports of fatigue, reaction time, number of lapses). Each regression model was examined for outliers and influential data points using Cook’s Distance, using a threshold of greater than one to indicate a significantly influential outlying data point\(^3\). This led to the exclusion of one case. Regression model homoscedasticity was examined with residual plots. All statistical analyses were performed using SPSS (Version 26; IBM, Armonk, NY).

### 3.3 Results

#### 3.3.1 Participant Characteristics

Female and male participants were similar in age and body mass index ($p \geq 0.07$), though males were taller, heavier and stronger than females ($p \leq 0.005$; Table 3.1). On the MFI, females reported greater levels of fatigue than males ($p = 0.02$), but females and males had similar sleep quality and moderate-vigorous PA levels ($p = 0.07$).

<table>
<thead>
<tr>
<th>Table 3.1 Participant characteristics</th>
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<tr>
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<td>BMI (kg/m(^2))</td>
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<td><strong>Males</strong></td>
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<td>Weight (kg)</td>
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<td>BMI (kg/m(^2))</td>
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</table>
3.3.2 Mental Fatigue

On the mental fatigue day, 30 min of PVT performance successfully induced mental fatigue. During the last five minutes of the PVT, participants had a slower reaction time ($p < 0.001; \eta^2_p = 0.41$) and committed a greater number of lapses ($p = 0.01; \eta^2_p = 0.20$) compared to the first five minutes of the PVT (Figure 3.2). Females had slower reaction times than males ($p = 0.04; \eta^2_p = 0.15$) and committed a greater number of lapses ($p = 0.05; \eta^2_p = 0.13$). There were no significant sex and time interactions for reaction time or lapses ($p \geq 0.14$).
**Figure 3.2 PVT outcomes**

**A:** Reaction time was slower at the end of the PVT (min 26-30) compared to the start (min 1-5; *p* < 0.001); females had a slower reaction time than males (*p* = 0.04). **B:** Number of lapses (reaction time >500 ms) was greater at the end of the PVT compared to the start (*p* = 0.01); females had a greater number of lapses compared to males (*p* = 0.05). Data presented as mean ± standard deviation.

Perceived fatigue before and after the mental fatigue and control intervention was not significantly different between days (*p* = 0.09), however it was significantly greater post-intervention compared with pre (*p* < 0.01; η²_*p* = 0.53; Figure 3.3A). The pre-post intervention differences were primarily due to an increase in perceived fatigue on the mental fatigue day, as indicated by a significant interaction between day and time (*p* < 0.001; η²_*p* = 0.50). Pre-intervention, perceived fatigue was similar across days (*p* = 0.33) and significantly increased from pre- to post-PVT on the mental fatigue day (*p* < 0.001). However, there was no significant difference from pre- to post-documentary (*p* = 0.06)
on the control day. Post-intervention, perceived fatigue was greater on the mental fatigue day compared to control day ($p = 0.001$).

Overall, perceived fatigue was also significantly greater in females than males ($p = 0.03$; $\eta^2_p = 0.16$; Figure 3.3A). This sex difference was primarily due greater perceived fatigue in females at the post-intervention time point as there was a significant interaction between sex and time ($p = 0.02$; $\eta^2_p = 0.19$). Although males and females reported similar pre-intervention fatigue levels ($p = 0.24$), and both sexes reported an overall increase from pre- to post-intervention ($p \leq 0.04$), this increase was greater in females than in males ($p = 0.008$). There were no significant interactions between day and sex ($p = 0.75$) or day, time and sex ($p = 0.27$).

Motivation was similar between days ($p = 0.22$), time points ($p = 0.48$) and sexes ($p = 0.95$; Figure 3.3B). There were no significant two or three-way interactions of day, time and sex for motivation ($p \geq 0.21$).
Figure 3.3 Mental fatigue and control intervention outcomes

A: Perceived fatigue before and after 30 minutes of the mental fatigue and control tasks. Overall, perceived fatigue was greater post compared with pre ($p < 0.01$) and increased from pre to post on the mental fatigue...
day ($p < 0.001$) resulting in overall greater perceived fatigue post-intervention on the mental fatigue day than the control day ($p = 0.001$). Overall, females reported greater perceived fatigue than males ($p = 0.03$). Males and females reported greater perceived fatigue post compared to pre ($p \leq 0.04$) but females had higher post fatigue than males ($p = 0.008$). B: There were no significant differences for overall motivation towards the motor performance tasks. C: Dorsiflexion maximum voluntary contraction force was greater in males than females ($p \leq 0.001$). Data presented as mean ± standard deviation.

### 3.3.3 Motor Performance

During dual-task walking, there were no significant differences in the distance walked or serial seven subtraction performance between days ($p \geq 0.53$), time points ($p \geq 0.10$) or sexes ($p \geq 0.41$; Figure 3.4B, C). There were also no significant two or three-way interactions between day, time and sex for dual-task distance walked or serial seven subtraction performance ($p \geq 0.23$).

Distance walked during the 6MW test was also not significantly different between days ($p = 0.45$), time ($p = 0.07$), and sex ($p = 0.16$; Figure 3.4A). There were no significant two or three-way interactions for distance walked during the 6MW test ($p \geq 0.29$).
Figure 3.4 Single and dual task walking performance

There were no significant differences for: A: Distance walked during 6MW. B: Distance walked during dual task walking for one minute. C: Percent correct responses during serial seven subtractions as the
cognitive portion of dual task walking for one minute. 6MW, Six-minute walk test; m, meters. Data presented as mean ± standard deviation.

RPE was not significantly different between days ($p = 0.52$) or sexes ($p = 0.58$). However, there was a significant main effect of minute of the 6MW test, as RPE was higher during min 6 than min 1 ($p < 0.001$; $\eta^2_p = 0.84$; Table 3.2). There was also a significant interaction between minute of the 6MW and the pre-post intervention assessments ($p = 0.003$; $\eta^2_p = 0.28$). Post-hoc analysis revealed RPE increased from min 1 to min 6 on both mental fatigue and control days ($p < 0.001$). Further, at min 1, RPE was greater during the post-test compared to the pre-test ($p = 0.03$), however by min 6, RPE was similar between pre and post-tests ($p = 0.11$).

For perceived fatigue related to the 6MW test, there was a significant main effect of day as overall fatigue on the mental fatigue day was higher than the control day ($p = 0.05$; $\eta^2_p = 0.13$; Table 3.2). This was primarily due to greater fatigue during the post-test assessment on the mental fatigue day, as indicated by a significant interaction between pre-post intervention and day ($p = 0.009$, $\eta^2_p = 0.22$). While pre-intervention perceived fatigue was similar between mental fatigue and control days ($p = 0.67$), and fatigue increased from the pre to post-intervention assessment on both days ($p < 0.001$), post-intervention fatigue was greater on the mental fatigue day compared to the control day ($p = 0.005$).

There was also a significant main effect of sex for perceived fatigue related to the 6MW test as females overall reported greater fatigue than males ($p = 0.02$; $\eta^2_p = 0.18$; Table 3.2). This difference was related to greater fatigue in females than males at the post-intervention time point, as indicated by a significant interaction between sex and pre-post-test time points ($p < 0.001$; $\eta^2_p = 0.36$). Males and females reported similar perceived fatigue pre-intervention ($p = 0.71$) and both reported higher fatigue levels post-intervention compared to pre-intervention (F: $p < 0.001$; M: $p = 0.003$). However, females reported greater perceived fatigue than males during the post-intervention assessment ($p = 0.003$).
Further, there were significant main effects of pre-post time point, as perceived fatigue was higher during post compared to pre-intervention ($p < 0.001; \eta^2_p = 0.72$; Table 3.2), and start-end of the 6MW test with end of assessment fatigue ratings being higher than the start of the 6MW test ($p < 0.001; \eta^2_p = 0.66$). Further there was a significant interaction between pre-post time point and start-end of the 6MW test ($p < 0.001; \eta^2_p = 0.57$). Perceived fatigue increased from the start to the end of the 6MW during the pre- ($p < 0.001$) and post- ($p = 0.005$) intervention time points. Post-intervention perceived fatigue was higher than pre-intervention fatigue at the start ($p < 0.001$) and end ($p < 0.001$) of the 6MW.
<table>
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RPE start = min 1 of 6MW test, RPE end = min 6 of 6MW test. Significance (p ≤ 0.05) denoted by: *main effect of minute of the 6MW; †interaction between minute of the 6MW and pre-post assessments; Φmain effect of pre-post time; #main effect of day; ‡interaction between pre-post assessment and day; §main effect of sex; Ψinteraction between pre-post assessment and sex. See text for description of significant differences. Data presented as mean ± SD.
3.3.4 Neuromuscular Function

3.3.4.1 Maximum Voluntary Contraction

While males were stronger than females ($p < 0.001; \eta_p^2 = 0.62; \text{Figure 3.3C}$), performing the PVT and watching the documentary did not change DF MVC ($p = 0.25$). DF MVC was also similar between mental fatigue and control days ($p = 0.40$) and there were no significant two or three-way interactions of day, time and sex ($p \geq 0.11$).

3.3.4.2 Submaximal Force

During the 10% MVC contractions, mean relative force did not differ significantly between days ($p = 0.50$) or sexes ($p = 0.07$; Figure 3.5A). Overall, the relative mean force produced was lower at the post-intervention time point compared with pre ($p = 0.006; \eta_p^2 = 0.24$), but there was no significant interaction between day and time ($p = 0.40$). There was, however, a significant interaction between day and sex ($p = 0.02; \eta_p^2 = 0.19$). Post-hoc analysis revealed males and females produced similar mean relative force on the control day ($p = 0.65$) but females produced greater mean relative force than males on the mental fatigue day ($p = 0.003$). Further, while mean relative force was similar across days for females ($p = 0.20$), it was greater on the mental fatigue day than the control day for males ($p = 0.03$). There were no other significant two or three-way interactions ($p \geq 0.24$).

During the 20% MVC contractions, mean relative force did not differ significantly between days ($p = 0.52$), time points ($p = 0.61$) or sexes ($p = 0.37$; Figure 3.5B). However, there was a significant interaction between day and sex ($p = 0.02; \eta_p^2 = 0.18$). Post hoc analysis revealed mean relative force was similar between males and females on the control day ($p = 0.38$), while females produced greater mean relative force than males on the mental fatigue day ($p = 0.002$). Further, while males produced similar mean relative force across days ($p = 0.20$), females produced greater mean relative force on the mental fatigue day than the control day ($p = 0.03$). There were no other significant two or three-way interactions ($p \geq 0.24$).
During the 50% MVC contractions, mean relative force did not differ significantly between days ($p = 0.52$), time points ($p = 0.93$) or sexes ($p = 0.08$; Figure 3.5C). There was a significant interaction between day and sex ($p = 0.05$; $\eta^2_p = 0.13$). While males and females produced similar mean relative force on the control day ($p = 0.81$), females produced greater mean relative force than males on the mental fatigue day ($p = 0.007$). However, females ($p = 0.33$) and males ($p = 0.07$) produced similar mean relative force during the mental fatigue and control days. There were no other significant two or three-way interactions ($p \geq 0.10$).

### 3.3.4.3 Intramuscular EMG

The total number of motor units quantified per contraction in the 10% MVC contractions was: 223 pre-MF, 214 post-MF, 236 pre-control, 242 post-control. In the 20% MVC contractions, the total number of motor units quantified was: 255 pre-MF, 221 post-MF, 210 pre-control, 245 post-control. In the 50% MVC contractions, the total number of motor units quantified was: 114 pre-MF, 131 post-MF, 138 pre-control, 142 post-control.

Motor unit firing rate at 10% MVC was similar between days ($p = 0.34$), time points ($p = 0.13$) and sexes ($p = 0.41$; Figure 3.5D). There were no significant two or three-way interactions between day, time and sex for motor unit firing rate at 10% MVC ($p \geq 0.19$).

There was a significant main effect of time for motor unit firing rate at 20% MVC such that post-intervention motor unit firing rate was slower than pre-intervention ($p = 0.04$, $\eta^2_p = 0.15$; Figure 3.5E). Motor unit firing rate at 20% was similar between days ($p = 0.34$) and sexes ($p = 0.22$). There were no significant two or three-way interactions between day, time and sex for motor unit firing rate at 20% MVC ($p \geq 0.15$).

Motor unit firing rate at 50% MVC was similar between days ($p = 0.25$), time points ($p = 0.56$) and sexes ($p = 0.30$; Figure 3.5F). There were no significant two or three-way interactions between day, time and sex for motor unit firing rate at 50% MVC ($p \geq 0.29$).
**Figure 3.5 Mean relative force and motor unit firing rate**

A: Mean relative force at 10% MVC was lower at post compared to pre ($p = 0.006$). Females produced greater mean relative force than males on the mental fatigue day ($p = 0.003$) while males produced greater relative mean force on the control day than the mental fatigue day ($p = 0.03$). B: Mean relative force at 20% MVC was greater in females compared to males on the mental fatigue day ($p = 0.002$). Females produced greater mean relative force on the mental fatigue day than the control day ($p = 0.03$). C: Mean relative force at 50% MVC was greater in females compared to males on the mental fatigue day ($p = 0.007$). D: There were no significant differences for motor unit firing rate at 10% MVC. E: Motor unit firing rate at 20% MVC was slower post compared to pre ($p = 0.04$). F: There were no significant differences for motor unit firing rate at 50% MVC. MVC, maximum voluntary contraction; MUFR, motor unit firing rate. Data presented as mean ± standard deviation.

### 3.3.4.4 Surface EMG

#### 3.3.4.4.1 Tibialis Anterior RMS

In the 10% MVC contraction, TA RMS was similar between days ($p = 0.14$) and sexes ($p = 0.98$; Table 3.3). Overall, TA RMS was lower post-intervention compared to pre-intervention ($p = 0.03$, $\eta^2_p = 0.16$), but there was no significant interaction between day and time ($p = 0.50$). There was, however, a significant interaction between day and sex ($p = 0.03$, $\eta^2_p = 0.15$). TA RMS was similar between males and females on the control ($p = 0.43$) and mental fatigue ($p = 0.19$) days. However, within males, TA RMS was significantly greater on the control day compared to the mental fatigue day ($p = 0.01$).
with no significant difference across days for females \( (p = 0.60) \). There were no other significant two or three-way interactions \( (p \geq 0.27) \).

In the 20% MVC contraction, TA RMS was similar between days \( (p = 0.23) \), time points \( (p = 0.32) \) and sex \( (p = 0.92; \text{Table 3.3}) \). There was a significant interaction between day and sex \( (p = 0.02; \eta^2_p = 0.19) \). Post-hoc analysis revealed there was no significant difference in TA EMG RMS between males and females on the control \( (p = 0.34) \) or mental fatigue \( (p = 0.35) \) days. However, within males, TA RMS was significantly greater on the control day \( (p = 0.01) \) with no significant difference across days for females \( (p = 0.36) \). There were no other significant two or three-way interactions \( (p \geq 0.16) \).

In the 50% MVC contraction, there were no main effects of day \( (p = 0.42) \), time \( (p = 0.57) \) or sex \( (p = 0.78) \) for TA RMS \( (\text{Table 3.3}) \). There were also no significant two or three-way interactions between day, time and sex \( (p \geq 0.09) \).

### 3.3.4.4.2 Medial Gastrocnemius RMS

In the 10% and 20% MVC contractions, there were no significant two or three-way interactions between day, time and sex \( (p \geq 0.10) \) and no significant main effects of day \( (p = 0.63) \), time \( (p = 0.50) \) or sex \( (p = 0.06) \) for MG RMS \( (\text{Table 3.3}) \).

In the 50% contractions, there was a significant interaction between day and sex for MG RMS \( (p = 0.04; \eta^2_p = 0.15; \text{Table 3.3}) \). However, post-hoc analysis did not indicate any significant differences \( (p \geq 0.08) \). There were no other significant two or three-way interactions between day, time or sex \( (p \geq 0.26) \) and no significant main effects of day \( (p = 0.56) \), time \( (p = 0.89) \) or sex \( (p = 0.40) \).

### 3.3.4.4.3 MG:TA Co-contraction

In the 10, 20 and 50% contractions, there were no significant two or three-way interactions between day, time and sex \( (p \geq 0.19) \) and no significant main effects of day \( (p \geq 0.32) \), time \( (p \geq 0.34) \) or sex \( (p \geq 0.13) \) for MG:TA RMS co-contraction \( (\text{Table 3.3}) \).
<table>
<thead>
<tr>
<th></th>
<th>Mental Fatigue</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Pre</td>
<td>Post</td>
</tr>
<tr>
<td><strong>TA RMS – 10% MVC</strong></td>
<td></td>
<td></td>
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<tr>
<td>(%max)*,<strong>†</strong></td>
<td></td>
<td></td>
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<tr>
<td>Female</td>
<td>14.5 ± 3.5</td>
<td>14.2 ± 3.5</td>
</tr>
<tr>
<td>Male</td>
<td>12.9 ± 4.4</td>
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<tr>
<td><strong>TA RMS – 20% MVC</strong></td>
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<tr>
<td>(%max)<strong>†</strong></td>
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<tr>
<td>Female</td>
<td>22.8 ± 5.9</td>
<td>22.7 ± 7.2</td>
</tr>
<tr>
<td>Male</td>
<td>20.8 ± 7.0</td>
<td>20.0 ± 6.8</td>
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<tr>
<td><strong>TA RMS – 50% MVC</strong></td>
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<tr>
<td>(%max)</td>
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<tr>
<td>Female</td>
<td>57.4 ± 12.0</td>
<td>59.5 ± 16.0</td>
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<tr>
<td>Male</td>
<td>53.5 ± 13.7</td>
<td>53.6 ± 13.9</td>
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<tr>
<td><strong>MG RMS – 10% MVC</strong></td>
<td></td>
<td></td>
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<tr>
<td>(%max)</td>
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<td></td>
</tr>
<tr>
<td>Female</td>
<td>1.8 ± 2.2</td>
<td>1.9 ± 1.7</td>
</tr>
<tr>
<td>Male</td>
<td>1.1 ± 1.3</td>
<td>1.4 ± 1.6</td>
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<tr>
<td><strong>MG RMS – 20% MVC</strong></td>
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<tr>
<td>(%max)</td>
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<td></td>
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<tr>
<td>Female</td>
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<td>3.9 ± 3.2</td>
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<tr>
<td>Male</td>
<td>1.7 ± 1.7</td>
<td>2.0 ± 2.2</td>
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<tr>
<td><strong>MG RMS – 50% MVC</strong></td>
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<td>(%max)</td>
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<td>12.5 ± 8.6</td>
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<td>7.4 ± 7.1</td>
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<tr>
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<td>13.0 ± 14.9</td>
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<td><strong>MG:TA RMS – 50% MVC</strong></td>
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<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
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<td>23.4 ± 15.0</td>
</tr>
<tr>
<td>Male</td>
<td>16.1 ± 17.4</td>
<td>16.6 ± 18.2</td>
</tr>
</tbody>
</table>

Significance ($p \leq 0.05$) denoted by: *main effect of time; †interaction between day and sex. See text for description of significant differences. EMG, electromyography; MG, medial gastrocnemius; MVC,
maximum voluntary contraction; RMS, root mean square; TA, tibialis anterior. Data presented as mean ± standard deviation.

3.3.4.5 Transcranial Magnetic Stimulation

MEP amplitude was similar between days ($p = 0.86$), time points ($p = 0.07$) and sexes ($p = 0.26$). There were no significant two or three-way interactions between day, time and sex ($p ≥ 0.38$; Figure 3.6A).

CSP duration did not differ between days ($p = 0.65$) or sexes ($p = 0.18$) but was significantly longer post-intervention compared with pre ($p = 0.01$, $\eta^2_p = 0.22$; Figure 3.6B). However, there was no significant interaction between day and time ($p = 0.46$), suggesting CSP duration did not change differently on mental fatigue and control days. There were no other two or three-way interactions between day, time and sex ($p ≥ 0.20$).

![Figure 3.6 TMS Outcomes](image)

**Figure 3.6 TMS Outcomes**

A: There were no significant differences for motor evoked potential amplitude, represented as a percent of maximal M-wave amplitude. B: Cortical silent period duration, represented in milliseconds, was longer
post compared to pre \( (p = 0.01) \). CSP, cortical silent period; MEP, motor evoked potential; ms millisecond. Data presented as mean ± standard deviation.

### 3.3.4.6 M-wave

M-wave amplitude did not differ between control (F: \( 1.7 \pm 0.4 \) mV, M: \( 2.4 \pm 1.3 \) mV) and mental fatigue days (F: \( 1.8 \pm 0.8 \), M: \( 2.6 \pm 1.2; p = 0.29 \)), though males had a larger M-wave amplitude than females \( (p = 0.03, \eta_p^2 = 0.15) \). There was no significant interaction between day and sex for M-wave amplitude \( (p = 0.63) \).

### 3.3.5 Regression Analysis

No multivariate outliers were identified using a significance threshold of \( p < 0.001 \). As identified Using Cook’s distance, one highly influential data point was identified and subsequently removed. Dependent measures for regression analysis included the change in PVT outcome measures (perceived fatigue, reaction time, lapses). Using backward stepwise linear regression with sex, moderate-vigorous PA and PSQI scores as independent variables, there was no significant regression model associated with change in perceived fatigue (full model: \( p = 0.26, R^2 = 0.15 \)), reaction time (full model: \( p = 0.50, R^2 = 0.09 \)) or the number of lapses (full model: \( p = 0.32, R^2 = 0.13 \)).

### 3.4 Discussion

The purpose of this study was to investigate sex differences in the impact of mental fatigue on neuromuscular function and motor performance. Secondarily, we examined the relationship between factors which may influence the development of mental fatigue, such as sex, PA level and sleep quality. Thirty minutes of performing the PVT successfully induced mental fatigue, however it did not lead to significant changes in single or dual-task walking performance. After the mental fatigue and control task, both males and females demonstrated a decline in force during 10% MVCs, slowing of motor unit firing rate during 20% MVCs and a longer CSP duration. Sex, PA level and sleep quality were not significantly associated with change in PVT outcome measures.
3.4.1 Mental Fatigue

Performing the PVT for 30 minutes successfully induced mental fatigue in males and females. At the end of the PVT, both sexes reported greater fatigue levels, had a slower reaction time and committed a greater number of lapses compared to the start of the PVT. These changes are characteristic indices of fatigue induced by the PVT\(^2,3^9\), were large in magnitude and align with previous work\(^{11,12}\). Across days, females reported greater perceived fatigue than males at the post-intervention time point, despite similar fatigue levels pre-intervention. However, this finding was not specific to the mental fatigue day, suggesting females may be more likely to report greater fatigue levels following any prolonged sitting task requiring attention, such as watching a documentary. Consistent with previous work\(^14\), females in this study had significantly more fatigue than males on the MFI. Therefore, it is also possible greater levels of general fatigue mediated the increase in perceived fatigue in females after the mental fatigue and control condition. Further work is required to better understand factors which contribute to sex-specific differences in perceived fatigue. Taken together, these results suggest that males and females respond in a similar manner to a mentally fatiguing sustained attention task.

3.4.2 Motor Performance

For males and females, distance walked during the 6MW test did not change following performance of a mentally fatiguing task, despite greater perceived fatigue during the 6MW test after the mental fatigue task. This finding is inconsistent with previous work which demonstrates declines in submaximal endurance performance after performing a mentally fatiguing task\(^5,13,44\). In these studies, declines in performance were thought to be mediated by higher RPE during the submaximal endurance task and not due to declines in motivation\(^5,8,44\). In the current study, there were no changes to motivation but RPE was higher at min 1 of the 6MW test after the mental fatigue task compared to min 1 after the control task. However, by min 6, RPE was similar between days. Therefore, we may not have identified any changes in 6MW test performance as RPE was not elevated throughout the 6MW test after performing the mentally fatiguing task. Average RPE at the end of the 6MW test was between 11-12 on the 6-20 Borg scale, which corresponds to slightly greater than light effort\(^32\), or a moderate intensity exercise\(^45\). In studies which
demonstrate declines in submaximal exercise performance after a mentally fatiguing task, such as running a five kilometer time trial or cycling until exhaustion at 80% of peak power output, participants report end-exercise RPE of approximately 18.44, corresponding to hard-extremely hard effort32 or vigorous exercise45. Thus, the 6MW test may be an insufficient submaximal endurance challenge to increase RPE in young, healthy adults adequately enough to induce measurable declines in performance with mental fatigue.

Dual-task walking performance also did not change following performance of a mentally fatiguing task in both males and females. During one minute of dual task walking, distance walked and serial seven subtraction performance was similar between pre- and post-test assessments. While mental fatigue impairs attention allocation1, our results suggest young healthy adults can allocate sufficient attention to both walking and a cognitive task leading to maintenance of motor and cognitive performance. Others have demonstrated that mental fatigue does not change spatiotemporal gait characteristics in young adults, however gait variability during dual-task walking increases in older adults after a mentally fatiguing task46. Further research is required to examine gait speed during single and dual-task conditions in older adults after a mentally fatiguing task, as gait speed is an indicator of functional capacity and general health status in this population47.

3.4.3 Neuromuscular Function

3.4.3.1 Maximal Voluntary Contractions

There were no changes to DF MVC force in males or females in response to mental fatigue. This finding aligns with others who have demonstrated mental fatigue does not impair maximum force production8–10 and provides additional insight that males and females have a similar MVC response to mental fatigue. Further, no decline in MVC force suggests our mentally fatiguing protocol did not lead to peripheral fatigue. Therefore, any changes in neuromuscular function after the mental fatigue task are likely mediated from within the central nervous system.
3.4.3.2 Submaximal Contractions

Despite setting target force lines, relative mean DF force declined after the mental fatigue and control task in males and females in the 10% MVC condition. This decline in force was accompanied by a decrease in TA EMG activity, but no change in TA motor unit firing rate. As firing rate during the 10% MVC condition was 11-12 pulses per second, it is likely motor unit firing rate was already near minimum\(^48\). There were no changes to MG EMG activity or MG:TA co-contraction suggesting the declines in force and TA EMG activity were not due to alterations in co-contraction. Changes to motor unit recruitment or synergistic muscle activity, could have contributed to the declines in force and TA EMG. Force targets may not have been met secondary to prolonged activation of the ACC during the sustained attention task which leads to reductions in action monitoring and error detection\(^49,50\). However, as there were similar declines on both days, the response was not specific to mental fatigue. Additionally, while the declines in force and TA surface EMG were statistically significant with a large effect size, they represent a 5-6\% difference. Therefore, any alterations to neuromuscular function at 10% MVC in response to mental fatigue are likely small in nature.

In the 20% MVC condition, TA motor unit firing rate declined in males and females after the mental fatigue and control task, despite no change in DF force or TA surface EMG activity. This aligns with our previous work demonstrating a decline in motor unit firing rate after performance of a mentally fatiguing task in both males and females at 20% MVC\(^11\). The decline in motor unit firing rate was not likely a result of increases in co-contraction as there were no changes in MG EMG activity or MG:TA co-contraction. Additional motor units could have been recruited or synergistic muscles activated to maintain force and TA surface EMG activity while firing rate declined. Similar to the 10% MVCs, these alterations in motor control could have been mediated by prolonged activation of the ACC, which has extensive connections with motor planning regions of the brain\(^51,52\). However, like the changes to force and surface EMG in the 10% MVCs, the observed change in firing rate was also small (less than one pulse per second) and occurred in both the mental fatigue and control conditions. This suggests motor unit
firing rate is not likely to contribute substantially to declines in submaximal force production and it is not specific to mental fatigue.

In the 50% MVC condition, there were no changes to DF force, TA surface EMG or motor unit firing rate after the mental fatigue or control task in either males or females. This observation is inconsistent with our previous work, which demonstrated a decline in TA motor unit firing rate at 50% MVC after a mentally fatiguing task in males, while females maintained a stable firing rate\textsuperscript{11}. These differing results may be mediated by a larger number of participants, greater number of trials, or characteristics of the participants in the current study. However, any differences in participant characteristics would have likely been consistent across neuromuscular function measures, making this unlikely.

At all contraction intensities, there was a significant interaction between sex and experimental day for mean relative force. Additionally, there was a significant interaction between sex and experimental day for TA surface EMG at 10 and 20% MVC. While the magnitude of the interactions was large in effect, the absolute difference in force ranged from 0.7-1.3 N and surface EMG from 2.9 and 3.8% of RMS max. The differences between days is not likely to be due to a learning or order effect as participants were randomly assigned to either the control or mental fatigue day first in a counterbalanced order. Eight males and eight females were assigned to the mental fatigue day first. Considering the experimental design of the study and the low absolute difference in force and surface EMG, the overall impact of the differences in force and surface EMG between sexes and across days is minimal and likely has little impact on the interpretation of other outcome variables.

3.4.3.3 Corticospinal Excitability & Intracortical Inhibition

MEP amplitude did not change in males or females after the mental fatigue or control task, suggesting there were no changes to corticospinal excitability. This finding aligns with the work of others who demonstrated no change in MEP amplitude in young and old females\textsuperscript{12}. The current study provides further clarity that there are no sex-specific differences in corticospinal excitability after mental fatigue.
CSP duration lengthened in males and females after the mental fatigue and control tasks, suggesting an increase in intracortical inhibition. This is consistent with Morris & Christie (2020) who identified a strong trend with a medium effect size of a longer CSP duration in young and older females after a mentally fatiguing sustained attention task. Performing a sustained attention task leads to an increase in dopamine release in regions of the ACC. As greater dopamine is associated with a longer CSP duration, it is possible we saw a longer CSP duration due to higher levels of intracortical dopamine that was still present within five minutes of the end of each intervention. However, as we identified a longer CSP duration after the PVT and documentary, this suggests the increased intracortical inhibition was not specific to mental fatigue.

The Earth documentary was chosen as the control task as it is emotionally neutral, yet engaging, and has previously been used as a control condition for mental fatigue experiments. However, watching the documentary also involves some level of sustained attention. Therefore, it may elicit a similar prolonged activation of the ACC, as has been demonstrated with the PVT, leading to an equivalent neurophysiological response. Perceived fatigue after the documentary was not significantly different than before the documentary, so it is unlikely any changes in neuromuscular function were a result of increases in perceived fatigue. Alternatively, it is possible the identified neuromuscular function changes were a result of prolonged sitting rather than being specific to the mental fatigue task. Prolonged sitting influences cognitive and neuromuscular function through several systems, including vascular, neuroendocrine and metabolic, which could have contributed to our equivalent neuromuscular responses after mental fatigue and control interventions. This hypothesis is supported by a recent study in which balance control was altered in a similar manner after performing a mentally fatiguing task and watching the Earth documentary for 90 min. Further work is required to differentiate the effects of mental fatigue, sustained attention and prolonged sitting on neuromuscular function. An enhanced understanding of these different, and likely interacting, factors is important given the rise in sedentary occupations necessitating sustained attention in prolonged sitting positions.
3.4.4 Regression Analysis

Using sex, PA level and sleep quality as variables, no regression models emerged which significantly predicted change in PVT outcomes, including change in perceived fatigue, reaction time and number of lapses. Sex, PA level and sleep quality were chosen *a priori* as they have been shown to influence fatigue levels\textsuperscript{14,17} and moderate the development of mental fatigue\textsuperscript{16,17}. In this study, females had a greater change in perceived fatigue than males as they reported greater fatigue at the end of the intervention than males. Despite this difference, sex was not significantly associated with the change in perceived fatigue in response to the PVT. Moderate-vigorous PA level was also not associated with the development of mental fatigue, despite previous research demonstrating highly trained male athletes are less likely to develop mental fatigue following a prolonged cognitive task in comparison to recreational athletes\textsuperscript{16}. In the current study, the number of minutes of moderate-vigorous PA completed by our population of young, healthy adults was quite high, though not outside reports of others investigating young, healthy adults on a University campus\textsuperscript{60}. Further, the accelerometer was worn on the non-dominant wrist, which produces greater step counts than the hip worn position\textsuperscript{61}. Nonetheless, we may not have had a wide enough range of PA levels to identify an association between moderate-vigorous PA level and mental fatigue. Sleep quality was also not associated with the development of mental fatigue, despite sleep quality influencing fatigue levels\textsuperscript{17}. Further work is required to investigate sedentary individuals who engage in low PA levels and cognitive factors such as comprehensive measurements of executive function to better identify those who may be more susceptible to the development of mental fatigue.

3.4.5 Limitations

While post-test measurements began immediately upon completion of the mental fatigue and control task, it is possible participants recovered from mental fatigue during the post-test neuromuscular function and motor performance assessments. There is very little research investigating recovery from mental fatigue, however, a recent study suggests gross and fine motor skills recover between 15-45 minutes after completion of a mentally fatiguing task\textsuperscript{62}. Our post-test assessments were completed approximately 13-15 min
after the end of each intervention and participants reported higher perceived fatigue at the start of the post-test 6MW in the mental fatigue condition. Therefore, it is unlikely mental fatigue recovery substantially influenced our results. Additionally, as our participants engaged in high levels of moderate-vigorous PA, it is possible they were more resistant to the development of mental fatigue with subsequent maintenance of neuromuscular function and motor performance, similar to well-trained male athletes\textsuperscript{16}. The current study only included active, young healthy adults, which limits the generalizability of our findings. More research is needed to better understand the role of PA level, including those who are sedentary, in the impact of mental fatigue on neuromuscular function and motor performance. Additionally, future studies on the effects of mental fatigue should include older adults as fatigue in this population is associated with lower functional status and earlier onset of disability\textsuperscript{63}.

3.4.6 Conclusions

Our findings demonstrate that 30 min of a sustained attention task which induces mental fatigue does not lead to significant changes in single or dual-task walking performance or DF MVC force production in young adult males and females. Following the mental fatigue and control task, males and females demonstrated a decline in DF force production at 10% MVC, slowing of TA motor unit firing rate at 20% MVC, no changes to neuromuscular function at 50% MVC and a longer CSP duration. The absolute change in these measurements was small and was not specific to the mental fatigue condition. Thus, it is unlikely mental fatigue leads to substantial alterations to neuromuscular function during submaximal isometric contractions in young, healthy adults. Additionally, sex, moderate to vigorous PA level and sleep quality were not associated with the development of mental fatigue in males or females. However, this study provides novel information that males and females respond in a similar manner to both a mentally fatiguing sustained attention task and watching a documentary. Further work is required to differentiate the effects of mental fatigue and prolonged sitting on neuromuscular function and motor performance, and to investigate populations with higher fatigue, such as older adults.
3.4.7 References


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28. Matthews G, Campbell S, Falconer S. Assessment of motivational states in


due to the fulfilment of a continuous cognitive task or by the watching of a documentary. *Exp Brain Res* 2020; 238: 861–868.


Chapter 4

4 State and Trait Fatigue and Energy Associations with Postural Control and Gait

A version of this manuscript has been published: Kowalski KL, Boolani A and Christie AD. State and Trait Fatigue and Energy Predictors of Postural Control and Gait. Motor Control, 1(aop), 1-18, 2021.
4.1 Introduction

Fatigue is commonly reported across the lifespan, has a multidimensional etiology and contributes to declines in physical and cognitive function\textsuperscript{1-4}. The sensation of fatigue arises secondary to the interaction between changes in the two primary attributes of fatigue - performance fatigue and perceived fatigue\textsuperscript{3}. Performance fatigue develops due to declines in muscle activation and/or contractile function. In young, healthy adults, this results in declines in motor performance such as a slowing of gait speed, an increase in step width and gait variability\textsuperscript{5} and alterations to postural control\textsuperscript{5-7}. In contrast, perceived fatigue is the rise in sensations of feeling fatigued in response to changes in homeostasis and psychological state, such as mood, wakefulness and executive functioning\textsuperscript{3}. Perceived fatigue regulates motor performance during activity, in part, by altering perception of effort and attentional control\textsuperscript{3,8,9}. Tasks that increase perceived fatigue without performing physical activity, such as prolonged cognitive or sustained attention tasks, also lead to declines in motor performance. This includes alterations to postural control in young, healthy adults\textsuperscript{10} and increased gait variability in older adults\textsuperscript{11}, which has been suggested as a potential contributor to fall risk\textsuperscript{12}.

Motor control mechanisms responsible for altered motor performance during heightened perceived fatigue include regulation through the executive function system, particularly the anterior cingulate cortex (ACC) and prefrontal cortex\textsuperscript{9,13,14}. These systems are responsible for the modulation of perception of effort and allocation of attentional resources\textsuperscript{9,13}. Maintaining sustained attention on a task results in prolonged activation of the ACC, leading to alterations in attentional resources and increases in perception of effort during a physical task\textsuperscript{8,9,13}. Compromised attentional resources during heightened perceptions of fatigue has been suggested to alter the control of balance from being largely an automatic process to one that requires greater cognitive control in young, healthy adults\textsuperscript{10}. Balance stability and spatiotemporal parameters of gait, such as gait speed and step length, are also associated with performance on tasks of executive function\textsuperscript{15}. This suggests gait and postural control may be altered if executive function systems are compromised to due increases in perceptions of fatigue. While increasing
perceived fatigue results in alterations to motor control, it is unknown how baseline, resting levels of perceived fatigue impact postural control and gait.

Perceived fatigue measured at rest reflects an individual’s state level of fatigue, which is transient and fluid in nature\textsuperscript{16}. State fatigue can limit an individual’s perceived capacity to perform physical or mental activities (here termed physical and mental fatigue). The likelihood of developing state perceived physical or mental fatigue is not only influenced by environmental and psychological factors, but also an individual’s trait level of fatigue\textsuperscript{16}. Trait fatigue represents an individual’s usual feelings of fatigue, or predisposition to feel fatigued, and is a relatively stable characteristic over time. Trait fatigue can also influence motor performance as older adults who report higher levels of trait fatigue demonstrate lower levels of physical function, such as slower gait speed\textsuperscript{17}, however it is unknown how trait physical and mental fatigue influence gait and postural control in young, healthy adults.

While fatigue is often described as a lack of energy, evidence suggests fatigue and energy are separate, but related, constructs and not opposite ends of a continuum\textsuperscript{18}. For example, in young, healthy adults fatigue and energy are both correlated with and predicted by sleep quality\textsuperscript{19}, however each construct has independent predictors, such as physical activity (PA) and age\textsuperscript{19}. Fatigue and energy can also be independently influenced in young, healthy adults through interventions such as exercise\textsuperscript{20} and caffeine\textsuperscript{21}, suggesting some of the mechanisms contributing to fatigue and energy are distinct. Further, separate constructs of physical energy and mental energy have been defined and relate to the capacity to complete either physical or mental activities, respectively\textsuperscript{19,22}. In young, healthy adults physical and mental energy each have distinct predictors, such as PA and body mass index (BMI), and similar to physical and mental fatigue, can be described as state variables or trait characteristics\textsuperscript{19,23}. While declines in mental energy have previously been shown to be related to declines in postural control with eyes closed in older adults\textsuperscript{24}, it is unknown how the constructs of mental and physical energy as well as mental and physical fatigue differentially impact postural control and gait in young, healthy adults.
State and trait fatigue and energy levels are also influenced by demographic characteristics and lifestyle factors, such as sex, sleep quality and PA level\textsuperscript{1,23,25,26}. Females, particularly those with high trait fatigue\textsuperscript{23}, report higher state fatigue than males\textsuperscript{1,23}. Individuals with poor sleep quality\textsuperscript{23} and low PA levels\textsuperscript{1,25,26} report higher state fatigue and lower energy levels. Further, sleep quality moderates the relationship between state and trait fatigue and energy levels in a sex-specific manner\textsuperscript{23} and leads to declines in postural control\textsuperscript{27}. While sex, sleep quality and PA influence state and trait fatigue and energy, it is unknown how these variables influence the relationships between motor performance, physical and mental fatigue and energy as state variables and trait characteristics in young, healthy adults.

The purpose of this study was to evaluate the relationships between postural control, gait and perceived physical and mental fatigue and energy as state variables and trait characteristics in young, healthy adults. We also examined how these relationships were modified by sex, sleep quality and PA level. We hypothesized that high state and trait fatigue and low state and trait energy would be associated with postural control and gait characteristics indicative of unsteadiness, such as greater postural sway acceleration parameters, slower gait speed, greater DL support time and variability of gait parameters. Additionally, given the influence of sex, sleep quality and PA level on fatigue and energy\textsuperscript{1,23,26}, we hypothesized these associations would be stronger for females, those with poor sleep quality and low PA.

4.2 Methods

4.2.1 Participants

Participants included 119 individuals (73 females, 46 males, age range: 18-36 years) recruited from across the Clarkson University campus and within the local community using announcements in classes, flyers posted on and off campus and a campus-wide recruitment email sent to students, faculty and staff. Sample size was estimated using correlation coefficients from previous work examining associations between gait, postural control and cognition\textsuperscript{15}. This analysis indicated a minimum total sample size of 87 to detect a significant association using a linear multiple regression with $\alpha = 0.05$ and
β = 0.80. Further, the general sample size recommendation for multiple regression analysis is a minimum of 10 participants per predictor variable. With 119 participants and 11 predictor variables, the sample size exceeded both this minimum recommendation and the calculated sample size estimate.

All participants could stand and walk pain-free for two minutes without an assistive device, were free of neurological conditions, visual impairments, wounds or absent foot sensation, and did not have orthopedic surgery impacting their walking and balance within six months of study participation. Prior to the study session, participants refrained from caffeine and alcohol for 12 h. Participants provided written informed consent of the procedures approved by Institutional Review Board at Clarkson University (approval #18.39.1) and aligned with the standards of the Declaration of Helsinki.

4.2.2 Experimental Protocol

The experimental protocol was carried out between 9:30-11:30am for all participants. After providing informed consent, participants completed the state component of the Mental and Physical State and Trait Fatigue and Energy Scale. Participants were then instrumented with sensors before completing postural control and gait assessments, as described below. Finally, participants completed the Pittsburgh Sleep Quality Index (PSQI), International Physical Activity Questionnaire (IPAQ) and the trait component of the Mental and Physical State and Trait Fatigue and Energy Scale. The state component of the Mental and Physical State and Trait Fatigue and Energy scale was administered prior to postural control and gait assessments to quantify baseline state fatigue and energy. As this portion of the questionnaire takes one to three minutes to complete, it is unlikely to alter fatigue or energy levels in this population of young, healthy adults\textsuperscript{13,24}. However, to minimize any impact of questionnaire completion altering fatigue and energy levels, trait fatigue and energy were assessed after the postural control and gait assessments. As traits are long-standing predispositions requiring a long timeframe for change\textsuperscript{16,28}, it is unlikely the postural control and gait assessments would alter trait fatigue and energy levels.
4.2.3 Questionnaires

To measure fatigue and energy levels, the Mental and Physical State and Trait Energy and Fatigue Scale was used\textsuperscript{19,29,30}. In this questionnaire, state mental fatigue, physical fatigue, mental energy and physical energy are each evaluated through three questions that measure the intensity of the participants’ current feelings of fatigue or energy. Specifically, participants were asked “How do you feel right now with regard to your capacity to perform typical physical activities” with fatigue questions related to feelings of fatigue, exhaustion and being worn out and energy questions related to feeling energetic, vigor and full of pep. These fatigue and energy characteristics were also used with questions asking about typical mental activities to quantify mental fatigue and energy. For each question, participants mark a vertical line along a continuum between the anchor statements “absence of a feeling” and “strongest feeling ever experienced”. The anchors are spaced 100 mm apart and each question is scored by measuring the distance of the participant’s mark from the “absence of a feeling” anchor. As there are three questions per state construct, the range of scores is 0-300.

Trait mental fatigue, physical fatigue, mental energy and physical energy are each measured through three categorical questions that measure the frequency of usual feelings of fatigue or energy. Participants were asked “With regard to your capacity to perform physical activities, how often do you usually feel” with fatigue, exhaustion and feeling worn out as characteristics defining fatigue and energetic, vigor and full of pep as characteristics defining energy. This question stem and fatigue/energy characteristics were also used to evaluate participants capacity to perform mental activities. Responses are marked on a 5-point scale ranging from “never” (scored as zero points) to “always” (scored as four points) and the range of scores for each trait construct is 0-12. The reliability of this questionnaire has been demonstrated in previous work with young, healthy male and female adults\textsuperscript{19,23,30,31} and its discriminant and structural validity supported using a healthy adult population\textsuperscript{29,30,32}.

Sleep quality was assessed with the PSQI, a self-report questionnaire consisting of nine questions about sleeping patterns within the last month. Global PSQI scores range from 0-21 and a score greater than five is indicative of a poor sleeper\textsuperscript{33}. In young, healthy
adults, the PSQI is reliable and valid when compared to other subjective measures of sleep quality\textsuperscript{34}.

Physical activity was quantified as metabolic equivalent minutes of PA per week (MET min\textsuperscript{-1}wk\textsuperscript{-1}) using the IPAQ. This questionnaire asked about the frequency and duration of moderate and vigorous PA performed throughout a typical week at work, during recreational activities and as a mode of transportation\textsuperscript{18}. The IPAQ is a reliable and valid self-report physical activity questionnaire in young, healthy adults\textsuperscript{35}. Questionnaires were administered electronically using SurveyMonkey (SVMK Inc., San Mateo, California, USA, www.surveymonkey.com).

### 4.2.4 Instrumentation

Postural control and gait variables were obtained with valid, reliable procedures\textsuperscript{36,37} using inertial measurement units (Opal, APDM Wearable Technologies, Portland, Oregon, USA). Sensors were placed at the fifth lumbar vertebra, body of sternum, forehead, bilateral dorsal feet and posterior wrists. Data were wirelessly transmitted, sampled at 128 Hz and synchronized using Mobility Lab V2.0 (APDM Wearable Technologies, Portland, Oregon, USA)\textsuperscript{37}.

### 4.2.5 Postural Control

The modified Clinical Test of Sensory Integration and Balance (mCTSIB) was used to evaluate postural control\textsuperscript{38}. This test consists of standing for 30 seconds during four conditions: (1) eyes open, firm surface; (2) eyes closed, firm surface; (3) eyes open, foam surface; and (4) eyes closed, foam surface. Participants stood barefoot with hands on hips and stance width standardized by the width of the Mobility Lab Footplate (APDM Wearable Technologies, Portland, Oregon, USA). Postural sway variables measured during each condition included: root mean square (RMS) of center of mass acceleration in the coronal and sagittal planes, sway velocity in the transverse plane, and jerk in the transverse plane, as previously described\textsuperscript{36}. These outcome measures were selected based on previous research demonstrating they are reliable and sufficiently sensitive to identify differences in postural control in young individuals\textsuperscript{39} and populations characterized by
fatigue\textsuperscript{36,39,40}. Further, mCTSIB measures of balance are associated with aspects of cognition involved in postural control\textsuperscript{15}.

4.2.6 Gait

Gait variables were measured while participants walked in shoes at a self-selected, comfortable pace. A cone was placed on the floor 6 m in front of the starting position and participants walked around the cone and back to the starting position for 2 min continuously. Spatiotemporal gait variables were collected during straight path walking and included double limb (DL) support time, foot swing elevation, stride length and gait speed. Kinematic gait variables collected during straight path walking included lumbar range of motion (ROM) in the coronal and sagittal planes and arm swing ROM. Gait variability was calculated as the coefficient of variation (CV) of DL support, stride length and gait speed, as well as asymmetry of lateral step variability. During the 180° turns at the start and ends of the walkway, turn angle and velocity were measured. Stride length and gait speed were normalized to participant height and unilateral gait variables are presented from the left lower extremity. Calculations for these outcome measures have been previously described\textsuperscript{41}. These outcome measures were selected as they are associated with aspects of cognition and cortical control of gait impacted by fatigue\textsuperscript{15,42}, or have been previously identified as being associated with gait in individuals with high state or trait fatigue\textsuperscript{43}.

4.2.7 Statistical Analyses

Shapiro-Wilk tests were used to assess whether postural control and gait variables were normally distributed. Any failed test of normality resulted in a square root or natural log transformation to normalize the distribution. Due to unequal sample sizes across the sexes, homogeneity of variance was evaluating using Levene’s test for equality of variance and Welch’s independent samples t-tests were used to evaluate sex differences in participant characteristics, (age, height, weight, BMI, PSQI, MET min\textsuperscript{\textendash}wk\textsuperscript{\textsuperscript{-1}}), state and trait fatigue and energy levels, postural control and gait variables.

Mahalanobis distance was used to check for multivariate outliers in state and trait fatigue and energy variables, sex, PSQI scores and MET min\textsuperscript{\textendash}wk\textsuperscript{\textsuperscript{-1}}. No multivariate outliers were
identified using a significance threshold of \( p < 0.001 \). Forward stepwise hierarchical multivariate multiple linear regressions were used to determine regression models which best predicted postural control and gait from state and trait fatigue and energy variables. The predictor and predicted variables were chosen based on previous literature, as outlined in the sections above. The regression models were constructed in blocks, following established recommendations\(^4\). The first block contained all state and trait fatigue and energy variables while the second block also contained sex, PSQI scores and MET min\( \cdot \)wk\(^{-1} \). Each model was examined for outliers and influential data points using Cook’s Distance with a threshold of greater than one indicating a significantly influential outlying data point. This led to the exclusion of one case during the eyes open, firm condition of the mCTSIB for sway RMS. Regression model residuals were examined for heteroscedasticity. When more than one predictor variable emerged from the model, multicollinearity was assessed using the variance inflation factor. The largest variance inflation factor was 1.17, suggesting no influential collinearity among independent variables\(^4\). Statistical analyses were performed using SPSS (Version 26; IBM SPSS Statistics, Armonk, NY, US) and significance was set at \( p \leq 0.05 \).

4.3 Results

4.3.1 Participants

Participant characteristics are presented in Table 4.1. Males were taller and heavier than females \( p < 0.001 \), however there were no sex differences in age, BMI, PSQI or MET min\( \cdot \)wk\(^{-1} \) \( p \geq 0.25 \). Females reported higher state mental and physical fatigue and lower state physical energy than males \( p \leq 0.05 \). No sex differences were identified for state mental energy or any trait characteristic \( p \geq 0.11 \). Males and females did not differ in any measure of postural control but males had a higher mid-swing foot elevation, slower gait speed, less lumbar coronal and sagittal ROM, slower turning velocity and less arm swing amplitude than females \( p \leq 0.01 \); Table 4.2).
<table>
<thead>
<tr>
<th></th>
<th>Females</th>
<th>Males</th>
<th>( p ) value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, years</td>
<td>24.03 ± 3.81</td>
<td>24.54 ± 4.50</td>
<td>0.52</td>
</tr>
<tr>
<td>Height (m)</td>
<td>1.69 ± 6.36</td>
<td>1.80 ± 7.23</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>69.85 ± 14.72</td>
<td>81.74 ± 13.98</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>BMI (kg/m(^2))</td>
<td>24.38 ± 5.07</td>
<td>25.14 ± 3.67</td>
<td>0.35</td>
</tr>
<tr>
<td>PSQI</td>
<td>5.55 ± 2.83</td>
<td>5.00 ± 2.27</td>
<td>0.25</td>
</tr>
<tr>
<td>MET (min·wk(^{-1}))</td>
<td>2561.21 ± 2383.20</td>
<td>3132.55 ± 3443.31</td>
<td>0.33</td>
</tr>
<tr>
<td>State mental fatigue</td>
<td>117.92 ± 72.27</td>
<td>75.17 ± 67.23</td>
<td>0.001</td>
</tr>
<tr>
<td>State physical fatigue</td>
<td>113.56 ± 66.28</td>
<td>74.61 ± 70.69</td>
<td>0.004</td>
</tr>
<tr>
<td>State mental energy</td>
<td>134.9 ± 53.20</td>
<td>147.43 ± 65.85</td>
<td>0.28</td>
</tr>
<tr>
<td>State physical energy</td>
<td>142.16 ± 55.27</td>
<td>163.72 ± 57.84</td>
<td>0.05</td>
</tr>
<tr>
<td>Trait mental fatigue</td>
<td>4.97 ± 2.27</td>
<td>4.74 ± 2.51</td>
<td>0.61</td>
</tr>
<tr>
<td>Trait physical fatigue</td>
<td>4.64 ± 2.34</td>
<td>4.17 ± 2.51</td>
<td>0.31</td>
</tr>
<tr>
<td>Trait mental energy</td>
<td>6.25 ± 2.09</td>
<td>6.48 ± 2.04</td>
<td>0.55</td>
</tr>
<tr>
<td>Trait physical energy</td>
<td>3.47 ± 0.75</td>
<td>3.67 ± 0.63</td>
<td>0.11</td>
</tr>
</tbody>
</table>

Data are presented as mean ± SD. BMI, body mass index; PSQI, Pittsburgh Sleep Quality Index; MET, metabolic equivalents.
<table>
<thead>
<tr>
<th>Postural Control</th>
<th>Female</th>
<th>Male</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eyes open, firm surface</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RMS sway (m/s²)</td>
<td>0.06 ± 0.04</td>
<td>0.07 ± 0.07</td>
<td>0.45</td>
</tr>
<tr>
<td>Velocity (m/s)</td>
<td>0.13 ± 0.14</td>
<td>0.13 ± 0.15</td>
<td>0.91</td>
</tr>
<tr>
<td>Jerk (m²/s³)</td>
<td>1.06 ± 2.00</td>
<td>1.06 ± 1.67</td>
<td>0.89</td>
</tr>
<tr>
<td>Eyes open, foam surface</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RMS sway (m/s²)</td>
<td>0.06 ± 0.02</td>
<td>0.07 ± 0.02</td>
<td>0.45</td>
</tr>
<tr>
<td>Velocity (m/s)</td>
<td>0.11 ± 0.06</td>
<td>0.12 ± 0.06</td>
<td>0.51</td>
</tr>
<tr>
<td>Jerk (m²/s³)</td>
<td>1.08 ± 0.89</td>
<td>0.99 ± 0.62</td>
<td>0.75</td>
</tr>
<tr>
<td>Eyes closed, firm surface</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RMS sway (m/s²)</td>
<td>0.07 ± 0.02</td>
<td>0.07 ± 0.03</td>
<td>0.64</td>
</tr>
<tr>
<td>Velocity (m/s)</td>
<td>0.14 ± 0.07</td>
<td>0.14 ± 0.07</td>
<td>0.62</td>
</tr>
<tr>
<td>Jerk (m²/s³)</td>
<td>1.46 ± 1.27</td>
<td>1.45 ± 0.83</td>
<td>0.69</td>
</tr>
<tr>
<td>Eyes closed, foam surface</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>RMS sway (m/s²)</td>
<td>0.11 ± 0.03</td>
<td>0.12 ± 0.04</td>
<td>0.30</td>
</tr>
<tr>
<td>Velocity (m/s)</td>
<td>0.18 ± 0.08</td>
<td>0.21 ± 0.13</td>
<td>0.12</td>
</tr>
<tr>
<td>Jerk (m²/s³)</td>
<td>4.07 ± 3.53</td>
<td>4.20 ± 3.15</td>
<td>0.41</td>
</tr>
<tr>
<td>Gait</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Double limb support (%)</td>
<td>20.21 ± 2.96</td>
<td>21.04 ± 3.14</td>
<td>0.15</td>
</tr>
<tr>
<td>Swing elevation (cm)</td>
<td>1.17 ± 0.55</td>
<td>1.48 ± 0.69</td>
<td>0.01</td>
</tr>
<tr>
<td>Stride length (m x height⁻¹)</td>
<td>0.71 ± 0.05</td>
<td>0.68 ± 0.07</td>
<td>0.06</td>
</tr>
<tr>
<td>Gait speed (m/s x height⁻¹)</td>
<td>0.64 ± 0.09</td>
<td>0.58 ± 0.07</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lumbar coronal ROM (deg)</td>
<td>6.49 ± 2.11</td>
<td>5.08 ± 2.00</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Lumbar sagittal ROM (deg)</td>
<td>5.74 ± 1.68</td>
<td>4.84 ± 1.07</td>
<td>0.001</td>
</tr>
<tr>
<td>Turn angle (deg)</td>
<td>187.12 ± 4.35</td>
<td>185.93 ± 3.99</td>
<td>0.13</td>
</tr>
<tr>
<td>Turn velocity (deg/sec)</td>
<td>188.24 ± 29.28</td>
<td>170.26 ± 22.37</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Arm swing amplitude (ROM)</td>
<td>44.82 ± 16.26</td>
<td>37.31 ± 11.65</td>
<td>0.004</td>
</tr>
<tr>
<td>Asymmetry lateral step variability</td>
<td>10.45 ± 7.58</td>
<td>10.95 ± 7.38</td>
<td>0.72</td>
</tr>
<tr>
<td>CV double limb support (%)</td>
<td>6.05 ± 2.14</td>
<td>5.57 ± 1.80</td>
<td>0.19</td>
</tr>
<tr>
<td>CV stride length (%)</td>
<td>2.97 ± 1.10</td>
<td>3.22 ± 0.94</td>
<td>0.18</td>
</tr>
<tr>
<td>CV gait speed (%)</td>
<td>4.60 ± 1.90</td>
<td>4.74 ± 1.59</td>
<td>0.68</td>
</tr>
</tbody>
</table>
Data presented as means ± standard deviation. CV, coefficient of variation; cm, centimeters; deg, degrees; m, meters; RMS, root mean square; ROM, range of motion; s, second.

4.3.2 Balance

The multivariate multiple regression models for the mCTSIB are presented in Table 4.3. When standing with eyes open on a firm surface (Condition 1), the model that best predicted sway RMS, velocity and jerk included only trait physical energy, which explained 5% of the variance in RMS, 6% of velocity and 9% of jerk.

When standing with eyes closed on a firm surface (Condition 2), the model that best predicted sway RMS included trait mental fatigue, state physical fatigue and PSQI, with 13% of the variance in RMS explained by these variables. Sway velocity was best predicted by a model that included state physical fatigue and PSQI, with 11% of the variance explained by these variables. While the model of best prediction for sway jerk included only trait mental fatigue, explaining 10% of the variance.

When standing with eyes open on a foam surface (Condition 3), the model that best predicted sway RMS included only trait mental energy, explaining 4% of the variance. No regression model emerged that significantly predicted sway velocity \((p \geq 0.67, R^2 \leq 0.06)\) or jerk \((p \geq 0.62, R^2 \leq 0.07)\).

When standing with eyes closed on a foam surface (Condition 4), the model that best predicted sway RMS and jerk included only trait mental fatigue. Trait mental fatigue explained 4% of the variance in RMS and 7% of the variance in jerk. No regression model emerged that significantly predicted sway velocity \((p \geq 0.32, R^2 \leq 0.10)\).
<table>
<thead>
<tr>
<th>Condition</th>
<th>Dependent Variable</th>
<th>p</th>
<th>R</th>
<th>R²</th>
<th>Regression Model</th>
<th>Standardized Regression Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>RMS (m/s²)</td>
<td>0.02</td>
<td>0.21</td>
<td>0.05</td>
<td>0.30 – (0.02*TPE)</td>
<td>0.30 – (0.21*TPE)</td>
</tr>
<tr>
<td>1</td>
<td>velocity (m/s)</td>
<td>0.006</td>
<td>0.25</td>
<td>0.06</td>
<td>0.50 – (0.05*TPE)</td>
<td>0.50 – (0.25*TPE)</td>
</tr>
<tr>
<td>1</td>
<td>jerk (m²/s⁵)</td>
<td>0.001</td>
<td>0.30</td>
<td>0.09</td>
<td>1.67 – (0.22*TPE)</td>
<td>1.67 – (0.30*TPE)</td>
</tr>
<tr>
<td>2</td>
<td>RMS (m/s²)</td>
<td>0.001</td>
<td>0.35</td>
<td>0.13</td>
<td>0.23 + (0.002<em>TMF) – (1.3x10⁻⁴</em>SPF) + (0.003*PSQI)</td>
<td>0.23 + (0.15<em>TMF) – (0.24</em>SPF) + (0.24*PSQI)</td>
</tr>
<tr>
<td>2</td>
<td>velocity (m/s)</td>
<td>0.001</td>
<td>0.33</td>
<td>0.11</td>
<td>0.33 – (3.43x10⁻⁴<em>SPF) + (0.006</em>PSQI)</td>
<td>0.33 – (0.30<em>SPF) + (0.21</em>PSQI)</td>
</tr>
<tr>
<td>2</td>
<td>jerk (m²/s⁵)</td>
<td>&lt;0.001</td>
<td>0.32</td>
<td>0.10</td>
<td>0.45 + (0.04*TMF)</td>
<td>0.45 + (0.32*TMF)</td>
</tr>
<tr>
<td>3</td>
<td>RMS (m/s²)</td>
<td>0.02</td>
<td>0.21</td>
<td>0.04</td>
<td>0.29 – (0.004*TME)</td>
<td>0.29 – (0.21*TME)</td>
</tr>
<tr>
<td>4</td>
<td>RMS (m/s²)</td>
<td>0.04</td>
<td>0.19</td>
<td>0.04</td>
<td>0.31 + (0.004*TMF)</td>
<td>0.31 + (0.19*TMF)</td>
</tr>
<tr>
<td>4</td>
<td>jerk (m²/s⁵)</td>
<td>0.005</td>
<td>0.25</td>
<td>0.07</td>
<td>1.20 + (0.06*TMF)</td>
<td>1.20 + (0.25*TMF)</td>
</tr>
</tbody>
</table>

Condition 1: eyes open, firm surface; Condition 2: eyes closed, firm surface; Condition 3: eyes open, foam surface; Condition 4: eyes closed, foam surface.
4.3.3 Gait

The multivariate multiple regression models for gait are presented in Table 4.4. For spatiotemporal gait characteristics, no regression model emerged that significantly predicted DL support \( (p \geq 0.92, R^2 \leq 0.05) \) and the regression model that best predicted mid-swing elevation and stride length included only sex, explaining 6% of the variance in mid-swing elevation and 3% of the variance in stride length. Gait speed was best predicted by a model that included trait physical fatigue and sex, explaining 13% of the variance.

For kinematic gait characteristics, the regression model that best predicted lumbar coronal ROM included only sex, explaining 11% of the variance. Lumbar sagittal ROM was best predicted by a model including sex and state mental energy, explaining 11% of the variance. The model that best predicted arm swing ROM included sex and state physical energy, explaining 8% of the variance.

For gait variability, the model that best predicted CV of DL support included state physical energy, MET min·wk\(^{-1}\) and sex, explaining 10% of the variance. No regression model emerged that significantly predicted the CV of gait speed \( (p \geq 0.42, R^2 \leq 0.10) \). The CV of stride length was best predicted by a model only containing MET min·wk\(^{-1}\), explaining 5% of the variance. The model that best predicted asymmetry of lateral step variability included state physical fatigue, explaining 8% of the variance.

During turning 180°, no regression model emerged that significantly predicted turning angle \( (p \geq 0.43, R^2 \leq 0.10) \). Turn velocity was best predicted by a model which included state mental fatigue and sex, explaining 12% of the variance.
Table 4.4 Gait multivariate multiple regression analyses

<table>
<thead>
<tr>
<th></th>
<th>$p$</th>
<th>$R$</th>
<th>$R^2$</th>
<th>Regression Model</th>
<th>Standardized Regression Model</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mid-swing elevation (cm)</td>
<td>0.01</td>
<td>0.24</td>
<td>0.06</td>
<td>1.32 – (0.14*Sex)</td>
<td>1.32 – (0.24*Sex)</td>
</tr>
<tr>
<td>Stride length (m, height normalized)</td>
<td>0.05</td>
<td>0.18</td>
<td>0.03</td>
<td>0.66 + (0.02*Sex)</td>
<td>0.66 + (0.18*Sex)</td>
</tr>
<tr>
<td>Gait speed (m/s, height normalized)</td>
<td>&lt;0.001</td>
<td>0.36</td>
<td>0.13</td>
<td>0.50 + (0.01<em>TPF) + (0.06</em>Sex)</td>
<td>0.50 + (0.16<em>TPF) + (0.31</em>Sex)</td>
</tr>
<tr>
<td>Lumbar coronal (ROM)</td>
<td>&lt;0.001</td>
<td>0.34</td>
<td>0.11</td>
<td>1.55 + (0.21*Sex)</td>
<td>1.55 + (0.34*Sex)</td>
</tr>
<tr>
<td>Lumbar sagittal (ROM)</td>
<td>0.001</td>
<td>0.34</td>
<td>0.11</td>
<td>1.50 + (0.14<em>Sex) + (0.001</em>SME)</td>
<td>1.50 + (0.30<em>Sex) + (0.19</em>SME)</td>
</tr>
<tr>
<td>Arm swing amplitude (ROM)</td>
<td>0.007</td>
<td>0.29</td>
<td>0.08</td>
<td>4.82 + (0.62<em>Sex) + (0.004</em>SPE)</td>
<td>4.82 + (0.26<em>Sex) + (0.18</em>SPE)</td>
</tr>
<tr>
<td>CV DL support (%)</td>
<td>0.002</td>
<td>0.12</td>
<td>0.10</td>
<td>1.28 + (0.001<em>SPE) + (2.85x10^-5</em>MET) + (0.121*Sex)</td>
<td>1.28 + (0.19<em>SPE) + (0.25</em>MET) + (0.18*Sex)</td>
</tr>
<tr>
<td>CV stride length (%)</td>
<td>0.01</td>
<td>0.23</td>
<td>0.05</td>
<td>1.00 + (2.53x10^-5*MET)</td>
<td>1.00 + (0.23*MET)</td>
</tr>
<tr>
<td>Asymmetry lateral step variability</td>
<td>0.002</td>
<td>0.28</td>
<td>0.08</td>
<td>3.51 – (0.005*SPF)</td>
<td>3.51 – (0.28*SPF)</td>
</tr>
<tr>
<td>Turn velocity (m/s)</td>
<td>0.001</td>
<td>0.34</td>
<td>0.12</td>
<td>5.03 + (2.52x10^-4<em>SMF) + (0.09</em>Sex)</td>
<td>5.03 + (0.13<em>SMF) + (0.29</em>Sex)</td>
</tr>
</tbody>
</table>

For Sex: 1 = Male, 2 = Female. CV, coefficient of variation; DL, double limb; MET, metabolic equivalents in min·wk⁻¹; ROM, range of motion; SME, state mental energy; SPE, state physical energy; SMF, state mental fatigue; SPF, state physical fatigue; TPF, trait physical fatigue.
4.4 Discussion

The purpose of this study was to evaluate the relationships between postural control, gait and perceived physical and mental fatigue and energy as state variables and trait characteristics in young, healthy adults. We also examined how these relationships were modified by sex, sleep quality and PA level. The results suggest that in general, trait fatigue, trait energy and sleep quality are associated with postural control while state fatigue, state energy and sex are associated with gait in young, healthy adults. Although statistically significant, the variance explained by the regression models was low (range 3-13%), and thus the functional implications of these results remains to be determined.

4.4.1 Sex Differences in Fatigue

Females reported higher levels of state physical and mental fatigue and lower levels of state physical energy than males, consistent with previous reports\(^1\). Proposed mechanisms contributing to sex differences in state fatigue include factors\(^{1,17,46-48}\) such as females more readily reporting physical symptoms than males\(^ {47}\) and sex differences in reproductive function\(^ {48}\). Further work is required to determine the ways in which psychosocial, behavioral and physiological factors contribute to higher state fatigue reported by females, to implement interventions designed to reduce fatigue in females. The sex-specific differences in state and trait fatigue suggest that future research investigating the motor control of gait and posture may consider sex as an important covariate.

4.4.2 Balance

Trait fatigue and energy were the predominant variables associated with postural control across all conditions of the mCTSIB. These results suggest the long-standing predisposition of energy and fatigue may be more important for postural control in young adults than acute changes in feelings of energy and fatigue. Similarly, previous work has demonstrated balance is more closely associated with trait fatigue than state fatigue in individuals with Multiple Sclerosis\(^ {43}\). Others have also demonstrated no change in postural control after increased state mental fatigue in young women\(^ {49}\). In contrast, declines in postural control have been noted in young adults after inducing state mental
fatigue\textsuperscript{10}. Given these discrepancies and considering the low variance (4-13%) explained by our regression models for postural control, it is likely that the influence of trait fatigue and energy on postural control is small in young, healthy adults.

Nonetheless, it is interesting to note that trait physical and mental energy were associated with postural sway in the eyes open conditions while trait physical and mental fatigue were associated with postural sway in the eyes closed conditions of the mCTSIB. Removing visual sensory feedback increases the cognitive load and attentional demands of balance\textsuperscript{50}. Therefore, it is possible higher trait fatigue modulates the cognitive load and attentional demands associated with the eyes closed conditions of the mCTSIB, leading to increased postural sway in young, healthy adults. Similarly, individuals with high levels of trait fatigue (e.g. individuals with Multiple Sclerosis) demonstrate greater postural sway during static stance with eyes closed compared to healthy controls\textsuperscript{43}. The motor control mechanisms responsible for this association may be related to the ACC. Through its extensive network of connections with the prefrontal and primary motor cortices as well as the executive function and limbic systems, the ACC is well-positioned to modulate the interaction between affective domain traits, cognition and motor control\textsuperscript{9,14}. Indeed, greater ACC activity is evident in individuals with high trait fatigue compared to individuals without high trait fatigue\textsuperscript{51}. Prolonged activation of the ACC due to high trait fatigue may have contributed to the observed associations in this study between high trait fatigue and postural sway.

Poor sleep quality was also associated with greater postural sway during the eyes closed, firm surface condition of the mCTSIB. This is consistent with previous work indicating poor sleep quality impairs postural control to a greater extent with eyes closed compared to eyes open\textsuperscript{27} and work evaluating the effects of sleep deprivation\textsuperscript{52}. Sleep deprivation reduces activity in the prefrontal and anterior cingulate cortices\textsuperscript{53}, leading to declines in attention, perception and cognition, and subsequent reduced capacity for sensory integration and coordinated motor output\textsuperscript{52,53}. It is possible poor sleep quality reduces postural control through similar mechanisms. However, sleep quality did not appear in the model for predicting sway on foam, suggesting that it may be not be associated with postural control with additional sensory challenges.
4.4.3 Gait

State fatigue and energy were the predominant variables associated with gait characteristics. This suggests current feelings of fatigue and energy (state variables) may be more important determinants of gait than usual feelings (trait characteristics) in young, healthy adults. This is consistent with previous work investigating state and trait fatigue in individuals with Multiple Sclerosis, in which state fatigue was more closely associated with alterations in gait characteristics than trait fatigue. Comfortable pace ambulation requires little attention and cognitive control for young, healthy adults, making it unlikely that acute changes in attentional reserve capacity would explain the observed relationships. It is possible the transient higher levels of resting state fatigue leads to alterations in gait characteristics through acute changes to motivation, arousal, executive function and mood.

While the associations between state fatigue and gait characteristics were statistically significant, the variance explained by the regression models was low (range 3-13%). This is in accordance with previous work demonstrating increases in state physical and mental fatigue lead to minimal changes in gait characteristics while walking on a treadmill in healthy young and older adults. While the use of a treadmill may have obscured fatigue-related changes in gait characteristics, others have demonstrated no change in over ground walking as a single-task after inducing mental fatigue. However, Behrens et al. (2018) did demonstrate increased gait variability in older adults during dual task walking in response to a mentally fatiguing task. Collectively, these findings lend further support for future work to determine the functional significance of our findings and expand them to dual task conditions in populations who experience higher fatigue and greater postural instability, such as older adults.

In this group of young, healthy adults, sex and PA were significant modifiers of the relationships between fatigue and energy variables and gait. Sex was particularly influential, which may be the product of sex differences in gait characteristics and self-reported fatigue levels. The positive relationship between PA and gait variability may underscore the ability of physically active individuals to adapt motor control strategies in response to internal and external demands, facilitating successful motor performance.
outcomes\textsuperscript{56}. However, this observation contrasts with the work of Ciprandi et al. (2017) in which PA was negatively correlated with gait variability in young and old females\textsuperscript{57}. Differences in the population studied may underlie the opposing outcomes. Further work is required to more clearly understand the interactions between PA, fatigue and gait variability.

4.4.4 Limitations

While this study provides insight into the relationships between state fatigue and energy variables, trait fatigue and energy characteristics, postural control and gait in young healthy adults, there are limitations. The magnitude of the relationships between fatigue and energy, postural control and gait are low. Additional factors not evaluated in this study, such as strength\textsuperscript{58}, ROM\textsuperscript{58} and pain\textsuperscript{59}, influence postural control and gait, and may enhance the predictive ability of the regression models. Further, given we ran several regression analyses, it is possible this led to inflation of type I error rate. However, this study suggests that further research is warranted in populations with higher fatigue and instability in postural control and gait, such as older adults, and during conditions where attentional capacity is reduced, such as dual task conditions. Additionally, PA was measured using self-report, which has a low-moderate correlation with quantitative measures of PA\textsuperscript{60}. Given the importance of PA in reducing fatigue\textsuperscript{26}, future work is warranted to better understand the relationships between quantitatively measured PA, fatigue, postural control and gait.

4.4.5 Conclusions

In young, healthy adults, postural sway and gait characteristics were associated with state and trait fatigue and energy. Postural control was associated with trait fatigue, trait energy and sleep quality, whereas gait characteristics were associated with state fatigue, state energy, sex and PA. While these relationships were statistically significant, the magnitude of the associations was low. Further work is required to extend these findings to populations which experience higher fatigue and instability in postural sway and gait, such as older adults. As well, given the sex-specific differences in state and trait fatigue,
our findings suggest sex may be an important covariate for future research examining the motor control characteristics of gait and postural control.
4.4.6 References


Chapter 5

5 Overall Discussion

With almost half of all adults in the United States experiencing moderate to very severe fatigue over the course of a week\textsuperscript{1}, fatigue is one of the most common reasons for primary care physician visits\textsuperscript{2}. It is associated with lower self-reported health status\textsuperscript{3} and greater co-morbidity of conditions\textsuperscript{4}. To alleviate the fatigue-related healthcare burden and improve health, wellness and function of people with fatigue, it is necessary to understand the development of fatigue and its impact on physical function.

The sensation of fatigue arises from the interaction between changes in performance and perceived fatigue\textsuperscript{5}. An increase in perceived fatigue due to sustained attention on a task, termed mental fatigue, leads to an increase in performance fatigue, such as declines in submaximal exercise performance\textsuperscript{6–8}. However, the neuromuscular mechanisms underlying this relationship are unclear\textsuperscript{9,10}. Further, there is very little literature describing sex-specific differences in response to a mentally fatiguing task, despite females commonly reporting greater fatigue than males\textsuperscript{3}. Accordingly, the overall objective of this dissertation was to examine sex-specific differences in the impact of mental fatigue on neuromuscular function and motor performance in young, healthy adults.

Chapters 2 and 3 involved investigations of the impact of a sustained attention task which induces mental fatigue (Psychomotor Vigilance Task, PVT) on neuromuscular function of the tibialis anterior (TA) in young, healthy adults. In chapter 2 neuromuscular measurements were collected during single task (contractions only) and dual task (contractions and performing PVT), including force characteristics, motor unit firing behavior and muscle contractile properties. After the mental fatigue task, motor unit firing rate declined at 20% MVC in males and females as a single task and in males only at 50% MVC as a single and dual task. The decline in motor unit firing rate occurred despite no change or slight increases in dorsiflexion (DF) force and no change in TA surface EMG activity. There were no changes to the variability in motor unit firing rate or
force production. Muscle contractile properties and M-wave amplitude also did not change following the mental fatigue task suggesting alterations to neuromuscular function are likely supraspinal in nature rather than peripheral. Supraspinal alterations to neuromuscular function may have impacted motor unit firing rate through alterations to muscle activation patterns, including activation of synergists, co-contraction, or motor unit recruitment. These results and hypothesized neuromuscular mechanisms informed the development of chapter 3, in which we expanded our measurements of neuromuscular function before and after mental fatigue to include investigations of central neuromuscular function, including the use of TMS and surface EMG for co-contraction.

Similar to chapter 2, chapter 3 evaluated neuromuscular function before and after mental fatigue. Our expanded neuromuscular function measurements included: intracortical inhibition, corticospinal excitability, motor unit firing rate, co-contraction between the dorsi- and plantar flexors and dorsiflexion force. We also addressed a limitation of chapter 2 by including a control condition. In this study, despite setting target force lines, DF force and TA surface EMG declined during 10% MVC and TA motor unit firing rate slowed at 20% MVC following the mental fatigue and control tasks in males and females. However, these alterations were not specific to mental fatigue and were not accompanied by a change in medial gastrocnemius (MG) EMG activity or MG:TA co-contraction, as hypothesized based on the results of Chapter 2. We were unable to replicate the decline in motor unit firing rate in males at 50% MVC after mental fatigue observed in chapter 2. This difference may be mediated by a larger number of participants, greater number of trials, or characteristics of the participants. There were no changes to corticospinal excitability while the cortical silent period (CSP) duration lengthened in males and females after the mental fatigue and control tasks, indicating increased intracortical inhibition. However, the changes to neuromuscular function were not specific to the mental fatigue task, suggesting the results of Chapter 2 may not be solely the result of mental fatigue.

The PVT is a simple reaction time, sustained attention task known to induce mental fatigue. As the impact of the PVT on neuromuscular function was equivalent to the control task of watching the Earth documentary, it is possible watching Earth was also a
sustained attention task. However, *Earth* is considered an engaging, emotionally neutral documentary and has previously been used as a control condition for mental fatigue experiments.\textsuperscript{10,14,15} Further, viewing *Earth* leads to a different brain activation profile than a sustained attention task similar in nature to the PVT\textsuperscript{16}. While these brain activation profiles were previously recorded with eight minutes of documentary viewing and performing the sustained attention task, our interventions were 30 min in chapter 3. Therefore, it is possible the longer duration of documentary viewing led to similar cortical activation patterns as the PVT with subsequent equivalent neuromuscular function responses in males and females.

It is also possible the neuromuscular function changes identified in the post-test assessment period in chapters 2 and 3 were a result of prolonged sitting. Through several interacting systems, such as vascular, neuroendocrine and metabolic, prolonged sitting impacts cognitive and neuromuscular function.\textsuperscript{17,18} As a result of these interactions, prolonged sitting can lead to functional alterations in cortical regions important to executive function, attention\textsuperscript{18} and the development of mental fatigue.\textsuperscript{11,19} Therefore, there may be interacting effects of prolonged sitting and sustained attention on the development of mental fatigue and neuromuscular function. This notion is supported by a recent study in which balance was similarly impacted by 90 min of a response inhibition task which induced mental fatigue and watching the *Earth* documentary.\textsuperscript{14} The authors of this study hypothesized the similar balance response between conditions was secondary to the effects of prolonged sitting during the interventions.\textsuperscript{14} Further work is required to differentiate the effects of mental fatigue, sustained attention and prolonged sitting on neuromuscular function.

While the alterations to neuromuscular function observed in chapters 2 and 3 were all statistically significant and large in magnitude, the absolute differences between pre- and post-assessments were small. These results suggest mental fatigue does not lead to substantial alterations in submaximal DF neuromuscular function. This outcome aligns with the work of others who have demonstrated no change in measures of neuromuscular function following a mentally fatiguing task, including MVC force, voluntary activation, EMG activity, M-wave amplitude and duration and muscle
contractile properties\textsuperscript{10,20,21} of the knee extensors and dorsiflexors. However, when considering muscles of the upper extremity, Bray et al. (2008) have demonstrated increased EMG activity in the wrist flexors during submaximal gripping at 50% MVC until exhaustion following less than four minutes of a modified Stroop task\textsuperscript{22}. This occurred in conjunction with earlier time to exhaustion, suggesting earlier onset of muscular fatigue in the wrist flexors after a short duration task which activates cortical regions implicated in mental fatigue\textsuperscript{23}. As there are greater corticospinal projections to the cervical spine than the lumbar spine\textsuperscript{24}, these differences in neuromuscular function may be related to the muscle under investigation. Future work should seek to compare neuromuscular function in upper and lower limb muscles after cognitive or sustained attention tasks which induce mental fatigue.

The lack of substantial alterations to neuromuscular function in the lower extremities after mental fatigue suggests declines in submaximal exercise performance are mediated by non-motor brain regions. Sustained attention and cognitive task which induce mental fatigue result in prolonged activation of the anterior cingulate cortex (ACC)\textsuperscript{6,11,19}. The ACC has extensive connections with motor planning regions of the brain and therefore prolonged ACC activation could have altered motor control strategies. Our results from chapter 3 suggest there are no changes to co-contraction between the TA and medial gastrocnemius. However, activation of synergistic muscle groups or changes to motor unit recruitment are possible mechanisms we were unable to examine with our outcome measures. Further, mental fatigue may have a larger effect on tasks involving whole-body movements and more complex motor planning than the isometric contractions investigated in this dissertation.

The ACC is also responsible for evaluating the costs and rewards of ongoing participation in an activity, is intimately involved in effort-based decision making and the generation of perception of effort\textsuperscript{19}. A higher rating of perceived exertion (RPE) during submaximal exercise performance after a mentally fatiguing task is a common observation\textsuperscript{6,8,10,25,26}. Perception of effort is associated with changes to cortical neurotransmitter concentrations, such as adenosine and dopamine\textsuperscript{19,26}, which are known to change in concentration after sustained attention and cognitive tasks\textsuperscript{26–28}. Future work
should investigate non-motor brain regions, such as neurotransmitter concentrations with the use of magnetic resonance spectroscopy, to better understand the central response to a mentally fatiguing task.

While much of the literature on mental fatigue and exercise performance involves submaximal performance performed at a vigorous intensity level\textsuperscript{6,8,10,29}, there is little research evaluating the impact of mental fatigue on light to moderate submaximal exercise performance. In Chapters 3 and 4, we investigated the impact of mental fatigue on measures of walking performance in young, healthy adults. Specifically, in chapter 3 we examined the impact of mental fatigue on single and dual task walking performance. After the mental fatigue and the control task, there were no changes to distance walked during a 6MW test or during one minute of walking as quickly as possible while performing serial seven subtraction. Performance on the serial seven subtraction task also did not change after the mental fatigue or control condition. These motor performance responses were similar between males and females. These results suggest that mental fatigue does not impair walking capacity in young, healthy adults as a single or dual task.

RPE is an important factor contributing to declines in submaximal exercise performance after a mentally fatiguing task\textsuperscript{6,8,25,26}. We may not have observed a change in 6MW test performance because RPE at the end of the 6MW test was approximately 11-12 on the 6-20 Borg scale, corresponding to slightly greater than light effort\textsuperscript{30}. This is in comparison to RPE of approximately 18, or hard to extremely hard effort, in studies which have demonstrated mental fatigue-related declines in submaximal exercise performance, such as running a five-kilometer time trial\textsuperscript{8} and cycling until exhaustion at 80% of peak power output\textsuperscript{6}. Thus, there appears to be range of RPE which is most susceptible to mental fatigue. Exercise intensities with perceived effort at light (chapter 3) and maximum\textsuperscript{20,31} levels are not impacted by mental fatigue, but intensities with efforts at moderate to vigorous levels are\textsuperscript{6,8}. Further work is necessary to support this hypothesis.

Similar to chapter 3, chapter 4 examined the relationships between walking performance and fatigue. While chapter 3 did not identify a change in walking capacity following mental fatigue, chapter 4 examined the relationships between how people walk (gait
characteristics), postural control, mental and physical fatigue and energy, both as state variables and trait characteristics. We also determined if these relationships were modified by sex, PA and sleep quality. Using a forward stepwise hierarchical multivariate multiple linear regression, the models that best predicted gait characteristics included state fatigue, state energy and sex. Regression models which best predicted postural control included trait fatigue, trait energy and sleep quality. While the mechanisms responsible for this may involve attentional regulation, the ACC or alteration to psychological state\textsuperscript{5,19,32}, the variance explained by the regression models was low (3-13%), suggesting trait and state fatigue and energy are unlikely to have substantial impacts on gait characteristics and postural control in young, healthy adults. These results align with the work of others who have observed young adults demonstrate minimal to no changes in gait characteristics after an increase in state mental fatigue when walking on a treadmill\textsuperscript{33} and overground\textsuperscript{15}. However, older adults demonstrate increased gait variability following a mentally fatiguing task\textsuperscript{15}. Further research is therefore needed in the older adult population to examine walking performance after a mentally fatiguing task as gait speed is an indicator of functional capacity\textsuperscript{34} and higher fatigue is associated with lower functional status\textsuperscript{35}.

Chapters 3 and 4 also included an analysis of the influence of sex, PA level and sleep quality on the development of mental fatigue and the relationship between mental fatigue and motor performance. In chapter 3, regression analyses indicated that sex, moderate to vigorous PA level and sleep quality were not significantly associated with the development of mental fatigue. In chapter 4, regression analyses indicated that sex, PA level and sleep quality had small relationships with some measures of postural control and gait. Overall, these results demonstrate that sex, PA level and sleep quality do not substantially influence the development of mental fatigue or moderate the relationship between mental fatigue and motor performance in young, healthy adults. Future work should include sedentary populations, older adults and comprehensive measurements of executive function to better identify those who may be more susceptible to the development of mental fatigue and subsequent declines in motor performance.
5.1 Limitations

As the neurophysiological response to the PVT was equivalent to watching the documentary, it is possible the PVT was not substantially different than sustaining attention on a documentary. However, objective indices of mental fatigue were present after performing the PVT (e.g. slowing of reaction time, increases in perceived fatigue). While we did not take measures of reaction time after the documentary, perceived fatigue was not significantly higher after the documentary compared to before, suggesting the two tasks had differential influences on fatigue. Additionally, the neuromuscular function measures in this dissertation were acquired during isometric contractions. Given the declines in motor performance after mental fatigue occur during whole-body, dynamic exercise, we may not have identified substantial changes to neuromuscular function due to the isometric nature of the contractions. Further, the motor performance tasks used in this study were completed at a low intensity level, requiring low effort for young, healthy adults. This may have limited our ability to identify changes to motor performance in this population. The young, healthy participants in this dissertation were all highly active and therefore may been more resistant to the development of mental fatigue and subsequent declines in motor performance, as is seen in highly trained athletes²⁹.

5.2 Future Research

Mental fatigue negatively impacts submaximal performance during running and cycling, however the physiological mechanisms underpinning these motor performance decrements are still unclear. While this dissertation suggests motor unit firing rate and intracortical inhibition may be involved, more research is needed to better understand the mechanistic causes. Future research should focus on neuromuscular function during dynamic contractions and investigate non-motor brain regions, such as using magnetic resonance spectroscopy to detail neurotransmitter concentrations. Additionally, future research should include older adults as this population, particularly older women, experience higher levels of fatigue³⁵,³⁶ with age-related changes to neuromuscular function³⁷,³⁸ and motor performance³⁸. Further, including participants with a wide range of PA levels will provide greater insight into the potential role of PA to mitigate the influence of mental fatigue on neuromuscular function and motor performance.
5.3 Conclusion

In conclusion, the sum of this dissertation suggests mental fatigue does not substantially alter neuromuscular function of the TA during submaximal isometric contractions in young adult males or females. Further, mental fatigue does not lead to declines in single or dual task walking performance in young adult males and females. When fatigue is viewed as a state variable or trait characteristic, physical and mental fatigue do not have substantial impacts on gait characteristics and postural control in young adult adults. Additionally, sex, PA level and sleep quality do not substantially influence the development of mental fatigue or the relationships between state and trait fatigue, gait and postural control. However, this dissertation provides novel information that males and females respond in a similar manner to mental fatigue and highlights the complex relationship between mental fatigue, sustained attention, neuromuscular function and motor performance. Insights from this dissertation provide several avenues for future research, including investigating sedentary populations and people with higher fatigue and lower functional abilities, such as older adults. It also underscores the need for a greater focus on the neurophysiological response to mental fatigue in non-motor brain regions.
5.4 References

1. Blackwell D. Percentage of adults who often felt very tired or exhausted in the past 3 months, by sex and age group - National Health Interview Survey, United States, 2010-2011, https://www.cdc.gov/mmwr/preview/mmwrhtml/mm6214a5.htm (2013).


27. Schweimer J, Hauber W. Dopamine D1 receptors in the anterior cingulate cortex


Appendices

Appendix 1 Ethics Approval

Dear Professor Anita Christie

The Western University Health Science Research Ethics Board (HSREB) has reviewed and approved the above-mentioned study as described in the WREEM application form, as of the HSREB Initial Approval. Due to the study design described, this study is to be conducted by the investigator noted above. All other required institutional approvals must also be obtained prior to the conduct of the study.

Documents Approved:

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No deviations from, or changes to, the protocol or WREEM application should be initiated without prior written approval of an appropriate amendment from Western HSREB, except where necessary to eliminate immediate hazard(s) to study participants or when the change(s) involves only administrative or logistical aspects of the trial.

HSREB members involved in the research project do not participate in the review, discussion, or decision.

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Please do not hesitate to contact us if you have any questions.

Sincerely,
Nicola Geoghegan-Murphy, Ethics Officer on behalf of Dr. Philip Jones, HSREB Vice-Chair
Appendix 2 Copywrite Approval

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# Curriculum Vitae

**Name:** Katie Kowalski  
**Post-secondary Education and Degrees:**

- University of Wisconsin - Madison  
  Madison, Wisconsin, United States  
  2003-2007 BS

- University of Wisconsin - Madison  
  Madison, Wisconsin, United States  
  2008-2011 DPT

- University of Oregon  
  Eugene, Oregon, United States  
  2015-2017 MS

- The University of Western Ontario  
  London, Ontario, Canada  
  2017-2021 PhD

**Honours and Awards:**

- American College of Sports Medicine Foundation Doctoral Student research grant, $4800  
  2020-2021

- Nan Phillipson Award for Excellence in Teaching Assistants  
  2019

- Province of Ontario Graduate Scholarship  
  2019-2020

- American Physiological Society Physiology Education Community of Practice Fellow  
  2018-2019

- General University Scholarship, University of Oregon  
  2018

- Sue Moshberger Scholarship, University of Oregon  
  2018

- American College of Sports Medicine Northwest, Outstanding Masters oral presentation  
  2017
### Related Work Experience

- **Graduate student research assistant**  
  School of Physical Therapy  
  The University of Western Ontario, 2021-current

- **Teaching Assistant**  
  The University of Western Ontario  
  2018-2021

- **Physical Therapist**  
  2011-current

- **Instructor, Human Anatomy II**  
  University of Oregon  
  2018

- **Graduate Teaching Fellow**  
  University of Oregon  
  2015-2018

### Publications:


4. **Kowalski KL**, Boolani A, Christie AD. Sex Differences in the Impact of State and Trait Fatigue on Gait Variability. (in review)

### Conference Presentations:


3) **Kowalski KL** & Christie AD. Force Steadiness and Motor Unit Firing Variability Following Mental Fatigue in Young Adults. Podium presentation at annual Exercise Neuroscience Group meeting, 2019.


5) **Kowalski KL** & Christie AD. The Impact of Mental Fatigue on Force and Motor Unit Firing Variability in Young Adults. Podium presentation at American College of Sports Medicine annual meeting, 2019.


**Knowledge Translation:**

1) **Kowalski KL**. Strength training reduces fatigue in female breast cancer survivors, but combining vitamin C and E supplementation with strength training did not provide any further reduction in fatigue. Canadian Society for Exercise Physiology, October 2020 Communique.

2) **Kowalski KL**. High-intensity interval training improves memory in older adults. Canadian Society for Exercise Physiology, August 2020 Communique.

3) **Kowalski KL**. Fatiguing muscle contractions of a small hand muscle can lead to fatigue of the same and other muscles in the opposite limb. Canadian Society for Exercise Physiology, Oct 2019 Communique.