Modern analytical approaches to understand the sex-specific effects of fatigue on multi-dimensional synergies during repetitive whole-limb tasks

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Abstract

From the perspective of dynamical systems, different degrees of freedom (DoFs) need to coordinate and be integrated into synergistic relations to maintain the performance of goal-directed movements. However, how DoFs are coordinated during repetitive whole-limb tasks, and how this is affected by fatigue and may differ between the sexes, is less clear. This dissertation aimed to apply modern linear and nonlinear approaches to investigate the sex-specific effects of fatigue on multi-dimensional synergies during repetitive movements. In addition, we studied repetitive tasks of both the upper limbs and of the lower limbs, so as to verify if general conclusions on multijoint coordination control could apply to both of the body's upper and lower limbs.

This thesis work is based on two retrospective analyses of previously collected datasets, and results from a novel experimental protocol. The retrospective analyses were conducted on data collected from healthy young adults who performed a forward-backward pointing task with the dominant upper limb until reaching fatigue. Analyses were performed on surface electromyography (sEMG) signals collected from four muscles of the upper limb. Continuous wavelet transform and entropy estimates were used to assess sEMG signals in time-frequency and complexity domains. Muscle synergy analysis was used to assess multimuscle coordination. Findings show that fatigue led to decreased complexity and mean frequency of upper arm EMG. Muscle synergy structures and recruitment patterns remained unchanged with fatigue. Females showed higher complexity and mean frequency of biceps brachii and more relative weight of biceps brachii EMG compared to males after fatigue. These results emphasize the important role of biceps brachii to distinguish male from female movements.

The novel experiment was conducted to study a treadmill running task in highly trained endurance runners. Kinematic data were collected using inertial measurement units motion capture

and continuous relative phase analysis was used to quantify coordination between joints of the lower limb. Results showed that fatigue led to an in-phase and variable Ankle-Knee joint coupling pattern during shock attenuation phases after fatigue. Sex differences were observed in the coordination of Pelvis-Hip couplings, with a more in-phase and variable coordination pattern in females with fatigue. These results emphasize the importance of hip-pelvis control to distinguish male and female locomotion with fatigue.

In conclusion, most indicators of multijoint coordination were unchanged with fatigue during which variability plays a useful role in preserving coordination. Sex differences in upper limb control involve the role of biceps brachii, whereas in lower limb control they involve the coordination of proximal hip-pelvis joint, two body areas with known anthropometrical differences between the sexes. This dissertation adds to the growing evidence that advanced modern analytical metrics can reveal subtle biomechanical changes with fatigue, as well as some sex-specific fatigue manifestations. The potential long-term application of this dissertation is to advance sex-specific features of software design to advance performance and prevent injuries.

Abrégé

Du point de vue des systèmes dynamiques, différents degrés de liberté (DL) doivent se coordonner et être intégrés dans des relations synergiques pour maintenir la performance des mouvements orientés vers un but. Cependant, la façon dont les DL sont coordonnés pendant les tâches répétitives multiarticulaires, et la façon dont cela est affecté par la fatigue et peut différer entre les sexes, sont moins claires. Cette thèse visait à appliquer des approches linéaires et non linéaires modernes pour étudier les effets sexospécifiques de la fatigue sur les synergies multidimensionnelles pendant les mouvements répétitifs. De plus, nous avons étudié des tâches répétitives des membres supérieurs et des membres inférieurs de façon à dégager des constats généraux sur le contrôle corporel de tâches multiarticulaires.

Ce travail de thèse est basé sur deux analyses rétrospectives d'ensembles de données collectées précédemment et sur les résultats d'un nouveau protocole expérimental. Les analyses rétrospectives ont été menées sur des données recueillies auprès de jeunes adultes en bonne santé qui ont effectué une tâche de pointage avant-arrière avec le membre supérieur dominant jusqu'à la fatigue. Les analyses ont porté sur les signaux électromyographiques de surface (sEMG) recueillis sur quatre muscles du membre supérieur. La transformée en ondelettes continue et les estimations d'entropie ont été utilisées pour évaluer les signaux sEMG dans les domaines temps-fréquence et de complexité. L'analyse de la synergie musculaire a été utilisée pour évaluer la coordination multimusculaire. Les résultats montrent que la fatigue entraîne une diminution de la complexité et de la fréquence moyenne de l’EMG du bras. Les structures de synergie musculaire et les schémas de recrutement sont restés inchangés avec la fatigue. Les femmes ont montré une complexité et une fréquence moyenne plus élevées du biceps brachii et un poids relatif plus important de l’EMG

du biceps brachii par rapport aux hommes après la fatigue. Ces résultats soulignent le rôle important du biceps brachii pour distinguer les mouvements masculins des mouvements féminins.

Finalement, la nouvelle expérience a été menée pour étudier une tâche de course sur tapis roulant chez des coureurs d'endurance très entraînés. Les données cinématiques ont été recueillies à l'aide d'unités de mesure inertielle et d'une analyse continue de la phase relative pour quantifier la coordination entre les articulations des membres inférieurs. Les résultats ont montré que la fatigue entraînait un modèle de couplage en phase et variable entre l'articulation cheville-genou pendant les phases d'atténuation des chocs après la fatigue. Des différences entre les sexes ont été observées dans la coordination des couplages bassin-hanche, avec un modèle de coordination plus en phase et plus variable chez les femmes avec la fatigue. Ces résultats soulignent l'importance du contrôle de la hanche et du bassin pour distinguer la locomotion masculine de la locomotion féminine en cas de fatigue.

En conclusion, la plupart des indicateurs de coordination multi-articulaire restent inchangés avec la fatigue, au cours de laquelle la variabilité joue un rôle utile dans la préservation de coordination. Les différences entre les sexes dans le contrôle des membres supérieurs concernent le rôle du biceps brachii, alors que dans le contrôle des membres inférieurs elles concernent la coordination de la hanche et du bassin, deux régions corporelles dont l'anthropométrie est clairement différente entre les sexes. Cette thèse ajoute aux preuves de plus en plus nombreuses que les mesures analytiques modernes avancées peuvent révéler des changements biomécaniques subtils avec la fatigue, ainsi que certaines manifestations de fatigue spécifiques au sexe. L'application potentielle à long terme de cette thèse est de faire progresser les caractéristiques sexospécifiques de la conception des logiciels afin d'améliorer les performances et de prévenir les blessures.

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Contribution to Original Knowledge

This thesis is comprised of three manuscripts. Chapter 3 has been published. Chapter 4 and 5 are in preparation for submission.

Chapter 3, titled "*Few sex-specific effects of fatigue on muscle synergies in a repetitive pointing task*", is the first study to evaluate the effects of fatigue on upper limb muscle synergies in dynamic multijoint upper limb movements. This study is also the first to evaluate the upper limb muscle synergies in a sex-specific way.

Chapter 4, titled "*Sex-specific myoelectric manifestations of fatigue in time-frequency and complexity domains during a repetitive pointing task*", is the first study to apply analyses in time-frequency and complexity domains to determine the effects of fatigue on arm muscle activation during dynamic multijoint upper limb movements. This study is also the first to evaluate time-frequency and complexity characteristics of arm muscle activation in a sex-specific way.

Chapter 5, titled "*Sex-specific effects of fatigue on lower limb coordination and coordination variability in highly trained endurance runners*", is the first study to evaluate the effects of fatigue on inter-joint relative phase relations during running in highly trained endurance runners. This study is also the first to evaluate the inter-joint relative phase relations of highly trained endurance runners in a sex-specific way.

Contributions of Authors

The three manuscripts forming this thesis are primarily the work of Ms. Yiyang Chen, including conceptualization, data curation, data analysis, visualization, results interpretation, and writing-first draft and editing. Therefore, she was the 1st author of each of these manuscripts. As the director of the laboratory where all three studies took place and as Ms. Yiyang Chen's thesis supervisor, Dr. Julie Côté is the last (senior) author on all three manuscripts.

Chapter 3 and 4 are based on two retrospective analyses of previously collected datasets in Dr. Julie Côté's lab. Ms. Chen led the conceptualization, data curation, data analysis, visualization, results interpretation, and writing-original draft and editing of both manuscripts. Dr. Chen Yang was the senior Ph.D. student in the lab who guided Ms. Chen with data curation and provided insights into conceptualization, validation of the data analysis and statistical analysis, results interpretation, and writing-review and editing. For this reason, Dr. Yang was included as 2nd author in Chapter 3. Ms. Di Kang was a Master's student in Mechanical Engineering at the University of Ottawa at the time of this work. Ms. Kang was invited and contributed to conceptualization, data analysis, results interpretation, and writing-review and editing. Therefore, Ms. Kang was included as 2nd author in Chapter 4. Dr. Côté supervised these projects and provided funding acquisition, management of support from highly qualified personnel, guidance on conceptualization, data analysis, results interpretation, visualization, and writing-review and editing. Therefore, she was assigned the final position (3rd and senior author) for both manuscripts.

For Chapter 6, Ms. Chen led the conceptualization, data collection, data curation, data analysis, visualization, results interpretation, and writing-original draft and editing. Dr. Côté supervised the project, was a co-investigator on the grant received to fund the project within which this data was collected, and provided guidance on conceptualization, data analysis, results interpretation, visualization, and writing-review and editing. Therefore, she was assigned the final position (2nd and senior author).

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List of Abbreviations

AD	Anterior Deltoid
ANOVA	Analysis of Variance
BIC	Biceps Brachii
CI	Confidence Interval
CIHR	Canadian Institutes of Health Research
CNS	Central Nervous System
CRP	Continuous Relative Phase
CSC	China Scholarship Council
CWT	Continuous Wavelet Transform
DoFs	Degrees of Freedom
DP	Deviation Phase
EMG	Electromyography
FRQS	Fond de Recherche du Québec – Santé
FT	Fatigue-terminal
GEE	Generalized Estimating Equations
iMNF	Instantaneous Mean Frequency
IMUs	Inertial Measurement Units
MARP	Mean Absolute Relative Phase
MD	Mean Difference
MdPF	Median Power Frequency
MMF	Myoelectric Manifestations of Fatigue
MSDs	Musculoskeletal Disorders

MVC	Maximal Voluntary Contraction
NF	Non-fatigue
NMF	Non-negative Matrix Factorization
NSERC	Natural Sciences and Engineering Research Council of Canada
PCA	Principal Component Analysis
RMS	Root Mean Square
RPE	Rating of Perceived Exertion
RPT	Repetitive Pointing Task
RRIs	Running-related Injuries
SampEn	Sample Entropy
SD	Standard Deviation
sEMG	Surface Electromyography
SPM	Statistical Parametric Mapping
TRI	Triceps Brachii
UT	Upper Trapezius
VAF	Variance Accounted For
VC	Vector Coding
WMSDs	Work-related Musculoskeletal Disorders

Chapter 1: Introduction

1.1 Rationale

Musculoskeletal disorders (MSDs) are the leading cause of disability and chronic pain worldwide. In 2019, MSDs were reported to have the highest prevalence rate among 25 diseases in 204 countries analysed. Up to 1.71 billion people were reported to live with MSDs globally (Cieza et al., 2020). In Canada, the prevalence rate of MSDs increased from 23.0% in 1990 to 27.8% in 2017. The total disease burden of MSDs ranked third in Canada, after cancer and cardiovascular diseases (Kopec et al., 2019). MSDs prevalence rates differ for males and females. Studies on general and working populations report a systematically higher prevalence of MSDs in females compared to males (Serna Arnau et al., 2023; Wijnhoven et al., 2006). In exercise populations, the MSDs injury profiles are less clear and vary between anatomical sites, types of sports, and performance levels (Haljaste et al., 2010). For instance, in running, female runners have been shown to sustain a higher rate of overuse running injuries compared to males. Overall, the highest running injury prevalence was observed at the knee, but this differed between sexes. Females showed the greatest running injury prevalence at the lower leg and calf, while males showed the greatest injury prevalence at the hip, pelvis, and upper leg regions (Dempster et al., 2021). The mechanisms responsible for the differences in injury risks of MSDs between sexes are not fully clear and may be multifactorial.

1.2 Problem statement

1.2.1 Fatigue and musculoskeletal disorders

Whole-limb repetitive movements are common in workplaces, as well as in sports and daily activities. The repetitive movements involving prolonged muscle contractions induce overload onto muscle fibres (Hägg, 2000). Over time, the excessive overloads may lead to muscle fatigue, chronic pain, discomfort and MSDs (Côté, 2014). Therefore, fatigue is a pathway to chronic and overuse injuries. Individuals who better adapt to fatigue may be more likely to prevent the development of overuse MSDs. However, how individuals adapt to fatigue during repetitive movements remains unclear.

1.2.2 Biomechanical manifestations of fatigue

Fatigue is defined as “a disabling symptom in which physical and cognitive function is limited by interactions between performance fatigability and perceived fatigability” (Enoka & Duchateau, 2016). Previous studies have shown that fatigue manifests in different degrees of freedom (DoFs) of the human body (e.g., muscle and joint) during repetitive tasks. A series of studies using an experimental upper limb repetitive pointing task to simulate common occupational repetitive tasks showed that participants can adjust their trunk posture and shift their body weight toward the non-moving and unfatigued arm (Bouffard et al., 2018; Fuller et al., 2009). Repetitive upper limb motion-induced fatigue has also been shown to lead to an increased movement variability (Fuller et al., 2011), both at individual joints and in their coordination patterns (Yang et al., 2018). In studies when fatigue was induced gradually with repetitive sub-maximal efforts, these changes in biomechanical patterns during fatigued movement are thought to reflect strategies to help maintain task performance, which could differ from patterns observed when the system fails, at exhaustion. However, the mechanisms underlying these hypothesized voluntary adaptations as fatigue gradually develops are yet to be fully elucidated.

Since these previously observed changes in whole-body features as a result of fatigue have been attributed to the highly rhythmic and repetitive nature of the tasks, we hypothesized that fatigue adaptations in coordination might also occur in rhythmic, repetitive lower limb tasks, such as running. Running is one of the most popular activities. The number of participants in world marathon races increased 13-fold from 1970 to 2017 (Vitti et al., 2019). However, there is also a high incidence of lower limb running-related injuries, with rates reaching up to 79.3% (van Gent et al., 2007). Fatigue has been identified as one of the risk factors for overuse running injuries, induced by overloading forces from repetitive strides (Hreljac, 2004). Fatigue has been shown to increase step length variability, reduce lower leg stiffness, and alter knee and hip joint angles during running (García-Pinillos et al., 2020; Luo et al., 2019). However, the changes of repetitive whole-limb motion-induced fatigue have been studied extensively in muscle activation and joint kinematics through the pathway of single DoFs, and less is known about how the multiple joints coordinate together in response to repetitive motion-induced fatigue.

1.2.3 Applying modern dynamical system approaches to study repetitive motion-induced fatigue

From the perspective of dynamical systems, different DoFs of the human body need to be coordinated and integrated into synergistic relations to maintain the performance of goal-directed movements (Robertson et al., 2013). In recent years, advanced dynamical system approaches have been developed to assess coordination and its variability, in ways to advance the understanding of how the human movement system organizes when it performs multijoint movements. The continuous relative phase technique has been regarded as a sensitive measurement approach to quantify multijoint coordination variability, due to its ability to incorporate spatial-temporal information in the measurement of multijoint coordination (Hamill et al., 1999). Muscle synergy analysis, which provides the advantage of reducing multiple muscle activation signals to low-dimensional synergistic muscle groups (Ting & McKay, 2007), has been recently applied to measure multimuscle coordination during tasks of postural control (Chvatal et al., 2011) and walking (Clark et al., 2010). Finally, most previous studies chose traditional amplitude and spectral metrics (e.g., root mean square and mean frequency) to assess myoelectric manifestations of muscle fatigue. However, given the non-stationary and nonlinear nature of muscle activation signals during dynamic contractions, traditional amplitude and spectral metrics in time and frequency domains, which assume that muscle activation signals are stationary, may not be well suited for dynamic contractions (Rampichini et al., 2020). Applying nonlinear and time-frequency metrics, such as the recently developed entropy and wavelet analyses, to study electromyographical manifestations of fatigue may provide a new perspective to more deeply understand how mechanisms of activation of muscles, and of control of coordinated muscle groups, may be affected by repetitive motion-induced fatigue.

1.2.4 Sex-specific manifestations of fatigue

Since males and females have shown different chronic injury profiles, and fatigue is a known injury risk factor, previous studies have attempted to determine whether there is a sex specificity to both the simple and complex fatigue manifestations. A previous study using continuous relative phase approach showed that females displayed increased humerothoracic elevation angle variability, while males showed decreased humerothoracic elevation angles after repetitive upper limb motion-induced fatigue (Bouffard et al., 2018). However, regardless of fatigue, females showed greater upper thoracic and lower thoracic spine variability than males (Yang & Côté, 2022), suggesting that there may be basic sex differences in movement features before fatigue develops and that could be relevant to sex differences to early exposure to injuries. Moreover, from the perspective of neuromuscular fatigue adaptations, no sex difference was found in the time domain of upper limb muscle activation amplitude with repetitive upper limb motion-induced fatigue (Srinivasan et al., 2016). However, males exhibited a greater increase in shoulder stabilizer (upper trapezius) muscle activation variability after fatigue, while females showed a higher increase in shoulder and elbow mover (biceps brachii) muscle activation variability after fatigue (Srinivasan et al., 2016), suggesting sex differences that vary between muscle roles. In the frequency domain, males showed higher median frequency in most upper limb muscles during the performance of the repetitive upper limb task compared to females (Yoon et al., 2021). It is likely that the contribution of different muscles and joints in maintaining task performance is different between sexes. Males and females may use different muscle coordination/synergy strategies to preserve performance with fatigue. However, no studies to date have compared multimuscle coordination, time-frequency and complexity aspects of muscle activation in fatiguing upper limb motions between sexes.

Previous studies have also identified sex differences in how males and females adapt to lower limb motion-induced fatigue. For instance, Bazuelo-Ruiz et al. (2018) found that male recreational runners displayed decreased plantar flexion at toe-off when fatigued compared to females, resulting in higher peak propulsive forces during shock absorption. In a simulation study, Willson et al. (2015) calculated that females would produce lower hamstring forces and peak hip extension moments after fatigue compared to male runners. Nevertheless, these changes observed to occur with running-induced fatigue in a single joint do not provide any information on how coordination might be affected by fatigue. Inter-joint coordination analyses can further reveal the coordination patterns of adjacent joints and help determine the impact of modified coordination patterns on task performance. However, to our knowledge, no studies have measured how fatigue affects running-related inter-joint coordination in both males and females.

1.3 General aim and research framework

1.3.1 General aim

This thesis aimed to apply modern linear and nonlinear analytical approaches to investigate the effects of fatigue on the coordination of repetitive movements and to explore the origin of sex differences during fatiguing repetitive motions. Moreover, we studied repetitive movements of both the upper limbs and lower limbs, in order to identify similarities and differences in how fatigue affects the coordination of both upper and lower limb movements. The first aim was to examine the sex-specific effects of fatigue on muscle synergies in a repetitive upper limb pointing task. The second aim was to investigate the sex-specific myoelectric manifestations of fatigue in time-frequency and complexity domains during a repetitive upper limb pointing task. The first two aims were accomplished through work based on two retrospective analyses of previously collected datasets in the Centre for Interdisciplinary Research in Rehabilitation of Greater Montreal at the Jewish Rehabilitation Hospital in Laval, Canada and the Biomechanics of Occupation and Sport Laboratory in Montreal, Canada. To expand our observations to lower limbs, we investigated the sex-specific effects of fatigue on lower limb coordination and coordination variability in running. This third aim was achieved by conducting a novel experimental protocol in the Human Brain Control of Locomotion Laboratory and the Biomechanics of Occupation and Sport Laboratory in Montreal, Canada.

1.3.2 Research framework development

The development of a research framework began with a literature review on measurements of fatigue-induced changes in coordination. A repetitive upper limb forward-backward pointing task was selected to mimic common occupational tasks. This task had been used in a series of experiments to study biomechanical and physiological adaptations of upper limb repetitive motion-induced fatigue, whereas most of these studies had focused on fatigue effects manifested in a single joint and muscle. This led to a research question of how the human movement system coordinates multijoint and multimuscle to deal with fatigue and how the coordination strategies differ between sexes (Study 1). The surface electromyography (EMG) approach was used to measure myoelectric muscle activities. An optoelectronic motion capture system was used to record kinematics for movement cycle partition. Muscle synergy analysis was used to quantify multimuscle coordination.

After study 1, the following research gap identified was how time-frequency and complexity analyses could further reveal myoelectric manifestations of muscle fatigue between sexes. In study 2, using the same dataset as in study 1, we further examined the time-frequency and complexity characteristics of EMG signals of upper arm muscle between sexes using continuous wavelet transform and entropy analyses.

After study 2, we endeavoured to explore if similar general conclusions on sex-specific multijoint coordination control could apply to both upper and lower limbs. Due to the sex differences in running injury profiles, running was chosen as an experimental model of lower limb repetitive tasks in study 3. Continuous relative phase approach was used to access inter-joint coordination in running. An inertial measurement unit system was used to record lower limb kinematics during running. Specific rationales, objectives, and hypotheses for each study are detailed in the next section.

1.4 Objectives and hypotheses

1.4.1 Chapter 3: Few sex-specific effects of fatigue on muscle synergies in a repetitive pointing task

Previous research has highlighted some sex-specific effects of fatigue on the activation patterns of individual muscles during a repetitive pointing task. However, there is limited understanding of how fatigue affects indicators of multimuscle coordination in both males and females. ***The first study aimed to investigate the effects of fatigue on muscle synergies during a repetitive upper limb pointing task in males and females. We hypothesized that fatigue would***

not alter the number and structure of muscle synergies. Sex differences would be found in the relative weight of individual muscles with fatigue.

1.4.2 Chapter 4: Sex-specific myoelectric manifestations of fatigue in time-frequency and complexity domains during a repetitive pointing task

Previous research has found some sex differences in amplitude and spectrum characteristics of muscle activation during fatigued dynamic tasks. Time-frequency and complexity analyses can offer a more detailed insight into EMG changes with fatigue. However, these methods have not yet been applied to investigate sex-specific upper limb fatigue. ***Therefore, the second study aimed to investigate sex-specific myoelectric manifestations of fatigue in time-frequency and complexity domains during a repetitive pointing task. We hypothesized fatigue would shift the energy to lower frequencies. A less complex EMG pattern would be found after fatigue. Sex differences would be found in EMG complexities.***

1.4.3 Chapter 5: Sex-specific effects of fatigue on lower limb coordination and coordination variability in highly trained endurance runners

Previous studies have shown some sex differences in lower limb kinematics after running-induced fatigue. Little is known about the fatigue adaptations of lower limb coordination between sexes. ***The third study aimed to compare the fatigue adaptations of lower limb coordination and coordination variability between highly trained endurance male and female runners. We hypothesized that fatigue would lead to an increased coordination variability of lower limb joint pairs during the loading phases. Males and females would show different variability patterns for different joint pairs.***

Chapter 2: Literature Review

2.1 Sex/gender differences

According to the scientific literature, “Sex” refers to the biological differences between males and females (National Academies of Sciences, Engineering, and Medicine, 2022). Sex is a multidimensional biological construct that encompasses several components, such as anatomy, physiology, genetics, and hormones. “Gender” can be broadly defined as socially constructed and enacted roles and behaviours that occur in a historical and cultural context. Understandings of gender vary across societies and over time and are associated with certain biological components (National Academies of Sciences, Engineering, and Medicine, 2022). Therefore, sex and gender describe connected but different constructs. Sex has been considered as a biological variable, while gender has been considered as a social variable in health research (National Institutes of Health, 2022). Research has identified important biological sex differences in body composition and anthropometrics (Bredella, 2017), muscle strength, power and endurance (Faber et al., 2006; Senefeld et al., 2019), muscle morphology (Nuzzo, 2024), hormones, X and Y chromosome gene expression (Ferguson-Smith & Bavington, 2014), and fuel metabolism and exercise performance (Hunter et al., 2023). These biological differences may help identify the sex-specific biomechanical metrics associated with musculoskeletal disorders (MSDs) in occupational and sports tasks.

2.1.1 Body composition and anthropometrics

In healthy populations, females on average are shorter and lighter than males (López-Ortega & Arroyo, 2016). Adult females are 8% shorter than males, with shorter upper and lower limbs. Adult females have less muscle and bone mass and a greater percentage of fat mass compared to males (Gallagher et al., 1997; Janssen et al., 2000). They are also 17% to 18% lighter than adult males, as females have less lean body mass (Fryar et al., 2012). In sports, research has also shown some sex differences specific to sporting tasks. Demographic profiles obtained from 693 elite athletes have shown that female athletes had a lean body mass that was 85% of that of male athletes and a fat mass percentage that was 5% to 10% greater (Healy et al., 2014). Lower fat mass is considered an advantage for males during weight-attenuation tasks such as endurance running. A greater body fat percentage in females was shown to account for up to 70% of the sex differences in vertical and horizontal jump performance (Mansour et al., 2021).

2.1.2 Muscle mass and mechanical output

Greater muscle mass in males is associated with greater muscle strength and power; therefore, males usually have larger muscle strength and muscle power compared to females (Alcazar et al., 2020). In active adults, the strength of upper limb muscles, such as elbow flexor muscles, in females is approximately 50% to 60% that of males. The strength of lower limb muscles, such as knee extensors, in females ranges from 60% to 80% that of males (Miller et al., 1993). Larger sex differences in muscle mass and strength were found in the upper limb than in the lower limb across different age groups (Janssen et al., 2000). In workplaces, Faber et al. (2006) found that males had greater maximal handgrip strength and maximal muscle strength of back flexors and back extensors compared to females in a sample of 423 employees. Females have been shown to exert less torque, work, and power during functional occupational tasks compared to males when the perceived workloads were controlled between sexes (Esmail et al., 1995). In athletes, males showed greater upper and lower body power adjusted for lean body mass compared to females (Bartolomei et al., 2021; Mansour et al., 2021).

2.1.3 Muscle fibre composition

These aforementioned sex differences in muscle mass and strength can be explained by structural differences, as well as by the different muscle fibre composition between sexes. In healthy populations, active adult males have been shown to have a larger cross-sectional area for all fibre types and a greater distribution percentage for Type 2 fibres, while females generally have a higher distribution percentage of Type 1 fibres (Nuzzo, 2024). Accordingly, males typically have greater faster muscle contractile properties than females. Conversely, females possess larger slower muscle contractile properties, potentially leading to a less fatigable muscle contractile ability compared to males of similar contraction intensity (Hunter, 2014). Sex differences in fibre composition can also be observed in individual upper and lower limbs. In upper limbs, females were reported to have a smaller fibre cross-sectional area of upper trapezius and biceps brachii compared to males (Lindman et al., 1991; Miller et al., 1993). In lower limbs, males have been shown to exhibit greater cross-sectional areas of all fibre types and smaller distribution percentages of Type 1 fibre of vastus lateralis (Nuzzo, 2024). Similarly, in vastus lateralis, males have shown better capabilities of muscle fibre repair and hypertrophy compared to females (Horwath et al., 2021). These aforementioned sex differences are mainly observed in general populations or recreationally active adults. Sex differences in muscle fibre composition are less clear in well-trained athletes, especially within a given sport. For instance, in elite endurance and power athletes, limited data have shown that elite male athletes possess a larger proportional area of Type 2 fibres (Alway et al., 1989; Costill et al., 1976).

2.2 Fatigue assessment and available metrics

2.2.1 Fatigue definition and mechanisms

Enoka and Duchateau (2016) defined fatigue as “a disabling symptom in which physical and cognitive function is limited by interactions between performance fatigability and perceived fatigability” based on the original definition proposed by Mosso (Mosso, 1904). Performance fatigability, also known as neuromuscular fatigue or muscle fatigue, can be defined as “the progressive change that occurs in the central nervous system (CNS) and muscles due to exercise, resulting in a force output that is less than anticipated for a given voluntary contraction or stimulation" (MacIntosh & Rassier, 2002). Performance fatigability depends on the contractile functions of involved muscles, modulated by calcium kinetics, force capacity, blood flow, and metabolism and products. Performance fatigability also depends on the activation capabilities of the nervous system for the given task, including functions of voluntary activation, afferent feedback, and neuromuscular propagation (Kluger et al., 2013). In contrast to performance fatigability, perceived fatigability is attributable to the deviation of the changes in the sensations that regulate the integrity of the performer, depending on the homeostasis and psychological state of the individual (Enoka & Duchateau, 2016; Kluger et al., 2013). Due to the complex interactions between those multiple modulating factors, fatigue definitions based on different modulating factors have been considered to be too vague to be distinguished, such as central fatigue, peripheral fatigue, and supraspinal fatigue (Enoka & Duchateau, 2016). Accordingly, fatigue is not the time of muscle exhaustion or task failure. Rather, fatigue has been proposed to be an ongoing and disabling symptom (Enoka & Duchateau, 2008; Enoka & Stuart, 1992). It develops gradually along the sustained task and is regulated by many adjustments that occur within or between performance and perceived fatigability.

Vøllestad (1997) has suggested that fatigue assessments can be categorized into direct and indirect assessments. Direct assessments include tests of Maximal Voluntary Contraction (MVC) force generation and power output. Indirect assessments include methods of muscle fibre twitch interpolation, performance criteria (e.g., walking endurance time), and electromyography (EMG). Fatigue can also be measured by the changes in self-reported ratings of exertion (RPE; Rannou et al., 2019) during a sustained task. By using different assessment methods, fatigue has been assessed by a wide variety of metrics in various settings (Gandevia, 2001; Kent-Braun et al., 2012; Morales-Alamo et al., 2015; Sidhu et al., 2013).

2.2.2 Performance criterion

As a way to explore the fatigue-related adjustments that limit the performance, a performance criterion is needed to assess fatigue specific to individual tasks and populations. These criteria include walking endurance of healthy adults (Justice et al., 2014), time trials by endurance athletes (Klass et al., 2012), and questionnaires and inventories such as the scale of physical aspects of fatigue in persons with multiple sclerosis (Learmonth et al., 2013).

2.2.3 Rating of perceived exertion

Fatigue can also be measured by self-reported ratings, such as the rating of visual analog scales and perceived exertion (RPE; Rannou et al., 2019). A common method of measuring RPE in adults is the Borg RPE scale, including the Borg Category-Ratio-10 scale (CR10) and the Borg 6–20 Category Scale (Borg, 1982). Due to the close relationship between Borg RPE scales and work intensity (Jakobsen et al., 2014), Borg RPE scales have been extensively used to assess fatigue in various occupational tasks, such as a repetitive lifting task (Yin et al., 2019), an upper limb pointing task (Fuller et al., 2009), multidirectional reaching tasks (Dupuis et al., 2021), and reaching-picking tasks in workplaces (Qin et al., 2014). In sports, Borg RPE scales can be used to detect fatigue in even more settings and sporting tasks attributable to its relationships between exercise intensity, training status, and pacing strategy (de Melo dos Santos, 2017; Eston, 2012). Therefore, Borg RPE scales have been suggested as a reliable measurement of subjective feelings of fatigue, effort, and exertion during physical work and exercise (Thorpe et al., 2017; Williams, 2017).

2.2.4 Force capacity

Measurements of force capacity of localized muscles have been considered validated and direct assessments of fatigue. Some commonly used techniques to measure muscle fatigue are to perform voluntary or electrically evoked maximal contractions to quantify the decline in the maximal force generation. The capacity of MVC force generation has been regarded as a classic metric to quantify muscle fatigue. The fall in the MVC force during sustained low-intensity exercise is largely due to an activation signal reduction controlled by the CNS (Taylor & Gandevia, 2008), whereas the decline in the MVC force after high-intensity exercise is more likely attributable to a reduction in contractile function (Westerblad et al., 2010). These differences demonstrate that the site of fatigue-related impairment and underlying mechanisms of fatigue vary across tasks, which is known as task dependency of fatigue (Enoka & Stuart, 1992). Therefore, rather than the direct assessment of fatigue by measuring force capacity, the task-dependent indirect assessments have also shown valid results in quantifying the changes in fatigue-related impairment.

2.2.5 Myoelectric manifestations of muscle fatigue in different domains

Electromyography (EMG) is one of the most commonly used indirect assessments of fatigue. An electromyogram is the profile of the electrical signal detected by an electrode placed on a muscle. EMG is the ensemble of techniques used to detect electromyograms. It has been applied to continuously record trains of electrophysiological events in muscle contraction with time, with the ability to reveal the characteristics of motor units (e.g., motor unit discharge rate and waveform of action potentials; Rampichini et al., 2020). Surface electromyography (sEMG) is widely used in biomechanical research because of its non-invasiveness and real-time recording capabilities during single-limb and dynamic tasks. Muscle fatigue has been shown to manifest prior to the fatigue onset, suggesting that the susceptibility of muscles to fatigue could be assessed by sEMG. These early signs of myoelectric alterations are termed myoelectric manifestations of muscle fatigue (MMF; Rainoldi et al., 2004). MMF are often assessed in time, frequency, and time-frequency domains. Moreover, because of the nonlinear nature of sEMG signals, many indicators calculated by nonlinear time series analysis in the complexity domain have been proposed to explore additional information on the interaction process between MMF and the neuromuscular system (Rampichini et al., 2020).

2.2.5.1 MMF in time and frequency domains

Time metrics often convey information related to the amplitude of EMG signals and spectral metrics are related to the distribution of energy across EMG frequencies and are usually used to characterize the EMG power spectrum (e.g., mean and median frequency). Both amplitude and spectral metrics have been considered to assess MMF during fatiguing tasks. A compressed power spectrum is usually detected with fatigue, indicating a relative shift in energy from high to low frequencies (Brody et al., 1991). An increased EMG amplitude may be found because of the recruitment of fresh motor units with the progression of fatigue. Root mean square (RMS) is one of the most widely used amplitude metrics in EMG analyses, given its sensitivity to the discharge rate of the motor unit and the number of units excited. RMS is also sensitive to many other confounding factors affecting the shape and the energy of the action potentials of each motor unit, such as the direction of sEMG electrodes and the location of spectral dip (Mottram et al., 2005; Vigotsky et al., 2018). In contrast, since the spectral metrics are equivalently affected by the different types of fatigue, they have shown more consistent results compared to amplitude metrics in MMF studies (Rampichini et al., 2020). The most widely considered spectral metrics are mean frequency and median frequency extracted by the Fourier transform, which have consistently been shown to decrease with fatigue during either isometric or dynamic contractions (Cifrek et al., 2009).

The aforementioned amplitude and spectral metrics are all calculated based on the assumption that the recorded EMG signal is stationary, or at least wide-sense stationary, such as the sustained isometric contraction during short-time intervals (0.5-2 s). These metrics are not well suited to dynamic contractions where the EMG signal is non-stationary due to alternations in muscle force, contraction velocity, and muscle length (Croce et al., 2014; Vitor-Costa et al., 2012). Alternative time-frequency methods are needed for selecting appropriate time-frequency resolution, especially for dynamic cyclical movements.

2.2.5.2 MMF in time-frequency domain

Alternatively, wavelet approaches can decompose the signal in both frequency and time into a series of basic functions, whose characteristics can be tailored to meet specific analysis needs (Karlsson et al., 2000). This makes wavelet approaches suitable for assessing the spectral content of EMG signals during dynamic contractions. The most accurate and precise time-frequency solution during fatiguing dynamic contractions has been suggested to be the continuous wavelet transform (CWT), as CWT allows for freely selecting wavelet scales corresponding to frequency and time values, thereby providing fine control over frequency resolution compared to the Short-Term Fourier Transform, Wigner-Ville distribution, and Choi-Williams distribution (Karlsson et al., 2000). During dynamic upper and lower limb tasks, such as a repetitive elbow flexion-extension motion (Triwiyanto et al., 2017), squatting (Smale et al., 2016), and cycling (Graham et al., 2015), previous studies have observed a decreased instantaneous mean frequency, major frequency, and a shift in the EMG spectrum when calculated using CWT. However, there is no information about how CWT measures differ between sexes during both upper and lower limb multimuscle tasks.

2.2.5.3 MMF in complexity domain

EMG signals contain both deterministic elements and stochastic or random components, meaning that they are nonlinear and chaotic (Clancy and Farry, 2000; Potvin and Brown, 2004). Because of this, nonlinear metrics in the complexity domain may provide additional information on the EMG changes of stochastic components with fatigue that linear metrics could not reveal. Nonlinear metrics derived from fractal, correlation, and entropy analyses have been shown to detect MMF efficiently (Rampichini et al., 2020). For example, fractal analysis is the most widely applied analytical method in MMF studies. It can be used to estimate the self-similarity of time series signals. Decreased fractal measures are typically observed with fatigue, suggesting a loss of self-similarity of the EMG signals (Arjunan & Kumar, 2014; Mesin et al., 2016). The recurrence quantification analysis is a two-dimensional geometrical tool used to present the correlations at all scales of time series data (Bradley & Mantilla, 2002). Local MMF has been shown to be accompanied by an increase in recurrence metrics, indicating an increase in motor unit synchronization and a more similar waveform of motor unit action potential with fatigue (Felici et al., 2001; Ikegawa et al., 2000). Compared to spectral metrics, recurrence metrics present a higher sensitivity to detect EMG drifts, thereby representing a reliable tool for revealing MMF during challenging motor tasks (Farina et al., 2002). In the context of biological time series, entropy is defined as “the probability that similar patterns of behaviour will not be followed by additional similar patterns” (Stergiou, 2018), thus providing nonlinear indices of the unpredictability and irregularity of EMG data. The entropy indices typically show a clear decline with fatigue, representing a more regular pattern of EMG signals. It is speculated that these decreased entropy estimates might result from decreased amplitude and velocity of motor unit action potential due to alterations in metabolic and enzymatic events involved in muscle contractions (Hernandez & Camic, 2019; Tong et al., 2016; Xie et al., 2010). In terms of sex effects, a previous study found that females showed less increase in fractal measures of biceps brachii during upper limb elbow isometric contractions at 60% MVC (Meduri et al., 2016). How males and females differ in complexity characteristics of both upper and lower limb muscles during multimuscle movements is less clear.

2.3 Movement variability and synergy

The concept of synergy in motor control has been used since the 19th century as a synonym of the word *coordination*. Bernstein incorporated this concept into his famous theory, "motor redundancy", which describes a multi-level hierarchical scheme for movement control. According to Bernstein, in order to exhibit goal-directed functional movement, the human body is required to integrate different degrees of freedom (DoFs; i.e., elements) at each spatiotemporal scale into synergetic relations under the control of the CNS (Bernstein, 1967). During the integration, synergy serves the main function of organizing numerous elements into groups. The CNS selects these synergetic groups and eliminates redundant DoFs to find the "optimal" solutions for movement control. Joints, segments and muscles are integrated and organized into controllable groups at individual spatiotemporal scales (Bernstein, 1967; Robertson et al., 2013).

2.3.1 Muscle synergy and factorization methods

It has been proposed that the CNS may reduce the dimensionality of neuromuscular system by activating synergistic muscle groups to complete movements (Ting & McKay, 2007). This low-dimensional muscle activation module is regarded as muscle synergy, with a group of muscles cooperating to execute motor tasks. Muscle synergy is typically recorded via EMG of multiple muscles while performing a task of interest (Bizzi & Cheung, 2013). Recent studies suggest that muscle coordination patterns of multijoint movements can be explained with a low-dimensional group of muscle synergies during stepping postural behaviours (Chvatal et al., 2011), postural perturbations (Safavynia & Ting, 2012), running (Hajiloo et al., 2020), cycling (Esmaeili & Maleki, 2019), circle-drawing movements (Wang et al., 2021), and multidirectional upper limb tasks (Ortega-Auriol et al., 2018). Muscle synergy analysis could be an appealing method to assess muscle coordination patterns of multijoint movements (Safavynia et al., 2011). Different factorization methods have been used to extract the synergy components from recorded EMG signals to quantify muscle synergies.

The aim of factorization is to form a reduced set of vectors in the muscle activation space whose linear combination can account for most of the variance in dataset. By using different types of factorization methods, two synergy components are usually extracted to reconstruct the EMG signals: 1) synergy vector and 2) activation coefficient. The activation coefficient represents the synergy activation pattern at a time, and the synergy structure denotes the fixed module organization of each synergy. The most commonly used factorization methods reported in the literature in muscle synergy analysis are principal component analysis (PCA; 23.11%) and non-negative matrix factorization (NMF; 62.28%; Rabbi et al., 2020). Each method is developed based on a different assumption regarding the variance of the recorded EMG signals and calculated using a different algorithm.

2.3.1.1 Principal component analysis (PCA)

PCA is one of the most early developed and widely applied factorization methods in muscle synergy research. It identifies muscle synergies by extracting those that most accurately explain the variance in the dataset while minimizing the covariance of the synergy vectors. This method is particularly effective with datasets that follow a Gaussian distribution (Lambert-Shirzad & Van Der Loos, 2017). The minimization of synergy vectors is achieved through analytical solutions using singular value decomposition. As a result, the muscle synergy vectors identified by PCA correspond to the eigenvectors of the data's covariance matrix (Rabbi et al., 2020). PCA is known for its dimensionality reduction capabilities (Halilaj et al., 2018), but it may have limitations in handling data with a non-Gaussian distribution and interpreting the synergy results based on the characteristics of principal components. PCA has been used to study multijoint muscle synergy with fatigue in different movements, such as an upper limb rope-turning motion (Bruce et al., 2017) and a rowing task (Turpin et al., 2011). In general, these studies have consistently shown that fatigue changes the activation profiles of muscle synergies. However, the results on the structure of synergy calculated by PCA are inconsistent, indicating that how fatigue influences the modular organization of multimuscle coordination is less clear.

2.3.1.2 Non-negative matrix factorization (NMF)

The NMF method is employed using the multiplicative update algorithms based on Euclidian distance objective function (Lee & Seung, 1999), gradient descent (Lin, 2007) or least square methods (Tresch et al., 2006). NMF is able to constrain muscle synergies to be non-negative, which aligns with the physiological interpretation of muscle activation patterns (Torres-Oviedo & Ting, 2007). To obtain a higher accuracy of factorization, it uses a lower-rank approximation to extract synergies that account for the largest variance of the EMG input signals. NMF can also be implemented into both Gaussian and non-Gaussian datasets (Rabbi et al., 2020). This highlights the versatility of NMF in different EMG datasets. Previous studies that evaluated EMG changes with fatigue using the NMF method have shown that fatigue did not change the number and the structures of synergies. However, fatigue did affect the activation coefficient of synergies and the synergy vector of individual muscles. This is consistent across different tasks, such as upper limb elbow isometric contractions, lower limb side cutting, and running movements (Hajiloo et al., 2018; Matsunaga et al., 2021; Ortega-Auriol et al., 2018). These findings generally suggest that fatigue influences activation but preserves the structure of muscle synergies, as quantified using the NMF method, in whole-limb motions. Regarding sex differences, Santuz et al. (2022) evaluated the sex-specific muscle synergy patterns for walking and running in young and older adults using NMF method. Their results showed that the synergy structures were similar between sexes. Some sex differences were observed in the synergy vectors of hip extensors, knee extensors and foot dorsiflexors. Lower activation coefficients were found in young females during walking propulsion and weight acceptance compared to males. Together, sex-specific effects of fatigue on both PCA- and NMF-based muscle synergies during whole-limb motions remain unclear.

2.3.2 Kinematic inter-joint coordination and coordination approaches

The control of muscles and muscle synergies would then lead to movement outcomes that are measurable at the joint, and joint coordination level. Hence, understanding human functional movements requires the analysis of not only isolated joints but also the organization of these joints and their coordination (Irwin et al., 2020). A dynamical systems approach derived from the concept of coordination has been developed to identify the nature of transition processes and stability in human movement (Kelso, 1994). From the perspective of dynamical systems, the variability in coordination plays a vital role in establishing a combination of flexibility and stability of movement. Coordination variability represents the range of coordination systems that the organism exhibits to master the redundancy of systems while performing a movement task (Wheat & Glazier, 2020). A loss of variability may be considered as fewer interactions between human DoFs and a decreased ability to master the redundancy of systems, leading to task failure (Lipsitz, 2002).

Relative phase (i.e., discrete and continuous relative phase) and vector coding techniques have been developed to quantify inter-joint/inter-segmental coordination and coordination variability.

2.3.2.1 Vector coding (VC)

VC has been defined as a vector-based coding scheme that keeps data on a ratio scale for the quantification and analysis of relative motion (Field-fote & Tepavac, 2001). Field-fote and their colleagues identified the direction and magnitude of the frame-to-frame intervals on the angle-angle diagrams and calculated the magnitude and direction of the vector connecting the two adjunct points in the diagrams. The advantages of the VC technique include no requirement for normalization (Hamill et al., 2000), which is helpful in maintaining more spatial information. However, Heiderscheit et al. (2002) pointed out that when joint motion changes directions during the movement, the proximities of consecutive data points might lead to abruptly increased VC variability, suggesting that the movement patterns of interest need to be considered before using the VC technique. VC technique has been applied to evaluate the effects of fatigue on coordination in lower limb running, walking turns, and cutting. A more out-of-phase VC coordination of hip-knee and pelvis-thigh joints with fatigue was observed during running (Brown et al., 2016; Mo & Chow, 2019). A decreased lower limb VC variability of trunk-pelvis and hip-knee joints with fatigue was observed during walking turns and a cutting maneuver (Samaan et al., 2015; Smith et al., 2021). Unchanged lower limb VC variabilities with fatigue were observed in runners with iliotibial band syndrome (Hafer & Boyer, 2017). In terms of sex effects, a higher thigh-shank VC variability was observed in young females compared to males (Boyer et al., 2017).

2.3.2.2 Relative phase techniques

Continuous relative phase (CRP) represents the phase relation between two oscillators (i.e., the segment or joint angles) at each sample point throughout the movement cycle. CRP has the advantage of containing spatial-temporal information in the coordination measurement, which is considered to be a higher-dimensional analysis (Hamill et al., 1999). The angular velocity involved in CRP analysis makes CRP a more sensitive measurement of coordination variability (Robertson et al., 2013). Moreover, CRP continuously measures coordination across the entire cycle. This makes the CRP useful for interpreting the coordination results of gait in conjunction with the functional demands of gait cycles (Heiderscheit et al., 2002). Despite these advantages, the results extracted from CRP analyses need cautious interpretation as some of the raw information may be masked from the higher-dimensional calculations (Lamb & Stöckl, 2014). CRP method has been used to evaluate inter-joint and inter-segmental coordination with fatigue in both upper and lower limb motions, such as a repetitive upper arm task (Yang et al. 2018, 2019), fatiguing running tasks (Bailey et al., 2018; Dal Pupo et al., 2017), and a vertical jump movement (Knihs et al., 2022). CRP and CRP variability changed significantly with fatigue in long-distance running (Bailey et al., 2018), while they showed no changes with fatigue in simulated futsal sprinting and jumping tasks (Dal Pupo et al., 2017; Knihs et al., 2022). An increased CRP variability was observed in a repetitive upper arm task (Yang et al., 2018). However, the results on which joint pair is affected by fatigue and how fatigue affects the CRP patterns (e.g., in-phase or antiphase) are inconsistent, which may be due to the less comparable fatigue protocols and variations in CRP calculations between studies. To compare the coordination patterns between sexes, CRP method has also been used to study lower limb walking (Ghanavati et al., 2014) and running movements (Hannigan & Chou, 2019). Significant sex differences in CRP and CRP variability were observed in pelvis-thigh couplings. However, together, how fatigue changes VC- and CRP-based coordination and coordination variability between sexes in whole-limb motions is less clear.

2.4 Application of fatigue metrics in repetitive upper and lower limb motions

The study of how fatigue affects the coordination of repetitive tasks is fairly recent, and has benefitted from the methodological developments associated to all of the newly developed metrics presented in the aforementioned sections, in a way that helps understand how the CNS deals with fatigue to maintain repetitive coordination as fatigue develops. In a series of studies using an experimental repetitive pointing task (RPT) to simulate common occupational repetitive tasks, it was demonstrated that participants adjusted their trunk posture and shifted their bodies towards the non-moving, unfatigued arm. This suggests active adaptations to mitigate the effects of fatigue, specifically by adjusting the task to decrease humerothoracic elevation and shoulder abduction angles, which are more are more challenging to maintain due to shoulder fatigue (Bouffard et al., 2018; Fuller et al., 2009). Additionally, fatigue has been shown to increase variability in human movement (Fuller et al., 2011). In protocols using the RPT, this variability was evidenced by increased shoulder and elbow angle variability and shoulder-elbow coordination variability, calculated using the CRP approach (Yang et al., 2018). These increased variabilities were further shown to result in a dominant role of multijoint stabilizing patterns with fatigue, as quantified by uncontrolled manifold analyses, which can distinguish between “good” and “bad” variability components for stabilizing the task (Hasanbarani et al., 2021). When evaluating different fatigue locations (i.e., shoulder, elbow, and trunk), shoulder fatigue induced the greatest angular changes at all three joints (Yang et al., 2019), further affecting performance stability and necessitating greater reorganization in redundant structures compared to elbow and trunk fatigue (Slopecki et al., 2022). One possible strategy in response to repetitive motion-induced fatigue could be changing muscle activation amplitudes and spectral distributions. Previous sEMG studies have shown decreased mean frequency and increased RMS amplitude of upper limb muscles during a fatiguing RPT in time and frequency domains (Srinivasan et al., 2016; Yoon et al., 2021). In the time-frequency domain, a decreased instantaneous mean frequency and a shift of the EMG spectrum, calculated using CWT, have been found during a dynamic elbow flexion task (Hostens et al., 2004; Triwiyanto et al., 2017) and a box lifting task (Falla et al., 2017). In the complexity domain, by using fractal estimates, fatigue has been shown to lead to increased fractal dimension of biceps brachii during sustained upper limb elbow contractions (Meduri et al., 2016). By using entropy estimates, fatigue has been shown to result in significantly reduced multiscale fuzzy approximate entropy and multiscale entropy values of biceps brachii during upper limb isometric elbow contractions and dynamic tasks (Cashaback et al., 2013; Navaneethakrishna et al., 2015), suggesting a less complex activation pattern of biceps brachii muscle. The other upper arm muscles are less studied, particularly during multimuscle dynamic tasks. It is still unclear how RPT-induced fatigue could affect MMF of upper limb muscles in time-frequency and complexity domains. Recent studies suggest that complex spatiotemporal patterns of muscle activation could be explained with a low-dimensional group of muscle synergies (Chvatal & Ting, 2012). Research using the NMF algorithm in muscle synergy analysis observed alterations in the recruitment, but not structure, of muscle synergies with fatigue in healthy populations executing a fatiguing upper limb task (Ortega-Auriol et al., 2018). Muscle synergy analysis using the PCA algorithm showed similar results in multimuscle coordination during an upper limb rope-turning motion (Bruce et al., 2017) and a rowing task (Turpin et al., 2011). The results of these studies showed that synergy structure was unchanged with fatigue. Slight modifications were observed in activation profiles of extracted synergies and synergy vectors of individual muscles. Overall, maintaining the synergy structure but changing the activation profiles of the synergies could be one possible strategy to adapt to fatigue and maintain performance. However, to our knowledge, no studies have studied muscle synergies in a fatiguing RPT.

A common and popular sporting task requiring repetitive lower limb movement is running. Fatigue has been shown to increase step variability, lower leg stiffness, and knee and hip joint angles during running, whereas it did not significantly cause adaptations in lower limb joint moments and change characteristics of ground reaction force (García-Pinillos et al., 2020; Luo et al., 2019; Möhler et al., 2021). Dal Pupo et al. (2017) found that the inter-segmental CRP coordination of thigh-leg and leg-foot couplings was not influenced by fatigue after a fatiguing sprinting protocol (Dal Pupo et al., 2017). After an endurance run with higher perceived fatigue, increased CRP variabilities of lower limb joint pairs during transition phases were revealed (Bailey et al., 2020). After an incremental run protocol, increases in CRP and CRP variability of the sagittal plane pelvis-hip joint pair were found in asymptomatic college students (Khaleghi Tazji et al., 2023). By using VC technique, a more out-of-phase coordination of frontal-sagittal plane hip-knee and sagittal plane pelvis-thigh joints with fatigue was observed in experienced runners (Brown et al., 2016; Mo & Chow, 2019). An unchanged lower limb VC variability in the sagittal plane and an increased VC variability in the frontal plane were found during the early stance phase in recreational runners after a fatiguing half marathon (Chen et al., 2022). The running task performance was maintained by regulating both “good” (variability components that do not impact task performance) and “bad” variabilities (variability components that negatively affect the task objective) within the synergy structure during a “fatigue-speed” treadmill run until exhaustion (Möhler et al., 2019). Given the fatigue-related changes in joint kinematics, research has been conducted to identify how fatigue affects lower limb muscle activities. In a 30-minute anaerobic threshold speed running, a significant increase in the instantaneous EMG of gastrocnemius muscles was observed during the fatiguing run (Mizrahi et al., 2000). Over a much longer distance (i.e., a 130-minute run), a similar pattern of EMG amplitude was found, where instantaneous EMG of vastus lateralis muscle was significantly increased with fatigue (Hausswirth et al., 2000). In the time-frequency domain, a decreased instantaneous mean frequency calculated by CWT was found in lower limb muscles when running with fatigue (Koenig et al., 2018; Wakeling et al., 2001). Hajiloo et al. (2020) compared the effects of fatigue on the synergy of lower limb muscles after an incremental run protocol. They found that fatigue did not change the number of synergies but modified the contribution of several muscles within a synergy. Together, running-induced fatigue has been shown to alter lower limb inter-joint and inter-segmental coordination during the stance phases of running. However, the results on coordination are inconsistent, which may be due to different methods to quantify coordination, less comparable fatigue protocols, and different performance levels of participants. The influence of fatigue on lower limb coordination seems more pronounced in novice runners. However, a potential reason could be that fewer studies were focused on highly trained experienced runners. The muscle synergy patterns that were identified in recreational runners with fatigue should also be verified in experienced runners in future studies.

2.5 Sex-specific adaptations of fatigue in repetitive upper and lower limb motions

Given that sex differences have been shown to affect injury risk and fatigue mechanisms, some previous studies have attempted to compare how males and females differ in their response to fatigue. During a RPT, males and females have shown to exhibit different kinematic adaptations to fatigue. Males displayed decreased humerothoracic elevation angles, while females displayed increased variability in humerothoracic elevation angles after a fatiguing RPT (Bouffard et al., 2018). Additionally, females displayed greater variability in upper thoracic and lower thoracic spine movements compared to males (Yang & Côté, 2022). This suggests that males and females might employ different motor control strategies, involving different joints, to reallocate the redundant structures in response to fatigue (Hasanbarani et al., 2021). Previous sEMG studies have shown no sex difference in the activation amplitude of several upper limb muscles after a fatiguing RPT in the time domain. However, males exhibited a higher increase in trapezius muscle activation variability with fatigue compared to females, whereas females showed a higher increase in biceps brachii muscle activation variability (Srinivasan et al., 2016). In the frequency domain, males have shown a higher median frequency of upper trapezius, biceps and supraspinatus with RPT-induced fatigue compared to females (Yoon et al., 2021). When investigating different fatigue locations, RMS of triceps brachii was greater in females after shoulder, elbow, and trunk fatigue (Renda et al., 2022). Hence, in order to adapt to fatigue and preserve task-specific performance, males and females could use different muscular coordination/synergy strategies, that could be evidenced by variables other than kinematic or EMG amplitude, to adapt to repetitive upper limb motion-induced fatigue. However, to our knowledge, no studies have compared muscle synergies in fatiguing upper limb movement control between males and females. Moreover, a combined application of linear and nonlinear metrics to study RPT may provide insight into the mechanisms underlying the sex difference in MMF. It remains unclear whether males and females would display similar time-frequency and complexity characteristics of upper limb muscles in response to RPT-induced fatigue.

In running, most fatigue studies have analyzed the kinematic and kinetic adaptations in males (Clansey et al., 2012; Gao et al., 2020) or in females only (Brown et al., 2014, 2016). Bazuelo-Ruiz et al. (2018) compared 28 male and 29 female recreational runners. The results showed that fatigue decreased dorsiflexion at foot strike in females and plantar flexion at toe-off in males. These changes led to a decreased ground reaction loading rate and the impact peak in females and increased peak propulsive forces in males with fatigue. However, no sex difference was found in patellofemoral joint kinetics, hip adduction excursion angle, ground reaction force loading rate, and step length with fatigue (Willson et al., 2015). Factors such as different fatigue protocols, running populations and running surfaces may contribute to these inconsistent results. Besides the biomechanical metrics calculated for an individual joint, the assessment of coordination patterns of lower limbs between sexes may reveal more in-depth information on how males and females coordinate these adjacent joints to adapt to task-specific fatigue. However, most running studies including both sexes have focused on the multijoint and multimuscle coordination in a non-fatigue condition (Boyer et al., 2017; Hannigan & Chou, 2019; Santuz et al., 2022). How males and females perform intra-limb coordination strategies in response to fatigue is less studied. Furthermore, how both sexes would coordinate these joints and reorganize the coordination/synergy structure to maintain the running task performance remains unclear. Sex-specific muscle coordination/synergy with running-induced fatigue, and MMF in time-frequency and complexity domains need further exploration.

Chapter 3: Few sex-specific effects of fatigue on muscle synergies in a repetitive pointing task

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3.1 Abstract

Previous studies have identified some sex differences in how individual muscles change their activation during repetitive multi-joint arm motion-induced fatigue. However, little is known about how indicators of multi-muscle coordination change with fatigue in males and females. Fifty-six (29 females) asymptomatic young adults performed a repetitive, forward-backward pointing task until scoring 8/10 on a Borg CR10 scale while surface electromyographic activity of upper trapezius, anterior deltoid, biceps brachii, and triceps brachii was recorded. Activation coefficient, synergy structure, and relative weight of each muscle within synergies were calculated using the non-negative matrix factorization method. Two muscle synergies were extracted from the fatiguing task. The synergy structures were mostly preserved after fatigue, while the activation coefficients were altered. A significant Sex × Fatigue interaction effect showed more use of the anterior deltoid in males especially before fatigue in synergy 1 during shoulder stabilization ($p = 0.04$). As for synergy 2, it was characterized by variations in the relative weight of biceps, which was higher by 16% in females compared to males ($p = 0.04$), and increased with fatigue ($p = 0.03$) during the elbow flexion acceleration phase and the deceleration phase of the backward pointing movement. Findings suggest that both sexes adapted to fatigue similarly, using fixed synergy structures, with alterations in synergy activation patterns and relative weights of individual muscles. Results support previous findings of an important role for the biceps and anterior deltoid in explaining sex differences in patterns of repetitive motion-induced upper limb fatigue.

Keywords

Muscle synergy, Non-negative matrix factorization, Repetitive work, Sex differences, Upper limb

3.2 Introduction

Work-related musculoskeletal disorders (WMSDs) affect more than 40% of workers in various occupational groups, inducing neck/shoulder pain syndromes and placing large economic burdens (Sarquis et al., 2016; Virta et al., 2012). In the workplace, repetitive low-intensity tasks can cause fatigue, an ongoing process that develops over time with the potential to lead to WMSDs (CCOHS, 2019; Côté, 2014; Jones & Hunter, 1983). Females have shown a higher prevalence of neck/shoulder complaints compared to males (Nordander et al., 2016). Therefore, repetitive work, fatigue, and sex differences have been identified as risk factors for upper limb WMSDs (Côté, 2012; Da Costa & Vieira, 2010; van der Windt et al., 2000).

In a series of studies using an experimental, repetitive pointing task (RPT) to mimic common occupational repetitive tasks, it was shown that participants can change their trunk posture and shift their bodies towards the unfatigued arm, suggesting active adaptations to mitigate the fatigue effects, in that case adjusting the task to the decreased humerothoracic elevation and shoulder abduction angles occurring due to shoulder fatigue (Bouffard et al., 2018; Fuller et al., 2009). With fatigue, human movement has also been shown to become more variable (Fuller et al., 2011). In protocols using the RPT, this was manifested through increased shoulder and elbow angle variability, and shoulder-elbow coordination variability (Yang et al., 2018). When investigating different fatigue locations (i.e., shoulder, elbow, and trunk fatigue), shoulder fatigue induced the greatest angular changes at all three joints (Yang et al., 2019), further affecting task stability and forcing greater reorganization in redundant structures compared to elbow and trunk fatigue (Slopecki et al., 2022). However, the neuromuscular correlates to these adaptations have been less clearly demonstrated so far.

Additionally, males and females have shown different kinematic adaptations specific to fatigue during the RPT. Males showed decreased humerothoracic elevation angles, while females showed an increased humerothoracic elevation angle variability after a fatiguing RPT (Bouffard et al., 2018). In addition, females showed greater upper thoracic and lower thoracic spine variability compared to males (Yang & Côté, 2022). None of these sex differences were found before fatigue. This suggests that males and females might use different motor control strategies, involving different joints, to reallocate the redundant structures to adapt to fatigue (Hasanbarani et al., 2021).

One possible strategy in response to fatigue during the RPT could be changing muscle activation amplitudes. Previous surface electromyography (sEMG) studies have shown no sex difference in the activation amplitude of several upper limb muscles after a fatiguing RPT. However, males exhibited a higher increase in trapezius muscle activation variability with fatigue compared to females, whereas females had a higher increase in biceps muscle activation variability (Srinivasan et al., 2016). Hence, in order to adapt to fatigue and preserve task-specific performance, males and females could use different coordination strategies, that could be evidenced by variables other than kinematic or EMG amplitude, to adapt to repetitive upper limb motion-induced fatigue.

Recent studies suggests that complex spatiotemporal patterns of muscle activation can be explained with a low-dimensional group of muscle synergies (Chvatal et al., 2011; Chvatal & Ting, 2012; Safavynia et al., 2011; Safavynia & Ting, 2012; Taborri et al., 2018; Torres-Oviedo & Ting, 2007) or “muscle-modes” (Falaki et al., 2014, 2017; Krishnamoorthy et al., 2003a, 2003b; Krishnamoorthy et al., 2007; Latash et al., 2007; Singh et al., 2012; Wang et al., 2006). It has been proposed that the Central Nervous System (CNS) may reduce the dimensionality of neuromuscular systems by activating synergistic muscle groups to complete movements (Ting & McKay, 2007).

This low-dimensional muscle activation module is regarded as muscle synergy, with a group of muscles cooperating to execute motor tasks (Taborri et al., 2018). Hence, muscle synergy analysis could be an appealing method to assess muscle coordination patterns of multi-joint movements (Coscia et al., 2014; Esmaeili & Maleki, 2019).

Non-negative matrix factorization (NMF) is commonly used in muscle synergy analysis as it performs the highest accuracy in EMG signal reconstruction compared to other factorization methods (e.g., principal component and independent component analysis; Rabbi et al., 2020). Recently, muscle synergy extraction using NMF has been applied in motor control (Baggen et al., 2020; Ortega-Auriol et al., 2018), clinical (Coscia et al., 2014; Lencioni et al., 2021; Pellegrino et al., 2018; Tang et al., 2017), robotics (Wang et al., 2021) and sports research (Esmaeili & Maleki, 2019; Hajiloo et al., 2020; Nishida et al., 2017; Saito et al., 2018). Research using NMF analyses observed alterations in the recruitment, but not structure, of muscle synergies with fatigue in healthy populations executing a fatiguing upper limb task (Ortega-Auriol et al., 2018). Hajiloo et al. (2020) compared the effects of fatigue on the synergy of lower limb muscles during running. They found that fatigue did not change the number of synergies but modified the contribution of several muscles within a synergy. Similarly, after a fatiguing one-legged squatting movement, the contribution of knee extensors in synergies increased in response to fatigue (Smale et al., 2016). The modulations of the relative weight of muscles with synergies could be one possible strategy to adapt to fatigue and maintain performance. However, to our knowledge, no studies have compared muscle synergies in fatiguing upper limb movement control between males and females.

The aim of the study was to investigate the adaptations of muscle synergies during a repetitive fatiguing upper limb task in both sexes. Since the structure and the number of synergies generally reflect the complexity of the movement (Cheung et al., 2009), we hypothesized that the

RPT-induced fatigue would not change the structure and the number of extracted synergies. Sex difference would be found in the relative weight of individual muscles with fatigue, given the different fatigue-induced adaptations in EMG variability between sexes.

3.3. Methods

3.3.1 Participants

A retrospective analysis was performed on data collected in multiple projects using the same experimental task. Twenty-seven healthy males and 29 females were included in the study (Table 3.1). All the participants self-reported being right-handed. Participants were excluded if they self-reported history of pain or diagnosed injury in the upper limb, shoulder, or back regions; a history of neurological or vestibular dysfunctions or any other conditions that influence balance. Written informed consent was given to the participant prior to participation. The research protocol was approved by the ethics committee of the Center for Interdisciplinary Research in Rehabilitation of Greater Montreal.

Table 3.1 Demographic data. Values for each group are mean ± standard deviation.

Group	Height (kg)	Weight (cm)	Age (year)	Endurance Time (minutes)
Males	177.74 ± 7.55	73.97 ± 6.37	25.41 ± 6.61	8.04 ± 3.97
Females	164.95 ± 6.12	60.57 ± 7.82	26.68 ± 6.19	7.45 ± 4.37

3.3.2 Data acquisition

The participant performed a repetitive pointing task (RPT), as first described in Fuller et al. (2009), and that has been extensively studied (Bouffard et al., 2018; Lomond & Côté, 2011; Savin et al., 2021; Srinivasan et al., 2016; Figure 3.1). The participant moved the dominant arm to touch a proximal (30% of arm length) and a distal target (100% of arm length) aligned with the body midline at shoulder height in standing position using the index finger. The touch-sensitive targets (length 6 cm, radius 0.5 cm, Quantum Research Group Ltd) provided auditory feedback for the participant to maintain a metronome rhythm at 1 Hz (i.e., one forward or backward pointing movement per second). An elliptical mesh barrier was placed under the elbow joint range of motion to ensure that the elbow position was maintained throughout the RPT. During the RPT, participants rated their perceived level of exertion (RPE) using a Borg CR10 scale at the end of every minute (Borg, 1982). The task was terminated when the participant reached an RPE of 8/10. The endurance time of the task ranged from 2 to 20 minutes in females and 3 to 17 minutes in males (Table 3.1). The first 30-s after the beginning of RPT and the last 30-s before task termination were defined as non-fatigue (NF) and fatigue-terminal (FT) conditions, respectively.

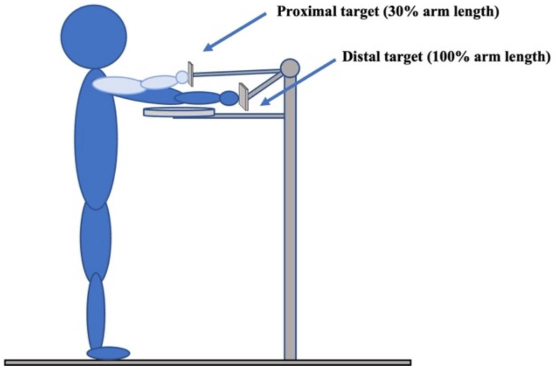

Figure 3.1 Side view of the experimental set up. * Note that the vertical coordinates of both targets are adjusted to each individual's shoulder height.

Surface electromyography (sEMG) signals were recorded during the RPT from four muscles of the right arm: Upper Trapezius (UT; midpoint between the acromion and C7 spinous process), Anterior Deltoid (AD; vertically below the lateral end of the clavicle), Biceps Brachii (BIC; midpoint between the acromioclavicular and elbow joints) and Triceps Brachii — Longhead (TRI; midpoint and 2 cm medial of the line between posterior crista of the acromion and the olecranon). The skin of the four muscle sites was cleaned with alcohol and shaven. Ag–AgCl disposable surface electrodes (Ambu™, Denmark; 1 cm diameter) were positioned and applied with a 3 cm inter-electrode distance, parallel to the muscle fibres on each of the muscle sites (Besomi et al., 2019, Srinivasan et al., 2016). EMG data were collected using a Telemyo 900 (Noraxon, USA) measurement system and sampled at 1080 Hz.

3.3.3 Data analysis

To determine individual forward and backward pointing movements, EMG data were partitioned using the touch-sensitive target signals. Within each NF or FT condition, 15 pointing cycles were collected. One pointing cycle consisted of one forward and one backward movement.

3.3.3.1 EMG data preprocessing

The partitioned EMG data were band-pass filtered (Butterworth 2nd, 20-450 Hz) and full-waved rectified to obtain the linear-enveloped EMG data. EMG data were then time-normalized into 101 samples using cubic interpolation. A submaximal method was used for amplitude normalization. Maximum activities of the muscles were detected first in each cycle and then, EMG data in each channel was divided by the corresponding maximum value in each cycle to get the amplitude-normalized EMG in each repetition (Hajiloo et al., 2020). Lastly, EMG time series were averaged over all the 15 movement cycles to obtain one cycle (i.e., a 4 × 101 matrix for every participant in each NF and FT condition), used for muscle synergy analysis as described below.

3.3.3.2 Non-negative matrix factorization (NMF)

The non-negative matrix factorization (NMF) method was used in this study (Rabbi et al., 2020). The NMF algorithm decomposed the enveloped EMG signals ($\boldsymbol{EMG^{exp}}$) into synergy structure (i.e., synergy vector; $\boldsymbol{W}$), activation coefficient ($\boldsymbol{C}$), and reconstruction error ($\boldsymbol{E}$).

As shown in equation 1, $\boldsymbol{N}$ is the number of muscles, $\boldsymbol{k}$ denotes the number of synergies, and $\boldsymbol{t}$ is the number of data points ($\boldsymbol{t}$ = 1, … ,101). To achieve the best reconstruction performance, NMF minimizes $\boldsymbol{E}$ by updating and iterating the synergy coefficients. Activation coefficient represents the synergy activation pattern at time, and the synergy structure denotes the fixed module organization of each synergy. The relative weight of each muscle was also calculated.

$$\boldsymbol{EMG_{N\times t}^{exp} = W_{N\times k} \times C_{k\times t} + E} \qquad (1)$$

Variance accounted for (VAF) was used to evaluate the accuracy of the reconstructed EMG matrix ($\boldsymbol{EMG^{rec}}$) and select the number of synergies. The number of synergies was defined as the minimum number of synergies required to achieve a mean global VAF while satisfying the criteria of local VAF for each muscle (Clark et al., 2010; Roh et al., 2013). To achieve this, we first calculated global VAF for each dataset of males and females in each fatigue condition, while varying the number of synergies from one to four. Then, to determine the minimum number of synergies needed to adequately reconstruct $\boldsymbol{EMG^{exp}}$, a global VAF > 90% needed to be satisfied for each dataset (Roh et al., 2013)**.** As for the local VAF, local VAF for each of the four muscles needed to be exceed 80% (Roh et al., 2013). Otherwise, additional synergies were needed until all muscles achieved 80% local VAF or until adding an additional synergy did not increase VAF by 5% for the muscle(s) with the lowest local VAF (Clark et al., 2010; equation 2). Cross-validation was conducted to confirm that the synergies extracted from $\boldsymbol{EMG^{rec}}$ were not biased by the NMF algorithm (Roh et al., 2013).

$$VAF = 1 - \frac{\sum_{t=1}^{101} EMG_t^{rec} - EMG_t^{exp}}{\sum_{t=1}^{101} EMG_t^{exp}} \tag{2}$$

Angle cosine (*r*) between two synergy vectors was evaluated as a criterion for comparing the similarities of synergy structures of both sexes between NF and FT condition. Each synergy vector was first normalized by its norm. Then the angle cosine was defined as the inner product of two synergy vectors (Nishida et al., 2017). A cosine similarity value of threshold of 0.8 was chosen, since values above 0.8 have been regarded as showing high similarity between two synergy structures (Esmaeili & Maleki, 2019). All data analyses were conducted through customized MATLAB scripts (version R2020b, MathWorks, Natick, USA).

3.3.4 Statistical analysis

Two-way (Fatigue × Sex) repeated-measures ANOVA was used to examine activation coefficients and relative weights of four muscles in synergies. Statistical parametric mapping (SPM) on two-way ANOVA was used to compare activation coefficients through movement time between NF and FT conditions (Kobayashi et al., 2022; Mehryar et al., 2020; Smale et al., 2016).

3.4 Results

Synergy 1 involved UT, AD, BIC, and TRI. This synergy corresponds to a period of stabilization of the shoulder. Synergy 2 involved the same four upper limb muscles. Synergy 2 seemed to be mainly responsible for the flexion and extension of the elbow. The interpretations of these synergy functions are further discussed in section 3.5.1.

3.4.1 Number of synergies

NMF algorithms were applied to the ***EMG***^{exp} for four interactions. As shown in Table 3.2, global VAF with two synergies was > 90% for each of the dataset. Meanwhile, local VAF with two synergies was > 80% for each of the four muscles. No significant differences in local VAF of four muscles were found between sexes and between fatigue conditions. To have a quantitative confirmation, we also illustrated the results of VAF varying from one to four synergies in Figure 3.2. Therefore, given the accurate overall reconstruction provided by two synergies, we retained and selected two synergies to facilitate between- and within-group comparisons and to be used in the subsequent analyses.

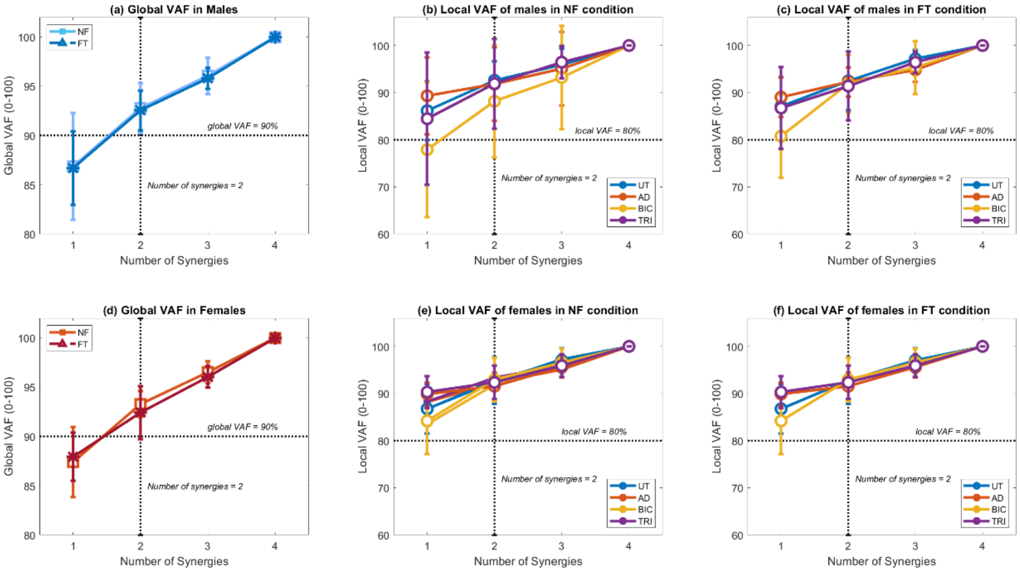

Figure 3.2 Global and local VAFs between- and within- groups. VAF: variance accounted for, UT: upper trapezius, AD: anterior deltoid, BIC: biceps brachii, TRI: triceps brachii, NF: non-fatigue, FT: fatigue-terminal.

Table 3.2 Descriptive data of global and local VAFs (means ± SD).

	Males		Females	
	NF	FT	NF	FT
Global VAF (%)				
With one synergy	86.88 ± 5.42	86.69 ± 3.73	87.39 ± 3.57	87.92 ± 2.45
With two synergies	92.77 ± 2.54	92.55 ± 2.02	93.28 ± 1.31	92.41 ± 2.69
With three synergies	96.06 ± 1.85	95.79 ± 1.06	96.50 ± 1.10	96.04 ± 1.09
With four synergies	100	100	100	100
Local VAFs with one synergy (%)				
UT	86.17 ± 6.24	87.11 ± 6.25	86.75 ± 5.25	86.76 ± 5.28
AD	89.34 ±8.18	89.04 ± 4.14	88.20 ± 5.88	89.90 ± 2.40
BIC	77.91 ± 14.31	80.76 ± 8.85	83.51 ± 10.49	84.19 ± 7.09
TRI	84.47 ± 14.04	86.74 ± 8.70	88.29 ± 5.67	90.33 ± 3.38
Local VAFs *with two synergies* (%)				
UT	92.60 ± 4.06	92.48 ± 6.21	92.48 ± 4.15	92.77 ± 4.89
AD	91.83 ± 7.84	92.25 ± 3.12	92.27 ± 4.39	91.56 ± 2.88
BIC	88.17 ± 11.96	91.91 ± 6.08	91.88 ± 10.31	92.95 ± 4.66
TRI	91.90 ± 9.51	91.41 ± 7.30	93.36 ± 3.25	92.35 ± 3.54

Notes: NF: non-fatigue, FT: fatigue-terminal, VAF: variance accounted for, UT: upper trapezius, AD: anterior deltoid, BIC: biceps brachii, TRI: triceps brachii.

3.4.2 Similarities of synergy structures

Angle cosine (*r*) between two synergy vectors was evaluated as a criterion for comparing the similarities of synergy structures of both sexes between NF and FT conditions. Overall, high cosine similarities of synergy structures were found in both sexes after fatigue. A high cosine similarity of synergy structures was found between fatigue conditions in both sexes (Figure 3.4a). A high cosine similarity of synergy structures was found between males and females (Figure 3.4b).

3.4.3 Distributions of relative weight of each muscle within two synergies

In synergy 1, there was a significant Sex × Fatigue interaction effect on the relative weight of AD as indicated by the red *F*S* letters in Figure 3.3a (F = 4.39, $p = 0.04$, $\eta^2 = 0.08$; Table 3.3 and Figure 3.5). There was generally more relative weight of AD in males especially before fatigue, although no significant differences were found in the post-hoc pairwise comparisons.

As for synergy 2, there was no Sex × Fatigue interaction on the relative weights of four muscles. However, significant main effects of Fatigue (F = 4.84, $p = 0.03$, $\eta^2 = 0.08$) and Sex (F = 4.36, $p = 0.04$, $\eta^2 = 0.08$) were found on relative weight of BIC. The relative weight of BIC significantly increased after fatigue (Mean difference (MD) = 0.05, 95% CI [0.005 - 0.10]). In addition, females displayed significant higher relative weight of BIC compared to males (MD = 0.07, 95% CI [0.003 - 0.14]; Table 3.3 and Figure 3.3d.

Table 3.3 Comparison of relative weight of four muscles and activation coefficient (means ± SD) in synergies before and after fatigue in males and females.

		Males		Females		p values		
		NF	FT	NF	FT	Fatigue effects	Sex effects	Interaction effects
Synergy 1								
Relative weight (0-1)	UT	0.43 ± 0.18	0.50 ± 0.15	0.49 ± 0.15	0.48 ± 0.12	0.25	0.52	0.11
	AD	0.54 ± 0.19	0.49 ± 0.10	0.45 ± 0.16	0.49 ± 0.08	0.84	0.15	**0.04**
	BIC	0.36 ± 0.19	0.44 ± 0.17	0.46 ± 0.20	0.45 ± 0.16	0.21	0.16	0.09
	TRI	0.51 ± 0.20	0.49 ± 0.14	0.49 ± 0.14	0.53 ± 0.09	0.60	0.80	0.19
*Activation coefficient (*0-1)		0.31 ± 0.09	0.37 ± 0.10	0.31 ± 0.06	0.36 ± 0.06	**<0.001**	0.75	0.81
Synergy 2								
Relative weight (0-1)	UT	0.53 ± 0.16	0.54 ± 0.14	0.50 ± 0.13	0.53 ± 0.13	0.33	0.42	0.68
	AD	0.49 ± 0.16	0.47 ± 0.13	0.48 ± 0.16	0.46 ± 0.11	0.50	0.66	0.10
	BIC	0.35 ± 0.16	0.40 ± 0.15	0.42 ± 0.16	0.48 ± 0.14	**0.03**	**0.04**	0.72
	TRI	0.50 ± 0.18	0.49 ± 0.15	0.52 ± 0.14	0.47 ± 0.11	0.19	0.97	0.30
*Activation coefficient (*0-1)		0.23 ± 0.07	0.28 ± 0.08	0.21 ± 0.05	0.26 ± 0.05	**<0.001**	0.15	0.88
						0.03 (SPM results, main effects of fatigue found at 62% and 98% of movement cycle in both sexes)		

Notes: NF: non-fatigue, FT: fatigue-terminal, UT: upper trapezius, AD: anterior deltoid, BIC: biceps brachii, TRI: triceps brachii, a significant difference was set at $p < 0.05$

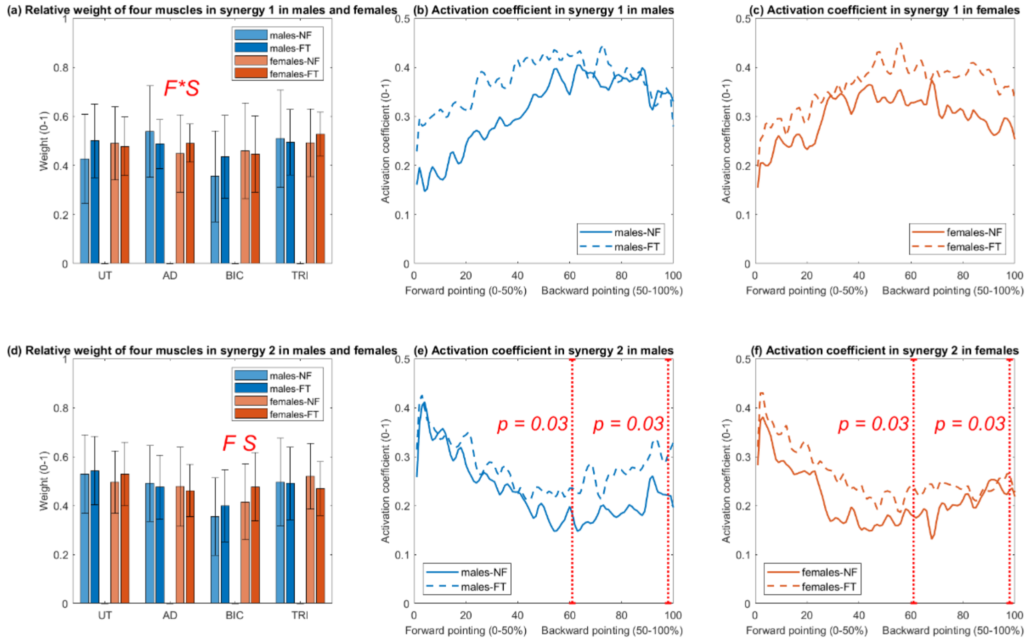

Figure 3.3 Synergy structure and activation coefficients, displayed as a function of Sex and Fatigue, overall (a) and as a function of movement time for synergy 1 in males (b) and females (c), and overall (d) and as a function of movement time for synergy 2 in males (e) and females (f). In synergy 1, males showed more relative weight of AD before fatigue (a). In synergy 2, the relative weight of BIC increased with fatigue, and females showed higher relative weight of BIC compared to males (d), and both sexes had an increased activation coefficient after fatigue at 62% and 98% of the RPT movement (b, c, e, and f). UT: upper trapezius, AD: anterior deltoid, BIC: biceps brachii, TRI: triceps brachii, RPT: repetitive pointing task, NF: non-fatigue, FT: fatigue-terminal, F*S: significant interaction effect between Sex and Fatigue, F: significant main effect of Fatigue, S: significant main effect of Sex ($p < 0.05$), the vertical dotted lines on subplot (e) and (f) represent times in the cycle where main fatigue effects were found using the SPM method.

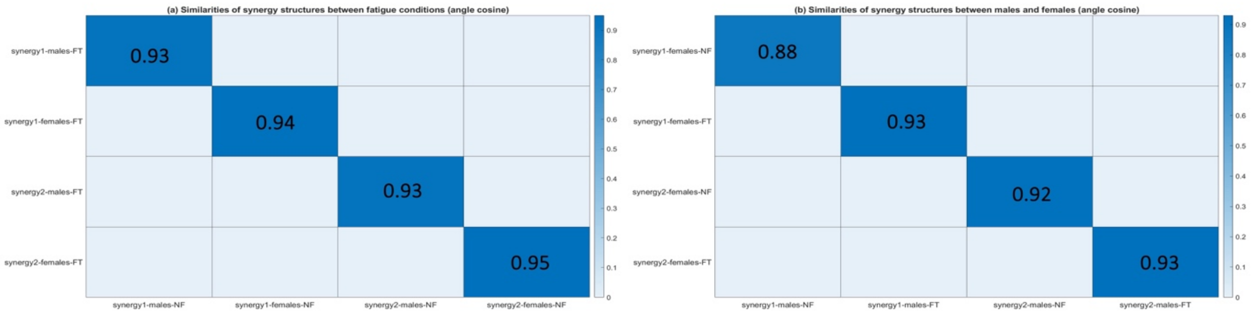

Figure 3.4 Similarities of synergy structures of sexes after fatigue. A high cosine similarity of synergy structures was found between fatigue conditions in both sexes (a). A high cosine similarity of synergy structures was found between males and females (b). NF: non-fatigue, FT: fatigue-terminal.

3.4.4 Characteristics of activation coefficients in two synergies

There was no Sex × Fatigue interaction on activation coefficient in synergy 1 and synergy 2. A significant main effect of Fatigue was found in synergy 1 (F = 28.12, $p < 0.001$, $\eta^2 = 0.34$) and synergy 2 (F = 42.01, $p < 0.001$, $\eta^2 = 0.44$), showing an increase after fatigue in both synergies (synergy 1: MD = 0.06, 95% CI [0.03 - 0.08], synergy 2: MD = 0.05, 95% CI [0.04 - 0.07]; Table 3.3).

3.4.5 Synergy characteristics as a function of time

SPM results showed that in synergy 1, there were no sex, fatigue or interaction effects occurring at any specific time of the movement cycle (Figure 3.3b and 3.3c). However, in synergy 2, both sexes had an increased activation coefficient after fatigue at 62% ($p = 0.03$) and 98% of RPT movement ($p = 0.03$; Table 3.3; Figure 3.3e and 3.3f), i.e. towards the acceleration (62%) and deceleration (98%) phases of the backward movement (from the distal to the proximal target).

3.4.6 Time and spectral EMG characteristics

There were no significant interaction effects on RMS or MdPF of four muscles. A significant main effect of fatigue was found on MdPF of AD (F = 94.02, $p < 0.001$, $\eta^2 = 0.64$), BIC (F = 25.27, $p < 0.001$, $\eta^2 = 0.32$), and TRI (F = 56.12, $p < 0.001$, $\eta^2 = 0.51$), showing a decrease after fatigue (AD: MD = –14.05, 95% CI [–16.95 - –11.14], BIC: MD = –7.27, 95% CI [–10.17 - –4.37], TRI: MD = –10.57, 95% CI [–13.39 - –7.74]; Table 3.4).

Table 3.4 Comparison of muscle activation amplitude (RMS) and median power frequency (MdPF) before and after fatigue in males and females (means ± SD).

	Males		Females		*p* values		
	NF	FT	NF	FT	Fatigue effect	Sex effect	two-way interaction
RMS (%)							
UT	42.60 ± 11.43	44.87 ± 14.37	47.10 ± 12.42	46.87 ± 9.35	0.57	0.23	0.49
AD	42.03 ± 15.37	46.21 ± 12.23	46.70 ± 16.67	44.49 ± 12.05	0.69	0.61	0.20
BIC	43.21 ± 15.50	40.31 ± 14.43	48.38 ± 12.42	43.40 ± 13.29	0.11	0.15	0.67
TRI	42.28 ± 18.18	45.40 ± 17.95	48.52 ± 15.03	46.26 ± 15.20	0.85	0.35	0.25
MdPF (Hz)							
UT	70.38 ± 37.65	70.38 ± 36.82	62.59 ± 15.57	62.16 ± 14.41	0.76	0.29	0.09
AD	77.03 ± 9.76	63.74 ± 9.12	76.38 ± 17.78	61.58 ± 12.93	**< 0.001**	0.66	0.61
BIC	71.49 ± 12.44	62.13 ± 10.91	66.10 ± 13.09	60.91 ± 10.08	**< 0.001**	0.24	0.16
TRI	84.01 ± 45.20	70.87 ± 38.40	67.53 ± 12.58	59.55 ± 10.42	**< 0.001**	0.09	0.07

Notes: NF: non-fatigue, FT: fatigue-terminal, RMS: root mean square, MdPF: median power frequency, UT: upper trapezius, AD: anterior deltoid, BIC: biceps brachii, TRI: triceps brachii, a significant difference was set at $p < 0.05$.

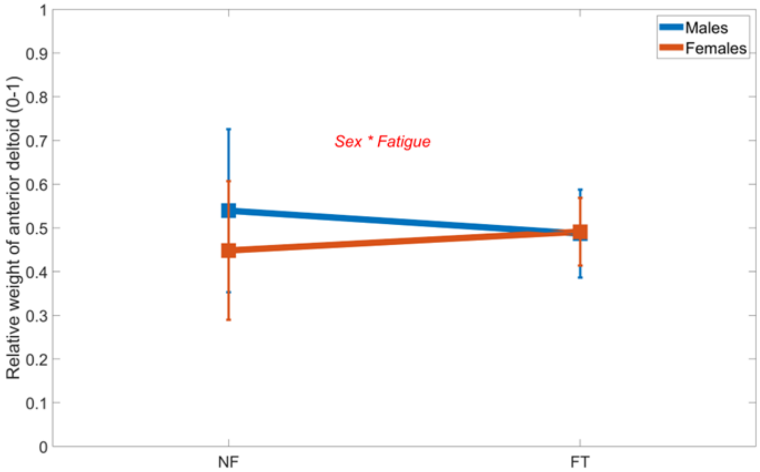

Figure 3.5 Relative weight of anterior deltoid in synergy 1 before and after fatigue in males and females. NF: non-fatigue, FT: fatigue-terminal, Sex * Fatigue: significant interaction effect between Sex and Fatigue ($p < 0.05$).

3.5 Discussion

This study aimed to investigate the spatial and temporal characteristics of muscle synergies in response to a fatiguing repetitive arm task between males and females. The main findings of the study are: 1) two muscle synergies were extracted, and the number of synergies did not change according to sex or fatigue. 2) There were strong similarities of synergy structures before and after fatigue. 3) There were few, but some, sex differences, with less relative weight of biceps after fatigue in males compared to females in synergy 2 during the elbow flexion acceleration phase and the deceleration phase of the backward pointing movement. 4) Conversely, there was more use of the anterior deltoid in males especially before fatigue in synergy 1 during shoulder stabilization.

3.5.1 Muscle synergies in repetitive pointing task

The current study is the first to include the analysis of the backward pointing phase of the repetitive pointing task in the synergy analysis, whereas many previous studies only analyzed the forward movement phase (Srinivasan et al., 2016; Yoon et al., 2021). We found that two synergies could account for 90% global variance of the dataset. The number of synergies generally reflect the complexity of the movement and the amount of movement planes of interest (Cheung et al., 2009). The experimental task used in our study was a single-plane movement, constrained by the start and end finger position. The number of synergies that were extracted in this study is in line with previous research (Muceli et al., 2010). For instance, during a dynamic shoulder extension-flexion movement, two synergies were extracted and able to reconstruct the movement, while three to four synergies were found in multi-directional reaching tasks in 12 directions (Muceli et al., 2010).

In looking more closely at what each synergy reflects, synergy 1 was active during the entire task (Figure 3.3b and 3.3c), suggesting that this synergy facilitated the stabilization of the shoulder throughout the task, during which fatigue is mainly induced by the need to maintain the entire arm at shoulder height during both forward and backward movement phases. Fatigue led to a significant increase in activation coefficient temporally. Biceps, anterior deltoid, upper trapezius, and triceps showed similar relative weights with fatigue (Table 3.3). Therefore, all four muscles increased their muscular activation and contributed similarly to stabilize shoulder and elbow joints in response to fatigue in synergy 1. As for synergy 2, it was mainly responsible for the flexion and extension of the elbow during the task. In this synergy, both sexes exhibited increased relative weight of biceps with fatigue (Table 3.3). Activation coefficients were mainly active at the beginning phase of forward pointing and the latter phase of backward pointing (Figure 3.3e and 3.3f), where participants would generally initialize elbow extension to accelerate the forward pointing and terminate elbow flexion to decelerate the backward pointing, respectively. The biceps made more contributions to synergy 2 with fatigue, especially during the elbow flexion acceleration phase and the deceleration phase, where biceps contracted concentrically and eccentrically to maintain the elbow position.

3.5.2 Similarities and differences between sexes

In the current study, males and females exhibited many similarities in their synergy structure organization in response to fatigue. The preservation of the synergy structure aligns with the hypothesis that muscle synergies are fixed modules organized by the CNS and built within the spinal circuit (Emilio Bizzi & Cheung, 2013; Lencioni et al., 2021). This is in line with the previous suggestions from the literature that the fatigue manifestations stem from peripheral changes stemming from fatigue. At the peripheral level, receptors could produce afferent inputs to modulate the activity of motoneurons, thereby progressively facilitating the firing rate of motor units and altering their activation patterns (Gandevia, 2001; Macefield et al., 1993).

Despite the many similarities between the sexes, there were some differences highlighted in our results. For instance, even though the synergy structure was maintained with fatigue in both sexes, our study highlighted that males utilized more of their anterior deltoid to stabilize the shoulder before fatigue, while females utilized more of their biceps after fatigue during elbow flexion and extension. The addition of the backward phase to our analysis further reinforces the important role of the biceps and anterior deltoid in explaining sex-specific fatigue effects during repetitive upper limb tasks, since both muscles are involved in synergies highly activated in both forward and backward phases of movement. Thus, our findings are in line with previous ones that suggest that males and females execute the same task with many similarities, but slight differences in their coordination patterns (Ansdell et al., 2020; Côté, 2012; Hunter, 2014; Srinivasan et al., 2016). However, the origin of these slight sex differences is unclear, and is likely multifactorial. Although males and females have similar fibre compositions in several muscles, females were reported to have a smaller fibre cross-sectional area of upper trapezius and biceps compared to males (Lindman et al., 1991; Miller et al., 1993). In addition, males on average have heavier upper limbs which required more contribution of anterior deltoid to lift the arm and stabilize it; arm weight, and its anthropometric load, has previously been suggested to be a part of the mechanisms underlying sex-specificity in the muscle activity response to repetitive arm motion-induced shoulder fatigue (Slopecki et al., 2020). Moreover, Yoon et al. (2021) found that males and females had similar power spectrum of median power frequency of biceps, but males showed more biceps swelling following a fatiguing repetitive forward reaching task, suggesting that the sex-specific mechanisms in the fatigue response could also involve hemodynamic factors. Further, the relationship between task-specific fatigue and motor variability has also shown some sex-specificity, with increased biceps EMG variability and humerothoracic elevation variability in females with fatigue (Bouffard et al., 2018; Srinivasan et al., 2016). Males may use a "shoulder-based" strategy to stabilize the should before fatigue; however, with the development of fatigue, females may adopt an "elbow-based" strategy to adapt to fatigue during the repetitive pointing task (Srinivasan et al., 2016). Thus, the current findings, in line with those previous ones, do identify many similarities, but some differences, in sex-specific mechanisms of the fatigue response, which may further help explain a higher incidence of neck-shoulder WMSDs in females (Côté, 2012).

3.5.3 Limitations

The present study had some limitations. Firstly, the number of muscles collected in our study is smaller than in other studies. The activities of deep shoulder and elbow muscles should be recorded to help us better extract muscle synergies and interpret each muscle's role within the synergy. Despite the small number of muscles, it has been suggested that two synergies were sufficient to reconstruct the pointing task, given the complexity of the task (Ortega-Auriol et al., 2018), although more synergies with lesser weights were observed but ignored from further analyses. Further research is needed to include more upper limb muscles to explore the sex-specific effects of fatigue on muscle synergies in a repetitive pointing task. Secondly, the use of surface electrodes may lead to inconsistent results on EMG signals, such as subcutaneous tissue thickness and the skin-electrode impedance, although care was taken with amplitude normalization and taping, to minimize the error. Lastly, while this study focused on exploring biological sex-specific effects of fatigue on muscle synergies using a computational method, potential social and individual risk factors, such as the work environment encountered by males and females and morphology difference between sexes should be considered in the future when investigating sex differences in neck-shoulder WMSDs

3.6 CRediT authorship contribution statement

Yiyang Chen: Conceptualization, Methodology, Software, Validation, Formal analysis, Data Curation, Writing – Original Draft, and Visualization. **Chen Yang**: Conceptualization, Methodology, Validation, Formal Analysis, Data Curation, Writing – Review & Editing, and Project Administration. **Julie N. Côté**: Conceptualization, Methodology, Validation, Resources, Writing – Review & Editing, Supervision, and Funding Acquisition.

3.7 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.

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Bridge between Chapter 3 and 4

In line with a series of similar experimental studies using traditional time and frequency EMG metrics (e.g., root mean square and median frequency; Erika et al., 2022; Slopecki et al., 2020; Yoon et al., 2021), muscle synergy analysis in Chapter 3 further reveals and supports the critical roles of biceps brachii and anterior deltoid in explaining sex differences in multimuscle activation patterns with repetitive motion-induced upper limb fatigue. It is worth noting that muscle synergy analysis, along with the traditional EMG metrics, all assume the EMG signals are linear and stationary. However, it is now well agreed that the EMG signals are non-stationary in nature. EMG signals contain both deterministic and stochastic components; therefore, they cannot be fully characterized by linear metrics. This led to a research question of whether the general conclusion of sex-specific manifestations of upper limb fatigue would remain the same by using nonlinear and time-frequency EMG metrics.

To answer this question, Chapter 4 presents further analyses of the same dataset as that used in Chapter 3. The same surface electromyography and optoelectronic motion capture systems were used to record myoelectric muscle activities of upper limb muscles and kinematics of upper limb motions. We chose continuous wavelet transform analysis to access the frequency components of EMG signals of upper limb muscles in the time-frequency domain. We used sample entropy method to measure the similarity and regularity of EMG signals in the complexity domain. Time-frequency characteristics of EMG were computed as the mean frequency calculated by continuous wavelet transform and major frequency extracted from the wavelet scalograms. Complexity characteristics of EMG were measured as the sample entropy value. Results from Chapter 4 build on findings of Chapter 3 by adding time-frequency and complexity information to understand more features of the impact of fatigue on upper limb muscle activation.

Chapter 4: Sex-specific myoelectric manifestations of fatigue in time-frequency and complexity domains during a repetitive pointing task

Yiyang Chen, Di Kang, Julie N. Côté

Chapter 4 is a copy of the manuscript being prepared for submission to *Motor Control.*

4.1 Abstract

Previous studies have shown sex differences in muscle activation amplitude and spectrum during fatigued dynamic tasks. However, time-frequency and complexity analyses may provide a more in-depth assessment of changes in the electromyographic activities with fatigue, but have never been used to study sex-specific upper limb fatigue effects. Fifty-five (29 females) asymptomatic young adults performed a repetitive, forward-backward pointing task until scoring 8/10 on a Borg CR10 scale while surface electromyography (EMG) of upper trapezius, anterior deltoid, biceps brachii, and triceps brachii was recorded. 1) all muscles displayed decreased sample entropy and mean frequency with fatigue; 2) fatigue led to decreased major frequency (i.e., frequency component of the region with the highest power on the wavelet scalogram) of anterior deltoid, biceps brachii, and triceps but not upper trapezius; 3) females' biceps brachii mean frequency in forward pointing was 5% significantly higher than males'; all other frequency components were similar between sexes; 4) females showed a significantly higher complexity of biceps brachii by 7% during forward pointing and 8% during backward pointing. Females showed a significantly lower complexity of anterior deltoid by 3%, but only in backward pointing phase. Our results suggest that entropy and continuous wavelet transform analyses are capable of revealing new effects of sex and fatigue in myoelectric manifestations of repetitive fatiguing tasks.

Keywords

Muscle fatigue; Upper limb; Time-frequency analysis; Complexity analysis; Sex differences

4.2 Introduction

Work-related musculoskeletal disorders (WMSDs) have been reported to affect more than 40% of workers, with females showing a higher prevalence of neck/shoulder complaints compared to males (Nordander et al., 2016). Sustained low-force tasks in workplaces can lead to a decreased functional capacity of muscles, inducing declines in the task performance and changes in sensation. Fatigue is defined as “a disabling symptom in which physical and cognitive function is limited by interactions between performance fatigability and perceived fatigability” (Enoka & Duchateau, 2016). The electromyography (EMG) is usually used to record the changes in the electrical activities of muscles during fatiguing contractions. Myoelectric manifestations of fatigue (MMF) previously reported to occur with various tasks include a shift towards lower frequencies in the EMG power spectrum in frequency domain due to changes in muscle fibre conduction velocity and increased EMG amplitude and variability in time domain (Farina et al., 2002a; Fedorowich et al., 2013; Srinivasan et al., 2012; Vigotsky et al., 2018). Due to differences in muscle fibre composition, hormonal influences, and metabolic responses to fatigue, sex differences have been observed in MMF (Hicks et al., 2001). However, the extent to which these MMF differ between sexes may vary between muscles, type of tasks performed, and the extracted MMF measures.

The link between MMF and WMSDs has been investigated by a series of studies using a repetitive pointing task (RPT; Fuller et al., 2009; Moyen-Sylvestre et al., 2022; Renda et al., 2022; Savin et al., 2021). The task requires the participant to repetitively move their dominant arm between a proximal and a distal target placed at shoulder height in a standing position. The mimicked static load on the neck/shoulder elevators and dynamic load on the shoulder movers, added to the prolongation of muscle contraction over time observed to occur with this task, are in line with common risk factors in workplaces associated with WMSDs (van der Windt et al., 2000). Changes in MMF in response to repetitive upper limb tasks, and how these differ between males and females, have been measured in time and frequency domains. A previous study has shown that the median frequency of upper limb muscles decreased with fatigue in both sexes, with males having a higher median frequency of upper trapezius, biceps brachii and supraspinatus compared to females (Yoon et al., 2021). In the time domain, males showed a higher increase than females in trapezius and anterior deltoid muscle activation variability with fatigue, but females showed a higher increase in biceps brachii and triceps muscle activation variability (Srinivasan et al., 2016). However, the reliability of amplitude and spectral measures may be affected by the application of Fourier-based techniques. These approaches are not well suited for dynamic contractions where the EMG signal is non-stationary due to alterations in muscle force, contraction velocity, and muscle length (Costa et al., 2012; Croce et al., 2014). Wavelet methods enable the decomposition of a signal into frequency and time across a range of fundamental functions, which can be tailored to meet specific analytical requirements for different types of signals (Bertoli et al., 2019). Among various wavelet approaches, the continuous wavelet transform (CWT) offers the flexibility to choose wavelet scales that match specific frequency and time values, allowing for precise adjustment of frequency resolution (Costa et al., 2012), which makes it suitable for dynamic muscle contractions. A decreased instantaneous mean frequency and a shift of the EMG spectrum calculated by CWT have been found during dynamic upper-limb tasks (Hostens et al., 2004; Triwiyanto et al., 2017). However, there is no information about the sex-specific time-frequency characteristics in a fatiguing dynamic multijoint arm task.

Biological systems are regulated by physiological control processes that operate across various time scales (Costa et al., 2005), manifested as noisy and chaotic signals. Entropy measures the probability that existing patterns of signals will not be succeeded by further similar patterns, thus offering nonlinear indices of the unpredictability and irregularity of biological data. Approximate entropy was developed for the application of entropy measures to chaotic biological data, as a way to estimate the “likelihood that runs of patterns that are similar remain similar on next incremental comparisons" (Pincus, 1991). To avoid the main issue of self-matches in approximate entropy approach, an index of sample entropy (SampEn) was developed and represents the similarity and regularity of signals, as a way to provide better consistency in measuring the regularity of time series (Richman & Moorman, 2000). Due to the chaotic nature of EMG signals, the complex EMG signals include both deterministic elements and stochastic or random components (Clancy & Farry, 2000; Potvin & Brown, 2004). Additionally, the complexity metrics have been shown to be linearly correlated with muscle activation (Anmuth et al., 1994), potentially providing further insight into the MMF assessment.

A few recent studies have used nonlinear approaches to characterize MMF. They have shown that fatigue results in a significant loss in EMG complexity during isometric contractions and dynamic tasks (Rampichini et al., 2020). Within different types of complexity metrics, entropy measures show promising results in underlying the onset of MMF in a way that is in line with the known evolution of metabolic and enzymatic events involved in muscle contractions with fatigue (Hernandez & Camic, 2019; Tong et al., 2016; Xie et al., 2010). The entropy values typically show a clear decline with fatigue, representing a more regular (and likely more realistic) fatigue-related evolution of EMG signals. However, it remains unknown whether males and females would display similar time-based changes in entropy estimates in response to RPT-induced fatigue.

This study aimed to 1) detect the time-based effects of fatigue on time-frequency and complexity characteristics of EMG signals during a RPT and 2) investigate if males and females would respond similarly. We hypothesized that fatigue would shift the energy from high to low frequencies, that a less complex EMG signal would be detected after fatigue, and that there would be sex differences in the complexity domain of the EMG signals.

4.3 Methods

4.3.1 Participants

A retrospective analysis was performed on data collected in multiple projects using the same experimental task. Twenty-six healthy males and 29 females were included in the study (Table 4.1). All participants self-reported being right-handed. Participants were excluded from the study if they reported having experienced pain or were diagnosed with an injury in the upper limb, shoulder, or back regions, a history of neurological or vestibular dysfunctions or any other conditions that influence balance. Written informed consent was given to the participant prior to participation. The research protocol was approved by the ethics committee of the Center for Interdisciplinary Research in Rehabilitation of Greater Montreal.

Table 4.1 Demographic data (mean ± standard deviation).

Group	Height (kg)	Weight (cm)	Age (year)	Endurance Time (minutes)
Males	176.82 ± 6.89	73.92 ± 6.31	25.30 ± 6.31	8.02 ± 3.30
Females	164.95 ± 6.12	60.57 ± 7.82	26.68 ± 6.19	7.45 ± 4.37

4.3.2 Data acquisition

The participant performed a repetitive pointing task (RPT) that has been extensively studied and described elsewhere since Fuller et al. (2009; Moyen-Sylvestre et al., 2022; Renda et al., 2022; Savin et al., 2021). The task was terminated when the participant reported an RPE of 8/10 (Borg, 1982). The first 30-second after the beginning of RPT and the last 30-second before task termination were defined as non-fatigue and fatigue-terminal conditions, respectively.

SENIAM guidelines were followed to determine the electrode location (Hermens et al., 2000). Surface EMG signals were recorded from four muscles of the right arm: Upper Trapezius (UT; midpoint between the acromion and C7 spinous process), Anterior Deltoid (AD; vertically below the lateral end of the clavicle), Biceps Brachii (BIC; midpoint between the elbow joint and acromioclavicular) and Triceps Brachii – Longhead (TRI; midpoint and 20 mm medial of the line between the posterior crista of the acromion and the olecranon). The skin of the four muscle sites was cleaned with alcohol and shaven. Bipolar Ag–AgCl disposable surface electrodes (Ambu™, Denmark; 1 cm diameter) were positioned and applied with a 3 cm inter-electrode distance, parallel to the muscle fibres on each of the muscle sites (Besomi et al., 2019; Srinivasan et al., 2016). Surface EMG data were recorded through a Telemyo 900 (Noraxon, USA) measurement system and sampled at 1080 Hz.

4.3.3 Data analyses

Each pointing cycle was partitioned into forward and backward phases using the signals from the touch-sensitive targets (0.5 cm radius, 6 cm length, Quantum Research Group Ltd). The partitioned EMG data were band-pass filtered (Butterworth 2nd, 20-450 Hz) and then put into the entropy and time-frequency analysis.

4.3.3.1 Entropy estimates

The multiscale entropy algorithm was used to quantify the complexity of time series data over multiple scales (Costa et al., 2002). For each repetition $\boldsymbol{X}$, a coarse-grained time series $\boldsymbol{Y}^{(\tau)}$ was constructed, determined by non-overlapping windows of length τ (i.e., scale factor; $1 < \tau < 20$; equation 1).

$$Y_i^{(\tau)} = \frac{1}{\tau}\sum_{j=(i-1)\tau+1}^{i\tau} x_j \qquad (1)$$

The modified sample entropy (SampEn) value was then calculated for each $\boldsymbol{Y}$ based on a given vector length m, threshold value r, and scale factor τ, where $\boldsymbol{A}^{(m)}(r, \tau)$ and $\boldsymbol{B}^{(m)}(r, \tau)$ are the counts of similar patterns of length m+1 and m in $\boldsymbol{Y}^{(\tau)}$, respectively (equation 2). Similar patterns indicate that the distance between two $\boldsymbol{Y}$ is smaller than r (Costa et al., 2003).

$$\text{SampEn}\ (\text{m}, \text{r}, \tau) = -\ln\left(\frac{A^{(m)}(r,\tau)}{B^{(m)}(r,\tau)}\right) \qquad (2)$$

We selected the *m* ($2 \le m \le 8$) and *r* ($0.1 \le r \le 0.9$) by calculating the minimal value of probabilistic cost ***J*** for the biceps brachii EMG signals, which is quantified as the maximum of the relative error of the entropy values and conditional probability (Cashaback et al., 2013; equation 3). *m* =2 and *r* = 0.6 were selected based on the conditional probability analysis (Figure 4.1).

$$J(m,r) = \max\left(\frac{\sigma_{CP}}{CP}, \frac{\sigma_{CP}}{-\log(CP)CP}\right) \qquad (3)$$

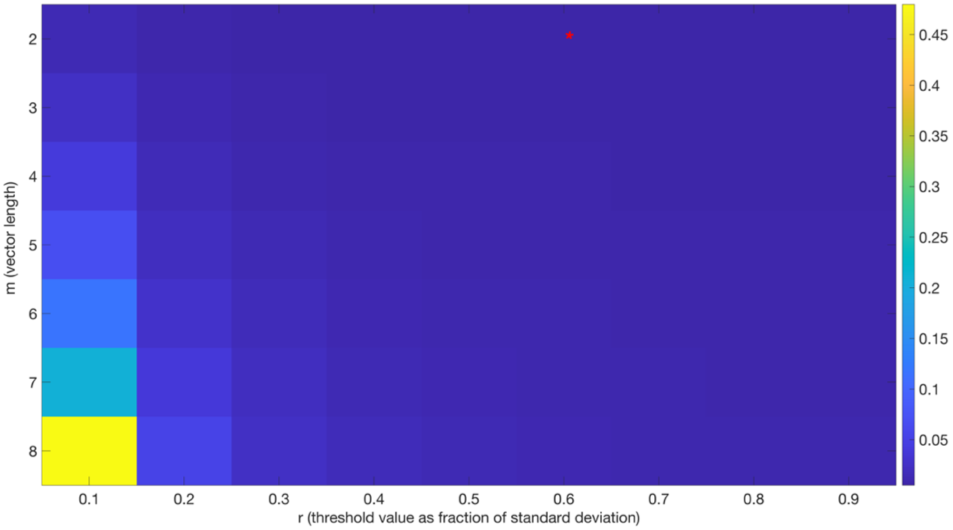

Figure 4.1 Conditional probability of sample entropy changing with *m* ($2 \le m \le 8$) and *r* ($0.1 \le r \le 0.9$). * on the heat map represents the optimal conditional probability with *m* = 2 and *r* = 0.6. *m*: vector length m, *r*: threshold value.

The SampEn estimates were computed for each scale τ, creating a profile of entropy values across scales. To compare the SampEn between and within groups, mean SampEn with $\tau = 3$ was calculated and averaged over all the 15 movement cycles for every participant in each fatigue condition (Rampichini et al., 2020). A higher SampEn value indicates lower regularity.

4.3.3.2 Frequency components

The continuous wavelet transform (CWT) scalogram of each forward and backward repetition was extracted by using CWT (MATLAB cwt function, Morlet wavelet family) from pre-processed EMG signals (Figure 4.2A). The CWT of a continuous signal *x(t)* is defined by the integral transform of x(t) with respect to the Morlet wavelet family (Ψ; equation 4), where $\Psi_{(\tau,s)}$ donates that wavelet coefficient at scale s and position τ. The minimum and maximum s are automatically established according to the distribution of energy of the wavelet across frequency and time.

$$\Psi_{\tau,s}(\mathrm{t}) = \int_{-\infty}^{\infty} x(t)\frac{1}{\sqrt{|s|}}\Psi^{*}\left(\frac{t-\tau}{s}\right)dt \qquad (4)$$

Instantaneous mean frequencies at each scale s were calculated based on the scalograms and then averaged to determine the mean frequency of each trial (Figure 4.2B). Then, to extract the major frequency, the high magnitude area on a CWT scalogram is identified. The CWT of each trial was first normalized and remapped into 101 points. The region with the highest power/magnitudes in forward and backward pointing phases was identified on the remapped scalograms (Figure 4.2C). These areas with higher magnitudes correspond to scales and times where the signal has significant components, indicating the presence of strong frequency components at specific time points. The corresponding frequency at which high-magnitude area occur is defined as major frequency (Graham et al., 2015). All data analyses were conducted through customized MATLAB scripts (version R2020b, MathWorks, Natick, USA).

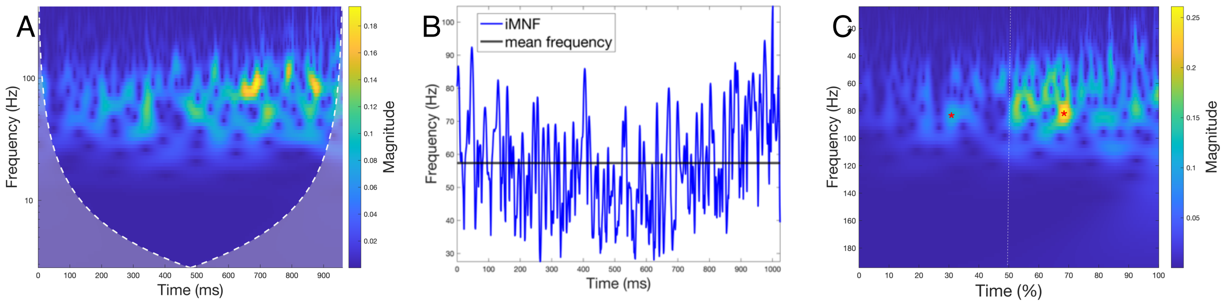

Figure 4.2 An example of detection of frequency components of a biceps brachii contraction during one pointing cycle. (A) a continuous wavelet transform scalogram. (B) Evolution of iMNF and mean frequency over time. (C) A remapped scalogram. * on Fig 2 (C) represents two major frequency components. The magnitude shows the intensity of frequencies in local time, with a higher value representing higher intensity. iMNF: instantaneous mean frequency.

4.3.4 Statistical analysis

Shapiro–Wilk test was used to assess the data for normal distribution. Generalized estimating equations were used to compare the measures between sexes before and after fatigue. In the case when the data was normally distributed, Identity link function was used in the model. Otherwise, Gamma log link was chosen. The significance level was set at $p < 0.05$. Pairwise comparisons with sequential Bonferroni tests were used to adjust for multiple comparisons (SPSS Statistics v24, IBM Corp., US). Hedges' g was calculated as effect size (Rosenthal, 1994).

4.4 Results

4.4.1 SampEn

In the forward phase of the RPT, significant main effects of fatigue were found on SampEn value of four muscles (UT: $\chi2 = 3.15$, $p = 0.04$, g = 0.18; AD: $\chi2 = 26.09$, $p < 0.001$, g = 0.78; BIC: $\chi2 = 3.24$, $p = 0.001$, g = 0.37; TRI: $\chi2 = 20.09$, $p < 0.001$, g = 0.58; Table 4.2). The SampEn value of four muscles significantly decreased after fatigue (UT: Mean difference (MD) = -0.03; AD: MD = -0.09; BIC: MD = -0.06; TRI: MD = -0.07). Significant main effects of sex were only found in

BIC ($\chi2$ = 4.36, p = 0.02, g = 0.68), where females showed greater SampEn value compared to males (MD = 0.09).

In the backward pointing phase, there were significant main effects of fatigue in AD ($\chi2$ = 43.14, $p < 0.001$, g = 0.71), BIC ($\chi2$ = 13.06, $p < 0.001$, g = 0.69), and TRI ($\chi2$ = 7.70, $p < 0.001$, g = 0.70), where SampEn values decreased after fatigue (AD: MD = -0.11; BIC: MD = -0.09; TRI: MD = -0.06). There were significant main sex effects in AD ($\chi2$ = 4.64, p = 0.04, g = 0.42) and BIC ($\chi2$ = 3.20, p = 0.03, g = 0.44). Males showed greater SampEn values of AD (MD = 0.05), but lower SampEn values of BIC (MD = -0.07) compared to females (Table 4.2).

Table 4.2 Comparison of SampEn (means ± SD) before and after fatigue in males and females.

Notes: NF: non-fatigue condition, FT: fatigue-terminal condition, UT: upper trapezius, AD: anterior deltoid, BIC: biceps brachii, TRI: triceps brachii, a significant difference was set at $p < 0.05$.

	males		females		*p* values		
	NF	FT	NF	FT	Fatigue effect	Sex effect	two-way interaction
Forward pointing							
UT	0.74 ± 0.17	0.71 ± 0.20	0.75 ± 0.15	0.74 ± 0.15	**0.04**	0.66	0.25
AD	0.87 ± 0.12	0.77 ± 0.13	0.81 ± 0.12	0.74 ± 0.08	**<0.001**	0.09	0.39
BIC	0.72 ± 0.21	0.67 ± 0.16	0.82 ± 0.11	0.75 ± 0.13	**0.001**	**0.02**	0.77
TRI	0.89 ± 0.15	0.83 ± 0.15	0.90 ± 0.78	0.82 ± 0.09	**<0.001**	0.89	0.46
Backward pointing							
UT	0.74 ± 0.15	0.70 ± 0.20	0.73 ± 0.15	0.73 ± 0.16	0.19	0.81	0.14
AD	0.89 ± 0.09	0.77 ± 0.12	0.83 ± 0.12	0.73 ± 0.10	**<0.001**	**0.04**	0.72
BIC	0.82 ± 0.16	0.72 ± 0.15	0.88 ± 0.08	0.79 ± 0.12	**<0.001**	**0.03**	0.60
TRI	0.91 ± 0.12	0.86 ± 0.13	0.92 ± 0.06	0.85 ± 0.09	**<0.001**	0.97	0.18

4.4.2 Mean frequency

There were no Sex × Fatigue interactions in any mean frequency measure in either forward or backward pointing phases. In the forward phase, significant main effects of fatigue were found on all four muscles (UT: $\chi2 = 9.44$, $p = 0.002$, g = 0.24; AD: $\chi2 = 61.21$, $p < 0.001$, g = 0.71; BIC: $\chi2 = 63.44$, $p < 0.001$, g = 0.50; TRI: $\chi2 = 117.65$, $p < 0.001$, g = 0.29), all showing decreases (UT: MD = -1.93; AD: MD = -6.86; BIC: MD = -6.34; TRI: MD = -5.32). Significant main effects of sex were only found on mean frequency of BIC ($\chi2 = 4.31$, $p = 0.04$, g = 0.45). with higher frequency in females (MD = 3.30; Figure 4.3A).

In the backward pointing phase, there were significant main effects of fatigue in UT ($\chi2 = 7.39$, $p = 0.007$, g = 0.17), AD ($\chi2 = 56.12$, $p < 0.001$, g = 0.85), BIC ($\chi2 = 50.46$, $p < 0.001$, g = 0.93), and TRI ($\chi2 = 110.16$, $p < 0.001$, g = 0.64), all showing decreases with fatigue (UT: MD = -2.10; AD: MD = -7.20; BIC: MD = -6.14; TRI = -4.57; Figure 4.3B). There were no significant differences between the sexes in any of these measures.

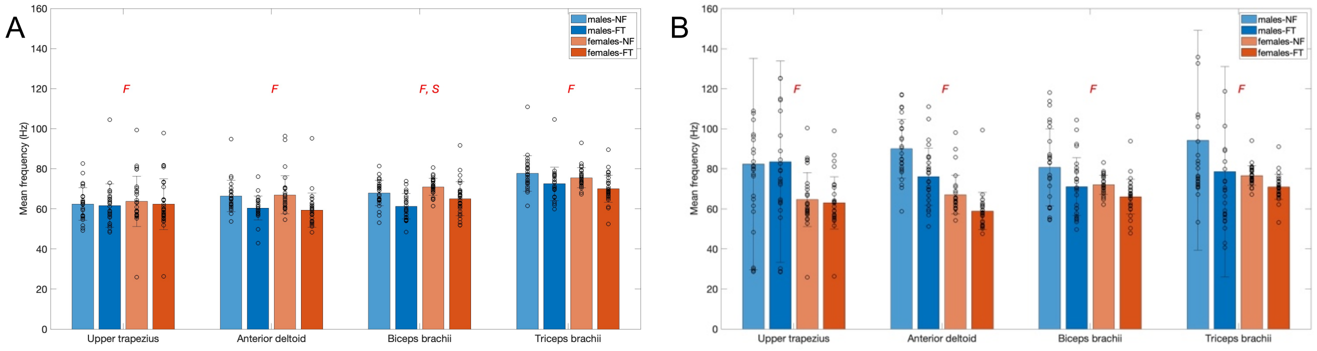

Figure 4.3 Mean frequency displayed as a function of sex and fatigue in (A) forward and (B) backward pointing phases. F: significant main effect of fatigue, S: significant main effect of sex ($p < 0.05$), NF: non-fatigue, FT: fatigue-terminal. Circular markers represent individual data points.

4.4.3 Major frequency

Similar trend of major frequency was observed in backward and forward point phases. There was no interaction or sex main effects in any of the four muscles during either forward or backward pointing phase. However, there were significant main effects of fatigue in AD, BIC, and TRI in both forward (AD: $\chi2 = 71.42$, $p < 0.001$, g = 0.73; BIC: $\chi2 = 13.89$, $p < 0.001$, g = 0.54; TRI: $\chi2 = 37.81$, $p < 0.001$, g = 0.33) and backward pointing phases (AD: $\chi2 = 50.90$, $p < 0.001$, g = 0.58; BIC: $\chi2 = 12.76$, $p < 0.001$, g = 0.49; TRI: $\chi2 = 41.74$, $p < 0.001$, g = 0.31), all showing decreases with fatigue (forward: AD: MD = -16.18; BIC: MD =-9.21; TRI: MD = -13.40; Figure 4.4A; backward: AD: MD = -15.54; BIC: MD =-8.52; TRI: MD = -12.50; Figure 4.4B).

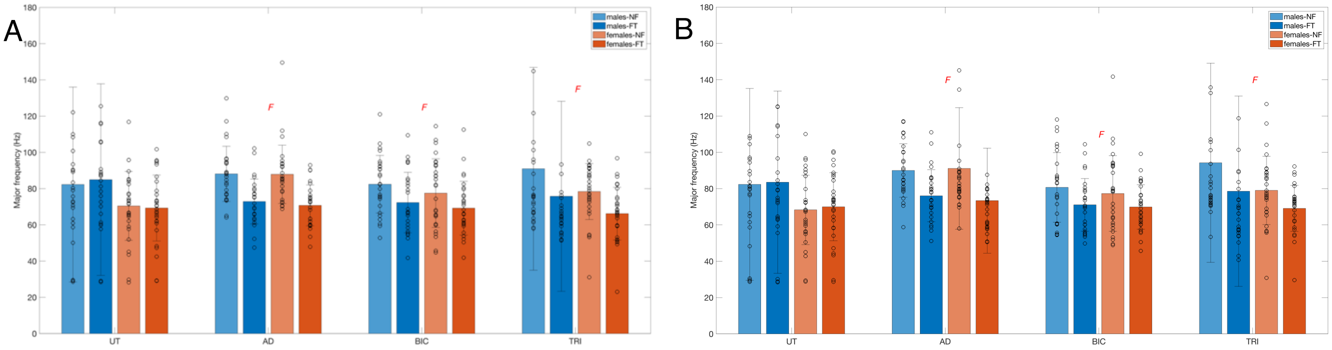

Figure 4.4 Major frequencies displayed as a function of sex and fatigue in (A) forward and (B) backward pointing phases. F: significant main effect of fatigue ($p < 0.05$), NF: non-fatigue, FT: fatigue-terminal. Circular markers represent individual data points.

4.5 Discussion

This study aimed to measure the sex-specific effects of fatigue on the time-frequency and complexity characteristics of EMG signals of upper limb muscles during a repetitive pointing task. The main findings of the study are: 1) overall, all four upper limb muscles displayed a decreased entropy and mean frequency with fatigue through the pointing cycle; 2) fatigue led to a decreased major frequency of anterior deltoid, biceps brachii, and triceps, but not upper trapezius, throughout the task; 3) females showed a higher mean frequency of biceps brachii compared to males during the forward pointing phase; 4) females showed a higher complexity of biceps brachii throughout the task and lower complexity of anterior deltoid, but only in backward pointing phase.

4.5.1 Fatigue effects on EMG characteristics

The repetitive pointing task requires the upper trapezius to work as the shoulder (scapulothoracic) stabilizer and the biceps brachii to work as the stabilizer for both shoulder (glenohumeral) and forearm in the forward direction (Renda et al., 2022). In frequency domain, we found that anterior deltoid, biceps brachii, triceps, and upper trapezius all displayed decreased mean frequency after the pointing task in both the forward and backward pointing phases. Although this has been shown previously, the current study is the first to apply the analysis of time-frequency transformation to obtain estimates of instantaneous muscle frequency in a dynamical upper-arm pointing task, whereas previous study only quantified spectral estimators using the traditional Fourier transform (Renda et al., 2022; Yoon et al., 2021). Using the same experimental protocol where fatigue was also induced by repetitive movements, Yoon et al. (2021) found a decreased median frequency of all upper arm and shoulder muscles of interest (i.e., upper trapezius, biceps brachii, and supraspinatus). Renda et al. (2022) found that when fatigue was induced using localized elbow fatigue efforts performed by individual joints until exhaustion instead of repetitive pointing task, the triceps, a prime mover of elbow movement in the pointing task, displayed a trend of decreased mean frequency, after localized elbow fatigue.

To gather further information, we extracted the major frequency from the wavelet scalograms. As part of our main findings, we found no difference in the major frequency of upper trapezius with fatigue. This may be explained by the functional role of upper trapezius in the repetitive pointing task. As a stabilizer of the neck/shoulder region, upper trapezius would be consistently activated throughout the fatiguing task in which the entire arm is kept moving in a horizontal plane at shoulder height, as opposed to the functional roles of all other muscles investigated, which all have a joint-moving component. Another possible explanation could be related to muscle fibre composition and related recruitment patterns of muscle fibres in upper trapezius (Lindman et al., 1991). During fatiguing contractions, at the beginning when fatigue is manifested early, the firing rate of signals sent to Type 2 fibres may slow down first, which would lead to a reduction in mean frequency. Type 2 muscle fibres usually operate at higher frequencies. As fatigue sets in, it is possible that more Type 1 muscle fibres in upper trapezius were recruited as they are more fatigue-resistant. Type 1 fibres generally operate at lower frequencies. As a result, the dominant frequency would decrease, which could explain why the major frequency in EMG did not shift much, even as overall fatigue causes the mean frequency to drop. However, these results could also be impacted by sources of error associated with our protocol. The electrode position of upper trapezius is another factor that may affect major frequency changes, as the position recommended by published guidelines for electrode placement may cover the innervation zone of upper trapezius (Farina et al., 2002c). With the progression of fatigue, we found lower major frequencies in the magnitude or power of the EMG signal of the other three upper limb muscles. Indeed, our results show that biceps brachii, triceps, and anterior deltoid showed significant decreases in major frequency after fatigue. This further confirms the downward shifts in the frequency domain occurring with fatigue. The mechanism behind this shift could be due to a reduction in conduction velocity and decreased action potential propagation (González-lzal et al., 2012). It has also been suggested that increased synchronization might contribute to the observed decrease in signal frequency, as the variance in the timing of action potentials across different motor units decreases (Keenan et al., 2005). However, the exact ways in which the increased synchronization of motor units may affect changes in EMG frequency and power spectrum are still poorly understood.

The present study showed that the repetitive multijoint arm motion-induced fatigue resulted in a significantly decreased SampEn and a loss in EMG complexity. From a physiological perspective, since healthy biological systems exhibit significantly greater complexity than those that are compromised, lower entropy values usually indicate a lower systematic movement variability and a state of dysfunction (Rampichini et al., 2020). The temporal and spectral profiles of EMG depend on the motor unit recruitment and discharge rate, and previous studies have used the complexity approach to assess changes in EMG with pathology and with aging (Kang & Dingwell, 2016; Sung et al., 2007). For instance, it has been shown that although the spectral characteristics of EMG remained similar between groups with chronic low-back pain and healthy controls, the complexity of EMG signals of erector spinae was lower in individuals with low-back pain (Sung et al., 2007). Fatigue is another physiological process that can lead to adaptation in patterns of motor unit recruitment and discharge and in complexity patterns of the EMG signals. Cashaback et al. (2013) found that fatigue reduced the complexity of biceps brachii activity during isometric contraction by using multiscale sample entropy. By using metrics calculated based on a single time scale (i.e., root-mean-square), Srinivasan et al. (2021) only found significant fatigue effects on root-mean-square cycle-to-cycle standard deviation in upper trapezius, anterior deltoid, and biceps brachii, and root-mean-square cycle-to-cycle coefficients of variation in upper trapezius and anterior deltoid during forward pointing phase. However, using the same experimental protocol as Srinivasan et al. (2021), this current study found reduced complexity in all four muscles, including triceps, during forward pointing phase. The difference may be due to the nature of biological signals, as a previous study has shown a nonlinear relationship between EMG amplitude and excitation (Keenan et al., 2005). Our findings add to the evidence that complexity measures may be able to reveal subtle EMG changes with MMF compared to traditional linear metrics (Cashaback et al., 2013).

4.5.2 Sex differences and similarities in EMG characteristics

The current study is also the first one to include the analysis of the backward pointing phase of the repetitive pointing task in any frequency analysis. Despite the several similarities between forward and backward phases of the task, there were some differences. Females displayed higher mean frequency and complexity of biceps brachii compared to males in the forward pointing phase; in the backward pointing phase, females showed a lower complexity of anterior deltoid and higher complexity of biceps brachii compared to males. The addition of the backward phase to our analysis further reinforces the important role of the biceps brachii and anterior deltoid in explaining sex differences during repetitive arm tasks. In frequency domain, we found that females displayed a higher mean frequency of biceps brachii compared to males, regardless of fatigue. Males and females have different muscle fibre characteristics, as it has been previously reported that females have a smaller fibre cross-sectional area of biceps brachii than males (Lindman et al., 1991; Miller et al., 1993). Generally, males have larger muscle mass and larger cross-sectional area in the biceps brachii, which affects the force generation and mean power frequency of the biceps brachii. This could suggest higher motor unit firing rates due to higher relative effort of biceps brachii in females. Chen et al. (2024) found that the activation of upper limb muscles showed a trend of earlier activation in females compared to males during the same repetitive pointing task. The sex differences in activation timing and power spectrum could reflect a different strategy based on differences in force production capacity. Different from our results, Yoon et al. (2021) found that males and females displayed similar median power frequency of biceps brachii, while males showed more biceps brachii swelling after a fatiguing repetitive forward reaching task, suggesting that hemodynamic factors could explain the sex-specific mechanisms in fatigue responses in biceps brachii. However, this current study did not find any differences in fatigue-related changes of power spectrum in upper limb muscles between sexes. Given the prominent sex differences in muscle size and strength of biceps brachii, it is possible that the predominant role of anthropometry of biceps brachii may in large part explain the sex differences in upper limb control.

Main effects of sex were found in the complexity of muscle activities of biceps brachii and anterior deltoid. We observed a higher complexity of biceps brachii activity in females during both forward and backward pointing, suggesting females may use a biceps-based control strategy during repetitive upper limb motions. However, a lower complexity of anterior deltoid activity was found in females and limited to backward pointing phase. One of the explanations associated to the lower EMG complexity is the less activated motor units and the lower level of motor unit short-term synchronization (Farina et al., 2002c; Kang & Dingwell, 2016), causing females' insufficient relative effort of anterior deltoid when it functions as shoulder agonist during backward pointing. As a result, the anterior deltoid may be less vulnerable to external perturbation, which could be associated to the higher incidence rates of neck/shoulder WMSDs in females. Previous results have shown different muscle activation strategies in how males and females respond to repetitive multijoint arm motion-induced fatigue in a single time scale. Females showed a higher increase in biceps brachii EMG amplitude cycle-to-cycle variability and a lower increase in anterior deltoid EMG amplitude cycle-to-cycle variability compared to males with fatigue (Srinivasan et al., 2016). Males might use a "shoulder-based" strategy to stabilize the repetitive pointing task before fatigue; with the development of fatigue, however, females might adopt an "elbow-based" strategy to mitigate fatigue (Renda et al., 2022; Srinivasan et al., 2016). Moreover, basic sex differences in strength, segment weight (anthropometric load), and skinfold thickness have also been proposed to affect the sex-specificity in the muscle activity with fatigue (Hunter et al., 2004; Otto et al., 2018; Slopecki et al., 2020). However, those fatigue-related changes were not observed in the complexity of upper limb muscle activation. This suggests that complexity analysis could be a better way of assessing muscle activity compared to linear analysis (Farina et al., 2002b).

4.5.3 Limitations

Surface electrodes having a diameter of 10 mm and inter-electrode distance of 30 mm may introduce spatial filtering and low frequency dips in the power spectrum (Merletti & Muceli, 2019), making our results less comparable with those of other authors using different electrode geometries. There are a few other limitations caused by dynamic muscle contractions that may not be completely attenuated by the CWT approach and entropy estimates. Firstly, the sliding of the innervation zone under the electrodes can cause changes in spectral and amplitude EMG features. Specifically, the placement of the electrodes on the upper trapezius may have covered the innervation zone, which could partly explain the lack of sex differences in this muscle (Barbero et al., 2012; Farina et al., 2002c). Secondly, the absolute values of spectral features are difficult to compare between subjects or groups because they depend on the thickness of subcutaneous layers and body fat. Some other metrics and approaches can also be considered in future work. As an alternative to the Morlet wavelets, intensity analysis using Cauchy wavelets, which provide discrete frequency information, gains popularity in EMG processing (Beck et al., 2008). Additionally, alternative measures, such as quantifying spectral features through pattern recognition approaches, can be considered in the future (Graham et al., 2015).

4.6 Conclusions

For the first time, our study compared the sex-specific effects of fatigue on the time-frequency and complexity characteristics of muscular activities of upper limb muscles during a repetitive upper limb task. Overall, upper limb muscles displayed a decreased complexity and mean frequency in response to repetitive motion-induced upper limb fatigue. Females showed higher mean frequency and complexity of biceps brachii muscle activities, and lower complexity of anterior deltoid muscular activities regardless of fatigue. These sex-specificities may support a compensation strategy, such that males might adopt a “shoulder-based” strategy, and females might use an “elbow-based” strategy with fatigue. Our findings add to the growing evidence that entropy and mean frequency measures are capable of capturing subtle EMG changes with MMF compared to traditional linear metrics. Fatigue and sex effects were not significant in major frequency of upper trapezius (i.e., frequency component of the region with the highest power on the wavelet scalogram). However, which linear or nonlinear descriptors demonstrate the greatest sensitivity and robustness for characterizing MMF is still a critical question and needs further investigation. Studies using different surface EMG electrode positionings and EMG descriptors should be considered to make our findings more comparable.

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4.8 Author contribution statement

Yiyang Chen: Conceptualization, Methodology, Software, Validation, Formal analysis, Data curation, Writing – original draft, Visualization, Project administration. Di Kang: Conceptualization, Methodology, Validation, Formal analysis, Data curation, Writing – review &

editing. Julie N. Côté: Conceptualization, Methodology, Validation, Resources, Writing – review & editing, Supervision, Funding acquisition.

4.9 Declarations

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Bridge between Chapter 3, 4 and 5

Sex-specific fatigue changes observed in the complexity and frequency components of biceps brachii and anterior deltoid muscle activities in Chapter 4 align with the sex differences found in these two major upper limb muscles in Chapter 3. Together, the findings from the previous two chapters suggest that the predominant role of anthropometry of upper limb muscles may explain the sex differences in upper limb control, as biceps brachii and anterior deltoid show the most prominent sex difference in muscle size and mechanical output. This led to a research question of whether the predominant role of anthropometry in explaining sex-specific fatigue changes observed in upper limb tasks would be supported by findings on a lower limb task.

Running is one of the most widespread activities during which repetitive strides may induce fatigue, with the potential to cause lower limb running-related overuse injuries. Therefore, to answer the research question, we chose running as a model to study fatigue-related lower limb motions in Chapter 5. An inertial measurement unit motion capture system was used to record lower limb kinematics during running. We know that the pelvis, hip, and knee joints are the joints that show the biggest sex differences in lower limb joint structure. In addition, the ankle joint plays an important role in attenuating high-impact ground reaction forces during running-induced loading. Therefore, motion of these four lower limb joints was analyzed in Chapter 5. Pelvis, hip, knee, and ankle joint angles were calculated during different phases of the gait cycle, and continuous relative phase and its variability of Pelvis-Hip, Hip-Knee, and Knee-Ankle joint pairs were further computed to assess inter-joint coordination and coordination variability. Mean absolute relative phase was calculated to represent coordination amplitude, and deviation phase was calculated as the cycle-to-cycle coordination variability.

Chapter 5: Sex-specific effects of fatigue on lower limb coordination and coordination variability in highly trained endurance runners

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Chapter 5 is a copy of the manuscript being prepared for submission to the *Journal of Sports Sciences.*

5.1 Abstract

This study aimed to compare the fatigue adaptations of lower limb coordination and its variability between highly trained endurance male and female runners using continuous relative phase (CRP) analysis. Thirty-two right-footed endurance runners (16 females; weekly running volume ≥ 40 km) performed an incremental running task on a treadmill until volitional exhaustion on a Borg CR (6–20) scale. The participants ran at 10 km/h for 30 seconds at the beginning and after the fatiguing running task, defined as pre-fatigue and post-fatigue conditions, while lower limb joint kinematics were recorded. CRP analysis based on Hilbert transform was used to quantify coordination amplitude and its variability for sagittal plane Pelvis-Hip, Hip-Knee and Knee-Ankle couplings. After fatigue, females showed significantly lower Hip-Pelvis coordination amplitude by 41% to 56% during all gait phases and higher Hip-Pelvis coordination variability by 25% during loading stance phase compared to males. Ankle-Knee coordination amplitude significantly decreased by 21% during both loading stance and midstance phases after fatigue in both sexes. Ankle-Knee coordination variability significantly increased by 26% during loading stance phase after fatigue in both sexes. Overall, after fatigue, sex differences were only observed in the coordination of proximal joints (pelvis-hip), with a more in-phase coordination pattern in females. Results can help better understand sex-specific mechanisms of running-related injuries.

Keywords

Running, Sex difference, Fatigue, Coordination, Variability, Continuous relative phase

5.2 Introduction

Running is a popular and accessible sporting task across one’s lifespan. Along with the benefits of this exercise comes a high incidence of lower extremity running-related injuries (RRIs) ranging between 19.4% and 79.3% (Kluitenberg et al., 2015; van Gent et al., 2007). The localization and types of RRIs have been suggested to differ between sexes (Hollander et al., 2021). A higher risk of bone stress injuries is typically found in female runners, while male runners typically show a higher risk for Achilles tendon injuries (Hollander et al., 2021). These different RRI profiles may be attributed to sex-specific risk factors for RRIs. Indeed, it has been reported that factors such as age, previous sports activity, and weekly running distance (48 to 62 km) were associated with a greater risk of RRIs in females than in males, whereas a history of injury and running for more than 62 km could contribute to the greater risk of RRIs in male than female runners (van der Worp et al., 2015). Therefore, incorporating sex differences in studying running mechanics is needed to clarify the risk profiles of RRIs for both sexes.

Fatigue is another risk factor linked to the RRIs. Within RRIs, 70% to 80% of running disorders are due to overuse during endurance running (Hreljac, 2004; Lopes et al., 2012), where the body is repetitively exposed to the loading forces over many strides. These accumulated forces may cause abnormal hip and knee joint kinematics, greater gluteal muscle activation, and greater retropatellar stress, resulting in the development of fatigue-related overuse injuries such as tibial fatigue fracture, patellofemoral pain, and iliotibial band syndrome (Bertelsen et al., 2017; Sheerin et al., 2019; Willson et al., 2012). Changes in running biomechanics with fatigue include increased stance time, knee flexion at initial contact, maximum knee flexion during swing, and rearfoot excursion (Dierks et al., 2010; Möhler et al., 2021; Zandbergen et al., 2023).

Besides the assessment of single joint or segment metrics, the assessment of coordination patterns of lower limbs may reveal more complex information on how runners adapt to fatigue. From the perspective of dynamical systems, the body's different degrees of freedom (DoFs) need to be coordinated and integrated into synergistic relations to maintain task performance in response to environmental constraints, such as fatigue. Coordination involves bringing the multiple DoFs at each level into proper relations, and its variability reflects the range of interactions between the DoFs of the body (Robertson et al., 2013). Similar to single-joint kinematics, patterns of inter-joint coordination and its variability change with running-induced fatigue. After a fatiguing run, Bailey et al. (2020) found that recreational runners with low perceived fatigue showed higher coordination variability of Knee (flexion/extension)-Foot (inversion/eversion) coupling at toe-off compared to runners with high perceived fatigue. After a fatiguing half marathon, Chen et al. (2022) reported that recreational runners maintained stable lower limb coordination variabilities in the sagittal plane while increased coordination variabilities in the frontal plane during the early stance phase. In contrast, increases in both coordination amplitude and coordination variability have been found in the sagittal plane for the Pelvis-Hip joint pair in asymptomatic college students after a fatiguing running task (Khaleghi Tazji et al., 2023). In addition, compared to recreational runners, experienced endurance runners exhibited a more in-phase sagittal plane Pelvis-Thigh and Knee-Ankle coupling and a more variable sagittal plane Hip-Knee and Shank-Foot coordination pattern after fatigue (Mo & Chow, 2019). Finally, associations between altered coordination patterns with fatigue and overuse RRIs have previously been observed (Miller et al., 2008). In summary, indicators of increased lower limb coordination variability have been found after fatiguing running, although controversy remains about which joint pairs and planes of motion these changes seem to affect the most.

Previous studies have also shown some sex differences in how runners adapt to fatigue. To optimize shock attenuation, male recreational runners have been shown to decrease plantar flexion at toe-off when fatigued compared to female runners. These changes may lead to higher peak propulsive forces during shock absorption but may also be associated with the higher prevalence of patellar tendinopathy in males (Bazuelo-Ruiz et al., 2018). However, to our knowledge, no previous studies have compared males to females' changes in running coordination patterns with fatigue. Given the different RRIs profiles between sexes, it is conceivable that males and females perform unique changes in coordination patterns in response to fatigue, and that clarifying this issue could help better understand the origin of sex differences in RRIs.

The aim of the current study was to compare the fatigue adaptations of lower limb coordination and its variability between highly trained endurance male and female runners. We hypothesized that (1) fatigue would lead to an increased coordination variability of lower limb couplings during the loading phases (Mo & Chow, 2019) and (2) male and female runners would display unique variability patterns at different coupling levels (e.g., Pelvis-Hip or Knee-Ankle couplings; Hannigan & Chou, 2019).

5.3 Methods

5.3.1 Participants

Thirty-two highly trained endurance runners (16 females; effect size = 0.26, power = 0.8) who had a minimum weekly running volume of 40 km and were competing in events of mid- to long-distance running for at least three consecutive years participated in this study. The participant self-declared their training profiles. All the participants self-reported being right-footed. The exclusion criteria were a self-reported history of musculoskeletal injury in the year preceding the study, a history of neurological disease, or a history or current use of doping substances listed on the banned substances list of the Canadian Centre for Ethics in Sport. Females on oral contraceptives were tested during the placebo pill week to minimize the possibility of hormonal differences within the female group and between sexes. Eumenorrheic participants with a menstrual cycle length between 21 to 35 days participated in this study during the early follicular phase (days 1–5) when estrogen and progesterone levels were low (McNulty et al., 2020). Females using an intrauterine device were included if eumenorrheic. The menstrual function and use of contraceptives questionnaire were administered before the study. Written informed consent was given to the participant prior to participation. The research protocol was approved by the ethics committee of the Faculty of Medicine and Health Science at McGill University (A00-M35-21B/21-05-055).

5.3.2 Data acquisition

Anthropometric data were collected upon arrival (i.e., body weight, height, leg length). Leg length was measured from the anterior superior iliac spine to the medial malleolus using a measuring tape. The participant performed a five- to seven-minute warm-up on the treadmill at a self-selected speed (Trackmaster, model number: TMX428CP 220, Newton, Kansas, USA). The fatigue protocol required that the participant start running at 10 km/h, followed by a 1 km/h speed increase every 2 minutes. The participant ran at 10 km/h for 30 seconds at the beginning of the fatigue protocol, defined as pre-fatigue condition. The speed increased until the participant reached their maximal exertion during the incremental run. After the fatigue protocol, the participant ran at 10 km/h for another 30 seconds, defined as post-fatigue condition. The participant reported their rate of perceived exertion (RPE) in both pre-fatigue and post-fatigue conditions. The time between the end of the fatigue protocol and the start of the post-fatigue session was 54 ± 25 seconds in males and 53 ± 22 seconds in females (no significant sex difference).

Lower limb kinematic data were acquired at 128 Hz using inertial measurement units (IMUs; Opals, APDM Inc., Portland, OR, USA) within APDM Moveo Explorer system. Before the warm-up, seven IMUs were placed on the main landmarks of the pelvis (Lumbar vertebrae 4–5; at the height of the anterior superior iliac spine), bilateral thighs (middle lateral thigh; 50% of the length between knee and hip joints) and shanks (on the flat surface of the tibia, below and close to the knee joint), and feet (front upper part of the foot over the distal end of the third and fourth metatarsal bones), and reinforced with APDM straps, tapes and Coban wraps. A 3-second static N-pose calibration was performed before the start of data collection.

5.3.3 Data analysis

Sensor fusion for obtaining the orientation data, time syncing, and data interpolation for missing entries was pre-processed and embedded onboard within ADPM IMU system. Pre-processed data were exported and read in MATLAB (R2020b, The MathWorks, Natick, USA) and filtered using a 4th-order lowpass Butterworth filter with a cutoff frequency of 6 Hz. The local minima method was used to detect initial contact and toe-off using the anteroposterior acceleration obtained from the foot-mounted IMU (Chew et al., 2018). Stance and swing phase and subphases of stance (i.e., loading stance, midstance, terminal stance, and pre-swing phases) were identified based on the detected gait events (Mo & Chow, 2019). Approximately 40 strides were obtained per fatigue condition. The joint angles of the pelvis, hip, knee, and ankle were calculated using OpenSense workflow (4.4, Sim TK; Al Borno et al., 2022). Pre-processed IMU data were converted into OpenSim's file format in Python. IMU data were calibrated to the Rajagopal et al. (2016) OpenSim model to find the initial orientations of the IMU frames relative to the OpenSim body segments (Rajagopal et al., 2016). Joint angles were estimated using inverse kinematics in OpenSense based on the IMU orientation data. Mean pelvis, hip, knee, and ankle joint angles of the right leg in the sagittal plane were calculated for each running phase.

Continuous relative phase (CRP) analysis was used to quantify coordination and coordination variability for the Hip-Pelvis, knee-Hip and Ankle-Knee joint pairs. The first and the last running gait cycles of each 30s recording served as data pads to help control edge effects associated with the CRP approach (Ippersiel et al., 2019). Phase angles for the pelvis, hip, knee, and ankle joints were determined using the Hilbert-transform method. Data pads were removed afterwards. CRP values were time-normalized to 101 frames and calculated as the absolute point-by-point difference between phase angles of two adjacent joints for each stride of each fatigue condition, resulting in n CRP curves per condition (n × 101 frames). CRP values greater than 180 were subtracted from 360 to adjust for discontinuities in data, resulting in CRP values ranging between 0 and 180. The CRP value of 0 represents fully in-phase coupling, while 180 represent fully out-of-phase coupling (Hamill et al., 1999). CRP curves of Hip-Pelvis, knee-Hip and Ankle-Knee joint pairs were partitioned into stance and swing phase and the subphases of stance. Mean absolute relative phase (MARP) and deviation phase (DP) were calculated as mean and standard deviation of n CRP curves for each running gait phase and joint pair before and after fatigue. MARP quantifies coordination amplitude, and DP represents the within-individual coordination variability.

5.3.4 Statistical analysis

Independent samples *t-tests* were used to compare the descriptive data of the participants between sexes. Shapiro–Wilk tests were used to verify the normality of data. Generalized estimating equations (GEE) were used to compare the MARP and DP of each joint pair and the mean angles of lower limb joints between sexes (between-subject factor, male/female) and with fatigue (within-subject factor, before/after). If data was normally distributed, Identity link function was used in the GEE model. Otherwise, Gamma log link was chosen. The significance level was set at $p < 0.05$. Pairwise comparisons with sequential Bonferroni tests were used to adjust for multiple comparisons (SPSS Statistics v24, IBM Corp., USA). Hedges' g was calculated to measure effect size for the reported significant effects.

5.4 Results

5.4.1 Group characteristics

Descriptive statistics are displayed in Table 5.1. There were significant differences in body height ($p = 0.001$), leg length ($p = 0.04$), weight ($p < 0.001$), 5 km personal best ($p < 0.001$), and 10 km personal best ($p < 0.001$) between female and male participants. There were significant main effects of fatigue ($p < 0.001$), but no significant main effects of sex in RPE pre-and post-fatigue ($p = 0.10$; Table 5.1).

Table 5.1 Descriptive characteristics of the participants. Mean ± standard deviation.

	Males	Females
Height (cm)	177.1 ± 7.0	168.4 ± 5.9*
Leg length (cm)	94.4 ± 4.0	90.5 ± 6.3*
Weight (kg)	70.0 ± 5.8	60.2 ± 6.7*
Age (y)	30 ± 7	32 ± 7
5 km personal best (minutes)	17.77 ± 1.82	21.75 ± 1.86*
10 km personal best (minutes)	37.42 ± 3.78	45.90 ± 3.16*
Weekly training sessions	5.5 ± 1.7	6.1 ± 3.2
Weekly running distance (km)	68.0 ± 30.1	59.0 ± 25.7
Endurance time of the fatigue protocol (minutes)	22.98 ± 2.68	18.42 ± 1.62
RPE in the pre-fatigue condition	8.5 ± 1.6	9.3 ± 1.6
RPE at the end of the fatigue protocol	18.4 ± 1.8	18.9 ± 1.1
RPE in the post-fatigue condition	12.1 ± 2.0	12.6 ± 2.0

Notes: * represents significant sex difference ($p < 0.05$).

5.4.2 Joint angles

There was a significant Sex × Fatigue interaction effect on the mean pelvis tilt joint angle during swing (χ^2= 4.10, p = 0.04; Table 5.2). After fatigue, females showed significantly higher mean pelvis tilt during swing phase compared to males (more anterior pelvis tilt; MD = 3.37, g = 0.71). Significant main effects of fatigue were found on mean hip flexion angles during pre-swing phase (χ^2= 4.57, p = 0.03). The mean hip flexion angle was significantly decreased after fatigue in both sexes during pre-swing (more hip extension; MD = -9.22, g = 0.34).

Table 5.2 Comparison of mean joint angles (means ± SD) before and after fatigue in male and female runners.

		Males		Females		*p* values		
		NF	FT	NF	FT	Fatigue effect	Sex effect	Interaction
Pelvis tilt	Loading stance	-0.57 ± 2.20	-1.64 ± 4.54	0.32 ± 4.51	-0.25 ± 3.86	0.65	0.16	0.55
	Midstance	0..32 ± 2.77	-0.95 ± 3.41	-0.26 ± 3.39	-0.17 ± 4.72	0.59	0.88	0.46
	Terminal stance	0.48 ± 4.08	-0.64 ± 4.13	-0.10 ± 3.41	0.33 ± 3.27	0.92	0.72	0.25
	Pre-swing	0.19 ± 3.63	-1.55 ± 5.07	-0.74 ± 2.97	0.32 ± 2.87	0.79	0.55	0.12
	Swing	0.32 ± 3.83	-2.45 ± 3.64	-0.25 ± 2.48	0.33 ± 4.20	0.28	0.22	**0.04**
Hip flexion	Loading stance	13.52 ± 17.45	13.75 ± 16.35	13.60 ± 11.98	8.66 ± 16.47	0.50	0.55	0.46
	Midstance	13.20 ± 20.46	13.48 ± 15.54	11.06± 16.93	4.37 ± 18.88	0.34	0.18	0.31
	Terminal stance	13.33 ± 21.80	8.93 ± 16.99	9.12 ± 14.38	0.15 ± 22.00	0.26	0.09	0.54
	Pre-swing	12.51 ± 19.99	3.92 ± 17.17	10.28 ± 18.62	-0.36 ± 23.60	**0.03**	0.64	0.89
	swing	11.90 ± 11.29	6.31 ± 12.00	9.94 ± 10.65	9.31 ± 12.17	0.91	0.26	0.31
Knee flexion	Loading stance	37.06 ± 25.06	40.19 ± 27.24	35.28 ± 23.11	24.39 ± 20.05	0.22	0.41	0.14
	Midstance	38.20 ± 23.57	27.92 ± 25.72	29.01 ± 18.73	28.14 ± 24.14	0.53	0.24	0.35
	Terminal stance	37.77 ± 17.67	26.78 ± 14.06	28.42 ± 22.10	26.45 ± 17.00	0.35	0.13	0.32
	Pre-swing	36.93 ± 22.85	28.29 ± 21.15	33.99 ± 29.52	27.46 ± 19.23	0.72	0.27	0.87
	Swing	38.87 ± 14.81	34.88 ± 14.53	29.43 ± 13.72	36.66 ± 13.85	0.42	0.68	0.09
Ankle dorsiflexion	Loading stance	-17.76 ± 37.90	-3.08 ± 25.28	-3.98 ± 22.68	-2.96 ± 27.54	0.34	0.29	0.36
	Midstance	-10.00 ± 31.55	-1.82 ± 20.97	-0.83 ± 19.80	-5.28 ± 30.34	0.68	0.77	0.14
	Terminal stance	0.34 ± 36.66	-3.14 ± 20.44	2.58 ± 29.12	-11.32 ± 28.06	0.77	0.14	0.35
	Pre-swing	-2.46 ± 41.94	-7.29 ± 27.82	2.02 ± 32.10	-21.84 ± 20.47	0.49	0.09	0.25
	Swing	-9.46 ± 32.87	-15.90 ± 21.29	-14.44 ± 18.50	-11.24 ± 11.18	0.89	0.90	0.22

Notes: NF: non-fatigue, FT: fatigue-terminal, a significant difference was set at $p < 0.05$.

5.4.3 Mean absolute relative phase (MARP)

For the Hip-Pelvis joint pair, there were significant Sex × Fatigue interaction effects on MARP during all gait phases (loading stance: χ^2= 5.09, p = 0.02; midstance: χ^2= 5.26, p = 0.02; terminal stance: χ^2= 6.35, p = 0.01; pre-swing: χ^2= 6.37, p = 0.01; swing: χ^2= 5.34, p = 0.02; Figure 5.1). In males, there was a significant increase in MARP of Hip-Pelvis coupling after fatigue for all gait phases (loading stance: MD = 24.57, g = 0.58; midstance: MD = 25.07, g = 0.33; terminal stance: MD = 25.57, g = 0.68; pre-swing: MD = 27.54, g = 0.77; swing: MD = 24.21, g = 0.69). After fatigue, females showed significantly lower MARP during all gait phases compared to males (loading stance: MD = -37.62, g = 0.95; midstance: MD = -34.18, g = 0.90; terminal stance: MD = -35.99, g = 0.88; pre-swing: MD = -36.64, g = 0.98; swing: MD = 26.23, g = 0.97).

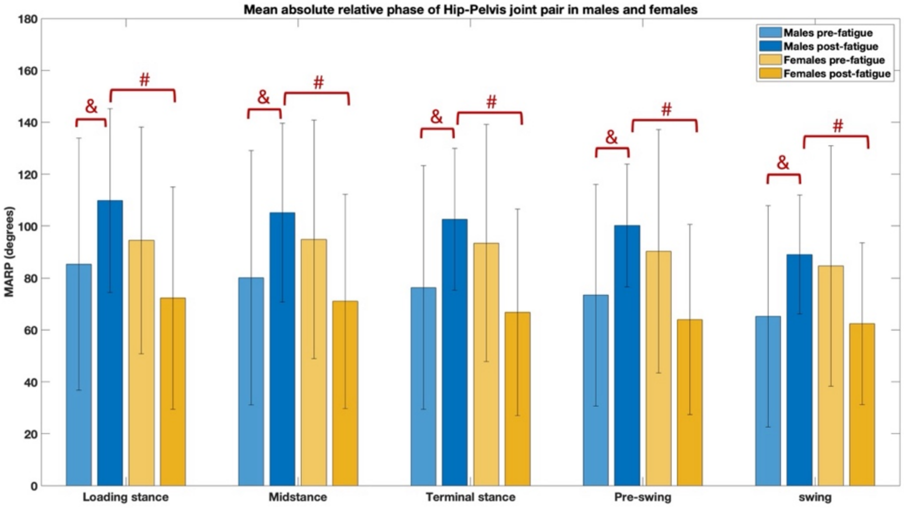

Figure 5.1 Mean absolute relative phase (MARP) of the Hip-Pelvis joint pair in males and females at different phases of the running cycle. Error bars represent the standard deviation of all MARP of each condition (the four conditions indicated in figure legend) at different phases of the running cycle. Significant interaction effects were found for all gait phases. &: significant difference between non-fatigue and fatigue-terminal conditions in males ($p < 0.05$). #: significant difference between males and females in fatigue-terminal condition ($p < 0.05$).

For the Knee-Hip joint pair, there were no significant Sex × Fatigue interaction effects on MARP during any gait phases (loading stance: $p = 0.80$; midstance: $p = 0.72$; terminal stance: $p = 0.60$; pre-swing: $p = 0.58$; swing: $p = 0.53$). There were no significant main effects of fatigue (loading stance: $p = 0.17$; midstance: $p = 0.24$; terminal stance: $p = 0.35$; pre-swing: $p = 0.24$; swing: $p = 0.48$) or main effects of sex (loading stance: $p = 0.92$; midstance: $p = 0.53$; terminal stance: $p = 0.37$; pre-swing: $p = 0.37$; swing: $p = 0.40$) during any gait phases.

For the Ankle-Knee joint pair, there were no significant Sex × Fatigue interaction effects on MARP during any gait phases (loading stance: $p = 0.07$; midstance: $p = 0.16$; terminal stance: $p = 0.20$; pre-swing: $p = 0.20$; swing: $p = 0.78$). Significant main effects of fatigue were observed during loading stance ($\chi^2= 4.60$, $p = 0.03$) and midstance ($\chi^2= 4.06$; $p = 0.04$; Figure 5.2). The MARP of Ankle-Knee coupling decreased significantly after fatigue during loading stance (MD = -22.83, g = 0.55) and midstance (MD = -21.66, g = 0.55).

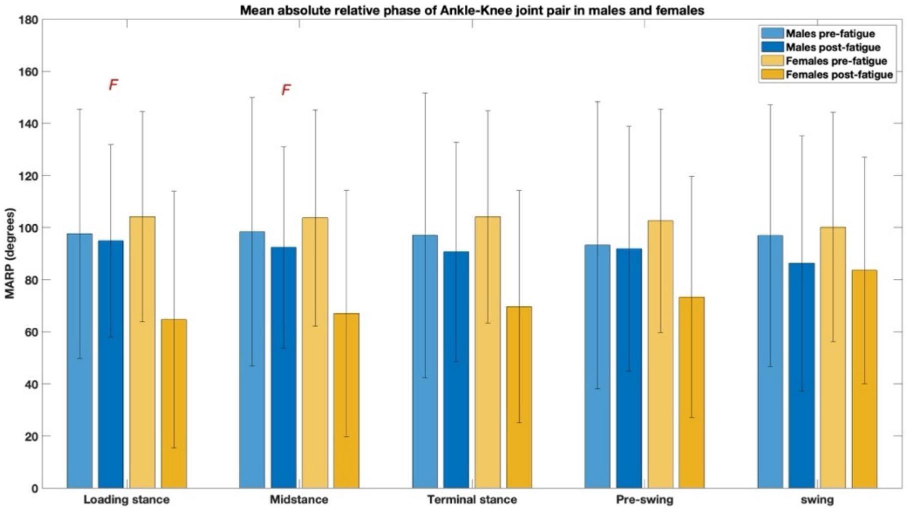

Figure 5.2 Mean absolute relative phase (MARP) of the Ankle-Knee joint pair before and after fatigue in males and females at different phases of the running cycle. Error bars represent the standard deviation of all MARP of each condition (the four conditions indicated in figure legend) at different phases of the running cycle. F: significant main effects of fatigue ($p < 0.05$).

5.4.4 Deviation phase (DP)

For the Hip-Pelvis joint pair, there was a significant Sex × Fatigue interaction effect on DP during loading stance (χ^2= 5.44, p = 0.02; Figure 5.3). After fatigue, females showed significantly higher DP of the Hip-Pelvis joint pair during that phase compared to males (MD = 7.76, g = 0.88). There were no significant main effects of fatigue (loading stance: p = 0.70; midstance: p = 0.61; terminal stance: p = 0.98; pre-swing: p = 0.91; swing: p = 0.81) or main effects of sex (loading stance: p = 0.43; midstance: p = 0.37; terminal stance: p = 0.68; pre-swing: p = 0.99; swing: p = 0.58) on DP during any gait phases.

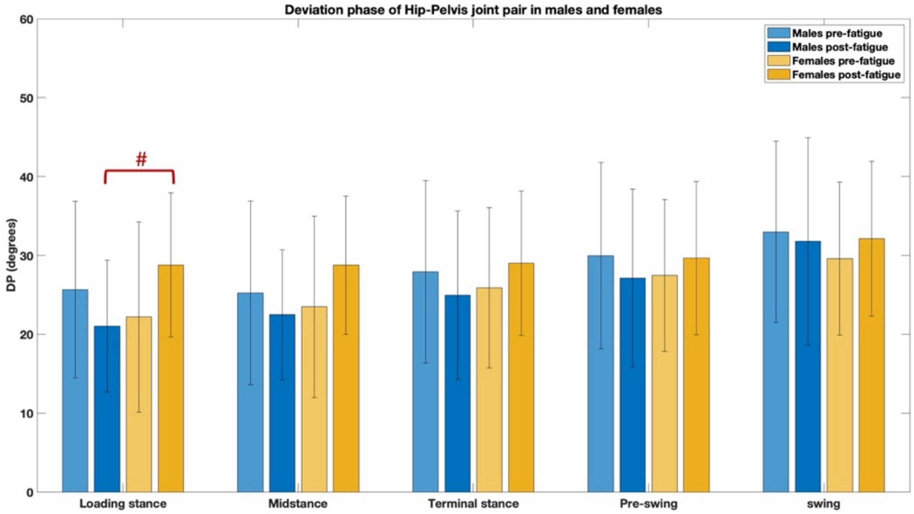

Figure 5.3 Deviation phase (DP) of the Hip-Pelvis joint pair before and after fatigue in males and females at different phases of the running cycle. Significant interaction effect was found during loading stance phase. Error bars represent the standard deviation of all DP of each condition (the four conditions indicated in figure legend) at different phases of the running cycle. #: significant difference between males and females in fatigue-terminal condition ($p < 0.05$).

For the Knee-Hip joint pair, there were no significant Sex × Fatigue interaction effects on DP during any gait phases (loading stance: p = 0.97; midstance: p = 0.76; terminal stance: p = 0.66; pre-swing: p = 0.55; swing: p = 0.32). There were no significant main effects of fatigue (loading stance: $p = 0.67$; midstance: $p = 0.82$; terminal stance: $p = 0.62$; pre-swing: $p = 0.32$; swing: $p = 0.61$) or main effects of sex (loading stance: $p = 0.14$; midstance: $p = 0.06$; terminal stance: $p = 0.09$; pre-swing: $p = 0.23$; swing: $p = 0.30$) during any gait phases.

For the Ankle-Knee joint pair, there were no significant Sex × Fatigue interaction effects on DP during any of the gait phases (loading stance: $p = 0.83$; midstance: $p = 0.74$; terminal stance: $p = 0.56$; pre-swing: $p = 0.52$; swing: $p = 0.75$). Significant main effects of fatigue were found on DP of Ankle-Knee joint pair during loading stance ($\chi^2 = 4.46$, $p = 0.04$; Figure 5.4). DP of Ankle-Knee joint pair significantly increased after fatigue during loading stance (MD = 3.84, g = 0.36).

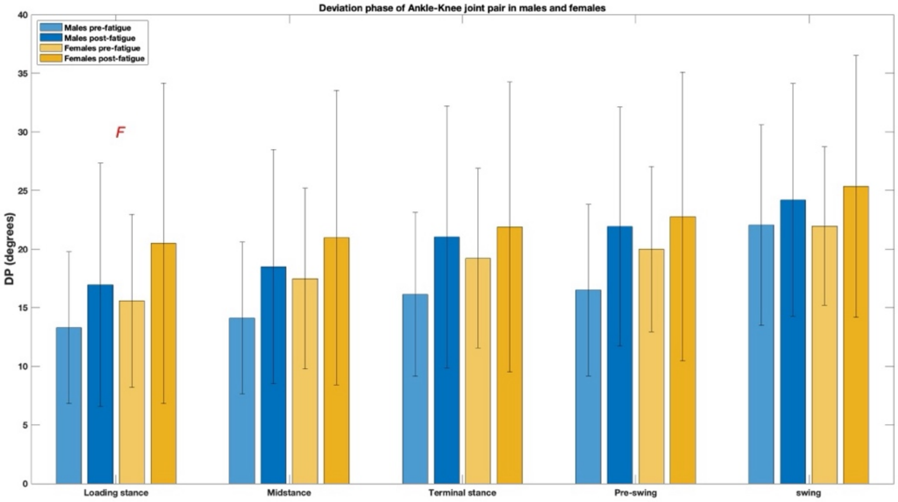

Figure 5.4 Deviation phase (DP) of the Ankle-Knee joint pair before and after fatigue in males and females at different phases of the running cycle. Error bars represent the standard deviation of all DP of each condition (the four conditions indicated in figure legend) at different phases of the running cycle. F: significant main effect of fatigue ($p < 0.05$).

5.5 Discussion

This study aimed to investigate the coordination and coordination variability of lower limb joints in the sagittal plane in response to a fatiguing treadmill run in highly trained endurance male and female runners. The main findings of the study are: 1) Female runners use a more in-phase Hip-Pelvis coupling pattern across all gait phases, and a higher Hip-Pelvis coordination variability during loading stance, compared to male runners, 2) both male and female runners use a more in-phase and variable Ankle-Knee joint coupling pattern during loading and midstance phases after fatigue, 3) any sex differences in sagittal plane coordination occurs between the Hip-Pelvis joint.

5.5.1 Fatigue and sex effects on proximal joints

The current study is the first to compare the fatigue changes in lower limb coordination patterns between highly trained endurance male and female runners. In the current study, sex-specific fatigue changes were mainly found in coordination in proximal joints. Female runners displayed a more in-phase Hip-Pelvis coordination pattern during all gait phases and a higher Hip-Pelvis coordination variability during loading stance phase compared to male runners after fatigue. At single joint, female runners displayed more anterior pelvis tilt during swing phase compared to male runners after fatigue. Dynamical systems perspectives have shown that a loss of variability may be associated with a reduction in the effective use of DoFs and synergies to maintain task performance (Lipsitz, 2002; Yang et al., 2018). In previous running-related studies, a lower coordination variability has been related to an injured or pathological state, while a higher coordination variability has been regarded as a healthy state (Hamill et al., 2012). Thus, we postulated that, compared to male runners, female runners would show a more variable pattern of proximal joint coordination during the loading phase with fatigue, in line with the higher incidence of injury at the hip and pelvis region in males (Dempster et al., 2021). Our results indeed agree with this hypothesis; however, too much variability is also problematic and may be related to an injured state (Hamill et al., 2012). Therefore, the relationship between the level of coordination variability and injury profiles of both sexes needs further investigation. The mechanism behind fatigue-related coordination changes of Hip-Pelvis joint pairs between sexes is not clear based on the findings from this current study. A potential pathway could be that female runners might utilize different groups of synergetic hip muscles to increase the Hip-Pelvis interactions. Vannatta and Kernozek (2021) investigated gluteal muscle force between experienced male and female runners at a controlled speed of 3.52–3.89 m/s down a 20-meter runway, using force estimates from kinematic and kinetic data. They found that female runners produced greater peak gluteus medius, minimus, and hamstring force but lesser greater peak gluteus maximus force during stance phase than male runners. It has been previously shown that after fatigue, experienced female runners produced lower peak hip extension moments and estimated hamstring forces during stance phase than male runners (Willson et al., 2015). It is likely that this lower hamstring force may induce more anterior pelvis tilt in females after fatigue, as we found in this current study. This difference in force generation of hip muscles may imply that females tend to utilize more gluteus medius, gluteus minimus, and hamstring before fatigue and increase the use of gluteus maximus in the progression of fatigue. The sex differences in force generation of hip muscles with fatigue could be related to the sex differences that we observed in coordination changes of Hip-Pelvis joint pairs. Further work on fatigue-related changes in lower limb muscle activity and synergistic muscle control appears necessary in sex-specific running research.

Despite these sex differences, there were some similarities between sexes found in this study. Both sexes showed more hip extension after fatigue during pre-swing phase. Rather, the knee flexion/extension angles and the coordination of Hip-Knee joint pairs were not affected by fatigue and sex during all gait phases, suggesting that males and females display unchanged and rigid Hip-Knee interactions with fatigue. There is some evidence that females produced higher estimated patellofemoral joint force during running (Sinclair & Selfe, 2015). Therefore, given the altered patellofemoral joint kinetics and higher injury rate of patellofemoral pain in females, it is possible that this rigid coordination strategy of Hip-Knee joints may be problematic for females. Future studies of Hip-Knee coordination and sex bias for running-related knee injuries appear necessary.

Different from our findings, a few studies found a more out-of-phase coupling pattern of Hip-Knee and Pelvis-Thigh joints with fatigue in experienced runners (Brown et al., 2016; Mo & Chow, 2019). However, the participants ran at their individual anaerobic threshold speed, and the sex of the participants was not reported in Mo and Chow (2019), or, the participants ran at 3.35 m/s, and only female runners were recruited in Brown et al. (2016). Additionally, the coordination in these studies was quantified using vector coding technique. These differences in study design and data analysis make the coordination results less comparable.

5.5.2 Fatigue and sex effects on distal joints

Our findings showed an in-phase and a higher variability of Ankle-Knee joint coordination pattern during early stance after fatigue. No sex difference was found in Ankle-Knee joint coordination pattern. At single joint, the ankle dorsiflexion/plantarflexion was not affected by fatigue or sex. From the perspective of lower limb muscular activation, Hajiloo et al. (2020) found that recreational runners increased the muscular activation of tibialis anterior, gastrocnemius medialis, and rectus femoris together during the shock absorption phase with fatigue, possibly suggesting a reduced ability to attenuate vertical ground reaction forces with fatigued distal muscles. However, it remains unclear if the pattern of multimuscle activation would be similar in experienced and highly trained endurance runners. With respect to coordination variability, we found that highly trained endurance runners display an increased coordination variability of Ankle-Knee joint pairs with fatigue during pre-loading phase, indicating more interaction and flexibility of distal joint pairs. Similar to our findings, Bailey et al. (2020) found that experienced endurance runners with higher perceived fatigue displayed more coordination variability after fatigue, with the adjustments occurring during the transition portion of the gait cycle. Compared to novice runners, experienced runners exhibited more coordination variability in Hip-Knee and Shank-Foot couplings after fatigue (Mo & Chow, 2019). Given that the participants in this current study are experienced and asymptomatic runners, it is likely that this increased coordination variability could be a learned and beneficial response to fatigue in experienced runners. Overall, based on our findings on fatigue effects, it is indicated that highly trained runners may display an in-phase and flexible coupling pattern of the distal joints with fatigue during early stance, in a way to prepare for the upcoming propulsion.

5.5.3 Limitations

Several limitations of this study should be noted. An IMU motion capture system was used, given its consistency in detecting sex-based differences (Miqueleiz et al., 2024). However, only sagittal plane kinematics were calculated in this study. It is likely that examining the frontal plane motion may have revealed different findings. Anatomical differences between sexes support that the wider pelvis in females may require female runners to exhibit greater hip adduction to bring the lower extremity close to the body midline during the stance phase of running (Barber, 2004). The frontal plane joint motion analysis may help explore how this anatomical difference could relate to a higher injury rate of patellofemoral pain and iliotibial band syndrome in females (Brown et al., 2016; Willson et al., 2015). However, it has been reported that the IMU (iSEN IMU system) was only able to provide reliable measurements of sagittal plane motions and showed low reliability in measuring motions in the frontal and horizontal planes (Zeng et al., 2023), which is why we chose to limit our analysis to the sagittal plane. Marker-based motion capture systems may provide more reliable profiles for the frontal plane motions. Additionally, we did not control for footwear and had the participants wear their own preferred running shoes. Since footwear can influence running mechanics, this may have affected the coordination patterns observed in this study.

5.6 Conclusions

After fatigue, we observed sex differences in the coordination of proximal joints (hip-pelvis), with a more in-phase coordination pattern and a higher coordination variability with fatigue in females. Both males and females showed the same fatigue-related changes in the knee-hip coordination patterns, and finally, both sexes showed more in-phase coordination patterns and higher coordination variabilities of the ankle-knee joint. The fatigue-related changes in different joint pairs between sexes may help explain the sex bias of developing knee and hip injuries. The sex differences found in this study also suggest that future research should incorporate sex-specific analyses to reveal the mechanisms of running-related injuries of different localizations and types.

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5.8 Disclosure statement

The authors report there are no competing interests to declare.

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Chapter 6: Comprehensive Discussion

The general objective of this thesis was to investigate the effects of fatigue on coordination of repetitive whole-limb tasks and to explore the origin of sex differences during fatiguing whole-limb movements. The overall hypotheses of this thesis were: 1) repetitive motion-induced fatigue would change the measures of multijoint and multimuscle coordination, and 2) sex differences would be found in multimuscle coordination. Key findings are summarized as follows:

6.1 Key findings of this thesis

1. The multimuscle synergy structure and multijoint coordination were maintained constant with fatigue in both upper limb and lower limb tasks. This indicates that the human movement system may prioritize the maintenance of some simplified motor control strategy of grouping multiple muscles and joints together in controlling upper and lower limb repetitive multipoint movements with fatigue.
2. Despite this, some indicators of motor variability changed with fatigue in both tasks. In the study on the upper limb, fatigue led to decreased activation variability of shoulder agonist (anterior deltoid), elbow agonist (triceps brachii), and elbow antagonist (biceps brachii) of forward pointing movement, and shoulder stabilizer (anterior deltoid), elbow agonist (biceps brachii), and elbow antagonist (triceps brachii) of backward pointing movement. Fatigue induced no changes in the activation variability of scapulothoracic stabilizer (upper trapezius) during backward pointing movement. In the study on the lower limb (running), fatigue led to a more variable ankle-knee coordination pattern during the loading and midstance phase of running. One interpretation can be that the changed motor variability reflects some control strategy whereby the human movement system is able to adapt to fatigue so as to be able to keep the multijoint coordination and multimuscle synergy structure constant even with fatigue.

3. Sex differences were observed in some indicators of multijoint coordination and multimuscle synergy. After repetitive motion-induced upper limb fatigue, there were more contributions and higher activation complexities of the biceps brachii (i.e., the elbow agonist during backward pointing and the elbow antagonist during forward pointing) in females compared to males. After running-induced fatigue, females showed a more in-phase coordination of the proximal joint (hip-pelvis) throughout the running cycle and a more variable coordination pattern during loading stance phase compared to males. Together, results suggest that females' coordination may be controlled by proximal joints and may reflect an advantageous fatigue response compared to males. Together, this thesis found that the biceps brachii and hip-pelvis joints may be central to those sex differences, which supports an important role of muscle strength and anthropometry in explaining the biomechanical origin of sex differences in coordination patterns and how they change with fatigue during both repetitive upper limb and lower limb tasks.

6.2 What is preserved with fatigue in repetitive whole-limb movements: motor synergy

This thesis found that the multimuscle synergy structure and multijoint coordination of most of the joint pairs were preserved with fatigue in both upper and lower limb tasks. This thesis studied motor synergies at several levels of human body DoFs in the form of coordinated joint and muscle groups. The extracted coordinated joints and muscle groups have been suggested to represent movement modules or "templates" with low DoFs, that can in turn be used in a way that simplifies the control of multiple DoFs. In Chapter 3, both synergy structures were preserved after repetitive upper limb motion-induced fatigue. In Chapter 4, no fatigue-related changes were found in lower limb inter-joint coordination for most joint pairs (i.e., hip-pelvis and knee-hip joint) after running-induced fatigue. The unchanged synergy structure and coordination found in this thesis align with previous results. Previous studies on repetitive upper limb motion found no change with fatigue in movement frequency and endpoint trajectory of hammering and sawing (Côté et al. 2002, 2008). No changes with fatigue were also observed in endpoint spatial variability and shoulder-elbow inter-joint coordination of the same repetitive pointing task (Yang et al., 2018). In repetitive lower limb motions during running, similar findings of invariant global coordination variables were found in inter-segmental coordination of thigh-leg and leg-foot couplings (Dal Pupo et al., 2017). Those unchanged coordination patterns further reinforce the hypothesis that motor synergies are used to control repetitive whole-limb motions using simplified modules organized at a central level. This advantageous strategy may also facilitate the adaptation of the human movement system when dealing with perturbations to the normal state, such as during repetitive motion-induced fatigue.

6.3 What is changed with fatigue in repetitive whole-limb movements: motor variability and mechanical and functional roles of muscles and joints

6.3.1 Motor variability changes with fatigue

Despite the maintained parameters of motor synergy, some fatigue-induced changes were found in both upper and lower limb tasks. This thesis found that fatigue led to a lower activation variability of most of the arm muscles during upper limb tasks and a more variable ankle-knee coordination pattern during the braking phase of running. By using the same experimental repetitive upper limb task, previous research found a more variable shoulder-elbow coordination pattern during the forward pointing phase (Yang et al., 2018). The changed motor variability at both muscle and joint levels supports the adaptive aspects of variability under the dynamical system framework. The human movement system may decrease the interactions between individual muscles and joints, potentially leading to a path to impairment with fatigue. However, the system may increase the interactions between low coordinated joints and muscle groups, in a way to preserve global task performance with fatigue. Together with the main finding of constant parameters of motor synergy that we discussed in the preceding section, our results may reflect the adaptability of motor variability even in the presence of fatigue.

6.3.2 Muscles and joints working as decelerators with fatigue

Our findings suggest some similarities in how upper and lower limbs' roles change in response to fatigue. The upper limb elbow agonist and lower limb proximal joints may share similar roles as decelerators in responding to whole-limb motion-induced fatigue. An elbow control strategy may be used for fatiguing upper limb task, and a distal control strategy may be used for a lower limb task. Biomechanically, the elbow agonist (triceps brachii) and shoulder agonist (anterior deltoid) of the forward pointing movement work together as accelerators and decelerators to initiate and end the forward pointing movement. The elbow agonist (biceps brachii) of the backward pointing movement works as accelerator and decelerator for initiating and ending the backward pointing movement. For both forward and backward movements, the upper trapezius works as scapulothoracic stabilizer. In running, during the braking phases of stance (i.e., loading and midstance phase), Hamner et al. (2010) found that the quadriceps muscle group played a significant role, contributing to both braking and support. It provided twice the peak braking acceleration and nearly half of the peak vertical support of the body's center of mass. The gluteus maximus, gluteus medius, and adductor magnus collectively contributed approximately half of the peak vertical support following initial contact. During the propulsion phase of stance (i.e., terminal stance and pre-swing phase), the soleus and gastrocnemius were the primary muscles responsible for propulsion and support. They provided more than twice the peak forward acceleration and over half of the peak vertical support of the body's center of mass. Meanwhile, the quadriceps continued to resist forward motion. Towards the end of the stance, the hamstrings, tibialis anterior, and iliopsoas accelerated the body's center of mass downward (Hamner et al., 2010).

In taking a closer look at the function of muscles and joints within the synergy for both upper and lower limb tasks, this thesis found that the elbow agonist (biceps brachii) made more activation contributions to accelerate and deaccelerate the elbow flexion of backward pointing as part of the fatigued coordination pattern. Fatigue led to decreased major frequency of shoulder agonist and stabilizer (anterior deltoid), elbow agonist and antagonist (biceps brachii and triceps brachii) but not the scapulothoracic stabilizer (upper trapezius) during both forward and backward pointing. After running-induced whole-limb fatigue, this thesis found that the ankle-knee joint pair showed a more in-phase and variable coordination pattern during loading and midstance phase of running. Fatigue changes were only observed in the distal ankle-knee joint pairs, not the proximal pelvis-hip and hip-knee joint pairs. From those two sets of results from fatigued upper limb and lower limb movements, we can therefore conclude that upper limb elbow agonist and lower limb proximal joints may share similar roles as decelerators with whole-limb motion-induced fatigue.

6.4 Sex differences in motor synergies in repetitive whole-limb movements

Findings from Chapters 3 and 4 support muscle specificity of patterns between sexes executing the same upper limb fatiguing task, with emphasis on the involvement of biceps brachii in females. This thesis found that the females utilized more of their elbow agonist and antagonist (biceps brachii) in multimuscle coordination during elbow flexion and extension. Females showed a more variable and complex pattern of the elbow agonist and antagonist muscle activity compared to males. But despite this, interestingly, the task performance was similar after fatigue between sexes. Our findings suggest that males and females may use different coordination strategies of biceps brachii to arrive at the same preservation of task performance. Sex differences have been previously observed in biceps brachii, with females showing a greater increase in biceps brachii EMG variability and less biceps brachii swelling after performing the same experimental upper limb fatiguing task (Srinivasan et al., 2016; Yoon et al., 2021). Females generally have less biceps brachii muscle mass and a smaller cross-sectional area of muscle fibres than males, resulting in a lower biceps brachii muscle force in females (Lindman et al., 1991; Miller et al., 1993). To maintain the same task performance as males, females may activate more of their biceps brachii motor units and increase the movement variability of biceps brachii to compensate for the lower force capacity compared to males. This higher contribution and usage of the elbow primary mover, biceps brachii, could be associated with the higher prevalence of neck/shoulder complaints in females in workplaces (Nordander et al., 2016).

Despite these sex differences, there were still many similarities between the sexes. For instance, our results suggest that males and females show similar organization of muscle synergy structures and activation patterns (Chapter 3; Chen et al., 2024), complexity and time-frequency characteristics of upper limb muscles (Chapter 4). This had also been suggested in previous studies from our lab showing no sex difference in multijoint stabilization in response to repetitive motion-induced upper limb fatigue (Hasanbarani et al., 2021). In sum, this thesis highlights the sex-specific impact of fatigue on control of biceps brachii in repetitive movement-induced upper limb fatigue patterns while supporting many similarities of motor synergies between sexes.

Given the highly rhythmic and repetitive nature of whole-body tasks, it was hypothesized that the sex-specific effects of fatigue that we observed in the upper limb tasks could also be observed in common lower limb tasks, such as walking and running. In Chapter 5, sex differences were observed in pelvis and hip joints after running-induced fatigue, with females showing more in-phase and variable hip-pelvis coordination and greater pelvis tilt angles compared to males. Our findings on the role of the pelvis and hip joint movement in distinguishing males from females agree with previous findings on walking (Konishi et al., 2024) and running (Hannigan & Chou, 2019) and may be attributed to the known sex difference in anthropometry of hips. Females generally have a greater pelvic width and a higher ratio of pelvic width to thigh length compared to males (Lewis et al., 2017; Horton & Hall, 1989). Despite this, no sex difference in stride width has been previously observed during either running (Takabayashi et al., 2017) or walking (Bruening et al., 2015). This suggests that the lower limb alignment is distinct between sexes, where movement strategies are optimized to maintain task performance and respond to perturbing conditions like fatigue. It is reported that females exhibit greater hip adduction and internal rotation amplitude during walking (Chehab et al., 2017; Rowe et al., 2021) and running (Almonroeder & Benson, 2017; Sakaguchi et al., 2014), hypothesized to reflect sex-specific strategies to position the feet closer to the vertical axis of the body in females in comparison to males. Together, Chapter 5 suggested an important role of hip and pelvis joints in explaining sex differences in movement control in response to running-induced fatigue.

Combining results of sex differences across all chapters of this thesis, one interpretation can be that females may use a biceps strategy to deal with upper limb fatigue, and a hip-pelvis strategy to deal with lower limb fatigue. In turn, the common aspect of both strategies could be related to the predominant role of anthropometry in explaining sex differences in biomechanics. The biceps brachii is the muscle that shows the most prominent sex difference in muscle mass, muscle fibre cross-sectional area, and force output in the upper limb (Miller et al., 1993). Males usually have longer arms compared to females. In the lower limb, the pelvis and hip joints are the joints that show significant sex differences in joint geometry. Together, these results further reinforce the role of anthropometry in explaining musculoskeletal system function. Moreover, these sex-based group differences observed in this thesis suggest that the overall sex difference is larger than inter-individual differences specifically in characteristics of the biceps brachii and of the pelvis and hip point, further reinforcing the importance of accounting for sex differences in at least the parameters as dimorphic as those, when modelling the biomechanics of the human body.

6.5 Methodological considerations

6.5.1 Choice of muscles for the upper limb task

In Chapter 3 and 4, the four muscles that we selected are the prime movers of the elbow and shoulder joints and the main stabilizers of the shoulder joint. The repetitive pointing task in forward pointing phase requires the participants to abduct their shoulder and extend their elbow in the horizontal plane. Therefore, the prime elbow mover and the prime shoulder mover for the forward pointing movement are triceps and anterior deltoid. In backward pointing phase, the pointing movement in the backward direction requires the participants to adduct their shoulder and flex their elbow. Biceps brachii is the prime elbow mover for the backward pointing movement. For both forward and backward pointing movements, the upper trapezius works as a shoulder stabilizer for the pointing task.

6.5.2 Interpretation of muscle synergies

In Chapter 3, we interpreted the functions of two synergies as 1) shoulder stabilization and 2) elbow flexion and extension as discussed in section 3.5.1. However, there are other possible functions of the synergies based on different interpretations. For instance, as shown in Figure 3.3, synergy 1 is most active at the start of the backward pointing phase, and synergy 2 is most active at the start of the forward pointing phase. The biggest difference between the males and females seems to be that the females activate synergy 1 earlier in the cycle, which could be indicative of needing an earlier activation of that synergy to end the forward pointing phase and initiate the backward pointing phase, possibly because of less force generation capacity for elbow flexion (eccentrically and concentrically). Thus, another possible interpretation could be that synergy 1 is related to the backward pointing phase and that synergy 2 is related to the forward pointing phase. The observed difference in activation patterns may be explained by a different ability to generate stiffness and damping in the elbow musculature between the two sexes. In Chapter 4, a higher mean frequency was found in females compared to males. This could suggest higher motor unit firing rates due to higher relative effort. The difference in synergy activation timing, with each synergy seeming to ramp up earlier in females than males, could reflect a different strategy based on differences in force production capacity for generating muscle stiffness and damping. Lastly, we used EMG to measure muscle activation and analyze muscle synergies. What we observe with EMG, however, is not the neural signals to the muscles, but the electrical activity in the muscles. Because of that, the synergies that we see from EMG could change even if the synergies coming from the CNS do not, because different muscles may experience different physiological effects that change their EMG profiles.

6.5.3 EMG normalization

In Chapter 3, we normalized the EMG to the maximum value of each pointing trial. This normalization method is more flexible but lacks a common reference point for comparison between trials and participants compared to normalization to maximal voluntary contraction. However, since muscle synergy analysis was performed across trials within the group, differences in the maximal voluntary contraction between individuals may not influence the muscle synergy analysis. A similar EMG normalization design using the maximal value of each trial was previously used to investigate the effects of fatigue on synergy of lower limb muscles in running (Hajiloo et al., 2020). This previous study, together with Chapter 3, found fatigue-related changes in muscle synergies during repetitive movements, indicating that the EMG normalization method of maximal value of each trial is able to detect fatigue-related synergy changes. However, future studies should also consider the EMG normalization method of maximal voluntary contraction in muscle synergy analysis for more fatigue-relevant comparisons.

6.5.4 Data analysis of time and spectral EMG characteristics

Given that the time and spectral EMG characteristics (i.e., RMS and median power frequency) were not primary outcomes in Chapter 3, we did not include the data analysis of RMS and median power frequency in Chapter 3. To describe how we calculated these metrics in detail, we have included them below. Partitioned EMG data were de-meaned, band-pass filtered (Butterworth 2nd, 20–450 Hz), and full-wave rectified. A moving RMS average (100 ms time-window) was then applied to the rectified data to obtain the RMS curve of each pointing phase and each muscle. The mean RMS value was calculated for each RMS curve. To calculate the median power frequency, Fast Fourier Transform was applied to the filtered EMG data. EMG amplitude and spectrum were determined by calculating the averaged mean RMS value and median power frequency of the 15 repetitions for each fatigue condition.

6.5.5 How anthropometric differences can influence the findings in biceps and anterior deltoid?

Previous studies have found sex-specific differences in upper limb motor control strategies even with arm's anthropometric load and strength controlled between sexes. A previous study investigated the effects of fatigue during a sustained, sub-maximal elbow flexion task, with sex groups matched based on maximal wrist extensor strength. While the strength-matched groups experienced similar reductions in maximal strength following the fatiguing task, differences in EMG activity were observed between sexes. Notably, females exhibited a greater increase in EMG bursts by the end of the task. These findings suggested the presence of sex-specific differences in motor control strategies employed to sustain performance with fatigue (Hunter et al., 2004). Arm's anthropometric load has also been studied in comparing the upper limb muscle activation amplitude with repetitive motion-induced fatigue between sexes. It has been reported that arm's anthropometric load did not group participants differently by sex. However, when arm's anthropometric load was included as a covariate in the statistical analysis model, a significant sex main effect was found, showing that females exhibited a significantly greater fatigue-related increase in anterior deltoid activation amplitude compared to males, though this effect was not observed in upper trapezius. Notably, when arm's anthropometric load was excluded as a covariate, the sex effect disappeared. This indicates that, while arm's anthropometric load itself was not a significant covariate, its inclusion enhanced the accuracy of the statistical analysis model (Slopecki et al., 2020). Therefore, it is hypothesized that there may still be sex-specific motor control strategies with repetitive upper motion-induced fatigue even when strength is accounted for. Anthropometric differences may play roles in fatigue-related upper limb muscle activity between males and females regardless of sex. However, these hypotheses need future studies to further investigate.

6.6 Practical/applied aspects of findings

This thesis highlights that sex differences in upper limb coordination pertain to the function of the biceps brachii. This suggests that in the ergonomics setting, injury prevention in jobs involving repetitive upper limb tasks should consider potential sex differences in upper limb fatigue and injury risk especially if they relate to the role of the biceps brachii (e.g., elbow-based tasks). When a higher risk is identified for females, interventions should be designed around impacting the effort on the biceps brachii muscle. Alternatively, injury prevention approaches could focus on biceps brachii strengthening interventions for females to prevent them from working near their biceps brachii capacity. As for running, this thesis highlights that sex differences in lower limb coordination are central to the hip and pelvis joint pair. Our findings support that the hip is affected differently in females, indicating that there could be differences in hip injury preventative approaches for female runners. However, the higher rates of running-related hip injuries in males also support that either the fatigue patterns identified in females are protective of injury, or alternatively, that factors other than biomechanics could explain the higher injury rates in males.

6.7 Limitations

A few limitations affected the generalizability of our findings. First, our experiments were conducted in laboratory settings, which places a constraint on the ecological validity of findings. The performance of the upper limb and lower limb tasks in laboratory settings cannot predict the fatigue-related control strategies of our participants in real-world settings. Future studies could replicate studies of this thesis but through real-world data collection methods. For instance, future work could design occupational experiments to study upper limb motions in real-world workplace. Future work could consider collecting real-time lower limb motions during real-time running training sessions and races. Moreover, different upper limb and lower limb models and experimental tasks could also be chosen (e.g., drawing and walking), in order to broaden the scope of transferability of results. Second, our participants were healthy young adults (Chapter 3 & 4) and highly trained endurance runners (Chapter 5), which limits the generalizability of our results beyond those groups. Future work could consider a broader range of populations. For example, in workplace, future work could recruit healthy controls and individuals with upper limb MSDs of different ages. In running, runners of different performance levels and those with different types of running-related injuries could be recruited.

6.8 Future research

6.8.1 A complete assessment of motor synergy and variability during repetitive whole-body repetitive movements

This thesis aimed to investigate movement variability and synergy at levels of joints and muscles. However, due to the limited transportation ability of EMG system, we only captured the lower limb kinematics by using the inertial measurement units in the third study. Therefore, we only assessed the inter-joint coordination and its variability during repetitive lower limb motions in Chapter 5. A combined study of multijoint and multimuscle synergy, as well as movement variability, may provide a more complete picture of multi-dimensional synergies during repetitive tasks. To investigate the multijoint synergy and the stability of task-specific performance, the uncontrolled manifold and goal equivalent manifold approaches, developed based on the theory of motor abundance, can be considered in the future, to help determine which variability components are useful and which ones are harmful in terms of overall performance goals and injury risks. Nonlinear analyses, such as fractal and entropy approaches, can be further used to quantify dynamic and temporal aspects of kinematics, in a way to provide insight into the nonlinear dynamics of motor control.

6.8.2 Novel artificial intelligence approaches to extract the sex-specific features during fatiguing whole-body movements

Like all complex analyses of motor behaviour, results of this thesis that have to do with motor synergy and variability features contain higher-dimensional information and can be challenging to interpret. Novel artificial intelligence approaches have the ability to process complex biomechanical data and reveal the relationships underlying the multiple features. For instance, multilayer artificial neural network models allow input features to be automatically extracted from raw data and transformed to handle unstructured data. This direct input avoids several data processing steps required in traditional machine learning techniques, reducing overall computational times. Multilayer artificial neural networks and deep learning algorithms have shown promising results in human activity recognition (Xu et al., 2022) and biomechanical variable prediction (Girka et al., 2020) in both laboratory settings and real-world environments. As such, novel artificial intelligence approaches can be promising tools to predict the continuous changes of fatigue during locomotion and recognize sex-specific biomechanical features in the future (Halilaj et al., 2018). Nevertheless, findings from this thesis will be helpful towards such approaches for the future, in helping identify which variables should be approached and modelled in a sex-specific way. In turn, both men's and women's health will benefit from the increased knowledge that this thesis provides about sex similarities and differences in biomechanical outcomes.

Chapter 7: Summary and Conclusions

7.1 Final conclusion

This dissertation aimed to apply modern linear and nonlinear analytical approaches to assess the multi-dimensional synergies during fatiguing repetitive whole-limb motions. Additionally, we studied upper and lower limb tasks in both sexes to explore the origin of sex differences during fatiguing whole-limb movements. A repetitive upper limb pointing task and a treadmill running task were studied to mimic common whole-limb movements. Continuous relative phase approach and muscle synergy analysis were used to quantify multijoint and multimuscle coordination patterns. Continuous wavelet transform technique and entropy analysis were used to assess myoelectric manifestations of muscle fatigue in time-frequency and complexity domains. Results of this thesis show that the structure of the upper limb multimuscle synergy and lower limb inter-joint coordination was maintained constant with fatigue, while fatigue led to a less complex activation pattern in most arm muscles and a more variable ankle-knee coordination pattern. This indicates a useful function of motor variability in both linear and nonlinear aspects, demonstrating how variability helps maintain coordination even in the presence of fatigue. Females displayed more contributions and higher activation complexities of biceps brachii in upper limb multimuscle coordination. In lower limb multijoint coordination, females showed a more in-phase and variable hip-pelvis coordination pattern with fatigue. The sex-specific patterns of biceps brachii and hip-pelvis control in females may reflect the predominant roles of anthropometry, as biceps brachii and hip-pelvis joints show significant sex differences in muscle mass, muscle fibre content, and joint anatomy.

7.2 Implications of findings

Our results provide new insights into the personalization of sex-specific musculoskeletal injury prevention and rehabilitation interventions for occupational and running populations.

Clinicians and coaches should keep track of the injury history and performance during daily work and sports training. This could be monitored through wearable electronics and smart textiles specifically targeting biceps brachii and hip joints of both sexes.

Our results also serve as a recommendation to consider biological sex differences in software engineering for fatigue monitoring and performance analysis. For instance, models and algorithms designed to predict how the human body adapts its multijoint repetitive movements to fatigue should make sure to personalize data on biceps brachii muscle strength and hip geometry for males and females. Moreover, our results help identify specific coordination metrics that show sex-specific effects of fatigue, which can be incorporated into biofeedback or app-based approaches for movement tracking and injury prevention. This dissertation contributes to the growing body of evidence that advanced linear and nonlinear analytical approaches can detect biomechanical sex-specific fatigue adaptations. This gives insight and advice for biomechanists to include advanced metrics in software design. Together, results from this thesis can help identify which metrics could be used for movement tracking and software engineering and design in workplace and sports applications, and among those keep variables, which ones should come with different guidelines to personalize sex-specific injury prevention.

Dissertation References

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Appendices

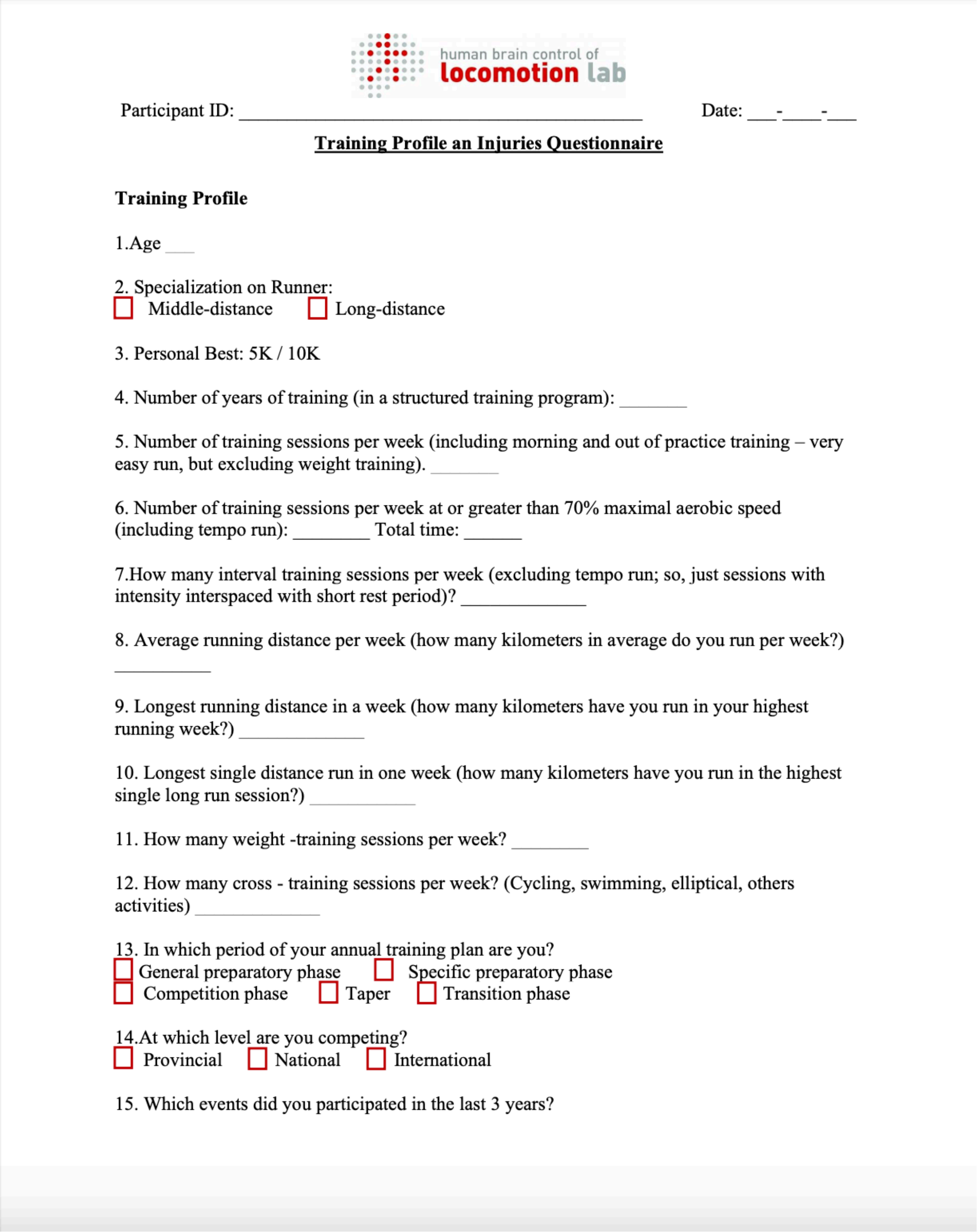
Appendix 1. Borg CR10 Scale

Rating	Description
0	Nothing at all
0.5	Very, very light
1	Very light
2	Light
3	Moderate
4	Somewhat hard
5	Hard
6	
7	Very hard
8	
9	
10	Maximal

Appendix 2. Borg CR (6–20) Scale

RPE	Level of Exertion	Physical Fatigue Levels
6	No exertion	
7		
7.5	Extremely light	
8		Low
9	Very light	
10		
11	Light	
12		
13	Somewhat hard	Moderate
14		
15	Hard	Heavy
16		
17	Very Hard	
18		Severe
19	Extremely Hard	

Appendix 3. Training Injury Profile Questionnaire



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Participant ID: ____ Date: ___-____-___

Training Profile an Injuries Questionnaire

Training Profile

1.Age ___

2. Specialization on Runner:
☐ Middle-distance ☐ Long-distance

3. Personal Best: 5K / 10K

4. Number of years of training (in a structured training program): _______

5. Number of training sessions per week (including morning and out of practice training – very easy run, but excluding weight training). _______

6. Number of training sessions per week at or greater than 70% maximal aerobic speed (including tempo run): ________ Total time: ______

7.How many interval training sessions per week (excluding tempo run; so, just sessions with intensity interspaced with short rest period)? _____________

8. Average running distance per week (how many kilometers in average do you run per week?) __________

9. Longest running distance in a week (how many kilometers have you run in your highest running week?) _____________

10. Longest single distance run in one week (how many kilometers have you run in the highest single long run session?) ___________

11. How many weight -training sessions per week? ________

12. How many cross - training sessions per week? (Cycling, swimming, elliptical, others activities) _____________

13. In which period of your annual training plan are you?
☐ General preparatory phase ☐ Specific preparatory phase
☐ Competition phase ☐ Taper ☐ Transition phase

14.At which level are you competing?
☐ Provincial ☐ National ☐ International

15. Which events did you participated in the last 3 years?

Primary events:
____
____

Secondary events:
____
____

Injuries
Mark the response that most accurately describes your situation

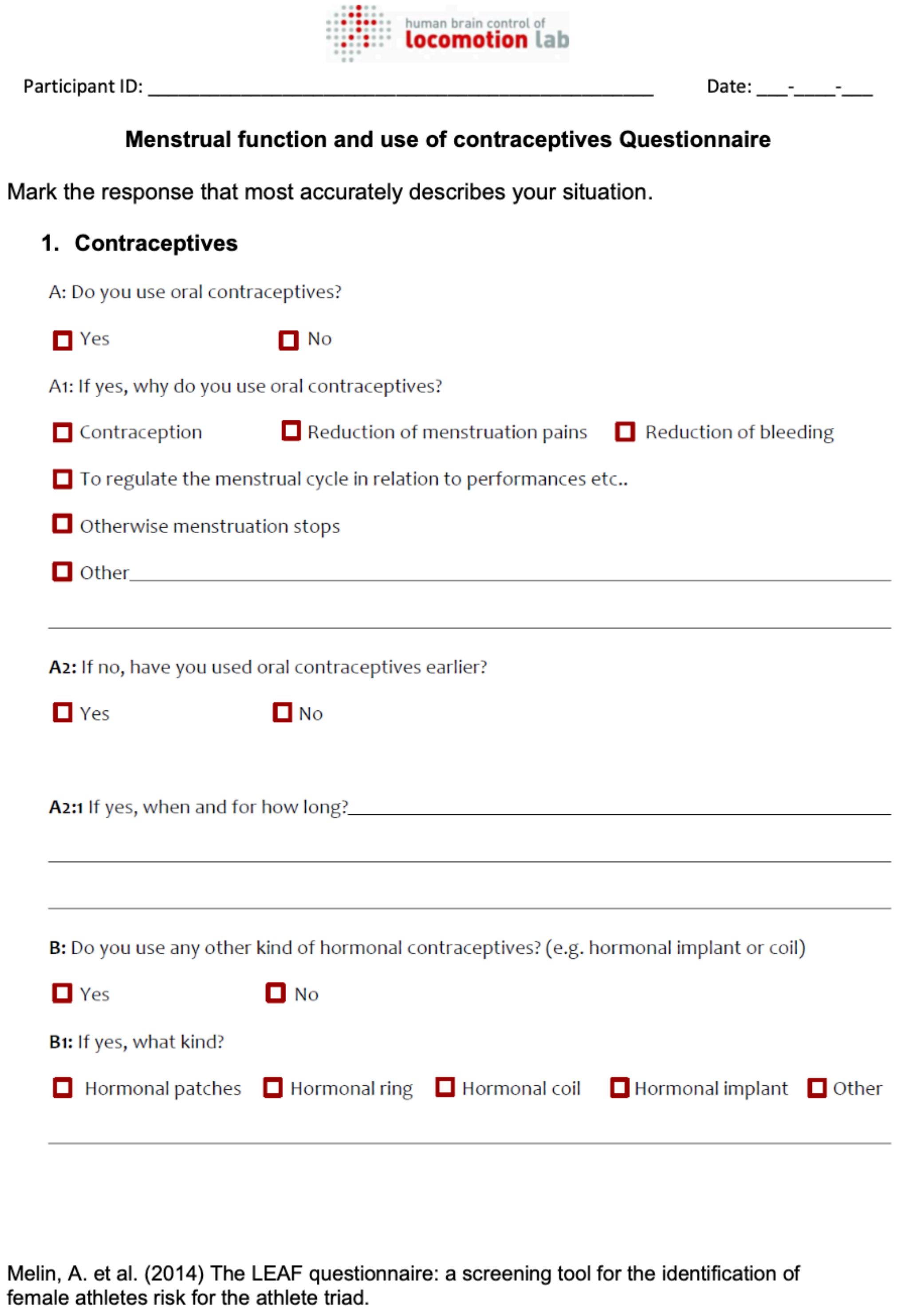
1. Have you had absences from your training, or participation in competitions during the last year due to injuries?
☐ No, not at all ☐ Yes, once or twice ☐ Yes, three or four times ☐ Yes, five or more

2. If yes, for how many days absence from training or participation in competition due to injuries have you had in the last year?
☐ 1-7 days ☐ 8-14 days ☐ 15-21 days ☐ 22 days or more

3. If yes what kind or injury have you had in the last year?____
____
____

4. Comments or further information regarding injuries:
____
____
____

Appendix 4. Menstrual Function and Contraceptive Questionnaire



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Participant ID: ______________________________ Date: ___-____-___

Menstrual function and use of contraceptives Questionnaire

Mark the response that most accurately describes your situation.

1. Contraceptives

A: Do you use oral contraceptives?

☐ Yes ☐ No

A1: If yes, why do you use oral contraceptives?

☐ Contraception ☐ Reduction of menstruation pains ☐ Reduction of bleeding

☐ To regulate the menstrual cycle in relation to performances etc..

☐ Otherwise menstruation stops

☐ Other______________________________

____

A2: If no, have you used oral contraceptives earlier?

☐ Yes ☐ No

A2:1 If yes, when and for how long?______________________________

____

____

B: Do you use any other kind of hormonal contraceptives? (e.g. hormonal implant or coil)

☐ Yes ☐ No

B1: If yes, what kind?

☐ Hormonal patches ☐ Hormonal ring ☐ Hormonal coil ☐ Hormonal implant ☐ Other

____

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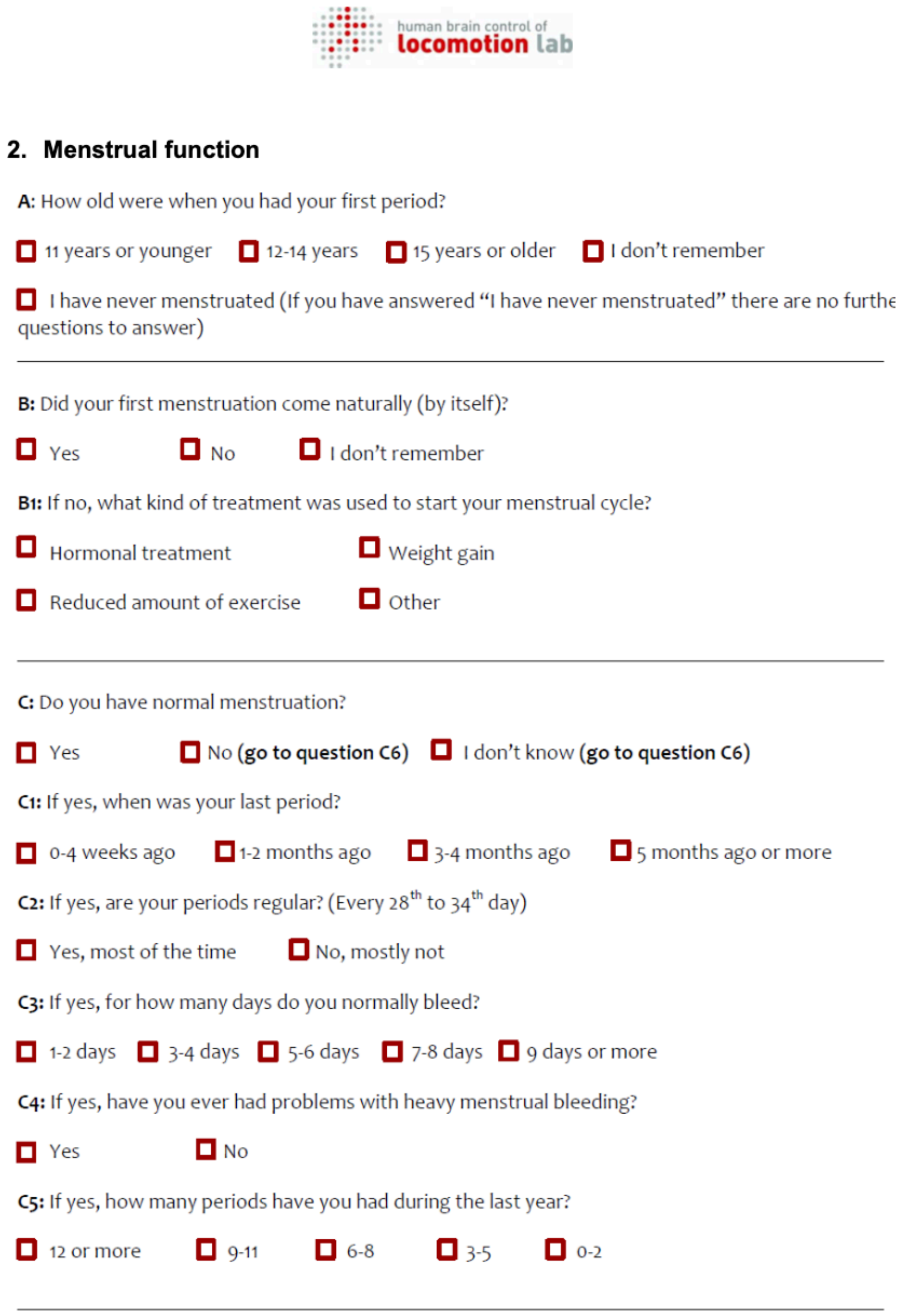

human brain control of locomotion lab

2. Menstrual function

A: How old were when you had your first period?

☐ 11 years or younger ☐ 12-14 years ☐ 15 years or older ☐ I don't remember

☐ I have never menstruated (If you have answered "I have never menstruated" there are no furthe questions to answer)

B: Did your first menstruation come naturally (by itself)?

☐ Yes ☐ No ☐ I don't remember

B1: If no, what kind of treatment was used to start your menstrual cycle?

☐ Hormonal treatment ☐ Weight gain

☐ Reduced amount of exercise ☐ Other

C: Do you have normal menstruation?

☐ Yes ☐ No **(go to question C6)** ☐ I don't know **(go to question C6)**

C1: If yes, when was your last period?

☐ 0-4 weeks ago ☐ 1-2 months ago ☐ 3-4 months ago ☐ 5 months ago or more

C2: If yes, are your periods regular? (Every 28th to 34th day)

☐ Yes, most of the time ☐ No, mostly not

C3: If yes, for how many days do you normally bleed?

☐ 1-2 days ☐ 3-4 days ☐ 5-6 days ☐ 7-8 days ☐ 9 days or more

C4: If yes, have you ever had problems with heavy menstrual bleeding?

☐ Yes ☐ No

C5: If yes, how many periods have you had during the last year?

☐ 12 or more ☐ 9-11 ☐ 6-8 ☐ 3-5 ☐ 0-2

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C6: If no or "I don't remember", when did you have your last period?

☐ 2-3 months ago ☐ 4-5 months ago ☐ 6 months ago or more

☐ I'm pregnant and therefore do not menstruate

D: Have your periods ever stopped for 3 consecutive months or longer (besides pregnancy)?

☐ No, never ☐ Yes, it has happened before ☐ Yes, that's the situation now

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E: Do you experience that your menstruation changes when you increase your exercise intensity, frequency or duration?

☐ Yes ☐ No

E1: If yes, how? (Check one or more options)

☐ I bleed less ☐ I bleed fewer days ☐ My menstruations stops

☐ I bleed more ☐ I bleed more days

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