The effects of exercise-induced ankle muscle fatigue on static postural control in healthy young adult males and females

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To my God almighty

My grace is sufficient for you, for my power is perfected in weakness.

2 Corinthian 12:7

This thesis is dedicated to my loving wife, Ha-Young Song, who has always encouraged and supported me to go through this Ph.D. journey and to my loving mom, dad, and sister who trust and love me.

STATEMENT OF COVID-19 IMPACT

The planned initial focus of this thesis was to determine the effects of muscle fatigue on postural control and fear of falling according to aging. However, COVID-19 and the associated prolonged uncertainty concerning research-related restrictions led to constraints with regards to data collection, particularly with older adults. Given these circumstances, the Faculty of Health Sciences encouraged doctoral students and their supervisors at the end of September 2020 to examine research alternatives that would ensure that students could progress in their studies and complete their degree in a timely manner. Thus, the initial plan was changed, with approval from the thesis advisory committee (TAC), to the current topic of this thesis, which focused on sex differences in muscle fatigue mechanisms and postural control. This thesis thus includes one systematic scoping review (article 1; planned and conducted after changing the initial plan), two experimental studies (articles 2 and 3) finalized with data that had been already collected before COVID-19 and for which Donguk Jo was the lead investigator, and a last experimental study (article 4), modified from the original plan to focus on sex differences and carried out during the pandemic.

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AUTHOR CONTRIBUTIONS

This thesis includes one scoping review (article 1) and three experimental studies (articles 1-3).

Article 1: *Rating of perceived exertion (RPE) in studies of fatigue-induced postural control alterations in healthy adults: scoping review of quantitative evidence.* The author (Donguk Jo) and the supervisor (Dr. Martin Bilodeau) conceptualized the study. The author carried out data identification, data screenings (title, abstract, and full text), data synthesis, and wrote and edited the manuscript. The supervisor (Dr. Martin Bilodeau) participated in the concept and design of the study and full-text screening, provided advice and content expertise, and revised the manuscript.

Article 2: *Sex differences in central and peripheral fatigue induced by sustained isometric ankle plantar flexion.* The author (Donguk Jo) and the supervisor (Dr. Martin Bilodeau) conceptualized the study. The author carried out data collection, statistical analyses, and wrote and edited the manuscript. The supervisor (Dr. Martin Bilodeau) participated in all research aspects of the study and provided advice and content expertise. The co-author (Miriam Goubran) participated in the data collection and reviewed the manuscript.

Article 3: *Sex differences in the effect of muscle fatigue on static postural control under different vision and task conditions.* The author (Donguk Jo), the supervisor (Dr. Martin Bilodeau), and co-authors (Maya Pannetier, Sophie Drouin, Sarah Bassil, and Caroline Matte) conceptualized the study. The author provided guidance and assistance for data collection, organized data and performed statistical analyses, and wrote and edited the manuscript. The supervisor (Dr. Martin Bilodeau) participated in all research aspects of the study and provided advice and content expertise. The co-authors participated in data collection/curation and reviewed the manuscript.

Article 4: *Sex differences in effects of ankle muscle fatigue on static postural control and ankle spinal motoneuron activities.* The author (Donguk Jo) and the supervisor (Dr. Martin Bilodeau) conceptualized the study. The author carried out data collection, statistical analyses, and wrote and edited the manuscript. The supervisor (Dr. Martin Bilodeau) participated in all research aspects of the study and provided advice and content expertise and reviewed the manuscript.

ABSTRACT

This thesis describes a series of experiments to investigate sex differences in neuromuscular fatigue mechanisms of the ankle muscles and related postural control changes in healthy young adults. We found that isometric exercise-induced ankle muscle fatigue led not only to significant declines in twitch contractile function and voluntary activation (using twitch interpolation technique, Article 2) but also to significant changes in the center of pressure (COP) sway (backward/right shifts of the COP position and/or increased COP sway velocity) during quiet standing and/or standing forward leaning (FL) task with eyes open and/or eyes closed (Articles 3 and 4). However, we found minor or no significant sex differences in the fatigue mechanisms and fatigue-induced COP sway changes regardless of task difficulty, except for a significant sex X fatigue interaction for COP sway velocity (Article 3). The interaction effect was due to a significant increase in sway velocity in males during the FL task with eyes closed (but not in females), suggesting that males may preferentially rely on ankle control during a relatively challenging task (as compared to females). The general lack of sex differences is not surprising given similar performance and/or perceived fatigability between the sex groups (Articles 2-4), which could be explained by the relatively small differences in contractile function (and/or muscle strength) between males and females for ankle plantar and dorsi flexors compared with other muscle groups. In addition, this thesis involves a scoping review (Article 1), which summarized the broad range of rating of perceived exertion (RPE) values documented in studies observing an effect of muscle fatigue on postural control and suggested the potential effect of various fatigue levels on postural changes. Collectively, these findings advance our understanding of sex-specific fatigue mechanisms and postural control behavior. These findings also indirectly contribute to the understanding of sex differences in

injury risks during physically or stability-demanding tasks and sports, as well as to the improvement in the prescription of physical training or rehabilitation exercise.

DEFINITION OF TERMS

Anthropometric parameters: are defined as variables (e.g., height, weight, etc.) quantifying the size of the human body, and whose changes can affect postural control in this thesis.

Anticipatory postural adjustment: is "a specific form of feedforward control wherein a pattern of muscle activation acting to counter the destabilizing effects of a volitional movement is released prior to, or in conjunction with, the volitional movement activity" (Maki & McIlroy, 1996).

Attention: is the cognitive process to "selectively enhance the information most relevant to one's current behavior" (Buschman & Kastner, 2015).

Automatic process (an): is a postural control process that is automatically carried out without directing attention to such process in performing a low demand-cognitive task and benefits postural stability.

Base of support: is the area of the body in contact with the support surface.

Center of pressure (COP): is **"**the location on the supporting surface where the resultant vertical force vector would act if it could be considered to have a single point of application" (Benda et al., 1994). The ground reaction force vector indicates the sum of all forces acting between individuals and their supporting surface (Benda et al., 1994; Cavanagh, 1978). A shift in the COP indirectly represents a change in postural sway, which could be used not only as an indicator of an individual's ability to maintain stability and related neuromuscular control (Gribble & Hertel, 2004b), but also as a precursor to a fall (Fernie et al., 1982). The equation to obtain COP position is as follows (Lafond et al., 2004): $COP_x = \frac{-M_y + F_x + Z_0}{F_z} + X_0$ and

$COP_y = \frac{M_x + F_y + Z_0}{F_z} + Y_0$. M = moment; F = reaction force; x, y and z = mediolateral, anteroposterior and vertical directions, respectively; and X0; Y0; Z0 = offsets from the geometric center of the force platform.

Center of mass (COM): is "an imaginary point at which the total body mass can be assumed to be concentrated" (Lafond et al., 2004). The COM is considered a controlled variable in the inverted pendulum model, which relates to a controlling variable (COP) (Winter et al., 1998). The equation of the COM location is as follows: $COM = \frac{1}{N}\sum_{i=1}^{n} COM_i \times M_i$. M = total body mass; m_i = the mass of *i*th segment, COM_i = the coordinate of *i*th segment; and N = the number of segments defining the body COM.

Dynamic stability: has been defined as the ability to maintain the center of mass (COM) within the base of support (BOS) while the body faces "expected (voluntary displacement) or unexpected (externally triggered displacement) perturbations of the center of gravity (COG)" (Winter et al., 1990). Dynamic tasks, for example, are those involving either voluntary movements (e.g., gait, and upright standing with voluntary arm (s) or leg movements) and/or perturbations (e.g., upright standing on movable surface, sagittal/frontal lean in a standing position induced by muscle/tendon vibrations) (Papa et al., 2015).

Fall (a): is defined as "unintentionally coming to rest on the ground or other lower level not as a consequence of a major intrinsic occurrence (e g., stroke, or seizure) or a devastating external hazard (e g., hit by a vehicle)" (Gibson, Andres, Isaacs, Radebaugh, 1987).

Feedback control: is "a mode of postural control that uses sensory information about the orientation and motion of the body to update the ongoing stabilizing muscle activation"(Maki & McIlroy, 1996).

Feedforward control: is “a mode of postural control in which a preprogrammed pattern of muscle activation is released without further modification” (Maki & McIlroy, 1996).

Hoffmann (H) reflex: is the neurophysiological “response of the motoneuron pool to a volley from large-diameter primary muscle afferents” evoked by electrical stimulation of a peripheral nerve (McNeil et al., 2013).

Gender: “refers to the socially constructed roles, behaviours, expressions and identities of girls, women, boys, men, and gender diverse people” (Canadian Institutes of Health Research).

Impairments: are “problems in body function or structure such as a significant deviation or loss” (World Health Organization, 2002)**.**

Limit of stability: is “the area over which an individual can move their COM and maintain equilibrium without changing the base of support” (Horak, 2006)

Muscle fatigue: is defined as any exercise-induced loss of ability to generate force or power within a muscle or muscle group (Bigland-Ritchie, Woods, & Bigland-Ritchie, 1984; Gandevia, 2001). In this thesis, the term “muscle fatigue” is exchangeable with the term “neuromuscular fatigue”. Muscle fatigue (or neuromuscular fatigue) is also defined in the context of “performance fatigability”, which is defined as “the decline in an objective measure of performance over a discrete period” (Enoka & Duchateau, 2016). The objective measure typically includes muscle torque (or force) and the time to task failure (Enoka & Duchateau, 2016; Kluger et al., 2013). Also, the experiments included in this thesis only focuses on muscle fatigue produced by local muscular exercise (or resistance exercise) generating segmental movements (e.g., weight-based tiptoes) or force (e.g., isometric exercise, not by general muscular exercise involving whole-body movements (e.g., walking and running) (Paillard, 2012). Because local muscular exercise is the main focus of this thesis, the potential influence of general muscular exercise and related changes in the cardiac and respiratory systems on postural control are not described in this thesis.

Motor unit (a): consists of a motor neuron and all the skeletal muscle fibers innervated by it.

Neuromuscular junction (a): is a synapse formed by the contact between a motor neuron (axon) and a muscle fiber.

Perceived fatigability: is defined as a change in the sensations (e.g., perceived muscle exertion and pain) that regulate task performance (Enoka & Duchateau, 2016)

Postural stability (or balance or equilibrium): is one component of postural control, which is the ability to control the center of mass (COM) in relation to the base of support (BOS) (Shumway-Cook & Woollacott, 2012).

Postural control: involves neural control of postural stability and postural orientation.

Postural orientation: is another component of postural control, which is "the ability to maintain an appropriate relation between the body segments, and between the body and the environment for a task (Shumway-Cook & Woollacott, 2012).

Proprioception: is defined as a sense of position and sense of movement of the limbs and trunk in space (Sherrington, 1907). Proprioception has also been suggested to involve the sense of effort, sense of force, and sense of heaviness (Proske & Gandevia, 2012; Proske & Gandevia, 2009).

Sensory systems: in the context of this document, sensory systems are the nervous systems responsible for processing sensory information from visual, vestibular, and somatosensory (proprioceptive and cutaneous) receptors.

Sex: “refers to a set of biological attributes in humans”, which “is usually be categorized into female or male” (Canadian Institutes of Health Research). Because this thesis focuses on neurophysiological behaviors in human, the terms of “sex”, “female”, and “male” are used throughout this thesis document, instead of the terms of “gender”, “women”, and “men”.

Static stability: in this thesis, is defined as the capability to maintain upright posture on a firm and stable surface when at rest. Static tasks, for example, are those involving upright standing on different BOS (e.g., on one or two legs) and with different vision conditions (e.g., eye open and closed).

Stiffening behavior (a): in this thesis, is defined as a behavior caused by an increase in co-contraction of agonist and antagonist muscles (e.g., tibialis anterior and lateral gastrocnemius lateralis), and/or their neuromuscular activations around the ankle joint. This concept has also been termed “muscular stiffness,” “stiffness,” and “stiffening strategy” in previous studies (Caron, 2004; Young & Mark Williams, 2015).

Stretch reflex (a): is an automatic muscle response produced in response to imposed stretches of the muscle as a result of activation of muscle spindle afferents.

Voluntary activation (or drive): reflects the level of activation of motoneurons from descending motor tracts (Gandevia, 2001). It is commonly estimated by evoking a response from the motor nerve (through electrical stimulation) or motor cortex (through TMS) which is superimposed during an isometric maximal voluntary contraction (MVC) (Taylor et al., 2006).

LIST OF ABBREVIATIONS

AP: anteroposterior

BOS: base of support

CNS: central nervous system

COG: center of gravity

COM: center of mass

COP: center of pressure

CR10: Category-Ratio scale

DF: ankle dorsiflexors

EMG: electromyography

FL: standing forward lean

HRT: half relaxation time of resting twitch torque

GL: gastrocnemius lateralis

LFF: low frequency fatigue

LOS: limit of stability

ML: mediolateral

MV(I)C: Maximal voluntary (isometric) contraction

PF: ankle plantar flexors

PNS: peripheral nervous system

RPE: rating of perceived exertion

SD : standard deviation

SOL: soleus

ST: singlet twitch torque

TA: tibialis anterior

VA: voluntary activation

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CHAPTER 1. INTRODUCTION

The inability to maintain postural stability could be an indicator of injury risks in young adults when performing stability-demanding tasks; injuries such as sports injuries (e.g., ankle strain and ACL injury) (Lehmann et al., 2017; Ross & Guskiewicz, 2004) and workplace injuries (e.g., due to exertion produced by weight-lifting, slips, trips, and falls) (Bannon et al., 2018; Guerin et al., 2020). A stability assessment could thus provide guidance for rehabilitation or fitness training to prevent musculoskeletal injuries and improve task performance efficiency during stability-demanding tasks in young adult males and females (Punakallio, 2003; Sell et al., 2018).

It has been reported that females are likely to have greater postural stability than males during some tasks due to the advantage of anthropometric factors such as smaller body height, lesser body mass, and a lower COM caused by a wider pelvic base and proportionally lighter (muscle) mass of the upper body in females compared to males (Era et al., 2006; Gribble et al., 2009; Zeller et al., 2003). However, reports of sex differences in postural control for young adults are still contradictory. For example, some studies found less stability in females (Ericksen & Gribble, 2012; Hsue & Su, 2014; Kim et al., 2010; Nagai et al., 2013), while others found less in males (Greve et al., 2013; Ołpińska-Lischka et al., 2021; Sell et al., 2018) and still others found no sex differences (Ku et al., 2012; Røgind et al., 2003; Sell et al., 2018) during static and dynamic tasks. These contrasting findings have been suggested to be mainly due to variations in stability measures (e.g., postural task and variable), postural data standardization (e.g., data normalized or not by different anthropometrical factors) (Era et al., 2006; Kim et al., 2010) and an individual's physiological conditions such as neuromuscular function (Ericksen & Gribble, 2012; Faraldo-García et al., 2011) and phases of the menstrual cycle in females (Khowailed & Lee, 2021; Lee & Yim, 2016).

Acute muscle fatigue produced by resistance exercise (or local muscular exercise) can lead to alterations in the peripheral and central nervous systems (PNS and CNS) associated with a given muscle, as well as a decline in contractile function of the muscle (Enoka & Duchateau, 2016). Such fatigue-induced changes can have significant effects on postural control during some tasks (Paillard, 2012), which may be different between males and females, given sex differences in performance fatigability (Hunter, 2014; Hunter, 2016). More specifically, Hunter (2016) reported by summarizing previous findings (from 1975 to 2015) that females generally have lesser performance fatigability (e.g., a lesser reduction in muscle torque and/or a longer time to task failure) in performing low to moderate isometric exercise of various muscles (e.g., neck, trunk, and upper and lower limbs) as compared with males. This sex difference has been suggested to be mainly due to a greater oxidative metabolic capacity (Russ et al., 2005), a greater proportion of fatigue-resistant muscle fibers (type I) within skeletal muscles (Toft et al., 2003), lesser muscle mass and strength limiting blood flow within the muscles (Hunter & Enoka, 2001; Miller et al., 1993), and lesser central fatigue during fatiguing tasks (Russ & Kent-Braun, 2003) in females compared with males.

Again, such sex differences in performance fatigability may lead to different postural control changes between males and females. For example, acute fatigue produced by exercise of the trunk and leg muscles (ankle, knee, and hip) in young adults can lead to a greater decrease in standing leg-reaching distance (Gribble et al., 2009) and a greater increase in anteroposterior (AP) and mediolateral (ML) postural sway (Springer & Pincivero, 2009) and sway velocity (only for males) (Bannon et al., 2018) during one-leg standing in males compared with females.

These results suggest greater postural control changes or impairments with fatigue in males compared to females.

Given the significant contributions of proximal joint control (e.g., hip and trunk) to postural stability (Aramaki et al., 2001; Creath et al., 2005; Zhang et al., 2007), the aforementioned results could also involve sex differences in postural control strategy with fatigue, for example, with males relying preferentially on ankle control but females relying on proximal joint control (e.g., knee, hip, and trunk). This is supported by previous findings, where greater ankle torque variability with ankle fatigue during feet-together standing in males compared with females (Wojcik et al., 2011) and an increase in trunk acceleration (accompanying decreased center of pressure (COP) velocity) with ankle fatigue in females (although males were not included) (Adlerton et al., 2003) were observed. However, studies regarding sex differences, not only in fatigue mechanisms but also in fatigue-induced postural control changes, are still contradictory and limited in number. Particularly, such sex-related differences in the context of ankle fatigue have only been sparsely studied despite the significant role of the ankle muscles in regulating active ankle stiffness to maintain postural stability during upright standing (Di Giulio et al., 2009; Loram & Lakie, 2002).

In considering the influence of ankle fatigue on postural control during static standing (Bisson et al., 2010, 2011, 2014; Boyas et al., 2011), alterations in proprioception (Paillard, 2012) via a change in spinal proprioceptive inputs from the ankle may be a possible mechanism contributing to observed postural control changes. For example, depression in the soleus (SOL) Hoffmann (H) reflex, which could reflect a reduction in spinal proprioceptive input at the ankle, has been found during quiet standing with fatigue of ankle plantar flexors (PF) (Laudani et al., 2009) and during unilateral perturbed standing in the presence of multi-muscle fatigue of the legs produced by repetitive jumps (Ritzmann et al., 2016). These authors also found an increased COP sway displacement (Laudani et al., 2009) or increased co-contraction in the proximal muscles (knee and hip) (Ritzmann et al., 2016), suggesting that such a reduction in spinal excitability with fatigue may lead to postural control changes during some tasks. However, in the context of postural control and muscle fatigue, the observation of SOL H-reflex modulations has only been sparsely studied, and at this time, sex differences have yet to be documented.

In summary, sex differences in performance fatigability and the significant role of ankle muscles in regulating stability have been documented in many studies of muscle fatigue. However, little is known about sex differences in the effects of ankle muscle fatigue on postural control and related ankle spinal proprioceptive inputs, as well as for ankle fatigue mechanisms. Therefore, the main goals of this thesis were to determine whether fatigue mechanisms (peripheral and central neural processes and contractile function) of PF are different between young adult males and females, and also whether ankle muscle fatigue leads to differences in postural alterations and related ankle spinal proprioceptive (afferents) inputs (SOL H-reflex) between the sex groups. In addition to these experimental studies, this thesis involves a scoping review, which systematically summarizes the rating of perceived exertion (RPE) values documented in studies reporting an effect of muscle fatigue on postural control, as the RPE value could help identify muscle fatigue levels affecting postural control.

In the following review of literature sections, postural control mechanisms (neuromuscular, sensory, and central processing systems) based on the conceptual model of postural control systems and related sex differences are first reviewed. The review next focuses on fatigue mechanisms and related sex differences, and also on how muscle fatigue affects postural control depending on task specificity and sex. Finally, SOL H-reflex measurements and how SOL H-reflex is modulated with postural instability, muscle fatigue, and sex are reviewed.

CHAPTER 2. LITERATURE REVIEW

2.1. Postural control

Postural control, consisting of the neural control of postural orientation and stability, demands a complex interaction between the musculoskeletal and neural systems (Shumway-Cook & Woollacott, 2012). Postural orientation is defined as “the ability to maintain an appropriate relation between the body segments, and between the body and the environment for a task” (Shumway-Cook & Woollacott, 2012). Postural stability is defined as the capability to control the center of mass (COM) with respect to the base of support (BOS) (Shumway-Cook & Woollacott, 2012). The COM is considered a controlled variable in the inverted pendulum model and relates to a controlling variable, the COP. Thus, the COP movements under the feet (which are controlled by the ankle muscles in the AP and ML directions in quiet standing) regulate the position of the COM (Winter et al., 1998). In the inverted pendulum model, Winter and colleagues (1998) also suggested that the difference between the COM and COP positions is proportional to the acceleration of the body.

Although all tasks require postural control, stability and orientation demands vary with different tasks and environments (Horak & Macpherson, 1996). In order to maintain proper orientation and stability under various tasks and environments, postural control is considered to require dynamic and complex interactions between motor, sensory, and central processing systems (Horak, 2006). These complex interactions for postural control are framed within the conceptual model of the postural control system developed by Shumway-Cook & Woollacott (2012) (see Figure 1). Therefore, this thesis makes use of this conceptual model in order to better interpret postural control changes with respect to muscle fatigue and sex in healthy young adults.

This section describes how the neuromuscular, sensory, and central processing (sensory reweighting) systems generally influence postural control and related sex differences. However, attentional demands, which could have an impact on postural control especially during dual task conditions (e.g., standing with a concurrent cognitive task such as working memory task) (Huxhold et al., 2006), are not described in this review. This is because the focus of this thesis is limited to the effects of fatigue-related neuromuscular and sensory changes on postural control during single postural task conditions.

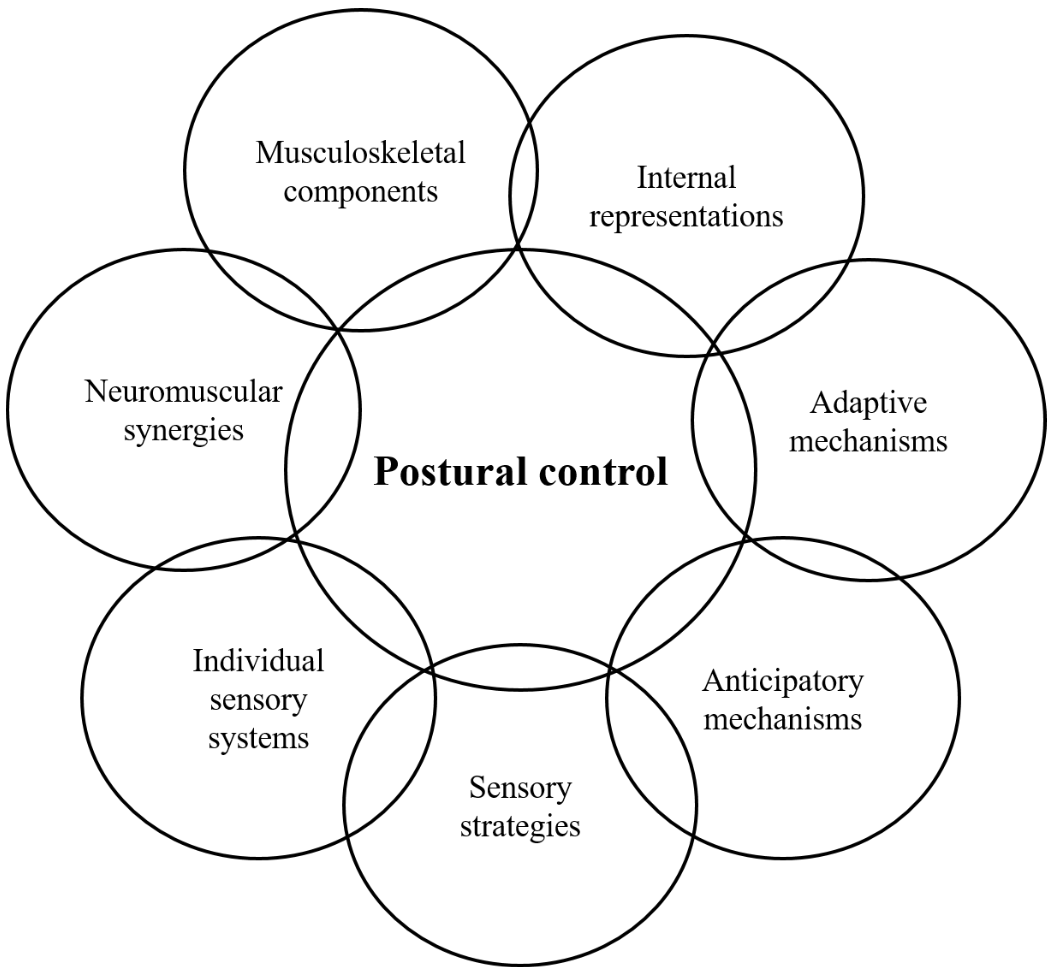

Figure 1. Conceptual model of the postural control system (Adapted from Shumway-Cook & Woollacott (2012), *Motor Control: Theory and Practical Applications*, 4th edition, Lipincott

Williams & Wilkins, p 165).

2.1.1. Neuromuscular system and postural control

Skeletal muscles and their nerve supply, including supraspinal and spinal motor pathways, support postural control through the coordination of forces for adjusting the body's position in space (Shumway-Cook & Woollacott, 2012). In this context, the ability to generate appropriate and/or sufficient muscle force, to react to sensory stimuli, and to adjust movement strategies (e.g., of the ankle and hip joints) to maintain stability are generally required.

2.1.1.1. Muscle strength

The strength of postural muscles (e.g., ankle, knee, hip, and trunk muscles) is considered to be one of the major contributors to maintaining standing stability (Horak, 2006). The information about the muscle strength and joint range of motion available, in addition to sensory inputs, can be important references for the CNS to determine the limits of stability (LOS) and also how to move the body to maintain postural stability (Horak, 2006). The importance of muscle strength for controlling stability is reflected in a recent systematic review of randomized control trials (Šarabon & Kozinc, 2020) reporting the effects of resistance exercise training on both muscle strength and stability improvements in young adults as well as in older adults. Several studies (observing young adults and athletes) included in this review showed increases in standing leg-reaching distances in multiple directions (e.g., see Tay et al., 2019) and decreased COP sway displacement and area (e.g., during one-leg standing in performing Taekwondo, see Yoo et al., 2018) with strength improvements following a 3- to 32-week resistance training of the trunk and lower legs. The significant role of muscle strength on postural control is also supported by many studies observing postural control impairments with acute muscle torque reductions during and at the end of exercise in young adults (see a review by Paillard 2012 and section 2.2.3 below for details).

2.1.1.2. Reaction time

The ability to react quickly and appropriately to maintain standing stability or avoid a fall when an individual encounters a postural challenge or threat is essential (Sturnieks et al., 2008). This ability is dependent on reaction time, which encompasses the amount of time needed to generate an appropriate motor command (or necessary control action) following a triggering sensory stimulus (CNS) as well as the time needed for the muscles to generate the needed force for the response (PNS) to maintain stability (Molnar et al., 2021; Sturnieks et al., 2008). In the context of postural control, a delay in reaction time (likely allowing the COM to come close to the edge of the BOS during some tasks) could lead to an impaired capacity to maintain stability in an unstable environment. Molnar and colleagues (2021), modeling human postural sway, for example, found a relationship between dynamic instability and reaction time delay (from the onset of visual stimulus to a mechanical action of the foot during standing on a sagittal plane-rolling board) in young adults. This may suggest the need for function training to improve the ability to properly respond to external stimuli in an unstable environment to prevent a loss of stability even in healthy young adults as well as in older adults (e.g., see Okubo et al., 2017).

2.1.1.3. Movement strategies

Movement strategies to maintain postural stability have been identified through metabolic and neuromechanical work (e.g. metabolic energy consumption, muscle activation and torque, and joint movement) (Afschrift et al., 2016; Blenkinsop et al., 2017; Runge et al., 1999). The identified strategies generally include an ankle strategy, a hip strategy, and a stepping strategy (Horak, 2006). The ankle strategy, in which "the body moves at the ankle as a flexible inverted pendulum" (Horak, 2006), typically represents patterns of distal-to-proximal muscle activation (from the ankle to the thigh and hip) and minimal movements around the ankle during upright standing on a firm surface (Horak & Nashner, 1986; Christoph Maurer & Peterka, 2005; Nashner & McCollum, 1985). An ankle stiffening behavior may play an important role within the ankle strategy to maintain stability, and has been suggested to be the consequence of increased co-contraction of agonist and antagonist muscles at the ankle (mainly caused by feedforward control) (Henry & Baudry, 2019; Loram & Lakie, 2002; Winter et al., 2001; Young & Mark Williams, 2015). This behavior could be a significant contributor to maintaining stability during challenging static tasks. This is supported the observation of greater co-contraction or muscle activation around the ankle in young adults during upright standing on reduced BOS (e.g., feet together, standing on one leg) compared to quiet (normal) standing (Pinar et al., 2010; Trimble & Koceja, 2001).

The hip strategy, in which "the body exerts torque at the hips to quickly move the body (COM)" (Horak, 2006), has generally been observed during tasks (e.g., standing on a narrow, compliant, tilting, or moving surface) that do not allow the appropriate use of ankle joint torque, and the strategy can lead to a proximal-to-distal muscle activation (from the hip to the thigh and ankle) (Horak & Nashner, 1986; Horak & Kuo, 2000; Nashner & McCollum, 1985). Co-occurrence of the ankle and hip strategies and smooth transitions between both strategies (e.g., from ankle to hip) have also been observed during some dynamic tasks, for example, during standing on a continuous AP moving platform (Mohd Ramli et al., 2019) or standing on a slow-tilting platform (Horak & Nashner, 1986; Nashner & McCollum, 1985). The co-occurrence and transition between ankle and hip strategies could involve the CNS operating basic patterns of postural coordination through a set of motor programs and at the same time adjusting those patterns based on mechanical limits, metabolic efficiency and sensory conditions (Bardy et al., 2002; Horak & Macpherson, 1996).

Lastly, the stepping strategy is a compensatory reaction to quickly take a step(s) (changing the BOS) when an individual is on the verge of falling (Horak, 2006; Maki & McIlroy, 2006). Such strategy has been examined in healthy young and older adults, for example, in response to a large and sudden horizontal perturbation (Maki et al., 2000), when standing on a forward-tilting platform (Chou et al., 2001), and with a forward fall from a forward-leaning standing position (Mademli et al., 2008; Patikas et al., 2016). All these results suggest that postural strategies and their transitions are task specific (e.g., dependent on the size of the BOS, surface conditions, etc.).

2.1.2. Sensory systems and postural control

To maintain postural stability, the CNS must rapidly integrate sensory information from the visual, vestibular, and somatosensory (proprioception and cutaneous sensations) systems (Maki & McIlroy, 1996). The CNS must also use this information selectively to produce complex motor responses (i.e., timing, direction, and magnitude) appropriate to the characteristics of the postural stability disturbances of the surrounding environment (Maki & McIlroy, 1996).

The visual system provides essential information to create a spatial map of the environment in order to assess object movement (e.g., speed and direction), the location of hazards, and body movements in regards to the environment (Grace Gaerlan et al., 2012; Sturnieks et al., 2008). Visual information can have a significant impact on postural stability during upright standing in healthy individuals (Grace Gaerlan et al., 2012; Rodrigues et al., 2017). Young adults, for example, show a significant increase in postural sway when their vision is occluded (EC) during quiet standing, as compared to when they have normal vision (EO with a fixed target) (Barbieri et al., 2019; Hazime et al., 2012), and this may be more significant in challenging tasks (e.g., one-leg standing) (Hazime et al., 2012). However, some specific altered vision inputs (e.g., saccadic or fast eye movement) may instead lead to postural control improvement (e.g. decreased AP COP sway) compared to normal vision, possibly due to an increase in automatic control (or process) regulated by lower-level brain structures such as the cerebellum or basal ganglia (Barbieri et al., 2019; Bonnet & Baudry, 2016; Rodrigues et al., 2017).

The vestibular system provides information on the position and motion of the head with respect to gravity and also contributes to sustaining visual fixation on an object during head movement, while interacting with the visual and somatosensory systems to maintain postural stability (Grace Gaerlan et al., 2012; Sturnieks et al., 2008). The afferent input from the vestibular system, which is transferred to the spinal cord, brainstem, and medulla (Peng, 1996), controls the vestibulo-ocular reflex to keep gaze fixation during head movements and the vestibulo-colic and spinal reflexes to help stabilize the head during upright standing, while coordinating head, neck, and trunk movements in order to adjust the standing posture (Brister et al., 2020; Diener & Dichgans, 1988; Peng et al., 1995; Peng, 1996; Straka, 2020; Sturnieks et al., 2008). The contribution of the vestibular system to postural control has been considered to be lesser compared to that of the somatosensory system in healthy adults during upright standing with a firm BOS (Horak, 2006). However, vestibular information loss could impair postural stability in task conditions where an individual cannot obtain appropriate proprioception and visual inputs to maintain stability (Peterka, 2018). This is supported by previous studies observing young adults (Assländer & Peterka, 2016; Horak & Hlavacka, 2001; Peterka, 2002) which showed an increase in sensory weighting to vestibular information during upright standing on a tilting surface and/or around rotating visual surround. These findings suggest that the vestibular system can provide precision (or compensatory) information to the CNS to maintain stability when visual and proprioceptive sensory systems are impaired.

The somatosensory system in the foot and ankle is considered the most important source of sensory information (proprioception and cutaneous sensation) for stability control during upright standing on a stable and firm surface (Henry & Baudry, 2019; Horak, 2006). The role of proprioception and cutaneous sensation has been emphasized (Shaffer & Harrison, 2007). The term *proprioception,* defined as the sense of position and sense of movement of the limbs and trunk in space, was passed down to us by Sherrington (1906). In addition to these senses, proprioception has also been suggested to include the sense of effort, sense of force, and sense of heaviness (Proske & Gandevia, 2012; Proske & Gandevia, 2009). These different types of information are provided to the CNS by several proprioceptive receptors (Henry & Baudry, 2019; Proske & Gandevia, 2012; Shaffer & Harrison, 2007): joint receptors (providing information about extreme joint position and limb movements), muscle spindles (providing information concerning the muscle's contraction velocity and length), and Golgi tendon organs (providing information about very slight changes in tensile force within the junction between muscle and tendon). Cutaneous sensation, which involves information on mechanical pressure, vibration, and stretch to the skin, is provided by cutaneous receptors: Meissner's corpuscles, Merkel disks, hair follicle receptors, Pacinian corpuscles, Ruffini's endings, and free nerve endings (Shaffer & Harrison, 2007).

Of these receptors, both muscle spindles and cutaneous receptors in the foot and ankle have been determined to play a critical role in controlling posture on a stable surface. This is supported by many studies observing postural sway changes when changing afferent inputs from the two receptors with muscle vibration at the ankle (spindle) and foot (cutaneous). For example, a backward body tilt in a standing position is evoked with muscle vibration of PF in response to an illusion of forward displacement (Kavounoudias, Gilhodes, et al., 1999; Smetanin et al., 2002), and also, increased sway is observed with vibration of both PF and DF (Borel & Ribot-Ciscar, 2016) during quiet standing. Changes in postural sway and/or muscle activation have been also reported with vibration of the plantar surface of the foot (Kavounoudias et al., 1998; Kavounoudias, Roll, et al., 1999; Roll et al., 2002) and with plantar desensitization (Billot et al., 2015; Hong et al., 2007; Meyer et al., 2004), suggesting that feedback from cutaneous receptors of the plantar surface of the foot can have a complementary contribution to postural control during some static tasks. The contribution of these two somatosensory sources has also been observed in a limited number of studies of dynamic tasks (e.g., see Thompson et al., 2011). Overall, the results obtained from muscle vibration studies indicate that afferent somatosensory information coming from both muscle spindles and cutaneous receptors within the ankle/foot complex (e.g., the features of the support surface and the forces generated against the surface) is likely to be the most critical source of somatic information to maintain postural stability during upright standing on a firm surface.

2.1.3. Sensory reweighting and postural control

The sensory reweighting model was introduced by Oie and colleagues (2002) and developed later by Peterka (2002). Sensory reweighting is the process of adjusting the relative contribution of each sensory system to control postural stability (Assländer & Peterka, 2014).

Many studies found shifts in the relative contribution of proprioception and vision by using sensory perturbations such as those provided by visual surround or platform tilts while observing changes in postural sway (e.g., COP, COM) (Assländer & Peterka, 2014; Maurer et al., 2006; Oie et al., 2002; Peterka, 2002; Polastri et al., 2012). The proper timing of sensory reweighting in response to such sensory perturbations is also suggested to be an essential factor to avoid stability loss or fall(s) (Assländer & Peterka, 2014; Peterka & Loughlin, 2004). This is reflected in aging studies (Jeka et al., 2010), which found a concurrence of postural instability (increased COM trajectory) and sensory reweighting delay (in response to visual motion stimulus) with age.

2.2. Sex and postural control

The effect of sex on postural control has been discussed in a limited number of studies, and the findings are contradictory. A few studies showed a lesser postural control (e.g., greater COP sway or lesser standing leg-reaching distance) in females compared to males during quiet standing (Kim et al., 2010) and dynamic tasks (e.g., stair descent, single-leg landing, and leg-reaching task) (Ericksen & Gribble, 2012; Hsue & Su, 2014; Nagai et al., 2013). By contrast, several studies found that males presented with a lesser ability to control posture (e.g., lower stability index or greater COP sway) during one- or two-leg standing with EO and EC, as compared with females (Greve et al., 2013; Ołpińska-Lischka et al., 2021; Sell et al., 2018). Some studies (Ku et al., 2012; Røgind et al., 2003; Sell et al., 2018) also found no sex differences in static and dynamic stability (Ku et al., 2012; Røgind et al., 2003; Sell et al., 2018). These contrasting findings could be explained by the varying extent of sex differences with regards to 1) the function of the neuromuscular and sensory systems, 2) anthropometry (e.g., weight, height, foot width), as well as 3) varying stability measures across studies.

2.2.1. Sex differences in the neuromuscular system and postural control

Sex differences in neuromuscular functions (strength and reaction time) may be beneficial to males for controlling stability. Males generally have greater muscle strength compared to females, possibly due to different anatomy and physiology between the sexes (Hunter, 2014). For example, larger skeletal muscles and a lesser proportional area of type I muscle fibers (the opposite is true for type II muscle fibers) (Porter et al., 2002; Roepstorff et al., 2006; Simoneau & Bouchard, 1989; Staron et al., 2000) have been reported in males compared with females. Such differences in the size of muscle and proportional fiber type area have been suggested to be attributed to sex differences in human skeletal muscle gene expression (using DNA microarrays) and sex-related hormonal differences (e.g., greater steroid hormone levels in males) (Liu et al., 2010; Maher et al., 2009; Roth et al., 2002; Welle et al., 2008). The greater muscle strength in males may, in turn, lead to greater joint stability (e.g., ankle) and thus better postural control (e.g., greater standing leg-reaching distance), as found by Erickson et al. (2012). Also, males may present with a shorter reaction time to generate a proper postural control action, given the reported negative relationship between muscle strength and reaction time (e.g., see Jiménez-García et al., 2021). This is supported by previously observed shorter response times from the onset of a visual stimulus until the onset of voluntarily moving the COG in males compared with females (Faraldo-García et al., 2011). However, this has only been sparsely studied at this time.

2.2.2. Sex differences in sensory processing and postural control

Sex differences have been found in sensory processing (e.g., vision and proprioception) in some environments. Males have shown greater visual acuity (sensitivity to fine detail and rapidly moving stimuli) and greater accuracy in pointing a far target compared with females (but the opposite is true for near target) (Abramov et al., 2012; Stancey & Turner, 2010; Velle, 1987). It has been suggested that such sex differences in sensory processing are due to sex differences in body and brain size and hormonal exposure (e.g., caused by the greater number of testosterone receptors in the cerebral cortex in males compared to females) (Baker & Cornelson, 2018; Vanston & Strother, 2017). In a few studies using oscillation of optic flow (e.g., see Koslucher et al., 2016), it was suggested that a relationship may exist between the sex differences in vision processing and postural control changes during the oscillation. However, how such sex differences in vision processing affect postural control in males and females is still unclear at this time.

In addition, sex differences in leg proprioception have been observed in a few studies. For example, a greater sense of joint position and movement of the leg (e.g., extension, flexion, and rotation in the knee and ankle joints) has been reported in young adult males compared with females (Muaidi, 2017; Nagai et al., 2012). Such sex differences have been suggested to be associated with a greater risk of musculoskeletal injuries of the leg (e.g., ACL ligament tear) in young female adults (or athletes) when performing stability-demanding tasks or sports (Caraffa et al., 1996; Cerulli et al., 2001; Sell et al., 2018). Given the significant role of proprioceptive information from the ankle and foot in controlling postural stability (see section 2.1.2), it would be interesting to determine the association between the extent of sex differences in leg proprioception and postural sway between males and females. As of now, only one study (Cug et al., 2016) has found no sex differences in both knee proprioception and dynamic stability during a leg-reaching task in both young adult athletes and sedentary young adults. The lack of sex effects may be due to similar anthropometric features (height and weight) reported between the sex groups in that study, as different anthropometric factors between males and females have been suggested to be a major contributor to sex differences in postural control (see below for details).

2.2.3. Sex differences in anthropometric features and postural control

Anthropometric variables (e.g., weight, height, foot features such as width, length, and arch area) have been found to be significantly correlated with postural sway during some tasks (Chiari et al., 2002; Ku et al., 2012). Of these variables, generally shorter height and lighter weight and a lower COM (caused by a wider pelvic base, greater valgus position of the legs, and proportionally lighter mass of the upper body) in females compared with males could be particularly beneficial for controlling standing posture (Era et al., 2006; Gribble et al., 2009; Paillard, 2012; Zeller et al., 2003). However, it has been reported that these anthropometric factors correlate differently with postural variables between males and females. For example, Glass and colleagues (2020) found that weight had a positive correlation with the standard deviation (SD) of AP COP sway displacement and mean ML COP velocity in females while height had a positive correlation with the SD in males. Kim and colleagues (2012) showed that both height and weight had a negative correlation with postural sway displacement in females (but not in males), despite there being no such difference in sway frequency between the two sex groups, suggesting sex differences in stability behavior. These findings indicate that anthropometric factors need to be controlled when determining sex differences in postural control in certain cases.

2.2.4. Effect of the menstrual cycle on postural control

The menstrual cycle, which is a sequence of natural hormonal changes in the female reproductive system (Richards, 2018), may become a confounding factor in determining sex differences in postural control as the hormonal changes have been suggested to affect leg proprioception (e.g., joint position sense) and neuromuscular function (e.g., muscle strength and coordination) (Aydoğ et al., 2005; Fridén et al., 2006; Hertel et al., 2006; Hu et al., 2020). This is supported by recent studies of young adults, which found variations in postural sway between the follicular and ovulation phases (Lee & Yim, 2016), and also a different ankle stiffening behavior and postural sway characteristics between ovulating females and males (Khowailed & Lee, 2021) during challenging static tasks. However, such hormonal changes were reported to have no effect on dynamic stability (e.g., leg-reaching distance, see Ericksen & Gribble, 2012). This contrasting finding suggests that the effects of the menstrual cycle on postural control could be task-dependent.

2.2.5. Stability measures and sex differences in postural control

Sex differences in postural control depend on the postural tasks studied and variables analyzed, as suggested by findings (Era et al., 2006; Kim et al., 2010). Era and colleagues, for example, found that young adult males had a lesser ML COP sway displacement compared to young adult females during normal standing with EO and EC, but the opposite was true during semi-tandem standing and no sex differences were found during tandem standing. The authors also found that the sex differences in AP COP sway displacement (males > females) were opposite to those in ML displacement (males < females) during the static tasks. These findings indicate that there are confounding factors to consider, such as the specific task and postural variables used, when studying sex differences in postural control.

Collectively, motor, sensory, and central processing systems are the key components in regulating standing stability. Sex differences in postural control can vary according to several factors, including neuromuscular and sensory function, anthropometric features, task and stability measures.

2.3. Muscle fatigue

In an individual, muscle fatigue can arise from repeated or sustained muscular exercise and activities of daily living. In laboratory-based studies, muscle fatigue is defined as any exercise-induced loss of ability to generate force or power within a muscle or muscle group (Bigland-Ritchie, Woods, & Bigland-Ritchie, 1984; Gandevia, 2001). In this thesis, muscle fatigue is exchangeable with the term 'neuromuscular fatigue'. More recently, the concept of muscle fatigue has been termed "performance fatigability" (in contrast with "perceived fatigability"), which has been used to describe the decline in objective measures of performance (e.g., the ability to generate muscle force or the time taken to reach task failure) over a certain period (Enoka & Duchateau, 2016; Kluger et al., 2013). For example, individuals (e.g., females) who present with less performance fatigability as compared with others (e.g., males), would need a longer time to reach the same level of muscle fatigue or have a greater reduction in MV(I)C torque during an exercise protocol with a fixed time limit. Muscle fatigue is dependent on the capacity of the CNS and PNS and the contractile function of a given muscle to sustain activity during the involved task (Enoka & Duchateau, 2016) (see Figure 2).

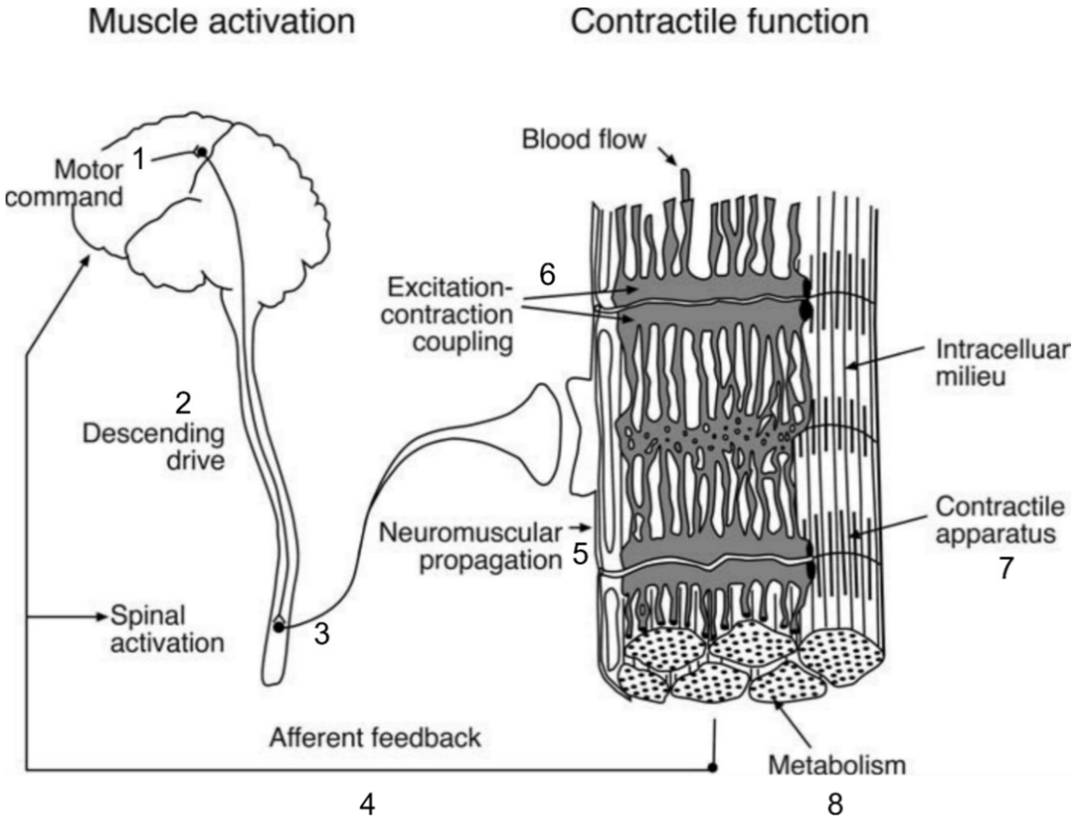

Figure 2. Mechanisms and sites of neuromuscular fatigue. Central fatigue can occur with alterations in 1) the activation of the brain (motor cortex), 2) the propagation of commands from the brain to the motor neurons, 3) the activation of the motor neuron axons, and 4) afferent feedback from the peripheral system within the muscle fiber. Peripheral fatigue could arise from changes in 5) the signal transmission across the neuromuscular junction between a motor neuron and a muscle fiber, 6 and 7) excitation-contraction coupling events (converting muscle membrane excitability through the T-tubule into muscle contraction performed by the sliding action of the actin and myosin cross-bridge), and 8) the metabolic energy supply. Reprinted with permission from (Enoka & Duchateau, 2016) and marked with numbers (1-8) on the reprinted figure.

In an attempt to organize and clarify the physiological mechanisms involved in performance fatigability, neuromuscular fatigue has been separated into two components, peripheral and central fatigue. Central fatigue is considered to be a progressive exercise-induced reduction in voluntary activation (VA) (Gandevia, 2001). A decrease in VA could arise from changes in the activation of the brain and motor neuron and the propagation of commands from the brain to motor neuron and may include afferent feedback from muscles. By contrast, peripheral fatigue is regarded as the loss of force caused by processes occurring at or distal to the neuromuscular junction (Gandevia, 2001). This is considered to be fatigue within the muscle itself, which is typically responsible for much of the reduction in force compared with central fatigue, which may be responsible for 20 to 25% of the decrease in force under some exercise conditions (Taylor et al., 2006).

The aforementioned performance fatigability and fatigue mechanisms can be different between males and females during some tasks (Hunter, 2014; Hunter, 2016b), which may lead to sex differences in postural control alterations with fatigue (Paillard, 2012). Therefore, the following sections describe sex differences in performance fatigability and related fatigue mechanisms. Then, postural control changes with fatigue and related sex differences are reviewed. But first, fatigue measurements generally used in previous studies are described.

2.3.1. Fatigue measurements

2.3.1.1. Central and peripheral fatigue measures

For central fatigue measures, VA is commonly measured by stimulating a peripheral (motor) nerve to a target muscle(s) when an individual performs an maximal voluntary isometric contraction (MVIC) of the muscle (Gandevia, 2001). A reduction in VA is reflected by an increase in the superimposed twitch torque generated by the stimulation during MVIC (Belanger & McComas, 1981; Merton, 1954), indicating insufficient recruitment or firing rate of motor units to produce optimal muscle torque at the moment of the stimulation (Herbert & Gandevia, 1999). Many studies examined such decrease in VA during and after exercise of various muscles or muscle groups (e.g., DF, knee extensors, and elbow flexors) in healthy young adults (Akagi et al., 2019; Albert et al., 2006; Kavanagh et al., 2020; Kent-Braun et al., 2002; Lee et al., 2017; Martin & Rattey, 2007; Russ & Kent-Braun, 2003; Yoon et al., 2007). Stimulation over the motor cortex, using transcranial magnetic stimulation (TMS), has also been used to determine the decline in VA from a supraspinal (cortical) level to a fatigued muscle (Hunter, Butler, et al., 2006; Taylor et al., 2000; Taylor et al., 2006; Vernillo et al., 2018). Such cortical stimulation, however, was considered to lack precision in evoking responses in target muscles, so it has been used in only a relatively limited number of studies (mainly studies involving elbow flexors) (Gandevia, 2001; Taylor et al., 2006). Also, central fatigue has been suggested to be associated with decreased EMG amplitude (integrated and rectified), which could reflect the decreased firing rate and recruitment of the motor neurons innervating fatigued muscle(s) (Davis, 2010).

By contrast, peripheral fatigue can be reflected by alterations in the twitch contractile properties of a fatigued muscle by electrically stimulating the peripheral nerve while the muscle is at rest. Such fatigue-induced alterations generally include reduced twitch peak torque (Taylor & Gandevia, 2008), increased twitch half-relaxation time (the time needed for twitch torque to decrease from its peak value to half of this value) (Boyas, Remaud, et al., 2013; Smith-Ryan et al., 2014), and decreased low frequency fatigue (LFF) index (ratio of low frequency twitch torque to high frequency twitch torque) (Vøllestad, 1997). These changes in twitch contractile properties involve metabolic inhibition of muscle contractile processes (e.g., reduced pH level within a fatigued muscle) (Kent-Braun, 1999), reduced Ca^{2+} release from the sarcoplasmic reticulum and a related reduction in the amount of Ca^{2+} binding to myofilaments (Keeton & Binder-Macleod, 2006; Vøllestad, 1997), and slowing of Ca^{2+} re-uptake by the sarcoplasmic reticulum and Ca^{2+} detachment from myofilaments (Allen et al., 2008; Neyroud et al., 2016). Peripheral fatigue may also be reflected by a decline in the ratio of muscle torque (or force) to EMG amplitude, possibly indicating decreased neuromuscular contractile efficacy (Milner-Brown & Lee, 1975). These central and peripheral neurophysiological processes can interact with perceived fatigue (or exertion) (Enoka et al., 2021; Enoka & Duchateau, 2016; Kluger et al., 2013).

2.3.1.2. Rating of perceived exertion (RPE)

The Borg RPE (or 6-20 Borg) and Category-Ratio (or CR10) scales were established and are commonly used to assess the level of perceived exertion (or fatigue) with respect to cardiovascular (e.g., augmented heart rate and breathing difficulty) and muscular (e.g., muscle exertion and pain) loads during physical activity (Borg, 1982; Williams, 2017). The 6-20 Borg scale and CR10 scale range from "6" (no exertion) to "20" (maximal exertion) and "0" (no exertion) to "10" (maximal exertion), respectively (Borg, 1982; Williams, 2017). The Borg scales have been validated to be estimators of the degree of muscle fatigue (or physical exertion) in previous studies. For example, an increased RPE value assessed with the CR10 scale has been correlated with a decreased MVIC (Whittaker et al., 2019) and increased EMG amplitude (muscle activation) (Cruz-Montecinos et al., 2019) during exercise progression. An increased RPE value estimated with the 6-20 Borg scale has also shown a significant correlation with increased heart rate during high-intensity or interval cycling (Fusco et al., 2020; Green et al., 2006). Interestingly, such changes in the RPE value may be associated to a greater extent with central fatigue mechanisms (e.g., the observation of a concomitant gradual reduction in cortical VA with an increase in RPE value during fatigue of elbow flexors, see Smith et al., 2007; Søgaard et al., 2006). However, it has been argued that the interaction between perceived fatigue and performance fatigability is not straightforward and needs to be clarified (Enoka & Duchateau, 2016; Kluger et al., 2013). Because the CR10 scale has been considered to be more suitable for evaluating subjective symptoms such as muscle exertion and pain compared to the 6-20 Borg scale (Borg, 1982; Williams, 2017), this thesis (for article 4) used a modified Borg CR-10 scale (Whittaker et al., 2019) to (indirectly) assess the level of ankle muscle fatigue.

2.3.2. Muscle fatigue and sex differences

It has been suggested that females are generally less fatigable compared to males (Hunter, 2014; Hunter, 2016). More specifically, young adult males have shown a greater reduction in muscle torque and a shorter time to task failure compared with young adult females during isometric and dynamic fatiguing tasks such as single-limb isometric contraction (e.g., elbow flexion and DF) (Dearth et al., 2010; Russ & Kent-Braun, 2003) and slow- to moderate-velocity contractions (e.g., knee flexion and extension and elbow flexion) (Pincivero, Gandaio, & Ito, 2003; Yoon, Doyel, Widule, & Hunter, 2015). This difference has been suggested to be mainly due to a greater oxidative metabolic capacity (Russ et al., 2005), a greater proportion of fatigue-resistant muscle fibers (type I) within skeletal muscles (Toft et al., 2003), lesser muscle mass and strength limiting blood flow within the muscles (Hunter & Enoka, 2001; Miller et al., 1993), and lesser central fatigue during fatiguing tasks (Russ & Kent-Braun, 2003) in females compared with males.

However, with regards to the differences in the contributions of central versus peripheral fatigue mechanisms between young adult males and females, inconsistent results have been found in the limited number of studies on the topic, even when observing greater performance fatigability in males than females. For example, some studies using isometric exercise protocols of leg extensors (Martin & Rattey, 2007) and of DF (Russ & Kent-Braun,

2003) found greater central fatigue (greater reductions in VA) during and at the end of the exercise protocol in males compared with females, while showing no significant sex differences in peripheral fatigue (similar decreases in resting twitch peak torque in both sex groups). By contrast, several studies using low to moderate isometric exercise protocols of the elbow flexors and/or knee extensors (Akagi et al., 2019; Albert et al., 2006; Hunter, Butler, et al., 2006; Kavanagh et al., 2020) found greater reductions in resting twitch peak torque and slower twitch relaxation following the exercise protocols in males compared with females, while not observing sex differences in central fatigue. Also, similar reductions in both VA and resting twitch peak torque between males and females following low- to high-intensity isometric or dynamic exercise have been shown, even with shorter time to task failure in males compared to females (e.g., see Lee et al., 2017; Yoon et al., 2007). These contrasting findings emphasize the need for further evidence regarding such sex differences, particularly for PF which have not yet been studied extensively (Hunter, 2016b).

Sex differences in performance fatigability and related mechanisms could be dependent on task specificity and other confounding factors, such as different phases of the menstrual cycle among females and unequal sex data (favoring males) in previous studies.

2.3.2.1. Task-dependent sex differences in performance fatigability

Different sites within the neuromuscular system can be affected depending on the demands of the fatiguing task (Enoka & Stuart, 1992), which could differ for males and females (Hunter, 2014; Hunter, 2009, 2016b). Task-related factors that could affect sex differences in performance fatigability include contraction type, contraction velocity, target muscle(s), and exercise intensity.

Contraction type: The type of muscle contraction is partially accountable for the sex differences in performance fatigability. Females are typically less fatigable compared to males when performing a low to moderate isometric fatiguing exercise of similar intensity, but such sex difference has been less clear for dynamic fatiguing exercise (shortening and lengthening contractions) in a limited number of studies, as reported in review papers (Hunter, 2014; Hunter, 2016b). Many previous studies of sustained and/or intermittent isometric fatiguing exercise, for example, have reported that females show a longer time to task failure or lesser reductions in muscle torque during and at the end of a fatiguing exercise of different muscle groups such as finger flexors and forearm (Hunter et al., 2009; Hunter, Schletty, et al., 2006), elbow flexors (Hunter & Enoka, 2001; Hunter et al., 2002; Kavanagh et al., 2020), adductor pollicis (Fulco et al., 1999), back extensors (Clark et al., 2003), DF (Russ & Kent-Braun, 2003), and knee extensors (Clark et al., 2003; Maughan et al., 1986).

Regarding the type of isometric contraction (sustained vs. intermittent), different fatigue mechanisms could be responsible for sex differences in performance fatigability. It has been reported that the sex differences during sustained isometric exercise with low to moderate intensity could be mainly due to the greater muscle mass and/or strength (which would limit blood flow and lead to the accumulation of metabolites within muscle fibers) in males compared with females (Hunter & Enoka, 2001; Kavanagh et al., 2020; Miller et al., 1993). This is supported by the observation of no sex differences in performance fatigability during sustained isometric exercise when matching the strength of young adult participants (e.g., for elbow flexors, see Hunter et al., 2004a). By contrast, a difference in muscle mass and strength between males and females may not be a major contributor to sex differences in performance fatigability produced by intermittent isometric exercise. Hunter and colleagues (2004b) showed greater fatigability in males compared with females during a moderate intermittent isometric exercise of elbow flexors, even when matching muscle strength between sexes. Sex differences in the performance of intermittent exercises may rather involve differences in oxidative metabolism within fatigued muscles (which could lead to associated differences in VA) between males and females (e.g., see Russ & Kent-Braun, 2003), although this is still uncertain (e.g., reports of no sex differences in VA, see Kavanagh et al., 2020).

Dynamic fatiguing exercise, which generates muscle force with target muscles shortening (concentric contraction) or elongating (eccentric contraction), has led to contradictory findings in a limited number of studies. For example, some studies showed a lesser reduction in peak torque or a greater number of repetitions during repeated submaximal concentric contractions of PF (HeBert-Losier & Holmberg, 2014), elbow flexors (Maughan et al., 1986), and knee extensor and flexors (Pincivero et al., 2003) in females compared with males. A few studies, however, showed no sex differences in fatigability during and/or at the end of concentric contractions of hip and lumbar extensors (Clark et al., 2003) and elbow flexors (Senefeld et al., 2013). Also, for eccentric fatiguing exercises, a relatively limited number of studies have reported not only no sex differences in muscle torque or power decrease (Hubal & Clarkson, 2009; Lee et al., 2017; Power et al., 2010; Rinard et al., 2000), but also greater fatigue in females (Power et al., 2013; Sewright et al., 2008). These findings could be related to exercise-induced soreness (Semmler et al., 2013) which has a threshold reported to be lower in females compared with males (Fillingim et al., 2009; Racine et al., 2012), although the association between muscle fatigue and pain has yet to be determined. These contradictory findings about dynamic contraction exercise could be partly due to contraction velocity (see below).

Contraction velocity: The extent of sex differences in performance fatigability may be dependent on the velocity of concentric fatiguing exercise. Yoon and colleagues (2015) found that a slow-velocity exercise of elbow flexors led to a shorter time to failure of concentric contraction of elbow flexors with a fixed time limit in males compared with females. This was accompanied by slower muscle relaxation in males, suggesting that muscle contractile mechanisms (e.g., excitation-contraction coupling) could be accountable for such sex difference in a low-velocity concentric exercise. By contrast, when performing high-velocity contractions of both elbow flexors and knee extensors, a similar reduction in muscle power between males and females was found (Senefeld et al., 2013). Regarding eccentric exercise, sex differences in velocity-dependent fatigability has yet to be studied.

Target muscle(s) fatigued: Sex differences in performance fatigability could be reliant on the specific muscle(s) studied, possibly due to different physiological and structural characteristics across muscles (e.g., muscle metabolism, fiber-type proportional area, muscle mass, etc.), as reported in two recent reviews (Hunter, 2014; Hunter, 2016b), where the extent of sex differences in performance fatigability is summarized from a total of 62 studies (46 isometric and 16 dynamic fatiguing exercises). Most studies of isometric exercise showed lesser performance fatigability of various muscles (neck, trunk, and upper and low limbs) in females compared to males. Of these muscles, the reviews showed that the ankle muscles (PF and DF) generally showed a lesser extent of sex differences in fatigability as compared with other muscle groups. For example, Avin and colleagues (2010) found a lesser extent of sex differences in the time to failure during sustained isometric exercise of DF (female > males: 9%) compared with elbow flexors (40 %). Such lesser sex differences in performance fatigability of PF and DF could be due to somewhat lesser sex differences in the relative area of type I (fatigue-resistant) muscle fibers of the ankle compared with other muscle groups (Coggan et al., 1992; Larsson et al., 2006; Miller et al., 1993; Porter et al., 2002; Staron et al., 2000), which would contribute to the relatively similar fatigability between males and females directly and through muscle metabolism (Hunter, 2016, 2014).

Exercise intensity: For sustained isometric exercise, the extent of sex differences in performance fatigability tends to be greater when performing the exercise at low intensity (e.g., 20% MVIC) compared with moderate- to high-intensity exercise (e.g., 50% to 80%) as observed for elbow flexors (Yoon et al., 2007) and knee extensors (Maughan et al., 1986). This may be explained by greater sex differences in muscle perfusion (females > males) during such low-intensity exercise compared to moderate- to high-intensity exercise (Hunter, 2014; Hunter, 2016b). Interestingly, Yoon and colleagues (2007) examined similar peripheral and central fatigue between males and females regardless of exercise intensity (20% vs. 80% MVIC), although observing sex differences in performance fatigability. This suggests a complex relationship between performance fatigability and fatigue mechanisms (Enoka & Duchateau, 2016; Kluger et al., 2013). By contrast, Hunter (2014) did not find any relationship between sex differences in fatigability and exercise intensity across 16 studies on dynamic exercise, although one study (Maughan et al., 1986) found such a relationship when performing moderate- to high-intensity concentric exercise.

2.3.2.2. Confounding factors to sex differences in performance fatigability

Other than task specificity, factors such as the menstrual cycle and sex bias in previous fatigue research may have a confounding effect on reported sex differences in performance fatigability.

Menstrual cycle: The phases of the menstrual cycle could have an impact on muscle contractile function and exercise performance in females (Janse De Jonge, 2003). This might affect sex differences in performance fatigability, but this has been contradictory in previous studies. For example, slight but significant changes in both muscle strength and fatigue have been observed throughout the menstrual phases of young adult females due to varying steroid hormonal levels across the phases (e.g., changes in handgrip strength and fatigue rate, see Pallavi et al., 2017). By contrast, such change across the menstrual cycle did not affect exercise-induced muscle fatigue in several studies, showing no alterations in the time to failure of sustained isometric contraction of elbow flexors throughout the different phases of the menstrual cycle (Hunter, Critchlow, & Enoka, 2004; Keller et al., 2011). These inconsistent findings suggest that the menstrual cycle may not be a major confounding factor to sex differences in performance fatigability, and, in fact, it has been suggested that general physiological differences between males and females have a greater impact on sex differences in performance fatigability than the effects of the menstrual cycle (Hunter, 2016b).

Sex-related research bias: Previous findings of sex differences in fatigability may be somewhat biased due to the unequal number of tested males versus females, as reported in Hunter (2016b). More specifically, Hunter reported the number of male versus female participants in 200 studies of fatigability from the last four decades (1972 to 2015; see their Figure 1) and found a smaller number of tested females (~60%) compared to males across the studies (Hunter (2016b). The author suggested that this disproportionate testing between the sex groups is likely to hide the true extent of sex differences in fatigability. However, the author reported that the low ratio of females to males across those studies is mainly due to numerous studies involving only males. Because most studies of sex and fatigability cited in this thesis compared fatigability between similar numbers of males and females, a potential research bias related to unequal data between the sex groups does not apply.

In summary, previous findings indicate that young adult females typically present with lesser performance fatigability than young adult males when performing low to moderate isometric exercises, but this is less clear for dynamic fatiguing exercises.

2.4. Muscle fatigue and postural control

Local muscular fatigue leads to decrements in force production capacity (Papa et al., 2015) and modifications in both the peripheral proprioceptive system and central processing of sensory inputs (Enoka et al., 2011). These changes can cause clumsiness and diminished precision of motor and postural control (Paillard, 2012; Tripp et al., 2007). Postural control changes (or strategy) with fatigue can depend on exercise demands (e.g., the extent and location of muscle fatigue) and postural task (e.g., static vs. dynamic task).

2.4.1. Extent of fatigue and postural control

Many studies observing fatigue-induced postural control alterations have observed a reduction in muscle force production capacity produced by exercise protocols using different types of pre-established cutoffs such as muscle force and torque or joint angle (% of maximum value) (Bisson et al., 2011; Mademli et al., 2008; Paillard et al., 2014; Sant'Anna do Carmo Aprigio et al., 2020), sustained contraction duration (Caron, 2004; Davidson et al., 2009), dynamic contraction velocity (Gimmon et al., 2011; Vuillerme & Boisgontier, 2010), and the maximum number of repetitions in a pre-determined set or sets (e.g., squat and tiptoes) (Bannon et al., 2018; Bisson et al., 2010; Bryanton & Bilodeau, 2016; Laudani et al., 2009; Walsh et al., 2011). Different exercise protocols can lead to varying levels of muscle fatigue as discussed in a review study by Paillard (2012). In this review, the author states that most fatigue is likely to cause declines in postural stability when MVC reduction is greater than or equal to 25-30%, regardless of the location of fatigue. Nevertheless, a 6% loss of MVIC following prolonged exercise (30 min) of knee extensors induced an increase in mean COP velocity, suggesting a potential contribution of central descending drive decline to the postural control change rather than the loss of strength (Paillard et al., 2010). These findings indicate that not only the deterioration of muscle contractility but also the degradation of neuromuscular control could be accountable for postural control disturbance with muscle fatigue, as reported in a review (Paillard et al., 2012). However, the effect of the extent of muscle fatigue on postural control is still unclear and needs to be studied further. For example, Boyas and colleagues (2013) showed similar alterations in COP sway variables regardless of different extents of muscle fatigue (25%, 50%, and 75% loss of MVIC of PF). By contrast, greater COP sway velocity with relatively greater fatigue (70% loss of MVC from alternating PF and DF contractions) compared to lesser fatigue (50% loss of MVC) has been observed (Harkins et al., 2005).

In addition, the level of perceived exertion can be an alternative for indirectly assessing the degree of exercise-induced fatigue (previously mentioned in section 2.3.1) in the context of postural control. Within the literature pertaining to the effect of exercise-induced fatigue on postural control, many studies assessed RPE values using the 6-20 and CR10 Borg scales, with typical values ranging from 15.5 to 17.2 (Adlerton et al., 2003; Adlerton & Moritz, 2001; Paillard et al., 2014) and 5.4 to 8.7 (Adlerton et al., 2003; Adlerton & Moritz, 2001; Bannon et al., 2018; Bryanton & Bilodeau, 2016; Gimmon et al., 2011; Pinsault & Vuillerme, 2008; Sant'Anna do Carmo Aprigio et al., 2020; Vuillerme et al., 2009; Vuillerme & Boisgontier,

2010) following fatiguing exercise protocols of the ankle, knee, and hip muscles until task failure, indicating "hard" or "strong" to "extremely hard" or "almost maximal" (Borg, 1982). This range of RPE values immediately following or at the end of exercise indicates that a moderate to high level of local muscle fatigue has typically been used to affect postural control in past studies. However, this has not been studied systematically. A systematic summary of RPE values documented in studies of muscle fatigue and postural control would provide useful information, given the potential relationship between fatigue-induced instability and musculoskeletal injuries during stability-demanding tasks and sports in young adults (Bannon et al., 2018; Sell et al., 2018).

2.4.2. Localization of fatigue and postural control

The fatigue of postural muscles (e.g., neck, trunk, thigh, shank, and foot) can lead to changes in postural control. In particular, many studies have shown the effect of fatiguing PF and/or DF on AP/ML sway in healthy young adults (Bisson et al., 2010, 2011, 2014; Boyas et al., 2011; Sant'Anna do Carmo Aprigio et al., 2020). The findings are not surprising, given the fact that ankle muscles play an important role in controlling upright standing (Loram & Lakie, 2002). During one-leg standing, however, fatigue of the hip and/or knee muscles was shown to have a greater effect than fatigue of ankle muscles on frontal plane postural control (Bisson et al., 2011; Gribble & Hertel, 2004b, 2004a). This may be due to the compensation of the proximal muscles, mainly for frontal plane postural stability when ankle muscles are fatigued (Paillard, 2012).

2.4.3. Compensatory strategies

Postural strategies used with fatigue can be dependent on the type of postural task. In the context of local muscle fatigue, several compensatory strategies for maintaining postural stability have been considered, as detailed in a review study (Paillard, 2012). One of the common strategies assumes that fatigue of distal muscles evokes the recruitment of proximal muscles to maintain postural stability (e.g., hip strategy). This adaptation is supported by the work of Gribble & Hertel (2004a, 2004b), where no effect of ankle muscle fatigue on postural stability during one-leg standing was observed, suggesting compensation by hip muscles for fatigued ankle muscles. Other possible strategies used with fatigue, such as a stiffening behavior, sensory reweighting, and anticipatory postural adjustment (APA), could also be used to maintain postural stability in different task conditions. Again, the preference for using these compensation strategies with fatigue is different with the type of postural task (e.g., static vs. dynamic).

2.4.3.1. Compensation strategy for static postural control

In the context of static stability, several studies have determined the effect of local muscle fatigue, for example, observing changes in COP variables (e.g., increased COP sway amplitude, velocity, and frequencies) during quiet standing on either one leg or both legs, and with eyes either opened or closed (Bisson et al., 2010, 2011; Chaubet et al., 2012). These reported changes may be the consequence of a stiffening behavior at the ankle. Such stiffening behavior could be caused by alterations in the sensitivity of muscle spindles and related sensory reweighting, leading to reorganization of multi-joint coordination and altered stability control via the CNS (Paillard, 2012).

A series of two studies (Caron, 2003, 2004), for example, showed increases in COP displacements at high frequencies in the AP direction during quiet standing following a fatiguing exercise of PF in young adults. At the same time, no changes in COG displacements were reported in the corresponding direction, suggesting that increased muscle stiffness was used for postural stability. Such an increase in stiffness could explain the increased COP sway velocity observed immediately following a fatiguing exercise of the same muscle group during one-leg standing (Boyas, Hajj, et al., 2013; Boyas, McGown, et al., 2013; Boyas, Remaud, et al., 2013). Such COP changes, however, need to be carefully considered in conjunction with other postural variables (e.g., EMG of ankle muscles and/or proximal joint movement) before inferring ankle stiffness modulation, as it was reported that COP sway velocity is highly correlated with COM sway acceleration (Masani et al., 2014) (potentially reflecting ankle corrective action regardless of stiffness), and ankle fatigue increases hip movements as well as sway velocity (Boyas, McGown, et al., 2013).

2.4.3.2. Compensation strategies for dynamic postural control

Dynamic tasks are typically categorized into perturbed stability and voluntary movements (Papa et al., 2015; Sell, 2012). The former mainly involves reactive postural control (feedback control), which accompanies actions of sensory and motor systems in response to an external perturbation (Shumway-Cook & Woollacott, 2012). By contrast, the latter involves anticipatory postural adjustments (APAs), which utilize feedforward control before the action of the prime movers (Bouisset & Zattara, 1981), followed by feedback control in response to the movement to ensure stability.

The stiffening behavior may have negative consequences for dynamic stability, different from its likely positive (stabilizing) effect on static stance, as described in the previous section. This could be due to the restriction of efficient movements of the lower limb (Khanmohammadi et al., 2016; Young & Mark Williams, 2015). This is supported by the findings of Davidson and colleagues (2009), who observed a fatigue-related decrease in time to peak COP velocity following a perturbation (impact on the chest or back), which they explained as being due to increased muscle stiffness. At the same time, they observed slower recovery of the COM following the perturbation, which suggests that a fatigue-induced stiffening behavior reduces the ability to recover postural stability. Granacher and colleagues (2010), however, suggested that the observed stiffening behavior of the ankle compensated (stabilizing effect) for the fatigued ankle muscles during perturbed walking. These results indicate that the stiffening behavior may play a different role as a compensatory strategy for the control of postural stability between dynamic tasks.

In addition to the stiffening behavior, acute muscle fatigue can lead to changes in re-weighing sensory information during perturbed standing. Pinsault & Vuillerme (2008) observed an increased reliance on vestibular and neck proprioceptive information following fatigue of ankle muscles during a standing task performed under different sensory conditions. This is also supported by the findings of previous studies (Ledin et al., 2004; Vuillerme et al., 2002), where it was observed that vibration of fatigued PF did not significantly produce a further increase in postural sway during upright standing. These findings suggest a lesser reliance on proprioception of the fatigued ankle muscles for regulating postural control during standing when perturbed with muscle vibration.

Lastly, anticipatory postural adjustments (APAs) are observed during upright standing perturbed with voluntary focal movements (Paillard, 2012). A series of studies (Strang et al., 2009; Strang & Berg, 2007) reported that fatigue of thigh and lumbar muscles led to earlier onsets of APAs in fatigued and non-fatigued muscles, as compared to those in a non-fatigued state, during upright standing perturbed with quick arm(s) raises. At the same time, no decline in postural stability was found following fatigue of the postural muscles. These findings suggested that early APA onsets may counteract decreases in force production capacity of fatigued muscles to maintain postural stability. Some of these postural control changes or strategies with fatigue may be different between young adult males and females.

2.4.4. Sex differences in postural control alterations with fatigue

Only a limited number of studies have investigated sex differences in postural control changes with fatigue of the leg and trunk muscles. For example, a greater reduction in the distance of a standing leg-reaching task (Gribble et al., 2009) and a greater increase in AP/ML COP sway displacement during one-leg standing (Springer & Pincivero, 2009) in males compared to females have been found. Bannon and colleagues (2018) also found increased COP velocity during one-leg standing only for males (not for females) following the repetitive lifting of a weighted box. These findings could suggest greater postural control changes or impairments with fatigue in males compared to females. It was suggested that such sex differences may be due to the aforementioned lesser fatigability and advantages related to anthropometric factors in females compared with males (Paillard, 2012).

Given the possible contribution of proximal joints (e.g., hip and trunk) to static and dynamic (perturbed) stability (Aramaki et al., 2001; Creath et al., 2005; Zhang et al., 2007), the aforementioned results could also suggest the use of different postural control strategies with fatigue between males and females, for example, with males preferentially relying more on ankle control, but females relying more on proximal joint control. In line with this, males have been shown to present with increased ankle torque variability during feet-together standing with EC following a fatiguing exercise of PF, but females did not (Wojcik et al., 2011). Also, females showed increased trunk acceleration (induced by hip movement) accompanied with decreased COP velocity (possibly reduced ankle control or stiffness) during one-leg standing following a fatiguing exercise of PF, although males were not included in this experiment (Adlerton et al., 2003). However, Wojcik and colleagues (2011) also observed an increase in ankle torque variability in females (but not in males) with fatigue of other muscles (shoulder and lumbar muscles), and several other studies also found no sex differences in static or dynamic stability (assessing COP sway or balance score) with fatigue of PF (Boyas et al., 2019; Nelson & Johnson, 1973) and of hip abductors (McMullen et al., 2011).

These contrasting findings in a limited number of studies indicate the need for further systematic observations regarding sex differences in fatigue-induced postural control changes. Comparison of the duration of postural control disturbance with fatigue between males and females would also be interesting, given the previously observed longer recovery from muscle fatigue following sustained isometric exercise in males compared with females (e.g., see Albert et al., 2006; Martin & Rattey, 2007).

As previously mentioned, decreased postural control with muscle fatigue could be accompanied by a reduced contribution of proprioceptive inputs onto motor neurons during some tasks. This can be indirectly assessed through the H-reflex.

2.5. Hoffman (H) reflex

The Hoffmann reflex (H-reflex) was originally described by a German physician, Paul Hoffmann, in 1910. The H-reflex, which bypasses muscle spindles, is an electrically evoked response analogous to the stretch reflex (Palmieri et al., 2004; Zehr, 2002). The H-reflex is considered an index of the efficacy of the transmission between muscle spindle afferents (Ia afferents) and alpha motor neurons (spinal pathway) (Baudry, 2016). The H-reflex can be modulated by posture (Baudry, 2016; Chen & Zhou, 2011; Henry & Baudry, 2019) and muscle fatigue (Enoka et al., 2011; Taylor, Amann, Duchateau, Meeusen, & Rice, 2016). H-reflex variations due to sex, however, are still contradictory and have been observed in only a limited number of studies at this time. Before reviewing these SOL H-reflex modulations, the H-reflex measurement will be first described.

2.5.1. Soleus (SOL) H-reflex measurement

In many studies, the measurement of the H-reflex has been focused on the SOL (Tucker et al., 2005), particularly in studies concerned with postural stability (Baudry, 2016; Chen & Zhou, 2011; Henry & Baudry, 2019; Zehr, 2002).

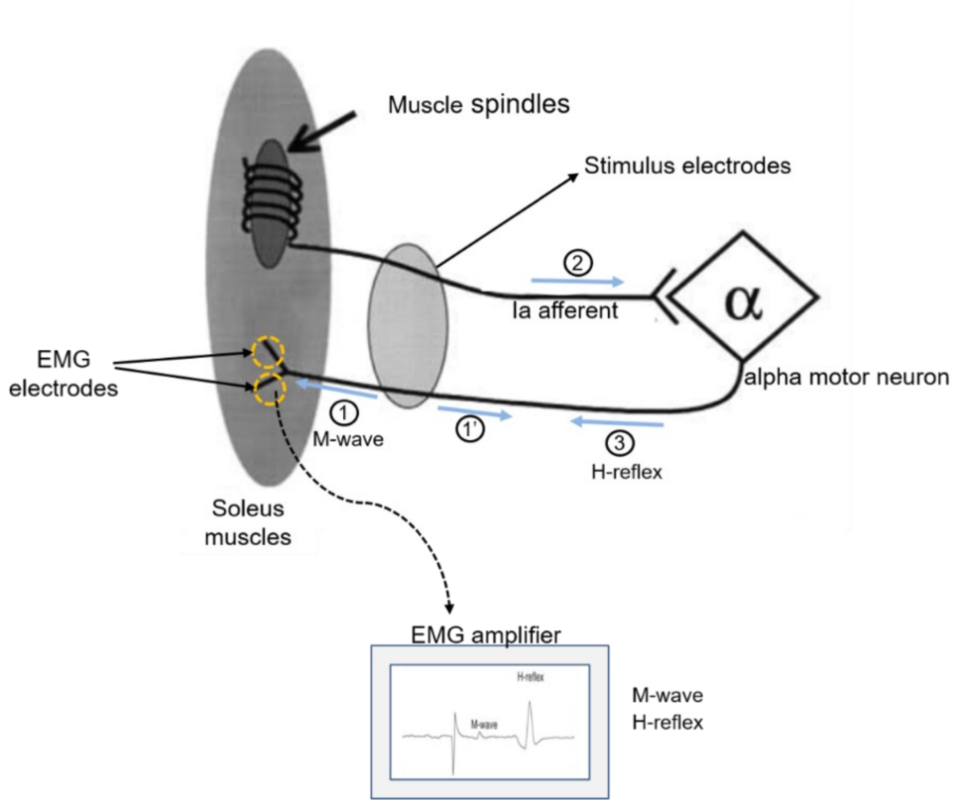

Figure 3. Measurement and pathway of the soleus Hoffmann (H) reflex and compound muscle action potential (M-wave). Modified from Zehr (2002).

For the measurement of the SOL H-reflex (see Figure 3 above), the response is initially recruited through activation of Ia afferent fibers (response 2) by progressively increasing the strength of an electrical stimulus imposed on the posterior tibial nerve. The signal from activated Ia afferents is relayed (mainly) monosynaptically to alpha motoneurons and activates such motoneurons. This then leads to the activation and contraction of SOL muscle fibers (response 3), which is recognized as the H-reflex recorded by an EMG system. A stronger stimulus intensity eventually evokes action potentials directly in axons of alpha motor neurons (response 1), which propagates distally and can be recorded at the muscle level as the M-wave. At the same time, other action potentials travel upward toward the spinal cord (response 1') and collide with the H-reflex (response 3), thereby decreasing its amplitude. The systematic documentation of the modulation of both the H-reflex and M-wave amplitude with increasing stimulus intensity constitutes both responses' recruitment curves, which can help determine the appropriate level of stimulus amplitude to evoke an optimal SOL H-reflex.

In order to measure an optimal SOL H-reflex, several recommendations have been offered, which include factors associated with: 1) the electrical stimulus, 2) the recording electrodes, and 3) the normalization procedure. First, the amplitude of the H-reflex can vary depending on the placement of the stimulating electrodes, stimulus-pulse duration, and stimulus interval (Tucker et al., 2005). The stimulus electrodes can be placed using either unipolar or bipolar stimulation configurations (Chen & Zhou, 2011; Tucker et al., 2005). For the unipolar configuration, the cathode is placed on the tibial nerve and the anode just above the patella, whereas for the bipolar configuration, a stimulating electrode with the cathode and anode (a few centimeters apart) is placed longitudinally along the length of the tibial nerve in the popliteal fossa. The optimal placement for the stimulating electrode has not been clearly determined. Palmieri and colleagues (2004), however, demonstrated that the bipolar configuration should be used when stimulating nerves that are located in a small area (e.g., the tibial nerve innervating the SOL) in order to avoid affecting surrounding nerves.

Different pulse durations (0.05, 0.2, 0.5, and 1.0 ms) have been used to elicit the H-reflex (Chen & Zhou, 2011), possibly leading to some of the variability observed in SOL H-reflex amplitudes (Tucker et al., 2005). Lagerquist and Collins (2008), however, observed no significant differences among SOL H-reflex amplitudes evoked by stimuli with different durations when the amplitudes were normalized to M-max. Lastly, a 2-10 s interval between stimuli for evoking SOL H-reflex has been recommended to prevent post-activation depression when the test muscle is both at rest and voluntarily contracting (Tucker et al., 2005; Zehr, 2002).

In addition to stimulus characteristics, the configuration and placement of recording electrodes can lead to variability in the SOL H-reflex. Two bipolar recording electrodes, although a single monopolar recording electrode configuration was suggested to be superior to the bipolar configuration (Gerilovsky et al., 1989), are commonly used to record the H-reflex (Pierrot-Deseilligny & Mazevet, 2000), due to reductions in common noise in the EMG signals (Tucker et al., 2005). Also, it is recommended that the bipolar electrodes be placed below the SOL muscles' motor point to reduce the probability of signal cancelation (Tucker et al., 2005).

Furthermore, two H-reflex normalization procedures have been strongly recommended to avoid either time- or movement-dependent variations (Chen & Zhou, 2011; Tucker et al., 2005; Zehr, 2002). The first one is to normalize a given submaximal H-reflex amplitude (evoked in the up-sloping portion of a full SOL H-reflex recruitment curve) to the M-max amplitude (Palmieri et al., 2004). The authors (Palmieri et al., 2004) suggested that this normalization method is useful in both clinical and research contexts that require short intervals for the H-reflex measure by using an initially fixed stimulus during an entire protocol.

Another common H-reflex measurement procedure is to normalize the maximal H-reflex (H-max) amplitude to M-max amplitude (Palmieri et al., 2004; Tucker et al., 2005; Zehr, 2002). Although this method has also been commonly used, it has some limitations. The H-max amplitude is considered to be highly variable (Palmieri et al., 2004) and also less susceptible to facilitation and inhibition under a given intervention condition (Crone et al., 1990). Also, this method could be time-consuming due to the need for obtaining the H-reflex recruitment curve at every H-reflex measure interval (Palmieri et al., 2004). These limitations can suggest that this method is not optimal for fatigue studies which require short intervals for repeated H-reflex measures.

In addition to these normalization procedures, it has been recommended that an evoked H-reflex be accompanied by a small reference M-wave (% of M-max) in order to ensure constant stimulus intensity (Tucker et al., 2005; Zehr, 2002). During postural tasks, the value of small M-waves observed in previous studies has typically been shown to be less than 8% of M-max: for example, 3 to 7% (Miranda et al., 2019), 4 to 8% (Masu & Muramatsu, 2015), and below 2.5% (Johannsson et al., 2019). Miranda and colleagues also accepted only the H-reflex data that include 2% variation in small M-wave amplitudes (% M-max) obtained from each participant (intra-subject; e.g., 1-3%, 3-5%, or 5-7%).

2.5.2. Soleus (SOL) H-reflex modulation

SOL H-reflex modulation can occur with different types of postural task and muscle fatigue, but modulation by sex is contradictory in a limited number of studies. Regarding the type of task, a challenging postural task can lead to depression in the H-reflex amplitude (Chen

& Zhou, 2011; Zehr, 2002), which may be linked to the degree of postural instability (Earles et al., 2000). Examples of the types of challenging task showing depression in H-reflex amplitude in previous studies (observing young adults) include: standing on foam and/or reduced BOS (Alizadehsaravi et al., 2020; Earles et al., 2000), standing on a fixed or movable platform with an interrupted visual cue (Day et al., 2017; Taube et al., 2008), and standing following a fatiguing exercise (repeated tiptoes) (Laudani et al., 2009), compared with control tasks (e.g., normal standing on a firm and flat surface). This depression with increased task difficulty is suggested to reflect an increase in presynaptic inhibition (McIlroy et al., 2003), which may play a positive role in preventing overload of the afferent response for optimal postural adjustments (Chalmers & Knutzen, 2002; Chen & Zhou, 2011).

The degree of such H-reflex modulations may depend on the position of the COP in the AP direction (i.e., forward vs. backward leaning). This is supported by a previous study (Tokuno et al., 2007) showing an increase (12%) in the SOL H-reflex amplitude (the ratio of H-max to M-max) evoked at the moment when the COP was shifting forward (forward lean) during quiet standing, as compared to when the COP was shifting backward (backward lean). However, the relatively small AP sway occurring during normal standing may not have a major impact on the relatively greater H-reflex modulations resulting from large AP postural movements elicited voluntarily or with an external perturbation. This is supported by a recent study (Miranda et al., 2019), which observed a much greater increase (~310 %) in the SOL H-reflex amplitude during standing on a forward-tilting platform (as compared to before the onset of the tilting) than the former (12%) from intrinsic forward leaning during quiet standing (Tokuno et al., 2007).

Local muscle fatigue has been described as causing a decrease in the amplitude of the H-reflex, potentially due to decreased muscle spindle firing and reduced efficacy of Ia afferent inputs to facilitate motoneurons, as discussed in review studies (Enoka et al., 2011; Taylor, Amann, Duchateau, Meeusen, & Rice, 2016). However, SOL H-reflex modulation with fatigue of the PF has shown variable results among several previous studies, for example: no change (Cresswell & Löscher, 2000; Stutzig & Siebert, 2017), a reduction (Grosprêtre et al., 2019; Walton et al., 2002), and an increase (Rupp et al., 2010) following and/or during submaximal sustained contraction(s). These variable results may be due to different experimental conditions, including exercise intensity, the number of electrical stimuli, and the duration of each experimental trial (Chen & Zhou, 2011). Fatigue-related H-reflex modulation may also depend on the type of exercise (e.g., dynamic elastic band exercise vs. isometric exercise of PF, see Grospretre et al., 2019). With regards to local muscle fatigue and postural control, only two studies have been found at this time, and both show a fatigue-induced SOL H-reflex depression during quiet standing (Laudani et al., 2009) and unilateral perturbed standing in healthy young adults (Ritzmann et al., 2016). Laudani and colleagues (2009) however, found that the SOL H-reflex responses varied (increased or decreased) among participants. Further observations are thus needed to help our understanding of the effects of muscle fatigue on SOL H-reflex, especially in the context of postural control.

Lastly, SOL H-reflex modulations according to sex are contradictory in the small number of studies currently available. Mendonca and colleagues (2020) showed a greater H-reflex amplitude (normalized to M-max) during low-level contraction (10% MVIC) of PF in a sitting position for young adult males compared to females. Similar sex differences were reported in biathlon athletes (Dornowski et al., 2017). It was suggested that this sex difference may be due to a greater level of ankle stiffening behavior (Mendonca et al., 2020) and the lesser muscle mass of the legs (Dornowski et al., 2017) in females compared with males. By contrast, one study found that females showed a greater H-reflex amplitude than males in young adults when both feet are in contact with the ground during gait (Cheng et al., 2007), potentially due to a greater increase in post-synaptic recurrent inhibition of SOL activation with fatigue of PF in males compared to females (Johnson et al., 2012). However, in the context of muscle fatigue and standing posture, no evidence for H-reflex modulation by sex has been found at this time.

Altogether, the condition and placement of electrodes (for electrical stimulation and recording) and the H-reflex normalization procedure should be carefully considered when measuring an SOL H-reflex. SOL H-reflex modulations have been reported based on the type of postural task and muscle fatigue, but H-reflex modulation according to sex has yet to be studied at this time, especially in the context of muscle fatigue and postural control. Such sex-related observation could provide interesting information on the role of proprioception and how it may vary between males and females.

2.6. Summary

The review of literature presented has shown sex differences in 1) performance fatigability and (central and peripheral) fatigue mechanisms, as well as in 2) the effects of muscle fatigue on standing postural control and spinal proprioceptive inputs at the ankle (SOL H-reflex). Females have typically been shown to be less fatigable than males during low to moderate isometric exercise regardless of fatigued muscles. However, sex differences in fatigue mechanisms and related postural control changes (e.g., in COP sway and ankle stiffness) have only been investigated in a limited number of studies and results are contradictory, particularly regarding fatigue of ankle muscles. In the context of postural control and muscle fatigue, a sex difference in SOL H-reflex has not been studied to date. Therefore, this thesis aims at addressing these issues, and the overall goal and objectives are stated below.

Objectives, hypotheses, and main results of the thesis

The overall goal of this thesis was to determine whether fatigue mechanisms of PF are different between young adult males and females and whether ankle muscle fatigue differently affects postural control and spinal motor neuron activations (SOL H-reflex) between the sex groups. Based on this goal, this thesis includes three experimental studies (articles 2-4). This thesis also includes a scoping review (article 1) that systematically summarized RPE values documented in studies observing a significant effect of muscle fatigue on postural control, because the assessment of muscle fatigue level (leading to instability) may be needed in the context of stability-demanding sports/tasks.

In article 1, the main aim of this scoping review was to map maximal RPE values assessed in studies that found significant effects of exercise-induced muscle fatigue on postural control in healthy adults, according to the type of exercise and different healthy populations. Secondary aims were to summarize the preference/purpose for the use of each of the two Borg scales (6-20 Borg and CR10) in the included studies, and also to determine whether any general associations could be found between fatigue-induced RPE values and postural control changes across the included studies.

In article 2, the main aim was to determine sex differences in central and peripheral fatigue of PF during a sustained isometric exercise in healthy young adults. It was hypothesized that males would show greater performance fatigability compared with females, and such fatigability differences would be associated with sex differences in central (VA) and peripheral (twitch contractile properties) fatigue. We, however, found only minor sex differences in central and peripheral fatigue variables, which could be explained by a similar performance fatigability (reduced muscle torques and time to task failure) between males and females.

In article 3, the main aim of this study was to determine sex differences in postural control changes generated by fatigue of ankle plantar flexors in healthy young adults in two postural tasks of varying difficulty: a quiet standing (QS) task and a forward lean (FL) task. The secondary aim was to determine the effects of vision (EO vs. EC) on postural changes with fatigue according to task difficulty. It was hypothesized that males would show greater fatigue-induced alterations in postural control compared with females, and such results would be more pronounced under relatively challenging task conditions (e.g., FL-EC) compared to lesser challenging conditions (e.g., QS-EO). Also, the withdrawal of vision would lead to greater fatigue-induced postural changes, which would be more pronounced during the FL task. These hypotheses are consistent with the findings of this study where males presented with a significant and prolonged increase in COP sway velocity, but females did not (sex X fatigue interaction), and fatigue-induced backward shifts was greater with EC compared to EO during recovery (vision X fatigue interaction).

In article 4, the main aim was to determine sex differences in postural control changes (sway and co-contraction) with ankle muscle fatigue during a standing forward leaning (FL) task in different vision conditions (EO vs EC). A secondary aim was to determine fatigue-induced changes in ankle spinal proprioceptive inputs (SOL H-reflex) according to sex and vision. It was hypothesized that males would show greater increases in both COP sway parameters and ankle stiffness (co-contraction) compared with females, and such results would be more pronounced with the withdrawal of vision. Also, we hypothesized that ankle muscle fatigue would lead to SOL H-reflex depression, and this depression would be more pronounced in males and with the removal of vision. We however found similar postural control changes with fatigue between males and females during the FL task regardless of vision conditions, as well as no significant effects of fatigue and interactions with sex and vision on SOL H-reflex.

CHAPTER 3. RESEARCH ARTICLES

List of research articles

Research article 1: Rating of perceived exertion (RPE) in studies of fatigue-induced postural control alterations in healthy adults: scoping review of quantitative evidence

Published in: *Gait & Posture (2021), 90, 167–178*

Research article 2: Sex differences in central and peripheral fatigue induced by sustained isometric ankle plantar flexion

Published in: *Journal of Electromyography and Kinesiology (2022), 65, 102676–102676*

Research article 3: Sex differences in the effect of muscle fatigue on static postural control under different vision and task conditions

Published in: *PLOS ONE (2022), 17(6), e0269705–e0269705*

Research article 4: Sex differences in effects of ankle muscle fatigue on static postural control and ankle spinal motoneuron activities

Submitted to: *Frontiers in Human Neuroscience (under revision)*

Research article 1

Title: Rating of perceived exertion (RPE) in studies of fatigue-induced postural control alterations in healthy adults: scoping review of quantitative evidence

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Keywords:

Rating of perceived exertion, Borg scale, postural control, muscle fatigue.

Abstract

Background: Amongst the literature researching the effects of exercise-induced fatigue on postural control in healthy adults, many studies have used the Borg scales to document the rating of perceived exertion (RPE) and have shown a broad range of RPE values. Our main aim was to map fatigue-induced RPE values in included publications. Secondary aims were to summarize the preference and purpose for the use of Borg scales within the included publications and to explore the potential associations between fatigue-induced RPE values and postural control changes.

Methods: Five databases (Ovid Medline, PubMed, CINAHL, Scopus, and SPORTDiscus) were systematically searched for synthesizing data among the publications that reported RPE values on the Borg RPE- and Category-Ratio (CR) 10 scales and also found fatigue effects on postural control in healthy adults. Spearman's rank correlations were conducted to assess potential associations between fatigue-induced RPE values and maximal postural control changes across the included publications (group data).

Results: 45 of 51 studies included in this review reported maximal RPE values following exercise and ranged from 10.4 to 20 (6-20 Borg RPE) or 0.9 to 10 (CR10) indicating "very light" or "very weak" to "maximal" exertions. The 6-20 Borg and CR10 scales were mainly used to assess cardiovascular and muscular exertion, respectively. The scales were used mostly to estimate fatigue levels (n=45), and to a lesser extent to produce a specific exercise intensity (n=5) and as the criterion for exercise termination (n=1). In general, there was no significant association between RPE and postural control changes across studies.

Conclusion: The broad range of RPE values and weak correlations may suggest that various fatigue levels can lead to postural control changes. However, one should be careful in comparing the extent of fatigue from RPE values and its potential effect on postural control in the light of many confounding factors.

1. Introduction

Postural stability is regarded as the capability to control the center of mass with respect to the base of support [1]. To maintain postural stability, the central nervous system must rapidly integrate sensory information from the visual, vestibular, and somatosensory systems [2]. The central nervous system must also use this information selectively to produce complex motor responses (i.e., timing, direction, and magnitude), appropriate to the characteristics of the postural stability disturbances of the surrounding environment [2].

Exercise-induced muscle fatigue can affect some of the sensory information and motor commands required to regulate postural control [3]. This is supported by several review studies, which concluded that muscular fatigue leads to modifications in the peripheral proprioceptive system and central processing of sensory inputs [4], as well as decrements in force production capacity [5]. Muscle fatigue could also lead to an increase in cardiac and respiratory (breathing) frequency caused by increased metabolic demands, particularly when performing whole-body exercise (e.g.., aerobic exercise, circuit training, etc.), possibly generating postural control alterations [3]. Thus, fatigue-induced changes in the neuromuscular and cardiovascular systems can adversely affect postural control performance.

Many studies have found fatigue-induced changes in postural control variables in healthy adults and athletes following various types of exercise such as: strenuous bouts of resistance exercise of targeted muscle groups (e.g., trunk, hip, knee, and ankle) [6–16], aerobic exercise (e.g., walking, cycling, running) [17–20], and mixed exercise (e.g., circuit training) [21–23]. Other than following exercise, studies using occupational tasks have also shown impaired balance control, for example, after walking in a heated environment simulating the work of firefighters [24] and load-carrying tasks [25].

Borg's rating of perceived exertion (RPE) (or 6-20 Borg) and Category-Ratio (or CR10) scales were developed to rate the level of perceived exertion in regards to cardiovascular (e.g., increased heart rate and breathing difficulty) and muscular (e.g., muscle exertion and pain) loads during physical activity [26,27]. The 6-20 Borg scale ranges from "6" (no exertion) to "20" (maximal exertion), while the CR10 scale ranges from "0" (no exertion) to "10" (maximal exertion) [26,27]. These two scales have been validated to be indicators of the degree of physical exertion in several studies. For example, an increase in the RPE value using the CR10 scale has been correlated with a reduction in maximal voluntary muscle force [28] and increased muscle activation [29] during exercise progression. An increase in RPE measured with the 6-20 Borg scale has shown a significant association with increased heart rate during high-intensity cycling [30].

Within the literature pertaining to the effect of exercise-induced fatigue on postural control, many studies have used the Borg scales to rate perceived exertion with a wide range of tasks; for example: fitness exercises in healthy adults [16,17,21,31–33], high-intensity circuit/interval training in athletes [20,23,34,35] and occupational tasks [24,25,36]. In these studies, the range of maximal RPE values recorded is broad, possibly indicating that various fatigue levels can affect postural control. A systematic summary of RPE values documented in the literature in the context of exercise-induced fatigue and related postural control changes would be beneficial to researchers or exercise practitioners who have to guide individuals in performing an exercise but avoid stability loss and potentially related injuries.

Therefore, the main aim of this review was to map maximal RPE values assessed in studies that found significant effects of exercise-induced muscle fatigue on postural control in healthy adults, according to the type of exercise and different healthy populations. Secondary aims were to summarize the preference/purpose for the use of each of the two Borg scales (6-20 Borg and CR10) in the included studies, and also to determine whether any general associations can be found between fatigue-induced RPE values and postural control changes across the included studies.

2. Method

The methodology for this review was based on the guidance for conducting a systematic scoping review by the Joanna Briggs Institute [37]. The use of these guidelines was justified because our aims did not concern health practice and delivery (e.g., exercise intervention), which is commonly the focus of "systematic reviews" [37,38], but rather mapped and summarized broad data [37]. Following these guidelines, the method section consists of 1) the research questions, 2) inclusion criteria, 3) types of participants, 4) database sources/search strategy, 5) study selection and 6) data summary/synthesis. A statistical analysis section is also included and describes the methods used to perform correlations between fatigue-induced RPE values and maximal postural control changes chosen from each of the included studies.

2.1. Research questions

This review was developed to answer our main research question: "What is the level of perceived exertion in healthy adults when their postural muscles are in a state of acute muscle fatigue after exercise and, at the same time, changed or impaired postural control is present?" In addition, the following three secondary questions were formulated concerning the use of the Borg scales and the potential general relationship between exercise-induced fatigue and related postural control changes: "Which Borg scale is preferred for reporting RPE values for different types of exercise in studies looking at the effect of muscle fatigue on postural control? ", "What is the purpose(s) of assessing RPE using the Borg scales in studies looking at the effect of muscle fatigue on postural control?", and, "Is there a general association between RPE values and the extent of postural control changes produced by fatiguing exercise or tasks across the included studies?"

2.2. Inclusion criteria for studies

The following criteria were used for inclusion of studies into the scoping review: 1) fatiguing exercise (or a task) using postural muscles (trunk and lower limbs), 2) presence of a significant effect of acute muscle fatigue on postural control (however, see discussion section for how results from a few studies which documented no fatigue effect on postural control compare), 3) quantitative study measuring postural stability-related variables (e.g., COP/COM sway parameters, foot pressures, stability index, etc.) during a standing postural task (not including gait), including both static (e.g., quiet standing on one leg or both legs) and dynamic tasks (e.g., upright standing on firm surface, foam, or movable platform, and standing reaching one leg), and 4) record of RPE value(s) using the 6-20 Borg or (modified) CR10 scales in the state of muscle fatigue. This review did include the Foster scale [22], the Borg dyspnea scale [39], and the Borg Visual Analog scale [40], as all these have a similar structure to the CR10 scale.

2.3. Type of participants

All participants in the articles included in this review had to be healthy adults who have the ability to ambulate independently and are 18 years of age or older. None of them were to present with any disease which could adversely affect postural control. In cases where studies included both non-healthy adults as well as healthy adults, we synthesized data only from the healthy adults.

2.4. Database sources and search strategy

Five databases were searched: Ovid Medline, PubMed, CINAHL, Scopus, and SPORTDiscus. The following combination of search terms was used to identify articles: “postural control or posture or postural balance or postural stability” AND “muscle fatigue or muscular fatigue or fatigue exercise or fatiguing exercise” AND “Borg scale or perceived exertion”. This search was limited to articles published in English and available in full text, with no limit on date.

2.5. Study selection

The studies included in this review were selected through two screening steps (see Figure 1). First, the two authors independently assessed all titles and abstracts of the studies identified from the electronic database searches to exclude those that did not meet the inclusion criteria. One author (JD) screened titles/abstracts of all references in studies included after the first screening and from relevant review papers [3,5,41,42] to identify additional articles. After the initial identification, the two authors reviewed the full-text of each article to confirm the inclusion in the final set of articles. When questions occurred about eligibility, the two authors came to a consensus via discussion.

2.6. Data summary and synthesis

A standardized form was developed in order to facilitate the synthesis of data from all selected articles. Using "Mendeley Desktop" (Version, 1, 19, 4), basic information about each article was imported into an excel worksheet and then summarized in the standardized form, where additional data screened from each article was input manually. The form consisted of a data table and included: study title, published year, journal, authors, country of origin, study aims, research field, used postural task (static vs. dynamic), used Borg scale(s), purpose of the use of the Borg scale(s), fatiguing protocol, experimental setting, maximal RPE value(s) after exercise or RPE value(s) during exercise, characteristics of participants, postural control measures, and fatigue effects on postural control. Based on the recommendations for scoping studies [43], the data table was used to synthesize qualitative findings because the heterogeneity among publications excluded the possibility of a meta-analysis.

2.7. Statistical analysis

In order to determine whether there is a broad association between fatigue-induced RPE values and the extent of postural control changes across the included studies, Spearman's rank correlation analyses (nonparametric bivariate correlation coefficients) were performed using "IBM SPSS Statistics 27.0". These correlations were based on an analysis of group data across the included studies and not an analysis of data across individuals. The choice of the non-parametric test was justified due to selected postural data being not normally distributed, and the 6-20 Borg scale constituting an ordinal scale. With regards to the postural control data (e.g., COP sway parameters, stability index/score) reported in each included study, the variable(s) showing the greatest change immediately following exercise(s) for each population(s) was selected, and the change in the pre to immediately post-exercise value was normalized to the pre-exercise value (which represents the percentage change from the pre-fatigue value). RPE values assessed immediately after exercise were considered to represent the level of exertion induced by the fatiguing exercise and were selected for the correlation analysis. These post-exercise RPE values were normalized to the maximum of the scale, 10 for the CR10 scale or 20 for the 6-20 Borg scale, to allow pooling of data from all studies. Subsets of data were used to perform different correlations between fatigue-induced RPE values and maximal postural control changes, with respect to 1) the type of Borg scales (all Borg vs. 6-20 Borg vs. CR10), 2) the type of postural control variables (all COP sway parameters vs. COP sway displacement vs. COP sway velocity vs. COP sway area vs. stability index/score), 3) the type of exercise (aerobic: running, cycling, and walking vs. anerobic: resistance exercise vs. mixed exercise: high intensity circuit/interval training), and 4) different populations (young adults vs. athletes vs. older adults). In cases where the number of studies for a given subset was not sufficient ($n < 7$), no correlation was performed. These data sets did not include the data from one publication [46], as there was a delay between postural variable measurements (at 5min) and RPE assessment (immediately) after the exercise protocol.

3. Results

A flow chart of the process for the selection of articles is shown in Figure 1. A total of 998 studies were identified, which included 19 from Ovid Medline, 71 from PubMed, 16 from CINAHL, 653 from Scopus, and 239 from SPORTDiscus. Because the Scopus database led to different sets of identified articles depending on the order of keywords, 653 studies from this database included records from a first (n=170) and second (n=483) searches. After removing duplicates, a total of 759 articles had their title and abstract assessed, resulting in a total of 94 studies extracted. These 94 studies included 17 articles extracted through screening 304 records that were identified from all references in the 94 studies as well as from four relevant review papers [3,5,41,42]. After the full-text assessment, 43 studies which did not meet all of the inclusion criteria (see details in Figure 1) were excluded, leaving a total of 51 studies for the data synthesis. The data synthesis includes the general characteristics in the included studies as well as the key items relevant to our stated aims.

3.1 General characteristics and research focus of the included studies

The general characteristics and research focus of the included studies are shown in Tables 1 and 2, respectively. These characteristics include publication year, country of origin, general field of study, population, number of participants, experimental setting, postural control measures, fatiguing protocol, and variables used to identify fatigue.

3.2. Key results

3.2.1 Range of maximal RPE reported

Maximal RPE values after exercise reported in the included studies were mapped and are summarized in Table 3 in Figure 2. The RPE values reported in 6 studies [17,21,23,31,32,47] were excluded as those were reported during exercise and thus considered not to be maximal. However, these RPE values were included in the data synthesis for the secondary aims. The maximal RPE value following exercise ranged from 10.4 to 20 for the 6-20 Borg scale and 0.9 to 10 for the CR10 scale, indicating "very light" or "very weak" up to maximal exertion. These maximal RPE values showed different trends depending on population and type of exercise. Maximal RPE values reported after exercise for young adults showed a broader range, from 9.7 to 20 (6-20 Borg) and 2.3 to 8.7 (CR10), as compared with athletes showing generally higher values, ranging from 15.2 to 20 (6-20 Borg) and 5.0 to 10

(CR10), and also older adults typically showing lower values, from 11.4 to 16.9 (6-20 Borg) and 0.92 to 6.0 (CR10).

With regards to the type of exercise, the range of maximal RPE values after aerobic exercise was broader, with values between 10.4 to 20.0 (6-20 Borg) and 0.9 to 7.0 (CR10), as compared with those ranging from 15.5 to 20 (6-20 Borg) and 5.4 to 8.7 (CR10) following anaerobic exercise, as well as 13.0 to 19.3 (6-20 Borg) and 7.5 to 10 (CR10) after mixed exercise. Regarding aerobic exercise, maximal RPE values on the 6-20 Borg scale ranged from 11.4 to 20.0, 10.4 to 20.0, and 11.2 to 14.0 after cycling (number of RPEs=10) [19,48–54], running (n=11) [20,35,44,55–60], and walking protocols (n=2) [61], respectively. Using the (modified) CR 10 scale, maximal RPE values (n=2) were 6.5 following each of cycling and running protocols [46], while maximal RPE values (n=6) ranged from 0.9 to 7.0 following walking protocols [18,33,62,63]. Regarding anaerobic exercise protocols, maximal RPE values of the 6-20 Borg scale ranged from 15.5 to 17.2, and 17.0 to 18.8 following resistance exercise protocols (n=5) [64–66] and cycling/sprints at a maximal speed (n=5) [44,48,49,54,60], respectively. Using the CR10 Borg scale, maximal RPE values (n=11) ranged from 5.4 to 8.7 following resistance exercise protocols [16,36,39,40,64,65,67–69] whereas there were no measures using cycling/running protocols at maximal speed.

Mixed exercise protocols used in the included studies involved high-intensity circuits/interval training protocols [22,23,34,44,45,70–74], moderate-intensity physical activity protocols (e.g., step-ups, lunges, and stepping over obstacles) [21,31,32], sports matches (soccer and badminton) [75,76], and occupational task (load carriage task) [25]. Following circuit/interval training, maximal RPE values (n=11) of the 6-20 Borg scale [34,44,45,70–74] ranged from 15.9 to 19.3, whereas one study [22] reported a maximal RPE value of 10.0 using the CR10. During physical activity protocols, RPE values of 13.0 on the 6-20 Borg scale were reported in 3 studies [21,31,32], but were not included in the summary of the extent of maximal RPE values, as those were not maximal. Regarding sports match, one study [75] assessed a maximal RPE values of 15.2 using the 6-20 Borg scale after a soccer match (90 mins), while one study using the Borg CR10 scale [76] showed a maximal RPE value of 7.5 after a competitive badminton match. Following an occupational task (load carriage task), one study [25] reported a maximal RPE value of 19.0 using the 6-20 Borg scale.

3.2.2. Preference in the Borg scale used

In the included studies (n=51), the number of studies using the 6-20 Borg scale (n=33, 64.7%) [19–21,23,25,31,32,34,35,44,45,48–56,58–61,66,70–75,77,78] was twice as those using the modified CR10 scale (n=16, 31.4%) [16–18,22,33,36,39,40,46,47,62,63,67–69,76]. Two studies (4.0%) [64,65] used both the 6-20 Borg and CR10 scales. The (modified) CR10 scales included the 0-10 CR10 (n=12) [16–18,33,36,46,47,62,67–69,76], 1-10 CR10 (n=1) [63], 0-10 Visual Analog scale (n=1) [40], 0-10 Borg dyspnea scale (n=1) [39], and 0-10 Foster scale (n=1) [22]. With regards to the type of exercise (Table 3), the use of the 6-20 Borg scale was predominant in studies using cycling (n=8 out of 9 studies) [19,48–54], running (n=9 out of 12) [20,35,44,55–60], and high intensity circuit/interval training (n=9 out of 10) [23,34,44,45,71–74,78] protocols. In contrast, the CR10 scale was used mainly in studies using resistance exercise (n=9 out of 10) [16,36,39,40,64,65,67–69] and walking (n=4 out of 5) [18,33,62,63] protocols.

3.2.3. Purpose for using the Borg scales

The purpose for using the Borg scales was not the same across different studies. In most studies included (n=45, 88.2%) [16,18–20,22,25,33–36,39,40,44–46,48–76,78], the Borg scales were used to indirectly measure the level of fatigue produced by low-to-high intensity exercise protocols. Also, 5 studies (9.8%) [17,21,31,32,47] used RPE values to produce a specific exercise intensity during exercise. More specifically, these studies guided participants to perform a certain moderate-intensity exercise corresponding to an RPE value of 13 (6-20 Borg) [21,31,32] and 3 or 5-6 (CR10) [17,47] until the end of the exercise protocols. Besides these two uses, one study [23] used an RPE value of 18 (6-20 Borg) as a criterion for exercise termination during a high-intensity circuit training protocol in which participants were asked to stop performing the protocol when reaching this RPE value.

3.2.4. Correlations between RPE values and maximal postural control changes

There were no significant correlations, whether tested overall or with the different subsets according to RPE scales used (Table 4), different postural variables (Table 5), and type of exercise (Table 6). However, there were a few significant correlations when considering the data from young adults only, between all postural variables and RPEs assessed with all Borg scales ($r_s = 0.351$, $p = 0.033$), with a greater correlation for the 6-20 Borg scale ($r_s = 0.513$, $p = 0.010$) (Table 7).

4. Discussion

The main aim of this review was to map RPE values assessed immediately after exercise protocols that lead to significant postural control changes in healthy adults. In addition, our secondary aims were to summarize the preference and purpose for the use of the Borg RPE scales, as well as to determine whether any broad associations could be found between fatigue-induced RPE values and the extent of postural control changes across the included studies.

4.1. Rating of perceived exertion (RPE) values

The range of maximal RPE values reported in the included studies was very broad, ranging from "very light" or "very weak" to "maximal" exertion. This broad range of maximal RPE values suggests that various fatigue levels can affect postural control performance.

Several potential factors can contribute to the broad range of RPE values in the included studies; amongst factors identified in these studies are task-specificity (exercise intensity, location of fatigued muscles and exercise design), participant's characteristics such as sex, and dehydration during exercise. Exercise intensity can be an obvious key factor, as RPE is used as a subjective indicator of exercise intensity, which has been validated through significant associations between exercise-induced RPE values and fatigue-related physiological changes such as heart rate and lactate accumulation [26,27]. A previous study [79], for example, showed significant correlations between RPE values and the level of blood lactate during cycling with different loads corresponding to levels of maximal oxygen uptake (VO2 max) and respiratory threshold. Studies included in this review using various levels of aerobic exercise intensity (low to high) showed a broader range of maximal RPE values than those using mostly high intensities for the other types of exercise. For example, studies using walking protocols with different speeds [33,63] and grades [62] showed a broad range of maximal RPE values with the CR10 scale, from 0.9 (very weak) to 7.0 (too strong). In contrast, most studies using anaerobic- and mixed exercise requiring maximal efforts generally reported much higher maximal RPE values showing more than "hard" (6-20 Borg) and "strong" (CR10) ratings. Such variations were also found in the different populations (young adults, older adults, and athletes) tested in the included studies. For example, healthy young adults showed a broad range of RPE values from “very light” to “maximal” (6-20 Borg and CR 10) immediately after performing low-to-high intensity exercises such as from walking [61] or submaximal running [57] to repetitive lifting until failure [36] or cycling until exhaustion [50]. In contrast, athletes performing high-intensity interval training and running until failure [22,34,56] showed high RPE values from “hard” to “maximal” (6-20 Borg and CR 10), while older adults generally performing exercise at low to moderate intensity, expectedly, showed relatively low RPE values, ranging from “fairly light” or “very weak” to “somewhat strong” (6-20 Borg and CR10).

Exercising/fatiguing different muscle groups could also lead to variations in maximal RPE values. In the included studies, maximal RPE values (“very strong” or “very hard”) following resistance exercise targeting proximal muscle groups (thigh, hip, and back muscles) [16,36,66] tend to be greater than those (less than “very strong”) following exercise targeting distal muscle groups (ankle muscles) [39,64,65], even though all exercise protocols were performed until exhaustion. Such different RPE values based on the location of fatigued muscle could be associated with different fatigue effects on postural control. This would be in line with previous findings [11,80,81] where fatigue of the hip and/or knee muscles was shown to have a greater effect on postural control than the fatigue of ankle muscles (however, see section 4.2). Differences in maximal RPE values on the 6-20 Borg scale were also shown according to exercise-design specificity. For example, different RPE values were found between exercise protocols for backward walking (RPE of “14.0”) versus forward walking (“11.2”) [61] and 10 x 400 m (“16.0”) versus 40 x 100 m (“15.1”) interval training [71], even though each pair of protocols was designed with the same exercise intensity.

Regarding potential sex differences for RPE, two studies [36,73] found that females reported slightly higher maximal RPE values following resistance exercise and high-intensity circuit/interval training compared to males, potentially indicating greater muscle fatigue in the females than the males. These results are in contrast with those of several previous studies [82–85] where females were shown to have greater fatigue resistance than males, likely due to a greater oxidative metabolic capacity [86], a greater proportion of fatigue-resistant muscle fibers (type I) within skeletal muscles [87], and lesser voluntary activation during fatiguing tasks [85]. These contrasting findings might be explained by the dynamic and functional exercise protocols used in the two studies reporting RPE values in males and females [36,73]. This would be in line with the review paper by Hunter (2016) [88], in which it was suggested that sex differences in fatigability induced by a dynamic fatiguing task are not consistent amongst the limited number of studies. Dehydration during exercise affected RPE values in the included studies. Two articles [53,57] observed that dehydration during aerobic exercise led to greater maximal RPEs (6-20 Borg) of 16.6 and 10.4 following exercise compared with 10.4 and 9.9 reported in no-dehydration conditions.

Although not included in the present data synthesis, we did look at the RPE values in 4 studies [89–92] that showed no fatiguing effects on postural control. We did not find any obvious differences in the RPE values reported in those four studies (showing more than “very hard” or “strong”), compared with those in the studies included in the data synthesis, where a significant effect of fatigue on postural control was found. This suggests that several potential confounding factors may affect the interaction between muscle fatigue and postural control (see section 4.4).

4.2 Use of the 6-20 Borg and CR10 scales

In the studies included in this review, twice as many used the 6-20 Borg scale compared with those which used the (modified) CR10 scale. The use of the 6-20 Borg scale was predominant for studies using cycling and running protocols. Most of these studies [19,20,35,44,48–60] monitored changes in aerobic exertion level (e.g., heart rate, respiratory exchange rate, blood lactate, VO2 max, etc.). In contrast, the CR10 scale was mostly used in studies looking at resistance exercise [16,36,39,40,64,65,67–69], even if the scale was used to observe aerobic exertion levels in a small number of studies [22,46,47,62,63]. The specific use of these Borg scales is likely the result of their characteristics of origin. The 6-20 Borg scale was developed given linear correlations with exercise intensity for cycle ergometer [26,27], while the CR10 scale was considered to be more suitable for evaluating subjective symptoms such as exertion and pain [26,27].

4.3 Purpose for using the Borg scales

In the included studies, RPE values were used: 1) to assess fatigue levels during/following exercise, 2) to guide participants in maintaining a certain submaximal intensity for the duration of the exercise protocol, and 3) as a criterion for exercise termination in order to potentially produce the same fatigue level across participants. Most of the studies used RPE values to estimate fatigue levels during exercise progression. For example, a gradual increase in RPE values (CR10) in young adults was reported every minute from the beginning of a repetitive sit-to-stand task performed until failure. At the same time, greater postural sway (COP) was observed at the halfway and endpoint of the task, compared with the starting point [16]. This use of RPE values could help determine a range of fatigue levels affecting postural stability.

Five studies used a target RPE value to guide participants at a selected exercise intensity level. For example, two studies using the CR10 scale [17,47], paced young adults at a moderate exercise level corresponding to either RPE values of “3” or “5-6” during entire treadmill running protocols by controlling treadmill speed. Three studies using the 6-20 Borg scale [21,31,32] paced young and older adults to perform a physical activity protocol at a moderate intensity level corresponding to an RPE value of 13. This is consistent with guidelines for exercise in older adults [113], and this approach could allow to monitor fatigability in frail individuals who may be at risk of stability loss and related injuries when performing higher intensity exercise or exercise until failure. Besides these two approaches, one study [23] used a specific RPE value as the criterion for exercise termination to potentially generate the same fatigue level amongst participants. In this study, participants were asked to stop a high-intensity circuit training protocol when reporting a value of 18 on the 6-20 Borg scale. This approach was based on findings from previous studies [20,35], which recognized an RPE value of 17 as a fatigued state when performing a running exercise until failure. Such an approach may help produce a standardized fatigue level and thus lead to more reliable fatigue effects on postural control.

4.4. Correlations between RPE values and the extent of postural control changes following muscle fatigue

The correlation between RPE values (all Borg scale) and maximal postural control changes (all postural variables) produced by fatiguing exercise across the included studies was, in general, not significant, except when considering data from young adults only (with a greater correlation shown within the subset of studies using the 6-20 Borg scale). These results suggest that the characteristics of the population under study have an influence on the correlation, possibly due to different fatigability and postural control ability/strategy between populations, especially between young and older adults. For example, many studies on muscle fatigue have demonstrated that older adults have greater fatigue resistance than younger adults [93–97] possibly due to factors such as a decrease in maximal motor unit discharge rates [98,99], a greater proportion of fatigue-resistant muscle fibers (e.g., type I) [100], and a greater dependence on oxidative phosphorylation within the muscle [101,102]. Many studies have also observed postural alterations (e.g., increased COP sway displacement) or adaptations (e.g., greater reliance on vision and/or greater stiffness) in older compared with young adults during static [103–105] and dynamic tasks [106–109]. However, how these age-related effects influence the correlations in this review is unknown as there are a number of other potential confounding factors affecting RPE values and/or postural control amongst the included studies.

Amongst potential confounding factors are those affecting RPE values as discussed in section 4.1. Exercise intensity, which will be closely associated with fatigue and RPE as discussed above, may not lead to corresponding changes in the extent of postural control alterations. For example, our group [13], as shown that a more pronounced change in postural control variables following greater levels of fatigue is not necessarily observed in all instances, even when the different levels of fatigue involve different physiological mechanisms (e.g., central versus peripheral). A higher correlation was obtained for the ‘walking’ subset, the activity with the lowest reported RPE levels, as compared to the other medium-to-high intensity activities (Table 6). This suggests that the association between fatigue-induced RPE level and the extent of postural control changes might vary between activities involving high versus low levels of exertion (or exercise intensity). Because we generally did not find any significant correlations regardless of the type of exercise in the included studies (aerobic, anaerobic, mixed), it appears that the type of exercise may be not a major potential confounding factor. Accordingly, both aerobic and resistance exercises (matched for intensity and duration), for example, can lead to similar RPE values (CR10) reported after each bout [110].

Varied levels of postural task difficulty may also constitute a key potential confounding factor, as it could affect the magnitude of fatigue-related alterations in postural control. For example, Koyama and Yamauchi (2017) [74] showed significant decreases in postural stability during relatively challenging tasks (both one-leg standing with eyes open and two-leg standing with eyes closed) from pre to post-exercise, but not during a less challenging task (two-leg standing with eyes open) following the same exercise in healthy young adults. This trend has also been found in healthy older adults, for example, in a previous study [111] showing greater fatigue-related postural sway alterations on a compliant compared to a firm surface. Postural task difficulty is a multifaceted factor that can be influenced, not only by the biomechanical demands of a given task (e.g., unipedal versus bipedal, base of support variations), but also by the availability of quality sensory information to perform the task optimally (e.g., eyes closed versus opened, firm versus compliant surface) (see Bisson et al., 2010 [112] for example). Because task difficulty and determining factors vary widely across the studies included in the present review (e.g., quiet standing [47,59], single-leg standings [22,74], standing on unstable/movable surfaces [25,56], and standing with different sensory conditions (e.g., visual, somatosensory) [68,74]), it is not surprising to generally find little association between RPE and postural control changes following exercise.

Another potential confounding factor that may explain the lack of a broad association between RPE and the extent of postural control changes with fatigue in the included studies is related to the selected postural variable(s). COP sway parameters showed weaker correlations with RPE values compared with stability index/scores (Table 5). This could be due to the wide range of parameters used to quantify COP movements across the included studies and because fatigue does not necessarily have the same effect on all these COP variables [13,35,48,66]. COP parameters included COP sway displacement (e.g., AP sway displacement [40], ML sway displacement [50], and total sway displacement [72]), COP sway velocity (e.g., sway area velocity [17], AP sway velocity [19], and ML sway velocity [35]), and COP sway area (e.g.,90% or 95% confidence of sway ellipse area [61,68] and surface area covered by the path of the COP sway [69,74]). In contrast, the correlation between the changes in stability index/score with RPE from all Borg scales was close to reaching significance ($p = 0.086$). Such stronger association may be due to the reporting of only two variables (overall stability index [56] and balance error score [60]), and that these measures were standardized across publications.

A few limitations should be considered for this review. First, most of the included studies did not provide all relevant details concerning RPE assessments that may affect recorded values, such as: the precise timing of the recording of an RPE value following exercise and in what posture (e.g., standing and sitting) the RPE value was obtained. In addition, this review was limited to 'standing' postural control, although exercise and fatigue can also affect gait performance. Furthermore, none of the included studies directly investigated the relationship between RPE and fatigue-induced postural control changes, and individual RPE and postural control data could not be extracted in all studies. Therefore, all correlations whether tested overall or with different subsets of data in this review were based on an analysis of "group" results from the included studies, thus limiting our ability to generate strong conclusions concerning the relationship between fatigue-induced RPE values and postural control changes with the necessary control of a number of confounding factors. However, our discussion on such potential confounding factors may be helpful for future studies examining fatigue-induced postural changes which have to control potential confounding factors related to fatigue or RPE and/or postural control.

5. Conclusion

In this review, 51 studies, which showed significant effects of exercise-induced fatigue on static and dynamic postural control, were identified/selected through searches from the Ovid Medline, PubMed, CINAHL, Scopus, and SPORTDiscus databases. The included studies showed a broad range of RPE values (6-20 Borg and CR10) in a fatigued state, which led to postural control alterations. In general, there was no significant correlations between fatigue-induced RPE values and the extent of postural control changes found across studies. These results suggest that various fatigue/exertion levels can lead to postural control changes, however, this can be influenced by several confounding factors. The Borg scales were mainly used to assess cardiovascular (6-20 Borg) and muscle (CR10) fatigue/exertion in the included studies. Our overview on the range of fatigue-induced RPE values (Borg scales) and the use of the scales may be useful for future studies or clinical/sport practitioners that have to estimate muscle fatigue levels affecting postural control in healthy adults, especially when measures of fatigue-related neuromuscular and physiological changes (e.g., EMG, muscle force, blood lactate, heart rate, etc.) cannot be obtained. However, more work is needed to further our understanding of the effect of exercise/fatigue on postural control.

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Figure 1. Flow chart illustrating the screening process for study selection

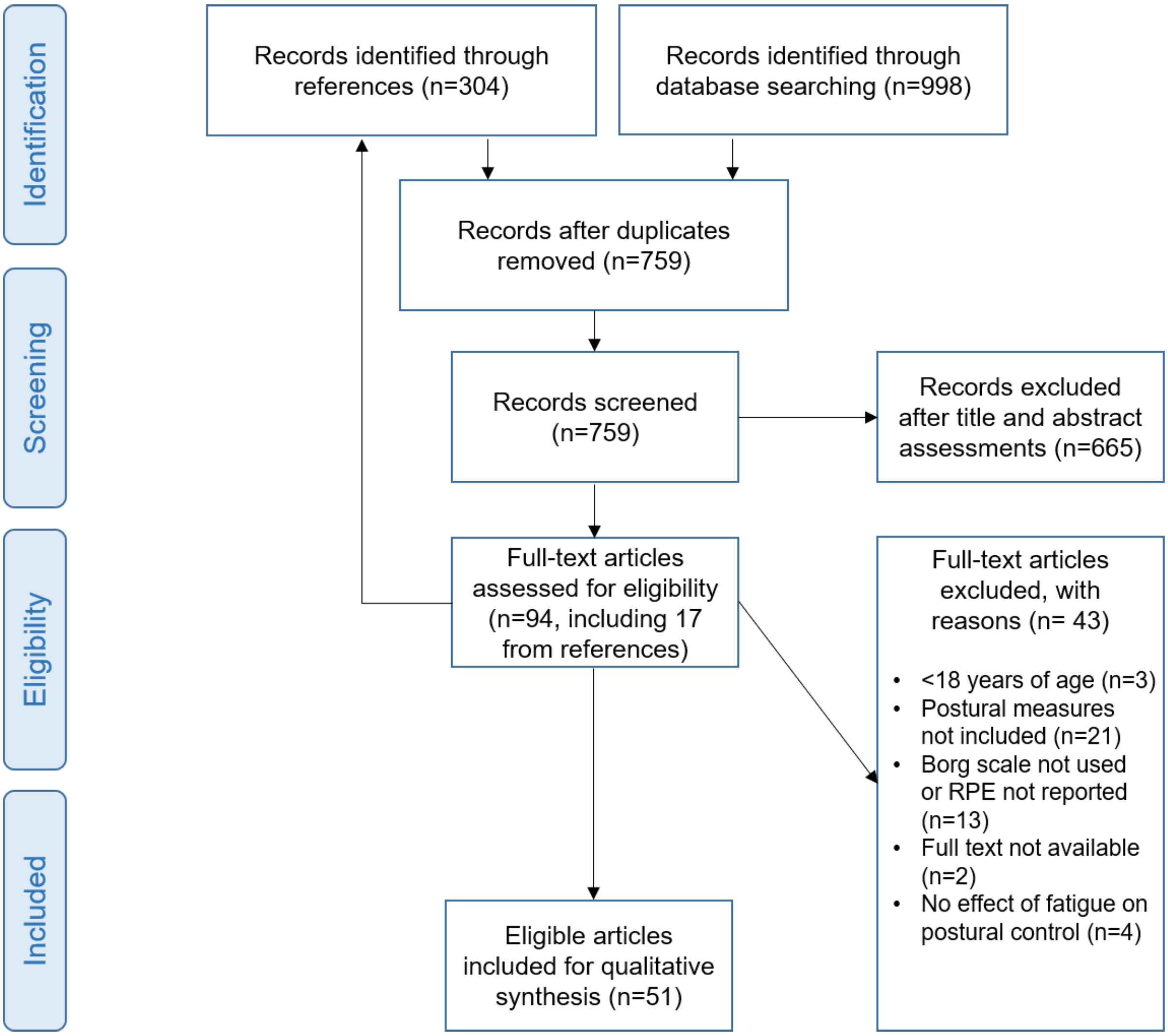

Figure 2. Ranges of the rating of perceived exertion (RPE) overall (A) and according to population (B) and exercise (C). The area of circles indicates the range of RPE assessed with the 6-20 Borg scale or the CR10 scale. The numbers at the left and right sides of the circles indicate lowest and highest RPE values of the CR10 scale. The numbers at the bottom and top indicate lowest and highest RPE values of the 6-20 Borg scale.

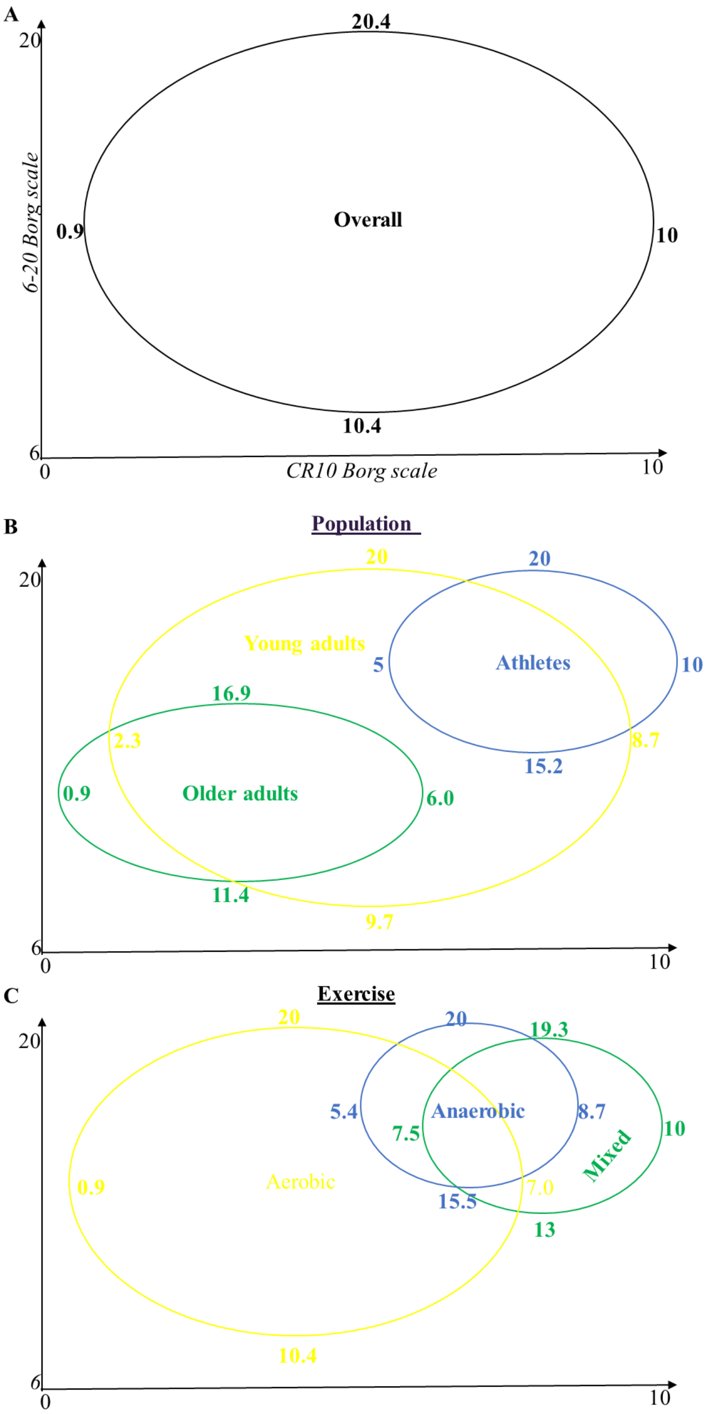

Table 1. General characteristics of the included studies. HR: heart rate; VO2: oxygen uptake; CO2: carbon dioxide production; MVC: maximal voluntary contraction torque; EMG: electromyography; VA: voluntary activation.

Characteristics	Number (*n*= 51)	Percentage (%)
Publication year		
Prior to 1997	0	0
1997-2000	3	5.9
2000-2009	14	27.5
2010-October 2020	34	66.6
Country of origin		
North America	11	21.5
Asia	6	11.8
Europe	28	55.0
South America	2	3.9
Australia-Oceania	4	7.8
Research fields		
Healthy human movement and strategy	34	66.7
Sports performance	13	25.5
Occupational performance	2	3.9
Athletic therapy	2	3.9

Population		
Healthy young adults	30	58.9
Healthy older adults	4	7.8
Both young and older adults	4	7.8
Athletes	13	25.5
Number of participants		
< 10	4	7.8
10-19	24	47.1
20-49	18	35.3
50-100	5	9.8
Experimental setting		
Laboratory	40	78.4
Gym or outside	8	15.7
Unclear	3	5.9
Postural control task		
Static	34	66.7
Dynamic	11	21.6
Both static and dynamic	6	11.8
Fatiguing protocol		
Aerobic exercise	18	35.3
Anaerobic exercise	10	19.6

Mixed exercise	16	31.4
Aerobic vs. Anaerobic	6	11.8
Aerobic vs. Anaerobic vs. Mixed exercise	1	2.0
Variables used to identify fatigue (other than RPE values)		
Physiological variables (e.g., HR, VO2, CO2, blood lactate, respiratory rate)	21	43.1
Neuromuscular variables (e.g., MVC, EMG, VA)	13	25.4
None (only RPE value)	19	37.2

Table 2. Research topics in the included studies with regards to the research fields

Research fields (number of study, percentage)	Research topics in the context of muscle fatigue (number of study)
Healthy human movement and strategy (n=34, 66.7%)	• Postural control performance (n=15) in healthy young adults [16,17,39,40,46,51,58,62–64,66,67,69,74,78] and healthy older adults (n=4) [18,19,33,52] • Type of exercise on postural control performance in healthy young adults (n=7): backward vs. forward walking [61]; aquatic vs. land running [47]; 10 x 400 m vs. 40 x 100 m interval running [71]; anaerobic vs. aerobic exercise [48–50], anaerobic vs. aerobic exercise vs. mixed exercise [44] • Aging on postural control performance (n=4) [21,31,32,65] • Fluid condition on postural control performance in healthy young adults (n=2) [53,57] • Cognitive demand on postural control performance in healthy young adults (n=1) [49] • Somatosensory condition on postural control performance in healthy young adults (n=1) [68]
Sports performance (n=13, 25.5%)	• Postural control performance in athletes (n=6) [22,34,45,70,73,75] • Type of exercise on postural control performance in athletes (n=2): aerobic and anaerob ic exercise [56,60] • Ankle stability on postural control performance in athletes (n=2) [20,35] • Different stability measures on postural control performance in athletes (n=1): COP swa y parameter- and foot pressure measures in athletes [59] • Postural control performance and injury mechanisms in athletes (n=1) [76] • Sex difference on postural control performance in athletes (n=1) [23]

Occupational performance (n=2, 3.9%)	• Footwear and load carrying on postural control performance in healthy young adults (n= 1) [25] • Sex difference and load lifting on postural performance control in healthy young adults (n=1) [36]
Athletic therapy (n=2, 3.9%)	• Postural stability assessment for sports concussion management in healthy young adults (n=2) [54,72]

Table 3. The extent of maximal ratings of perceived exertion (RPE) values on the 6-20 Borg and CR10 scales with respect to the type of fatiguing protocol. RPE values on the CR10 scale included those on the Borg Visual Analog scale, Borg dyspnea scale, and Foster scale as they have a similar structure to the CR10 scale. All RPE values reported in this table are maximal RPE values assessed after fatiguing protocols, except for RPE* which was measured during exercise and thus not maximal. RPE* thus was excluded in the extent of maximal RPE values. YA: healthy young adults; OA: healthy older adults; AT: athletes; n: the number of RPE values.

Type of exercise (number of protocols)	Maximal RPE of 6-20 Borg (SD)	Maximal RPE of Borg CR10 (SD)	Participants
Aerobic exercise			
Cycling			
10-min cycling (60% of maximum)[19]	11.4(2.9)	N/A	OA
10-min cycling (60% of maximum)[52]	12	N/A	OA
30-min cycling (50% of maximum)[49]	13(1.0)	N/A	YA
30-min cycling (50% of maximum)[50]	13(2.0)	N/A	YA
60-min cycling (50% of maximal aerobic power)[48]	14.5(1.9)	N/A	YA
120-min cycling (55-60% VO2 max) without dehydration[53]	14.5(2.1)	N/A	YA
15-min cycling (75-85% of maximal HR)[54]	15(2.0)	N/A	YA
120-min cycling (55-60% VO2 max) with dehydration[53]	16.6(1.9)	N/A	YA
15-min cycling exercise of 200 W[51]	17.8(2.6)	N/A	YA
Cycling with an incremental load until exhaustion[50]	20.0(0.0)	N/A	YA
25-min cycling with an incremental work load[46]	N/A	6.5(2)	YA
Extent of maximal RPE value(s) of 6-20 Borg (n=10) and CR10 (n=1)	***11.4-20***	***6.5***	N/A
Running			
60-min treadmill running (75–85% of maximal HR) with water intake[57]	9.7(2.4)	N/A	YA
60-min treadmill running (75–85% of maximal HR) with sports drink intake[57]	9.9(3.0)	N/A	YA
60-min treadmill running (75–85% of maximal HR) with no fluid[57]	10.4(2.8)	N/A	YA
171-km mountain ultra-trail race [59]	16 (3.0)	N/A	AT
15.5-mile run[55]	16.1	N/A	YA
Submaximal treadmill running until exhaustion[44]	18.1(0.4)	N/A	YA
Submaximal shuttle running intervals until task failure [60]	18.3	N/A	AT
Treadmill Bruce protocol until exhaustion[58]	18.5(1.0)	N/A	YA
Treadmill Bruce protocol until exhaustion[56]	18-20	N/A	AT
Submaximal treadmill running until exhaustion [35]	19.5(0.6)	N/A	AT
Submaximal treadmill running until exhaustion [20]	19.7(0.7)	N/A	AT
20-min landing or aqua treadmill running[47]	N/A	3*	YA

25-min moderate treadmill running[17]	N/A	5-6*	AT
25-min treadmill running with an incremental grade and speed[46]	N/A	6.5 (0.2)	YA
Extent of maximal RPE value(s) of 6-20 Borg (n=11) and CR10 (n=1)	***10.4-20***	***6.5***	N/A
Walking			
15-min treadmill forward walking[61]	11.2(2.2)	N/A	YA
15-min treadmill backward walking[61]	14(2.6)	N/A	YA
6-min walking test protocol on walking course[33]	N/A	0.92	OA
35-min treadmill walking at PWS[63]	N/A	2.3(0.7)	YA
35-min treadmill walking at 120%-PWS[63]	N/A	3.2(1.1)	YA
32-min treadmill walking[18]	N/A	3.9(0.4)	OA
35-min treadmill walking 140%-PWS[63]	N/A	4.8(1.7)	YA
25-min treadmill uphill walking[62]	N/A	5-7	YA
Extent of maximal RPE value(s) of 6-20 Borg (n=2) and CR10 (n=6)	***11.2 and 14.0***	***0.9-7.0***	N/A
Extent of maximal RPE values after aerobic exercise	**10.4-20**	**0.9-7.0**	
Anaerobic exercise			
Resistance exercise			
Repeated heel rises of the right leg until task failure[64]	15.5	6.7	YA
Repeated heel rises of the right leg until task failure[65]	16.9	6.0	OA
Repeated heel rises of the right leg until task failure[65]	16.9	6.2	YA
Bilateral quadriceps contractions until task failure[66]	17.2(1.2)	N/A	YA
Unilateral quadriceps contractions until task failure[66]	17.2(1.3)	N/A	YA
Concentric-eccentric ankle plantar flexor contractions until exhaustion[40]	N/A	5.4(2.1)	YA
Sustained (isometric) heel rise until exhaustion[39]	N/A	6.0(2.0)	YA
Repetitive lifting at incremental weights until fatigue[36]	N/A	8.44(men)	YA
Repeated toe-lifts until task failure[68]	N/A	8.5	YA
Repeated heel rises of the dominant leg until task failure[69]	N/A	8.6(1.0)	YA
Repetitive sit-to-stand exercise until task failure[16]	N/A	8.6(2.0)	YA
Repetitive lifting at incremental weights until fatigue[36]	N/A	8.69(women)	YA
Side-lying repetitive hip abduction until task failure[67]	N/A	8.7(0.5)	YA
Extent of maximal RPE value(s) of 6-20 Borg (n=5) and CR10 (n=11)	***15.5-17.2***	***5.4-8.7***	N/A
Cycling or running at maximal speed			
High intensity cycling at more than 85% of HR [54]	17.0(2.7)	N/A	YA
20-m maximal sprint intervals during 2 mins [60]	17.6	N/A	AT
Cycling as hard and fast as possible during 30 seconds [49]	18.0(1.0)	N/A	YA
Maximal treadmill running until exhaustion [44]	18.4(0.5)	N/A	YA
Maximal voluntary pedaling exercise for 10 seconds [48]	18.8(1.1)	N/A	YA
Extent of maximal RPE value(s) of 6-20 Borg (n=5) and CR10 (n=0)	***17.0-18.8***	***N/A***	N/A

Extent of maximal RPE values after anaerobic exercise	**15.5-18.8**	**5.4-8.7**	
Mixed exercise			
High intensity circuit and interval training			
40 x 100 m interval running[71]	15.1(1.1)	N/A	YA
20-min circuit training (jog/sprint/push-up/sit-up/step-up)[72]	15.6(0.8)	N/A	YA
20-min circuit training (jog/sprint/push-up/sit-up/step-up)[70]	15.9(2.4)	N/A	AT
10 x 400 m interval running[71]	16.0(1.2)	N/A	YA
60-min fatiguing exercise(agility/balance ball/ankle exercise)[74]	16.6(2.6)	N/A	YA
20-min circuit training (jog/sprint/push-up/sit-up/step-up)[45]	17.1	N/A	AT
20-min circuit training (jog/sprint/push-up/sit-up/step-up)[78]	17.8(1.7)	N/A	YA
Circuit training (sprints/jumps/side steps)[23]	18*	N/A	AT
20-min circuit training (jog/sprint/push-up/sit-up/step-up)[44]	18.1(0.3)	N/A	YA
Multi-ball training session (practicing topspin, backspin, etc.)[73]	18.5(1.1): men	N/A	AT
90-min shuttle run protocol (submaximal and maximal sprints)[34]	19.0(1.0)	N/A	AT
Multi-ball training session (practicing topspin, backspin, etc.)[73]	19.3(0.5): women	N/A	AT
Circuit training(sprint/sidestep/jumping/landing/shifting) until task failure [22]	N/A	10	AT
Extent of maximal RPE value(s) of 6-20 Borg (n=11) and CR10 (n=1)	***15.9-19.3***	***10***	N/A
Physical activity protocol (n=3)			
14-min moderate exercise (step-ups/lunges/stepping over obstacles)[21,31,32]	13.0*	N/A	YA/OA
Sports match (n=2)			
90-min soccer match [75]	15.2	N/A	AT
Competitive badminton match[76]	N/A	7.5(2.1)	AT
Extent of maximal RPE value(s) of 6-20 Borg (n=1) and CR10 (n=1)	***15.2***	***7.5***	N/A
Occupational task			
27-min high intensity load carrying treadmill walking with incremental	19.0(STB)	N/A	YA
speed and grade, with wearing different military boots (STB vs MTB)[25]	19.0(MTB)	N/A	YA
Extent of maximal RPE values after mixed exercise	**13.0-19.3**	**7.5-10**	
Extent of maximal RPE values after all types of exercise	**10.4-20.0**	**0.9-10**	

Table 4. Spearman's correlations between exercise-induced RPE values (all Borg scales vs. 6-20 Borg vs. CR 10) and maximal postural control changes (MPCC) from pre to post-exercise in the included studies. n: number of data points in a given set (RPE and MPCC); r: Spearman's correlation coefficient; CI: confidence interval.

Items	r	95% CI of r	p-value
RPE values of all Borg scales and MPCC (n=52)	0.169	-0.102–0.417	0.230
RPE values of 6-20 Borg Scale and MPCC (n=35)	0.252	-0.101–0.563	0.144
RPE values of CR10 and MPCC (n=17)	0.345	-0.224–0.716	0.175

Table 5. Spearman's correlations between maximal exercise-induced changes in different postural control variables (COP sway parameters vs. COP displacement vs. COP velocity vs. COP area vs. stability index) and exercise-induced RPE values of Borg scales in the included studies. Stability index/score included overall stability index and balance error score. n: number of data points in a given set (RPE and MPCC); r: Spearman's correlation coefficient; CI: confidence interval.

Items	r	95% CI of r	p-values
COP sway parameters and RPE (n=35)	0.247	-0.760–0.526	0.153
COP sway displacement and RPE (n=12)	0.179	-0.535–0.772	0.578
COP sway velocity and RPE (n=13)	0.300	-0.715–0.330	0.319
COP sway area and RPE (n=8)	0.443	-0.316–0.975	0.272
Stability index/score and RPE (n=8)	0.643	-0.103–0.950	0.086

Table 6. Spearman's correlations between RPE values of Borg scales with postural control changes immediately following the different types of exercise (Aerobic vs. Anaerobic vs. Mixed) in the included studies. n: number of data points in a given set (RPE and MPCC); N/A: In case n < 7; r: Spearman's correlation coefficient; CI: confidence interval.

Items	r	95% CI of r	p-values
RPE and MPCC after all aerobic exercise (n=28)	0.243	-0.095–0.526	0.212
Running (n=11)	0.255	-0.570–0.917	0.450
Cycling (n=9)	-0.235	-0.815–0.581	0.542
Walking (n=8)	0.707	-0.105–1.000	0.050
RPE and MPCC after all anaerobic exercise (n=19)	0.134	-0.640–0.381	0.584
Resistance exercise (n=16)	-0.103	0.716–0.505	0.703
Cycling or running at maximal speed	N/A	N/A	N/A
RPE and MPCC after all mixed exercise (n=21)	0.279	-0.258–0.643	0.221
High intensity circuit/interval training	-0.175	-0.815–0.484	0.587
Sport match/physical activity and occupational tasks	N/A	N/A	N/A

Table 7. Spearman's correlations between exercise-induced RPE values (all Borg scales vs. 6-20 Borg vs. CR 10) and maximal postural control changes (MPCC) from pre to post-exercise with regards to different populations (young adults vs. athletes vs. older adults) in the included studies. n: number of data points in a given set (RPE and MPCC); r: Spearman's correlation coefficient; CI: confidence interval.

Items	r	95% CI of r	p-values
RPE values of all Borg scales and MPCC in young adults (n=37)	**0.351***	0.060–0.582	0.033
6-20 Borg and MPCC (n=24)	**0.513***	0.096–0.792	0.010
CR10 and MPCC (n=13)	0.418	-0.258–0.845	0.156
RPE values of all Borg scales and MPCC in athletes (n=11)	0.027	-0.641–0.583	0.936
6-20 Borg and MPCC (n=9)	0.084	-0.690–0.670	0.831
CR10 and MPCC (N/A)	N/A	N/A	N/A
RPE values of all Borg scales and MPCC in older adults (n=9)	-0.664	-0.986–0.098	0.051
6-20 Borg and MPCC (N/A)	N/A	N/A	N/A
CR10 and MPCC (N/A)	N/A	N/A	N/A

Research article 2

Sex differences in central and peripheral fatigue induced by sustained isometric ankle plantar flexion

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Keywords

Exercise, neuromuscular fatigue, central fatigue, peripheral fatigue, and sex

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Abstract

The main aim of this study was to determine sex differences in central and peripheral fatigue produced by a sustained isometric exercise of ankle plantar flexors in healthy young adults. Ten males and fourteen females performed a sustained isometric ankle exercise until task failure. Maximal voluntary isometric contraction (MVIC) torque (plantarflexion), voluntary activation level (using the twitch interpolation technique), and resting twitch contractile properties [twitch peak torque (ST), twitch half relaxation time, and low frequency fatigue (LFF) ratio] were measured before, immediately after, and throughout a recovery period (1, 2, 5, and 10 min) following the exercise protocol in order to characterize neuromuscular fatigue. Fatigue had effects ($p \leq 0.05$) on all dependent variables (reduction in MVIC, VA and twitch torque and slowing of relaxation time). However, no significant differences in performance fatigability markers (MVIC torque decline and time to fatigue) and only minor differences in the variables reflecting central and peripheral fatigue mechanisms were found between males and females. A regression analysis did suggest a somewhat greater role of central fatigue in males compared with females. Females also showed a slightly greater and more prolonged decline in ST and LFF after exercise compared with males. The presence of only minor differences in central and peripheral fatigue mechanisms between males and females in the present study could be explained by the lack of important sex differences in performance fatigability, which could be due to lesser sex differences in the relative area of type I muscle fibers and in contractile function (muscle strength) of ankle plantar flexors as compared with other muscle groups.

1. Introduction

The limits of an individual's performance during athletic events, occupational tasks, daily activities, or exercise can be partly explained by fatigue associated with acute changes in the neuromuscular system [Hunter, 2018]. The concept of performance fatigability (in contrast to perceived fatigability) has been used to describe "the decline in an objective measure of performance over a discrete period" [Enoka and Duchateau, 2016]. Performance fatigability can be reflected in the observation of a loss in the ability to generate muscle force (or power) over time or in the time taken to reach task failure during a submaximal exercise in a laboratory setting [Enoka and Duchateau, 2016; Kluger et al., 2013]. Performance fatigability is dependent on the contractile function of a given muscle and the capacity of the central and peripheral nervous system to sustain activity during the involved task [Enoka and Duchateau, 2016].

In an attempt to organize and clarify the role of these limiting factors, neuromuscular fatigue has been divided into two components, central and peripheral fatigue [Enoka and Duchateau, 2016]. Central fatigue represents a progressive exercise-induced reduction in the neural drive to muscle (termed voluntary activation (VA)) [Gandevia, 2001]. Such a decrease in VA has been found for various muscles (e.g., ankle dorsiflexors, knee extensors, and elbow flexors) in healthy young adults [Akagi et al., 2019; Albert et al., 2006; Kavanagh et al., 2020; Kent-Braun et al., 2002; Lee et al., 2017; Martin and Rattey, 2007; Russ and Kent-Braun, 2003; Yoon et al., 2007]. In contrast, peripheral fatigue is caused by processes occurring at or distal to the neuromuscular junction [Gandevia, 2001]. Peripheral fatigue can be assessed by looking at changes in twitch contractile properties of a given fatigued muscle by electrically stimulating the peripheral nerve while the muscle is at rest. Such fatigue-induced alterations generally include: reduced twitch peak torque (Taylor and Gandevia, 2008), increased twitch half-relaxation time (Boyas et al., 2013; Smith-Ryan et al., 2014) and decreased low frequency fatigue (LFF) index (ratio of low frequency twitch torque to high frequency twitch torque) (Vøllestad, 1997).

Males have been shown to generally exhibit greater performance fatigability for various muscle groups compared with females for isometric fatiguing tasks, although such sex differences are less evident for dynamic fatiguing exercise (concentric and eccentric contractions) [Hunter, 2016]. For example, several previous studies of sustained/intermittent isometric fatiguing exercise have reported that males show a shorter time to task failure or a greater reduction in torque with fatigue of different muscle groups such as: finger flexors and forearm (Hunter et al., 2009, 2006b), elbow flexors (Hunter et al., 2002; Hunter and Enoka, 2001; Kavanagh et al., 2020), adductor pollicis (Fulco et al., 1999), back extensors (Clark et al., 2003), ankle dorsiflexors (Russ and Kent-Braun, 2003), and knee extensors (Clark et al., 2003; Maughan et al., 1986). However, ankle muscles have shown less pronounced sex differences in fatigability as compared with other muscle groups (especially elbow flexors) [Hunter, 2018, 2016, 2014], potentially due to larger area of type I (fatigue resistant) muscle fibers of the ankle compared with other muscle groups (Coggan et al., 1992; Larsson et al., 2006; Miller et al., 1993; Staron et al., 2000). For example, Avin and colleagues (2010) found a smaller sex difference in time to failure during a sustained isometric exercise of ankle dorsiflexors (female > males: 9%) compared to elbow flexors (female > males: 40 %). However, such sex differences have only been sparsely studied in ankle plantar flexors [Hunter, 2016].

The greater fatigability in males compared with females has been suggested to be due to a lesser oxidative metabolic capacity [Russ et al., 2005], a smaller proportion of fatigue-resistant muscle fibers (type I) within skeletal muscles [Toft et al., 2003], and a greater reduction in neural drive to muscles during fatiguing tasks [Russ and Kent-Braun, 2003] in males compared with females. Sex differences in these fatigue mechanisms (related to contractile function and muscle activation) have been indirectly determined by comparing twitch contractile properties (peripheral fatigue) and VA (central fatigue) between males and females in a limited number of studies. Furthermore, these studies have shown inconsistent findings concerning the respective role of central and peripheral fatigue in males versus females during sustained or intermittent isometric exercise, in contrast to the consistent observation of greater performance fatigability in males compared with females. For example, studies of knee extensors and elbow flexors [Akagi et al., 2019; Albert et al., 2006; Hunter et al., 2006; Kavanagh et al., 2020; Yoon et al., 2007] have observed greater peripheral fatigue in males compared with females, but no differences in central fatigue. In contrast, studies of knee extensors and ankle dorsiflexors [Martin and Rattey, 2007; Russ and Kent-Braun, 2003] found greater central fatigue in males compared with females, but showed no sex differences in peripheral fatigue.

Altogether, although males have typically shown greater performance fatigability than females during isometric exercise, sex differences in neuromuscular fatigue have only been sparsely studied for ankle plantar flexors, despite the primary role of this muscle group in standing stability [Loram and Lakie, 2002]. Our main aim was to determine sex differences in central and peripheral fatigue of ankle plantar flexors during a sustained isometric exercise in healthy young adults. Based on the limited literature available [see Hunter, 2016; Martin and

Rattey, 2007], it was hypothesized that a small difference in performance fatigability favoring males compared with females would be associated with greater central, but not peripheral fatigue in the former group.

2. Methods

2.1. Participants and data exclusion

Fifteen males and fifteen females initially volunteered for this study, of which five males and one female were excluded due to exceptionally low levels of VA at pre-exercise (< 70%; n = 1) or post-exercise (< 50 %; n = 3) and technical issues with the timing of the electrical stimulus (n = 2). The results of the remaining ten healthy young males (27.3 ± 5.3 years; 183.5 ± 5.8 cm; 91.5 ± 11.4 kg) and fourteen healthy young females (29.4 ± 4.9 years; 167.4 ± 7.3 cm; 62.9 ± 9.8 kg) are reported. Participants had no neurological disorders or musculoskeletal injuries to the lower leg, as confirmed by a health questionnaire. Both sex groups (overall: 8.6 ± 2.2 out of 15) showed a similar moderate-to-high physical activity level (males: 9.5 ± 2.4 vs. females: 8.0 ± 1.9), as reported on a habitual physical activity questionnaire associated with work, sport, and leisure time [Baecke et al., 1982]. The study was approved by the research ethics boards of the University of Ottawa (# H11-14-23) and Bruyère Continuing Care (#M16-08-038). Participants were informed of all procedures before enrolling in the study.

2.2. Experimental procedure

All participants volunteered for a single session, which was held during regular daytime hours (between 9am and 5pm). Participants were asked to avoid strenuous or prolonged physical activity for 24 hours before their session. The protocol (Figure 1A) began by determining the supramaximal intensity of electrical stimulation at the popliteal fossa needed to generate the maximal twitch torque from ankle plantar flexors of the dominant leg (see below for details). Participants then familiarized themselves with the main task by generating bilateral submaximal intermittent isometric contractions of ankle plantar flexors in a sitting position on a dynamometer (Figure 1B). Once comfortable with the task, they were asked to perform three maximal voluntary isometric contractions (MVICs) in ankle plantar flexion (approximately 3-5 s in duration), with a 2-min interval between each MVIC. During each MVIC, one doublet stimulus was delivered at the maximum (plateau) of the MVIC torque to record a superimposed doublet torque (dominant leg). Immediately after each MVIC, one doublet stimulus and then one singlet stimulus were delivered with a 2-s interval while the ankle plantar flexors were at rest in order to measure resting double/singlet twitch peak torque (DT and ST, respectively). After these pre-fatigue measures, participants performed a sustained isometric ankle plantarflexion with both legs in a sitting position until task failure in order to produce plantar flexors fatigue. Post-fatigue MVICs were then performed after 1, 2, 5, and 10 min of recovery following the fatiguing exercise. Doublet and singlet electrical stimuli were delivered during and after each MVIC as was done for the pre-fatigue measures, as well as immediately after the exercise.

2.3. MVIC and twitch torque recording

A dynamometer (Biodex System 3 Pro ®, Biodex medical systems, Shirley, USA) was used to record MVIC peak torque, superimposed twitch torque, and DT and ST (all isometric). Participants sat on the dynamometer chair with their hip at about a 80^o angle, legs extended forward and both feet placed on a custom footplate at a 90^o angle (aligning the external malleoli with the center of rotation of the leg apparatus; see Bisson et al., 2012). Their feet, chest, and thighs were secured with non-elastic straps. The torque measurement position and straps were used to minimize the contribution of other body segments/muscle groups to the production of plantarflexion torque.

2.4. Electrical stimulation

Two stimulating electrodes (diameter: 8 mm) were placed longitudinally along the length of the posterior tibial nerve in the popliteal fossa of the dominant leg (Figure 1B). A constant current stimulator (Digitimer DS7AH, Digitimer Ltd, Hertfordshire, United Kingdom) delivered single (pulse duration = 200 µs) and doublet electrical pulses (two consecutive singlet stimuli separated by 10 ms). In order to determine a supramaximal intensity before the pre-fatigue measurements, singlet stimulus intensity was increased until an increase in voltage no longer generated an increment in twitch torque amplitude. The voltage was then increased by 10 to 15% to ensure supramaximal intensity, which was maintained for all subsequent stimuli.

2.5. Fatiguing exercise protocol

A sustained isometric exercise protocol was performed to produce fatigue of ankle plantar flexors. Participants were asked to sit on the dynamometer and keep pushing the footplate (plantarflexion) with both feet for as long as possible while producing a target torque corresponding to 30% of MVIC torque represented by a cursor on a computer screen. The fatiguing protocol stopped when participants no longer produced and maintained the target torque for 3 consecutive seconds, at which point a superimposed doublet was provided to estimate VA at the end of the fatigue task (before the participants were told to relax). Verbal encouragement was given throughout the fatiguing exercise.

2.6. Data analysis

MVIC peak torque, VA, ST, half relaxation time of ST (STHRT), and a LFF ratio were obtained before, immediately after the fatiguing exercise (or at the end of the exercise for VA only), and throughout a 10-min recovery period (1, 2, 5, and 10 min). The half-relaxation time is the time from the twitch peak torque to a 50% reduction in torque amplitude (Froyd et al., 2013). The LFF ratio is quantified by a ratio of ST to DT (Vøllestad, 1997). VA was calculated using the formula (Gandevia, 2001):

$$VA = 100 \times [1 - (superimposed\ doublet\ twitch\ torque \div resting\ doublet\ twitch\ torque)]$$

2.7. Statistical analysis

Minimum sample size required was calculated using G* power (version 3.1.9.4) and shown to be at least 10 participants per group, with a power of 0.95, an effect size of 0.71, and alpha of 0.05. The effect size was estimated from existing data, with respect to sex differences in fatigue-induced reductions in voluntary activation (Martin and Rattey, 2007).

Two-way ANOVAs with one between-subjects [sex (males vs. females)] and one within-subjects [repeated measures over time (pre-fatigue vs. fatigue (immediately or at the end of the exercise) vs. recovery period (1, 2, 5, and 10 min)] factor, were used to analyze the effect of fatigue, sex, and their interaction on the following dependent variables (non-normalized): MVIC peak torque, ST, VA, LFF ratio, and STHRT. In cases where Mauchly's test of sphericity (within-subjects effect) was significant, the Greenhouse-Geisser correction was used to determine significance. Pairwise comparisons and independent T-tests (for main simple, and interactional effects) were performed when significance was detected from the ANOVAs using a Bonferroni correction. Independent T-tests were also performed for determining sex differences in the time to task failure. The alpha level chosen for all analyses was set at 0.05.

A Pearson correlation analysis and multiple linear regression analyses were also performed to assess the association/contribution of changes in VA (central fatigue) and ST (peripheral fatigue) to changes in MVIC torque after 1 min of recovery. The linear regression analysis was conducted where all predictors (VA, ST, and sex) were entered into the regression equation at once, with the contributions of the predictors assessed with R^2 value at a significance level of $p < 0.05$. The regression analysis met the following criteria: 1) the association between each predictor and MVIC torque was linear, 2) predictors were not significantly correlated with one another (no multicollinearity), the values of the residuals were 3) independent and 4) normally distributed, 5) the variances of the residuals were constant, and 6) individual data points were not unduly affecting the regression analysis.

3. Results

3.1. Fatigue duration

The average time needed to reach the 70% decrement in MVIC torque (fatigue task duration) was 212 ± 72 s and was not significantly different ($p = 0.28$) between males (189 ± 64 s) and females (229 ± 76 s).

3.2. Maximal voluntary isometric contraction (MVIC) torque

A main effect of fatigue (F (4, 88) = 30.90; $p = <0.001$; partial $Eta^2 = 0.58$) was found for MVIC torque where a significant decrease was observed up to 5-10 min after exercise (overall: 10 min; and both sex groups separately: 5 min) (Figure 2 and Table 1). Even though there was a significant sex x fatigue interaction for MVIC torque (F (4, 88) = 4.24; p = 0.02; partial Eta^2 = 0.16), post-hoc t-tests comparing percent change in MVIC torque from pre to post fatigue between males (~27 %) and females (~22 %) did not show any significance (1 min: p = 0.35, 2 min: p = 0.89; 5 min: p = 0.07; and 10 min: p = 0.23). A main effect of sex was also significant (F (1, 22) = 12.92; p = 0.002; partial Eta^2 = 0.37), with males showing overall greater MVIC torque values (~48%) compared with females (Table 1).

3.3. Voluntary activation (VA)

A main effect of fatigue (F (5, 110) = 37.47; p = <0.001; partial Eta^2 = 0.63) was found for VA, where a significant decrease was observed at the end of exercise (overall: 35%; males: 38%; females: 33%), but quickly recovered (Figure 3 and Table 1). No significant effect of sex (F (1, 22) = 1.72; p = 0.20; partial Eta^2 = 0.08) nor a sex x fatigue interaction (F (5, 110) = 0.61; p = 0.61; partial Eta^2 = 0.03) were found for VA.

3.4. Resting singlet twitch peak torque (ST)

ST showed a main fatigue effect (F (5, 110) = 21.56; p = <0.001; partial Eta^2 = 0.50), where it was significantly decreased up to ~2 min after exercise (males and females combined); but with females presenting with a longer time to recover (>10 min vs 1 min for males) (Figure 4A and Table 1). The sex x fatigue interaction for ST was not significant (F (5, 110) = 1.28; p = 0.29; partial Eta^2 = 0.06), but a main effect of sex was found (F (1, 22) = 25.10; p = <0.001; partial Eta^2 = 0.53), where males showed greater ST values (~80 %) compared with females (Table 1).

3.5. Low frequency fatigue (LFF) ratio

The LFF ratio showed a main fatigue effect (F (5, 110) = 4.42; p = 0.02; partial Eta^2 = 0.17), with the ratio significantly decreased immediately after exercise and at 1 min of recovery. When separated for each of the sex groups, post hoc tests for the effect of fatigue showed a significant decrease for only females at 1 min post-fatigue (Figure 4B and Table 1). However, we found no significant main effect of sex (F (1, 22) = 2.02; p = 0.17; partial Eta^2 = 0.08) nor a sex x fatigue interaction (F (5, 110) = 1.12; p = 0.34; partial Eta^2 = 0.05).

3.6. Singlet half relaxation time (STHRT)

STHRT showed a main fatigue effect (F (5, 110) = 46.95; p = <0.001; partial Eta^2 = 0.68), where STHRT was significantly increased up to 1 min after fatigue (Figure 4C). No significant sex x fatigue interaction was found for STHRT (F (5, 110) = 1.01; p = 0.39; partial Eta^2 = 0.04). A main sex effect was found (F (1, 22) = 5.26; p = 0.03; partial Eta^2 = 0.19), with females presenting with longer STHRT values (~27 %) compared with males (Table 1).

3.7. Pearson's correlation and multiple regression analyses

Changes in VA and ST both contributed to the pre to 1 min post-exercise change in MVIC torque with all participants (males and females) included in the model. By contrast, only VA contributed to the MVC torque change in males. None of the predictor variables reached significance in the separate model with only females included (Tables 2 and 3).

4. Discussion

The main aim of this study was to determine sex differences in central and peripheral fatigue produced by isometric ankle plantar flexors exercise in healthy young adults. Partly in accordance with our hypothesis, only small (mostly non-significant) differences were found in performance fatigability markers (MVIC torque decline and time to fatigue) and in the behavior of variables reflecting central and peripheral fatigue mechanisms between males and females. Mainly, no significant interaction between sex and fatigue was found for any of the dependent variables except for MVIC torque (significant in ANOVA but not in post-hoc t-tests). The regression analysis did suggest a greater role of central fatigue in males compared with females. Females also showed a slightly greater and more prolonged decline in ST and LFF after fatigue compared with males.

4.1. Overall fatigue (performance fatigability)

We observed a significant exercise-induced decrease (~24 %) in MVIC peak torque, which had not fully recovered 10 min following exercise. This is in line with previous findings, which showed a 30% reduction observed immediately after a 25% MVIC isometric exercise [Boyas et al., 2013], and also prolonged reductions following isometric exercise [Kennedy et al., 2011] for the same muscle group. Such performance fatigability can result from decreased contractile function within fatigued muscle (peripheral fatigue) and also reduced capacity of the nervous system to provide descending commands (central fatigue) for task performance [Enoka and Duchateau, 2016].

4.1. Central fatigue

We found a significant decrease in VA at the end of the fatigue task, when participants were assumed to be producing a maximal effort but failing to reach the 30% of MVIC target. The decreased VA then quickly recovered by 1 min after the termination of the fatigue task. These results are in line with previous findings showing reduced VA of ankle plantar flexor muscles immediately after a sustained 25% MVIC until exhaustion [Boyas et al., 2013] and also with studies showing a quick recovery, for example within 1 min or 2 min following fatigue of elbow extensors [Bilodeau, 2006] and ankle plantar and dorsiflexors [Kennedy et al., 2011], respectively. Such central fatigue has been suggested to be a significant contributor to performance fatigability (declined MVIC torque) during sustained low-intensity fatiguing exercise (e.g., see Taylor and Gandevia, 2008) compared with high-intensity exercise, with reduced contractile function being preferentially involved (see a review by Westerblad et al., 2010). This in line with the findings of the Pearson's correlation and regression analyses of the present study, which showed greater contributions of VA to pre to 1 min post-exercise MVIC torque changes compared with ST (Tables 3 and 4) for our low-intensity fatigue task.

4.2. Peripheral fatigue

Our results showed fatigue effects on twitch contractile properties, as reported in previous studies: reduced ST [Akagi et al., 2019; Kavanagh et al., 2020; Taylor and Gandevia, 2008], decreased LFF ratio [Keeton and Binder-Macleod, 2006; Vøllestad, 1997], and increased STHRT [Boyas et al., 2013; Kent-Braun et al., 2002; Martin and Rattey, 2007; Smith-Ryan et al., 2014]. These changes reflect potential alterations in neurotransmission and/or excitation–contraction coupling mechanisms and indicate the presence of peripheral fatigue [Hunter, 2018; Michaut et al., 2003]. More specifically, the reduction in ST immediately post-exercise observed here (Figure 4A) is in accordance with prior results from our group [Boyas et al., 2013] using a similar fatigue criterion (25% MVIC) in the same muscle group. A sustained reduction in ST by 10 min post-exercise is also in line with previous findings [Russ and Kent-Braun, 2003] showing a 14-min sustained decrease in ST following exercise of ankle dorsiflexors. Such decreases in the twitch peak torque potentially reflect metabolic inhibition of the muscle contractile processes, such as resulting from the fall in pH level within the fatigued muscle [Kent-Braun, 1999]. A decrease in the LFF ratio, which indicates the greater loss of ST compared to DT, was also statistically noted by 1min after the fatigue task (Figure 4B). This reduction potentially indicates decreased Ca^{2+} release from the sarcoplasmic reticulum and a related decrease in the amount of Ca^{2+} binding to myofilaments possibly limiting the amount of muscle force produced [Keeton and Binder-Macleod, 2006; Vøllestad, 1997]. Lastly, significant increases in STHRT were shown by 1 min after exercise (Figure 4C). Such slowing of muscle relaxation may result from slowing of Ca^{2+} re-uptake by the sarcoplasmic reticulum and slowed Ca^{2+} detachment from myofilaments [Allen et al., 2008; Neyroud et al., 2016].

4.3. Minimal sex differences in central and peripheral fatigue

We found no sex X fatigue interactions for changes in VA and all twitch torque-related variables in healthy young adults with a submaximal fatiguing exercise performed with the ankle plantar flexors, as found in previous studies of elbow flexors [Yoon et al., 2007] and knee extensors [Lee et al., 2017]. These findings are not surprising given the lack of significant differences in performance fatigability (reduced MVIC torque and time to task failure) between the sex groups in the present study.

In contrast to what has been reported for other lower extremity muscle groups [Akagi et al., 2019; Martin and Rattey, 2007; Russ and Kent-Braun, 2003], such overall lack of significant difference in fatigue mechanisms (as well as in performance fatigability) between males and females could be explained by a lesser sex difference in the relative area of type I (fatigue resistant) muscle fibers of ankle plantar flexors compared with other muscle groups [Coggan et al., 1992; Larsson et al., 2006; Miller et al., 1993; Staron et al., 2000]. This is because the relative area of type I fibers within a given muscle(s) can affect muscle contractile processes, but also have an impact on central processes through Group III and IV afferents, and therefore influence performance fatigability of the muscle [Hunter, 2016, 2014]. The present lack of sex differences is supported by the findings of a systematic review summarizing 46 studies of various fatigued muscles (Hunter 2016, see their Figure 2), where it is reported that ankle plantar flexors showed a smaller sex difference (less than 5 %) in performance fatigability, as compared with other muscle groups (especially elbow flexors; ~ 60 %).

Furthermore, muscle strength can affect the accumulation of perfusion-related metabolites in muscle, especially during isometric exercise, which may contribute to peripheral and central fatigue of a given muscle (Hunter 2016). Although we found significant sex differences in contractile function of ankle plantar flexors (MVIC and ST greater and STHRT shorter in males versus females), such differences (MVIC: 48% and ST: 80%) were less pronounced compared to those reported for other muscle groups; for example, greater MVIC torque (121 %) and resting twitch torque (153 %) for elbow flexors in males compared to females [Kavanagh et al., 2020]. This lesser sex difference in contractile function could partly explain the lack of sex difference in fatigue mechanisms as well as in performance fatigability in the present study. This is supported by previous studies showing similar performance fatigability of elbow flexors during sustained isometric exercise when matching for muscle strength between sex groups (e.g., see Hunter et al., 2004). Such effects of muscle strength (or contractile function) can be associated with sex differences in muscle mass (males were 29 kg heavier than females, see section 2.1).

Despite the lack of significant sex X fatigue interactions in variables reflecting central and peripheral mechanisms, we found that only males presented with a significant contribution of VA to the reduction in MVIC torque with fatigue (from pre to 1 min following exercise) according to the Pearson's correlation (Table 2) and multiple regression analyses (Table 3 and Figure 5). These results were accompanied by males showing a slightly more pronounced decrease (~5 %) in VA with fatigue compared with females (Figure 3). By contrast, only females presented with a significant decrease in LFF ratio at 1 min following exercise due to a relatively greater (~6 %) and longer reduction for ST compared to males (Figure 4A and B). These results suggest that males had a greater but non-significant contribution of central fatigue to performance fatigability, whereas females showed a more pronounced change in peripheral fatigue and related longer recovery. These differences, however, were not important enough to lead to significant sex x fatigue interactions with regards to the extent of central and peripheral fatigue, as well as performance fatigability.

A few limitations should be considered for the present study. Given the report that mechanisms responsible for central and peripheral fatigue can interact with one another and also be affected by other physiological and psychological factors (e.g., blood glucose, mood, pain, etc.) [Enoka and Duchateau, 2016], multifaceted measures documenting central and peripheral fatigue mechanisms should be considered in future studies. Within this context, the recording and analysis of EMG signals could have provided interesting complementary information to the present data. Although we had initially set out to record EMG signals from ankle muscles, we encountered a technical problem with our amplifier which led to non-physiological signals being recorded for most of our participants and therefore, could not be included in the present paper. We believe that the information provided is, however, still rather comprehensive and valuable. We did not obtain information on the phases of the menstrual cycle in female participants, which has been reported to affect both muscle strength and fatigue due to various steroid hormonal levels across the phases (Pallavi et al., 2017). However, this would likely not be a major confounding factor to sex differences in muscle fatigue, given the smaller effect of the menstrual cycle on fatigability compared to other general sex differences in fatigability (Hunter, 2016). Nevertheless, this study provides useful information regarding sex-specific responses to fatiguing exercise (in this case similar responses between males and females), which may inform the areas of physical training or rehabilitation exercise, given the reported sex differences in physical ability and potential injury risk during physical demanding tasks/sports (Arendt and Dick, 1995; Deitch et al., 2006; Swanik et al., 2007; Tessier-Sherman et al., 2014; Zelisko et al., 1982).

5. Conclusion

We observed only minor (mostly non-significant) sex differences in performance fatigability and fatigue mechanisms of ankle plantar flexors between young males and females. Our results suggest that males had a somewhat greater contribution of central fatigue (VA) as compared with females, who presented with slightly greater and longer lasting peripheral fatigue (ST and LFF). However, there were no significant sex x fatigue interactions for any of the dependent variables reflecting central or peripheral fatigue mechanisms. This lack of sex differences may be explained by the relatively small differences in performance fatigability and contractile function between males and females for ankle plantar flexors compared with other muscle groups.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Acknowledgement

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Table 1. Mean values (standard deviation) of all dependent variables. These values (MVIC torque, VA, ST, LFF ratio, and STHRT) changed before and immediately following fatiguing exercise, and throughout recovery (1, 2, 5, and 10 min).

	Variables	Mean values (standard deviation)					
		Pre	*Post 0*	*Post1*	*Post 2*	*Post 5*	*Post 10*
Overall (n=24)	MVIC (N/m)	136.3(39.6)	n/a	103.3(33.2)***	110.2(31.4)***	120.6(30.9)***	124.0(32.2)**
	VA (%)	92.8(6.0)	60.7(17.7)***	85.3(17.7)	87.5(13.1)	90.5(9.5)	93.3(9.1)
	ST (N/m)	20.6(7.9)	15.0(6.3)***	17.8(7.2)*	18.3(6.9)	18.7 (6.8)	17.7(6.3)
	LFF ratio (%)	64.8(9.7)	56.8(6.1)*	59.5(8.9)**	61.1(6.9)	62.2(8.0)	60.8(9.7)
	STHRT (sec)	0.09(0.02)	0.14(0.03)***	0.10(0.02)*	0.09(0.01)	0.08(0.02)	0.08(0.02)
Males (n=10)	MVIC§	168.4(33.0)	n/a	121.9(33.7)**	127.5(28.6)**	141.7(25.6)**	146.0(25.0)
	VA	91.6(7.1)	57.7(20.0)***	81.1(25.9)	81.9(15.1)	87.3(12.6)	90.0(8.2)
	ST§	26.8(5.6)	20.1(4.6)*	24.1(3.8)	23.8(4.0)	24.4(4.0)	22.6(4.5)
	LFF ratio	61.1(6.2)	57.0(4.9)	57.8(6.5)	59.6(5.2)	58.9(5.2)	57.7(6.7)
	STHRT§	0.08(0.01)	0.12(0.02)***	0.09(0.02)	0.08(0.01)	0.07(0.02)	0.07(0.01)
Females (n=14)	MVIC	113.4(25.9)	n/a	90.0(26.7)***	97.9(28.1)***	105.5(25.4)*	108.3(25.6)
	VA	93.6(5.3)	62.9(16.2)***	88.3(8.7)	91.5(10.3)	92.8(5.8)	91.5(9.9)
	ST	16.2(6.1)	11.3(4.5)***	13.4(5.4)**	14.3(5.7)	14.5(5.2)	14.1(4.9)
	LFF ratio	67.5(11.0)	56.6(6.9)	60.7(10.3)**	62.2(7.9)	64.6(9.0)	62.9(11.1)
	STHRT	0.10(0.02)	0.15(0.04)***	0.11(0.02)	0.09(0.02)	0.09(0.03)	0.08(0.02)

MVIC: maximal voluntary isometric contraction torque, ST: resting singlet twitch peak torque; VA: voluntary activation; LFF: low frequency fatigue; and STHRT: singlet twitch half-relaxation time.

Main and simple effect of fatigue (* = $p < 0.05$, ** = $p < 0.01$, and *** = <0.001) depicting differences from pre values.

Main effect of sex (§ = $p < 0.05$), values in males are significantly greater or lesser than in females.

Table 2. Pearson's correlations between pre-to-post (1min) changes in MVIC torque and central/peripheral fatigue properties. Results are presented for the pooled data and separated for each of the sex groups.

Items	r	95% CI of r	p-values
MVIC and ST	**0.419***	-0.047–0.774	**0.042**
MVIC and ST (males)	0.586	-0.030–0.953	0.075
MVIC and ST (females)	0.440	-0.212–0.835	0.116
MVIC and VA	**0.755****	0.406–0.891	**<0.001**
MVIC and VA (males)	**0.831****	0.594–0.946	**0.003**
MVIC and VA (females)	0.412	-0.048–0.839	0.143

** = $p<0.01$; * = $p<0.05$; MVIC: maximal voluntary isometric contraction; ST: resting singlet twitch peak torque; VA: voluntary activation.

Table 3. Summary of multiple linear regression models. These results are related to the contribution of peripheral and central fatigue parameters (predictors) to fatigue-induced changes (pre to 1min post-exercise) in MVIC torque.

Dependent variable	**Predictors**	**R^2**	**Adjusted R^2**	**Significance F**	**Standardized Coefficients**	**P-values**
ΔMVIC torque	Sex ST VA	0.692	0.645	<0.001	0.175 0.378 0.655	0.175 **0.012** **<0.001**
ΔMVIC torque (males)	ST VA	0.771	0.706	0.006	0.309 0.711	0.160 **0.008**
ΔMVIC torque (females)	ST VA	0.388	0.277	0.067	0.468 0.443	0.073 0.088

Δ: fatigue-induced changes (pre to 1 min post-exercise); MVIC: maximal voluntary isometric contraction; ST: resting singlet twitch peak torque; VA: voluntary activation.

Figure 1. Schematic representation of the experimental procedure (A) and schema of experimental setup (dynamometer; B). Circle: maximal twitch torque generated by the supramaximal intensity of singlet electrical stimuli; SVICs: submaximal voluntary isometric contractions; superimposed twitch torque (STT); MVICs: maximal voluntary isometric contractions; DT: resting doublet twitch torque; and ST: resting singlet twitch torque.

Figure 2. **Changes in maximal voluntary isometric contraction (MVIC) peak torque with fatigue and recovery.** The changes depicted are percent change from pre to post fatigue (1, 2, 5, and 10 min). *** (p<0.001), ** (p<0.01) and * (p<0.05) indicate significant decreases in MVIC peak torque compared with baseline torque (Pre) for each of males and females as well as for all participants.

Figure 3. Changes in voluntary activation (VA) with fatigue and recovery. The changes are depicted as percent change from pre to post fatigue (1, 2, 5, and 10 min). *** (p<0.001) indicates significant decreases in the VA at post-exercise compared to pre-exercise values (Pre) for each of males and females as well as for all participants.

Figure 4. **Changes in twitch torque-related variables with fatigue and recovery.** The changes are depicted as percent change from pre to post fatigue (1, 2, 5, and 10 min). The variables involve resting singlet twitch peak torques (ST, A), low frequency fatigue (LFF, B) ratio, and singlet twitch half-relaxation time (STHRT, C). *** (p<0.001), ** (p<0.01) and * (p<0.05) indicate significant reductions in the ST, LFF ratio, and STHRT following exercise compared with baseline values (Pre) for each of males (except for LFF) and females as well as for all participants.

Figure 5. Scatter plots related to the multiple regression analysis. Predicted values from the regression analysis, as well as changes in voluntary activation (VA) and resting singlet twitch peak torque (ST) from pre to 1 min post-exercise plotted against changes in maximal voluntary isometric contraction (MVIC) torque: overall (A; also involving the factor "sex" in predicted values), and for each of males (B) and females (C).

Figure 1. Schematic representation of the experimental procedure (A) and schema of experimental setup (dynamometer; B).

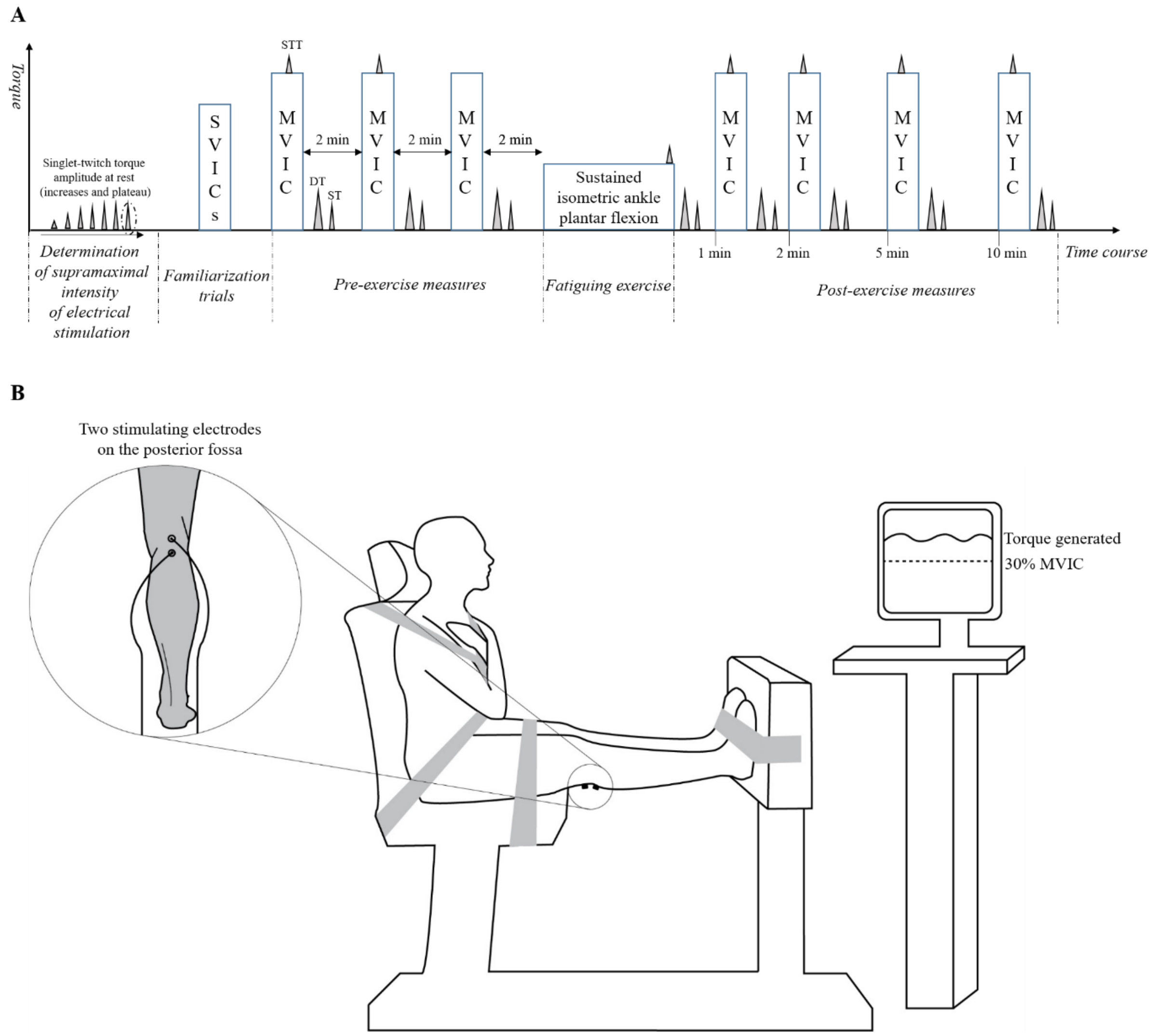


Figure 2. Changes in maximal voluntary isometric contraction (MVIC) peak torque with fatigue and recovery.

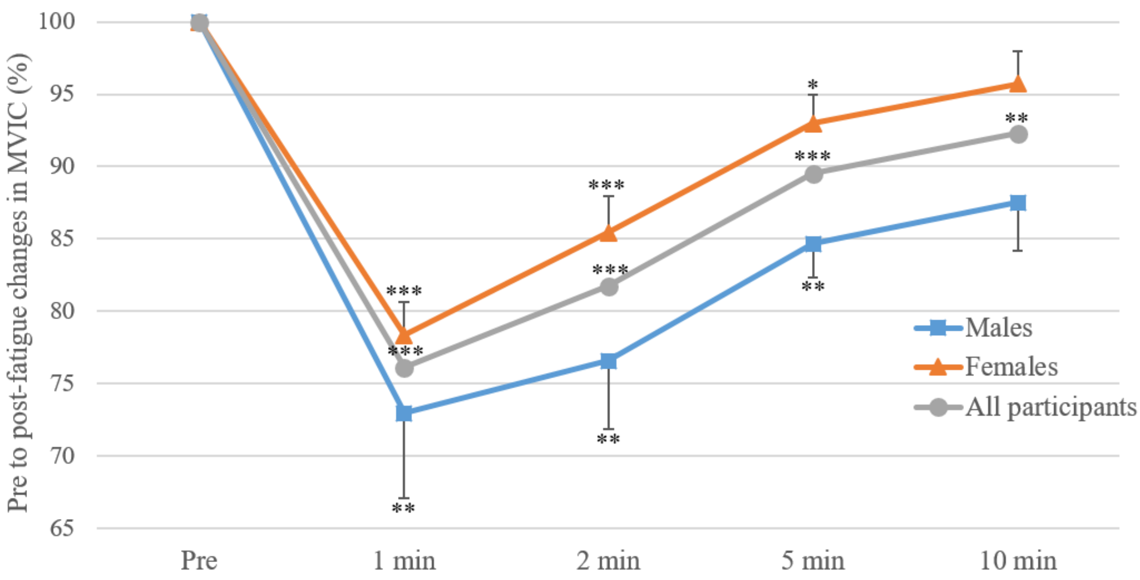


Figure 3. Changes in voluntary activation (VA) with fatigue and recovery.

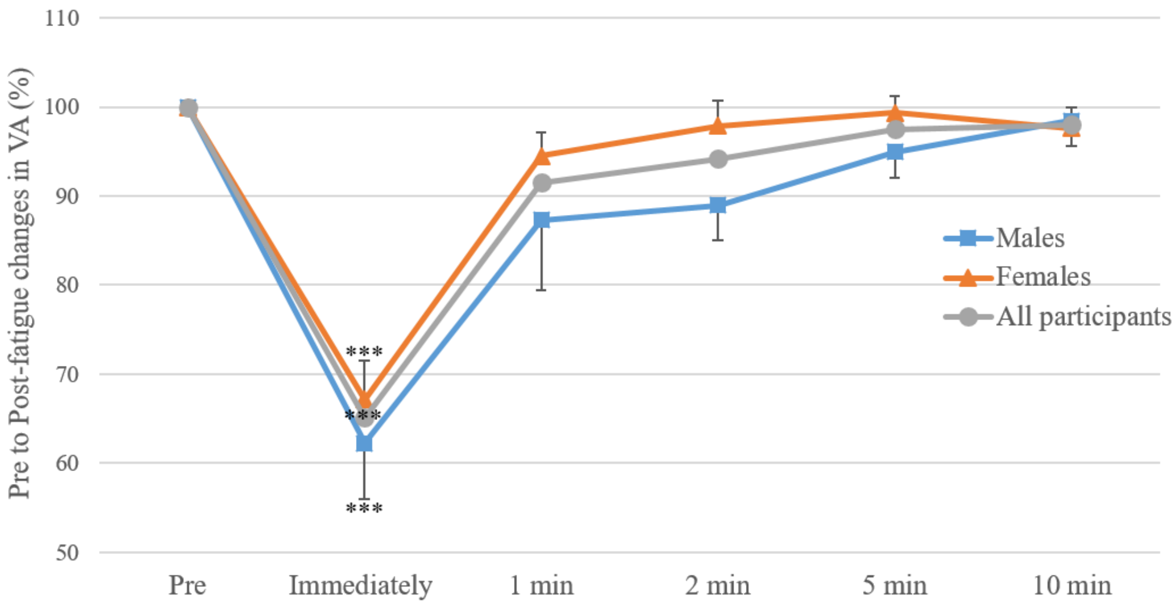


Figure 4. Changes in twitch torque-related variables with fatigue and recovery.

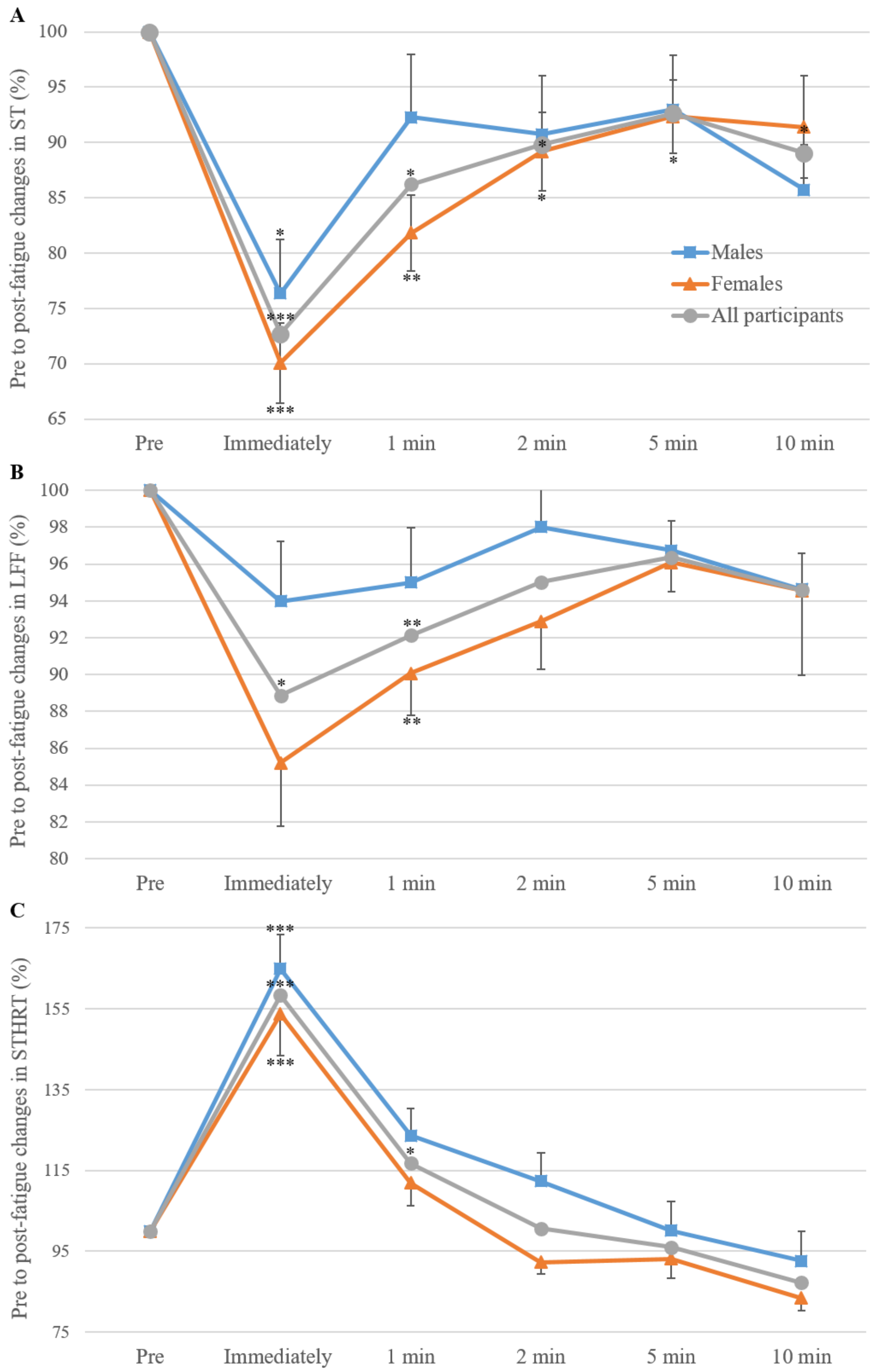
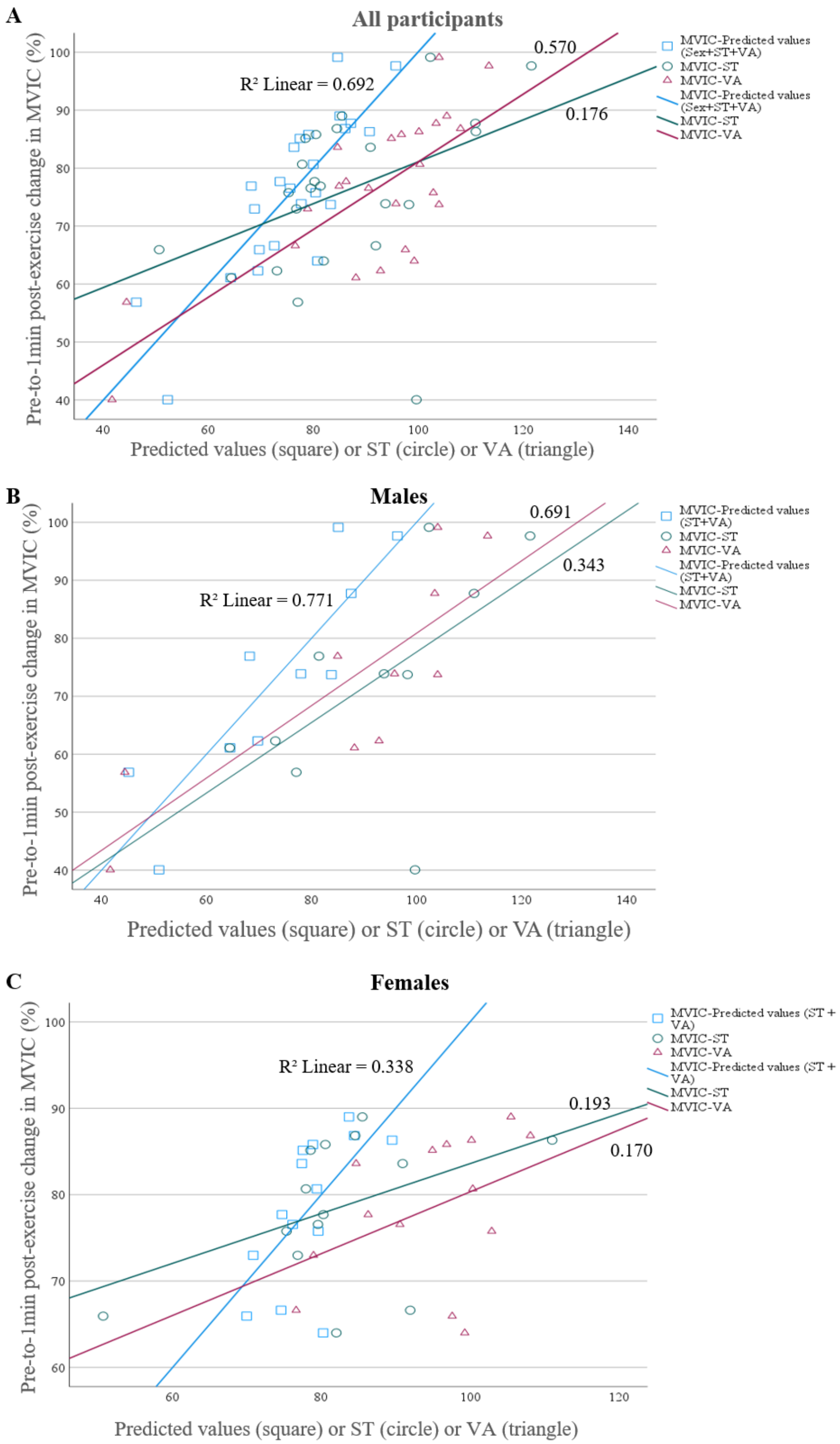


Figure 5. Scatter plots related to the multiple regression analysis.



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Research article 3

Title

Sex differences in the effect of muscle fatigue on static postural control under different vision and task conditions

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Abstract

The main aim of this study was to compare the effects of ankle plantar flexors fatigue on postural control between healthy young adult males and females. The secondary aim was to determine the effects of vision on the fatigue-induced postural changes. Ten healthy young males and nine females were asked to perform quiet standing (QS) and standing forward lean (FL) tasks with eyes open (EO) and closed (EC) before and immediately following exercise, and throughout a 15-min recovery period. A sustained isometric exercise of ankle plantar flexors was performed until participants were no longer able to maintain a target torque of 50% of maximal voluntary isometric contraction (MVIC). Mean anteroposterior (AP) and mediolateral (ML) positions of the center of pressure (COP), mean COP sway velocity, and 95% ellipse area of COP sway were measured. Ankle plantar flexors fatigue had significant effects on all dependent variables, except for sway area. A fatigue X sex interaction was found for sway velocity with the most challenging task condition (FL-EC), where males showed a significant increase in sway velocity up to 15 min following exercise, whereas females did not. Fatigue X vision interactions for AP position were also found, with the withdrawal of vision leading to a greater backward shift during recovery for both the QS (5 to 15 min) and FL (5 to 10 min) tasks. Our findings suggest the use of different postural control strategies with ankle fatigue between males and females, and also a contribution of vision to compensate for fatigue-induced instability that is not dependent on task difficulty.

Introduction

Postural stability is regarded as the capability to control the center of mass with respect to the base of support [1]. To maintain postural stability, the central nervous system must integrate sensory information from the visual, vestibular, and somatosensory systems [2]. The central nervous system must also use this information selectively to produce complex motor responses (i.e., timing, direction, and magnitude), appropriate to the characteristics of the postural stability disturbances of the surrounding environment [2].

Acute exercise-induced muscle fatigue can affect sensory information and motor commands required to regulate postural control [3]. This is supported by review studies [4,5], which conclude that muscle fatigue leads to modifications in the peripheral proprioceptive system and central processing of sensory inputs [4], in addition to the decrements in force production capacity [5]. Fatigue of postural muscles can thus alter or impair postural control performance. Many studies, for example, have found changes in static postural control following strenuous resistance exercise (isometric or isokinetic) of postural muscles (trunk, hip, knee, and ankle) in healthy adults [6–13]. In particular, ankle plantar flexors fatigue induced by such strenuous exercise can lead to significant changes in postural control during upright standing [8,12,14,15]. This can be attributed to the significant role of ankle plantar flexors in regulating active ankle stiffness to maintain postural stability during upright standing [16].

The rate and extent of fatigue can be affected by sex-related physiological differences [17,18], such as: a greater proportion of fatigue-resistant muscle fibers within skeletal muscles [17], lesser neural drive to the muscle [19] and greater oxidative metabolic capacity [20] in females compared to males. Such differences could lead to greater fatigability in males compared with females, especially when performing low-to-moderate isometric exercise [17,18], and this could lead to greater alterations in postural control in males during certain tasks. Only a limited number of studies have looked at sex differences with regards to the effect of fatiguing postural muscles on stability. For example, greater COP sway displacements [21], increased COP velocity (only in males) during one-leg standing [22], and reduced leg-reaching distance [23] have been observed in males compared with females. These findings suggest different postural control strategies between males and females with fatigue. Particularly, an ankle strategy, ankle joint control (or movements) to maintain stability, could be a primary contributor to such difference (e.g., during quiet standing, see [24]). However, the effect of sex on fatigue-related change in postural control is still unclear, including in challenging tasks, such as when leaning forward close to the limit of stability.

Furthermore, vision may affect the extent of fatigue-related changes in postural control depending on the postural task. A few studies [7,25,26] where fatigue of ankle plantar flexors was induced, found greater impairments in postural stability during one-leg standing with eyes closed (EC) compared with eyes open (EO). The withdrawal of vision, however, tended not to lead to greater fatigue-induced postural control changes with relatively easier postural tasks (e.g., quiet standing on both legs) (see [14,27] for example). These contrasting findings suggest that visual information may compensate for fatigue-induced impairments in postural stability depending on task difficulty.

The present study was carried out to provide further information on potential sex differences concerning the effect of ankle fatigue on postural control, and whether such effect could be dependent on postural task difficulty. Given the primary role of ankle muscles in standing stability [16], such information may contribute to basic knowledge of sex differences in injury risks during physically demanding tasks/sports that requires standing postural control in healthy young adults [28–32]. Therefore, the main aim of this study was to determine sex differences in postural control changes generated by fatigue of ankle plantar flexors in healthy young adults in two postural tasks of varying difficulty: a quiet standing (QS) task and a forward lean (FL) task. The secondary aim was to determine the effects of vision (EO vs. EC) on postural changes with fatigue according to task difficulty. It was hypothesized that males would show greater fatigue-induced alterations in postural control compared with females, and such results would be more pronounced under relatively challenging task conditions (e.g., FL-EC) compared to lesser challenging conditions (e.g., QS-EO). Also, the withdrawal of vision would lead to greater fatigue-induced postural changes, which would be more pronounced during the FL task.

Methods

Participants

Ten healthy young males and nine healthy young females volunteered for this study. Participants had no disorders or musculoskeletal injuries (e.g., ankle injury and instability) in the past year that could affect postural control, as confirmed verbally. The study was approved by the research ethics boards of the University of Ottawa (# H11-14-23) and Bruyère Continuing Care (#M16-08-038). All participants were informed of all procedures, and their signed consent was obtained prior to participation in this study.

Experimental procedure

A schematic of the experimental procedure is shown in Figure 1A. All participants volunteered for a single session, which was held during regular daytime hours (between 9am and 5pm). Participants were asked to avoid strenuous or prolonged physical activity for 24 hours before their session. Each participant was first asked to perform two sets of four postural tasks (QS-EO, QS-EC, FL-EO, and FL-EC) barefoot on a force platform. Before these pre-fatigue measures, all participants were allowed to practice each of the task conditions twice, with instructions to keep their body straight (no flexion at the hips) limiting the movement to the ankles when leaning forward and without lifting the heels off the platform. They then performed three bilateral maximal voluntary isometric contractions (MVICs) in ankle plantarflexion with a 2-min interval between each, from which the highest torque was used to set the target torque for the fatiguing exercise to be performed after the MVIC (see below for details). In order to ensure an adequate level of fatigue when testing the four different postural conditions, only two trials were tested (e.g., QS-EO/QS-EC or FL-EO/FL-EC) after the fatiguing exercise, which was repeated a total of four times. Each of the four postural tasks was then assessed at 2, 5, 10, and 15 min following the end of the fourth exercise protocol. The order of the postural tasks was counterbalanced across participants.

Figure 1. Schematics of the experimental protocol. The schematics include experimental procedures (A), and experimental setup for the postural tasks (QS vs. FL) performed on a force platform with the representation of the COP on a computer screen (B) and sustained isometric exercise of ankle plantar flexors on a dynamometer (C). QS: quiet standing; FL: standing forward lean task; EO: eyes open; EC: eyes closed; F1-F4: four submaximal fatiguing isometric

contractions of ankle plantar flexors; MVIC: maximal voluntary isometric contraction; circle: 70 % anterior limit of stability (LOS) target for the FL task; dotted circle: 0% LOS target for the QS task.

Postural tasks

Figure 1B shows a schematic of the experimental setup for the FL and QS tasks. Subjects were asked to align the tip of their toes with a line drawn on the force platform located 17 cm from the center of the platform. For the FL task, the limits of stability (LOS) were first obtained by measuring the maximum excursion of the COP while participants lean the whole body in a standing position (feet together and wearing no shoes) as far as possible forward, backward, and side-to-side on a force platform without lifting the heels and limiting the movement to the ankle. Afterward, participants were asked to track a target (small circle) with a representation of their COP on a computer screen placed in front of them. When the target moved upward to a position representing 70% of the anterior LOS on the force platform, the participants were required to maintain the 70% LOS target as closely as possible for 20 s with EO or EC. For the QS task, they were asked to maintain an initial target (representing 0% LOS of all directions) as closely as possible for 20 s while standing with feet together with EO or EC. For the EC condition, participants were first asked to match the 0% or 70% LOS target with EO and once they felt comfortable, to close their eyes and maintain the memorized target for the recorded 30-s trial.

Fatiguing exercise

Figure 1C shows a schematic of the experimental setup for the fatiguing exercise. Participants sat on the chair of a dynamometer apparatus (Biodex medical systems, Shirley, USA) with their legs straight forward and both feet placed on a footplate (aligning the external malleoli with the center of rotation of dynamometer). Their trunk, thighs, and feet were secured with non-elastic straps. For the fatigue task, they were asked to exert a plantarflexion isometric torque (with both feet) corresponding to 50% MVIC and represented by a trace and target on a computer screen located beside them. The fatiguing protocol stopped when participants no longer produced and maintained the target torque during three consecutive seconds. Verbal encouragement was given throughout.

Data analysis

COP data were recorded using an AMTI AcuGait force platform (Watertown, MA) at a 25 Hz sampling rate. The following variables were obtained from the Balance Trainer Software (version 1.05.02) from the unfiltered data: mean anteroposterior (AP) and mediolateral (ML) COP position (cm; average AP and ML sway displacement from the platform center = $\frac{1}{n} * \sum_{i=1}^{n} x_i$ and $\frac{1}{n} * \sum_{i=1}^{n} y_i$, respectively), mean COP sway velocity (cm/s; path length per unit time = $\frac{l_{path}}{t}$), and the 95% ellipse area of COP sway (cm^2; area of the 95th percentile ellipse = $\pi * \sqrt{F * (x_{sd}^2 + y_{sd}^2 + D)} * \sqrt{F * (x_{sd}^2 + y_{sd}^2 - D)}$): $l_{path} = \sum_{i=2}^{n} \sqrt{(x_i - x_{i-1})^2 + (y_i - y_{i-1})^2}$; D = $\sqrt{(x_{sd}^2 + y_{sd}^2)^2 - 4 * (x_{sd}^2 * y_{sd}^2) - \sigma_{xy}}$; and F statistics = 3.00.

Statistical analysis

The minimum sample size required was calculated using G* power (version 3.1.9.4) and shown to be at least 7 participants per group, with a power of 0.80, an effect size of 0.68, and alpha of 0.05. The effect size was estimated from existing data, with respect to sex differences in AP sway displacement changes produced by ankle plantar flexors fatigue [21].

Independent t-tests were used to compare demographic information of participants (age, height, weight, and BMI) and MVIC torques between males and females. A Pearsons' correlation analysis was conducted to determine the association between each of the four COP variables (mean AP and ML positions, sway velocity, and sway area) at pre-exercise and each of three anthropometric variables (height, weight, and BMI), not only overall but also for males and females separately. These correlations were conducted to determine whether sex differences in the anthropometric variables (e.g., smaller height and lesser weight in females compared to males) would be beneficial for controlling standing stability in females, as suggested in previous studies [3,23,33,34]

Separate three-way ANOVAs with one between-subject and two within-subject factors were used to assess the effects of fatigue [pre-fatigue vs. fatigue (immediately) vs. recovery (2, 5, 10, 15 min)], vision [EO vs. EC], sex (males and females) and their interactions for each of the QS and FL tasks on the four COP variables (mean AP and ML positions, sway velocity, and sway area). If Mauchly's test of Sphericity (within-subjects effect) was significant ($\leq$ 0.05), the Greenhouse–Geisser correction was used to determine significance. When the ANOVAs depicted significance, *post-hoc* t-tests with Bonferroni corrections were performed. In order to assess the impacts of the anthropometric variables on the COP variables according to fatigue and related interactions, the ANOVAs were performed and compared with the four types of COP data: 1) non-normalized, and normalized by 2) height, 3) weight and 4) BMI.

Results

Baseline information and measures

Height, weight, and MVIC torque were found to be significantly greater in males compared with females, while age and BMI were not (see details in Table 1). There were significant moderate-to-high negative correlations between both body height and weight and mean AP COP position (overall, as well as in females; see details in Table 2). No significant correlation was noted for the other COP variables (overall and in both females and males), except for sway area, with only males showing a significant correlation with height (r = 0.641; CI = 0.158 – 0.947; and p = 0.046) for the QS-EC task.

Table 1. Sex differences in demographics and MVIC

	Mean (SD)			P-values
	Overall	Males	Females	
Age (years)	25.3 (3.3)	25.6 (3.9)	25.0 (2.6)	0.702
Height (cm)	171.9 (10.1)	178.7 (7.6)	164.3 (6.5)	**<0.001**
Weight (kg)	75.2 (16.7)	85.6 (15.4)	63.5 (8.2)	**0.001**
BMI (kg/m^2)	25.6 (4.6)	26.9 (5.2)	23.5 (2.7)	0.091
MVIC torque (Nm)	219.4 (53.3)	245.7 (51.1)	190.1 (39.8)	**0.017**

BMI: body mass index = weight/(height)^2; MVIC: maximal voluntary isometric contraction.

Table 2. Results of Pearsons' correlation analysis of mean AP COP position with body height and weight.

Group	COP variable	Tasks	Height			Weight		
			r	95% CI of r	P-value	r	95% CI of r	P-value
Overall (n=19)	AP COP mean position	QSEO	**-0.629****	-0.81 – -0.39	0.004	**-0.514***	-0.83 – -0.23	0.024
		QSEC	**-0.547***	-0.79 – -0.25	0.015	**-0.495***	-0.82 – -0.17	0.031
		FLEO	-0.414	-0.68 – -0.11	0.078	-0.439	-0.80 – -0.12	0.060
		FLEC	**-0.533***	-0.78 – -0.21	0.019	**-0.526***	-0.83 – -0.24	0.021
Males (n=10)	AP COP mean position	QSEO	-0.192	-0.60 – 0.47	0.595	0.246	-0.34 – 0.80	0.494
		QSEC	0.151	-0.53 – 0.77	0.676	0.336	-0.20 – 0.81	0.342
		FLEO	0.392	-0.25 – 0.90	0.263	0.367	-0.35 – 0.76	0.296
		FLEC	0.386	-0.28 – 0.92	0.271	0.296	-0.47 – 0.70	0.406
Females (n=9)	AP COP mean position	QSEO	-0.406	-0.81 – 0.26	0.278	**-0.749***	-0.97 – -0.28	0.020
		QSEC	-0.458	-0.86 – 0.17	0.215	**-0.797***	-0.96 – -0.58	0.010
		FLEO	-0.250	-0.74 – 0.45	0.517	**-0.691***	-0.96 – 0.12	0.039
		FLEC	-0.388	-0.83 – 0.26	0.302	-0.637	-0.97 – 0.02	0.065

r: correlation coefficient; CI: confidence interval.

Fatiguing bouts duration

There were no significant sex differences in the duration of fatigue bouts, even though males presented with somewhat longer mean times to failure (± standard deviation) for the first (159.8 ± 69.7 s), second (106. 8 ± 38. 3 s), third (95.0 ± 29.9 s), and fourth exercise bouts (94.3 ± 38.3 s), compared with females (97.1 ± 21.3 s, 83.9 ± 18.6 s, 77.5 ± 24.5 s, and 74.4 ± 16.7 s, respectively).

COP sway parameters

Table 3 shows a summary of statistical results (ANOVAs) for non-normalized COP sway parameters for each of the QS and FL tasks. These results were not different from those with the COP data normalized by height or body weight, except for weight-normalized data eliminating a significant sex X fatigue interaction (shown in Table 3) on mean COP sway velocity during the FL task ($F(5, 85) = 1.729$, $p = 0.18$); this interaction elimination was described in the discussion section (see below). Results are thus reported only for the non-normalized data and do not focus on the effect of vision alone, as this was not the aim of our study.

Table 3. Summary of statistical results (ANOVAs) of COP sway parameters. These results depict the effects of fatigue (time), sex, vision, and fatigue-related interactions during quiet standing (QS) and standing forward leaning (FL) tasks. The results are shown for the COP data that are not normalized by anthropometric variables (weight, height, and BMI).

Type of task	**Effects**	**COP sway parameters**							
		AP position		*ML position*		*velocity*		*Area*	
		F	*P*	*F*	*P*	*F*	*p*	*F*	*P*
	Time	9.810	**<0.001**	4.150	**0.002**	3.404	**0.007**	2.679	**0.027**
	Sex	13.93	**0.002**	1.336	0.264	0.229	0.638	1.828	0.194
QS	*Vision*	4.104	0.059	0.022	0.883	95.63	**<0.001**	179.5	**<0.001**
	Time x sex	1.023	0.392	0.879	0.479	1.605	0.167	0.337	0.889
	Time x vision	9.167	**<0.001**	2.273	0.054	1.398	0.233	1.537	0.187

	Time x vision x sex	1.020	0.395	1.214	0.310	2.181	0.064	0.580	0.715
FL	*Time*	4.219	**0.002**	2.766	**0.023**	3.038	**0.014**	1.430	0.222
	Sex	14.96	**0.001**	1.385	0.255	0.317	0.581	0.542	0.472
	Vision	35.82	**<0.001**	0.085	0.774	87.90	**<0.001**	89.76	**<0.001**
	Time x sex	1.988	0.089	0.819	0.539	2.567	**0.033**	1.140	0.346
	Time x vision	3.921	**0.003**	1.664	0.152	1.862	0.110	0.624	0.682
	Time x vision x sex	2.298	0.052	1.623	0.163	1.052	0.393	0.820	0.539

BMI: body mass index = weight/(height)^2; the degrees of freedom between- and within-subjects are the numbers of 5 and 85 (for the time effects and related interactions), and of 1 and 17 (for the main effects of sex and vision) with regards to all the COP variables.

Mean AP COP position

The effects of sex, fatigue, and a fatigue X vision interaction were found for mean AP COP position for both QS and FL (Table 3). The sex effect was due to a greater mean anterior COP position during all task conditions (QS-EO: ~47 %; QS-EC: ~62 %; FL-EO: ~21 %; FL-EC: ~32%) in females compared to males. The mean AP COP position showed a significant backward shift (mean COP position decreased in value, which is associated with a more posterior location on the force platform) following exercise during QS-EC (~20%; 5min: p = 0.03, 10min: p = 0.005, and 15min: p = <0.001) and FL-EC (~4.9%; 5min: p = 0.04 and 10min: p = 0.001) (Figure 2A). Fatigue X vision interactions were due to greater backward shifts in mean AP position for both QS (10 min: p = 0.03 and 15 min: p = <0.001) and FL (5 min: p = 0.04 and 10 min: p = 0.005) with EC (~20%), as compared with EO (~2%) (Figure 2A).

Figure 2. Mean anteroposterior (AP) and mediolateral (ML) COP position. Mean AP and ML COP positions shown before and immediately following exercise, and throughout the recovery period (2, 5, 10, and 15 min). Panel A shows the AP position during both quiet standing (QS) and standing forward leaning (FL) tasks with eyes open (EO) and closed (EC). B represents ML position during QS-EO. * = fatigue effects ($p \leq 0.05$, compared to pre-exercise value), and a = effects of fatigue X vision ($p \leq 0.05$, in comparing EO to EC).

Mean ML COP position

A fatigue effect on mean ML COP position was due to a rightward displacement (56%) from pre to immediately post-exercise during QS-EO ($p = 0.03$) (Figure 2B).

Mean COP sway velocity

Fatigue effects and a sex X fatigue interaction (FL) were found for mean COP sway velocity (Table 3). The fatigue effects were due to significant increases in sway velocity following exercise for both QS-EO (~14%; 2 min: $p = 0.02$, 5 min: $p = 0.01$, 10min: $p = 0.05$, and 15 min: $p = 0.04$) and FL-EO (~18%; 2min: $p = 0.05$, 5min: $p = 0.02$ and 15min: $p = 0.03$) (Figure 3). Post hoc tests did not show such significant increases for the EC condition.

Figure 3. Mean COP sway velocity. Mean COP velocity shown before and immediately following exercise, and throughout the recovery period (2, 5, 10, and 15 min) for quiet standing (QS) and standing forward leaning (FL) tasks with eye open (EO). * = significant fatigue effects ($p \leq 0.05$, compared to pre-exercise) on sway velocity.

A sex X fatigue interaction (5min: $p = 0.05$ and 10min: $p = 0.02$) was found during FL-EC, where males had significant and prolonged increases (~18 %; immediately: $p = 0.04$, 5min: $p = 0.02$, 10 min: $p = 0.002$) in sway velocity following exercise, whereas females showed no significant change with fatigue and recovery (Figure 4).

Figure 4. Sex differences in fatigue effects on mean COP sway velocity. Mean COP velocity shown before, immediately following exercise, and throughout the recovery period (2, 5, 10, and 15 min) in males and females during the standing forward leaning task with eyes closed (FL-EC). * = fatigue effects for males and females ($p \leq 0.05$, compared to pre-exercise), and a = sex X fatigue interaction ($p \leq 0.05$, in comparing percentage changes from pre to post-exercise between males and females).

95% ellipse of COP sway area

A significant fatigue effect was found for sway area for the QS task. However, none of the *post-hoc* tests reached significance.

Discussion

The main aim of this study was to compare the effects of ankle plantar flexors fatigue on static postural control between healthy young males and females in tasks with varying levels of difficulty. Our findings showed a sex X fatigue interaction for COP sway velocity during the most challenging task (FL-EC), where males presented with a significant and prolonged increase in velocity, whereas females did not. This is partly consistent with our first hypothesis, which stated that males would show greater fatigue-induced postural control alterations compared with females, and such changes would be more pronounced under challenging task conditions. We also found vision X fatigue interactions for mean AP COP position during both QS and FL tasks, which were due to greater fatigue-induced backward shifts with EC compared with EO. This is partly in accordance with the secondary hypothesis, where it was proposed that the withdrawal of vision would lead to greater postural changes with fatigue, which would be more pronounced during the FL task.

Fatigue effects on postural control

Ankle plantar flexors fatigue led to changes in mean COP position and velocity. A gradual posterior shift in mean COP position (significant from 5 to 15 min) following exercise was observed during the no-vision tasks (QS-EC and FL-EC). This is in accordance with previous findings, but for unipedal standing tasks [7,35]. For example, Boyas and colleagues [35] observed a gradual and prolonged (at least 8 min) backward shift of the COP during one-leg standing after fatigue of ankle plantar flexors. This posterior shift could be a compensatory consequence in response to declines or changes in the force-producing capability and proprioception of fatigued ankle plantar flexors [3]. Particularly, the contribution of proprioception is supported by the observation that vibration of fatigued ankle plantar flexors does not significantly produce a further increase in postural sway during upright standing [36,37], suggesting a lesser reliance on proprioception of the fatigued ankle muscles for regulating postural control during standing. Interestingly, the fatigue-induced posterior shift (pre- to post-exercise) in the mean AP COP position with EC was more pronounced for the relatively lesser challenging task (QS; ~21 %) compared to the FL task (~4%). This may be explained by the initial position of the COP for the FL task with EC which was not as far forward compared with EO at pre-exercise. This was opposite to the QS task where the COP was positioned more forward with EC compared to EO at pre-exercise (Figure 2). The less forward COP position during the FL task with EC compared to EO at pre-exercise may be explained by a perceived threat of a forward fall when leaning the body forward to 70% of the LOS. This may be somewhat similar to the COP displacement seen with height-induced threats, which shows a shift away from the platform's edge (less anterior position) during quiet standing at height compared to relatively lower height or on the ground, possibly due to increased attention to postural control [38].

Interestingly, the significant backward shift was not observed before 5 min post-exercise. Sensory systems likely not affected by fatigue (e.g., vestibular and neck somatosensory inputs, see [39]) could play a initial compensatory role for the reduced ability of fatigued ankle plantar flexors to maintain stability. As well, an initial compensation by other muscle groups, such as ankle mediolateral stabilizers/dorsiflexors, toe flexors or more proximal muscle groups of the knee/hip/back as suggested in previous studies [35,40,41], could also be involved. For example, an increase in the contribution of proximal muscles and joint movements (e.g., hip) depending on the extent of ankle fatigue, could explain the backward shift in COP. The aforementioned study by Boyas et al. [35], showed greater increases in hip flexion of supporting and free legs immediately (8%) following exercise compared to during recovery (5%), which were accompanied by a smaller backward shift with fatigue compared with recovery. Such compensation could have taken place in the present study, such that changes in AP hip control may have eliminated or minimized the backward shift of the COP with fatigue of ankle plantar flexors, but mostly immediately after fatigue.

In addition, a fatigue-induced shift of the mean ML COP position to the right was found during the QS-EO task in the present study (shift to a more positive value indicating a shift to the right; Figure 2B), possibly suggesting a fatigue-induced asymmetry of posture. This would be consistent with the results of a recent study showing an increased asymmetry index between preferred and non-preferred legs (based on muscle activation during quiet standing) with ankle and hip muscle fatigue, possibly indicating a shift in the control of posture towards the preferred leg [42]. This suggests that the contribution of a more reliable leg to control posture could increase with fatigue. The right shift of the ML position during QS-EO in the present study could be thus explained by the fact that the right leg is generally observed to be dominant in young adults (e.g., more than 95% in both males and females, see [43]); although we did not assess leg dominance in our participants.

Post hoc tests revealed that significant fatigue-induced increases in sway velocity were found only during the QS-EO and FL-EO tasks. An increase in sway velocity is consistent with previous findings [7,15,35,44]. It has been suggested that increases in sway velocity and corresponding sway frequency could be the result of an increase in ankle stiffness to maintain stability [45]. The lack of a significant increase in sway velocity immediately following exercise (Figure 3) may also be explained by the aforementioned compensatory strategies at proximal joints with fatigue, which could minimize the effect of an increase in ankle stiffness with fatigue of ankle plantar flexors, although this cannot be confirmed in the present study.

Sex differences in postural control

We found that females had a greater mean anterior COP position than males (Table 3). This sex difference could be due to anthropometric differences (e.g., weight, height) between males and females rather than sex differences in postural control strategy (or ability), as found or suggested in previous studies for variables reflecting postural performance [34,46–48]. In the present study, greater height and weight in males compared to females (Table 1) and moderate-to-high negative correlations between anthropometric variables (height and weight) and AP position (but none of the other COP variables; table 2) were found. Interestingly, when analyzed separately for each sex group, we found significant correlations between AP position and body weight in females for all task conditions (except for FL-EC; Table 2), whereas males showed only one significant correlation between sway area and height during QS-EC, potentially suggesting sex-specific stability behavior related to body factors in young adults [49,50]. However, this should be interpreted with caution, as we still found a sex difference in the AP position normalized by each of height and weight, possibly indicating other contributors or confounding factors to the sex differences in COP behavior. For example, different foot size/feature (length, width, and arch area/height) between the sex groups (although not measured in the present study) may become another contributor, given the relationship between foot size and AP postural stability (e.g., see [51]).

Interactions between sex and fatigue on postural control

We found a sex X fatigue interaction for mean COP sway velocity during the most challenging task (FL-EC), where males showed a significant and prolonged increase in sway velocity (~28%) up to 15 min following exercise, whereas females showed a non-significant increase (~2%) and then recovered to a slightly lower value (~5 %) than baseline by 5-10 min post-exercise (Figure 4). This is consistent with a recent finding [22], where an increase in COP sway velocity during one-leg standing following a repetitive lifting task was observed in males, while females showed a slight decrease. This result could indicate an increased ankle stiffness strategy with fatigue, but only in males, to maintain stability. Given the similar fatigability (time to task failure) between the sex groups in the present study, the presence of the ankle stiffness strategy could be due to a disadvantage in terms of biomechanical factors (e.g., greater weight/height and related higher COM) for static stability in males compared with females, as reported in a review by Paillard [3]. Amongst potential biomechanical factors, greater body weight in males compared to females may be a primary contributor to the sex X fatigue interaction on COP sway velocity during the most challenging task because the interaction was eliminated with the COP velocity normalized by the weight of the participants.

Given the compensatory movements with ankle plantar flexors fatigue mentioned in the "Fatigue effects on postural control" section above, we speculate that the sex X fatigue interaction suggests the involvement of different postural control strategies with ankle fatigue between females and males, with males potentially relying preferentially on ankle/foot control (possibly relying on non-fatigued ankle invertors, evertors, dorsiflexors, and toe flexors), and females preferentially relying on proximal joint movements (e.g.., hip and trunk) to maintain stability. Such a sex difference in control strategy is supported by previously observed greater fatigue-induced ankle torque variability during feet-together standing with EC in males compared to females [24], and a fatigue-induced increase in trunk accelerations (induced by hip movement) accompanying a decrease in COP velocity (ankle control) in females during one-leg standing [52]. However, the sex X fatigue interaction and proposed potential control mechanisms involved should be interpreted with caution as we did not measure ankle/foot and proximal joint movements.

Interactions between vision and fatigue on postural control

A vision X fatigue interaction was found for mean AP COP position for both QS and FL tasks, which was due to a greater backward shift of the COP during recovery (from 5 to 15 min) for the tasks with EC (significant) compared with EO (not significant) (Figure 2A). This is consistent with previous findings of fatiguing ankle plantar flexors, which showed greater postural sway changes (or impairment) with no-vision and/or disturbed vision compared to normal vision during upright standing on one leg [7,14,25,27] or two legs [26,53]. This suggests a significant role of visual information for maintaining stability [54,55], compensating declines in the neuromuscular system and proprioception of fatigued ankle plantar flexors [3].

It was suggested that such vision effects could be dependent on task difficulty. For example, Bisson and colleagues (2010) found greater fatigue-induced COP sway displacement with EC compared to EO during one-leg standing, but not during two-leg standings (semi-tandem and feet together). However, this is not consistent with our findings showing similar fatigue X vision interactions during both QS and FL tasks (although different at 15 min, see Figure 2A). This could be explained by the use of the representation of the COP on a computer screen, which would enhance the role of vision for compensating instability with fatigue and lead to a vision effect regardless of task difficulty (QS vs. FL). This contrasting finding may also be attributed to the use of the relatively close vision target (1.8 m) in the present study compared to the relatively distant one (2.5 m) used by Bisson et al., given the effect of vision target distance on postural control [54]. This is supported by a previous study [53], which found the reduced contribution of vision to compensating fatigue-induced instability with a distant target (4 m) compared to near one (1 m). These findings showcase the importance of task specificity when determining vision effects on postural changes associated with fatigue.

A few limitations should be mentioned for the present study. A motion capture system and electromyographic (EMG) measures were not used to assess body movements and muscle activation to compare compensatory postural strategies (e.g., ankle, hip, and trunk movements) produced by fatigue of ankle plantar flexors between males and females. Vision impairments and correction and ankle stability in participants was not formally assessed in the present study. However, participants who typically wore glasses were asked to wear them for the session, and the absence of known ankle instability was confirmed verbally. Also, we did not obtain information on the phases of the menstrual cycle in female participants, which has been found to affect postural stability [56,57]. However, this would likely not be a major confounding factor to sex differences in postural control changes with fatigue, given the smaller effect of the menstrual cycle on fatigability compared to other general sex differences in fatigability [17]. Nevertheless, this study provides useful information regarding sex-specific postural control changes with fatigue, which may contribute to improve the design and prescription of stability-demanding physical training or rehabilitation exercise.

Conclusion

We found a sex X fatigue interaction for mean COP sway velocity during the most challenging task (FL-EO) in healthy young adults, where only males showed a significant increase in sway velocity after fatigue of ankle plantar flexion. This interaction suggests that different postural control strategies may be used with fatigue between sex groups. We also found a significant contribution of vision to AP stability with fatigue regardless of task difficulty (QS vs FL).

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Supporting information

S1 file. Data set. This data includes COP sway variables which were collected before and immediately after exercise, and throughout the recovery period (2, 5, 10, 15 min).

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Figure 1. Schematics of the experimental protocol.

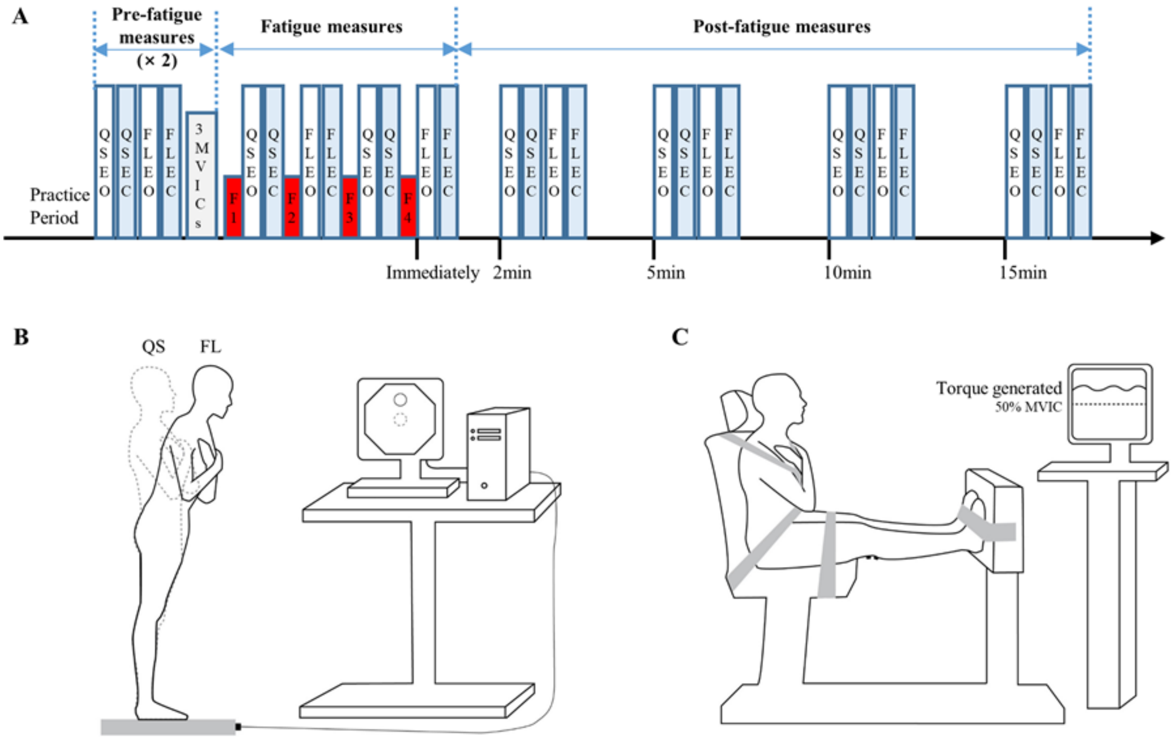
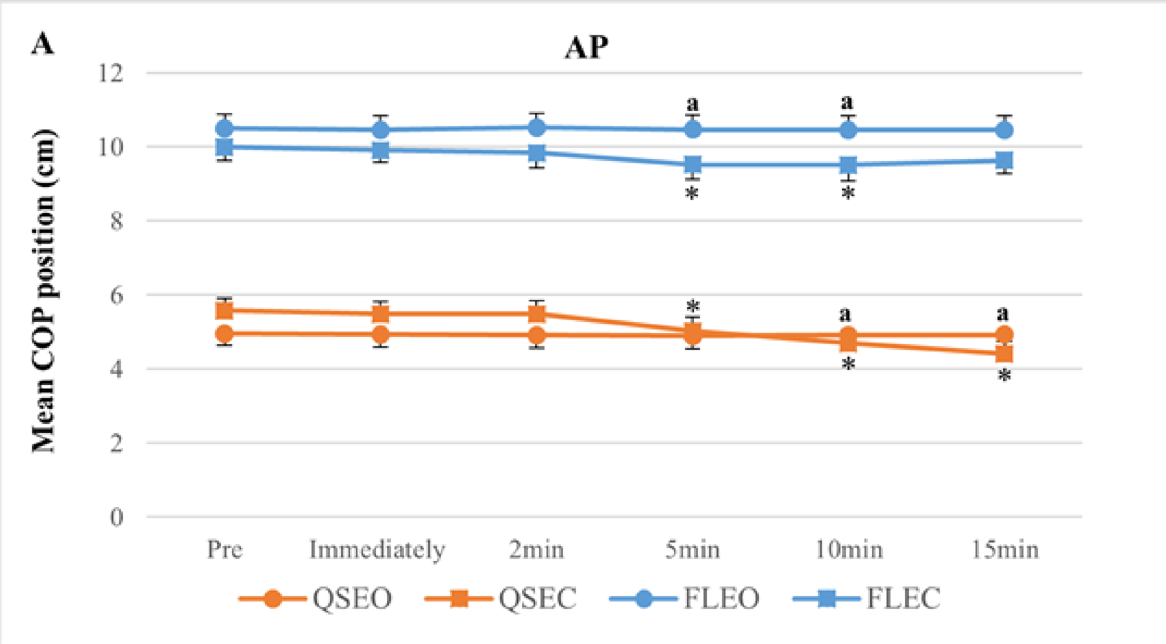


Figure 2. Mean anteroposterior (AP) and mediolateral (ML) COP position.



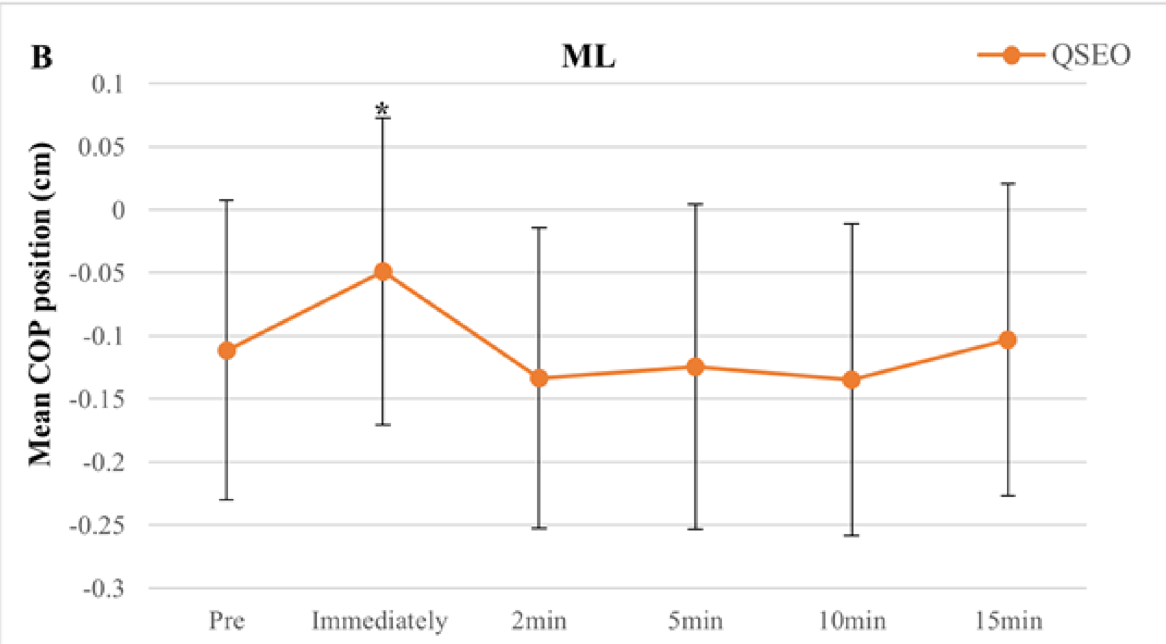


Figure 3. Mean COP sway velocity.

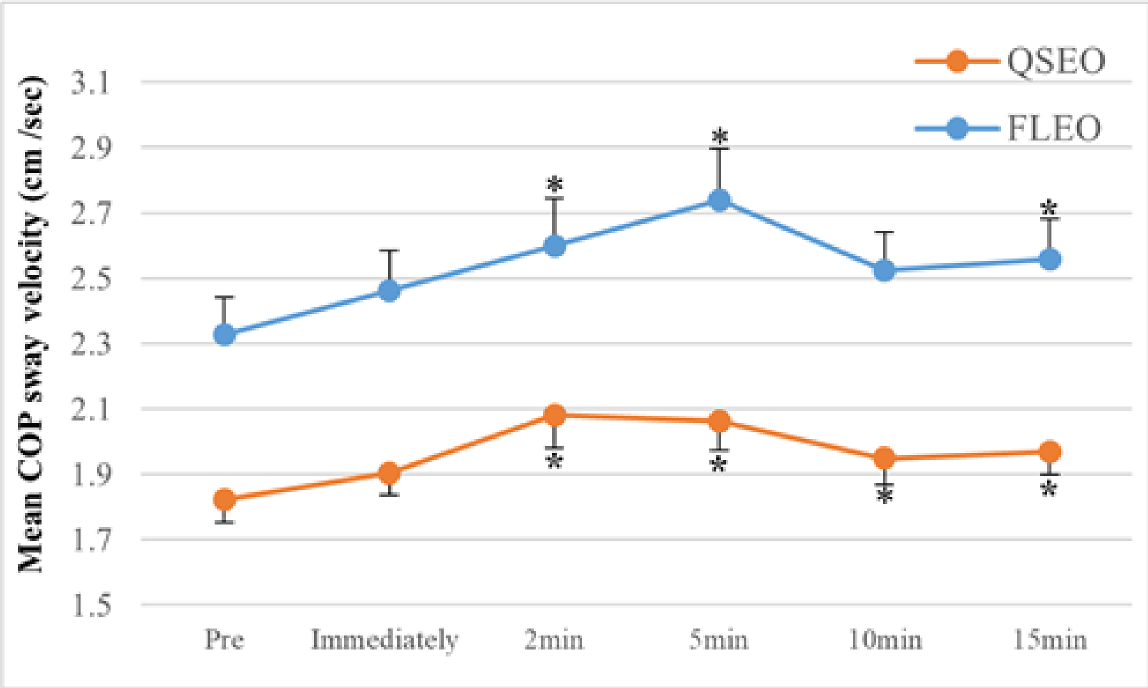
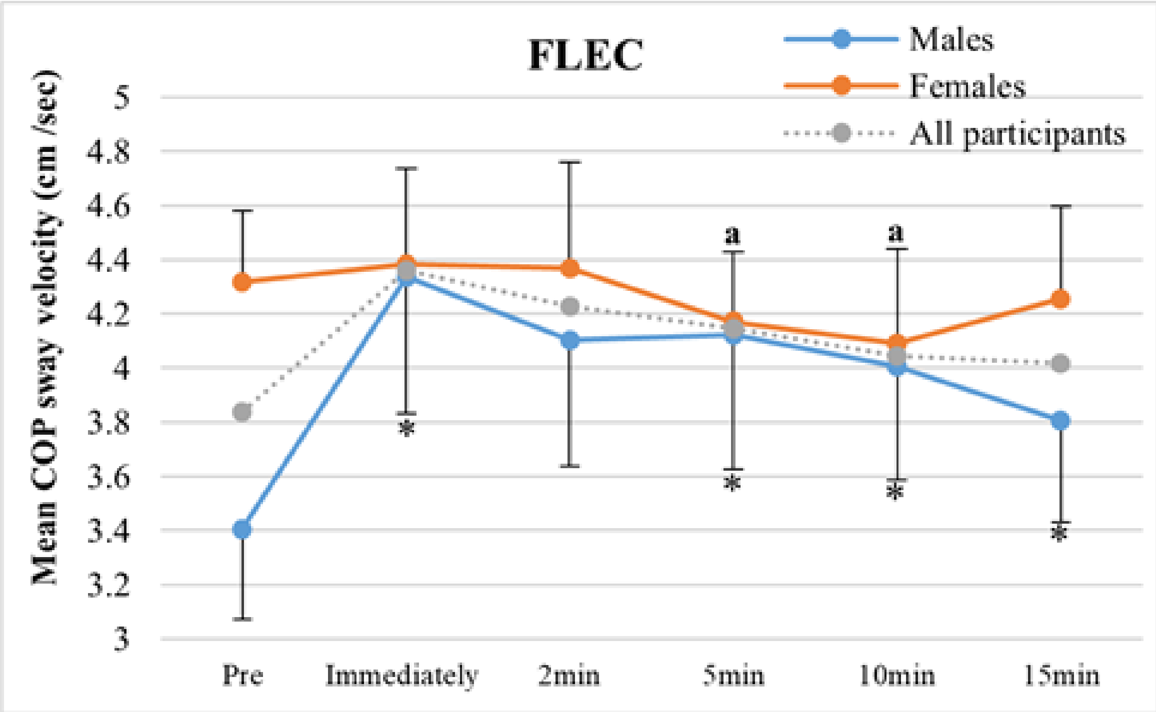


Figure 4. Sex differences in fatigue effects on mean COP sway velocity.



Research article 4

Sex differences concerning the effects of ankle muscle fatigue on static postural control and spinal proprioceptive input at the ankle

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Abstract

The main aim of this study was to determine sex differences in postural control changes with ankle muscle fatigue during a standing forward leaning (FL) task under different vision conditions. The secondary aim was to examine whether fatigue affects spinal proprioceptive inputs at the ankle during the task conditions differently according to sex. Fifteen healthy young adult males (mean age: 28.0 years) and sixteen healthy young adult females (mean age: 26.1 years) were asked to perform four consecutive FL tasks [30 s; two with eyes open (EO) and two with eyes closed (EC)] before, and immediately following a fatiguing exercise consisting of alternating ankle plantarflexion (6 s) and dorsiflexion (2 s) maximal isometric contractions, and at 5 and 10 min of recovery. Center of pressure (COP) sway variables (mean position, standard deviation, ellipse area and average velocity), an ankle co-contraction index, and a ratio of soleus (SOL) H-reflex to the maximum amplitude of the compound muscle action potential (M-max) were obtained during the FL tasks. A rating of perceived exertion (RPE) was also documented at the different time points. Time to task failure (reduction of 50% in maximal voluntary isometric contraction torque of ankle plantar flexors) and the increase in RPE value were not significantly different between males and females. Both sex groups showed similar and significant increases ($p<0.05$) in mean COP sway velocity with no significant changes in co-contraction indices. No significant effects of fatigue and related interactions were found for SOL H/M-max ratio. The absence of a significant sex difference in postural control change (sway and co-contraction) with fatigue could be explained by similar perceived (RPE) and performance fatigability (exercise duration) between males and females in the present study. Fatigue did not lead to significant changes in proprioceptive inputs from SOL.

Introduction

Postural stability is regarded as the capability to control the center of mass with respect to the base of support [1]. To maintain postural stability, the central nervous system must rapidly integrate sensory information from the visual, vestibular, and somatosensory systems and use this information selectively to produce complex motor responses (i.e., timing, direction, and magnitude), appropriate to the characteristics of the postural stability disturbances associated with a given task and of the surrounding environment [2].

Exercise-induced fatigue of postural muscles (trunk, hip, knee, and ankle) can alter or impair the control of postural stability, mainly due to fatigue-induced modifications in the peripheral proprioceptive system and central processing of sensory inputs, as well as decrements in force production capacity [3–5]. In particular, ankle muscle fatigue can lead to significant postural control alterations during tasks such as upright standing on one or two legs [6–9]. This effect could involve a change in ankle stiffness through increased coactivation of antagonists, given the significant role of ankle muscles in regulating active ankle stiffness to maintain postural stability [10,11]. For example, several studies [12–14] found increases in COP sway velocity and/or frequency with ankle muscle fatigue during static tasks, suggesting an increase in ankle stiffness to maintain stability optimally in a state of fatigue. Also, the absence of vision may increase the extent of such fatigue-related changes in postural control during relatively challenging static standing tasks. This has been observed in a few studies [13,15,16] where fatigue of ankle plantar flexors led to greater impairments in postural stability during one-leg standing with eyes closed (EC) compared with eyes open (EO).

Given such significant effects of muscle fatigue on postural control, sex differences in muscle fatigue may lead to different postural control changes between males and females. It has been suggested that females are generally less fatigable than males during isometric fatiguing exercise [17,18], mainly due to: a greater proportion of fatigue-resistant muscle fibers within skeletal muscles [17], lesser neural drive to the muscle [19], and greater oxidative metabolic capacity [20] in the former group. This sex difference in muscle fatigue may lead to greater postural control changes with fatigue in males compared with females. For example, greater center of pressure (COP) sway displacements [21], increased COP velocity (only in males) during one-leg standing [22], and reduced leg-reaching distance [23] have been found in males compared with females in a state of fatigue of ankle, knee, and hip muscles. These findings may be due to different postural control strategies used in the presence of fatigue between males and females. In particular, an ankle strategy (ankle joint control or movements) to maintain stability could be a primary contributor to such sex differences (e.g., during quiet standing, see [24]). However, sex differences in postural control changes with ankle muscle fatigue have only been sparsely studied, including in challenging tasks, such as when leaning forward close to the limit of stability.

Furthermore, ankle muscle fatigue could lead to a degradation in the information provided by proprioceptive afferents from the fatigued muscles, which could contribute to fatigue-induced changes in postural sway or performance [3]. Proprioceptive inputs from the ankle can be reflected by modulation of the soleus (SOL) H-reflex, which is an electrically evoked response analogous to the stretch reflex, but bypasses muscle spindles [25,26]. In the context of muscle fatigue and postural control, two studies at this moment have reported a decrease in SOL H-reflex amplitude following repetitive standing tiptoes [27] or jumps [28] in healthy young adults, which was accompanied by an increase or decrease in anteroposterior (AP) COP displacement during upright standing on a firm or movable surface. It was suggested that such SOL H-reflex depression (accompanying fatigue-induced postural changes) may be attributed to reciprocal inhibition due to an increased level of activation in the antagonists (e.g., tibialis anterior (TA)) to compensate for instability with fatigue [28]. The withdrawal of vision may also lead to a decrease in the SOL H-reflex through increased presynaptic inhibition of Ia afferents (e.g., see [29]). However, no studies have looked at SOL H-reflex modulation with fatigue in the context of postural control and potential differences based on sex.

The main aim of this study was to determine sex differences in postural control changes (sway and co-contraction) with ankle muscle fatigue during a standing forward leaning (FL) task in different vision conditions (EO vs EC). A secondary aim was to determine fatigue-induced changes in ankle spinal proprioceptive inputs (SOL H-reflex) according to sex and vision. It was hypothesized that males would show greater increases in both COP sway parameters and ankle stiffness (co-contraction) compared with females, and such results would be more pronounced with the withdrawal of vision. Also, we hypothesized that ankle muscle fatigue would lead to SOL H-reflex depression, and this depression would be more pronounced in males and with the removal of vision.

Methods

Participants

General information about participants is shown in Table 1. Fifteen healthy young males and sixteen healthy young females volunteered for this study. The participants had no disorders and musculoskeletal injuries. Both sex groups showed a similar moderate-to-high physical activity level (overall: 8.8 ± 1.5 out of 15; males: 8.7 ± 1.6; females: 8.9 ± 1.4), as reported on a habitual physical activity questionnaire documenting work, sport, and leisure time [30]. The study was approved by the research ethics boards of the University of Ottawa (# H11-14-23) and Bruyère Continuing Care (#M16-08-038). Participants were informed of all procedures and consented orally before enrolling in the study.

Table 1. Sex differences in demographics and MVIC torque of ankle muscles

	Mean (SD)			P-values
	Overall (n=31)	Males (n=15)	Females (n=16)	
Age (years)	27.3 (4.5)	28.00 (4.2)	26.1 (4.8)	0.383
Height (cm)	171.4 (9.7)	178.6 (7.3)	164.6 (6.1)	**<0.001**
Weight (kg)	66.2 (12.9)	74.0 (9.5)	59.0 (11.6)	**<0.001**
PF torque (Nm)	195.8 (62.6)	234.2 (57.0)	159.8 (44.3)	**<0.001**
DF torque (Nm)	64.8 (20.7)	82.69 (13.0)	48.1 (9.0)	**<0.001**

MVIC: maximal voluntary isometric contraction; PF: ankle plantar flexors; DF: ankle dorsiflexors

Experimental procedure

A schematic of the experimental procedure is shown in Figure 1A. All participants were first asked to practice each of two task conditions (FL-EO and FL-EC) twice. Then, two different levels of electrical stimulus intensity were determined to elicit the maximum amplitude (M-max) of the compound muscle action potential (M-wave) and submaximal SOL

H-reflex during FL-EO (see below for details). Participants were then required to perform four consecutive 30-s FL trials (2 FL-EO and 2 FL-EC) on a force platform. During the first trial of each pair (2 FL-EO or 2 FL-EC), six consecutive electrical stimuli with at least a 3-s interval (as recommended to prevent post-activation depression of the H-reflex [26]) were delivered to obtain five H-reflexes followed by one M-max. The second trial of each pair did not include the electrical stimuli and was recorded for the assessment of postural stability. Participants then performed a minimum of three bilateral maximal voluntary isometric contractions (MVICs) with each of ankle plantar flexors (PF) and dorsiflexors (DF), with a 2-min interval between each contraction. The MVICs were maintained over approximately 3 s after the presence of a plateau of the PF or DF torque amplitudes. The highest torque from PF MVICs was used to set a cut-off target (50% MVIC of PF) for an alternating PF-DF isometric fatiguing exercise (see below section 2.5 for details). After the fatiguing exercise, the four FL tasks were immediately assessed and also at 5 and 10 min of recovery. The order of the postural tasks (EO or EC) was counterbalanced across participants.

Figure 1. Schematics of the experimental protocol. The schematics include experimental procedures (A) and alternating isometric contractions of ankle plantar (for 6 s) and dorsiflexors (for 2 s) on a dynamometer (B). PT: practice of standing forward lean (FL) tasks with eyes open (EO) and eyes closed (EC); H/M: determination of electrical stimuli intensities for obtaining submaximal H-reflex and maximum M-wave (M-max); FLEO/FLEC: the FL task with eyes open and closed; 5H (5 blue arrows): five submaximal electrical stimuli for five H-reflexes; 1M (red arrow): supramaximal stimulus for one M-max; MVICs: maximal voluntary isometric contractions; RPE: rating of perceived exertion using a 12-point modified Borg's CR-10 scale. The order of the FL tasks has been counterbalanced.

The rating of perceived exertion (RPE) of the ankle muscles was also assessed using a 12-point modified Borg's CR-10 scale (0 = "No fatigue at all" to 10 = "Absolutely exhausted") [31] before and immediately after the fatiguing exercise and also after each block of four FL trials (immediately, 5 and 10-min post-exercise) (Figure 1A). The obtained RPE values were used to indirectly assess the degree of ankle muscle fatigue, as an increase in such RPE value has been significantly correlated with muscle fatigue (e.g., reduction in muscle force or torque [31] and increased muscle activation [32]).

Electromyographic (EMG) signal and center of pressure (COP) data recordings

Electromyographic (EMG) signals from SOL, gastrocnemius lateralis (GL), and tibialis anterior (TA) of the dominant leg were recorded using bipolar surface electrodes (width: 1 mm, length: 10 mm, and center-to-center interelectrode distance: 10 mm; DE-2.1, Delsys Inc., Boston, USA). The recording electrodes were placed according to the SENIAM recommendations [33]. The reference electrode was placed on the patella or the upper part of the tibia of the same leg. These EMG signals were amplified (X1000; common mode rejection ratio: 92 dB; channel frequency response: 20-450 Hz) and recorded at a sampling rate of 5000 Hz during the entire duration (30 s) of each FL task. During the same period, COP data (see below section 2.6 for details) were recorded using an AMTI AcuGait force platform (Watertown, MA) and the Balance Trainer software (version 1.05.02) at a 25 Hz sampling rate.

Soleus (SOL) H-reflex measurements

SOL H-reflex and M-wave recruitment curves were first obtained when participants with the arms crossed on the chest were standing as still as possible with feet together and staring at a target on a computer screen in front of them. Two stimulating circular electrodes (diameter: 8 mm) were placed longitudinally along the length of the posterior tibial nerve under the dominant knee. Electrical stimuli (pulse duration = 0.2 ms) [34] starting from 10 mA were evoked with 10-mA increments up to the presence of a plateau in the SOL M-wave to determine its maximum amplitude (M-max). A supramaximal intensity (10-mA above the intensity needed to reach M-max) was used thereafter to elicit M-max. Subsequently, a 1-mA increment was used starting back from 10 mA for the characterization of the SOL H-reflex recruitment curve up to the point where H-reflex amplitude started to decrease after observing the H-reflex maximum. From the H-reflex recruitment curve, the intensity of electrical stimulation to elicit the test H-reflex during the FL trials was set to meet the following criteria for each participant (Figure 2): 1) H-reflex accompanied by a small M-wave (less than 8% of M-max prior to the H-reflex [35,36]) to ensure constant stimulus intensity; and 2) placed on the rising portion of the H-reflex recruitment curve to be susceptible to facilitation and inhibition under a given intervention condition (e.g., pre vs. post-fatigue) [25]. The intensity of the electrical stimuli used to elicit the test H-reflex was sometimes slightly re-adjusted during an experiment to ensure that the amplitude of the accompanying small M-wave remained within a ~2% range for a given participant (intra-subject variation), as suggested by Miranda et al [35]. These criteria could not be met in six males and seven females, whose data was thus excluded from further analysis (the subset of valid H-reflex data thus included 9 males and 9 females).

Figure 2. Schematics of the experimental setup. The setup is for the standing forward leaning (FL) task with an example of electromyographic (EMG) signals from tibialis anterior (TA), gastrocnemius lateralis (GL), and soleus (SOL) during the FL task, as well as of SOL H-reflex for participant M12. The FL tasks with eyes open and closed were performed on a force platform with the representation of the COP on a computer screen. EMG data were obtained from the bipolar surface electrodes positioned as follows: 1: TA, 2: GL, and 3: SOL (for H-reflex as well). QS: quiet standing; STIM: electrical stimulation on popliteal fossa for obtaining SOL H-reflex and M-wave.

To characterize the potential influence of pre-stimulus muscle activation on H-reflex amplitude, the root mean square EMG amplitude of the ipsilateral antagonist (TA) and agonist muscles (GL and SOL) was calculated over a 50-ms window before the onset of the H-reflex. This was done in order to determine whether reciprocal inhibition (from antagonist activation) and AP postural sway position (which was reported to interact with agonist activation during quiet standing [37]) affect SOL H-reflex. An increase in TA activation could suggest an increase in reciprocal inhibition from the ankle that contributes to SOL H-reflex depression [26]. A posterior to anterior postural sway shift during quiet standing was reported to lead to a slight increase in the H/M ratio (as well as activation of ankle plantar flexors) [37].

Postural tasks

A schematic of the experimental setup for the FL task is shown in Figure 2. The limit of stability (LOS) was first obtained by measuring the maximum excursion of the COP while participants lean the whole body in a standing position (feet together) as far as possible forward, backward, and side-to-side on a force platform without lifting the heels or toes and limiting the movement to the ankle. Afterward, participants were asked to lean forward and reach a target set at 70% of the anterior LOS with a representation of their COP on a computer screen placed 1.8 m in front of them. They were required to maintain the 70% LOS target as closely as possible for 30 s with EO or EC. For the EC condition, participants first reached the 70% of anterior LOS target with EO, and then closed their eyes. For both EO and EC conditions, the participant indicated when they felt stable by saying ‘OK’ out loud, which triggered the researcher to begin the 30-s recording.

Fatiguing exercise

A schematic of the experimental setup for the fatiguing exercise is shown in Figure 1B. Participants sat on the chair of a Biodex system 3 Pro (Biodex medical systems, Shirley, USA) with their legs straight and both feet placed on a footplate at a 90^{o} angle (aligning the external malleoli with the center of rotation of the dynamometer). Their trunk, pelvis, and feet were secured with non-elastic straps. Because fatigue of both PF and DF was reported to have greater impact on postural control than fatigue of each muscle group separately [9], an alternating PF-DF isometric fatiguing exercise of both legs was performed in this study. A pilot test was conducted to determine the intensity and duration of contractions that generated simultaneous fatigue of both PF and DF to less than 50% of the pre-fatigue MVIC torque. Based on the pilot testing results and previous work [38], participants were asked to alternate between maximal isometric contractions of PF (for 6 s) and DF (for 2 s) for the fatigue exercise protocol. The fatigue protocol was stopped when PF torque was reduced to less than 50% of the pre-fatigue MVIC torque during consecutive 3 seconds. Verbal encouragement was given throughout.

Data analysis

The following COP variables were obtained from the Balance Trainer Software: mean anteroposterior (AP) and mediolateral (ML) COP position (cm; average AP and ML displacements from the platform center = $\frac{1}{n} * \sum_{i=1}^{n} x_i$ and $\frac{1}{n} * \sum_{i=1}^{n} y_i$, respectively), standard deviation (SD) of the AP/ML COP position (cm; $x_{SD} = \frac{1}{n} * \sqrt{\sum_{i=1}^{n} \left(x_i - x_{COP\ displacement}\right)^2}$ and $y_{SD} = \frac{1}{n} * \sqrt{\sum_{i=1}^{n} (y_i - y_{COP\ displacement})^2}$, respectively), mean COP sway velocity (cm/s; path length per unit time = $\frac{l_{path}}{t}$), and the area of the 95% confidence ellipse of COP sway (cm^2; area of the 95th percentile ellipse = $\pi * \sqrt{F * (x_{sd}^2 + y_{sd}^2 + D)} * \sqrt{F * (x_{sd}^2 + y_{sd}^2 - D)}$): $l_{path} = \sum_{i=2}^{n} \sqrt{(x_i - x_{i-1})^2 + (y_i - y_{i-1})^2}$; D = $\sqrt{(x_{sd}^2 + y_{sd}^2)^2 - 4 * (x_{sd}^2 * y_{sd}^2) - \sigma_{xy}}$; and F statistics = 3.00. SOL H-reflex peak-to-peak amplitude was normalized to the SOL M-max to form the H/M ratio. The amplitude (root mean square) of TA, GL and SOL EMG for a 50-ms window prior to the onset of the H-reflex was calculated. The level of co-contraction between TA and GL and between TA and SOL of the dominant leg during the FL tasks without electrical stimuli was also quantified using the formula described by Rudolph and colleagues (2001): co-contraction index = level of activity of the less active muscle (root mean square of EMG signal amplitude calculated over the 30-s window comprising a given FL task) / level of activity of the more active muscle(s) X sum of the activity of both muscles.

Statistical analysis

The minimum sample size required was calculated using G* power (version 3.1.9.4) and shown to be a total of at least 6 participants per group, with a power of 0.95, an effect size of 0.50, and an alpha of 0.05. The effect size was estimated from existing data, with respect to SOL H-reflex changes produced by ankle plantar flexors fatigue during upright standing [27].

Independent t-tests were used to compare demographic information (age, height, and weight) and MVIC torque of PF and DF between males and females. Separate three-way ANOVAs with one between-subject factor and two within-subjects factors were used to assess whether fatigue [pre-fatigue vs. post-fatigue (immediately, 5, and 10 min)], sex [males vs. females], vision [EO vs. EC], and their interactions were significant for 1) COP variables (mean AP and ML positions, SDs of the AP and ML positions, sway velocity, and sway area), 2) co-contraction indices (TA-GL and TA-SOL), and 3) the H/M ratio (only including pre and immediately-post fatigue data) during the FL task.

In order to assess the potential influence of anthropometric variables on the changes in COP variables with fatigue, the ANOVAs were performed and compared with three types of COP data: 1) non-normalized, and normalized by 2) height, and 3) weight. Two-way ANOVAs were also conducted to assess the effects of fatigue, sex, and their interaction for the RPE value. If Mauchly's test of Sphericity (within-subjects effect) was significant ($\leq$ 0.05), the Greenhouse–Geisser correction was used to determine significance. When significance was detected with ANOVA, pairwise comparisons or independent t-tests with a Bonferroni correction were performed.

Pearson's correlation analyses were conducted to assess the relationship between percent change (from pre to immediately post-fatigue) in COP sway variables and co-contraction indices (TA-GL and TA-SOL) during each of the FL tasks (FL-EO and FL-EC). Correlation analyses were also performed to assess the association between H/M ratio and EMG amplitude of each of GL, and SOL (for 50ms prior to SOL H-reflex) during each of the FL tasks at pre or post-exercise, and between pre to immediately post-fatigue changes in the H/M ratio and RPE value or EMG amplitude of TA (for 50ms prior to SOL H-reflex) during each of FL-EO and FL-EC.

Results

Baseline information and measures

Body height, weight, and MVIC torques of PF and DF were found to be significantly greater in males compared with females (Table 1).

Fatiguing exercise duration and RPE

Exercise duration (the average time needed to reach the 50% decrement in MVIC torque of PF) was 226.4 $\pm$ 201.1 s and was not significantly different ($p = 0.496$) between males (200.4 $\pm$ 182.9 s) and females (250 $\pm$ 219.8 s). A 58% reduction of DF MVIC torque was observed at the end of exercise. A significant fatigue effect was found for RPE with an expected increase in RPE value up to approximately 14 min following exercise (end of the last four postural tasks) (Figure 3). There was no significant fatigue x sex interaction for RPE.

Figure 3. Changes in the rating of perceived exertion (RPE). RPE scores shown pre-exercise and immediately following alternate isometric exercise of ankle plantar and dorsiflexors, and at the end of each of the four sets of four consecutive standing forward leaning tasks (approximately at 5, 9, and 14min of recovery). *** indicates p = <0.001.

COP sway variables

Statistical results (three-way ANOVAs) for non-normalized COP sway parameters were not different from those with the COP data normalized by height or weight, with respect to fatigue effects and related interactions. Results are therefore reported only for the non-normalized data.

Mean COP positions

Only a main effect of vision was significant for mean AP position (F (1, 29) = 16.04, p = <0.001, partial Eta^2 = 0.356), with an overall slightly more forward position with EO compared with EC (Table 2). For ML mean position, a sex x time (F (3, 87) = 3.331, p = 0.023, partial Eta^2 = 0.103) interaction were found to be significant, but none of the post hoc t-tests reached significance when comparing pre- to post-exercise percent changes in the ML position between males and females during FL-EO or FL-EC. A sex x vision x time (F (3, 87) = 3.293, p = 0.024, partial $Eta^2 = 0.102$) interaction was also found due to a significant left shift of the mean COP position during recovery (immediately to 5 min post-exercise; p = 0.02) in males but not in females and only during FL-EC (Table 2).

Table 2. Mean values (standard deviation) of COP variables. These values are assessed before (Pre) and immediately following fatiguing exercise (Post 0), and throughout recovery (5 and 10 min).

	COP variables	Mean values (standard deviation)							
		Eyes Open				*Eyes Closed*			
		Pre	*Post 0*	*Post 5*	*Post 10*	*Pre*	*Post 0*	*Post 5*	*Post 10*
Overall (n=24)	AP position (cm)†	8.316(1.26)	8.303(1.26)	8.279(1.24)	8.292(1.26)	7.915(1.25)	8.032(1.21)	7.775(1.43)	7.728(1.51)
	AP SD (cm)†	0.366(0.10)	0.375(0.08)	0.373(0.09)	0.377(0.16)	0.725(0.25)	0.784(0.21)	0.766(0.27)	0.776(0.27)
	ML position (cm)¶	-0.014(0.68)	-0.017(0.69)	-0.042(0.71)	-0.040(0.14)	0.072(0.75)	0.240(0.51)	0.111(0.78)	0.086(0.67)
	ML SD (cm)†	0.394(0.10)	0.408(0.10)	0.406(0.11)	0.415(0.12)	0.725(0.21)	0.725(0.23)	0.723(0.24)	0.718(0.26)
	Sway velocity (cm/s)†*	2.163(0.40)	2.470(0.56)	2.443(0.55)	2.408(0.51)	3.797(1.42)	4.376(1.61)	4.012(1.31)	4.004(1.53)
	Sway area (cm^2)†	2.798(1.54)	2.979(1.49)	2.946(1.39)	3.046(1.68)	10.44(6.56)	11.50(7.79)	11.24(7.98)	11.45(8.84)
Males (n=10)	AP position	8.105(1.25)	8.121(1.27)	8.082(1.26)	8.067(1.25)	7.584(1.09)	7.561(1.03)	7.381(1.49)	7.189(1.69)
	AP SD§	0.408(0.12)	0.434(0.12)	0.414(0.08)	0.394(0.08)	0.773(0.33)	0.891(0.33)	0.832(0.26)	0.895(0.35)
	ML position	-0.157(0.63)	-0.153(0.69)	-0.193(0.68)	-0.182(0.71)	-0.008(0.70)	0.221(0.55)	-0.240(0.84)	-0.029(0.76)
	ML SD	0.430(0.11)	0.437(0.09)	0.425(0.10)	0.444(0.11)	0.735(0.21)	0.813(0.26)	0.789(0.24)	0.791(0.28)
	Sway velocity	2.249(0.36)	2.615(0.51)	2.556(0.47)	2.510(0.39)	3.978(1.72)	4.694(1.84)	4.286(1.06)	4.415(1.62)
	Sway area	3.405(1.80)	3.657(1.67)	3.349(1.31)	3.337(1.31)	11.28(7.58)	14.55(9.52)	13.08(7.87)	14.34(10.46)
Females (n=14)	AP position	8.514(1.27)	8.474(1.25)	8.464(1.22)	8.503(1.27)	8.225(1.34)	8.475(1.22)	8.120(1.32)	8.200(1.19)
	AP SD	0.326(0.10)	0.321(0.08)	0.336(0.09)	0.361(0.16)	0.681(0.25)	0.684(0.21)	0.709(0.27)	0.671(0.27)
	ML position	0.120(0.72)	0.111(0.70)	0.100(0.72)	0.093(0.72)	0.148(0.81)	0.258(0.49)	0.419(0.59)	0.186(0.59)
	ML SD	0.359(0.08)	0.381(0.10)	0.389(0.11)	0.388(0.12)	0.715(0.21)	0.643(0.17)	0.665(0.24)	0.655(0.25)
	Sway velocity	2.083(0.44)	2.335(0.58)	2.337(0.61)	2.312(0.60)	3.628(1.09)	4.077(1.35)	3.773(1.49)	3.645(1.40)
	Sway area	2.230(1.01)	2.343(0.98)	2.569(1.40)	2.774(1.96)	9.656(5.59)	8.638(4.35)	9.626(7.96)	8.922(6.45)

AP: anteroposterior; SD: standard deviation; ML: mediolateral.
† Main effect of vision, values eyes open are significantly lower than with eyes closed (p < 0.001).
§ Main effect of sex, values in males are significantly greater than in females (p < 0.05).
* Main effect of time, a value during Pre (before exercise) is significantly greater than during Post 5 and 10 (5 and 10 min after exercise) (p < 0.001).
¶ Sex x time x vision interaction, only males have a significant left shift from Post 0 (immediately after exercise) to Post 5 during standing forward leaning task only with EC.

SDs of AP and ML COP positions

A main effect of vision was found for both AP SD ($F (1, 29) = 114.0$, $p = <0.001$, partial $Eta^2 = 0.797$) and ML SD ($F (1, 29) = 120.2$, $p = <0.001$, partial $Eta^2 = 0.806$), with greater values observed with EC than with EO (Table 2). A significant sex effect was also found for AP SD ($F (1, 29) = 4.334$, $p = 0.046$, partial $Eta^2 = 0.130$), with males presenting higher values compared with females (Table 2). However, no effects of fatigue or sex x fatigue interactions were found for SD of AP and ML COP positions.

Mean COP sway velocity

A significant effect of vision ($F (1, 29) = 74.79$, $p = <0.001$, partial $Eta^2 = 0.721$) was found for COP sway velocity, with higher values observed during the EC compared with the EO condition (Table 2). A significant fatigue effect was found due to a significant increase in mean COP sway velocity following exercise compared to pre (immediately: $p = <0.001$, 5 min: $p = 0.009$, and 10 min: $p = 0.031$) (Figure 4). No interactions were found for COP sway velocity.

Figure 4. Changes in mean COP sway velocity. Percent change from pre-exercise values are provided immediately after, and at 5 and 10 min following the alternate isometric exercise of ankle plantar and dorsiflexors during standing forward leaning with eyes open (EO) and closed (EC) and overall (EO + EC). ***, **, and * indicate $p = <0.001$, $p = < 0.01$, and $p = < 0.05$, respectively for overall changes as there were no significant vision x fatigue interactions.

95% ellipse of COP sway area

Only a main effect of vision was found for sway area ($F(1, 29) = 56.37$, $p = <0.001$, partial $Eta^2 = 0.660$), with higher values observed during the EC compared with EO condition (Table 2).

SOL H-reflex

No significant effects were found for the H/M ratio according to vision ($F(1, 16) = 0.727$, $p = 0.406$, partial $Eta^2 = 0.04$), sex ($F(1, 16) = 0.122$, $p = 0.732$, partial $Eta^2 = 0.01$), fatigue ($F(1, 16) = 0.167$, $p = 0.688$, partial $Eta^2 = 0.01$), and their interactions. Participants showed inconsistent changes in the ratio with fatigue regardless of sex and vision conditions (Figure 5). Because the criterion to elicit a comparable H reflex across time points (small M-wave with consistent amplitude) was not met in several participants during recovery (5- and 10-min post-exercise), only data for pre and immediately post-exercise were considered.

Figure 5. Changes in H/M ratio. H/M ratio shown before and immediately following alternate isometric exercise of ankle plantar and dorsiflexors during standing forward leaning tasks with eyes open (A) and closed (B). M (blue) and F (orange) indicate males and females, respectively.

Co-contraction index

At pre-fatigue, the mean activity level (% MVIC) of ankle muscles (TA, SOL, and GL) was 4.7, 24.1, and 16.1 during FL-EO, as well as 5.4, 25.8, 12.3 during FL-EC, respectively. Table 3 shows the mean values and standard deviations of the co-contraction index at all time points before and after exercise. No significant effects of vision, sex and fatigue (or their interaction) were found for either of the co-contraction indices (TA-GL and TA-SOL).

Table 3. Mean values (standard deviation) of co-contraction indices (TA-SOL and TA-GL). These values were assessed before and immediately following fatiguing exercise, and throughout recovery (5 and 10 min).

	Co-contraction Indices	Mean values (standard deviation)							
		Eyes Open				*Eyes Closed*			
		Pre	*Post 0*	*Post 5*	*Post 10*	*Pre*	*Post 0*	*Post 5*	*Post 10*
Overall (n=24)	TA-SOL	3.915(1.96))	3.978(1.94)	3.828(1.89)	4.107(1.92)	4.680(3.75)	5.124(4.14)	4.847(3.71)	5.428(3.50)
	TA-GL	4.454(2.09)	4.623(2.16)	4.300(1.92)	4.803(2.22)	4.817(3.81)	4.976(3.45)	5.380(3.53)	5.448(3.38)
Males (n=10)	TA-SOL	4.136(2.25)	4.161(2.30)	4.110(1.95)	4.312(2.58)	5.112(5.20)	5.603(4.59)	5.424(4.15)	6.150(3.81)
	TA-GL	4.137(2.47)	4.486(2.23)	4.128(2.28)	4.916(2.28)	5.169(4.69)	5.265(5.03)	5.533(4.80)	5.949(3.86)
Females (n=14)	TA-SOL	3.709(1.37)	3.806(1.68)	3.564(1.45)	3.914(1.58)	4.275(2.71)	4.675(3.19)	4.307(2.32)	4.751(3.09)
	TA-GL	4.752(1.95)	4.752(2.09)	4.461(1.95)	4.697(1.92)	4.488(1.87)	4.704(2.00)	5.236(2.96)	4.979(2.97)

TA-SOL: co-contraction index between tibialis anterior and soleus; and TA-GL: co-contraction index between tibialis anterior and gastrocnemius lateralis.

Pearsons' correlation

No significant correlation was found between pre to immediately post-fatigue changes in any COP variables and co-contraction indices (TA-SOL and TA-GL) (Table 4). There was also no significant correlation between the H/M ratio and the preceding 50-ms EMG amplitude of each of GL and SOL at each of pre and immediately post-exercise, and between pre to immediately post-exercise changes in the H/M ratio and the preceding 50-ms EMG amplitude of TA or RPE value (immediately after exercise) during each of FL-EO and FL-EC (Table 5).

Table 4. Results of Pearsons' correlation analyses. The correlations were assessed between pre to immediately post-fatigue changes in co-contraction indices (TA-GL and TA-SOL) and COP variables.

Vision	COP sway variables	Co-contraction Indices					
		TA-GL			TA-SOL		
		r	95% CI of r	P-value	r	95% CI of r	P-value
EO	ML position	0.115	-0347 – 0.541	0.538	0.169	-0.313 – 0.563	0.362
	AP position	-0.291	-0.521 – 0.064	0.112	-0.317	-0.518 – -0.011	0.082
	ML SD	-0.074	-0.428 – 0.026	0.694	-0.084	-0.471 – 0.196	0.652
	AP SD	-0.290	-0.551 – 0.087	0.113	-0.185	-0.471 – 0.218	0.319
	Sway velocity	-0.114	-0.365 – 0.150	0.541	-0.044	-0.252 – 0.213	0.816
	Sway area	-0.273	-0.604 – -0.022	0.138	-0.195	-0.529 – 0.026	0.292
EC	ML position	-0.016	-0.094 – 0.221	0.930	-0.014	-0.090 – 0.270	0.942
	AP position	0.165	-0.421 – 0.570	0.374	0.319	-0.219 – 0.646	0.081
	ML SD	-0.044	-0.363 – 0.461	0.813	-0.228	-0.497 – 0.146	0.218
	AP SD	0.099	-0.177 – 0.474	0.596	0.115	-0.169 – 0.573	0.406
	Sway velocity	-0.068	-0.320 – 0.289	0.715	-0.190	-0.414 – 0.132	0.306
	Sway area	0.024	-0.298 – 0.505	0.897	-0.056	-0.324 – 0.353	0.766

TA-GL = co-contraction index between tibialis anterior (TA) and gastrocnemius lateralis (GL); TA-SOL = co-contraction index between TA and soleus (SOL); EO = eyes open; EC = eyes closed; ML = mediolateral; AP = anteroposterior; SD = standard deviation; and r = correlation coefficient; and CI = confidence interval.

Table 5. Results of Pearsons' correlation analysis. The correlations are assessed between soleus (SOL) H/M ratio and either ankle muscle activation (for 50ms prior to the onset of H-reflex) or the rating of perceived exertion (RPE).

Time period (or point)	Muscle or RPE	H/M ratio					
		EO			EC		
		r	95% CI of r	P-value	r	95% CI of r	P-value
Pre to P0	TA	-0.015	-0.455 – 0.485	0.952	0.040	-0.307 – 0.428	0.875
Pre	SOL	0.273	-0.161 – 0.643	0.272	0.135	-0.233 – 0.590	0.593
P0	SOL	0.036	-0.300 – 0.308	0.888	0.114	-0.291 – 0.484	0.652
Pre	GL	0.162	-0.121 – 0.585	0.520	0.193	-0.128 – 0.565	0.442
P0	GL	0.018	-0.278 – 0.456	0.942	0.029	-0.332 – 0.385	0.910
P0	RPE	0.109	-0.308 – 0.593	0.689	0.412	0.020 – 0.728	0.113

H/M ratio = a ratio of soleus H-reflex to maximal M-wave amplitude; EO = eyes open; EC = eyes closed; Pre = before exercise; P0 = immediately after exercise; TA = tibialis anterior; GL = gastrocnemius lateralis; r = correlation coefficient; and CI = confidence interval.

Discussion

The main aim of this study was to compare postural control changes with ankle muscle fatigue during the FL task between healthy young males and females in different vision conditions (EO vs EC). The secondary aim was to determine fatigue-induced alterations in ankle spinal proprioceptive inputs during the FL task according to sex and vision. Our findings showed no significant differences in fatigue-induced COP sway changes (from pre to post exercise) between males and females during the FL task regardless of vision conditions, with no significant fatigue-induced changes in co-contraction indices. This study also found no significant effects of fatigue on the H/M ratio independent of sex and vision conditions. The findings are not consistent with our hypotheses, where we expected males to show greater postural alterations and SOL H-reflex depression with fatigue, and such results would be more pronounced with the withdrawal of vision.

Effects of ankle muscle fatigue on postural control

Fatigue of ankle plantarflexors and dorsiflexors led to a significant increase in overall mean COP sway velocity during the FL task up to 10 min following exercise. This is in line with previous findings of unipedal or bipedal quiet standing tasks [9,12–14]. It has been suggested that such an increase in sway velocity with fatigue may be the consequence of an increase in ankle stiffness to maintain postural stability [40]. Such stiffening behavior could be caused by alterations in sensitivity of muscle spindles and related sensory reweighting with fatigue, leading to reorganization of multi-joint coordination and altered or compensated stability control via the CNS [3].

However, we found no significant effect of ankle muscle fatigue on co-contraction indices, as well as no significant correlation between pre- to immediately post-fatigue changes in COP variables and co-contraction indices (Table 4). The present lack of a fatigue effect on co-contraction could be due to the requirements of the FL task. The forward leaning position, for example, involves greater activation (% MVIC) in both agonist and antagonist muscles (SOL: 26 %, GL: 12 %, and TA: 5 %) and greater co-contraction index (TA-SOL: 6.5 and TA-GL: 7.8), as compared with quiet standing (SOL: 10% and TA: 2 % [41]; and TA-SOL: 2.4 (our calculation based on [41])), which could limit the extent of agonist/antagonist modulation available to increase ankle stiffness to compensate for fatigue. Thus, in the present study, the fatigue-induced increase in sway velocity may instead indicate the use of more corrective actions at the ankle independent of stiffness, as COP sway velocity has been shown to be highly correlated with COM sway acceleration during quiet standing [42]. The increase in sway velocity may also indicate a potential increase in proximal joint contribution to maintaining postural control during challenging static tasks. For example, Boyas and colleagues [13,14] found that significant increases in ankle and/or hip flexion of the supporting and free legs with fatigue of ankle plantar flexors during one-leg standing were accompanied with increases in AP/ML COP sway velocity.

Such a potential compensatory change in proximal joint position, which could occur with insufficient ankle torque needed for optimal control [43], may also have led to the similar performance (amplitude of COP movement: AP/ML position, SD, and sway area) in participants after compared with before the fatiguing exercise. A compensation by other muscle groups, such as ankle mediolateral stabilizers and toe flexors, as suggested in previous studies [14,44,45], could also be involved. Furthermore, sensory systems likely not affected by fatigue (e.g., vestibular and neck somatosensory inputs, see [46]) could play a compensatory role for the reduced ability of fatigued ankle plantar flexors to maintain stability. Also, for the first block of COP data measured immediately after exercise in the present study, a time delay of approximately 1 min occurred for the transition from the dynamometer to the force platform, as well as for any adjustment to the electrical stimulation intensity. Given this delay, the lack of significant fatigue-induced changes in the COP amplitude variables may indicate that the effect of fatigue can be 'short lived'. This is consistent with previous results [14], where it was observed that COP variables were affected only immediately after a tiptoe standing exercise with no significant time delay between fatigue and testing, but not after a 60-s recovery period.

Sex differences in postural control

We found that males had greater SD of overall mean AP COP position and sway area as compared with females. These findings indicate that males may have lesser ability to regulate stability when leaning forward close to the limit of stability as compared with females. Such sex difference in postural stability could be due to documented advantages in biomechanical factors such as a lower COM caused by a wider pelvic base and a greater valgus position of the legs in females compared with males [3,23,47,48]. Although body height and weight could be significant contributors to sex difference in postural control during some tasks [48,49], we still observed the sex difference in SD of mean AP position with COP data normalized by height or weight.

Interactions between sex and fatigue on postural control

No significant sex x fatigue interactions were found for COP sway variables (except for mean ML COP position; however, not reflected in post-hoc t-tests) and the co-contraction indices, indicating generally similar postural control changes with fatigue between males and females. This is consistent with previous findings, which showed no significant sex differences in COP sway changes with fatigue of the ankle or hip muscles during unipedal standing tasks [50,51]. This is not necessarily surprising given similar performance fatigability (the time to task failure) and perceived fatigability (increase in RPE values following exercise, see Figure 3) between males and females [50].

The similar fatigability in males and females may be dependent on the specific exercise/task used to induce fatigue. It has often been reported that females can be less fatigable than males during sustained isometric exercise [17,18], mainly due to their typical lesser muscle mass and strength (limiting blood flow occlusion and accumulation of metabolites, as suggested in [52–54]). The extent of sex differences in performance fatigability during sustained isometric exercise of upper and lower limbs tends to be greater for low-intensity contractions (e.g., 20% MVIC) compared to moderate to high intensity contractions (e.g., 50% to 80%) [55,56]. This may be due to the greater extent of sex differences in muscle perfusion (females > males) during such low-intensity exercise compared to moderate to high intensity in the context of sustained isometric contraction [17,18]. In contrast to sustained low-intensity isometric exercise, the maximal intermittent isometric exercise used in the present study may not have favored the emergence of sex differences in muscle perfusion during the exercise

[17,18] and consequently in ankle muscle fatigue and ultimately in fatigue-induced postural changes.

Furthermore, the findings of a systematic review summarizing 46 studies of various fatigued muscle groups (Hunter 2016) suggest that ankle plantar and dorsiflexors show lesser sex differences in fatigability as compared with other muscle groups. This could be explained by smaller sex differences in relative area of type I (fatigue resistant) muscle fibers and muscle mass and/or strength for the ankle muscles compared with other muscle groups [53,57–59], which would contribute to the similar fatigability between males and females directly and through muscle metabolism (which can affect the accumulation of metabolites and motor neuron activation) [17,18]. Again, the absence of sex differences in fatigue-induced postural changes in the present study could thus be attributed to similar ankle muscle fatiguability between the sex groups.

Interactions between vision and fatigue on postural control

Several studies looking at fatigue of ankle plantar flexors have found greater postural sway changes (or impairment) with no-vision and/or disturbed vision compared to normal vision during upright standing on one leg [6,13,15,60] or two legs [16,61], suggesting a significant role of visual information on compensating declines in the neuromuscular system and proprioception of fatigued ankle plantar flexors to maintain stability [3]. However, we found no significant vision x fatigue interaction for any of the COP sway variables, as well as for both co-contraction indices, indicating that the withdrawal of vision did not significantly affect fatigue-induced postural control changes. These results are in accordance with a few studies investigating ankle plantar flexors fatigue.

For example, two previous studies [14,61] found that the removal of vision does not increase postural sway during one or two-leg standing following sustained or repeated tiptoes until task failure. These authors suggested that the presence of a significant level of fatigue may have restrained vision from compensating fatigue-induced postural changes [14], or the distance of the visual target used (4 m) may have eliminated the compensatory effect of vision on postural control changes with fatigue (which was different with a 1-m visual target leading to significant vision effects) [61]. Even though we used a relatively close visual 'target' distance (1.8 m), the specific characteristics of the postural task used in the present study, in contrast to a simple quiet standing task, may have lessen the potential effect of vision to compensate for fatigue-related alterations in postural control. The use of the representation of the COP on a computer screen to accomplish the FL task involved participants initially reaching the target (70% anterior LOS) before closing their eyes and thus likely memorizing the position where the COP position was to be maintained in the absence of vision. This may have reduced the potential effect of vision and would be different from the use of vision in the context of a quiet standing task while fixating a visual target. Lastly, compensatory proximal joint control could be prioritized rather than ankle control to maintain stability when removing vision in a state of ankle fatigue, which may have led to the lack of a vision effect. For example, Boyas and colleagues [14] found that a backward movement of the pelvis (hip flexion) produced by fatigue of ankle plantar flexors during one-leg standing task significantly increased with EC (15%) compared to EO, while observing a similar fatigue-induced increase in AP/ML COP sway velocity independent of vision conditions (EO vs. EC).

We did find a significant sex x time x vision interaction for mean ML sway position, where only males showed a left shift during recovery (immediately to 5 min after exercise) and only with EC. This may indicate a different postural control strategy with fatigue and recovery between males and females under certain conditions. However, we interpret this result with caution as none of the post-exercise values were different from pre-exercise.

Ankle spinal proprioceptive inputs

No significant effects were found for the H/M ratio according to all independent variables, as there was no consistent pattern of changes in the ratio with fatigue regardless of sex and vision conditions (Figure 5). This is consistent with previous findings by Laudani and colleagues [27], where different changes (increase or decrease) in H-reflex amplitude during quiet standing were found across healthy young adults immediately following an initial set of repetitive tiptoe movements (out of 5 sets).

The lack of fatigue effects on the H/M ratio may be attributed to different changes (increase or decrease) in presynaptic inhibition with ankle fatigue among the participants. In the present study, an increase in the H/M ratio with fatigue was noted in participants in 7 EO and 9 EC conditions. In those instances, fatiguing exercise could have led to descending inhibitory input onto the interneurons accountable for pre-synaptic inhibition of Ia afferents, causing an enhancement of the stretch reflex efficacy at the spinal level [62]. In contrast, a decrease in the H/M ratio with ankle fatigue in the other participants/conditions (11 EO and 9 EC) could be attributed to a potential increase in pre-synaptic inhibition of Ia afferents, possibly due to facilitation of small-diameter group III and IV afferents under the influence of muscle metabolic changes (e.g., reduced oxygen availability and accumulation of metabolites) [63–65]. Such depression in the H/M ratio could also have been caused by reciprocal inhibition due to increased activation of antagonists (TA) with fatigue [28]. However, we did not observe a significant association between pre-to-immediately post-fatigue changes in the H/M ratio and RPE value (which changes can be related to the metabolism within muscles [66,67]) or TA activation (taken immediately before the onset of SOL H-reflex).

Other than the neurophysiological factors mentioned above, psychological factors associated with the experimental conditions could contribute to the variability in the H/M ratio [34]. For example, anxiety imposed by a threat to postural stability (see [68]) could have played a role, especially during the FL-EC condition. Intrinsic forward or backward sway during the FL task at the moment when the SOL H-reflex is elicited may be another potential confounding factor. An increase in SOL H-reflex with intrinsic anterior sway during quiet standing has been reported [37]. We, however, found no significant correlation between the H/M ratio and each of SOL and GL activation (50 ms before the onset of SOL H-reflex), which is reported to be highly correlated with AP COP position [37]). The inconsistent changes in SOL H-reflex in the present study may thus be due to different neurophysiological and psychological conditions among the participants during their experimental session.

A few limitations should be mentioned for the present study. Movements and position of proximal joints/segments (e.g., hip and trunk movements) that could compensate for ankle muscle fatigue to maintain stability were not assessed. Also, the true relation between SOL H-reflex and COP data remains uncertain in the present study because COP data and SOL reflex were not assessed during the same FL task. Lastly, we did not obtain information on the phases of the menstrual cycle in female participants, which has been found to affect postural stability

[69,70]. However, this would likely not be a major confounding factor to sex differences in postural control changes with fatigue, given the smaller effect of the menstrual cycle on fatigability compared to other general sex differences in fatigability [17].

Conclusion

We found similar fatigue-induced postural control changes between males and females during the FL task regardless of vision conditions, where both sex groups had a significant increase in sway velocity following fatiguing exercise of ankle muscles, with no significant changes in ankle co-contraction. Also, no fatigue effect was found on SOL H-reflex, independent of sex and vision conditions (EO vs EC). The lack of sex differences on postural control and ankle proprioceptive inputs with fatigue is not surprising given similar performance and perceived fatigability between the sex groups in the present study. Our findings highlight the importance of considering (fatiguing and postural) task specificity, the muscle group studied, as well as individual characteristics when studying sex differences related to the effects of fatigue on postural control.

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Supporting information

S1 file. Data set. This data includes COP sway variables, ankle stiffness indices, and H/M-max ratios (from Pre to P0), which were collected before (Pre) and immediately (P0) after exercise, and throughout recovery period (5 and 10 min; P5 and P10).

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Figure 1. Schematics of the experimental protocol.

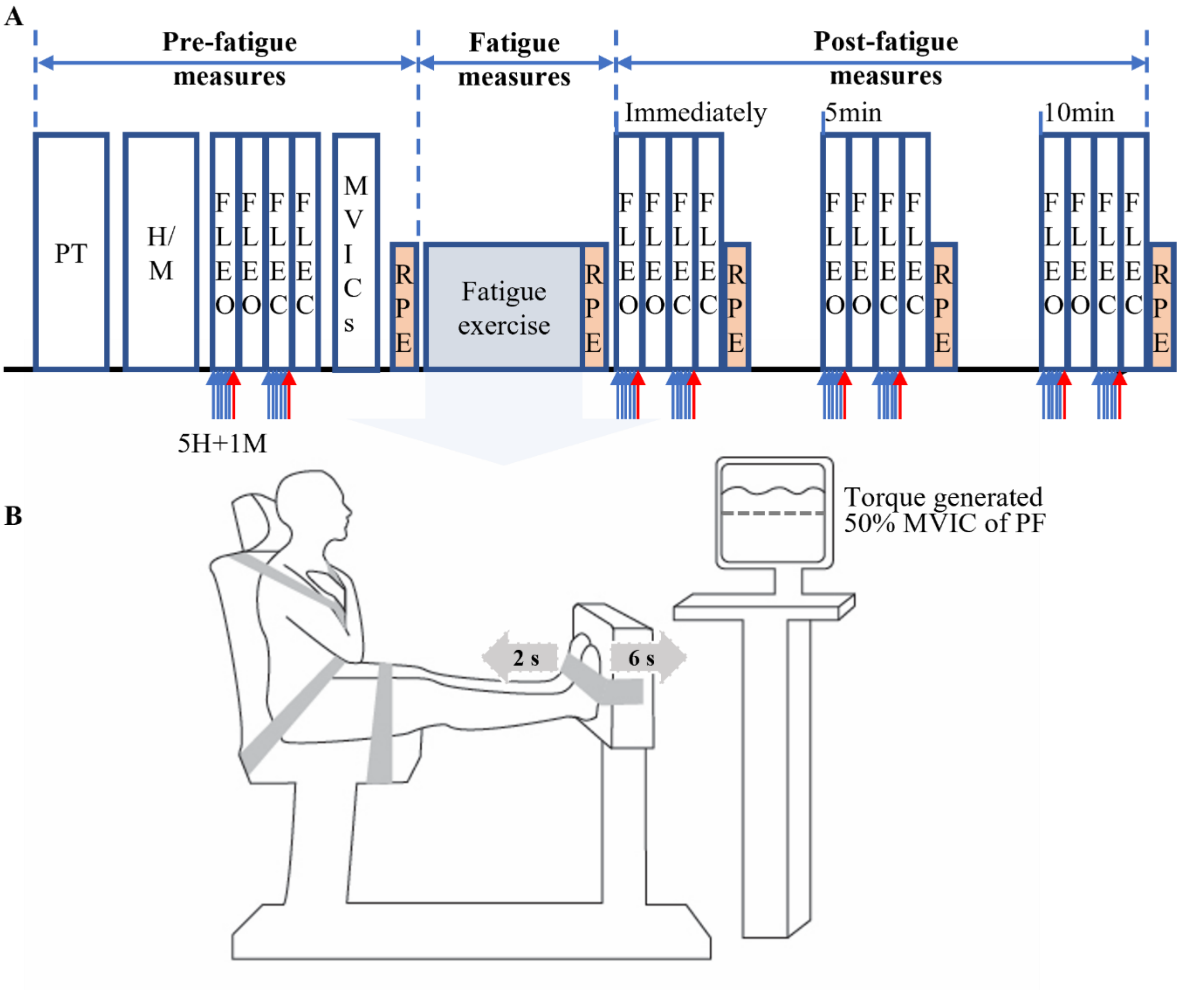


Figure 2. Schematics of the experimental setup.

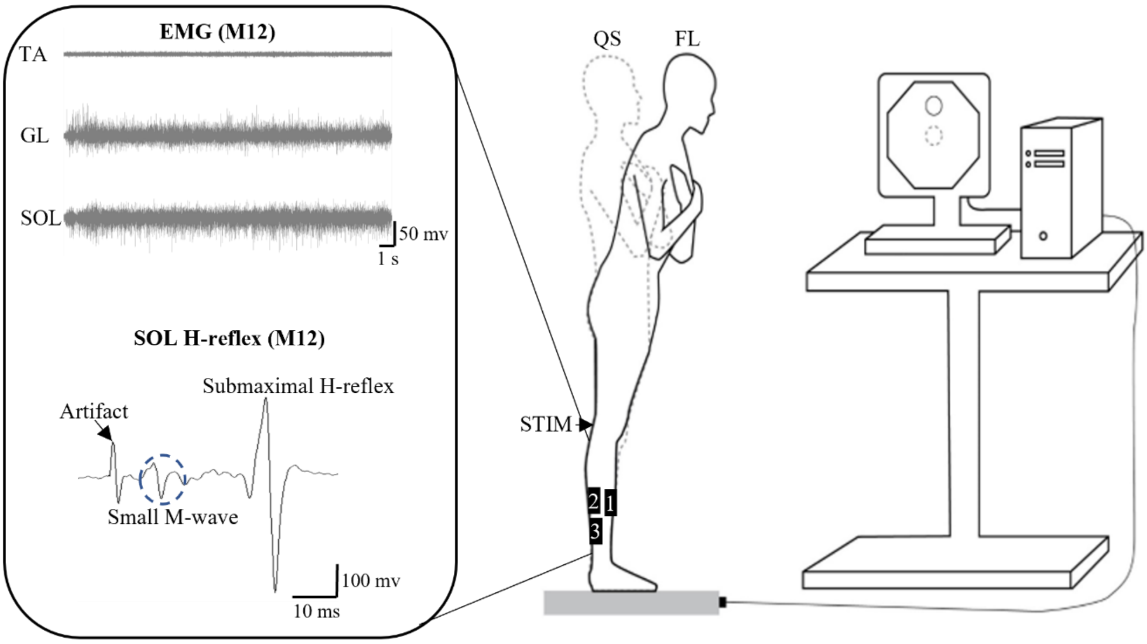


Figure 3. Changes in the rating of perceived exertion (RPE).

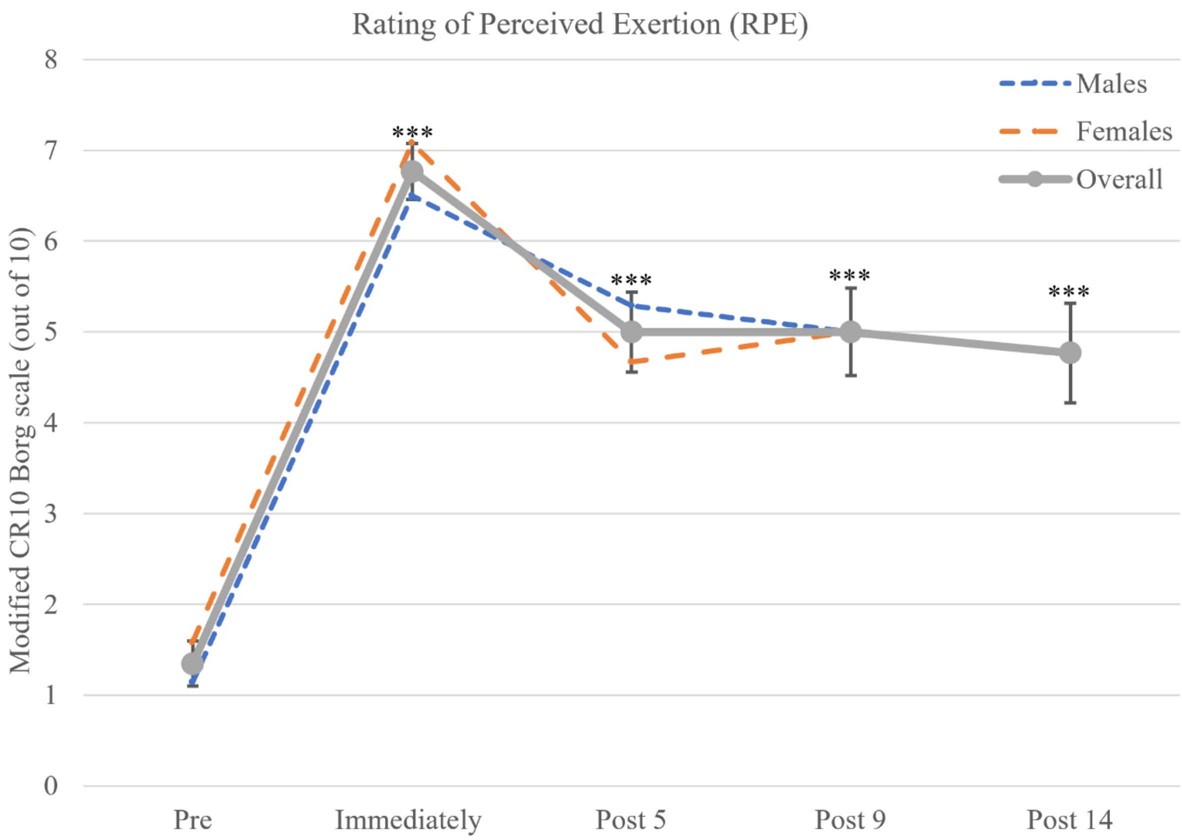


Figure 4. Changes in mean COP sway velocity.

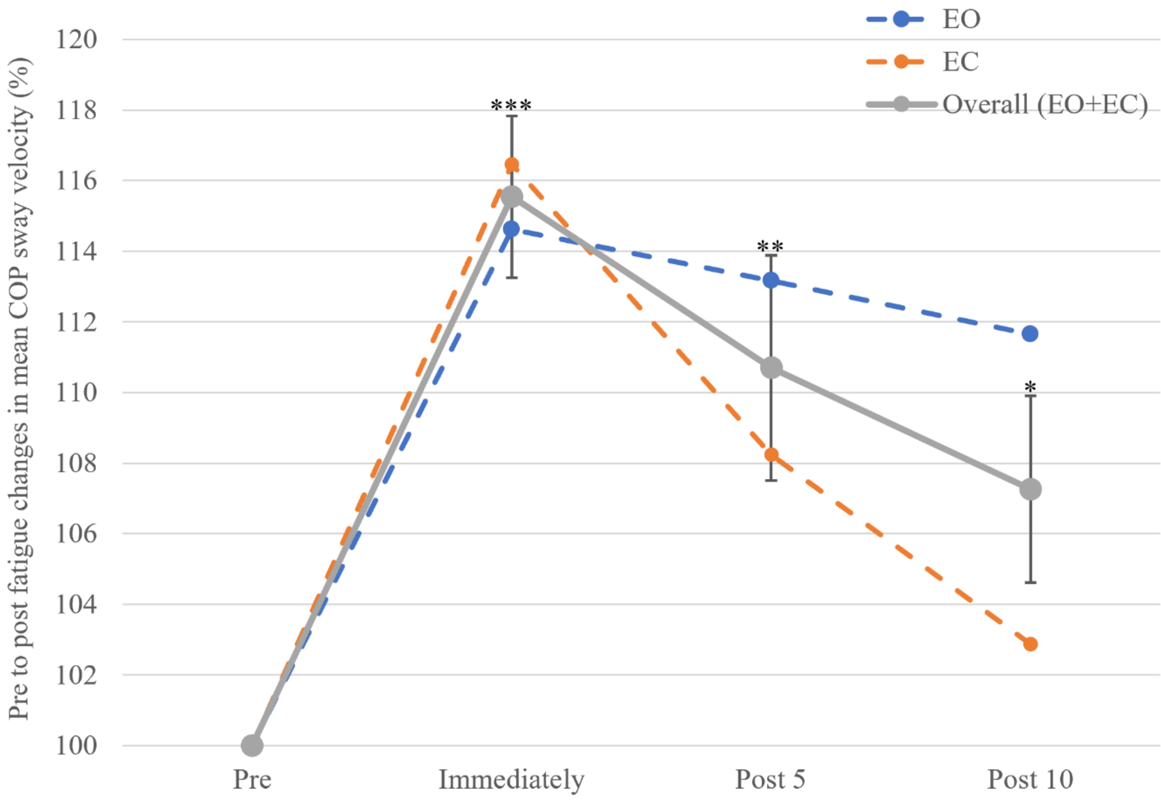
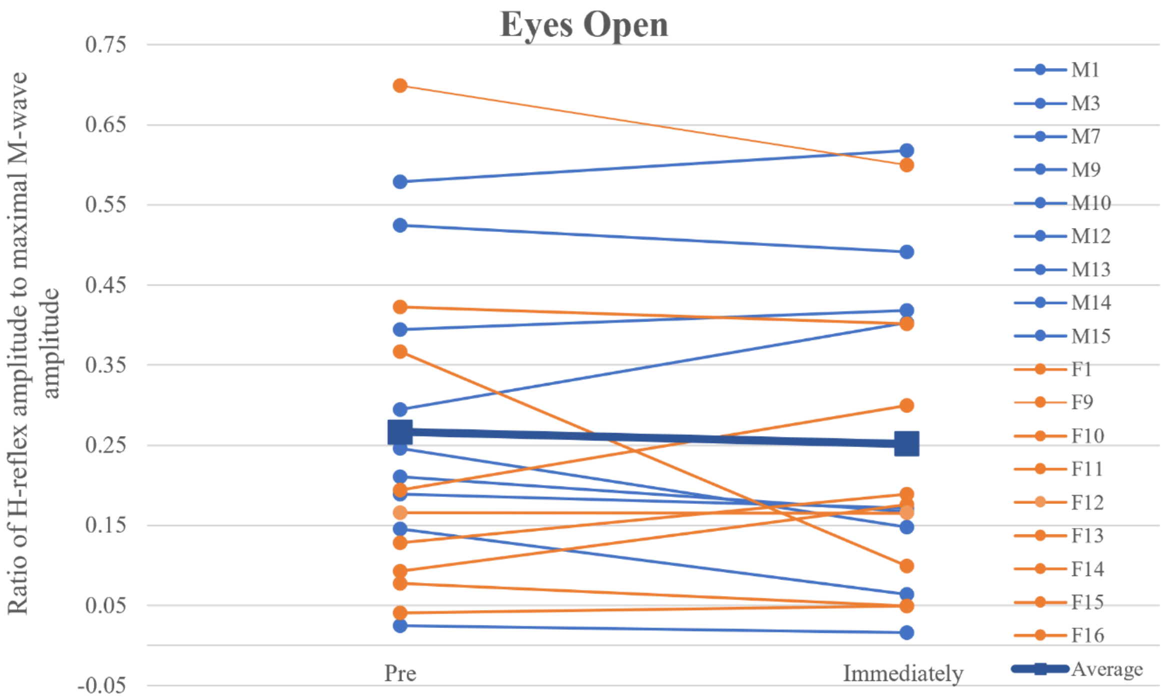
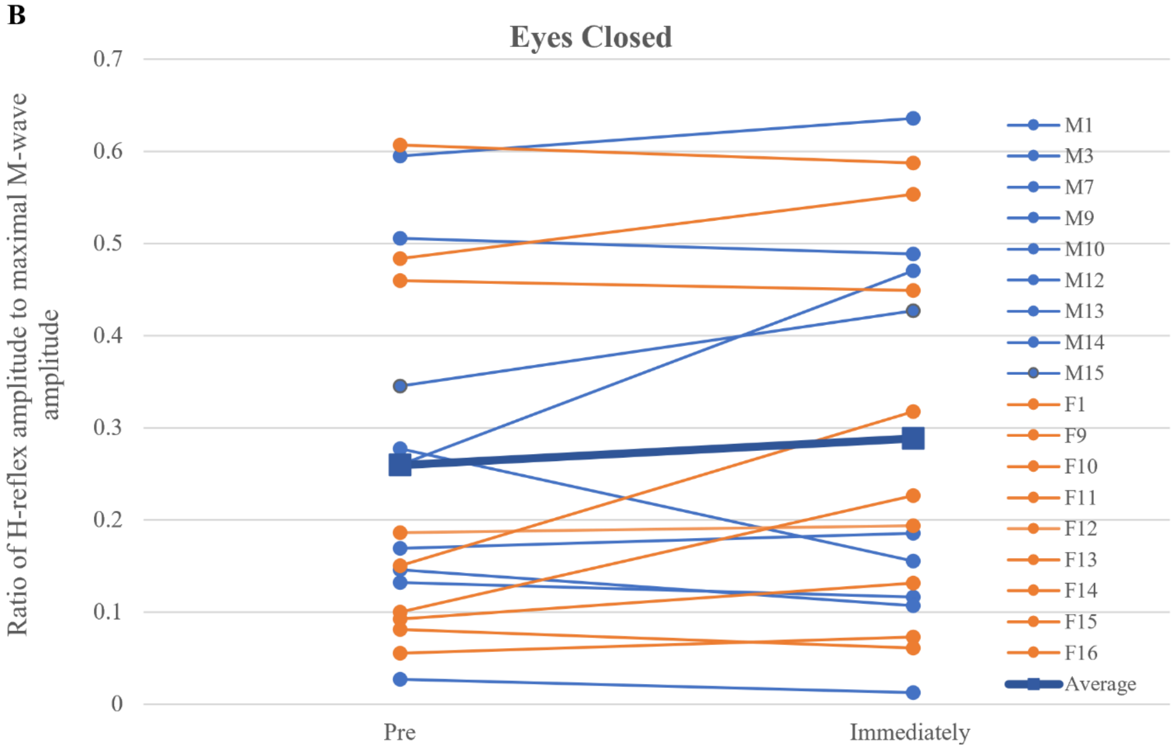


Figure 5. Changes in H/M ratio.

A



B



CHAPTER 4. GENERAL DISCUSSION AND CONCLUSION

The main results (see Table 1 below) for the one scoping review and three experimental articles of this thesis are discussed below.

Table 1. Summary of results of the one review and three experimental articles of this thesis

Study no.	Study type	Fatiguing task	Postural task	Effects	Dependent variables					
					Fatigue mechanisms			*Postural control/mechanisms*		
					FA	VA	TWT	COP sway	Ankle stiffness	SOL H-reflex
1	SR	n/a	n/a	n/a	RPE(SUM)	n/a	n/a	n/a	n/a	n/a
2	QE	(S)25% MVIC (PF)	n/a	Fat	**MVIC ↓**	↓	**ST↓ LFF↓ HRT↑**	n/a	n/a	n/a
				Fat X Sex	MVIC/TF (ns)	ns	ns	n/a	n/a	n/a
3	QE	(S)50% MVIC (PF)	QS/FL with EO/EC	Fat	n/a	n/a	n/a	**Vel (QS/FL-EO)↑ AP (QS/FL-EC)↓ ML (QS-EO)↑**	n/a	n/a
				Fat X Sex	TF (ns)	n/a	n/a	**Vel (FL-EC): Males > Females**	n/a	n/a
				Fat X Vis	n/a	n/a	n/a	**AP (QS/FL): EC < EO**	n/a	n/a
4	QE	(I)MVIC (PF/DF)	FL with EO/EC	Fat	**RPE ↑**	n/a	n/a	**Vel (EO+EC)↑**	ns	ns
				Fat X Sex	TF/RPE (ns)	n/a	n/a	ns	ns	ns
				Fat X Vis	n/a	n/a	n/a	ns	ns	ns

Note: Arrows (↑↓) indicate a significant increase or decrease with fatigue in each corresponding dependent variable. SR = scoping review; QE = quasi-experimental study; S = sustained; I = intermittent; MVIC = maximal voluntary isometric contraction torque; TF = time to task failure; PF = ankle plantar flexors; DF = ankle dorsiflexors; PF/DF = alternating between PF and DF; QS = quiet standing task; FL = standing forward leaning task; Fat = fatigue effects; Fat X sex = fatigue X sex interaction; Fat X vis = fatigue X vision interaction; FA = (perceived and performance) fatigability; VA = voluntary activation; TWT = twitch torque properties; ST = resting singlet twitch peak torque; LFF = low frequency fatigue; HRT = singlet twitch half-relaxation time; RPE = rating of perceived exertion; SUM = summary of a range of RPE values according to exercise type; COP = center of pressure; Vel = mean COP sway velocity; AP/ML = mean AP/ML COP positions; EO = eyes open; EC = eyes closed; SOL = soleus; n/a = not reported; ns = not significant.

4.1. General discussion

The two main goals of this thesis were to determine: 1) sex differences in central and peripheral fatigue mechanisms of PF and 2) sex differences in postural control alterations with ankle muscle fatigue in healthy young adults. Our experiments showed that low to moderate isometric exercise of the ankle muscles (PF and/or DF) led to behaviors of variables reflecting significant muscle fatigue: perceived and performance fatigability (increased RPE value and reduced MVIC torque), contractile function decline (changes in twitch contractile properties), and reduced neural drive to the fatigued ankle muscles (declined VA). Fatigue also induced significant backward and right shifts of the COP position and increases in sway velocity, somewhat dependent on task conditions (QS vs. FL or EO vs EC), despite no significant fatigue effects on co-contraction index and SOL H-reflex. However, we found only minor sex differences in fatigue mechanisms and fatigability, as well as only one significant sex difference in fatigue-induce sway velocity changes during FL-EO. Furthermore, our scoping review summarized RPE values following exercise in previous studies that found significant fatigue effects on postural control, where the range of RPE values found with local muscle fatigue were consistent with those found in our experiment. The following sections will discuss sex differences in ankle fatigue mechanisms, fatigue effects on standing postural control and related sex differences, and postural task-dependency for fatigue-induced postural control. Thereafter, the final two sections will describe the limitations of our studies and additional considerations for future research.

4.1.1. Sex differences in neuromuscular fatigue mechanisms of ankle plantar flexors

In article 2, our results demonstrated that the observed performance fatigability (a reduced MVIC torque) following a sustained 25% MVIC isometric exercise of PF until task failure, was accompanied by changes in variables reflecting both central and peripheral fatigue, namely: twitch contractile function decline (reduced ST and LFF and increased HRT of ST) and reduced VA. This is consistent with previous findings of fatiguing isometric exercise of different muscle groups (knee extensors, elbow flexors, PF, and DF), for example: reduced VA (Bilodeau, 2006; Boyas, Remaud, et al., 2013; Kennedy et al., 2011) and reduced ST (Akagi et al., 2019; Kavanagh et al., 2020), decreased LFF ratio (Keeton & Binder-Macleod, 2006), and increased HRT of ST (Boyas, Remaud, et al., 2013; Kent-Braun et al., 2002; Martin & Rattey, 2007; Smith-Ryan et al., 2014).

However, we did not find any significant sex differences in the ANOVAs related to central and peripheral fatigue mechanisms. This is not surprising given the lack of significant sex-differences in performance fatigability (reduced MVIC torque and/or time to task failure) reported in articles 2-4. This can also be explained by the similar perceived fatigability (increased RPE value assessed with the Borg's CR 10 scale) between males and females reported in article 4, given the significant relationship between performance and perceived fatigability (Cruz-Montecinos et al., 2019; Whittaker et al., 2019) as discussed in Chapter 2. Interestingly, our findings are in contrast with several previous findings of other lower extremity muscle groups, which showed greater performance fatigability and greater central or peripheral fatigue in males compared with females (Akagi et al., 2019; Martin & Rattey, 2007; Russ & Kent-Braun, 2003). This suggests that the extent of sex differences in fatigability and fatigue mechanisms could be dependent on the characteristics of the tested muscle group(s).

As partly discussed in article 2, the lack of significant sex differences in fatigue mechanisms and fatigability in our study could be explained by the characteristics of PF, which have been reported to show a lesser sex difference in the relative area of type I (fatigue resistant) muscle fibers compared with other muscle groups (Coggan et al., 1992; Larsson et al., 2006; Miller et al., 1993; Staron et al., 2000). This is related to the impact of the relative area of type I fibers within a given muscle(s) not only on muscle contractile processes, but potentially also on central processes through group III and IV afferents (Hunter, 2014; Hunter, 2016). Nevertheless, in our study, males showed a slightly greater central fatigue (reduced VA) contribution (accompanying a significant contribution of VA to the fatigue-induced reduction in MVIC torque according to the Pearson's correlation and multiple regression analyses, which was not observed in females), but lesser and shorter peripheral fatigue (reduced ST and/or increased LFF), as compared with females. The minor sex differences indicate the importance of using multifaceted measures when investigating sex-specific fatigue mechanisms.

4.1.2. Effects of ankle muscle fatigue on postural control and related sex differences

4.1.2.1. Effects of ankle muscle fatigue on postural control and soleus (SOL) H-reflex

In articles 3 and 4, our results showed significant postural sway changes following an isometric ankle fatiguing exercise. More specifically, our results demonstrated a significant and prolonged increase in mean COP sway velocity during the QS and FL task. This is in line with previous findings of unipedal or bipedal quiet standing tasks (Boyas et al., 2011; Boyas, Hajj, et al., 2013; Boyas, McGown, et al., 2013; Boyas, Remaud, et al., 2013), possibly suggesting an increase in ankle stiffening behavior to maintain stability (Winter et al., 1998). Nevertheless, our results did not show a significant fatigue effect on the ankle stiffening behavior as reflected by the increased co-contraction indices (TA-GL and TA-SOL) at the ankle nor significant correlations between pre to immediately post-fatigue changes in the co-contraction indices and COP variables. Therefore, our participants may have relied on compensatory ankle or hip corrective actions independent of ankle stiffness, as discussed in Article 4. Furthermore, a fatigue-induced right shift of the COP position was found during the QS task in article 3, which could indicate a shift in the control of posture towards the preferred leg, suggesting a fatigue-induced asymmetry of posture (Penedo et al., 2021).

However, our findings showed a lack of significant fatigue effects on the other COP variables (AP COP position, SD, and sway area; except for AP position during recovery in article 3), despite a significant and prolonged increase in the RPE values after fatiguing exercise (Article 4). The reported increase in RPE values (5-7 out of 10; assessed in the Borg's CR10 scale) after the alternating PF-DF isometric fatiguing exercise of article 4 is within the range of RPE values (5-8; assessed in the same scale) documented in previous studies that found a significant effect of local muscle fatigue (ankle, knee, and hip) on postural control in our scoping review (article 1; Jo and Bilodeau 2021). Thus, as discussed in Articles 3 and 4, the lack of a fatigue effect on sway amplitude variables may be explained by compensations from ankle mediolateral stabilizers or more proximal muscle groups to maintain stability with fatigue (Boyas, McGown, et al., 2013; Harkins et al., 2005; Lundin et al., 1993). Also, our findings (Article 4) showed a lack of significant fatigue effects on SOL H-reflex during the FL task regardless of vision conditions, which may potentially reflect the absence of a change in the contribution of spinal proprioceptive inputs at the ankle to compensate for fatigue to maintain stability. As discussed in Article 4, this could be due to different individual characteristics. For example, in our study, some participants showed a fatigue-induced increase in SOL H-reflex amplitude, potentially reflecting augmentation of the stretch reflex efficacy at the spinal level (Trimble & Harp, 1998). In contrast, the others presented with a fatigue-induced decrease in H-reflex amplitude, potentially due to an increase in pre-synaptic inhibition of Ia afferents (Duchateau & Hainaut, 1993; Kaufman et al., 1983; Sinoway et al., 1993).

Interestingly, the findings in article 4 appear to show a somewhat lesser fatigue effect on postural control, as compared with article 3. The former showed only a significant increase in sway velocity during the FL task, whereas the latter found a significant backward shift in mean AP position during recovery in addition to a significant increase in sway velocity during the same task. The relatively lesser fatigue effect may be partly due to a relatively greater time delay of approximately 1 min that occurred immediately following exercise for the transition from the dynamometer to the force platform, as well as for adjustment to the electrical stimulation intensity, as compared to article 3 (only requiring a 30-s transition). The greater time delay may have eliminated significant fatigue effects on AP position in article 4, given the fact that fatigue effects can recover relatively rapidly, e.g. within a 60-s time frame (Boyas, McGown, et al., 2013). The lesser fatigue effect may also be partly associated with the number of bouts of fatiguing exercise performed where only a single set was performed in article 4 in contrast to four bouts being conducted in article 3. However, these interpretations should be carefully considered as perceived fatigability after exercise was significant and prolonged in our study.

4.1.2.2. Minimal sex differences in fatigue-induced postural control changes

In articles 3 and 4, we initially expected significant sex differences in COP sway behaviors with fatigue of ankle muscles produced by the isometric exercises, as such isometric exercise generally has led to significant sex differences in performance fatigability (Hunter, 2016), and also ankle muscles play a significant role in controlling static stability (Loram & Lakie, 2002), as discussed in Chapter 2. However, our results in those two studies showed no significant sex differences in COP sway changes with fatigue (except for sway velocity), regardless of task conditions (QS vs. FL or EO vs. EC). This is consistent with previous findings, which showed no significant differences in COP sway changes between males and females with ankle or hip fatigue during unipedal standing tasks (McMullen et al., 2011; Nelson & Johnson, 1973). The lack of sex differences in postural control changes with fatigue may be explained by the absence of significant sex differences in fatigability and fatigue mechanisms observed in our studies and could be associated with similar relative area of type I muscle fibers and contractile function (or muscle strength) between males and females for the ankle muscles tested in this thesis, as previously mentioned in section 4.1.1.

Nevertheless, a significant sex difference in sway velocity with fatigue during the FL-EC condition was found in article 3, where males showed a significant and prolonged increase in sway velocity throughout the 15-min recovery following exercise, whereas females did not. This is in accordance with a recent finding (Bannon et al., 2018), where males had an increase in COP sway velocity during one-leg standing following a repetitive lifting task, while females did not have such a fatigue effect. The significant sex difference in sway velocity with fatigue in our study may indicate a potential increase in compensatory ankle corrective action for ankle fatigue to maintain stability in males (but not in females) during the most challenging static task.

As discussed in article 3, given the potential increased contribution of proximal joint (e.g., hip/pelvic) to compensate for ankle fatigue to maintain stability (Boyas, McGown, et al., 2013), our findings suggest different postural control strategies between males and females, where males may preferentially rely on ankle control, whereas females are likely to rely on proximal joint movements (e.g.., hip and trunk) to maintain stability. This is supported by previous findings, such as: greater fatigue-induced ankle torque variability during feet-together standing in males compared to females (Wojcik et al., 2011). Adlerton and colleagues (2003), who recruited healthy young females, also found an increase in trunk accelerations accompanied with a decrease in COP velocity with fatigue of ankle plantar flexors during one-leg standing, suggesting a changes in postural control strategy from ankle to hip with fatigue of the ankle muscles in this sex group. Also, the potential increased reliance on the ankle strategy with fatigue in males may be due to their disadvantage in biomechanical factors to control static stability as compared with females (Paillard, 2012) because, in article 3, a significant sex X fatigue interaction in non-normalized COP velocity was eliminated with the COP data normalized by the weight of the participants.

Interestingly, such a significant sex difference in sway velocity changes with fatigue was not found in article 4 where an intermittent maximal isometric exercise was used to induce fatigue of PF and DF, which was different from the sustained submaximal (50% MVIC) isometric exercise of PF used in article 3. It has often been reported that females can be less fatigable than males during sustained submaximal isometric exercise (Hunter, 2014; Hunter, 2016), because their typical lesser muscle mass and strength could have a smaller impact on blood flow occlusion and accumulation of metabolites compared with males during such type of exercise, as suggested in previous studies (Hunter & Enoka, 2001; Kavanagh et al., 2020; Miller et al., 1993). Thus, as discussed and suggested in Chapter 2 and article 4, in contrast to the sustained submaximal isometric exercise, the maximal intermittent isometric exercise used in article 4 may have minimized sex differences in muscle perfusion during the exercise and, consequently, in ankle muscle fatigue (Hunter 2014, 2016) and fatigue-induced postural alterations. Also, although fatigue of both PF and DF was reported to have a greater impact on unipedal postural control than isolated PF fatigue (Boyas et al., 2011), fatigue of both muscle groups in article 4 did not lead to a greater impact on bipedal postural control and did not lead to sex differences in postural control with fatigue.

In addition to this task specificity, a potential variation in the menstrual cycle across the female participants at the time of the experiments (articles 3 and 4) may have had a minor contribution to the small but contradictory sex-specific COP behaviors with fatigue between the two studies. This is because, as discussed in Chapter 2, natural hormonal changes across the menstrual cycle could affect leg proprioception and neuromuscular function (Aydoğ et al., 2005; Fridén et al., 2006; Hertel et al., 2006; Hu et al., 2020), which may lead to variations in muscle fatigue (Pallavi et al., 2017) and standing postural control (Khowailed & Lee, 2021; H. Lee & Yim, 2016) in female participants. However, we cannot confirm the effects of the menstrual cycle on the sex-specific behaviors in this thesis as information on the phases of the menstrual cycle in the female participants was not obtained (as discussed in the limitations of articles 2-4). Our results suggest that task specificity (exercise intensity, contraction type and the specific muscle(s) fatigued) and individual characteristics (e.g., the menstrual cycle) should be carefully considered when studying sex differences in postural control in the context of muscle fatigue.

4.1.3. Postural task-dependency

In addition to our primary goals, in articles 3 and 4, we noted that fatigue-induced COP changes were dependent on postural task conditions (QS vs. FL and/or EO vs. EC). Significant and greater backward shifts of the AP COP position with fatigue were found during recovery for the QS and FL tasks with EC compared with EO, suggesting a significant role of visual information for compensating ankle fatigue to maintain stability (Gaerlan et al., 2012; Paillard, 2012; Rodrigues et al., 2017). As discussed in article 3, the significant effects of vision could be due to the use of the representation of the COP on a computer screen, as well as the use of a relatively close visual target (Rodrigues et al., 2017), which would enhance the role of vision for compensating instability with fatigue. Interestingly, the visual effect was greater during the QS task as compared to the FL task, potentially due to the presence of a perceived threat of forward fall and increased ankle stiffness during the FL compared to QS (see below for details), which may have reduced the role of vision to compensate for ankle fatigue during the FL task. Such characteristics of the FL task may also have led to the lack of a fatigue effect on ankle stiffening behavior (co-contraction index), as discussed in article 4. For example, leaning forward close to the limit of stability during the task could reduce the extent of antagonist (TA) versus agonist (SOL or GL) modulation available to enhance ankle stiffness to counteract ankle fatigue. This is supported by our observation of greater co-contraction indices (TA-SOL and TA-GL) during the FL task at baseline, compared to quiet standing (Donath et al., 2016). However, in our study, postural task-dependency had no significant impact on sex differences in postural control with fatigue.

4.1.4. Limitations

Although specific limitations have been reported in each article, a few additional limitations are considered here. First, in article 4, one COP datum was obtained for each postural task condition at each time point before and after exercise as another group of the four postural tasks was performed to obtain the H-reflex data at each time point. However, time-related changes in the COP data in article 4 are analogous to the average COP data (from two trials at each timeframe) obtained in article 3. Also, as previously discussed, a time delay was present immediately following exercise in article 4, which may have minimized the effects of fatigue on postural data and SOL H-reflex. Third, fatigability of foot/toe flexors in participants was not assessed but could have affected postural control during the FL task. Lastly, although an interest in dynamic postural control (e.g., gait) is increasing, our experiments were limited to static postural control, but with a challenging postural task of FL.

4.1.5. Clinical implication

The main focus of this thesis was to advance our basic knowledge of sex differences in fatigue mechanisms and static postural control with fatigue. Nevertheless, our findings also indirectly contribute to the improvement in the sex-specific prescription of physical training or rehabilitation exercise, given the sex differences in injury risks during physically or stability-demanding tasks and sports (Arendt & Dick, 1995; Bannon et al., 2018; Deitch et al., 2006; Swanik et al., 2007; Zelisko et al., 1982). For example, our findings may indirectly inform clinical practitioners on how to develop a rehabilitation intervention for recovery from ankle instability (including the use of an isometric exercise of ankle muscles), in considering an optimal ankle fatigue level (perceived and physical) and recovery time (or interval) between and/or after bouts of isometric exercises to avoid an instability-related potential injury. The approach for such ankle exercise intervention may be similar for males and females, based on our findings that generally showed similar sex behaviors in ankle muscle fatigue and related standing postural control changes.

4.1.6. Future considerations

We propose additional considerations for future research when studying sex differences in neuromuscular fatigue mechanisms and postural control with fatigue. In article 2, we observed only minor sex differences in central and peripheral fatigue mechanisms by only reporting data on twitch torque and using the twitch interpolation technique. Additional measures for fatigue mechanisms (e.g., muscle activation, metabolic changes, perceived exertion level) should be concurrently considered, as muscle fatigue can be caused by neurophysiological and psychological factors from multiple central and peripheral sites (Enoka & Duchateau, 2016).

In Articles 3 and 4, our findings, which are based on the observation of COP sway and muscle activation at the ankle, found a general lack of significant sex differences in postural control. Additional postural measures (e.g., body segment movements and muscle synergies from ankle to hip or trunk) should be assessed to compare postural strategy changes between males and females with fatigue in the context of both static and dynamic postural tasks. It would be interesting to compare such sex differences in fatigue-induced postural control changes between different muscle groups (e.g., ankle vs. hip), given that the extent of sex differences in performance fatigability is muscle group-dependent (Hunter, 2014; Hunter, 2016). Testing the effects of the menstrual cycle on such sex differences would also be interesting.

Furthermore, our findings were based on the performance of isometric fatiguing exercise and static postural tasks. The use of dynamic postural and fatiguing tasks would help not only understand sex-specific differences in muscle fatigue and postural control, but also sex differences in injury risks (e.g., knee and lower back) during tasks that require continuous dynamic muscle contraction and stability, such as required in sports (e.g., soccer and basketball) (Arendt & Dick, 1995; Deitch et al., 2006; Swanik et al., 2007; Zelisko et al., 1982) and occupational tasks (e.g., repetitive weight lifting) (Bannon et al., 2018). Particularly, the use of dynamic (or functional) postural tasks with fatigue of proximal postural muscles (e.g., knee and hip) may have a great opportunity to observe such sex differences, as such dynamic tasks can mainly require the proximal muscles' movements to maintain stability (e.g., a forward step from forward falling; see Patikas et al., 2016), and these proximal muscles could be more susceptible to fatigue and show a greater extent of sex differences in fatigability (as compared with the ankle muscles, see Hunter, 2014, 2016). This, however, should be carefully considered due to possible confounding factors (e.g., analyzed postural variables) affecting the relationship between muscle fatigue and postural control, as reported in Chapter 2 and article 1 (scoping review). For example, two previous studies found no significant fatigue effects of knee/entire leg muscles on functional tasks (e.g., a forward step from a forward fall or leg-reaching tasks; see Mademli et al., 2008; Zech et al., 2012) with the observations of postural variables (not including COP data; anterior margin of stability, COM, BOS, and leg-reaching distance). In contrast, one of the two found significant changes in COP sway behaviors with fatigue of the legs even during quiet standing (Zech et al., 2012), possibly indicating that the extent of fatigue effects on postural control could be postural variable-dependent.

In addition to these experimental considerations, our scoping review (Article 1) was limited to articles reporting on 'standing' postural control, which corresponded to the focus of our experiments. Gait performance, which can also be affected by muscle fatigue in healthy young and older adults (Barbieri et al., 2016; Dos Santos et al., 2020; Lehnen et al., 2020), could be the focus of a future systematic review study.

4.2. Conclusions

Our findings contribute to improving sex-specific knowledge of fatigue mechanisms and static postural control with fatigue in healthy young adults, as there are only a limited number of studies in this area at the moment. In this regard, our results showed minimal sex differences in central and peripheral fatigue mechanisms induced by PF. This may be due to the small sex differences in type I muscle fiber area and contractile function, as compared to other muscle groups. Furthermore, to our knowledge, this is the first time that sex differences are determined in a standing forward leaning task in the presence of ankle muscle fatigue. A significant sex difference in sway velocity change induced by a submaximal sustained isometric exercise was found during FL-EC. We suggest that males may rely more on the ankle strategy, in contrast with females who may rely more on a hip strategy to compensate for ankle fatigue to maintain challenging static stability. Such a sex difference, however, was not observed following a maximal intermittent isometric exercise. Also, the range of RPE values documented with ankle fatigue in our experiment was analogous to RPE values documented with local muscle fatigue in previous studies that found significant fatigue effects on standing postural control in our scoping review. Altogether, our findings suggest that the specific details of fatiguing and postural tasks should be considered when studying sex differences in muscle fatigue and related postural control changes.

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APPENDIXES

Appendix A. Research Ethic Board approval (renewal) letters (University of Ottawa)

From: ETHICS2 <ethics2@uottawa.ca>
Subject: Ethics File #H11-14-23 Renewal
Date: December 10, 2019 at 1:27:26 PM EST
To: Martin Bilodeau <Martin.Bilodeau@uottawa.ca>, "Heidi Sveistrup (HSveistrup@bruyere.org)" <HSveistrup@bruyere.org>, Heidi Sveistrup <hsveist@uottawa.ca>

Dear Researchers,

Thank you for submitting an Annual Status Report for your research project entitled "**Acute effects of exercise-induced neuromuscular fatigue on posture control with aging**" (uOttawa ethics file #: H11-14-23)

Your ethics approval has been renewed and is **valid December 1st, 2020** (same as Bruyère REB). In order to help us keep your file up to date, please forward us a copy of any and all renewal, amendment and/or closure reports submitted to and approved by the Bruyère REB, as they become available.

Tara Martin and Simon Darbhanga have been added to the research team as volunteers.

If you have a grant for your research, you must provide a copy of this email to Research Management Services (https://research.uottawa.ca/rms/about).

Please don't hesitate to contact us if you have questions.

Best regards,

Stéphanie Léger
Pour / On behalf of

Marc Alain Bonenfant
Coordonateur / Coordinator
Bureau d'éthique et d'intégrité de la recherche / Office of Research Ethics and Integrity
Université d'Ottawa / University of Ottawa
Tél : 613-562-5387
550 Cumberland (TBT 154)
Ottawa, ON K1N 6N5
http://recherche.uottawa.ca/deontologie/

From: Kim Thompson <Kim.Thompson@uOttawa.ca>
Subject: uOttawa Ethics File #H11-14-23 - Renewed
Date: December 18, 2020 at 3:11:52 PM EST
To: Martin Bilodeau <Martin.Bilodeau@uottawa.ca>

Dear Researcher,

Thank you for submitting the renewal certificate from OHSN for your research project entitled "**Acute effects of exercise-induced neuromuscular fatigue on posture control with aging**" (uOttawa ethics file #: **H11-14-23**).

Your ethics approval has been renewed and is **valid until December 1, 2021** (same as Bruyère-REB).

In order to help us keep your file up to date, please forward us a copy of any and all renewal, amendment and/or closure reports submitted to and approved by the Bruyère-REB, as they become available.

If you have a grant for your research, you must provide a copy of this email to Research Management Services (https://research.uottawa.ca/rms/about).

Please don't hesitate to contact us if you have questions.

Best regards *– and Happy Holidays!*,
Kim

From: ETHICS2 <ethics2@uottawa.ca>
Subject: Ethics File #H11-14-23 Renewal
Date: December 2, 2021 at 2:53:38 PM EST
To: Martin Bilodeau <Martin.Bilodeau@uottawa.ca>

Dear Researchers,

Thank you for submitting an Renewal Report for your research project entitled "**Acute Effects of exercise-included neuromuscular fatigue on posture control with aging**" (uOttawa ethics file #: **H11-14-23**)

Your ethics approval has been renewed and is **valid until December 1st, 2022** (same as Bruyère REB). In order to help us keep your file up to date, please forward us a copy of any and all renewal, amendment and/or closure reports submitted to and approved by the Bruyère REB, as they become available.

If you have a grant for your research, you must provide a copy of this email to Research Management Services (https://research.uottawa.ca/rms/about).

Please don't hesitate to contact us if you have questions.

Best regards,

Stéphanie Léger
Pour / On behalf of

Catherine Paquet
Directrice / Director
Bureau d'éthique et d'intégrité de la recherche / Office of Research Ethics and Integrity
Université d'Ottawa / University of Ottawa
Tél : 613-562-5387
550 Cumberland (TBT 154)

Appendix B. Research Ethic Board approval (renewal) letters (Bruyere Research Institute)

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November 11, 2019

Dr. Martin Bilodeau

RE: Acute Effects of Exercise-Induced Neuromuscular Fatigue on Posture Control with Aging (Bruyère REB project M16-08-038)

Renewal/Extension Approval

Dear Dr. Bilodeau,

Thank you for submitting an annual renewal form for the above named study. The Bruyère Continuing Care Research Ethics Board is pleased to extend ethical approval for the above named project from December 1, 2019 to December 1, 2020.

All projects reviewed by the Bruyère Research Ethics Board must be renewed every 12 months or as otherwise determined by the Board. According to our policies, if we do not receive the renewal request in a timely manner the REB approval may be terminated and the file closed. In the future please submit an annual renewal/termination report 6 weeks in advance of the last approved renewal end date.

We wish you best of luck as you proceed with this study.

Sincerely,

Gordon DuVal, SJD
Chair, Bruyère Research Ethics Board
Bruyère Continuing Care
gduval@bruyere.org

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December 17th, 2020

Dr. Martin Bilodeau

RE: Acute Effects of Exercise-Induced Neuromuscular Fatigue on Posture Control with Aging (Bruyère REB project M16-08-038)

Renewal/Extension Approval

Dear Dr. Bilodeau,

Thank you for submitting an annual renewal form for the above named study. The Bruyère Continuing Care Research Ethics Board is pleased to extend ethical approval for the above named project from **December 1, 2020 to December 1, 2021.**

All projects reviewed by the Bruyère Research Ethics Board must be renewed every 12 months or as otherwise determined by the Board. According to our policies, if we do not receive the renewal request in a timely manner the REB approval may be terminated and the file closed. In the future please submit an annual renewal/termination report 6 weeks in advance of the last approved renewal end date.

We wish you best of luck as you proceed with this study.

Sincerely,

Gordon DuVal, SJD
Chair, Bruyère Research Ethics Board
Bruyère Continuing Care
gduval@bruyere.org

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Monday, November 15, 2021

Dr. Martin Bilodeau

Re: "Acute effects of exercise-induced neuromuscular fatigue on posture control with aging" (Bruyère REB Protocol # M16-08-038)

Renewal/Extension Approval

Dear Dr. Bilodeau,

Thank-you for submitting an annual renewal form for the above named study. The Bruyère Continuing Care Research Ethics Board is pleased to extend ethical approval for the above named project from December 1, 2021 to December 1, 2022.

We wish you best of luck as you proceed with this study.

Sincerely,

Gordon DuVal, SJD
Chair, Research Ethics Board
Bruyère Continuing Care
gduval@bruyere.org

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Appendix C. Consent form (for articles 2-4)

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Soins continus Bruyère Continuing Care — Institut de recherche Bruyère Research Institute
Affilié à l'Université d'Ottawa
Affiliated with the University of Ottawa

INFORMATION LETTER AND CONSENT FORM

Acute effects of exercise-induced neuromuscular fatigue on posture control with aging

Adresse postale
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Corporate Office
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Palliative Care Education and Research
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Téléc./Fax: 613-562-6371

Centre de recherche C.T. Lamont en soins de santé primaires
C.T. Lamont Primary Health Care Research Centre
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Recherche sur les soins aux aînés
Care of the Elderly Research
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Téléc./Fax: 613-562-4266

INVESTIGATOR

Martin Bilodeau, Ph.D., PT,
Bruyère Research Institute & School of Rehabilitation Sciences,
Faculty of Health Sciences, University of Ottawa
Telephone: (613) 562-6262, ext. 1358
Email: martin.bilodeau@uottawa.ca

Funding: This program of research is partly funded through a Discovery grant from the Natural Sciences and Engineering Research Council of Canada.

Invitation to participate: I am invited to participate in the research "Acute effects of exercise-induced neuromuscular fatigue on posture control with aging" conducted by the research team headed by Dr. Martin Bilodeau. I am a healthy adult between 18 and 35 years old, or between 40 and 55 years old or older than 65 years of age.

Purpose of the study: The purpose of this research study is to assess and compare the effects of muscular fatigue of the leg on mobility and/or balance in young and older adults.

Participation: If I agree to participate, my involvement will consist of at least one and up to a maximum of three visits (with about one week interval) to the Aging and Movement Research Laboratory at the Bruyère Research Institute. Some participants may be asked to participate in sessions done at the University of Ottawa's Lees Campus or Roger Guindon Campus. Each visit will last between 30 and 90 minutes. For each of the experimental visits, the following tasks may be performed.

1) First, surface electrodes may be taped to my skin over three to six of my leg muscles. To facilitate this, I will be asked to wear shorts. Some of the electrodes will be placed below my knee, and some may be placed above the knee on the thigh and on the side of my buttock. I will then have to briefly push as hard as I can with my leg against an apparatus or the hands

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of a researcher in three to six different directions. Small electronic devices may also be taped to the skin at my ankles, knees and hips to measure changes in the position of those joints. Changes in joint position may also be measured with a system consisting of eight infrared cameras and small markers taped to the skin.

2) My mobility and/or balance on one or two legs will be tested. I will be asked to perform one or more of the following activities: 1) stand still on one of my legs or on both legs on a platform able to measure how much I sway for bouts of 30-60 seconds; 2) lean in different directions by matching targets presented on a screen placed in front of me; 3) keep my balance while a platform I am standing on moves once or continuously for 1 min; 4) walk 8 meters to a memorized target on the floor while blindfolded; or, 5) sit down and stand up from a chair or the floor. I may also be asked to listen to or give a verbal response to a tone or give a verbal response or push a button as fast as possible in response to a light, before and/or while my balance is tested.

3) After this, my strength may be assessed using a device designed to measure muscular strength and for rehabilitation exercises. If so, I will be asked to sit with one of my legs strapped to avoid unwanted movement. Then, I will be asked to push or pull as hard as I can up to five times with either my hip, knee or ankle.

4) Then my leg muscles may be fatigued by performing one of the following activities: 1) in the same position as for the maximal force test, I may be asked to do continuous repetitions of maximal efforts or hold a target force level with my ankle, knee or hip until my force decreases by a given percentage (25, 50 or 75%) of my maximum force; 2) I may be asked to raise-up on my toes and maintain this position for as long as I can; 3) I may be asked to go up and down a flight of stairs or a platform until my heart rate increases to a pre-determined level; or 4) I may be asked to rise up and sit down from a chair repeatedly until I can no longer maintain a given pace.

5) Immediately and up to 30 minutes after fatigue is reached, I will be asked to execute the same task as described in 2.

6) During post fatigue assessments, the level of fatigue of my muscles may be maintained by repeating the step in 4 between balance trials.

7) I may be asked to perform the mobility/balance task described in 2 while wearing a weighted suit, goggles to diminish my vision and earplugs.

8) My participation may involve the electrical stimulation of one of my muscle. If so, from five to ten brief (5/1000 of one second) pulses of electrical stimulation will be given to my muscle.

9) My hearing may also be tested by the researchers in a sound booth.

Risks: I understand that the possible risks associated with participating in this research project are as follows:

1) **Minor irritation** of the skin at the surface electrode sites is possible, but uncommon because of the use of non-irritating, non-abrasive, non-sensitizing conductive cream.

If present, the irritation should disappear in a few hours. Also, some discomfort is possible when removing the surface recording electrodes (like removing a band-aid).

2) **Muscle soreness** associated with performing maximal contractions with my leg might be experienced after the experimental visits. However, a warm-up period before testing begins will be provided and should minimize the muscle soreness. For my safety and well-being, the investigators may decide to end a session at any time.

3) **The loss of balance** during testing is possible but any fall will be prevented through the use of a harness and rope system anchored to the ceiling or a belt worn around my waist. A member of the research team will be in appropriate proximity to provide additional support when necessary.

4) If applicable, **discomfort** from electrical stimulation may be present as the sensation is similar or somewhat stronger than from a shock experienced with static electricity. In our experience, participants do tolerate these shocks relatively well. However, if the stimulation was to become too uncomfortable for given individuals, the study would be ended. Subjects will be reminded periodically that they are free to end the session if they feel uncomfortable for any reasons.

Benefits: I understand that I may not benefit personally from participating in this study. However, we hope that, in the future, other people might benefit from this study because of the increased knowledge of factors affecting balance, postural control and falls with aging.

Cost: I will not have any costs for participating in this research study. I will be compensated to cover expenses associated with my participation in the study. By providing consent to participate in this research study and receiving payment for participation, we wish to inform you that a research administrator at the Institute will be reviewing the participant lists of all research studies of this nature (in which participant payments are made) once per year. He or she will sign a confidentiality pledge and will keep your personal information confidential. However, in the event that the research administrator identifies that you have received more than $500 per year in payments for your involvement in research studies at our organization, he/she will notify our Finance Department so that a T4A form can be issued to you for income tax reporting purposes (at which time your SIN number will be required).

Confidentiality and anonymity: I understand that the investigators will keep my participation in this research study confidential. My identity will be kept confidential by using a subject code or number instead of personal information. Any document with my personal information and data will only be accessed by the investigators and will be kept in a locked cabinet in Dr. Bilodeau's office.

Data Conservation: I understand that the results of this study (including mine), will be presented at scientific meetings and submitted for publication in scientific journals. When a report or article is written about this study, the results will be described in a summarized manner so that I cannot be identified. I understand that all data will be destroyed after 10 years.

Voluntary Participation: I understand that taking part in this research study is completely voluntary. I may choose not to take part at all. If I decide to be in this study, I may stop participating at any time. If I decide not to be in this study, or if I stop participating at any time, I will not be penalized and will still receive the reimbursement for expenses for which I otherwise qualify; furthermore my data/records will be destroyed.

Acceptance: I, ________________________________ *(name of participant),* accept to participate in this research conducted by the research team headed by Dr. Martin Bilodeau from the Élisabeth Bruyère Research Institute and the Faculty of Health Sciences of the University of Ottawa.

Questions: I am encouraged to ask questions. If I have any questions about the research study itself, I can contact: Dr. Martin Bilodeau at the Élisabeth Bruyère Research Institute, 43 Bruyère Street, Ottawa, Ontario, K1N 5C8, tel: (613) 562-6262, ext. 1358.

If I have questions about the rights of research subjects or I have ethical concerns about this study, I understand that I can contact the Director of Ethics at Bruyère Continuing Care at (613) 562-6262 x4003 or I can contact the Protocol Officer for Ethics in Research, University of Ottawa, Tabaret Hall, 550, Cumberland Street, room 154, Ottawa, ON K1N 6N5, at (613) 562-5387 or at ethics@uottawa.ca.

There are two copies of this form, one of which is for you to keep.

____________________________________ ______ / ____ / ____

Signature of participant yyyy mm dd

____________________________________ ______ / ____ / ____

Signature of the researcher yyyy mm dd

Appendix D. Approval letter and guideline of COVID-19 screening procedures for participants' onsite visit (Bruyère Research Institute) with COVID-19 screening questionnaire tool and COVID-19 verbal consent form (for article 4)

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Centre de médecine familiale Primrose
Primrose Family Medicine Centre
35, rue Primrose St.
Ottawa ON K1R 0A1
Tél./Tel.: 613-230-7788
Téléc./Fax: 613-230-7778

Institut de recherche Bruyère
Bruyère Research Institute
43, rue Bruyère St.
Ottawa ON K1N 5C8
Tél./Tel.: 613-562-6045
Téléc./Fax: 613-562-4266

Fondation Bruyère Foundation
43, rue Bruyère St.
Ottawa ON K1N 5C8
Tél./Tel.: 613-562-6319
Téléc./Fax: 613-562-6023

Affilié à / Affiliated with

uOttawa

Friday, April 23, 2021

Dr. Martin Bilodeau

Re: "Acute effects of exercise-induced neuromuscular fatigue on posture control with aging" (Bruyère REB Protocol #M16-08-038)

Addendum Approval

Addendum dated: April 22, 2021

Dear Dr. Bilodeau,

Thank you for submitting an addendum request for the above named project.

The following has been approved:

- ✓ COREB Application;
- ✓ Appendix A – Bruyère-approved COVID-19 Screening Questionnaire for Visitors;
- ✓ Appendix B – COVID Consent Form: On-Site;
- ✓ 4.1 On-site Outpatient Research Visits

The information received has been reviewed and I hereby give approval on behalf of the REB.

Sincerely,

Gordon DuVal, SJD
Chair, Research Ethics Board
Bruyère Continuing Care
gduval@bruyere.org

À Bruyère, nous vous promettons... bonté • sécurité • bienveillance
At Bruyère, we promise you... Kind • Safe • Care

4.0 PROCEDURES

4.1 On-site Outpatient Research Visits [1]

4.1.1 Number of RPs and SPs (if applicable) Outpatients Permitted on Site	Onsite outpatient research visits must be limited to only one RP and one SP (if applicable) in the research area at any one time [2].
4.1.2 Scheduling Call	A scheduling call **must** be made prior to the on-site visit, at which time the research team will; **Step 1**: Complete the latest version of the Bruyère-approved COVID-19 Visitor Screening Questionnaire with the RP/SP. See Appendix A. ▪ If passed by the RP/SP proceed to Step 2. ▪ If failed by the RP/SP contact the RP/SP in 14 days for another scheduling call. **Step 2**: Complete the verbal COVID Consent Form with the RP/SP. See Appendix B. ▪ If verbal consent is obtained from the RP/SP proceed to Step 3. ▪ If verbal approval is not received from the RP/SP the visit cannot occur. **Step 3**: Schedule the research visit and inform the RP/SP that if the RP/SP become symptomatic or if others around them are confirmed to have COVID before the scheduled visit, they must communicate that information to the research team, the visit will be cancelled and another scheduling call will be booked in 14 days.
4.1.3 Reminder Call	A reminder call **must** be done 24 hours before the visit or the Friday before a Monday morning visit with the RP/SP, at which time the research team will; **Step 1**: Complete the latest version of the Bruyère-approved COVID-19 Visitor Screening Questionnaire with the RP/SP. ▪ If passed by the RP/SP proceed to Step 2. ▪ If failed by the RP/SP inform the RP/SP that they will be contacted in 14 days for another scheduling call.

[1] *In the event that a SP is required to accompany the RP to the on-site research visit, both the RP and SP must pass the Bruyère COVID screening questionnaire and provide verbal consent for the Covid Consent Form, before they are allowed on site.*

[2] *If research teams have approval to run multiple face-to-face research studies that share a common research space, only one RP with their SP (if applicable) are allowed in the research space at any one time. The research area must be thoroughly cleaned between RPs.*

	Step 2: ▪ Remind the RP/SP of the requirements in the COVID Consent Form, including that if they feel unwell on the day of the appointment they should call the research team to reschedule[3]. ▪ Provide the RP/SP with the following information for their arrival to Bruyère; ○ Your contact details. ○ Arrival entrance: ▪ Research being conducted at EBH on 2Y – 75 Bruyère Street. ▪ Research being conducted at EBH on 7th – 43 Bruyère Street. ○ Wear their own mask while going through the entrance screening process. ○ Complete the Bruyère-approved COVID-19 visitor screening questionnaire at the entrance. ○ Complete hand hygiene. ○ Replace their mask with a procedural mask and wear a face shield provided by Bruyère. ○ Wait in the designated entrance area for a member of the research team to come and accompany the RP/SP to the research area.
4.1.4 Bruyère Entrance Screening Notification Procedure	The Bruyère entrance screening staff must be made aware of the RP/SP visit **at least 24 hours** prior to the visit. An email must be sent to Bruyère Screening Team at telecebp@bruyere.org with a copy sent to Marie Maksoudian (Screening Manager) at MMaksoudian@bruyere.org. The following information must be included in the email. ▪ Name of RP/SP ▪ Site location and entrance ▪ Visit date and time ▪ **Research team phone extension**
4.1.5 Arrival at Bruyère	When the RP/SP arrive on site and pass the screening procedure, research staff; ▪ Will be notified by the screeners that the RP/SP has arrived. ▪ Should proceed to the appropriate Bruyère entrance to accompany the RP/SP to the research area. ▪ Ensure that hand hygiene is completed by the RP/SP before entering the research area. In the event that the RP/SP do not pass the Bruyère entrance screening, the RP/SP will be asked to leave the building and research staff [4]; ▪ Will be notified by the screeners that the RP/SP did not pass the screening questionnaire.

[3] *If the RP/SP revoke their consent to the COVID Consent Form during the reminder call the visit must be cancelled.*
[4] *Ensuring that the Reminder Call is done prior to the on-site visit will reduce the chance of this happening.*

	▪ Should follow-up with the RP/SP to re-schedule at a later date pending passing the screening questionnaire..
4.1.6 Procedure during the Visit	During the visit, research staff must ensure that the RP/SP; ▪ Complete hand hygiene when entering and leaving the research area. ▪ Limit the touching of surfaces. ▪ Follow masking and physical distancing 2 metre rules. ▪ Are accompanied by research staff when needing to use the washrooms. ▪ Hand hygiene and 2 meter physical distancing is completed when the RP and/or SP (if applicable) need to remove their mask for any reason, including a hydration or nutrition break. ▪ Are provided with a disinfected table to put food and/ or drinks on. ▪ Do not use microwaves, water fountains, kettles, refrigerators, and coffee machines. Throughout the visit research staff must disinfect all equipment before and after use as per section 4.4. Personal Protective Equipment (PPE), Lab Coats and Cleaning. At the end of the visit, research staff must; ▪ Accompany the RP/SP to the exit of the Bruyère site. ▪ Disinfect all equipment and research surfaces that were used during the research visit.

APPENDIX A – Bruyère-approved COVID-19 Screening Questionnaire for Visitors

Bruyère

Screening Tool for COVID-19 Hospital Visitors

Your information will be shared with Ottawa Public Health, when requested, to assist in their contact tracing initiatives.

Date:	Location: ☐ÉBH ☐SVH ☐SLR ☐ÉBR
First name: (Please Print)	Last name: (Please Print)
Patient visited:	Phone:

Are you experiencing any NEW OR WORSENING SYMPTOMS listed in section #1 and #2? If YES, identify your symptom(s) from the list below.

1.	☐ Fever ☐ Difficulty breathing or shortness of breath ☐ Cough ☐ Conjunctivitis (pink eye)	☐ Loss of taste/smell ☐ New diagnosis of pneumonia ☐ Sore throat ☐ Difficulty swallowing	☐ Runny nose or nasal congestion ☐ Digestive symptoms (including nausea, vomiting, diarrhea, abdominal pain)
2.	☐ Unexplained fatigue/malaise or myalgia (muscle pain)	☐ Different or worsening Headaches	☐ Chills

3.	Have you travelled internationally (anywhere outside Canada) within the past 14 days?	☐ YES	☐ NO
4.	Have you been in close contact with a confirmed case of COVID-19 OR had close contact with a person who has any of the above symptoms (section #1 and #2) within the last 14 days?	☐ YES	☐ NO
5.	Have you worked any shift, volunteered or visited on a declared COVID-19 outbreak unit in another healthcare organization other than Bruyère, Élisabeth Bruyère Residence or Saint-Louis Residence within the last 14 days?	☐ YES	☐ NO
6.	Have you cared for a **probable or confirmed** COVID-19 case in another healthcare organization other than Bruyère, Élisabeth Bruyère Residence or Saint-Louis Residence within the last 14 days?	☐ YES	☐ NO
	– If yes, have you been cleared to return to work by your employer's OHSS?	☐ YES	☐ NO
7.	If you are 70 years of age or older, are you experiencing any of the following symptoms:		
	– Sudden or unexplained confusion?	☐ YES	☐ NO
	– Unexplained or increased number of falls?	☐ YES	☐ NO
	– Acute functional decline?	☐ YES	☐ NO
	– Worsening of chronic conditions?	☐ YES	☐ NO
8.	I have read the visitation guidelines and will adhere to them.	☐ YES	☐ NO

☐ **I declare that the information shared is true to the best of my knowledge.**

Signature:

Outcome of screening: ☐ Passed screening ☐ Failed screening	
Screener Signature:	**Date:**

COVID-19 (English version) *September 30, 2020*

Appendix B – COVID Consent Form: On-Site

Please note that all new studies applying for REB approval to begin their face-to-face research must include the new Verbal Consent for Face-to-Face Participant during COVID-19.

Verbal Consent for Face-to-Face On-Site Participation during COVID-19

Version Date: March 11, 2021

Bruyère Research Ethics Board Approval

Date of Approval: [03/10/2021]

Overview

This document contains important information regarding face-to-face study participation at the Bruyère Research Institute (Bruyère RI) during the COVID-19 pandemic. The purpose of this document is to inform you of the steps that we are taking at Bruyère RI to keep research participants and study partners safe and to lower the risk of COVID-19 exposure. It also outlines your responsibilities if you choose to come into the Bruyère RI to participate in research. These steps were built with direction from Ottawa Public Health, the province and Bruyère.

This form is intended to help you understand what is required of you so that you can decide whether you agree to commit to these safety measures for the duration of the COVID-19 pandemic.

Before providing verbal approval of this form, please ask all of the questions you might have, take as much time as you need, and consult with others as you wish.

Risks of face-to-face on-site study visits

Although we are taking multiple steps to reduce the risk of exposure to COVID-19 within our hospital, there is still a risk that you may be exposed to COVID-19. Due to the nature of the virus, carriers of the virus may not always show symptoms and may still be contagious.

Public health guidelines currently allow us to conduct face-to-face on-site study visits. However, in the event that these public health guidelines change, face-to-face visits may need to be stopped and/or the study might need to be put on hold. If this happens, you will be informed promptly by someone from the study team and instructed on plans for your specific study.

What we are doing to minimize risk of exposure:

- Screening everyone who enters Bruyère.
- Following universal masking and face shield protocols, which means that all staff must wear a procedural mask and face shield at all times while working at Bruyère.

- Maintaining physical distancing of 2 metres between all individuals who are not from the same household, where possible.
- During medical procedures, staff will always wear a lab coat and during biological specimen collection gloves will be worn. Staff will also thoroughly wash their hands before and after all procedures.
- Limiting the touching of surfaces. Only staff will touch things like door handles and elevator buttons during your visit.
- Following Bruyère Infection Prevention and Control (IPAC) guidelines for proper hand hygiene and disinfecting surfaces.
- Restricting access for staff, participants and study partners (if applicable) to certain areas in the hospital.
- Accompanying participants and their study partners (if applicable) to and from their visits to the Bruyère entrance/exit.
- Reducing the number of staff in the research area at any given time.
- Allowing no more than one participant and their study partner (if applicable) into the research area at any given time.
- Notify the participant and study partner (if applicable) as soon as possible if any member of the research team they have come in contact with during their visit becomes symptomatic and COVID is confirmed.

Your responsibility to minimize exposure/transmission

In order to continue to participate in face-to-face study visits at Bruyère RI, you must agree to follow the safety measures below. These precautions have been put into place to help keep you, the study team, and patients at Bruyère safe, and to prevent possible COVID-19 exposure. If you do not agree to follow these safety precautions, you will be asked to stop attending the Bruyère RI for face-to-face visits, which may impact your ability to participate in our research studies.

- You and your study partner (if applicable) agree to complete all the necessary COVID-19 screening procedures, which include:
    - Phone screening during your scheduling call,
    - Phone screening at your reminder call which can be 24 hours before your visit or the Friday before your Monday visit.
    - In-person screening at the Bruyère Street entrance that you will be asked to come to at the hospital on the day of your visit
- You agree to wear your own mask when you come to the entrance of Bruyère.
- You agree to change your mask and wear the mask and face shield that will be provided to you at the screening entrance for the entirety of your visit.
- You agree not to remove the mask or face shield unless you are instructed to do so by a member of the study team.
- You agree to maintain 2 metres of distance between you and others that are not in your household during your visit where possible, and except during medicals interventions and procedures that do not allow for 2 meter distancing.
- If you require beverages or food during your visit because of medical reasons or due the length of the visit, you agree to bring your own beverages and food and follow the instructions provided by the research staff on when and how to consume them.
- You will inform the study team immediately [Martin Bilodeau at] if you experience any COVID-19 related symptoms (e.g. new or worsening cough, shortness of breath, fever, chills, fatigue or weakness, new loss of smell or taste) or if you test positive for COVID-19 within 14 days following your visit to the Bruyère RI .
- You agree to have the Bruyère RI provide your name and contact information to Bruyère Occupational Health and Safety and /or other public health officials if needed to facilitate

prompt contact tracing and understand that by providing this information your anonymity cannot be maintained.

These policies/procedures have been reviewed and approved by the Bruyère Research Institute and the Bruyère Continuing Care Research Ethics Board.

If you require further information or have questions at any time about the information outlined above please contact [Martin Bilodeau at martin.bilodeau@uottawa.ca].

SIGNATURE OF PERSON OBTAINING CONSENT

I have personally explained the consent form to the participant (name of the participant – print) ______________________________________, and the study partner (if applicable) (name of the study partner-print) _____________________________and answered all of his/her/their questions. I believe that s/he/they understands the information described in this document and freely consents to participate.

I (name of person obtaining informed consent (print) ____,

Witnessed verbal consent by telephone on (date: dd/mmm/yyyy) ________________________________

at (time: hh:mm) ____

Signature ______________________________ Date Signed ________________________

Appendix E. Acceptance letters for the publication of articles 2 and 3.

An acceptance email for article 2:

From: em.jek.0.7bb301.7c829113@editorialmanager.com <em.jek.0.7bb301.7c829113@editorialmanager.com> on behalf of Journal of Electromyography and Kinesiology <em@editorialmanager.com>
Sent: Wednesday, June 1, 2022 2:03:22 AM
To: Donguk Jo
Subject: Decision on submission to Journal of Electromyography and Kinesiology

Attention : courriel externe | external email

Manuscript Number: JEK-D-21-00371R2

Sex differences in central and peripheral fatigue induced by sustained isometric ankle plantar flexion

Dear Mr. Jo,

Thank you for submitting your manuscript to Journal of Electromyography and Kinesiology.

I am pleased to inform you that your manuscript has been accepted for publication.

My comments, and any reviewer comments, are below.
Your accepted manuscript will now be transferred to our production department. We will create a proof which you will be asked to check, and you will also be asked to complete a number of online forms required for publication. If we need additional information from you during the production process, we will contact you directly.

We appreciate you submitting your manuscript to Journal of Electromyography and Kinesiology and hope you will consider us again for future submissions.

Kind regards,
Dario Farina
Editor-in-Chief

Journal of Electromyography and Kinesiology

An acceptance email for article 3:

You are being carbon copied ("cc:'d") on an e-mail "To" "Martin Bilodeau" martin.bilodeau@uottawa.ca

Sex differences in the effect of muscle fatigue on static postural control under different vision and task conditions
PONE-D-22-01230R1

Dear Dr. Bilodeau,

We're pleased to inform you that your manuscript has been judged scientifically suitable for publication and will be formally accepted for publication once it meets all outstanding technical requirements.

Within one week, you'll receive an e-mail detailing the required amendments. When these have been addressed, you'll receive a formal acceptance letter and your manuscript will be scheduled for publication.

An invoice for payment will follow shortly after the formal acceptance. To ensure an efficient process, please log into Editorial Manager at http://www.editorialmanager.com/pone/, click the 'Update My Information' link at the top of the page, and double check that your user information is up-to-date. If you have any billing related questions, please contact our Author Billing department directly at authorbilling@plos.org.

If your institution or institutions have a press office, please notify them about your upcoming paper to help maximize its impact. If they'll be preparing press materials, please inform our press team as soon as possible -- no later than 48 hours after receiving the formal acceptance. Your manuscript will remain under strict press embargo until 2 pm Eastern Time on the date of publication. For more information, please contact onepress@plos.org.

Kind regards,

Pierre Denise, Ph.D, M.D.
Academic Editor
PLOS ONE