Motor Adaptation to Muscle Fatigue: Moderating Factors and Implications

by

Jeffrey C. Cowley

A dissertation submitted in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
(Kinesiology)
in The University of Michigan
2017

Doctoral Committee:

Assistant Professor Deanna H. Gates, Chair
Associate Professor Susan H. Brown
Professor Daniel P. Ferris
Associate Professor R. Brent Gillespie
Associate Professor Richard E Hughes

Jeffrey C. Cowley

jccowle@umich.edu

ORCID iD: 0000-0003-0925-3330

Dedication

For Rachel, Lissy, Peter, Talmage, and more.

Acknowledgements

It is incredible to arrive at the end of this journey. I am grateful to so many people who have helped me reach this point. Looking back, it is clear that I've made it by the Grace that brought me all of your support. There were many bumps along the way where my flaws were so evident. My advisor, Deanna Gates, has worked with me with immense patience, and this dissertation would not be possible without her vital guidance and support – not to mention the MATLAB skills she taught me. Likewise, each of my committee members has provided valuable insights and feedback in the development of this work. I've benefitted from the efforts and input of collaborators, David Lipps and Josh Leonardis, and undergraduate assistants: Ann Starling, Ronnie Trower, Nick Dolnicek, Cassandra Cuyawa, Amanda Stark, and others. I can't thank them enough.

I would also like to thank my family for taking care of me on my best and worst days. More than anyone, my wife, Rachel has always believed in me even when I didn't have much hope for myself. More times than I can count, it was her support that kept me going as we laughed and cried our way through this process. My kids have helped me keep my perspective by constantly reminding me that I am no smarter than a 1st grader and by greeting me with smiles, wrestling matches, bad knock-knock jokes, and the occasional punch to the esophagus, all of which can be very energizing after a long day.

Finally, thanks to my RBL lab mates who made the basement a pretty delightful place to work, endured some pretty awful lab-meeting puns, and helped me stay sane.

Table of Contents

List of Figures

List of Tables

List of Appendices

Abstract

Muscle fatigue reduces the force that a muscle can produce and causes sensations of weakness and discomfort. People can adapt to muscle fatigue by adopting new movement patterns and control strategies. These motor adaptations can affect performance and sometimes predispose people to injuries. However, the effects of fatigue are situation-dependent. This research examined how the effects of muscle fatigue are moderated by which muscles are fatigued, the fatigue state, and the sensation of pain. It was expected that these moderating factors would affect the motor adaptations that people use when fatigued, the rate of muscle fatigue, and the risk of error and injury.

Since different joints make different contributions to the completion of movement tasks, fatigue that is localized in different muscle groups is expected to affect movement differently. *Aim 1* compared changes in whole-body movement coordination following fatigue of proximal and distal muscle groups in the upper extremity. Subjects maintained task performance after both proximal and distal fatigue. Proximal fatigue led to widespread movement changes across several joints, but distal fatigue primarily caused changes at the distal joints. The observed changes after proximal fatigue may increase the risk of back pain and injury, while changes after distal fatigue may predispose people to errors in manipulation.

Muscle fatigue is a complex, multifactorial process, and people may adapt to fatigue by changing the movement patterns of many joints. It is difficult to quantify the effects of muscle fatigue on multi-joint coordination. In *Aim 2*, I used principal components analyses to determine how multi-joint coordination changes during and after muscle fatigue. During fatigue, inter-joint

coordination decreased, and subjects utilized a stiffening strategy that may have reduced the complexity of movement. However, these changes began to reverse after cessation of a fatiguing task. The observed changes suggest that people learn novel coordinative patterns as they adapt to muscle fatigue.

Adapting to muscle fatigue is a cognitively demanding process. In working environments, biological stimuli such as pain may compete for limited cognitive resources during movement tasks. *Aim 3* used a goal equivalent manifold (GEM) approach to determine how experimental pain influences the ability to adapt to muscle fatigue. Ischemic muscle pain in the contralateral arm caused people to reduce movement control, but this did not lead to significantly faster fatigue rates. However, order of the painful, and non-painful experimental sessions had a significant effect on fatigue rate. Furthermore, people who exhibit catastrophic thinking used different movement strategies than those who did not exhibit catastrophic thinking.

Together these results demonstrate that the fatigue state of the muscles and the presence of a noxious stimulus moderate the way that people adapt to muscle fatigue. People can adapt to muscle fatigue by modifying their movement patterns, but motor adaptation does not necessarily lead to optimal movement strategies. While motor adaptation did not affect the task outcome in these or previous fatigue studies, the lack of performance deficits is likely attributable to the selection of simple experimental tasks in highly controlled environments. The moderating factors examined here are likely to affect complex fatiguing situations encountered in real world environments where the observed reduction in movement coordination and control could negatively impact task execution and lead to inefficient movement and injury. The current results emphasize the need to better understand how fatigue affects movement in realistic working environments.

CHAPTER 1. Introduction

1.1. Muscle Fatigue and Motor Adaptation

Muscle fatigue is defined as a reduction in the ability of muscle to generate force (De Luca 1984, Gandevia 2001, Enoka et al. 2008). The process of muscle fatigue begins at the onset of muscle activity (Bigland-Ritchie et al. 1984). Muscle fatigue results from a combination of several physiological, neurological, and psychological mechanisms (Enoka et al. 1992). During muscle contractions, depletion of energy substrates (e.g., glycogen, ATP) and accumulation of metabolic wastes (e.g., phosphate, hydrogen ions) in the active muscle cells alters the chemical environment of the muscle (Fitts 1994, Allen et al. 2008). Additionally, the maximum signaling rate of the motor neurons may decline (Bigland-Ritchie et al. 1984). These changes can affect muscle excitation and contraction limiting the contractile strength of muscle fibers. The reduction in strength due to factors distal to the spinal motor neurons is categorized as peripheral muscle fatigue (Davis 1995). Peripheral mechanisms are usually considered the predominant cause of muscle fatigue. However, muscle excitation is dependent on the ability of the central nervous system to voluntarily activate the muscles. Central muscle fatigue is a reduction in muscle force due to insufficient neural signals originating in the central nervous system (Davis 1995). Sensations of discomfort and other afferent feedback from fatiguing muscles can lead to central muscle fatigue in the form of reduced central drive or motor-neuron inhibition (Gandevia 2001).

As individual motor units become fatigued, the central nervous system must activate a greater number of motor units to generate the same force (Marcora 2009), and the motor units are activated in a more synchronized pattern (Chaffin 1973). These changes are detectable using surface electromyography (EMG) which shows an increase in signal amplitude (Bigland-Ritchie

et al. 1986) and a decrease in signal frequency (Hostens et al. 2004) during muscle fatigue. Due to the activation of additional motor units, the efferent signals generated in the central nervous system are larger when the muscles are fatigued. The increase in signal size is perceived by the individual as a sensation of weakness or increased effort, and this perception may eventually contribute to a voluntary or involuntary reduction in force output (Enoka et al. 1992, Marcora 2009).

Due to the physiological and neurological changes that occur during fatigue, muscle fatigue can affect movement in a variety of ways. Muscle fatigue impairs reaction time (Wilder et al. 1996) and proprioception (Myers et al. 1999) and increases force variability (Lorist et al. 2002) and cognitive load (Terrier et al. 2009). Fatigue has also been observed to cause changes in peak joint angles (McDonald et al. 2015), posture (Fuller et al. 2013), and movement variability (Qin et al. 2014). These changes may be a direct result of decreased force output and changes in motor recruitment, or they may represent an adaptive strategy intended to reduce the load on fatiguing muscles.

In some tasks, muscle fatigue impairs task execution (Lyons et al. 2006, Missenard et al. 2008). However, during many tasks people are able to adapt their movement patterns to continue meeting the task goal (Huffenus et al. 2006, Selen et al. 2007, Gates et al. 2008, Fuller et al. 2013, Cowley et al. 2014). In spite of muscle fatigue, people maintain timing accuracy during repetitive sawing (Gates et al. 2008, Cowley et al. 2014) and spatial accuracy during targeted reaching (Fuller et al. 2013), target tracking (Selen et al. 2007), and throwing (Huffenus et al. 2006). The flexibility of the neuromuscular system allows individuals to vary their movements and find a motor solution that maintains task execution (Fuller et al. 2011, Srinivasan et al. 2012). Thus people can adapt to fatigue by changing their inter-muscular (Gorelick et al. 2003, Madeleine et al. 2008) and inter-joint coordination (Côté et al. 2005, Gates et al. 2011), movement control strategies (Selen et al. 2007, Gates et al. 2008), postures (Fuller et al. 2009, Madeleine 2010), or movement kinematics (McDonald et al. 2015).

1.2. Muscle Fatigue and Injury

Muscle fatigue may contribute to injury through various mechanisms (Yoshikawa et al. 1994, Wilder et al. 1996, Sjøgaard 1998, Ebaugh et al. 2006). In particular, muscle fatigue has been associated with the development of repetitive motion injuries (Rempel et al. 1992, Bosch et al. 2012, Roy 2014). These injuries, known as repetitive stress injuries (RSIs) (Latko et al. 1999), are a major cause of lost work days (Baldwin et al. 2006, Bureau of Labor Statistics 2015) (Baldwin et al. 2006). RSIs of the upper extremity cause longer periods of lost work days than any workplace injury except fractures (Bureau of Labor Statistics 2015). In the U.S. and Canada, compensation claims for upper extremity RSIs have been calculated to average up to $8000, nearly twice the average claim (Baldwin et al. 2006). The total cost may be much higher, because many people who experience these injuries may continue their activities with reduced productivity (Baldwin et al. 2006, Roy 2014).

Fatigue may contribute to micro (Friden et al. 1992) or macro-injuries (Mair et al. 1996) within the muscle itself. Additionally, changes in movement coordination, control, and variability during muscle fatigue may alter the magnitude and frequency of mechanical stresses placed on body structures. Thus, muscle fatigue may contribute to the risk of injury in other tissues (Yoshikawa et al. 1994, Ebaugh et al. 2006). Changes in movement patterns or muscle activity can be beneficial when they help individuals to prevent or recover from fatigue and discomfort (Farina et al. 2004, Madeleine et al. 2008, Cote et al. 2010, Srinivasan et al. 2012) or enable people to continue executing a task in the presence of fatigue (Côté et al. 2002, Selen et al. 2007, Gates et al. 2008, Fuller et al. 2009). However, some movement changes predispose people to injury (Sparto et al. 1997, Ebaugh et al. 2006). Muscle fatigue in the back extensors may impair spinal stabilization and thus lead to and back pain (Wilder et al. 1996). Fatigue of the shoulder muscles can decrease humeral external rotation during overhead lifting and thus increase the risk of shoulder impingement syndrome (Ebaugh et al. 2006). Distally, wrist range of motion increased

after shoulder fatigue during sawing (Côté et al. 2002), and force sharing among the fingers was altered by fatigue (Danion et al. 2001). These changes in wrist posture or grasping may affect mechanical forces between the median nerve and surrounding tendons (Armstrong et al. 1979) leading to deformation or compression of the median nerve (Loh et al. 2014, Wang et al. 2014, Cowley et al. 2017). The effects of fatigue and the associated risks vary depending on the task (Bosch et al. 2011, Gates et al. 2011), the individual (Côté et al. 2005, Gates et al. 2008, Fuller et al. 2011), and the muscles that are fatigued (Gorelick et al. 2003, Huffenus et al. 2006, Cowley et al. 2014).

1.3. Location of Muscle Fatigue

The way a person adapts to muscle fatigue may be impacted by a variety of factors, one of which is the location of fatigue. A majority of the aforementioned studies explored changes after fatigue of a single muscle or muscle group. The localization of the fatigue can impact the variety of movement solutions available to the individual. In fact, we previously found that when fatigue is localized in a single muscle group, it has greater effects on movement patterns than fatigue that is widespread in several muscle groups (Cowley et al. 2014). The effects of localized fatigue are also expected to be different for different muscle groups. Indeed, fatigue that was localized in different arm muscles was found to have different effects on inter-joint coordination (Huffenus et al. 2006), presumably because the different joints of the arm have unique, task-specific roles. Proximal joints are used to position the entire arm, while distal joints are used to fine tune the movement to achieve the task goal (Dounskaia 2010). Fatigue that is localized in different arm muscles may differentially impact the way a person can safely modify their movement patterns.

Few studies have systematically examined the effects of fatigue that is localized in different muscle groups and those studies examined simple tasks that involved only a few degrees of

freedom. In a grasp and lift task, fatigue of the gripping muscles caused changes in the coordination of grip and lift forces, but fatigue of the lifting muscles did not (Emge et al. 2014). In a two joint, disc throwing task, fatigue of the elbow extensor muscles caused large changes in joint kinematics and torques, and people used less variable movement patterns after fatigue of wrist muscles (Huffenus et al. 2006). However, the simple disc throwing task does not adequately represent many complex movements that people perform in daily life. Further research is needed to better understand how fatigue of proximal and distal muscles differentially affects multi-joint movement patterns.

1.4. Muscle Fatigue and Coordination

Fatigue may result in a continuous series of small changes at many joints. Several studies have analyzed the effects of fatigue across many degrees of freedom (Côté et al. 2002, Côté et al. 2008, McDonald et al. 2015). For example, during sawing, fatigue of the triceps caused elbow range of motion to decrease and trunk range of motion to increase (Côté et al. 2002). While these changes suggest a change in inter-joint coordination due to fatigue, quantifying movement coordination during multi-joint movements is challenging because numerous (redundant) degrees of freedom contribute to movement. Most previous analyses only examined variables at discreet time points during motion. Therefore, they cannot fully address the problem of movement coordination because they do not explain how multiple degrees of freedom are coordinated to produce a movement. Multivariate statistical analyses such as principal components or factor analysis can be used to assess coordination across many degrees of freedom (Bockemühl et al. 2010). These types of analyses are needed to better understand the effects of muscle fatigue on movement coordination.

1.5. Muscle Fatigue and Movement Variability

During repetitive tasks people may increase or decrease movement variability across time or movement repetitions (Qin et al. 2014, Srinivasan et al. 2014). For instance, when fatigued, people may frequently change their movement (increased variability) as they search for a strategy that relieves fatigued muscles (Fuller et al. 2011, Qin et al. 2014), or they may maintain a more stereotyped movement pattern (decreased variability) to reduce errors (Cowley et al. 2014). Variability may increase at one joint and decrease at another during the same task to maintain task execution and alleviate fatigue (Qin et al. 2014). Clearly, people take advantage of a redundant neuromuscular system to adapt to muscle fatigue.

Movement variability likely has optimal upper and lower limits (Stergiou et al. 2006). In general, greater movement variability is considered beneficial because it limits repeated biomechanical exposure (Mathiassen 2006, Madeleine 2010, Srinivasan et al. 2012). Low variability of muscle activations may be associated with faster fatigue rates (van Dieën et al. 1993, Madeleine et al. 2008). Low variability of inter-joint coordination may increase the risk movement errors (Chiu et al. 2013), and low movement variability has been implicated in the development of musculoskeletal disorders because the same tissues are stressed repeatedly (Mathiassen et al. 2003, Stergiou et al. 2006, Srinivasan et al. 2012). Different working conditions (e.g. work pace or height) (Bosch et al. 2011, Gates et al. 2011, Srinivasan et al. 2014), skill levels (Madeleine et al. 2003), and muscle fatigue conditions (Cowley et al. 2014) affect the way that people can vary their movements.

1.6. Muscle Fatigue, Movement Control, and Task Execution

Daily life tasks require people to meet externally determined movement goals that require various degrees of spatial, temporal, and force accuracy. Muscle fatigue can cause people to

modify the movement control strategies they use to achieve these task goals. In one tracking task, researchers reported evidence of a vicious cycle in which people adapted to muscle fatigue with a strategy that could increase muscle force, thus accelerating the rate of fatigue (Huysmans et al. 2008). In a different tracking task, people adapted to fatigue by adopting a feed-forward control strategy (Selen et al. 2007). This strategy may reduce the rate of muscle fatigue, but it may also increase cognitive effort. The control strategies that people use during fatigue can affect the rate of muscle fatigue and the cognitive demand of the task.

One way to assess movement control is to determine how quickly people respond to deviations away from a task goal. A goal equivalent manifold (GEM) analysis provides a mathematical mapping between body variables and goal errors for a given task (Cusumano et al. 2006). By analyzing the dynamics of the body variables across multiple trials, we can assess how changes in body variables affect goal errors and measure how people control their movements across consecutive cycles (Gates et al. 2008, Dingwell et al. 2013). We previously used this method to demonstrate that people maintain movement timing by exerting greater control over movement distance and speed after localized shoulder muscle fatigue (Cowley et al. 2014). However, the controlled laboratory environments in which most previous fatigue studies were executed limit the amount of information that subjects must process during fatigue and therefore do not replicate many real-world environments where muscle fatigue often occurs.

1.7 Muscle Fatigue and Cognition

In complex, real-world environments, multiple stimuli may demand attention during motor tasks. During muscle fatigue, the central nervous system must monitor changes in the muscles and generate appropriate efferent signals to counteract the effects of fatigue (Demougeot et al. 2011, Monjo et al. 2014). Muscle fatigue can increase the demand for cognitive resources due to

increased central drive (Gandevia 2001) and movement adaptation (Terrier et al. 2009). Thus muscle fatigue can impair simultaneous performance of cognitive tasks (Terrier et al. 2009), and performing cognitive and fatigue tasks simultaneously can increase the rate of fatigue (Mehta et al. 2012). Attentionally-demanding stimuli may interfere with the process of fatigue adaptation and affect the rate of muscle fatigue.

1.8 Muscle Fatigue and Pain

Pain is a salient biological perception that may compete with other stimuli for cognitive resources (Moriarty et al. 2011). When people experience acute pain, they bias attention toward the painful area (Moseley et al. 2005). Thus, pain may limit the cognitive resources available for fatigue adaptation and affect the way that people adapt to muscle fatigue. Changes in motor coordination and control during muscle fatigue involve a process of motor learning (Monjo et al. 2015). Pain may alter this process and thus change the rate and effects of muscle fatigue. When reaching in a force field, pain caused larger movement errors and changed the control strategy that people used, and people retained this movement strategy after removal of the painful stimulus (Lamothe et al. 2014). Pain can enhance motor learning by increasing attention to painful areas of the body (Dancey et al. 2016). People who fear pain may increase their attention to painful stimuli, causing greater pain-related changes (Crombez et al. 1999). In young healthy adults, researchers observed greater declines in muscle strength in the presence of delayed onset muscle soreness in high fear compared to low fear subjects (George et al. 2007, Parr et al. 2012).

Like fatigue, pain can lead people to alter their motor patterns. Many pain adaptations may be intended to reduce stimulation of the painful area (Hodges et al. 2011). Experimental pain can lead people to modify their muscle activation (Ervilha et al. 2004), movement control strategies (Ervilha et al. 2005, Mista et al. 2015), and inter-joint coordination (Seeley et al. 2013) and can

increase the rate of muscle fatigue (Ciubotariu et al. 2004). However, the effects of muscle pain or joint pain may differ from skin pain or other types of pain (Lamothe et al. 2014), and the effects of pain that is localized in the active muscle or limb differ from those of remotely located pain (Dancey et al. 2016). While the effects of local muscle pain during muscle fatigue have been studied in several tasks, the effects of remote pain during muscle fatigue have not been examined.

1.9 Summary of Dissertation

Muscle fatigue is a universal effect of human movement. It is a complex, multifactorial process, and the way that people adapt to muscle fatigue depends on a variety of factors. Fatigue-related changes in movement kinematics, coordination, and control can affect injury risk, performance, and productivity. These effects of fatigue are not always immediately clear. This work will quantify how people change their movement coordination and control during repetitive arm movements in response to different muscle fatigue conditions and discuss the potential implications of these changes. The central hypothesis is that the rate and effects of muscle fatigue will be moderated by characteristics of the task and the individual performing it.

In Chapter 2, the aim was to compare the effects of proximal and distal muscle fatigue on movement coordination. In this study, fourteen (14) healthy adults performed a repetitive, timed wrench turning task before and after fatigue of either the proximal (shoulder flexor) muscles or distal (finger flexor) muscles. Pre/Post fatigue changes in 3-dimensional trunk, shoulder, elbow, and wrist kinematics were compared to determine how proximal and distal fatigue affected multi-joint movement patterns and variability. I expected the results to support the principle of hierarchical control wherein the proximal and distal joints have distinct task functions. I hypothesized that proximal fatigue would cause a significant reorganization of movement kinematics across several joints. In contrast, I expected distal fatigue to primarily affect distal joint

kinematics. I also hypothesized that movement variability would increase after proximal fatigue and decrease after distal fatigue.

The aim of the work recorded in Chapter 3 was to quantify changes in inter-joint coordination due to muscle fatigue. Sixteen (16) healthy adults performed a repetitive ratcheting task before, during, and after fatigue of the shoulder flexor muscles. Joint angle data from 13 degrees of freedom were decomposed into three representative variables using principal components analysis, and the amount of variance explained by each principal component was recorded. I expected the weightings of the joint angles on each principal component to change during fatigue as subjects modified their movement patterns. I hypothesized that coordination would decease during fatigue but that coordination would return to pre-fatigue levels after cessation of the fatiguing task while the variable weightings would remain different from pre-fatigue values.

The aim of the work presented in Chapter 4 was to analyze the effects of pain on movement control during a fatiguing task. Twenty-two (22) healthy subjects performed the same repetitive task with the dominant arm to voluntary exhaustion on two separate days. On one day, they simultaneously wore a blood pressure cuff on the non-dominant arm to induce ischemic pain. I expected that fatigue would cause people to modify their movement control strategies. I hypothesized that people would exert less control and commit larger movement errors during the pain session compared to the no pain session. I also hypothesized that people would reach voluntary exhaustion earlier in the pain session than the no pain session. Finally, I hypothesized that the effects of pain would be larger in people who exhibited high pain catastrophizing compared to low pain catastrophizing individuals.

Chapter 5 is a discussion of how different environmental and individual characteristics influence how people adapt to muscle fatigue and affect task execution. This work makes three unique contributions to our understanding of muscle fatigue adaptations. First, it systematically

compares changes in trunk and arm movement kinematics and variability following fatigue of different muscle groups. Second, this work quantifies how people modify their inter-joint coordination in response to fatigue during multi-joint movements. Third, this work determines how pain affects movement control during muscle fatigue. These contributions help to identify conditions that predispose people to performance deficits during fatiguing tasks.

CHAPTER 2. Proximal and Distal Muscle Fatigue Differentially Affect Movement Coordination[1]

2.1 Abstract

Muscle fatigue can cause people to change their movement patterns and these changes could contribute to acute or overuse injuries. However, these effects depend on which muscles are fatigued. The purpose of this study was to determine the differential effects of proximal and distal upper extremity muscle fatigue on repetitive movements. Fourteen subjects completed a repetitive ratcheting task before and after a fatigue protocol on separate days. The fatigue protocol either fatigued the proximal (shoulder flexor) or distal (finger flexor) muscles. Pre/Post changes in trunk, shoulder, elbow, and wrist kinematics were compared to determine how proximal and distal fatigue affected multi-joint movement patterns and variability. Proximal fatigue caused a significant increase (7 ˚, $p < 0.005$) in trunk lean and velocity, reduced humeral elevation (11 ˚, $p < 0.005$), and increased elbow flexion (4 ˚, $p < 0.01$). In contrast, distal fatigue caused small but significant changes in trunk angles (2 ˚, $p < 0.05$), increased velocity of wrench movement relative to the hand (17 ˚/s, $p < 0.001$), and earlier wrist extension (4 %, $p < 0.005$). Movement variability increased at proximal joints but not distal joints after both fatigue protocols ($p < 0.05$). Varying movements at proximal joints may help people adapt to fatigue at either proximal or distal joints. The identified differences between proximal and distal muscle fatigue adaptations could facilitate risk assessment of occupational tasks.

[1] A version of this chapter is published as Cowley, J.C. and D.H. Gates (2017) "Proximal and distal muscle fatigue differentially affect movement coordination." PloS One 12(2): e0172835.

2.2 Introduction

In 2014, more than 350,000 people in the U.S. missed work due to work related musculoskeletal disorders (Bureau of Labor Statistics 2015). Such injuries are caused either by a single event (acute) or the accumulation of repetitive stress (overuse) in a given area. Muscle fatigue has been implicated in both acute and overuse injuries. Fatigue impairs muscle strength (Enoka et al. 1992), reaction time (Wilder et al. 1996), and proprioception (Myers et al. 1999). Due to these changes, muscle fatigue may limit the ability to respond to sudden perturbations and can cause people to alter their kinematic patterns. Changes in kinematics can affect the distribution of forces on the body, leading to injuries.

Many factors influence the way that people change their movement patterns after fatigue. In particular, fatigue that is localized in a specific muscle group causes greater changes in muscle coordination (Gorelick et al. 2003) and movement amplitude and speed (Cowley et al. 2014) compared to fatigue that is widespread over several muscles. The direct relationship between muscle fatigue, movement, and injury is difficult to discern because the conditions that lead to fatigue and the activities performed while fatigued vary across worksites. Many complex work environments require people to perform a variety of tasks in no specific order throughout a work period. These kinds of jobs (e.g. construction, retail, health services) are among those with the highest rates of work related musculoskeletal disorders (Bonauto et al. 2006). In these working conditions, tasks that cause localized fatigue of one muscle group may be closely followed by different tasks. Thus, localized muscle fatigue can affect movement kinematics during various tasks.

Changes in kinematics due to muscle fatigue depend on which joints and muscles are affected (Côté et al. 2005, Huffenus et al. 2006) because different joints (and therefore muscles) are used for different task-specific objectives (Bernstein 1967, Dounskaia 2010). Proximal joints are generally responsible for the overall movement pattern of the arm, while distal joints primarily

fine-tune movements to achieve the task goal (Dounskaia 1998, Dounskaia 2010). Occupational tasks may lead to fatigue of proximal muscles (e.g. overhead lifting), distal muscles (e.g. assembly tasks), or simultaneous proximal and distal fatigue (e.g. overhead assembly). The unique functions of proximal and distal joints suggest that fatigue of proximal and distal muscles will have different effects on the movement patterns people use.

During multi-joint movement tasks, proximal or distal muscle fatigue has the potential to affect all the degrees of freedom in the kinematic chain (Côté et al. 2005, Qin et al. 2014). During repetitive sawing, fatigue of the elbow extensors caused the range of motion of the shoulder, trunk, and wrist to increase, while the elbow range of motion decreased (Côté et al. 2002). In a ball-throwing task, fatigue of the finger flexors and extensors caused motion of the forearm and hand to become more synchronized (Forestier et al. 1998). Generally, prior work has shown that proximal muscle fatigue causes widespread changes in joint angles and range of motion (Côté et al. 2002, Côté et al. 2005, Qin et al. 2014), and distal muscle fatigue causes changes in the timing of joint motion (Forestier et al. 1998). However, differences in task objectives, muscles fatigued, and types of analyses used limit the ability to compare the results of proximal and distal fatigue from different studies. One study examined the effects of proximal and distal fatigue separately during the same planar disc throwing task (Huffenus et al. 2006). While throwing performance was not affected by either condition, fatigue of the elbow flexors resulted in larger changes in joint kinetics and kinematics, whereas wrist extensor fatigue primarily caused changes in the timing of joint motion. Although these results support the distinct differences in fatigue of proximal and distal joints, the analysis was limited to a self-paced, planar, two degrees of freedom movement. Occupational tasks often include repetitive movements that involve many degrees of freedom and external timing constraints. The results of previous work may not apply to more complex multi-joint movements like those performed in working environments.

Proximal and distal muscle fatigue may also differentially affect kinematic variability. Low

variability can impair the ability to respond to perturbations and may cause tissues to be stressed repeatedly (Hamill et al. 1999), thus increasing the risk of soft tissue injury. In contrast, high variability can alleviate the load on tissues by distributing the stress to different areas (Mathiassen 2006) but may also increase the risk of errors or acute injury by increasing the likelihood of extreme movements (Sparto et al. 1997). Fatigue may cause variability to increase at affected joints, and decrease at unaffected joints. For example, shoulder fatigue led to increased kinematic variability of the shoulder and decreased variability at distal joints during reaching movements (Fuller et al. 2011) and assembly tasks (Qin et al. 2014). While this may imply that variability specifically increases at affected joints and decreases at unaffected joints, it is also possible that increasing variability at proximal joints and decreasing variability at distal joints is a generic strategy used to compensate for muscle fatigue.

The purpose of this study was to determine the effects of localized fatigue of proximal and distal upper extremity muscles on joint kinematics and kinematic variability during a repetitive, timed, multi-joint task. There are numerous occupational tasks, and these can require varying degrees of proximal and distal joint movement. In order to compare the effects of proximal and distal fatigue on movement patterns during the same task, I selected a ratcheting task that involved a similar dynamic range of motion at the shoulder and wrist joints. Subjects completed the repetitive ratcheting task in time with a metronome before and after fatigue of either the shoulder flexors (proximal) or finger flexors (distal). The proximal (shoulder and elbow) joints were responsible for the overall ratcheting movement pattern, while the distal (finger and wrist) joints were responsible for stabilizing the wrench on the bolt. I hypothesized that fatigue of the shoulder flexors would cause greater changes in multi-joint kinematic patterns compared to fatigue of the finger flexors because proximal joints control the overall position of the arm. Secondarily, I hypothesized that movement variability of the trunk, shoulder and elbow would increase after proximal fatigue and that variability of the wrist and elbow would decrease after distal fatigue.

2.3 Experimental Design

2.3.1 Subjects

Fourteen (7 female) healthy, right-handed adults participated in this study. Their mean age and BMI were 27 ± 13 (range: 18 – 64) years and 24.4 ± 3.3 kg/m^2, respectively. Handedness was verified using a modified version of the Edinburgh Inventory (Oldfield 1971). Individuals younger than 18, older than 65, or with any history of serious musculoskeletal, cardiovascular, neurological, respiratory, or visual problems were excluded.

2.3.2 Experimental Protocol

Prior to participation, subjects answered a series of questions about their habitual activity and tool use. They then completed two experimental sessions approximately one week apart in random order. Both sessions followed the same general protocol (Fig. 2.1). At the beginning of each session, baseline shoulder flexion and grip strength measures were recorded. Subjects then performed a pre-test consisting of three, one minute intervals of a repetitive ratcheting task (Fig. 2.1A) alternating with one minute rest periods (Fig. 2.1B). Following the pre-test, subjects completed one of two fatigue protocols to fatigue either proximal or distal muscles. Finally, subjects completed a post-test by performing three, one minute intervals of a repetitive work task, alternating with one minute periods in which they continued the fatiguing task. This protocol was designed to limit the development of muscle fatigue in the non-targeted muscle group during ratcheting while maintaining fatigue in the targeted muscle group. Throughout each session, muscle strength and ratings of perceived exertion (RPE) were assessed at regular intervals to measure the progression of fatigue (Fig. 2.1B).

Subjects performed a repetitive ratcheting task before and after fatigue. The ratcheting task was designed to require similar motion amplitude at the shoulder and wrist. In this task, subjects stood in front of a board placed 60% of arm length anterior to the toes while grasping a ratcheting

socket wrench (~ 0.4 kg) in the right hand (Fig. 2.1A). Subjects repeatedly rotated a bolt placed at eye level at 1 Hz. Subjects were instructed to end each rotation in time with a metronome beat but were not given explicit instruction on how far to rotate the bolt. The primary wrench movement in this task is generated at the shoulder and elbow joints using combined humeral rotation and elevation, and forearm supination. The joints of the wrist and hand play a stabilizing role to ensure

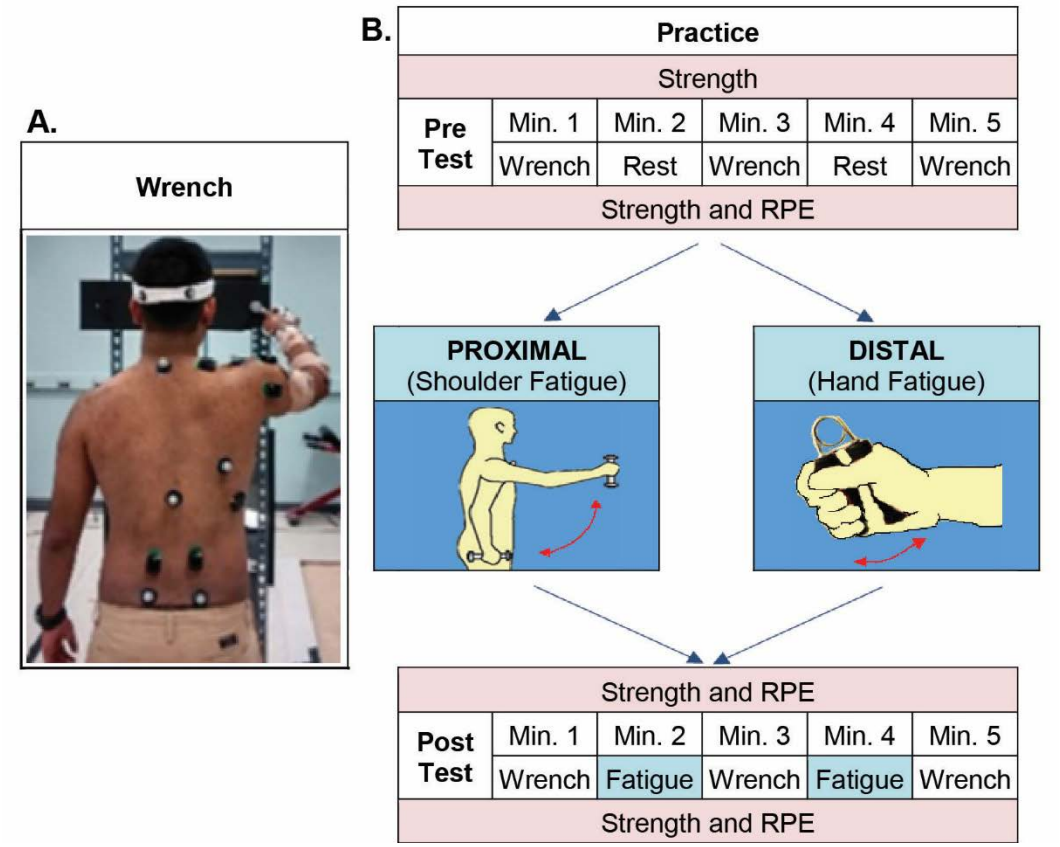


Figure 2.1. Proximal and distal fatigue procedure.

(**A**) Ratcheting Task. Subjects stood in front of a board placed at 60% of arm length in front of the toes, and rotated a bolt placed through the board at eye level using a ratcheting socket wrench. The torque required to rotate the bolt clockwise was ~ 4 Nm. (**B**) Experimental Session. Subjects performed three trials of a repetitive ratcheting task pre and post fatigue. Two different fatigue protocols (Proximal/Distal) were performed on separate days at least one week apart. Subjects performed the fatigue task during minutes 2 and 4 of the post-test to prevent recovery in the targeted muscle group. The order of test days was randomized. (**C**) Illustration of the wrench coordinate system.

that the force generated proximally is directed properly to rotate the bolt. Specifically, the hand and wrist must maintain the appropriate position of the wrench to prevent the bolt from slipping out of the socket. To reduce learning effects, subjects practiced the ratcheting task for one minute before each data collection.

Maximum isometric shoulder flexor and grip strength were measured using hand-held dynamometers. Peak shoulder flexion force (N) was measured with subjects sitting on a stool with the right arm raised to 90 degrees of shoulder flexion. Subjects pushed upward against a hand-held load cell (Lafayette Instruments, Lafayette, IN) for 4 s. A digital output displayed the peak force in Newtons. Grip strength (kg) was measured as the peak force obtained during 4 s of maximal gripping using a hydraulic hand dynamometer (Baseline, White Plains, NY). The maximum force was displayed on a dial measurement gauge in half-kilogram increments. The average of three peak forces was taken as the subject's maximum voluntary contraction (MVC). MVC at subsequent time intervals was expressed as a percentage of its initial value.

Static and dynamic muscle contractions may differentially affect muscle properties and fatigue (Masuda et al. 1999). Therefore, repetitive dynamic tasks were used for the proximal and distal fatigue protocols. The proximal fatigue protocol (Fig. 2.1B) was designed to fatigue the shoulder flexors. Subjects repeatedly raised and lowered a weight (~10 % max shoulder flexion strength) to shoulder height in the sagittal plane with the right arm straight at a frequency of 0.5 Hz. A custom strap was wrapped around the fingers to hold the hand closed and reduce the effort of distal muscles. The distal fatigue protocol (Fig. 2.1B) was designed to fatigue the intrinsic and extrinsic finger and wrist muscles. The right arm was placed in a static resting position, and subjects repeatedly squeezed a spring-loaded grip trainer with their right hand at a frequency of 1 Hz. A reflective marker was used to verify that all subjects compressed the spring, but the amount of compression was not enforced. During both fatigue tasks, subjects were instructed to match their movement phase (up-down, squeeze-release) with a metronome. Fatigue was verified using

ratings of perceived exertion (RPE) on the Borg CR-10 scale (Borg 1982). Subjects performed the fatigue tasks for three minutes or until they felt that they could no longer continue. If at the end of three minutes, a subject's RPE was < 8, the subject was asked to continue the task for another three minutes or until they could not continue.

The motion of six body segments and the wrench was tracked at 120 Hz with a 16 camera motion capture system (Motion Analysis, Santa Rosa, CA) using 34 reflective markers. Pelvis motion was tracked using markers placed bilaterally on the anterior and posterior superior iliac spines. The trunk was tracked using markers on the xiphoid process, sternal notch, seventh cervical vertebra, and eighth thoracic vertebra. To track head motion, subjects wore a headband with bilateral anterior and posterior markers attached approximately in a horizontal plane. Clusters of four markers each were used to track arm and forearm motion. The hand was tracked using markers on the third and fifth metacarpal heads, diaphysis of the second metacarpal, and base of the third metacarpal. Anatomical markers were also placed on the acromion process, medial and lateral humeral epicondyles, radial and ulnar styloids, and a reference marker was placed over the right scapula. To measure the effects of fatigue on wrench movement and task execution, the position of the wrench was tracked using four reflective markers attached to the wrench (Fig. 2.1C). Muscle activity in the right arm and trunk was recorded at 1200 Hz using 13 wireless electrodes (Delsys, Boston, MA) placed on right and left erector spinae and right side latissimus dorsi, trapezius, pectoralis major, anterior, middle, and posterior deltoid, triceps, biceps, wrist flexors, wrist extensors, and thenar muscles.

2.4 Data Analysis

A 6-segment model was created in Visual 3D (CMotion, Germantown, MA) using marker positions and joint centers, as described in (Gates et al. 2016). Trunk-pelvis, shoulder, elbow, and

wrist kinematics were calculated using Euler angles with rotation sequences recommended by the International Society of Biomechanics (Wu et al. 2005). In this convention, three planes of shoulder movement are defined as 1) humeral plane angle which approximately corresponds to horizontal adduction/abduction, 2) humeral elevation angle, and 3) humeral internal/external rotation. In the current work, all angles are labelled according to the positive direction of movement to improve clarity. For example, negative wrist flexion, or trunk right lean angles represent wrist extension and trunk left lean, respectively. The wrench-lab angle was calculated using an X-Y-Z rotation sequence, and the wrench-hand angle was calculated using a Z-Y-X rotation sequence (Fig. 2.1C).

Movement cycles were identified as the time between consecutive wrench-lab X angle minima (Fig. 2.2A) such that the start and end of a movement occurred with the wrench at its top position. Data was time normalized to 101 points (0 to 100% of the movement cycle. I calculated the maximum and minimum angle, and the magnitude and timing (% movement cycle) of peak joint velocity for each movement. Variability of the movement pattern was calculated as MeanSD (Dingwell et al. 2006): the average standard deviation of the joint angle across the movement cycle. Kinematic data were averaged across all movements (3 minutes).

EMG data were bandpass filtered to a range between 20 and 450 z. The instantaneous mean power frequency (IMPF) was calculated using a continuous wavelet transform algorithm with a Daubechies (‘db5’) wavelet (MATLAB 2015a, Mathworks, Natick, MA) as outlined in (Hostens et al. 2004, Gates et al. 2011). The mean IMPF value was obtained for each movement cycle of the fatigue protocol. The rate of decrease in frequency was calculated using the average IMPF from each cycle (Cowley et al. 2014). The IMPF was expected to decrease because muscle fatigue causes motor units to contract more synchronously leading to a decrease in high frequencies in the EMG signal (De Luca 1997, Gates et al. 2011).

2.5 Statistical Analysis

One sample t-tests were used to determine whether the IMPF slopes were less than zero. MVCs and RPEs were compared using 2-factor repeated measures ANOVAs to test for differences due to fatigue location (proximal vs. distal) and measurement time (pre, fatigue, post). For wrench variables (rotation, repetitions, variability, movement time, and velocity), 2-factor repeated measures ANOVAs were used to test for differences in performance due to fatigue location (proximal vs. distal) and fatigue state (pre vs. post). For each joint (trunk-pelvis, shoulder, elbow, wrist, wrench-hand), a series of 2-factor (PROX/DIST × PRE/POST) repeated measures MANOVAs was used to test for differences in joint angle, angular velocity, timing, and variability. For each significant MANOVA, univariate statistics were obtained. Mauchly's test of sphericity was used to test the assumption of equal variance. When Mauchly's test was significant, a Greenhouse-Geiser correction was applied to the F statistic and $\chi 2$ was reported. Significant interactions were further examined using estimated marginal means with a Bonferroni adjustment for multiple comparisons. Significance level was set at $p < 0.05$ for all comparisons.

2.6 Results

2.6.1 Muscle Fatigue

All subjects reached an RPE $\geq$ 8 during the fatiguing tasks. During shoulder fatigue, two subjects stopped before 3 minutes, seven subjects, were fatigued after 3 minutes, and five subjects continued longer than 3 minutes. During the hand fatigue task, four subjects stopped before 3 minutes, seven subjects were fatigued after 3 minutes, and 3 subjects continued longer than 3 minutes. No subject continued either task longer than 6 minutes. There was a main effect of time point ($F[2,12] = 118.131$; $p < 0.001$) and a PROX/DIST × time point interaction effect for RPE ($\chi^2 = 7.124$, $p = 0.028$; $F[1.382,17.96] = 6.564$, $p = 0.013$). During the post-test RPE was higher than the pre-test and lower than fatigue ($p < 0.005$). However there were no significant differences between sessions at any time point ($p = 0.054$; Fig. 2.2A).

During the hand fatigue task, IMPF slopes were negative for all muscles ($p < 0.05$) except anterior deltoid ($p = 0.751$). During the shoulder fatigue task, IMPF slopes were negative for all muscles ($p < 0.03$) except thenar muscles ($p > 0.417$). MVCs declined by about 20% after both proximal and distal fatigue ($F[2, 12] = 98.27$; $p < 0.001$). There was a PROX/DIST × time point interaction for MVC ($\chi^2 = 8.136$, $p = 0.017$; $F[1.34, 17.422] = 7.51$, $p = 0.009$). After the post-test, shoulder flexion MVC (68 ± 7%) was lower than grip MVC (78 ± 10%, $p = 0.005$). Shoulder flexion and grip MVCs did not differ at any other time point ($p > 0.19$; Fig. 2.2B and 2C). In the

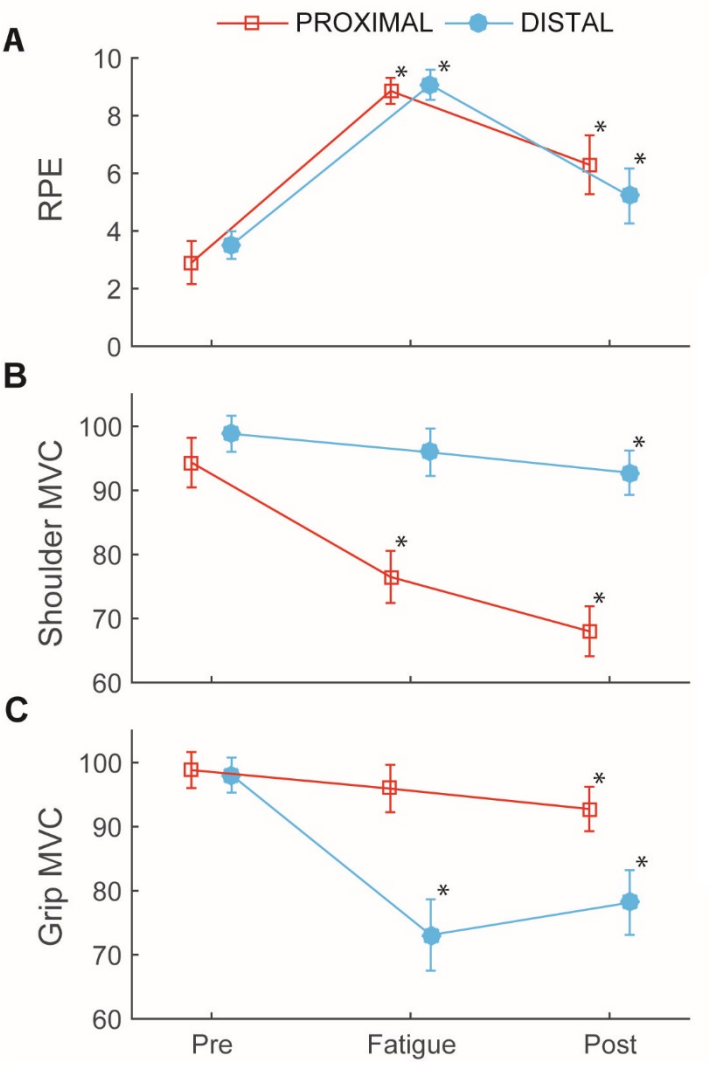


Figure 2.2. Measures of muscle fatigue during proximal and distal fatigue tasks.

(**A**) Average ratings of perceived exertion (RPE), (**B**) shoulder flexion maximum voluntary contraction (MVC), and (**C**) grip MVC for the proximal (squares) and distal (circles) fatigue sessions after the pre-test, fatigue, and post-test on each day. MVCs are reported as a percentage of the initial MVC. Error bars represent 95% confidence intervals. * indicates a difference from baseline strength.

non-targeted muscle group, MVCs declined by about 5% from baseline to the end of the session ($F[2, 11] = 7.745$, $p = 0.008$). There was no PROX/DIST × time point interaction in non-targeted muscles ($F[2, 11] = 1.323$, $p = 0.306$) (Fig. 2.2B and 2C).

2.6.2 Task Execution

There were no differences in movement time or peak speed after proximal or distal fatigue ($F[1,13] < 3.659$; $p > 0.05$) (Fig. 2.3). The wrench angle at the top position was ~ 2 degrees lower after fatigue ($F[1, 13] = 4.701$, $p = 0.049$; Fig. 2.3A). After fatigue, MeanSD for wrench-lab X (rotation) angle was greater ($F[1, 13] = 25.611$, $p < 0.001$), and subjects completed ~3 fewer

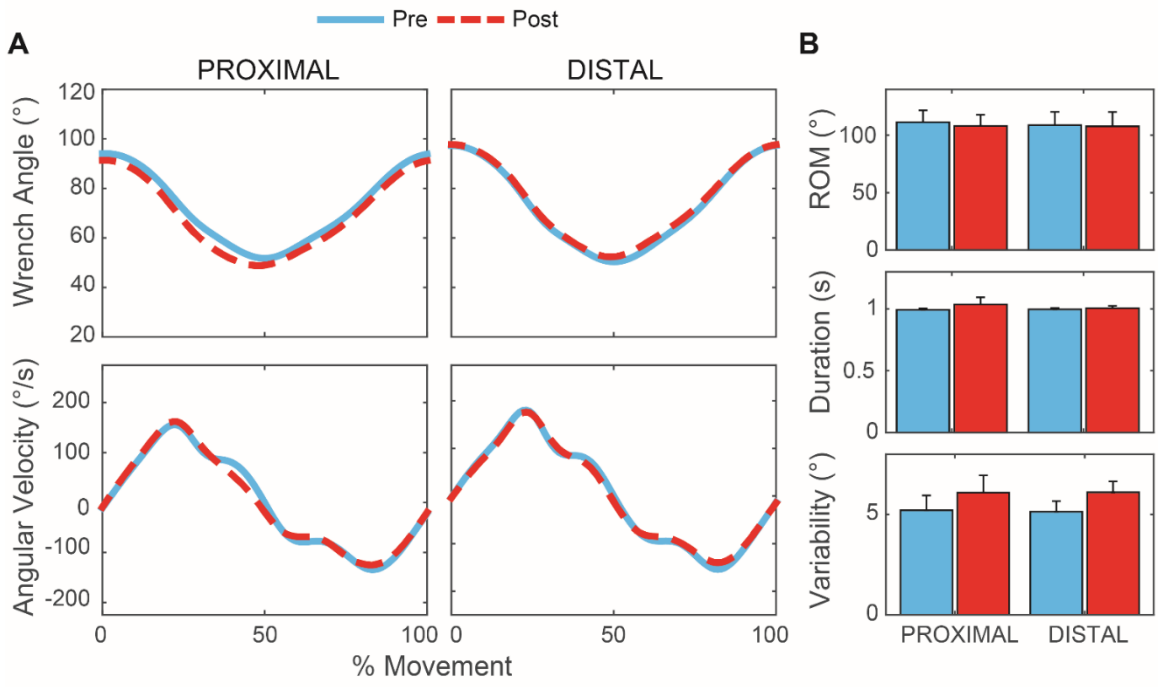


Figure 2.3. Ratcheting task execution pre and post fatigue.

(**A**) Average position and angular velocity of the wrench pre (blue) and post (red) fatigue across all subjects are shown for proximal and distal fatigue. Data are normalized to 100% of the movement cycle (top position to top position). (**B**) The average range of motion (top) and movement duration (middle) of the wrench cycles did not change, but wrench rotation variability (MeanSD) increased after both fatigue protocols (bottom). Error bars show 95% confidence intervals.

repetitions per minute ($F[1, 13] = 8.242$. $p = 0.013$). The amplitude of wrench rotation was not affected by fatigue ($F[1, 13] = 3.659$, $p = 0.078$; Fig. 2.3B). There were no differences between sessions and no significant PROX/DIST × PRE/POST interactions.

2.6.3 Maximum joint angles

For peak joint angle, MANOVAs showed PROX/DIST × PRE/POST interaction effects on the trunk ($F[6, 8] = 10.304$), shoulder (($F[6, 8] = 11.956$), and elbow joints ($F[4, 10] = 9.566$) ($p < 0.005$). Univariate analyses of these effects were significant for trunk lean, rotation and extension, humeral elevation and rotation, and elbow flexion ($F[1, 13] > 4.65$; $p < 0.05$). Humeral elevation decreased more after proximal (Pre: 101 ± 11°; Post: 90 ± 13°; $p < 0.001$) than distal fatigue (Pre: 103 ± 9°; Post: 102 ± 9°; $p = 0.003$) (Fig. 2.4). Trunk left rotation decreased after proximal fatigue, (Pre: 5 ± 5°; Post: 4 ± 6°; $p = 0.006$) but increased after distal fatigue (Pre: 5 ± 4°; Post: 7 ± 4°; $p = 0.037$). Generally changes were smaller after proximal than distal fatigue ($p < 0.02$; Fig. 2.4). Significant results from univariate analyses are summarized in Table 2.1.

2.6.4 Joint angular velocity

Results from MANOVAs showed main effects of fatigue on peak velocity for shoulder ($F[6, 8] = 10.673$, $p = 0.002$), elbow ($F[4, 10] = 7.568$, $p = 0.004$), and wrist ($F[4, 10] = 4.626$) ($p = 0.023$). There were also PROX/DIST × PRE/POST interaction effects on trunk ($F[6, 8] = 6.159$; $p = 0.011$) and wrench-hand velocity ($F[3, 11] = 6.159$; $p = 0.016$). There was a greater increase in trunk lean velocity after proximal (Pre: -9 ± 4°/s; Post: -15 ± 7°/s; $p < 0.001$) than distal fatigue (Pre: -9 ± 3°/s; Post: -11 ± 4°/s; $p = 0.015$). The wrench-hand Z angle had higher velocity after distal (Pre: 83 ± 34°/s; Post: 100 ± 34°/s; $p < 0.001$) but not proximal fatigue (Pre: 93 ± 28°/s; Post: 88 ± 27°/s; $p = 0.319$) (Fig. 2.5). Significant results are summarized in Table 2.2.

Table 2.1. Peak joint angles.
Maximum joint angles (degrees) are given as mean (standard deviation) across subjects. Probability statistics are for univariate ANOVAs.

		Proximal		Distal		P-value			
Joint	**Angle***	**Pre**	**Post**	**Pre**	**Post**	**Pre/Post**	**Prox/Dist × Pre/Post**	**Proximal#**	**Distal#**
Trunk	Right Lean	6 (2)	**13 (4)**	6 (2)	**8 (2)**	< 0.001	< 0.001	< 0.001	0.003
	Right Rotation	5 (5)	**4 (6)**	5 (4)	**7 (4)**		0.017	0.006	0.037
	Extension	4 (5)	**7 (4)**	4 (5)	4 (5)	< 0.001	0.001	< 0.001	0.201
Shoulder	Humeral Plane Angle	61 (12)	60 (12)	64 (13)	63 (12)		0.057		
	Humeral Elevation	101 (11)	**90 (13)**	103 (9)	**102 (9)**	< 0.001	< 0.001	< 0.001	0.003
	Internal Rotation	-40 (10)	**-45 (9)**	-42 (9)	-41 (8)	0.031	0.004	0.001	0.506
Elbow	Pronation	-18 (18)	-14 (17)	-20 (18)	-21 (16)				
	Flexion	76 (8)	**80 (11)**	76 (9)	75 (9)	0.049	0.010	0.008	0.332
Wrist	Ulnar Deviation	30 (11)	30 (10)	23 (12)	24 (12)				
	Flexion	-26 (13)	-26 (13)	-26 (9)	-28 (10)				
Wrench-hand	X	133 (11)	134 (11)	131 (10)	130 (10)				
	Y	13 (17)	14 (16)	11 (14)	12 (13)				
	Z	79 (18)	77 (18)	73 (17)	73 (19)				

*Angle titles refer to the positive direction of movement.
# Indicates post hoc pre/post comparison for proximal or distal fatigue only.
Bold values indicate a significant pre/post difference.

Table 2.2. Peak joint angular velocities.
Maximum joint angular velocities (degrees/second) are given as mean (standard deviation) across subjects. Probability statistics are for univariate ANOVAs.

		Proximal		Distal		P-value			
Joint	**Angle***	**Pre**	**Post**	**Pre**	**Post**	**Pre/Post**	**Prox/Dist × Pre/Post**	**Proximal#**	**Distal#**
Trunk	Right Lean	-9 (4)	**-15 (7)**	-9 (3)	**-11 (4)**	< 0.001	< 0.001	< 0.001	0.015
	Right Rotation	-15 (6)	**-22 (10)**	-15 (5)	**-17 (6)**	< 0.001	0.003	< 0.001	0.045
	Extension	-8 (3)	**-12 (6)**	-8 (3)	-10 (4)	< 0.001	0.047	0.001	0.091
Shoulder	Humeral Plane Angle	141 (49)	151 (56)	146 (60)	141 (54)				
	Humeral Elevation	126 (37)	113 (32)	140 (45)	127 (36)	0.009			
	Internal Rotation	-144 (40)	-164 (57)	-164 (41)	-164 (48)	0.068	0.095		
Elbow	Pronation	200 (67)	180 (55)	188 (56)	176 (53)	0.022			
	Flexion	93 (33)	102 (30)	94 (33)	101 (35)	0.009			
Wrist	Ulnar Deviation	146 (40)	137 (42)	139 (36)	136 (38)	0.007			
	Flexion	-143 (64)	-143 (61)	-131 (43)	-146 (48)				
Wrench-hand	X	67 (37)	68 (27)	62 (21)	66 (18)				
	Y	142 (49)	145 (46)	140 (50)	144 (59)				
	Z	93 (28)	88 (27)	83 (34)	**100 (34)**	0.09	0.001	0.319	< 0.001

*Angle titles refer to the positive direction of movement.
# Indicates post hoc pre/post comparison for proximal or distal fatigue only.
Bold values indicate a significant pre/post difference.

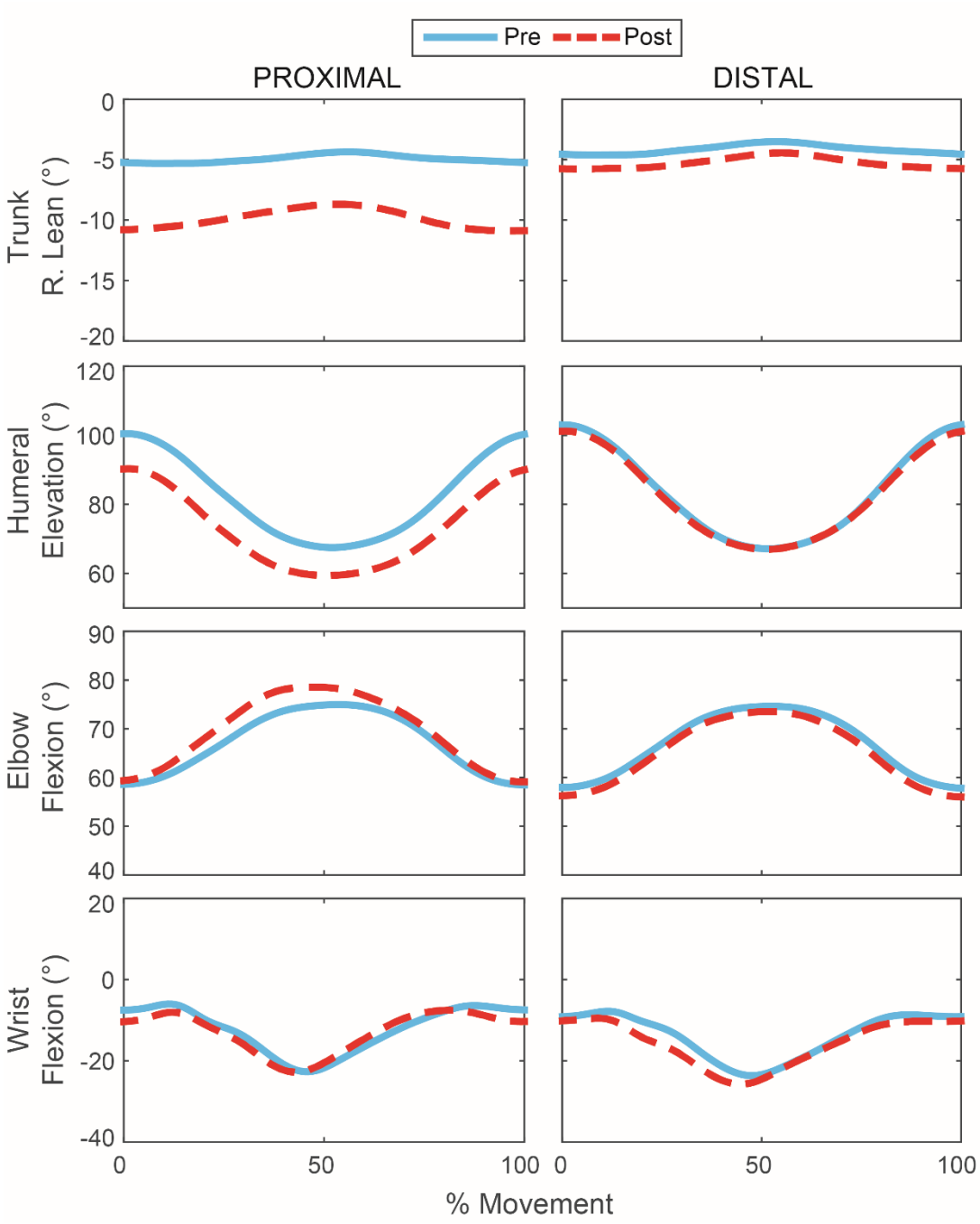


Figure 2.4. Selected joint kinematics pre and post fatigue.

Average joint angles across subjects for the ratcheting motion pre (blue) and post (red) two different fatigue protocols. Angles are normalized to 100% of the movement cycle (top position to top position). The angles shown represent those most affected by fatigue.

2.6.5 Joint Movement Timing

MANOVAs revealed a significant main effect of fatigue on time of peak velocity for the elbow ($F[2, 12] = 5.135$, $p = 0.024$). Univariate analyses showed that elbow supination peak time was earlier after fatigue on both days ($p = 0.01$). There was a PROX/DIST × PRE/POST interaction for the wrist ($F[2, 12] = 10.815$, $p = 0.002$). Univariate analyses showed an interaction effect for wrist extension ($p = 0.001$). Peak wrist extension velocity occurred earlier after fatigue. This effect was larger for distal (Pre: 30.1 ± 5.5%; Post: 28.9 ± 5.7%; $p = 0.001$) than proximal fatigue (Pre: 32.7 ± 5%; Post: 28.6 ± 6.5%;

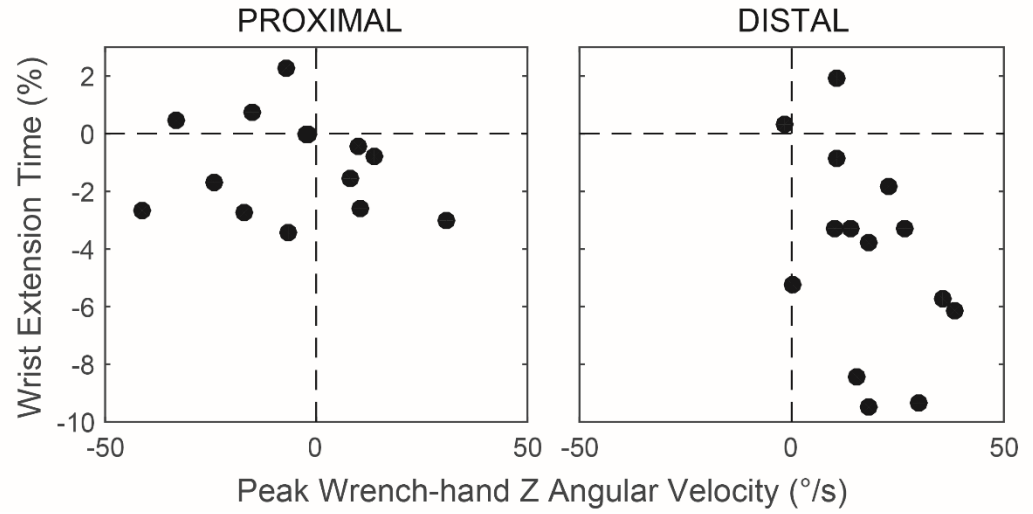


Figure 2.5. Effect of distal fatigue on distal joint motion.

The change (post - pre fatigue) in the peak angular velocity of the wrench relative to the hand about the wrench Z axis and the timing of peak wrist extension velocity for proximal and distal fatigue. Positive values indicate an increase after fatigue.

2.6.6 Joint variability

Results from MANOVAs showed main effects of fatigue on MeanSD for trunk ($F[3,11] = 15.351$, $p < 0.001$), shoulder ($F[3, 11] = 7.481$, $p = 0.005$), elbow ($F[2, 12] = 6.077$, $p = 0.015$), and wrench-hand angles ($F[3, 11] = 4.179$, $p = 0.033$). ANOVAs for these tests showed an increase in MeanSD after fatigue for all planes of trunk and shoulder motion ($p < 0.005$) and in elbow

flexion ($p = 0.01$), but there were no significant changes for wrench-hand angles ($p > 0.25$). There was a PROX/DIST × PRE/POST interaction for trunk MeanSD ($F[3, 11] = 4.707$, $p = 0.024$). Univariate tests showed significant interaction effects for trunk lean ($p = 0.008$) and extension ($p = 0.002$). For these angles, MeanSD was larger after proximal ($p < 0.001$) than distal fatigue ($p < 0.025$; Fig. 2.6; Table 2.3).

Table 2.3. Joint variability.
MeanSD for each joint angles is given as the mean (standard deviation across subjects. Probability statistics are for univariate ANOVAs.

		Proximal		**Distal**		**P-value**			
Joint	Angle*	Pre	Post	Pre	Post	Pre/Post	Prox/Dist × Pre/Post	Proximal[#]	Distal[#]
Trunk	Right Lean	1.5 (0.5)	**3.2 (1.3)**	1.5 (0.3)	**1.9 (0.8)**	< 0.001	0.008	< 0.001	0.025
	Right Rotation	1.3 (0.4)	2 (0.7)	1.2 (0.3)	1.5 (0.4)	0.001	0.069		
	Extension	1.3 (0.4)	**2.6 (0.9)**	1.3 (0.4)	**1.6 (0.5)**	< 0.001	0.002	< 0.001	0.012
Shoulder	Humeral Plane Angle	4.6 (1.3)	6 (1.6)	4.4 (0.9)	5 (1.1)	0.004			
	Humeral Elevation	3.8 (1.4)	5.3 (1.7)	3.6 (0.8)	3.8 (0.8)	0.004			
	Humeral Internal Rotation	3.5 (0.6)	4.4 (0.9)	3.6 (0.7)	4 (0.7)	< 0.001			
Elbow	Pronation	5.8 (2.1)	5.5 (1.9)	6.2 (2.8)	6.2 (3)				
	Flexion	4.4 (2)	5.6 (1.1)	4.3 (1)	5.4 (1.8)	0.010			
Wrist	Ulnar Deviation	3.9 (1.4)	3.8 (1.2)	3.8 (1.1)	3.7 (0.8)				
	Flexion	6.3 (1.9)	6.1 (1)	6.1 (2.5)	6.3 (2)				
Wrench-hand	X	3.2 (1.4)	3.1 (1.1)	3.1 (1.6)	3.9 (2)	0.294			
	Y	4.7 (1.8)	5 (1.7)	4.4 (1.4)	4.8 (1.3)	0.288			
	Z	6.9 (2.6)	6.4 (2)	7.2 (3.2)	7.5 (2.5)	0.768			

*Angle titles refer to the positive direction of movement.
[#] Indicates post hoc pre/post comparison for proximal or distal fatigue only.
Bold values indicate a significant pre/post difference.

2.7. Discussion

This study compared the differential effects of proximal and distal muscle fatigue on movement patterns during a repetitive ratcheting task. The relative muscle strength of the non-targeted muscle group did not differ at any measurement point suggesting that the ratcheting task had a similar effect on proximal and distal muscles in the absence of a fatigue intervention. The

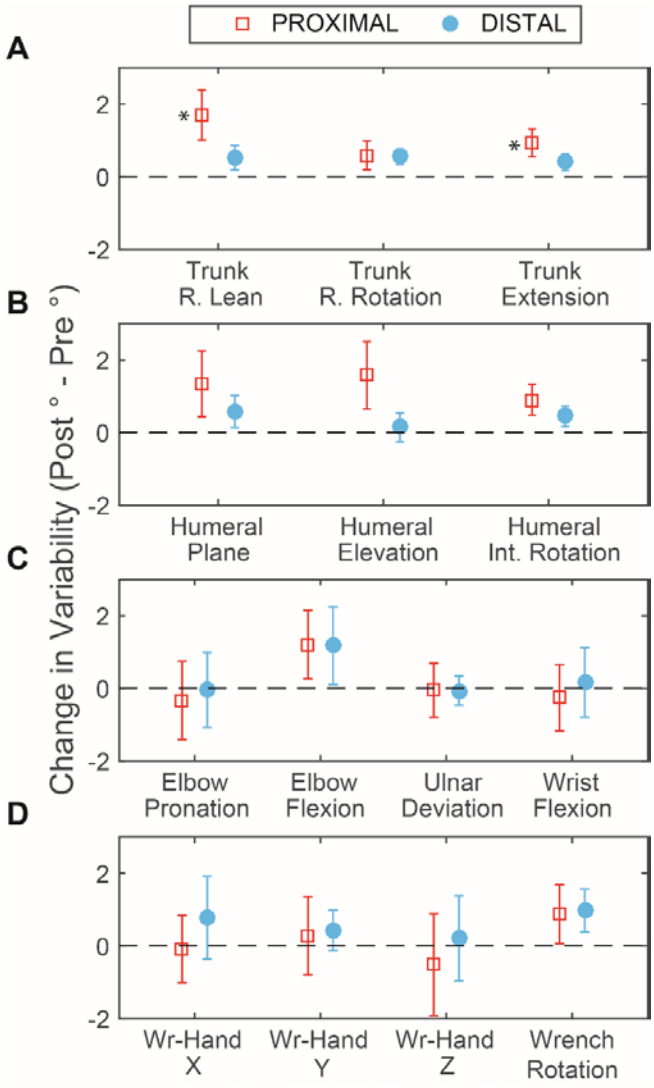


Figure 2.6. Effects of fatigue on joint variability.

Change in MeanSD at the trunk (**A**), shoulder (**B**), elbow and wrist (**C**), and hand and wrench (**D**) after proximal (squares) and distal (circles) fatigue. Positive values indicate that variability increased after fatigue. Error bars represent the 95% confidence interval. * indicates PROX/DIST × PRE/POST interaction effect.

high ratings of perceived exertion, negative IMPF slopes, and decreased maximum voluntary contractions demonstrate that subjects were fatigued after both fatigue protocols. The fatigue protocols caused MVC strength to decrease in the targeted muscle group by 18% and 24% for proximal and distal fatigue, respectively (Fig. 2.2B and 2C), while strength in the non-targeted muscle group declined to a much smaller degree (< 4%). These results confirm that the protocols successfully fatigued the targeted muscles.

2.7.1 Changes in Joint Kinematics

The hypothesis that fatigue of a proximal muscle group would cause greater kinematic changes than fatigue of a distal muscle group was supported. The primary effects of shoulder fatigue were reduced humeral elevation, increased elbow flexion, and increased left trunk lean angle and angular velocity. These changes are consistent with previous research and suggest a redistribution of loading to different areas (Côté et al. 2008). Conversely, fatigue of the finger flexors caused relatively small changes in movement organization. Distal fatigue primarily affected the movement velocity and timing of the wrist and hand. The distal fatigue protocol was expected to limit the ability to stabilize the wrist, hand, and wrench. When the gripping muscles were fatigued, the wrist joint extended earlier in the movement as the subjects began to apply clockwise torque to the wrench. The early wrist extension coincided with an increase in wrench–hand velocity indicating faster movement of the wrench between the proximal interphalangeal crease of the index finger and the palmar digital crease of the thumb. The increased velocity could be caused by reduced grip force and/or changes in the relative force vector between the wrench and hand. In spite of these changes, I did not observe changes in the execution of the task or the number of movement errors.

There were significant increases in trunk-pelvis angles and angular velocity after both proximal and distal fatigue. Even small changes in trunk angles can significantly affect endpoint kinematics (Fuller et al. 2009). In particular, left rotation decreased after proximal fatigue and increased after distal fatigue. This indicates that trunk movement changed in a way that specifically compensated for the different fatigue conditions. However, changes in trunk angles were two to four times smaller after distal than proximal fatigue. Overall the results suggest that distal fatigue predominantly affects the distal joints while proximal fatigue affects all joints in the kinematic chain.

2.7.2 Changes in Kinematic Variability

Our hypothesis that variability would increase after proximal but decrease after distal fatigue was not supported. Movement variability increased at proximal but not distal joints after both fatigue protocols. The increase in variability was larger after proximal fatigue. Results for proximal fatigue are consistent with previous studies which found increased movement variability after shoulder fatigue at proximal joints during sawing (Gates et al. 2011), reaching (Fuller et al. 2011), and assembly tasks (Qin et al. 2014). The current work expands previous findings as I found that proximal joint variability also increased when the hand muscles were fatigued. Muscle fatigue can increase neuromuscular noise and lead to increased kinematic variability. The observed increase in proximal joint variability after distal muscle fatigue might be the result of general increased descending motor drive. Alternatively, increasing kinematic variability at proximal joints might be a generic strategy to adapt to fatigue. One way to vary the load on fatigued distal muscles is to alter the pattern of proximal joint motion because this can alter the pattern of distal joint reaction torques. Thus varying proximal joint movement could change the force generated in distal muscles without necessarily varying distal joint kinematics. It is therefore possible that distal joint variability changed in ways that were not explored by the kinematic analyses used in this study (e.g. force, muscle activation patterns).

2.7.3 Injury Risk Factors Associated with Proximal and Distal Fatigue

Although subjects were not explicitly told to do so, they maintained a similar movement pattern of the wrench after fatigue. After shoulder fatigue, they did this by increasing trunk movement. These changes probably served to relieve the force in the fatigued shoulder muscles, but the observed increase in trunk motion and angular velocity can increase the risk of back injuries (Marras et al. 1993). In contrast, subjects maintained similar wrench movement after hand fatigue without major kinematic changes at the joints. Prior work has shown that wrist stiffness decreases

after muscle fatigue when people use power tools (Leger et al. 2000, Sesto et al. 2004). While I did not measure stiffness here, the observed changes in wrist extension time and wrench-hand velocity suggest that stiffness decreased after distal muscle fatigue. This strategy may have helped subjects recover grip strength during the post-test. However, these changes can increase force on the hand (Lin et al. 2001), and impair the ability to react to rapid forceful loading (Lin et al. 2003, Sesto et al. 2005).

2.7.4 Limitations

While there was no change in peak wrench velocity, the small decrease in movement repetitions may indicate that subjects moved more slowly after fatigue. However, subjects largely adhered to the instruction to follow the metronome beat. Still, there was high inter-subject variability in the way people responded to muscle fatigue. There may be large differences in fatigue for different subjects and even different muscle groups in the same subject. Some of these differences could be due to the different roles of individual muscles requiring static instead of dynamic muscle contraction. However, this is unlikely in the current study. Post hoc examination showed cyclic (dynamic) muscle activity in proximal and distal muscle groups during ratcheting.

Different work tasks could cause varying degrees of proximal and distal fatigue, but the progression and effects of the fatigue may be different for each person. Subjects may develop unique individual strategies in response to muscle fatigue. In the ratcheting task, performance stabilized within one minute of practice at the beginning of each session. However, the results demonstrate that subjects continued to modify their movement strategies throughout the sessions as they adapted to muscle fatigue. It is also likely that subjects learned and retained new movement strategies from trial to trial and day to day of the study. Some of these strategies could have helped subjects recover from fatigue. In particular, subjects began to recover from distal but not proximal fatigue during the post-test. This could be due to different movement strategies or different

recovery rates of proximal and distal muscles. In addition the recovery rate might be influenced by characteristics of the fatigue task. For example, during the distal fatigue protocol, the resistance of the grip trainer was not scaled to the subject's strength. Still, the MVCs indicate that grip strength was similarly impaired after fatigue and remained below the pre-test levels throughout the post-test indicating that the distal muscles remained fatigued.

People who use tools frequently might adapt to fatigue differently due to experience, strength, or other factors. I questioned subjects about the use of hand tools at the beginning of the experiment. One difference I observed was a change in wrist movement after distal fatigue. Wrist extension increased after hand fatigue in 10 of 14 subjects. However, in four subjects (3 male) who reported frequent tool use, wrist extension decreased. The differences in these subjects were not consistent across other measured variables, but experience with hand tools could affect both fatigue rate and movement strategy at the distal joints in particular.

Another potential factor that contributes to the fatigue response is gender. Lin et al. (2003) reported that female wrists are less stiff than male wrists. In the current balanced sample of males and females, the effects of distal fatigue were larger on average in females than males. However, these differences were small and influenced by a few outliers. Even small differences between males and females may be relevant to injury risk when they occur over a large number of repetitions. Future studies should further examine the effects of experience and gender and seek to identify characteristics that cause people to adopt different movement strategies during fatiguing tasks.

This study identified significant movement changes in trunk, shoulder, and elbow kinematics after proximal muscle fatigue in a repetitive, timed movement task. In contrast, after distal muscle fatigue, there were changes mainly in wrist and hand movement. Kinematic variability increased at proximal but not distal joints after both proximal and distal fatigue. These findings agree with previous research during disc throwing, and provide external validity to the

idea that fatigue adaptations are governed by hierarchical control principles. Furthermore, these results underscore the importance of considering the localization of muscle fatigue in order to assess the contributions of fatigue to injury risk. Further research is needed to understand how people modify the variability of different joints during fatigue and determine how consistent these changes are across tasks.

CHAPTER 3. Inter-joint Coordination Changes During and After Muscle Fatigue

3.1 Abstract

People produce coordinated movements by organizing many degrees of freedom into a few major covarying relationships. These relationships can be identified using data decomposition analyses (e.g. principal components analysis, non-negative matrix factorization). The purpose of this study was to determine how movement coordination changes during muscle fatigue as people modify their movements. Sixteen (16) healthy adults completed a continuous, timed ratcheting task with the right arm for three minutes pre, during, and post-fatigue. Joint angles from the right arm and trunk were tracked for subsequent principal components analysis. Principal component waveforms were constructed from the original joint angles, and changes in the waveforms during fatigue were assessed using cross-correlations. The variance explained by the first three principal components reached a maximum of 94.3% in the second minute of the pre-test and decreased to a minimum of 90.5% in the last minute of fatigue ($p = 0.001$). In the last minute of the post-test, explained variance (92.0%) did not differ from any other pre, fatigue, or post-test time point ($p > 0.23$). Changes in the principal component waveforms indicate that subjects adopted a more rigid movement strategy during fatigue. The results suggest that inter-joint coordination decreased during fatigue and increased during the post-test. Changes in movement patterns during fatigue may reduce inter-joint coordination leading to a more rigid movement strategy. However, the rigid movement strategy was not observed during the post-test suggesting that people learned to coordinate the degrees of freedom while using a new movement pattern.

3.2 Introduction

Muscle fatigue is defined as a reduction in muscle's capacity to generate force and is accompanied by a sensation of weakness (Enoka et al. 1992). Muscle fatigue leads to delayed muscle reaction time (Wilder et al. 1996) and increased variability of force (Huffenus et al. 2006, Côté et al. 2008) and movement (Enoka et al. 2008, Gates et al. 2011). The optimal movement strategy to execute a task in a fatigued state may differ from the non-fatigued state (Monjo et al. 2015). During repetitive tasks, people may compensate for muscle fatigue by reorganizing the movement patterns of individual degrees of freedom (DoF) (McDonald et al. 2015) or using different DoF to achieve the task (Côté et al. 2002, Côté et al. 2005). These changes may lead to altered inter-joint (Huffenus et al. 2006) and inter-muscular (Côté et al. 2008) coordination after muscle fatigue. In spite of these changes, people are able to coordinate their joint motions in a way that maintains performance when fatigued (Gates et al. 2008, Fuller et al. 2013, Cowley et al. 2014).

It is difficult to analyze inter-joint coordination because the musculoskeletal system is a multidimensional mechanical system with many (redundant) DoF. Fatigue studies frequently report only small changes (~3°) or find significant changes in the peak angles or range of motion of only a few joints, leading to the conclusion that movement reorganization may involve a sum of small changes at several DoF (Côté et al. 2002, McDonald et al. 2015, Tse et al. 2015). This is further complicated by the fact that the muscle fatigue state changes continuously throughout muscle fatigue and recovery. Moreover, different muscles have different fatigue and recovery rates (Caffier et al. 1992), and people continuously learn new movement strategies as they perform tasks (Selen et al. 2007, Dingwell et al. 2013). Thus adapting to fatigue requires people to respond to a complex combination of several nonlinear processes via the coordinated action of many DoF.

The way that people modify their inter-joint coordination during widespread movement

reorganization cannot be addressed by traditional analyses of individual biomechanical variables at discrete time points. Many studies have been limited to analyzing differences only between trials performed before and after fatigue. This approach reduces fatigue to two states (unfatigued or fatigued) and therefore cannot explain how people transition between movement patterns as fatigue progresses (or decreases). Recent studies examined the time course of kinematic changes during and after fatigue (Gates et al. 2011, Qin et al. 2014, McDonald et al. 2015). Joint angles grew increasingly different from baseline levels throughout a fatiguing task (Gates et al. 2011). During one hour of active recovery, some angles gradually returned to pre-fatigue levels, while others did not (McDonald et al. 2015). During simulated work, kinematic changes showed cyclic variations associated with rest-work cycles (Qin et al. 2014). It is clear from these studies that people continuously modify their movement patterns throughout the fatigue process. However, each of these previous analyses focused on average or maximum joint positions during movement. This approach does not quantify how multiple joints are coordinated to produce a movement. Previous findings emphasize the need for methods that can analyze the continuous fatigue response across multiple biomechanical DoF as measured by 3-dimensional kinematic analyses.

Multivariate statistical tools such as factor analysis, non-negative matrix factorization or principal components analysis (PCA) can be used to decompose data from multi-joint movements into smaller sets of highly representative variables. Each representative variable consists of a weighted combination of the original variables that describes a unique feature of the movement and accounts for a significant portion of the variance in the data (Daffertshofer et al. 2004). Generally, the combined effects of many variables can be represented well (e.g. > 90% variance explained) using a few linear combinations of covarying DoF (synergies). This indicates that many DoF are organized as a coordinated unit, and greater accuracy in representing the data reflects greater coordination (Chen et al. 2005). Inter-muscular (Steele et al. 2015) and inter-joint (Mah et

al. 1994) control strategies are thought to be simplified by organizing variables into synergies. PCA has often been used to quantify differences in multi-joint synergies across conditions and thus identify how different conditions affect movement strategies. Results from PCA show that multi-joint tasks are executed in a low dimensional space. Just a few synergies account for most of the variance in the multi-joint data which indicates high coordination among DoF (Mah et al. 1994, Sanger 2000, Chen et al. 2005, Bockemühl et al. 2010). PCA is sensitive to changes in explained variance and therefore well-suited to describe how coordination changes during muscle fatigue.

PCA could help to quantify how people modify their coordination during and after muscle fatigue and provide insight into the movement strategies that govern the response to fatigue. The purpose of the current study was to quantify how movement coordination changes over time during and after muscle fatigue. I hypothesized that changes in the movement pattern during muscle fatigue would cause inter-joint coordination to decrease. Further, I hypothesized that the inter-joint coordination would increase as subjects recovered after fatigue, but I expected the movement pattern to remain distinct from the pre-fatigue movements.

3.3 Methods

3.3.1 Subjects

Sixteen (8 female) healthy, right-handed subjects between the ages of 18 and 65 from the local community provided written informed consent and participated in an institutionally approved study. Subjects had a mean age and BMI of 29 ± 14 (range 18 – 64) years and 24.6 ± 3.3 kg/m2, respectively. Individuals with a history of serious musculoskeletal, cardiovascular, neurological, respiratory, or visual problems were excluded.

3.3.2 Experimental Protocol

Subjects completed one experimental session. First, baseline shoulder flexion strength was recorded using a hand-held dynamometer (Lafayette Instruments, Lafayette, IN). Subjects then performed nine minutes of a repetitive ratcheting task. The pre-test consisted of three, 1-minute intervals (pre1 – pre3) alternating with 1-minute rest periods (Fig. 3.1A). Subjects then completed a fatigue trial consisting of a repetitive lifting task alternating with three, 1-minute intervals of the ratcheting task (fatigue1 – fatigue3). After the fatigue protocol, subjects completed a post-test identical to the pre-test (post1 – post3). Muscle strength and ratings of perceived exertion (RPE) were assessed at regular intervals throughout the session to measure the progression of fatigue (Fig. 3.1A).

The ratcheting task consisted of repeatedly rotating a bolt (1 Hz) using a ratcheting socket wrench (~ 0.4 kg) with the right hand. The bolt was placed in a board at eye level and approximately 60% of arm length in front of the toes. Subjects were instructed to complete each ratcheting movement in time with a metronome beat but were not given explicit instruction on how far to rotate the bolt. Subjects completed a 1-minute practice trial at the start of the session to reduce learning effects.

Maximum isometric shoulder flexor strength (N) was measured with subjects seated on a stool and the right arm raised to 90 degrees of sagittal plane shoulder flexion. Subjects applied upward force on the hand-held dynamometer held against the upper arm for 4 s. The average of three peak force measurements was taken as the subject's maximum voluntary contraction (MVC). All MVCs were expressed as a percentage of the initial MVC value.

The fatigue task was designed to fatigue the shoulder flexors. Subjects repeatedly lifted and lowered a weight (~10% max shoulder flexion strength) to shoulder height in the sagittal plane with the right arm straight at a frequency of 0.5 Hz. Subjects were instructed to match their lifting

phase (up-down) with a metronome. Fatigue was verified using ratings of perceived exertion (RPE) on the Borg CR-10 scale (Borg 1982). During the first fatigue interval, subjects performed the lift task for three minutes or until they felt that they could no longer continue. If a subject's RPE was < 8 at the end of three minutes, the subject was asked to continue the task for three more minutes or until they could not continue. Subsequently, subjects performed ratcheting intervals fatigue1, fatigue2, and fatigue3 alternating with 1-minute lifting intervals (Fig. 3.1A).

Thirty-four reflective markers were placed on the head, trunk, pelvis, upper limb, and wrench to define motion of the body segments and wrench. The position of these markers was tracked at 120 Hz using a 16 camera motion capture system (Motion Analysis, Santa Rosa, CA). Markers were placed bilaterally over the anterior and posterior superior iliac spines to track pelvis motions. Trunk motions were tracked using markers placed over the sternal notch, xiphoid process, and spinous processes of C7 and T8 vertebrae. Motions of the head were tracked using four markers placed on a headband in bilateral anterior and posterior pairs approximately in the horizontal plane. The right arm and forearm were tracked using clusters of four markers attached to each segment. The right hand was tracked using markers over the 3rd and 5th metacarpal heads, diaphysis of the 2nd metacarpal, and base of the 3rd metacarpal. The position of the wrench was tracked using four reflective markers. Additional markers were placed over the right medial and lateral epicondyles of the humerus, radial and ulnar styloids, acromion, and right upper back.

3.4 Data Analysis

A 6-segment model was created in Visual 3D (CMotion, Germantown, MA) using marker positions and joint centers, as in (Gates et al. 2016). Trunk-pelvis, shoulder, elbow, and wrist kinematics were calculated using Euler angles according to International Society of Biomechanics recommendations (Wu et al. 2005). The wrench-lab angle was calculated using an X-Y-Z rotation

sequence where the ratcheting action of the wrench occurred about the X axis and the (vertical) Y axis aligned with the wrench handle. The wrench-hand angle was calculated using a Z-Y-X rotation sequence.

Movement cycles started and ended when the wrench handle was at its highest position. Time series of joint angles during each movement cycle were obtained for 13 degrees of freedom: trunk lean, flexion, and rotation, humeral abduction, plane, and rotation, elbow flexion, forearm pronation, wrist deviation and flexion, and three wrench-hand angles. Unsuccessful movement cycles in which the wrench slipped off the bolt were removed and all successful trials were concatenated resulting in data matrices of approximately 7000 × 13 for each 1-minute trial. Each data matrix was examined using principal components analysis.

Principal components analysis (PCA) uses a singular value decomposition to find the structure of variance in an original data set. The first principal component consists of a linear combination of weighted variables that explains the greatest amount of variance in the data. Subsequent principal components are orthogonal to all previous components with each subsequent component aligned with the greatest amount of the remaining variance in the data. The contribution of each variable to a given principal component is described by a weighting coefficient. Thus each principal component is represented by a set of *k* weighting coefficients where *k* is the number of variables in the data set. While the number of principal components can be as high as *k*, generally just a few principal components are needed to explain most of the variance in the data.

Preliminary analyses showed that 3 principal components explained > 90% of the variance in the ratcheting task. Therefore, the first three principal components for each one minute trial were retained for further analysis. I calculated the variance explained (EV) by each principal component and the weighting coefficients of the original variables on each component during each minute. Principal components were obtained by multiplying the original time series by the weighting coefficients yielding three new time series: pc1, pc2, and pc3 (Eq. 3.1).

$$pc(j) = \sum_{k=0}^{13} w_{kj}\theta_k \qquad (3.1)$$

Thus, each principal component, *pc(j)*, is the sum of all joint angles, θ_k, multiplied by their corresponding weighting coefficient, w_{kj}. Principal components were next separated into individual movement cycles and time normalized to 100 points (0 – 100 % movement cycle).

The average principal components during each minute of ratcheting (pre1 – post3) were obtained for each subject. The three components that were identified by the principal components analysis were similar across subjects and trials. However, the relative variance explained by the second and third principal components was not the same for all subjects. In order to analyze changes in coordination across trials, the average weighting coefficients from the second and third components for each subject were compared. For each subject, pc3 was defined as the component with the greatest weighting coefficient on humeral plane angle. This altered the order of pc2 and pc3 of four subjects. To assess changes in principal components, the time-normalized average principal components for pre2 – post3 were compared to the scores from the first pre-fatigue minute (pre1) using cross-correlations. The similarity between trials was defined as the highest correlation coefficient, and changes in movement timing (% movement cycle) were defined as the lag corresponding to the highest correlation.

3.5 Statistical Analysis

MVC, RPE, and EV were compared using single-factor (time point) ANOVAs to test for differences over time. To determine how the principal components changed over time, the average correlation coefficients and time lag values were compared using single factor (time point) ANOVAs. For all tests, significance was set at ($p = 0.05$), and a Bonferroni adjustment for family-wise error was applied. The shape of the principal components and the magnitude of the variable

weightings within the principal components were averaged across subjects and examined visually to determine how the movement pattern changed after fatigue.

3.6 Results

3.6.1 Muscle Fatigue

There were significant effects of time point on maximum voluntary contraction strength (MVC; $p < 0.001$) and rating of perceived exertion (RPE; $p < 0.001$). RPE was greater during the first lifting interval (8.9 ± 0.9) compared to all other time points ($p < 0.03$) except the last minute of fatigue (fatigue3; $p = 0.576$). RPE increased from fatigue1 to fatigue3 ($p = 0.004$) but did not change significantly during the pre-test ($p > 0.2$) or post-test ($p > 0.5$) (Fig. 3.1B). Shoulder MVC was lower after the first lifting interval (77% max), fatigue trial (fatigue 3; 69%), and post-test (72%) compared to the pre-test (95%; $p < 0.001$), and lower after the fatigue trial compared to the first lifting interval ($p = 0.001$). After the post-test, shoulder MVC did not differ from the first lifting interval or fatigue trial ($p > 0.15$) (Fig. 3.1C).

3.6.2 Principal Components

The three principal components obtained were similar for nearly all trials, but the weighting coefficients changed during and after fatigue. The first principal component (pc1) describes the nearly sinusoidal ratcheting motion (Fig. 3.2A). Forearm pronation, humeral elevation, and ulnar deviation were weighted heavily on pc1. During fatigue, the weighting of forearm pronation on pc1 decreased and the weighting of humeral rotation increased (Fig. 3.2D). The second principal component (pc2) describes coordination between the hand and wrench (Fig. 3.2B). The wrench-hand angle and wrist flexion were weighted heavily on pc2 (Fig. 3.2E). A small delay between arm and wrench movement which occurs as resistance increases in the first 30% of the movement was prominent in this component. The third principal component (pc3) describes variation in the

speed of wrench motion (Fig. 3.2C). Humeral plane angle was weighted heavily on pc3 (Fig. 3.2E). Fatigue primarily affected pc3 during the second half of the ratcheting cycle such that the counter-clockwise (upward) movement was slower after fatigue.

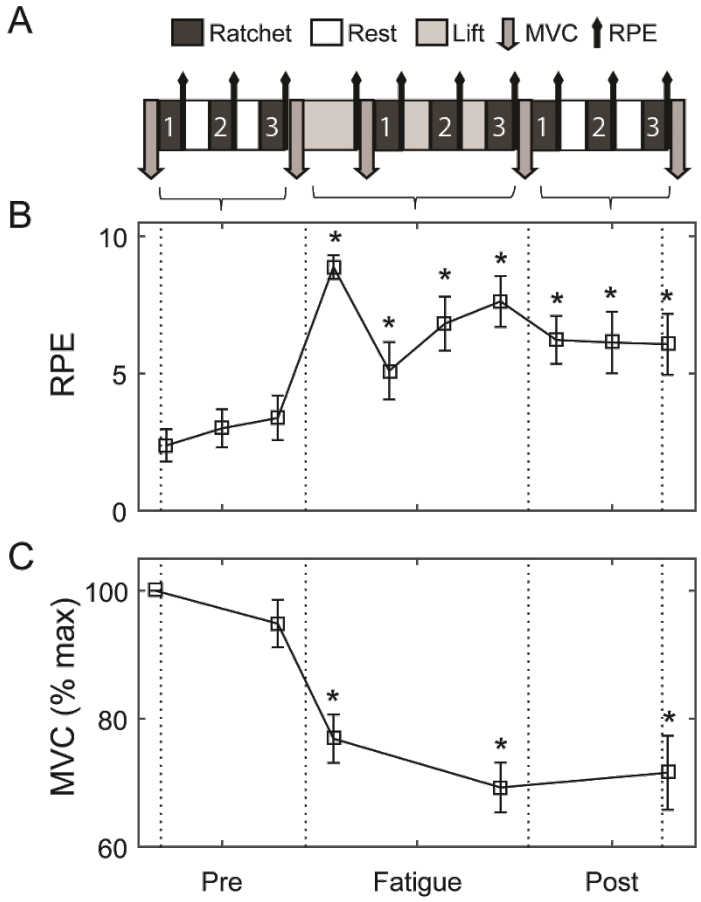


Figure 3.1. Experimental procedure and muscle fatigue measures.

A) Subjects performed a total of nine, 1-minute intervals of a ratcheting task (dark squares): three pre-test (pre1 – pre3), three fatigue (fatigue1 – fatigue3), and three post-test (post1 – post3). Ratcheting intervals alternated with 1 minute rest (white squares) or fatigue (lifting) intervals (light grey squares). The first lifting interval lasted until subjects reached an RPE of 8 or higher (see text for details). Ratings of perceived exertion (black arrows) and maximum voluntary contractions (grey arrows) were collected at regular intervals. **B**) Ratings of perceived exertion and (**C**) Maximum voluntary contraction strength at each time point. Error bars are the 95% confidence interval. * indicates a significant difference from the first measurement.

3.6.3 Inter-joint Coordination

The first three principal components accounted for approximately 78% (range: 53 – 93%), 9% (range: 2 – 27%), and 6% (range: 1 – 22%) of the variance in the data, respectively (Fig. 3.3). At least 90% of the variance in the data could be explained by three principal components during 118 of 144 trials. On average, explained variance (EV) was greater than 90% (range, 81 – 98%) during each minute of ratcheting indicating high inter-joint coordination. There was a main effect

of time point on EV ($p < 0.001$) (Fig. 3.3). EV was highest during the first two minutes of the pre-test (pre1, pre2: 94 ± 2%) and lowest during the last minute of fatigue (fatigue3: 90 ± 3%). Compared to pre1, EV was lower during the last two minutes of fatigue and first minute of the post-test (fatigue2, fatigue3, post1; $p < 0.05$). During the last minute of the post-test (post3: 92 ±

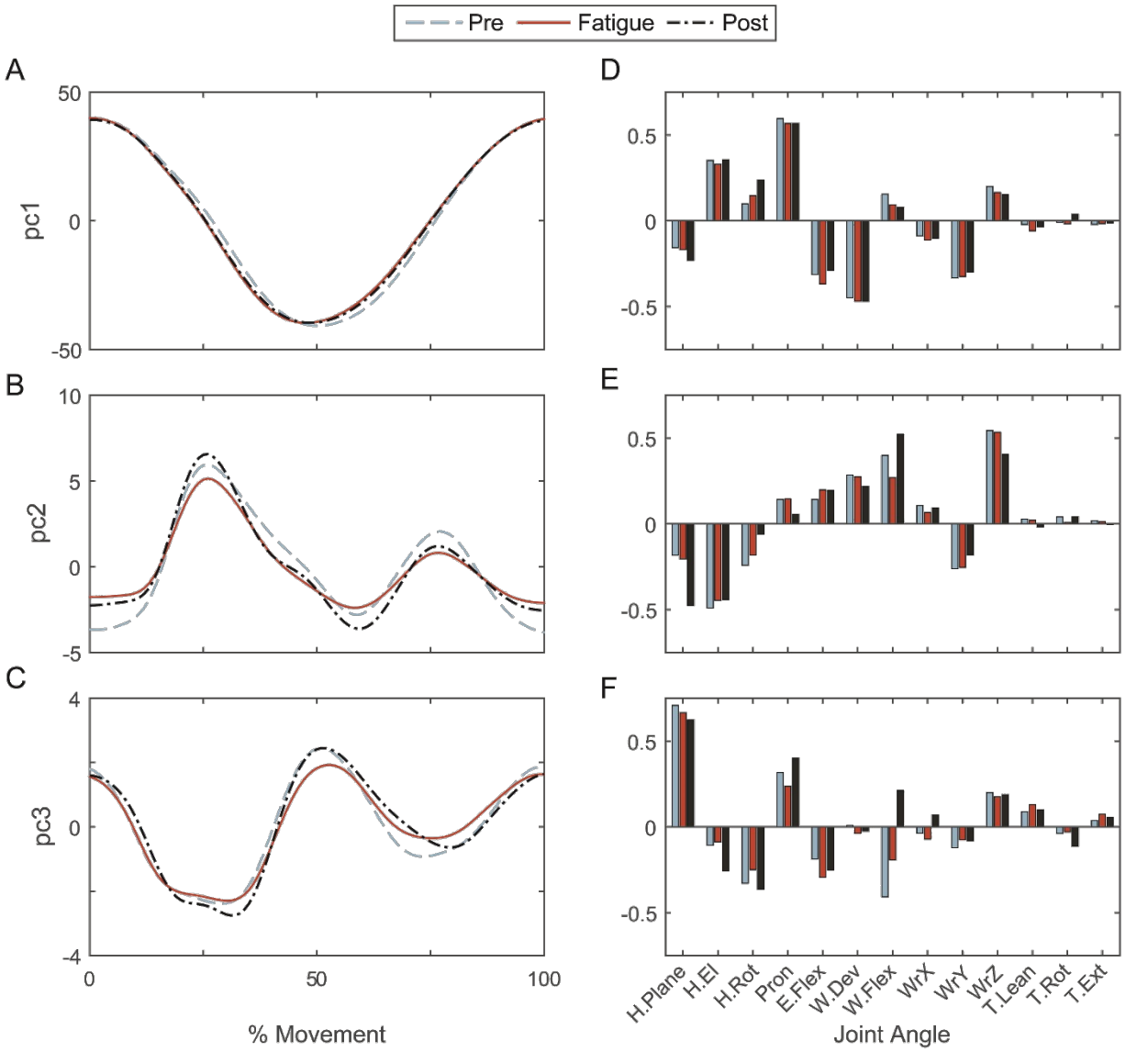


Figure 3.2. Principal components and weighting coefficients from the ratcheting task.

Average principal components (LEFT) and representative weighting coefficients for a single subject (RIGHT). Data are averaged across all minutes of pre-test (blue), fatigue (red), and post-test (black) for pc1 (**A, D**), pc2 (**B, E**), and pc3 (**C, F**).

3%), EV was not different from any other time point during the pre-test ($p > 0.2$) fatigue ($p > 0.3$) or post-test ($p > 0.9$; Fig. 3.3). The decrease in EV was most evident in pc1. There was a main effect of time point on variance explained by pc1 ($p < 0.001$) and pc2 ($p = 0.049$) but not pc3 ($p = 0.53$). Post hoc tests showed that the variance explained by pc1 was lower in the last minute of fatigue (fatigue3; $p = 0.014$) and first minute of the post-test (post1; $p = 0.027$) compared to the second minute of the pre-test (pre2). However, for pc2 post hoc tests were not significant ($p > 0.4$; Fig. 3.3).

3.6.4 Shape of Principal Components

The principal component waveforms were similar in shape to the first minute (pre1) with average correlation coefficients of approximately 0.98, 0.63, and 0.61 for pc1, pc2, and pc3,

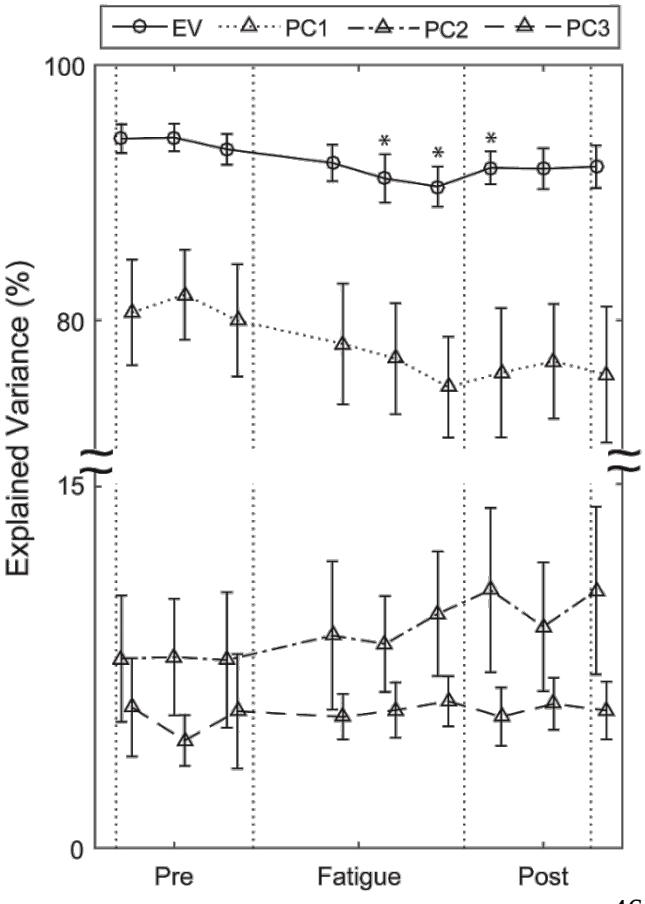


Figure 3.3. Explained variance during the ratcheting task.

Explained variance for each principal component (pc1, pc2, pc3: dashed lines) and the sum of three principal components (EV: solid line). Error bars are the 95% confidence interval. * indicates a significant difference from the first measurement time.

respectively (Fig. 3.4). There was a significant effect of time point on the correlation coefficients for pc1 (p=0.003), pc2 (p = 0.002), and pc3 (p = 0.003). However, post hoc tests showed no significant differences between minutes for pc1 or pc3 ($p > 0.05$). For pc2, correlation coefficients were larger for pre2 (r = 0.8) compared to the last two minutes of fatigue (fatigue2: r = 0.61; fatigue3: r = 0.54) and the last minute of the post-test (post3: r = 0.6; $p < 0.04$; Fig. 3.4B). There was no effect of time point on the time lags ($p > 0.28$).

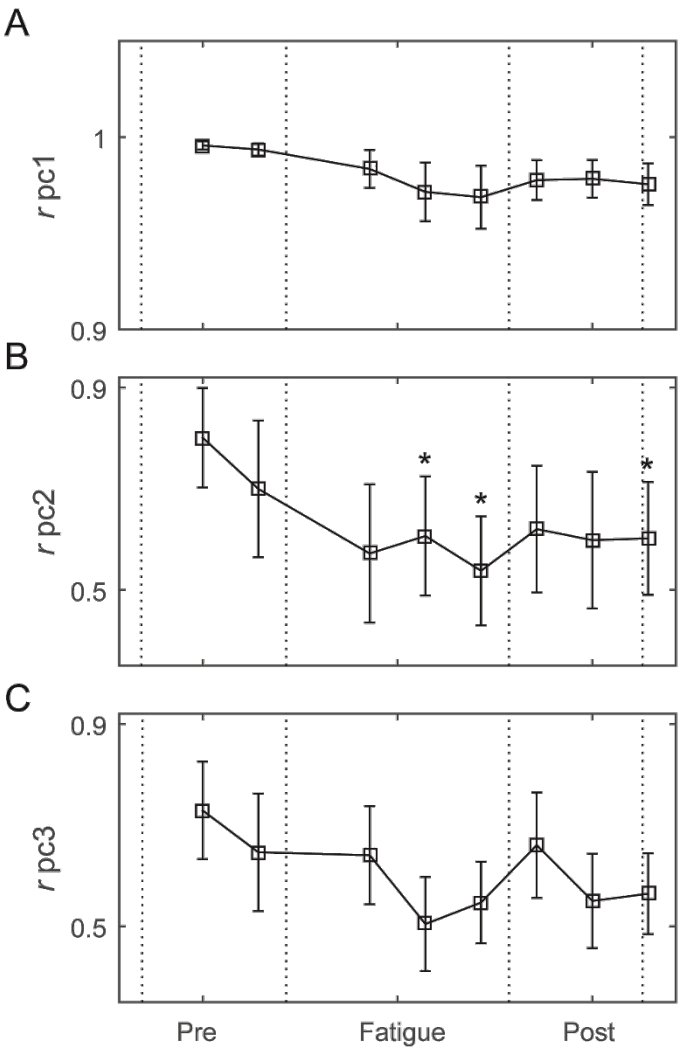


Figure 3.4. Correlation coefficients of principal components.

Average correlation coefficients for principal component waveforms, pc1 (A), pc2 (B), and pc3 (C). Correlations represent the relationship between the first pre-fatigue minute (pre1) and each subsequent minute. Error bars are the 95% confidence interval. * indicates a significant difference from the correlation between pre2 and pre1.

3.7 Discussion

In this study, I quantified movement coordination across minutes of a repetitive task executed before, during, and after fatigue. The decreased MVCs and high ratings of perceived exertion demonstrate that subjects were fatigued after the first lifting interval and that muscle fatigue persisted throughout the fatigue trial. Explained variance decreased during muscle fatigue. Although muscle strength did not recover significantly during the post-test, explained variance returned toward pre-fatigue levels. Overall, the results suggest that subjects adopted new movement patterns during muscle fatigue. The altered movement patterns initially caused coordination to decrease. However, inter-joint coordination increased during the post-test even though the movement patterns remained distinct from the pre-test.

Principal components analysis reduced this 13 dimensional data set to 3 variables that explain over 90% of the variance in the original data. These variables describe three distinct, relevant subtasks of the ratcheting movement: wrench rotation, wrench-hand coordination, and movement speed, respectively. The decrease in explained variance during the ratcheting movement primarily reflects a decline in the variance explained by the first principal component (Fig. 3.2). The results suggest that subjects increased joint motions that did not directly contribute to rotating the wrench when fatigued. This likely increased the complexity of the task after fatigue leading to decreased coordination. Movement complexity could increase due to frequent changes in movement strategy, postural adjustments, or increased range of motion at latent degrees of freedom (DoF; e.g. trunk). For example, there was a clear decrease in humeral elevation and an increase in trunk motion after fatigue. Thus subjects were completing the task in a different arm posture and increasingly using the trunk to assist the movement. Lower order principal components explained a small fraction of total variance but showed relatively large increases in explained variance after fatigue. These changes may be the result of joint rotations and postural changes that were not represented in high order principal components.

The same three basic waveforms emerged from the PCA during nearly all trials. This suggests that PCA identified a common set of neuromechanical synergies specific to the ratcheting task. Although the effects of muscle fatigue have been studied during many tasks, there is no single ideal task for studying muscle fatigue. It is likely that modifying task demands such as timing, accuracy, or position would change the observed results. However, it is also likely that major movement synergies will remain even when changing task demands (Mah et al. 1994, Bockemühl et al. 2010). Significantly, the major waveform features of the principal components were retained even though the fraction of explained variance and the variable weightings on the components changed from trial to trial. Similar results from PCA have been observed during walking over level ground and over obstacles (Mah et al. 1994) and during ball catching at multiple target locations (Bockemühl et al. 2010). Muscle fatigue affected the scale of major component features and led to new movement patterns, but changes in the movement patterns of multiple joints were executed in a way that preserved the overall component shape.

Muscle fatigue is a continuous process, and this was evident in the observed changes in movement patterns from minute to minute. The correlation coefficients demonstrated changes in the principal components which reached a maximum during fatigue (Fig. 3.4C). While the correlation coefficients showed that post-test trials generally tended to be more similar to pre-test than fatigue trials, the correlations between pre-test and post-test remained lower than the correlations between pre-test trials. This indicates that the movement patterns remained different from the pre-test (Fig. 3.4). Changes in the weighting coefficients from each principal component indicate that subjects adopted new movement patterns that affected many DoF. Some of these changes were transient and returned toward baseline during post-test (e.g., humeral elevation, elbow flexion, trunk lean: Fig. 3.2D). However, other changes persisted throughout the post-test, indicating that novel movement patterns were retained (e.g., humeral rotation, pronation: Fig. 3.2D; wrench-hand Z: Fig. 3.2E; humeral plane: Fig. 3.2F). These observations indicate that

kinematic changes spanning multiple joints did not occur simultaneously. Instead, changes at individual joints were observed at different times across minutes (and probably movement cycles). Further research is needed to better understand the control principles that underlie these changes in movement patterns and coordination during fatigue.

The current results support the idea that muscle fatigue adaptation is a process of learning to complete movements in a new body state (Monjo et al. 2015). This learning process is hard to measure as it involves small changes spanning many DoF. In previous work on motor learning, PCA showed that explained variance increased when learning a motor task (Chen et al. 2005). The greater explained variance of more skilled performance is considered to reflect a high level of coordination across a complex array of DoF (Verrel et al. 2013). Less skilled performers do not exhibit this level of coordination. Instead, they may reduce movement complexity by freezing DoF, thus moving multiple segments more like a single rigid unit (Bernstein 1967). Verrel et al. (2013) found that expert cello players used a larger range of motion at the wrist and elbow joints compared to novices, but PCA showed that the experts also exhibited more coordinated movement between these joints. In the current study, the coordination strategy of fatigued subjects was similar to that observed in early stages of learning. During the wrench task, the second principal component decreased in amplitude (Fig. 3.2B), reflecting a more sinusoidal overall movement pattern. These changes suggest that there was greater rigidity of the arm-wrench system during ratcheting. Similar effects have been observed after fatigue during throwing (Forestier et al. 1998) and are consistent with the idea of freezing DoF to reduce task complexity (Verrel et al. 2013). During the post-test, the amplitude of the second principal component increased suggesting that subjects began to restore a less rigid coordinative strategy as they learned to coordinate the DoF in the new movement pattern (Fig. 3.2B).

There were a few limitations in this study. First, the variance explained by each principal component varied from trial to trial and for each subject. Furthermore, subjects used a variety of

coordination strategies, and each subject uniquely modified coordination across minutes. The resulting principal component weightings were highly variable, even though the major waveform features were retained. Second, variables are often rescaled to unit variance before completing principal components analysis. This prevents variables with the highest movement amplitude (and thus high variance) from dominating the variable weightings. In this study, I did not scale to unit variance because movement amplitude is an important factor in fatigue adaptation. When unscaled, joint angles with small movement amplitude (e.g. trunk rotation) have low weightings on the principal components. However, the principal components are still a good representation of those joints if the joint angles are correlated (Mah et al. 1994). Furthermore, using the unscaled variables, small changes in joint range of motion have a large effect on component weightings which allows for a more intuitive interpretation when all variables are in the same units.

The results of this study support that people modify inter-joint coordination as the muscle fatigue state changes. Muscle fatigue reduces strength and increases perceived effort, and these effects can lead to changes in joint kinematics that increase movement complexity. The decrease in inter-joint coordination during muscle fatigue suggests that kinematic changes inhibit the ability to organize the DoF. However, the increase in inter-joint coordination during the post-test suggests that people learn new coordinative patterns after fatigue. Changes in inter-joint coordination after muscle fatigue may follow a pattern similar to that observed when learning novel motor tasks as people learn to organize multiple degrees of freedom in a new fatigue state.

CHAPTER 4. Influence of Pain and Fear on Perceived Effort and Muscle Endurance

4.1 Abstract

During fatiguing tasks people alter their movement control strategies to offset effects of muscle fatigue. Painful stimuli may compete for cognitive resources during muscle fatigue, thus impairing fatigue adaptation. The purpose of this study was to determine how pain affects movement control and muscle endurance during fatigue. 22 healthy young adults completed a repetitive task on separate days. Subjects slid a weighted sled back and forth along a low-friction surface in time with a metronome until voluntary exhaustion using continuous elbow flexion/extension motions. On one of the two days, subjects simultaneously experienced ischemic pain in the left arm. Subjective measures of pain, fatigue, and effort were recorded at regular intervals. Timing errors and movement distance and speed, were calculated for each movement throughout fatigue. A goal equivalent manifold was used to quantify goal-relevant and non-goal-relevant variability. Detrended fluctuation analysis was used to assess movement control during fatigue. Subjects made shorter, slower movements at the end of fatigue during both sessions. At the beginning of the pain session, subjects exerted less control over movement speed compared to the no pain session, but this effect was not present near the end of fatigue. However, these effects of pain and fatigue were dependent on session order. Fatigue time increased in the second session regardless of pain, but the effect was larger when the pain session was performed first. Subjects who scored high on the pain catastrophizing scale adopted more conservative movement strategies during fatigue regardless of pain. The effects of pain on muscle fatigue depend on familiarity with the painful stimulus and the fatiguing task.

4.2 Introduction

During fatiguing tasks, people vary their movement coordination and control patterns as they search for movement strategies that minimize discomfort and outcome errors caused by fatigue (Fuller et al. 2011). Adapting to fatigue requires the use of additional cognitive resources. The central nervous system must generate larger efferent signals to produce the same force in fatigued muscles. Feedback from group III and IV afferent nerves signals muscle fatigue and helps the central nervous system plan for these changes even before executing a movement (Demougeot et al. 2011, Monjo et al. 2014). Planning a movement in a fatigued state is likely a multi-step learning process that first requires continuous monitoring and interpretation of the afferent signals and creation of an efference copy, an internal copy of the set of outgoing motor commands. This is followed by formulation of an updated internal model based on the afferent feedback and the predicted effects of the efference copy before the new motor signals are generated (Monjo et al. 2014). The movement strategies a person adopts in response to fatigue could also increase the cognitive demand. For example, during target tracking tasks, people decreased co-contraction and remained closer to the target to maintain accuracy when fatigued, a strategy that relies on feedforward control (Selen et al. 2007, Missenard et al. 2008). Changes in the movement strategy and control patterns during fatigue may prolong task execution, but these adaptations rely on mechanisms that are cognitively demanding.

Muscle fatigue often occurs in complex environments with many cognitive demands. When multiple stimuli compete for cognitive resources, different aspects of performance may be prioritized or neglected. For example, a greater mental task workload may decrease force output (Bray et al. 2012), or performance on mental tasks may decrease when people exert higher force (Zijdewind et al. 2006). The cognitive effects of muscle fatigue adaptation have also been studied during dual tasks (Lorist et al. 2002, Terrier et al. 2009, Mehta et al. 2012). During muscle fatigue, movement reorganization leads to impaired reaction time on mental tasks (Terrier et al. 2009), and

when mental tasks compete for cognitive resources, the rate of muscle fatigue can increase (Mehta et al. 2012). The interactions between muscle fatigue and other cognitive stimuli are important factors in assessing productivity and safety during movement tasks.

Pain is another biological stimulus that demands cognitive resources. People tend to bias their attention toward a painful area (Moseley et al. 2005), and pain can alter the perception of the body schema (Bray et al. 2011, Bouffard et al. 2013). Like muscle fatigue, pain may impair performance on cognitive tasks (Moriarty et al. 2011). Continuously monitoring the fatigue state and executing motor-cognitive tasks requires a significant allocation of central nervous system resources, and painful sensations may interrupt this process. For example, chronic pain patients have difficulty regulating fatigue progression (Wallbom et al. 2002). Acute painful stimulation might also limit the process of movement reorganization and increase the rate of fatigue. In an isometric task, experimental pain decreased the endurance time and altered muscle activity during fatigue and recovery but did not significantly alter torque output (Ciubotariu et al. 2004, Ciubotariu et al. 2007).

Pain also causes people to modify their movement control strategies during motor tasks (Ervilha et al. 2005, Farina et al. 2005, Graven-Nielsen et al. 2010, Seeley et al. 2013, Mista et al. 2015). During maximum effort contractions, experimental muscle pain reduces voluntary but not evoked force output, suggesting that pain can cause central inhibition of muscle force (Graven-Nielsen et al. 2002). Similarly, experimental pain reduces EMG magnitude (Farina et al. 2005, Denning et al. 2014) and motor unit firing rate (Farina et al. 2004) and causes redistribution of motor unit activity (Madeleine et al. 2006) at submaximal force. Muscle pain also causes changes to inter-muscular (Ervilha et al. 2005) and inter-joint (Seeley et al. 2013) coordination during dynamic movements. These adaptations may be intended to reduce stimulation of the painful area.

Additionally, pain can affect the ability to learn and retain effective motor strategies. One study found that superficial pain led subjects to make larger movement errors and learn a different

control strategy with the painful arm compared to a control condition (Lamothe et al. 2014). However, most previous work on fatigue studied the effects of pain in muscles that were agonists or joints that were directly involved in the experimental task. While this method simulates many real-life conditions, many other conditions involve pain in remote areas of the body. Furthermore, this method cannot differentiate the effects of pain caused by muscle fatigue and that caused by another painful stimulus. Few studies have examined how remote pain affects motor control strategies. Pain in one hand was shown to slow the execution of a position matching task with the opposite hand (Moseley et al. 2005). In another study, local pain enhanced motor learning but remote pain did not (Dancey et al. 2016).

There is large variability in how different people respond to pain (Nielsen et al. 2009). One reason for this may be that some people experience fear or exaggerated negative emotions (catastrophize) which can affect how they interpret painful sensations. For example, people who catastrophize about pain also report more intense pain (Sullivan et al. 1995, George et al. 2007, Parr et al. 2012), and pain related fear is associated with more severe disability and lost work days (Waddell et al. 1993, Crombez et al. 1999, Vlaeyen et al. 2000) independent of actual physical capacity (Sullivan et al. 1998, Severeijns et al. 2001). In people with chronic back pain, fear of pain predicts disability better than actual pain ratings (Crombez et al. 1999). In young healthy adults, pain catastrophizing is associated with greater pain and disability 48-96 hours after exercise induced shoulder soreness (Parr et al. 2012). Given the potential effects of painful sensations on muscle fatigue (Farina et al. 2004, Cote et al. 2010), people who catastrophize about pain may exhibit exaggerated responses to painful stimuli during fatigue.

It is possible that remote pain draws attention away from the fatiguing area and limits the ability to learn successful movement strategies during muscle fatigue, but this has yet to be systematically tested. This research investigated the effects of remote ischemic pain on movement control during a fatiguing task. I hypothesized that pain would reduce the ability to develop

successful movement strategies during fatigue leading to reduced movement control, larger movement errors, and a faster rate of fatigue. I expected these changes to be larger in people with higher pain-related fear.

4.3 Methods

4.3.1 Subjects

Twenty-two (22) right-handed, healthy adult subjects (18 – 35 years; 11 females) participated in this institutionally approved study after providing written informed consent. Individuals with a history of serious musculoskeletal, cardiovascular, neurological, respiratory, or visual problems were excluded.

4.3.2 Experimental Protocol

Subjects completed two data collection sessions (pain/control) in random order on separate days at least four days apart. At the beginning of the first data collection session, subjects completed the Pain Catastrophizing Scale (PCS) (Sullivan et al. 1995, Sullivan 2009). This measures the degree to which a person experiences negative thoughts about pain. Patients rate their agreement with various statements on a 5-point scale ranging from 0 (not at all) to 4 (all the time). This scale has suitable reliability in clinical and nonclinical samples (Osman et al. 2000). During each session, subjects performed a fatiguing task to voluntary exhaustion with the right arm. The fatiguing task was identical in each session, but in the pain session subjects simultaneously experienced an ischemic pain protocol with the left arm. The fatiguing task consisted of repetitive, timed flexion/extension movements. Subjects were strapped to a chair in a seated position with the upper arm strapped to a solid brace and the arm raised to approximately 90 degrees of humeral elevation and about 30 degrees of horizontal adduction (Fig. 4.1A). They grasped a handle attached to a weighted sled and moved the weight back and forth on a low-friction surface in time to a

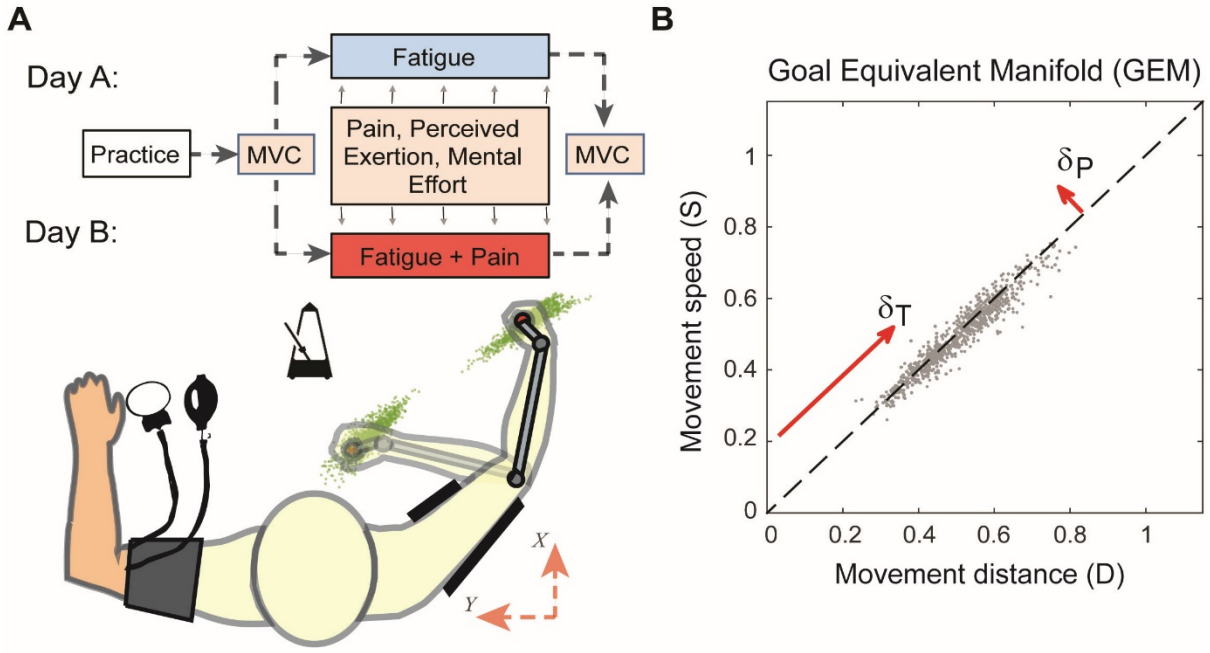


Figure 4.1. Experimental protocol and depiction of a goal equivalent manifold.

Subject setup and experimental procedure (A). Subjects were seated with their arm strapped to a rigid brace. They grasped a handle attached to a weighted sled and performed repetitive movements in time with a metronome. The goal of the task was to complete each movement in one metronome beat. A goal equivalent manifold (B) is represented by a dashed line. Data points for movements of an individual subject (grey) are shown with the non-dimensional distance, *D*, on the X-axis and non-dimensional speed, *S*, on the Y-axis. Points that lie on the dashed line satisfy the timing goal of the task, wherein $D/S = T$ and $T = 1$ metronome beat. Deviations away from the GEM (δ_P) affect performance. Deviations along the GEM (δ_T) do not (red arrows).

metronome until they felt could no longer continue. The weight of the sled was set to 15% of the subject's maximum elbow flexion/extension strength. The metronome was scaled to the length of the forearm (~2.6 Hz). Every 30 seconds and at the end of the fatiguing task, subjective ratings of perceived exertion (RPE) (Borg 1982), mental effort (Paas et al. 1994), and pain (Williamson et al. 2005) were obtained verbally using numeric scales.

At the beginning of the pain session, ischemic muscle pain was first induced in the left arm by applying a blood pressure cuff to the arm (Maixner et al. 1993) (Fig. 4.1A). Subjective pain

ratings were recorded every 30 seconds as soon as the cuff was inflated. When subjects reached a moderate pain rating (≥ 3/10), they began the fatiguing task with the right arm. Subjects wore the inflated cuff until the end of the fatiguing task or until they requested that the cuff be deflated or reached a maximum of 20 minutes. Subjects continued the fatiguing task until they felt they could no longer continue.

To quantify the degree of fatigue, maximal voluntary contraction (MVC) strength was measured during gripping, wrist flexion and extension, and elbow flexion and extension prior to and immediately following the fatiguing task. Strength was assessed with the subject strapped to the chair in the testing position described above. Grip strength (kg) was measured during maximal gripping efforts using a hydraulic hand dynamometer (Baseline, White Plains, NY). Wrist and elbow strength (N) were measured using a hand-held load cell (Lafayette Instruments, Lafayette, IN). For wrist flexion/extension MVC the forearm was pronated, and subjects were instructed to maintain the hand in a static horizontal position while a researcher applied upward (flexion) or downward (extension) force with the dynamometer on the hand. To assess elbow strength, subjects were instructed to maintain the elbow flexed to 90 degrees while a researcher applied pulling (flexion) or pushing (extension) force to the forearm (Gates et al. 2010). The peak force was recorded for each of three 4 second MVC trials. The average peak value for three trials was taken for grip, wrist, and elbow strength at each strength measurement.

The 3-dimensional position of a reflective marker placed on the handle of the sled was recorded at 120 Hz using a 16 camera motion capture system (Motion Analysis, Santa Rosa, CA). Muscle activity in the biceps, triceps, wrist flexors, and wrist extensors was recorded at 1200 Hz using wireless electrodes (Delsys Inc., Boston, MA). Marker and EMG data were collected continuously throughout the fatiguing task.

4.4 Data Analysis

EMG data were bandwidth filtered (20 - 450 Hz), and the instantaneous mean power frequency was calculated using a continuous wavelet transform algorithm with a Daubechies (db5) wavelet (MATLAB R2015a, Mathworks, Natick, MA) (Gates et al. 2011). The wavelet was scaled in one scale intervals from 1 – 39 (roughly 20 - 800 Hz). The maximum and minimum handle positions were used to identify the beginning and end of each flexion and extension movement. The IMPF data for each movement cycle (one consecutive flexion and extension movement) were averaged to obtain a single value for each cycle. The rate of decrease in IMPF was calculated as the slope of a line fit to the time series of all movement cycles (Cowley et al. 2014). A negative IMPF slope across cycles indicates progressing muscle fatigue because muscle fatigue leads to a decrease in the highest frequencies in the EMG signal (De Luca 1997, Gates et al. 2011).

For each movement, the timing error (E) was calculated as the time between movement reversal and the nearest metronome beat. Negative values of E indicate that movement reversal preceded the metronome beat. Movement distance was calculated as the total length of the path traveled by the handle marker, and movement speed was calculated as the average speed of the handle marker from the beginning to the end of each movement. Time series of movement distance and speed were rescaled by forearm length and metronome frequency to obtain non-dimensional distance (D) and speed (S). To assess how variations in movement affected the task outcome, I analyzed a goal-equivalent manifold (GEM). The GEM method maps body variables onto a mathematically defined goal space (Cusumano et al. 2006). The movement goal during the fatiguing task was to complete each movement in time, T, where T is the time between consecutive metronome beats. This goal could be accomplished with any constant error, E, across consecutive movements. The GEM is a set of all body state variables that exactly satisfy the task goal. For the timing goal of the fatiguing task, the GEM was defined as

$$D/S = T \quad (4.1)$$

where all [*D, S*] combinations that satisfy the goal equation lie on the GEM (Gates et al. 2008, Cowley et al. 2014). Using this GEM, variability in movement distance and speed was decomposed into a component that directly affects whether the timing goal is met (goal relevant) and one which has no effect on the timing goal (non-goal relevant). Thus, variability in *D* and *S* was decomposed into the new variables δ_P and δ_T which represent deviations perpendicular to the GEM (goal relevant) and deviations tangential the GEM (non-goal relevant), respectively.

Acceleration was calculated as the second derivative of the handle marker position, and the force applied to the handle (H_f) was estimated using the kinematic data according to

$$H_f = ma + \mu mg \quad (4.2)$$

where *m* is the mass of the weighted sled, *a* is the marker acceleration, μ is the coefficient of friction, and *g* is the gravitational acceleration constant. The magnitude of the peak force during each movement was recorded to obtain time series of peak handle force (*F*).

Finally, to determine how people controlled their movements during the fatiguing task, trial to trial fluctuation dynamics of each time series were quantified using detrended fluctuation analysis (Hausdorff et al. 1995, Peng et al. 1995). This procedure produces a scaling exponent, α, that describes statistical persistence in a time series. Time series of *N* data points were first integrated and then divided into non-overlapping bins of length *n*. Data in each bin were then detrended using a linear least-squares fit and the residuals were averaged. The average residual

size was calculated for bin lengths ranging from *n=4* to *n=N/4*. The variable α was defined as the slope of a line describing the relationship between the log of the bin length and the log of the average residual (Gates et al. 2008). Lower values of α indicate that deviations in one direction are more likely to be immediately corrected, meaning they are followed by deviations in the opposite direction. Higher values of alpha indicate that deviations in one direction are more likely to remain uncorrected, meaning they are followed by deviations in the same direction (Gates et al. 2008, Cowley et al. 2014). Thus, time series of variables that are tightly controlled yield lower α exponents than less controlled variables (Dingwell et al. 2010).

Five equally spaced bins of data from the muscle fatigue task were obtained for each session. Each bin consisted of 160 movement cycles (~1 minute) and the first and last bins were defined as first and last minutes the fatigue trial. For each time series (E, D, S, δ_P, δ_T, F), the average and DFA exponent (α) were quantified during each 1-minute interval. Additionally, to quantify differences in the rate of change in movement distance and speed, the slope of a line fit to each minute of D and S data was obtained.

4.5 Statistical Analysis

Subjects were categorized as pain catastrophizers if their score on the (PCS) was 20 (50^{th} percentile) or higher (Sullivan 2009). The durations of the fatiguing task from each session were compared using a 2-way mixed model (pain × catastrophizing) GLM to test for differences between sessions (pain vs. no pain) and groups (high vs. low catastrophizing). Subjective measures (RPE, mental effort, and pain) were resampled to 10 intervals using linear interpolation and examined using 3-factor mixed model (pain × time × catastrophizing) GLMs to test for differences between sessions, time intervals (1-10), and groups. IMPF slopes were excluded from the analysis

because I observed large changes in movement distance and speed during fatigue which would confound the IMPF results. Differences in muscle fatigue were assessed using 3-factor mixed model (pain × fatigue × catastrophizing) GLMs to determine whether the MVC strength in each muscle declined during each session (pre vs. post) and whether strength differed between sessions or groups. For each average, DFA exponent, and slope (E, D, S, δ_P, δ_T, F), a 3-factor mixed model (pain × fatigue × catastrophizing) GLM was used to test for effects of session, fatigue interval (1-5), and group. Initial review of the data revealed that the order of the sessions affected the outcome variables. Consequently, session order (Day 1 = pain vs. Day 2 = pain) was included as a covariate in all statistical tests to control for the sequence of exposure to the pain intervention. When session order was included in a significant interaction effect, additional mixed model (pain × fatigue × order) ANOVAS were performed to determine how session order affected the outcome variables. For all tests, Mauchly's test of sphericity was used to test the assumption of equal variances. When equal variance was violated, a Hyun-Feldt correction was applied. Estimated marginal means were used to further examine significant interaction effects. Significance level for all tests was set at $p < 0.05$, and a Sidak correction was applied for multiple comparisons. All statistical analyses were carried out in SPSS (IBM SPSS Statistics for Windows, Version 23.0. Armonk, NY).

4.6 Results

4.6.1 Pain

Eight subjects (4 male) were classified as pain catastrophizers (mean PCS score = 27 ± 6). The remaining subjects were classified as non-catastrophizers (mean PCS score = 9 ± 5). Main effects of pain and time ($p < 0.001$) showed that subjective pain ratings were higher in the pain session compared to the no pain session and increased throughout the fatigue trials ($p < 0.001$; Fig. 4.2A). There was also a time × group interaction effect ($p = 0.01$) on pain. Pain ratings were lower

in the high catastrophizing group than the low group during the last 30 % of the fatigue trials ($p < 0.04$).

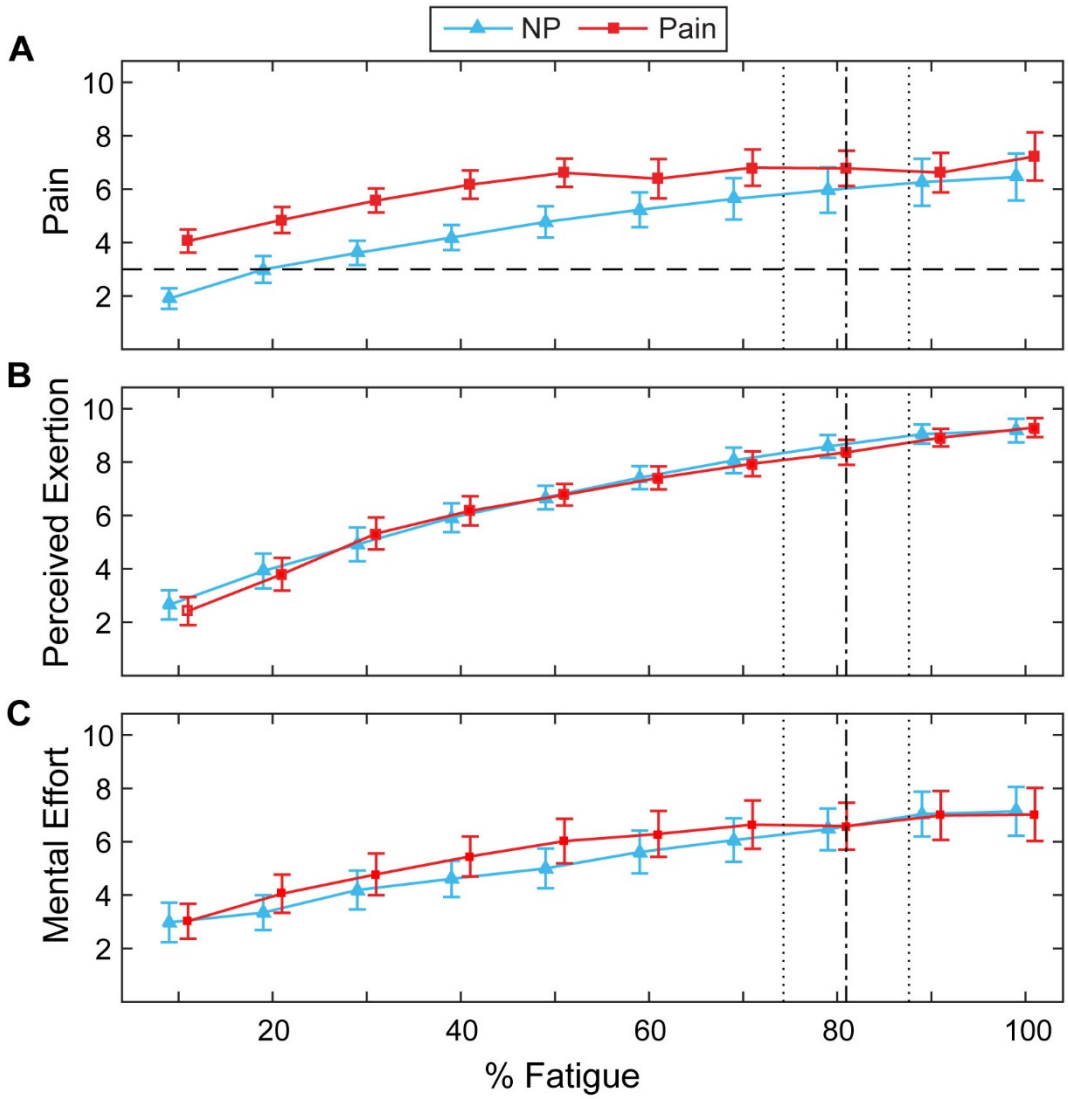


Figure 4.2. Subjective pain and effort during the fatiguing task.

Average subjective pain ratings (A), ratings of perceived exertion (RPE; B), and mental effort (C) during the fatigue trials during the pain and no pain sessions. Error bars are the 95% confidence interval. The horizontal dashed line shows the pain threshold of 3. Vertical dashed lines show the average cuff deflation time for the pain session. Vertical dotted lines show the 95% confidence interval for deflation time.

4.6.2 Muscle Fatigue

All subjects reached a rating of perceived exertion (RPE) of eight or greater during the fatiguing task (Fig. 4.2B). Compared to baseline measurements, maximum voluntary contraction (MVC) strength decreased in each muscle group after the fatigue task ($p < 0.004$). Wrist flexor MVC strength was higher in the no pain than the pain session ($p = 0.03$). There were no other significant effects of session ($p > 0.2$) and no interaction effects ($p > 0.079$) on MVC strength (Fig. 4.3).

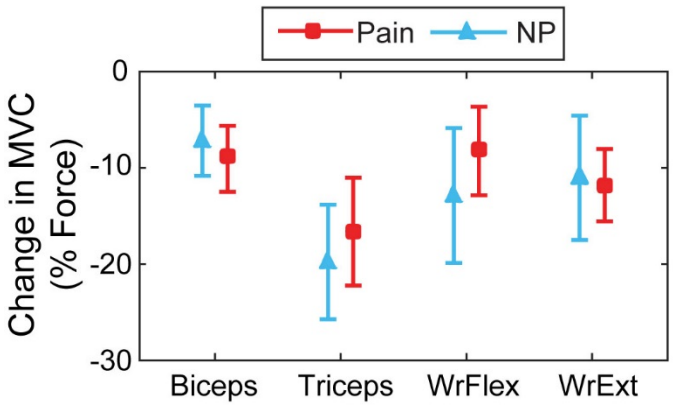


Figure 4.3. Maximum voluntary contraction strength before and after the fatiguing task. The change in maximum voluntary contraction strength (MVC) as a percentage of pre-fatigue MVC strength in each muscle. Error bars are the 95% confidence interval.

4.6.3 Subjective Effort

There was a main effect of time on RPE ($p < 0.001$; Fig. 4.2B). However, there were significant session × time × order ($p = 0.025$) and time × group interaction effects ($p = 0.007$). Subjects who completed the pain session first reported higher RPE between 20 and 60 % of the pain session compared to subjects who did the no pain session first ($p < 0.05$; Fig. 4.4B). There were no significant differences in RPE due to session order during the no pain session ($p > 0.27$;

Fig. 4.4A). The high catastrophizing group had a lower RPE between 60 % and 80 % of the fatigue task ($p < 0.03$) compared to the low catastrophizing ×group.

There was a significant effect of time ($p < 0.001$) and a session × time ($p = 0.003$) interaction effect on mental effort. Mental effort tended to be higher during the pain session compared to the no pain session, but post hoc tests were not significant ($p > 0.08$; Fig. 4.2C). There were no other significant main effects or interactions on RPE or mental effort ($p > 0.09$).

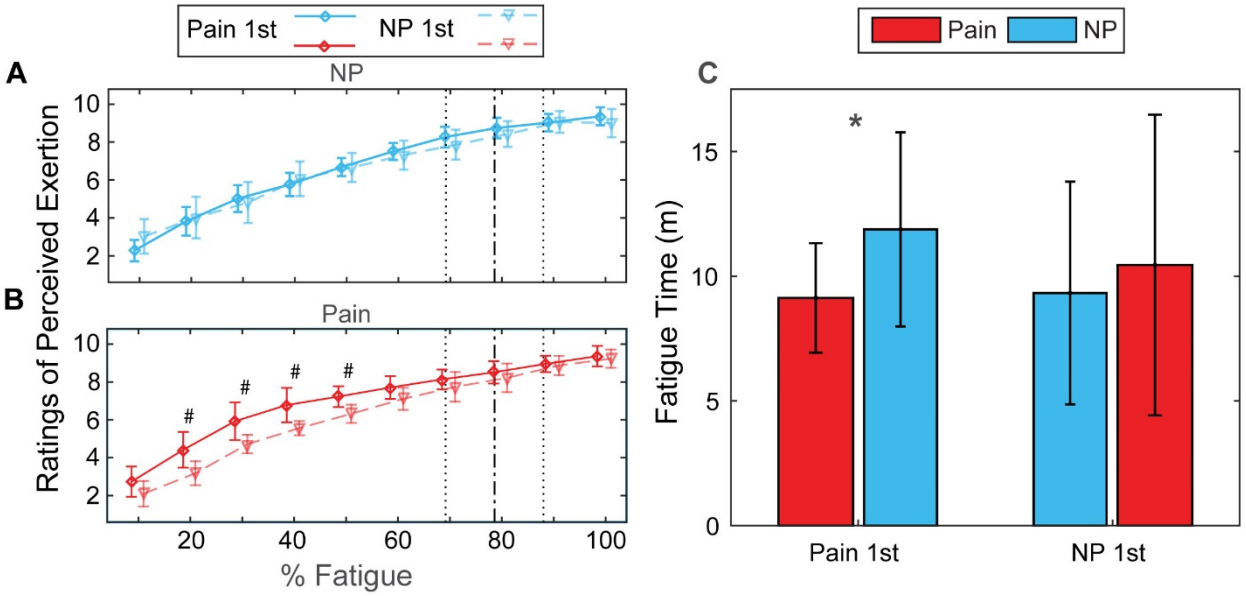


Figure 4.4. Effects of session order on RPE and endurance time.

Ratings of perceived exertion (RPE) during the no pain session (A) and pain session (B) for subjects who did the pain session first and those who did the no pain session first. Average endurance time (C) for subjects who did the pain session first and those who did the no pain session first. Error bars are the 95% confidence interval. * indicates a significant difference between sessions. # indicates a significant difference between pain first and no pain first subjects.

4.6.4 Fatigue Time

During the pain session, subjects reached a pain threshold of three and began the fatigue trial 1 min. (range: 0.1 – 3.2 min.) after the cuff was applied, on average. Subjects wore the cuff for 8.2 min. (range: 3.5 – 20 min.). One subject wore the cuff for 20 min. All others removed the

cuff or terminated the fatiguing task within 11.8 min. Subjects performed the fatiguing task for an average of 10.2 min. (Pain: 9.8 min., range: 3.4 – 40.6 min.; NP: 10.6 min., range: 3.4 – 30.3 min.). Four subjects ended the fatiguing task before deflating the cuff. The remaining subjects deflated the cuff an average of 3.2 min prior to terminating the fatiguing task (range: 0.3 –20 min.). The pain session was 0.8 min. (~65 cycles) shorter than no pain session, on average, but there was no main effect of pain ($p = 0.354$). The high catastrophizing group had a higher endurance time than the low catastrophizing group (high: 13.9 min.; low: 7.7 min.; $p = 0.036$). There were no group × order ($p = 0.308$) or session × group × order interaction effects ($p = 0.094$), but there was a session × order interaction effect ($p = 0.016$) on endurance time. Post hoc tests showed that subjects performed the fatigue task longer in their second session. When the pain session was first, time increased by 3.4 min. (~270 cycles) in the no pain session ($p = 0.014$). However, when the no pain session was first, time increased by just 1.1 min. (~87 cycles) in the pain session ($p = 0.346$; Fig. 4.4C).

4.6.5 Timing errors

There were no main effects or interaction effects on average timing errors, E, ($p > 0.05$; Fig. 4.6A) or the DFA exponent, α of E ($p > 0.1$; Fig. 4.4C).

4.6.6 Effects of Fatigue

There was a main effect of fatigue on movement distance, D, movement speed, S, and peak force (F) ($p < 0.001$). Subjects made shorter, slower movements during the last three fatigue intervals compared to the first two intervals ($p < 0.05$; Fig. 4.5A) and exerted higher force during the first interval than all subsequent intervals ($p < 0.001$). The average deviation (δ_T) along the goal equivalent manifold (GEM) also decreased during the fatigue task ($p< 0.001$), but deviations perpendicular to the GEM (δ_P) did not change ($p = 0.993$). There was a main effect of fatigue on

α of peak force (p = 034). During fatigue, there was a gradual increase in α. However, post hoc tests were not significant (p > 0.3; Fig.4.6). There were no other significant main effects of fatigue (p > 0.09).

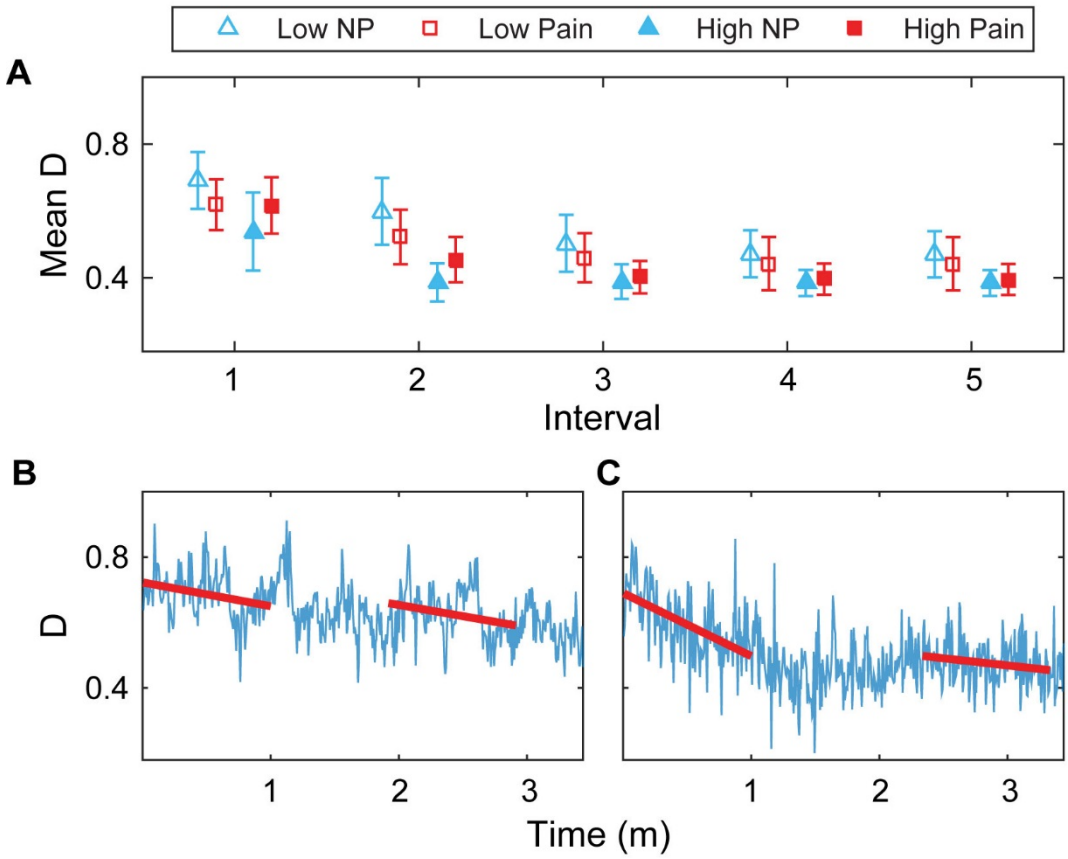


Figure 4.5. Effects of fatigue and catastrophizing on movement distance.

Average movement distance, *D*, during each interval of the movement (A) for low (empty markers) and high (filled markers) catastrophizing subjects during pain and no pain sessions. Error bars are the 95% confidence interval. Time series of *D* for representative low (B) and high (C) catastrophizing subjects. The slope of *D* during the first two ratcheting intervals is shown with red lines.

4.6.7 Effects of Pain

There were significant session × fatigue interaction effects on α of *D* (p = 0.017), α of *S* (p = 0.045), and α of δ_T (p = 0.019). Post hoc tests showed that α was higher at the beginning of the

pain session than the no pain session. However, this effect was only significant during the second fatigue interval for α of S (p = 0 .042; Fig. 4.6A-C). There were no differences between sessions for α of D, α of S, or α of δ_T at any other time point (p > 0.1) and no other main effects of pain (p > 0.06) or fatigue × pain interactions (p > 0.3).

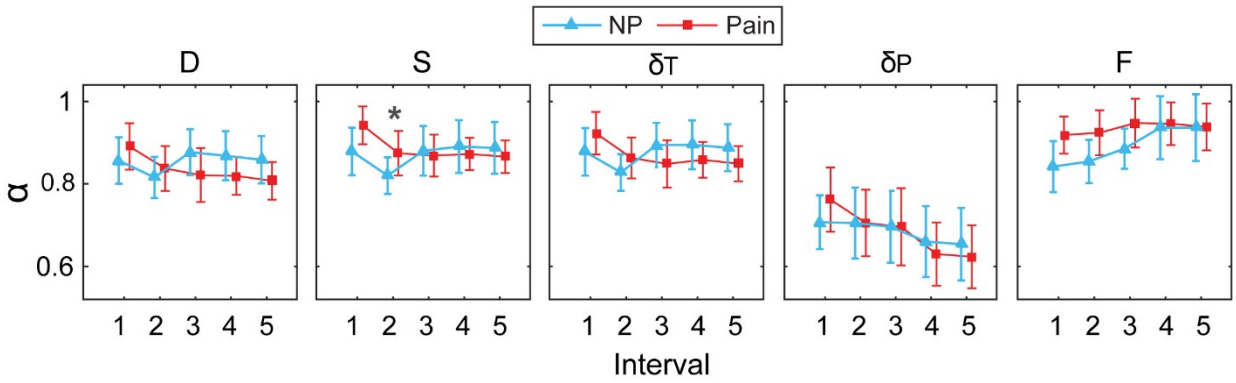


Figure 4.6. Effects of pain on movement control during the fatiguing task.

Average DFA exponent, α, during the pain and no pain sessions for D, S, δT, δ_P, and F during each interval of the fatigue task. Error bars are the 95% confidence interval. * indicates a significant difference between sessions.

4.6.8 Effects of Group

There was a significant main effect of group on α of δ_P (p = 0.041), indicating that α was lower in the high catastrophizing group compared to the low catastrophizing group (Fig. 4.6D). There were also session × group (p < 0.03) interaction effects on D, S, and δ_T. Low catastrophizing subjects made longer, faster movements (and thus higher δ_T) in the no pain session than the pain session (p < 0.035) but there was no difference between sessions in the high catastrophizing subjects (p > 0.15; Fig. 4.5A). On average, the slopes of D (p = 0.054) and S (p = 0.037) were lower in the high catastrophizing group than the low catastrophizing group. However, there were significant fatigue × group interaction effects on the slopes of D and S (p = 0.001). Post hoc tests showed that in the high catastrophizing group, movement distance and speed decreased faster during the first minute of fatigue than any other minute (p < 0.02; Fig.4.5C). There was no

difference between minutes in the slopes of the low catastrophizing group ($p > 0.06$; Fig. 4.5B). There were no other session × group ($p > 0.05$), fatigue × group ($p > 0.08$), or fatigue × session × group interaction effects ($p > 0.07$).

4.6.9 Effects of Order

There were session × order interaction effects on D, S, δ_T, and δ_P, and α of δ_P ($p < 0.045$). Subjects made longer, faster movements in the first session compared to the second session when they did the no pain session first ($p < 0.03$) but not when they did the pain session first ($p > 0.29$). Average δ_P tended to be lower in the second session than the first, but post hoc tests were not significant ($p > 0.11$). Subjects exhibited lower α of δ_P in the second session regardless of session order ($p < 0.05$). There were no other session × order ($p > 0.08$), fatigue × order ($p > 0.16$), or fatigue × session × order interaction effects ($p > 0.1$).

4.7 Discussion

The purpose of this study was to determine whether pain affects the control strategies that people use during a fatiguing task. Subjects reported higher pain ratings during the pain session indicating that the ischemic pain protocol successfully induced painful sensations. In addition, the high ratings of perceived exertion (RPE) and the decrease in maximum voluntary contraction strength (MVC) indicate that subjects experienced muscle fatigue during the repetitive task. I found significant effects of pain on movement control and endurance time during the fatiguing task. However, these effects were moderated by session order. Pain catastrophizing affected the movement strategies people used but did not change the way they responded to pain.

I hypothesized that subjects would reach voluntary exhaustion earlier during the pain session than the no pain session and that this effect would be amplified in the high catastrophizing subjects. Instead, subjects performed the task longer on the second test day, regardless of pain, and

high catastrophizing subjects continued the task longer than low catastrophizing subjects. However, subjects who completed the pain session on the first day of the study increased their endurance on day two by more than twice as much as the subjects who completed the pain session on the second day (Fig. 4.4C). Differences in the muscle endurance time were likely due to the movement strategies that subjects used. Subjects who completed the pain session first made shorter slower movements during the no pain session than those who did the no pain session first (Fig.4.4A). The high catastrophizing subjects reduced their movement distance and speed much faster than the low catastrophizing subjects during the fatigue trials on both days (Fig. 4.5B and C). The observed differences in the movement strategies between sessions and groups help to explain the different endurance times.

The order of testing also affected how effortful people perceived the task to be each day. Subjects who completed the pain session first reported higher RPE in the pain session compared to those who completed the no pain session first. Recent findings suggest that the limits of muscle fatigue are largely dependent on how effortful a task is perceived to be (Noakes 2004, Noakes 2008, Marcora et al. 2010). However, the similar decline in MVC strength in both sessions indicates that the muscles were fatigued to a similar degree on each day. Thus, the rate of fatigue differed, but the subjects reached voluntary exhaustion at a similar level of muscle fatigue. Furthermore, near the end of the fatigue task, the RPE was similar in all groups and conditions. (Fig. 4.2A and 4.4A and B). Thus the current pain task did not appear to limit the perception of muscle exertion at the highest levels of muscle effort.

Subjects modified their movement strategy during the fatiguing task to make shorter slower movements. These changes contributed to a reduction in handle force and presumably muscle forces. The reduction in movement distance and speed were similar to those observed during a timed sawing task after localized shoulder flexor fatigue (Cowley et al. 2014). However, in that task subjects also exerted greater control over movement distance and speed after fatigue. In the

current study, there was no effect of fatigue on the control of distance or speed, but there was a tendency for subjects to reduce control over peak handle force during fatigue. Overall, changes in movement distance, speed, and force were executed in a way that did not affect the task timing goal. In fact, the average reduction in d_P on the second study day indicates that subjects improved their ability to vary distance and speed without affecting the task outcome.

My hypothesis that pain would increase timing errors was not supported. Because pain affects motor planning and execution (Moseley et al. 2005, Babiloni et al. 2008, Bank et al. 2013), I expected remote pain to increase the magnitude of timing errors as subjects modified their movements during fatigue. Instead, I found no difference in the magnitude of timing errors due to pain or muscle fatigue. This is in agreement with previous studies of motor control during isolated muscle fatigue (Selen et al. 2007, Gates et al. 2008, Cowley et al. 2014) or pain (Birch et al. 2001, Smith et al. 2006). Although I did not observe changes in timing errors, during the pain session subjects tended to exert less control (higher α) over *D, S,* and d_T during early fatigue (Fig. 4.6). While the subjects initially showed reduced control during the pain session, they quickly developed a similar pattern of control to that observed in the no pain session. Additionally, subjects who did the no pain session first reduced their movement distance and speed during the pain session. While there was not a significant effect of session order on force ($p > 0.19$), reducing movement amplitude could reduce the magnitude of efferent signals due to a reduction in the muscle force required. Thus, the additional cognitive demand of monitoring the painful arm could be offset by using a less cognitively demanding movement strategy. These findings may explain why I observed only a minor increase in mental effort ratings during the pain session (Fig.4.2C). The results of the current study suggest that subjects acclimated to the pain quickly and redirected their attention to the fatiguing arm as fatigue progressed.

Pain has been found to augment (Lamothe et al. 2014) or impede (Dancey et al. 2016) motor learning in different contexts. In the current study, the order of exposure to the pain and no

pain conditions had a significant effect on the fatigue task. When subjects completed the pain session first, they reported higher RPE during the pain session compared to those who completed the no pain session first. Exposure to the painful stimulus during fatigue interfered with the perception of muscular effort only when subjects were unfamiliar with the fatigue task. Conversely, longer faster movements were observed during the no pain session of subjects who completed the no pain session first but not those who completed the pain session first. This suggests that those subjects who completed the pain session first adopted a more conservative movement strategy during the pain session which was retained when they returned for the no pain session. The results indicate that subjects learned new perceptual environments and movement strategies during the pain session, and some of this learning was retained across study sessions.

My hypothesis that pain catastrophizing subjects would exhibit larger effects of pain than low catastrophizing subjects was not strongly supported. Low catastrophizing subjects made longer, faster movements during the no pain session compared to the pain session, but high catastrophizing subjects did not. Indeed, the high catastrophizing subjects reduced their movement distance and speed quickly during the first minute of fatigue during both sessions, and this difference likely contributed to the greater endurance times in the high catastrophizing group. In one study, subjects who exhibited pain catastrophizing and negative beliefs about pain reduced the variability of muscle activation when a painful stimulus was applied during movement and retained the low variability when the pain was removed suggesting that these subjects tended to adopt a protective movement strategy (Moseley et al. 2006). In the current study, the high catastrophizing subjects adopted a protective strategy in the fatiguing task with or without pain. This may have been intended to delay sensations of discomfort related to muscle fatigue.

There were several limitations in this study. The effects of pain were highly dependent on session order and largely disappeared by the end of the fatigue task. I had limited power to identify interactions between session order and pain catastrophizing. Pain demands attention when a

painful stimulus is perceived to be threatening (Crombez et al. 1998, Moseley 2007). Ischemic muscle pain increases slowly. While the results suggest that subjects initially directed their attention to the painful arm, this did not continue throughout fatigue. It is probable that subjects did not perceive the ischemic pain to be threatening in the controlled laboratory setting and quickly acclimated to the pain. In future work, a less predictable painful stimulus might elicit larger effects. Furthermore, the fatigue task was also perceived to be painful. Near the end of the fatigue task, subjects may have directed their attention to the fatiguing muscles more than the ischemic arm. Like most previous work, this study included a relatively simple motor task. It is possible that in a more complicated motor task, performance would decline when people experience pain. In particular, tasks with varying outcome requirements (.e.g. variable movement times or endpoint locations) could be affected as pain may interfere with motor planning (Babiloni et al. 2008).

Another potential limitation is the way that subjects were classified as pain catastrophizers. In this study I used a cutoff score of 20 or higher on the PCS. This score corresponds to the 50^{th} percentile in a sample of injured workers (Sullivan 2009). While a score of 30 (75^{th} percentile) has been considered as a cutoff point in clinical populations, it is not clear how this cutoff point applies to young healthy subjects. In the current sample, only two subjects (1 male) scored above 30. The median PCS score was 13.

Including both genders in the study may have introduced additional variability. For example, previous work found higher catastrophizing scores in females than males. However, there was no difference between male and female subjects in the current sample (Female: 16 ± 9; Male: 14 ± 11; $p = 0.605$). Prior work has also demonstrated differences between males and females in muscle fatigue rate and pain perception. Females generally exhibit greater muscle endurance during submaximal tasks (Hicks et al. 2001, Clark et al. 2005, Hunter 2009, Hunter 2016) and report higher subjective pain ratings than males (Keogh et al. 2000). In the current study, endurance

time did not differ between males and females ($p > 0.5$). Females reported slightly higher pain ratings than males, but the difference was not significant ($p > 0.3$).

The results of this study are in agreement with previous studies on muscle fatigue which showed that subjects successfully adapt new movement control strategies to meet task goals when fatigued (Selen et al. 2007, Gates et al. 2008, Cowley et al. 2014). In addition, this work showed that remote ischemic pain initially caused subjects to reduce movement control, but the effects of pain were reduced quickly as subjects acclimated to the painful stimulus. Previous exposure to the fatigue task and the painful stimulation affected the perception of the task and the movement control during subsequent sessions. Pain catastrophizing affected how subjects executed the fatigue task, but not how they responded to pain. Further work is needed to understand how different types of painful stimulation affect movement control and fatigue, particularly in more complicated motor tasks. The current results suggest that exposure to a non-local painful stimulus during muscle fatigue may cause subjects to adopt simplified movement strategies.

CHAPTER 5. Conclusion

5.1 Summary

People respond to muscle fatigue by changing their movement patterns and control strategies. These fatigue-related changes can help people to maintain task execution when fatigued, but they can sometimes predispose people to further fatigue or injury. It is challenging to predict how people will be affected by muscle fatigue for several reasons. First, fatigue is a transient multifactorial process that usually affects multiple muscles and joints simultaneously. The redundancy of the neuromuscular system can impede the ability to quantify fatigue-related changes during multi-joint tasks. Second, the effects of fatigue depend on the characteristics of the task being performed and the individual performing it. In complex occupational or athletic environments, many factors may influence the way a person responds to muscle fatigue (e.g., mechanical, physiological, psychological, or cognitive task demands). Chapters 2, and 4 of this research investigated how different fatigue conditions moderate the way that people change their movement patterns and control strategies during repetitive tasks. Chapter 3 examined how movement coordination changes at different time points during an experimental fatigue session. Overall, the results of this work improved our understanding of how people adapt to muscle fatigue in different contexts and how these adaptations affect movement strategies and task execution.

The effects of muscle fatigue may be readily apparent with widespread movement changes or very subtle with little apparent change in movement kinematics. In Chapter 2, the effects of distal fatigue, in particular, were relatively minor. Even when fatigue causes minor movement changes, subtle effects of muscle fatigue can increase the likelihood of musculoskeletal injury (Chopp et al. 2010). The onset of many musculoskeletal disorders is insidious making it difficult

to identify how movement patterns influence risk. It is important to understand how people modify their movement patterns during fatiguing tasks. Even small changes may be important because they can alter the distribution of forces on tissues and may contribute to the rate of fatigue and the development of repetitive use injuries. However, for many musculoskeletal disorders, further work is needed to identify a direct causal relationship between muscle fatigue and injury.

Several previous studies found that muscle fatigue resulted in movement reorganization affecting multiple joints (Côté et al. 2002, Côté et al. 2005, Fuller et al. 2009, McDonald et al. 2015, Tse et al. 2015), and the results of Chapter 2 support these findings. Kinematic reorganization and increased variability during muscle fatigue can reduce the load on fatigued muscles. However, the results presented in Chapter 3 demonstrate that muscle fatigue also causes decreased movement coordination. A decrease in movement coordination could also reduce the overall efficiency of movement (Hodges et al. 2005, Wakeling et al. 2010), and lead to unwanted movement outcomes (Winter 1992, Chiu et al. 2013). It is unclear whether the reduction in coordination is a result of the observed movement reorganization or whether they occur simultaneously as a result of fatigue. It is possible that changes in one or two joint angles result in a chain of changes at other angles (reorganization), and this causes movement coordination to decrease because the CNS has not learned to effectively coordinate the joints in the new movement pattern. The extent to which this occurs could be assessed by experimentally constraining individual degrees of freedom to alter the movement pattern at specific joints and measuring the resulting coordination.

Muscle fatigue increases the variability of movement. While it is possible that movement variability increases due to neuromuscular noise (Wolpert et al. 1998), some have proposed that movement variability represents a form of motor exploration (Fuller et al. 2011, Srinivasan et al. 2012). In this sense, varying movement patterns enables people to identify new movement strategies that preserve movement execution and delay the progression of muscle fatigue. The

results of Chapter 4 demonstrate that people are able to vary their movements in task specific ways which do not affect the task outcome. The results in Chapter 2 suggest that motor variability does not exclusively increase at joints directly affected by fatigue. Instead, increases in motor variability during fatigue may occur primarily at proximal joints which have a large effect on task dynamics. Changes at proximal joints can influence the kinematic or kinetic patterns of distal joints in the kinematic chain and may thus reduce the load on fatiguing muscles. However further research is needed to determine to what extent changes in variability affect the rate of muscle fatigue.

Muscle fatigue did not have a significant effect on the execution of timed ratcheting or elbow flexion/extension movements. Previous research found that fatigue did not affect task execution in timed movements (Gates et al. 2008, Cowley et al. 2014), target tracking (Selen et al. 2007), or reaching movements (Fuller et al. 2011). In agreement with these studies, the current work demonstrates that when fatigued, people modify movement kinematics, coordination, and control strategies while maintaining the execution of externally defined task goals. This was true even in the final minute of a fatiguing task performed to voluntary exhaustion (Chapter 4). While the initial exposure to a painful stimulus had a mild impact on movement control, this did not affect task execution. In fact, experimental results where muscle fatigue limited the execution of repetitive motor tasks are limited (Jaric et al. 1999, Huysmans et al. 2008). These findings highlight the remarkable adaptability of the neuromuscular system. However, this also reflects a tendency to select relatively simple tasks and task environments for evaluation in experimental settings. While this approach is often necessary to limit the influence of confounding factors, there is a need for more studies of complex multi-joint tasks and realistic fatiguing environments. These kinds of experiments are likely to require more sophisticated measurement techniques and multivariate analyses such as principal components analysis.

While some work suggested that changes in the movement strategy during fatigue could accelerate the rate of muscle fatigue (Huysmans et al. 2008), in the current work there is no

evidence that fatigue adaptation initiates a cycle of further fatigue. Instead, the results of Chapter 4 support the idea that changes during fatigue reduce the load on fatigued muscles. However, in some cases, these adaptations may make movements more cognitively demanding (Lorist et al. 2002, Terrier et al. 2009). Muscle fatigue has a negative impact on simultaneously executed cognitive tasks (Terrier et al. 2009). This may be in part due to motor reorganization. The reduced coordination observed after fatigue in Chapter 3 suggests that muscle fatigue caused movement complexity to increase. Conversely, the observed reduction in movement amplitude during fatigue in Chapter 4 may have reduced the cognitive load of the movement task. This may explain why the reduction in movement amplitude was more pronounced when a painful stimulus was applied concurrently. Together the results of this and previous work suggest that people adopt movement strategies that satisfy the demands of their task environment. In some cases, fatigue adaptations may accelerate fatigue. In others, they may increase cognitive demand, and in others, they may limit successful execution of a task. Further work is needed to better understand how people balance these sometimes competing priorities in realistic environments. During tasks that emphasize muscle endurance, the limits of task execution may be more psychological than physiological (Noakes 2004, Marcora et al. 2010). People can continue performing a task until they decide they feel like they cannot. Individual characteristics that influence how a person interprets and responds to fatiguing sensations are therefore critical to this process.

Factors that influence the way a person responds to muscle fatigue range from genetics (e.g., sex, size) to personal experience (e.g., fitness, training) to psychological status (e.g., motivation, depression), and these characteristics are likely to interact in unique ways for each person. Furthermore, effects of these factors on fatigue adaptation may be operationalized through multiple aspects of motor-cognitive performance. Predicting how a fatigue scenario will affect an individual is therefore not trivial. For example, differences between males and females in muscle strength (Bambaeichi et al. 2004, Tenan et al. 2015), fatigue (Sarwar et al. 1996), pain sensitivity

(Hooper et al. 2011), motor control (Zoghi et al. 2015), reflexes (Casey et al. 2014), and cognition (Sundström Poromaa et al. 2014) may be exaggerated or minimized by hormone fluctuations during the female menstrual cycle. Research in this area has been inconclusive. Recent studies and reviews concluded that changes in fatigue (Hunter 2014, Julian et al. 2017) and pain sensitivity (Bartley et al. 2013, Iacovides et al. 2015) during the menstrual cycle are minimal. However, other recent studies urge caution and advocate a holistic approach. The effects of hormone levels on pain sensitivity can be affected by social-environmental factors such as romantic relationships (Vigil et al. 2014), and changes in cognition during the menstrual cycle may be the result of hormone-related emotional changes (Sundström Poromaa et al. 2014). The potential confounding effects of female hormonal fluctuations highlight the complexity of determining how a single variable (sex) affects fatigue adaptation. The lack of significant differences between males and females in the current work might be the result of intersubject variability related to the menstrual cycle. However, it is also likely that individual characteristics other than sex involve a similar level of complexity. Therefore, as experimental fatigue environments increase in complexity, it may be necessary to limit subject participation based on sex, psychology, or other individual characteristics in order to maintain sufficient scientific control.

Muscle fatigue is a complex process. While many studies reduce fatigue to two states (pre and post fatigue), the reality is that muscle fatigue is a continuously changing state. Motor adaptation is not only the result of the current fatigue state. The adaptations people make when fatigued also affect the future fatigue state. The results of this work demonstrate that the effects of muscle fatigue depend on which muscles are fatigued, and these effects continue to change during and after fatigue. Furthermore, the movement strategies that people use during fatigue can be moderated by a painful stimulus in a remote part of the body. From a practical standpoint, it is particularly important to limit muscle fatigue in occupational and athletic settings in order to avoid detrimental effects on performance and to reduce the risk of musculoskeletal disorders. Future

work should focus on identifying factors that can reduce the unwanted consequences of fatigue by limiting fatigue itself or enhancing the process of motor adaptation during fatigue. This will require studies in realistically complex fatiguing environments and the consideration of individual characteristics that influence muscle fatigue adaptation.

Appendices

Appendix A: Surveys and Subjective Scales

A1. Habitual Physical Activity

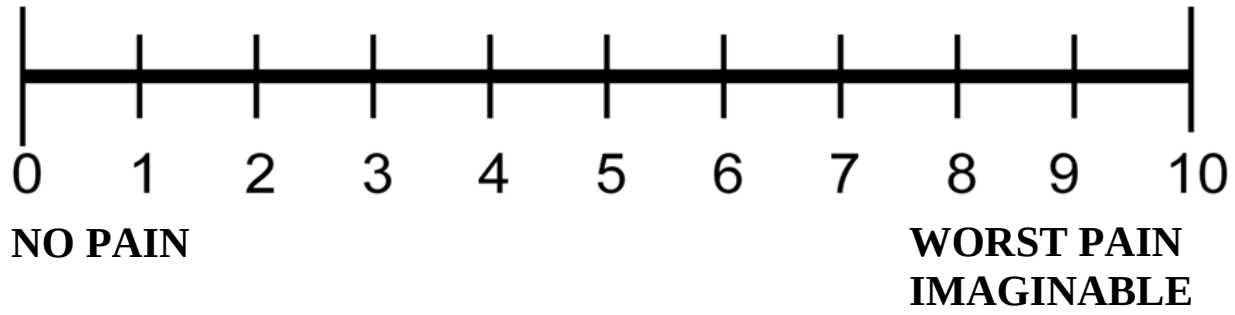
1. How do you rate your level of physical activity compared to other people your age?	very inactive	a little less active	about average	a little more active	very active
2. How often do you exercise?	never	less than once a week	once a week	2-3 times a week	almost every day
3. How hard do you usually exercise?	I don't exercise	I don't get breathless and sweaty	I get a little breathless and sweaty	I get very breathless and sweaty	I am almost totally exhausted
4. How often do you use wrenches or other hand tools?	almost never	a couple times a year	once a month	once a week	almost every day

A2. Pain Catastrophizing Scale

Everyone experiences painful situations at some point in their lives. We are interested in the types of thoughts and feeling that you have when you are in pain. Listed below are thirteen statements describing different thoughts and feelings that may be associated with pain. Using the scale, please indicate the degree to which you have these thoughts and feelings when you are experiencing pain.

	Not at all	To a slight degree	To a moderate degree	To a great degree	All the time
I worry all the time about whether the pain will end	0	1	2	3	4
I feel I can't go on	0	1	2	3	4
It's terrible and I think it's never going to get any better	0	1	2	3	4
It's awful and I feel that it overwhelms me	0	1	2	3	4
I feel I can't stand it anymore	0	1	2	3	4
I become afraid that the pain will get worse	0	1	2	3	4
I keep thinking of other painful events	0	1	2	3	4
I anxiously want the pain to go away	0	1	2	3	4
I can't seem to keep it out of my mind	0	1	2	3	4
I keep thinking about how much it hurts	0	1	2	3	4
I keep thinking about how badly I want the pain to stop	0	1	2	3	4
There's nothing I can do to reduce the intensity of the pain	0	1	2	3	4
I wonder whether something serious may happen	0	1	2	3	4

A3. Pain Scale



A4. Mental Effort Scale

1	Very, very low mental effort
2	Very low mental effort
3	Low mental effort
4	Rather low mental effort
5	Moderate mental effort
6	Rather high mental effort
7	High mental effort
8	Very high mental effort
9	Very, very high mental effort

Appendix B: Informed Consent

B1. Consent for Chapter 2 and Chapter 3

Consent to Participate in a Research Study

MOVEMENT CONTROL AFTER PROXIMAL AND DISTAL FATIGUE

Principal Investigator: **Jeffrey C. Cowley, M.S., School of Kinesiology, University of Michigan**

You are invited to be a part of a research study that looks at the way people move their upper body before and after muscle fatigue. The purpose of this study is to understand how healthy people adapt to fatigue of different muscles. The results of this study will help us understand how people control their movement when different parts of the body are fatigued.

If you agree to be part of the research study, you will be asked to participate in two testing sessions on separate days between 4 and 30 days apart. If you fail to return for a follow-up session within one month, your participation in the study may be discontinued. For each testing session, you will come to the Rehabilitation Biomechanics Lab in the Central Campus Recreation Building at the University of Michigan. You will complete a wrench turning task for several 3 minute periods. While you do this, we will monitor your movements with small reflective markers attached to your arms and torso with tape. We will also monitor your muscle activity using sensors attached with tape to the skin over muscles in your arm and torso. The areas of skin where muscle sensors need to be placed will first be shaved by a research assistant with a disposable safety razor and wiped clean with rubbing alcohol. You should come to lab in comfortable shoes and pants or shorts. Women will be asked to wear their sports bra or a tight fitting tank top (e.g., spandex) during testing. Men will be asked to remove their shirts during testing. The researchers who shave and attach markers to your skin may not necessarily be of your same gender.

Because this experiment will involve significant physical exertion, we ask that you avoid vigorous physical activity (beyond your normal daily routine) for at least 48 hours prior to each visit. Each testing session will take about 1 to 2 hours.

We would also like to videotape you so that we can ensure accuracy between the markers and your actual movement. You may still participate in the research even if you decide not to be videotaped.

At the beginning of the first testing session, we will take several measurements including your height, weight, and arm length. We will ask you to answer several questions to verify that you are right handed. We will also ask you to answer a series of questions to evaluate your attitude and emotions toward painful experiences. These tests will ask you to recall times when you experienced pain and to think about painful events, but they will not hurt you or cause you physical discomfort.

After you complete the questions you will warm up, stretch, and practice the wrench task. To perform the wrench task, you will stand in front of a shelf that has a bolt attached. We will ask you to hold a standard socket wrench and repeatedly turn the bolt. The bolt does not actually tighten, but it resists moving as you turn it. You will perform this repetitive wrench turning task, alternating with rest periods, before and after muscle fatigue. While your muscles are fatigued, you will perform the wrench task, alternating with periods of a muscle fatigue task. On each day you will complete a different muscle fatigue task to fatigue either your shoulder or hand muscles. To fatigue your shoulder muscles you will hold a weight set to 10 percent of your maximum shoulder strength and repeatedly raise your hand to shoulder height at a constant pace with your arm straight. To fatigue your hand muscles you will hold a spring-loaded hand grip trainer and repeatedly squeeze and release at a constant pace. During the fatigue tasks, you will be given vigorous verbal encouragement to help you perform the task as long as you possibly can, but not so long that you feel you might injure yourself if you were to continue further.

We will measure your muscle strength several times during the test session. To measure your strength, we will ask you to sit in a chair and hold your arm straight out in front of you. A researcher will push down against your arm with a device that measures force as you push up as hard as you can for 5 seconds. We will also ask you to hold a device that measures grip force and squeeze as hard as you can for 5 seconds. You will complete each of these tasks 3 times at several points during the session to determine the strength of your shoulder muscles and your grip strength.

While you may not receive a direct benefit from participating in this research, knowledge gained from this study may benefit others by contributing to a better understanding of how people control their movements when fatigued.

The researchers have taken steps to minimize the risks of this study. None of the procedures are expected to be dangerous in a healthy individual. You are likely to experience some discomfort during the fatigue tasks. This should not be greater than what you experience during typical exercise. If you experience severe or unusual pain during any procedures, you should tell the investigators and the procedure will be discontinued. You might develop muscle soreness 24 to 48 hours after a testing session. There is a small risk that you could experience muscular injury, such as a muscle strain. To help reduce these risks, a warm up and stretching session will be mandatory prior to performing these tests. Any muscle soreness should subside within 72 hours. You may also experience slight discomfort during shaving and alcohol preparation of the skin and during removal of reflective markers and sensors. Any skin irritation should subside within 24 hours.

By participating in this research there is a small chance of injury, as discussed above. In the event of injury, no treatment will be provided to you for any research related injury and no payment can be provided in the event of a medical problem.

We will keep the data we collect from you even after this study is complete. To keep your information safe, the data will be stored in a secure lab. It is very unlikely that anyone outside the study team will see your data or discover that you participated in this study because your name will not be attached to your data. Instead, a numeric code will be attached to the data, so

even if your data were accessed by someone else, it could not be traced back to you. Video files will be stored separately on a computer in a locked room, so it is very unlikely that anyone outside of this research team will see them. Videos will be destroyed as soon as the analysis is complete.

You will be compensated $10/hour for your time at the end of each session. If you decide to stop before a session is complete, you will not receive compensation for that session.

We plan to publish the results of this study, but will not include any information that would identify you or your family members.

There are some reasons why people other than the researchers may need to see information you provided as part of the study. This includes organizations responsible for making sure the research is done safely and properly, including the University of Michigan, or other government offices.

Participating in this study is completely voluntary. Even if you decide to participate now, you may change your mind and stop at any time. If you change your mind and decide you do not want video taken, we will destroy it. The researchers may terminate your participation in the study at any time if they feel that it has become unsafe for you to continue or if you fail to comply with instructions.

If you have questions about this research, including questions about scheduling or your compensation for participating, you may contact Deanna Gates, Ph.D., University of Michigan, School of Kinesiology, 401 Washtenaw Ave., Ann Arbor, MI 48108, (734) 647-2698, gatesd@umich.edu**.**

If you have questions about your rights as a research participant, or wish to obtain information, ask questions or discuss any concerns about this study with someone other than the researcher(s), please contact the University of Michigan Health Sciences and Behavioral Sciences Institutional Review Board, 2800 Plymouth Road, Building 520, Room 1169, Ann Arbor, MI 48109-2800, Phone: (734) 936-0933, or toll free, (866) 936-0933, Email: irbhsbs@umich.edu.

By signing this document, you are agreeing to be in the study. Participating in this study is completely voluntary. Even if you decide to participate now, you may change your mind and stop at any time. You will be given a copy of this document for your records and one copy will be kept with the study records. Be sure that questions you have about the study have been answered and that you understand what you are being asked to do. You may contact the researcher if you think of a question later.

I agree to participate in the study.

_____
Printed Name

_____ _____
Signature Date

Your permission to record digital video of you during your participation in this study is requested. Any photographs or video images we record will be used to interpret the findings of this study. **Your name will not be used in connection with any photos or videos.** If you give your permission to use your videos now, you can change your mind at any time. If you do change your mind please contact the researchers and let them know. Please check and initial the appropriate selection below.

☐ I ____(initials) allow photographs and digital video recordings to be taken of me during this study, and I allow these photographs and video recordings to be reviewed for this study.

☐ I ____(initials) **DO NOT** allow photographs and digital video recordings to be taken of me during this study.

_____ _____
Signature Date

B2. Consent for Chapter 4

UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

INFORMATION ABOUT THIS FORM

You may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of the study, and the risks and possible benefits of participating in the study.

Please take time to review this information carefully. After you have finished, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or other doctors) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

1. GENERAL INFORMATION ABOUT THIS STUDY AND THE RESEARCHERS

1.1 Study title:
Influence of Muscle Fatigue, Pain, and Task Goal on the Control of Repetitive Movements

1.2 Company or agency sponsoring the study:
School of Kinesiology, University of Michigan.

1.3 Names, degrees, and affiliations of the researchers conducting the study:
Deanna Gates, Ph.D., Assistant Professor, School of Kinesiology, University of Michigan (Principal Investigator)
Jeffrey Cowley, M.S., Ph.D. Candidate, School of Kinesiology, University of Michigan (Study Coordinator)

2. PURPOSE OF THIS STUDY

2.1 Study purpose: The purpose of this study is to understand how healthy people adapt to muscle fatigue in different situations. The results of this study will help us understand how people control their movement when they are fatigued. We hope the results will help to prevent workplace injuries.

3. INFORMATION ABOUT STUDY PARTICIPANTS (SUBJECTS)

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?
The study is restricted to healthy, right-handed individuals between the ages of 18-35, with a healthy Body Mass Index (BMI) (35 kg/m^2 or less). Participants should not have any history of major arm surgeries or injuries, cardiovascular, respiratory, or neurological disorders, or pain or impairment in the back or arms. People who are taking medications that can cause movement symptoms like shaking or weakness, or medications for blood clotting or thinning should not participate in this study. Pregnant women and people with uncorrected visual or auditory impairment will not be allowed to participate.

3.2 How many people (subjects) are expected to take part in this study?
We expect to have 25 participants in this study.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

We will ask you to answer several questions to verify that you are right handed. You will come to the Rehabilitation Biomechanics Lab in the Central Campus Recreation Building at the University of Michigan on three different days. On each day, you will sit on a chair in a harness that holds your back against the back of the chair. Your arm may also be comfortably strapped to a padded arm rest to prevent unwanted shoulder movement. You will perform a repetitive reaching task with your right arm until you can no longer continue. While you do the reaching task, we will monitor your movements with small reflective markers attached to your arms and torso with tape. We will record your motion with a high speed digital video camera to verify the accuracy of the marker data. We will also monitor your muscle activity and heart rate using sensors attached with tape to the skin over muscles in your arm and torso. The areas of skin where muscle sensors need to be placed will first be shaved with a disposable safety razor and wiped clean with rubbing alcohol. You should come to lab in comfortable clothing. Women will be asked to wear their sports bra or a tight fitting tank top (e.g., spandex) during testing. Men will be asked to wear a tank top or remove their shirt during testing. The researchers who shave and attach markers to your skin may not necessarily be of your same gender.

This experiment will involve significant physical exertion. We ask that you avoid vigorous physical activity (beyond your normal daily routine) for 48 hours prior to each visit. At the beginning of each testing session, we will take several measurements including your height, weight, and arm length. We will also ask you to answer a series of questions to evaluate your emotions toward painful experiences. The questions ask you to recall times when you experienced pain and to think about painful events, but they will not hurt you or cause you physical discomfort. For women, pain sensitivity might change during the menstrual cycle. If you are a female, we will also ask you to record how many days it has been since your last period started.

After you complete the questions, you will practice the reaching task. To perform the task, you will hold a weighted handle attached to a robot like the one in the images below. The robot will not move on its own, but it will help us measure how you move the handle. We will ask you to continuously move the handle back and forth between two different points displayed on a computer screen. You will perform the repetitive task until you can no longer continue. The weight of the handle will be set at 15-20% of your maximum strength. We expect most people to perform the reaching task for about 8 - 12 minutes. During the task, you will receive vigorous verbal encouragement to help you continue as long as you possibly can, but not so long that you feel you might injure yourself if you were to continue further.

On one day, we will ask you to complete the reaching task with your right arm while your left arm is in pain. You will wear an inflated blood pressure cuff on your left arm to make the left arm hurt while you are doing the reaching task. We will ask you to keep the cuff on as long as you can handle it. If you become too uncomfortable, you will be allowed to stop the pain task by deflating the cuff. If you deflate the cuff before your muscles are fatigued we will ask you to continue the reaching task until you cannot continue. We won't allow you to wear the cuff for more than 20 minutes. After deflating the cuff, the pain should subside within five minutes. We will ask you to remain in the chair until the pain is gone.

We will measure the strength of your arm, wrist, and hand before and after the fatigue task. To measure your arm strength, a member of the research team will push against your arm with a device that measures force as you push back as hard as you can for four seconds. To measure wrist strength, a member of the research team will push against your hand with the same device while you push back as hard as you can for four seconds. For grip strength measurements you will hold a device that measures grip force and squeeze as hard as you can for four seconds. You will complete each of these tasks three times before and after the fatigue task to determine the strength of your arm muscles and your grip strength.

4.2 How much of my time will be needed to take part in this study?
Each testing session will take about 1 1/2 hours. You will be asked to complete three sessions on different days between 4 and 14 days apart. If you fail to return for the follow-up sessions within one month, your participation will be discontinued. Participation in each session is completely voluntary.

4.3 When will my participation in the study be over?
Your participation will be over after you complete the third experimental session, unless you ask to discontinue your participation at an earlier time or your participation is discontinued by the researchers.

5. INFORMATION ABOUT RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?
The known or expected risks are: slightly more than minimal risk.

On the day that you complete the pain task, you will experience moderate to severe pain, tingling, and numbness in your left arm and hand while the cuff is inflated. You can end the pain task at any time. The pain will subside quickly when the cuff is deflated, and most people will have no pain within five minutes after the cuff is deflated. You may experience sensations of numbness, tingling, heaviness, and/or weakness in your arm and hand for 30 minutes after the pain task. The pain procedure is not expected to cause long term side effects or discomfort. Numbness or discomfort lasting more than 60 minutes is extremely rare in healthy individuals.

You are likely to experience discomfort during the reaching task on each day of the study. This should not be greater than what you experience during typical exercise or activities that fatigue your muscles. You might develop muscle soreness 24 to 48 hours after each testing session. Muscle soreness may last up to 72 hours. There is a small risk that you could experience muscular injury, such as a muscle strain. The risk involved in the reaching task is no more than that of performing daily activities or exercising at a gym.

You may also experience slight discomfort during shaving and alcohol preparation of the skin and during removal of reflective markers and sensors. Any skin irritation should subside within 24 hours. If you experience unusual or alarming pain during any procedures, you should tell the investigators and the procedure will be discontinued.

There is a small risk that someone other than the researchers could learn that you participated in this research because of the videos and data that we collect from you.

The researchers will try to minimize these risks by:
You will be allowed to terminate the pain and reaching tasks voluntarily at any time. We will not allow you to continue the pain task for more than 20 minutes. We will include a warm up and stretching session prior to performing the reaching tests to reduce the risk of muscle soreness and injury. We will ensure that all sensors, chairs, and devices are secure when in use, as well as providing constant supervision throughout the study. To reduce the risk that other people could identify you, all videos or images we collect from you will be stored on a password protected computer in a locked laboratory. Only members of the research team have access to the computer. It is unlikely that anyone outside the study team will see your data or discover that you participated in this study because your name will not be attached to your data. Instead, a numeric code will be attached to the data, so even if your data were accessed by someone else, it could not be traced back to you.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?
The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors. In the event of injury, no treatment or compensation will be provided to you for any research related injury.

5.3 If I take part in this study, can I also participate in other studies?
Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?
You may not receive any personal benefits from being in this study. Nonetheless, knowledge gained from this study may benefit others by contributing to a better understanding of how people control their movements during fatiguing tasks.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?
Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. OTHER OPTIONS

6.1 If I decide not to take part in this study, what other options do I have?
Your participation in this study is voluntary. You may choose not to take part in this particular data collection study.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?

You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 "Contact Information" (below).

7.2 Could there be any harm to me if I decide to leave the study before it is finished?
No, leaving this study at any time will not cause you harm.

7.3 Could the researchers take me out of the study even if I want to continue to participate?
Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- ✓ The researcher believes that it is not in your best interest to stay in the study.
- ✓ You become ineligible to participate.
- ✓ Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- ✓ You do not follow instructions from the researchers.
- ✓ The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?
The study will pay for research-related items or services that are provided only because you are in the study. These items include sensors, software and other devices or hardware needed to complete the study tasks. You or your health plan will not be billed for any study-related costs.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

8.2 Will I be paid or given anything for taking part in this study?
Your compensation for your time commitment will be in the form of a cash amount at a rate of $10/hour. If you choose to withdraw your participation during a session, you will paid for the completed session time up to the time of your withdrawal.

8.3 Who could profit or financially benefit from the study results?
No one will profit or financially benefit from the study results.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how your privacy and the confidentiality of your research records will be protected in this study.

9.1 How will the researchers protect my privacy?
All data collected in the study will be stored in a locked file cabinet or a password protected computer or server in a laboratory that is locked with a keypad. Your data will be associated with a number. Your

name will not be directly linked to data that we collect about you. Any identifiable data, such as video footage or images that include your face will only be accessible to the researchers in the study. Any published images or video footage will have your face and any identifiable features blurred, blocked or omitted in some other way.

9.2 What information about me could be seen by the researchers or by other people? Why? Who might see it?
Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required in order for you to take part in the study.

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University, Food and Drug Administration (FDA), and/or other government officials may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects
    - Analyze the results of the study
- If you receive any payments for taking part in this study, the University of Michigan accounting department may need your name, address, social security number, payment amount, and related information for tax reporting purposes.
- Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article or presented at a scientific meeting, but would not include any information that would let others know who you are. If identifiable video recordings or images of you will be used in any publications or presentations, the researchers will ask for your separate written permission.

9.3 What happens to information about me after the study is over or if I cancel my permission?
As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission expire?

Your permission to allow researchers to obtain, use, and share information about you collected as part of this study does not expire, unless you cancel it. The information that researchers obtain through this study will be kept indefinitely in order to compare with future studies. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below).

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished:
  Jeffrey Cowley, M.S.
  CCRB, room 1271A
  401 Washtenaw Avenue
  Ann Arbor, MI 48109
  jccowle@umich.edu

- Express a concern about the study:
  Deanna Gates, Ph.D.
  401 Washtenaw Ave.
  Ann Arbor, MI 48109
  gatesd@umich.edu

You may also express a concern about a study by contacting the Institutional Review Board listed below.

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road
Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768 (For International Studies: US Country Code: 001)
Fax: 734-763-1234
e-mail: irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.

When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

Your signature in the next section means that you have received copies of all of the following documents:

- This "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.)*

12. SIGNATURES

Consent/Assent to Participate in the Research Study

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with Jeffrey Cowley. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Date of Birth (mm/dd/yy): _____

Your permission to record digital video of you during your participation in this study is requested. Any photographs or video images we record will be used to interpret the findings of this study. **Your name will not be used in connection with any photos or videos.** If you give your permission to use your videos now, you can change your mind at any time. If you do change your mind please contact the researchers and let them know. Please check and initial the appropriate selection below. The recordings are necessary for analyzing the study data, and thus you will not be able to participate in the study if you refuse to give your consent below.

- ☐ I ____ (initials) allow photographs and digital video recordings to be taken of me during this study, and I allow these photographs and video recordings to be reviewed for this study.
- ☐ I ____ (initials) DO NOT allow photographs and digital video recordings to be taken of me during this study.

Signature: _____

Date of Signature (mm/dd/yy): _____

Bibliography

Allen, D. G., G. D. Lamb and H. Westerblad (2008). "Skeletal Muscle Fatigue: Cellular Mechanisms." Physiological Reviews **88**(1): 287-332.

Armstrong, T. J. and D. B. Chaffin (1979). "Some biomechanical aspects of the carpal tunnel." Journal of Biomechanics **12**(7): 567-570.

Babiloni, C., P. Capotosto, A. Brancucci, C. Del Percio, L. Petrini, M. Buttiglione, G. Cibelli, G. L. Romani, P. M. Rossini and L. Arendt-Nielsen (2008). "Cortical alpha rhythms are related to the anticipation of sensorimotor interaction between painful stimuli and movements: a high-resolution EEG study." The Journal of Pain **9**(10): 902-911.

Baldwin, M. L. and R. J. Butler (2006). "Upper extremity disorders in the workplace: costs and outcomes beyond the first return to work." Journal of Occupational Rehabilitation **16**(3): 303-323.

Bambaeichi, E., T. Reilly, N. T. Cable and M. Giacomoni (2004). "The isolated and combined effects of menstrual cycle phase and time-of-day on muscle strength of eumenorrheic females." Chronobiology International **21**(4-5): 645-660.

Bank, P. J. M., C. E. Peper, J. Marinus, P. J. Beek and J. J. van Hilten (2013). "Motor consequences of experimentally induced limb pain: A systematic review." European Journal of Pain **17**(2): 145-157.

Bartley, E. J. and J. L. Rhudy (2013). "Comparing pain sensitivity and the nociceptive flexion reflex threshold across the mid-follicular and late-luteal menstrual phases in healthy women." The Clinical Journal of Pain **29**(2): 154-161.

Bernstein, N. A. (1967). "The co-ordination and regulation of movements."

Bigland-Ritchie, B. and J. J. Woods (1984). "Changes in muscle contractile properties and neural control during human muscular fatigue." Muscle and Nerve **7**(9): 691-699.

Bigland-Ritchie, B. R., N. J. Dawson, R. S. Johansson and O. C. Lippold (1986). "Reflex origin for the slowing of motoneurone firing rates in fatigue of human voluntary contractions." The Journal of Physiology **379**(1): 451-459.

Birch, L., L. Arendt-Nielsen, T. Graven-Nielsen and H. Christensen (2001). "An investigation of how acute muscle pain modulates performance during computer work with digitizer and puck." Applied Ergonomics **32**(3): 281-286.

Bockemühl, T., N. F. Troje and V. Durr (2010). "Inter-joint coupling and joint angle synergies of human catching movements." Human Movement Science **29**(1): 73-93.

Bonauto, D., B. Silverstein, D. Adams and M. Foley (2006). "Prioritizing industries for occupational injury and illness prevention and research, Washington State Workers' compensation claims, 1999–2003." Journal of Occupational and Environmental Medicine **48**(8): 840-851.

Borg, G. A. (1982). "Psychophysical bases of perceived exertion." Medicine and Science in Sports and Exercise **14**(5): 377-381.

Bosch, T., S. E. Mathiassen, D. Hallman, M. P. de Looze, E. Lyskov, B. Visser and J. H. van Dieen (2012). "Temporal strategy and performance during a fatiguing short-cycle repetitive task." Ergonomics **55**(8): 863-873.

Bosch, T., S. E. Mathiassen, B. Visser, M. P. de Looze and J. H. van Dieen (2011). "The effect of work pace on workload, motor variability and fatigue during simulated light assembly work." Ergonomics **54**(2): 154-168.

Bouffard, J., M. Gagné and C. Mercier (2013). "Effect of Painful and Non-Painful Sensorimotor Manipulations on Subjective Body Midline." Frontiers in Human Neuroscience **7**(77).

Bray, H. and G. L. Moseley (2011). "Disrupted working body schema of the trunk in people with back pain." British Journal of Sports Medicine **45**(3): 168-173.

Bray, S. R., J. D. Graham, K. A. M. Ginis and A. L. Hicks (2012). "Cognitive task performance causes impaired maximum force production in human hand flexor muscles." Biological Psychology **89**(1): 195-200.

Bureau of Labor Statistics, U. S. D. o. L. (2015). Nonfatal Occupational Injuries and Illnesses Requiring Days Away from Work, 2014**:** 3.

Caffier, G., H. Rehfeldt, H. Kramer and R. Mucke (1992). "Fatigue during sustained maximal voluntary contraction of different muscles in humans: dependence on fibre type and body posture." European Journal of Applied Physiology and Occupational Physiology **64**(3): 237-243.

Casey, E., F. Hameed and Y. Y. Dhaher (2014). "The muscle stretch reflex throughout the menstrual cycle." Medicine and Science in Sports and Exercise **46**(3): 600-609.

Chaffin, D. B. (1973). "Localized muscle fatigue-definition and measurement." Journal of Occupational and Environmental Medicine **15**(4): 346-354.

Chen, H. H., Y. T. Liu, G. Mayer-Kress and K. M. Newell (2005). "Learning the pedalo locomotion task." Journal of Motor Behavior **37**(3): 247-256.

Chiu, S.-L. and L.-S. Chou (2013). "Variability in inter-joint coordination during walking of elderly adults and its association with clinical balance measures." Clinical Biomechanics **28**(4): 454-458.

Chopp, J. N., J. M. O'Neill, K. Hurley and C. R. Dickerson (2010). "Superior humeral head migration occurs after a protocol designed to fatigue the rotator cuff: a radiographic analysis." Journal of Shoulder and Elbow Surgery **19**(8): 1137-1144.

Ciubotariu, A., L. Arendt-Nielsen and T. Graven-Nielsen (2004). "The influence of muscle pain and fatigue on the activity of synergistic muscles of the leg." European Journal of Applied Physiology **91**(5-6): 604-614.

Ciubotariu, A., L. Arendt-Nielsen and T. Graven-Nielsen (2007). "Localized muscle pain causes prolonged recovery after fatiguing isometric contractions." Experimental Brain Research **181**(1): 147-158.

Clark, B. C., S. R. Collier, T. M. Manini and L. L. Ploutz-Snyder (2005). "Sex differences in muscle fatigability and activation patterns of the human quadriceps femoris." European Journal of Applied Physiology **94**(1-2): 196-206.

Cote, J. N. and M. K. H. Bement (2010). "Update on the relation between pain and movement: consequences for clinical practice." The Clinical Journal of Pain **26**(9): 754-762.

Côté, J. N., A. G. Feldman, P. A. Mathieu and M. F. Levin (2008). "Effects of fatigue on intermuscular coordination during repetitive hammering." Motor Control **12**(2): 79-92.

Côté, J. N., P. A. Mathieu, M. F. Levin and A. G. Feldman (2002). "Movement reorganization to compensate for fatigue during sawing." Experimental Brain Research **146**(3): 394-398.

Côté, J. N., D. Raymond, P. A. Mathieu, A. G. Feldman and M. F. Levin (2005). "Differences in multi-joint kinematic patterns of repetitive hammering in healthy, fatigued and shoulder-injured individuals." Clinical Biomechanics **20**(6): 581-590.

Cowley, J. C., J. B. Dingwell and D. H. Gates (2014). "Effects of local and widespread muscle fatigue on movement timing." Experimental Brain Research **232**(12): 3939-3948.

Cowley, J. C., J. Leonardis, D. B. Lipps and D. H. Gates (2017). "The influence of wrist posture, grip type, and grip force on median nerve shape and cross-sectional area." Clinical Anatomy **30**(4): 470-478.

Crombez, G., C. Eccleston, F. Baeyens and P. Eelen (1998). "When somatic information threatens, catastrophic thinking enhances attentional interference." Pain **75**(2): 187-198.

Crombez, G., J. W. Vlaeyen, P. H. Heuts and R. Lysens (1999). "Pain-related fear is more disabling than pain itself: evidence on the role of pain-related fear in chronic back pain disability." Pain **80**(1): 329-339.

Cusumano, J. P. and P. Cesari (2006). "Body-goal variability mapping in an aiming task." Biological Cybernetics **94**(5): 367-379.

Daffertshofer, A., C. J. Lamoth, O. G. Meijer and P. J. Beek (2004). "PCA in studying coordination and variability: a tutorial." Clinical Biomechanics **19**(4): 415-428.

Dancey, E., B. A. Murphy, D. Andrew and P. Yielder (2016). "The effect of local vs remote experimental pain on motor learning and sensorimotor integration using a complex typing task." Pain **157**(8): 1682-1695.

Danion, F., M. Latash, Z.-M. Li and V. Zatsiorsky (2001). "The effect of a fatiguing exercise by the index finger on single-and multi-finger force production tasks." Experimental Brain Research **138**(3): 322-329.

Davis, J. M. (1995). "Central and peripheral factors in fatigue." Journal of Sports Sciences **13 Spec No**: S49-53.

De Luca, C. J. (1984). "Myoelectrical manifestations of localized muscular fatigue in humans." Critical Reviews in Biomedical Engineering **11**(4): 251-279.

De Luca, C. J. (1997). "The use of surface electromyography in biomechanics." Journal of Applied Biomechanics **13**: 135-163.

Demougeot, L. and C. Papaxanthis (2011). "Muscle fatigue affects mental simulation of action." The Journal of Neuroscience **31**(29): 10712-10720.

Denning, W. M., S. Woodland, J. G. Winward, M. G. Leavitt, A. C. Parcell, J. T. Hopkins, D. Francom and M. K. Seeley (2014). "The influence of experimental anterior knee pain during running on electromyography and articular cartilage metabolism." Osteoarthritis and Cartilage **22**(8): 1111-1119.

Dingwell, J. B. and J. P. Cusumano (2010). "Re-interpreting detrended fluctuation analyses of stride-to-stride variability in human walking." Gait and Posture **32**(3): 348-353.

Dingwell, J. B. and L. C. Marin (2006). "Kinematic variability and local dynamic stability of upper body motions when walking at different speeds." Journal of Biomechanics **39**(3): 444-452.

Dingwell, J. B., R. F. Smallwood and J. P. Cusumano (2013). "Trial-to-Trial Dynamics and Learning in a Generalized, Redundant Reaching Task." Journal of Neurophysiology **109**(1): 225-237.

Dounskaia, N. (2010). "Control of human limb movements: the leading joint hypothesis and its practical applications." Exercise and Sport Sciences Reviews **38**(4): 201.

Dounskaia, N. V. (1998). "Hierarchical control of different elbow-wrist coordination patterns." Experimental Brain Research **121**(3): 239-254.

Ebaugh, D. D., P. W. McClure and A. R. Karduna (2006). "Effects of shoulder muscle fatigue caused by repetitive overhead activities on scapulothoracic and glenohumeral kinematics." Journal of Electromyography and Kinesiology **16**(3): 224-235.

Emge, N., M. Uygur, M. Radivoj, W. K. T, T. Royer and S. Jaric (2014). "Selective effects of arm proximal and distal muscles fatigue on force coordination in manipulation tasks." Journal of Motor Behavior **46**(4): 259-265.

Enoka, R. M. and J. Duchateau (2008). "Muscle fatigue: what, why and how it influences muscle function." The Journal of physiology **586**(1): 11-23.

Enoka, R. M. and D. G. Stuart (1992). "Neurobiology of muscle fatigue." Journal of Applied Physiology **72**(5): 1631-1648.

Ervilha, U. F., L. Arendt-Nielsen, M. Duarte and T. Graven-Nielsen (2004). "Effect of load level and muscle pain intensity on the motor control of elbow-flexion movements." European Journal of Applied Physiology **92**(1-2): 168-175.

Ervilha, U. F., D. Farina, L. Arendt-Nielsen and T. Graven-Nielsen (2005). "Experimental muscle pain changes motor control strategies in dynamic contractions." Experimental Brain Research **164**(2): 215-224.

Farina, D., L. Arendt-Nielsen and T. Graven-Nielsen (2005). "Experimental muscle pain decreases voluntary EMG activity but does not affect the muscle potential evoked by transcutaneous electrical stimulation." Clinical Neurophysiology **116**(7): 1558-1565.

Farina, D., L. Arendt-Nielsen, R. Merletti and T. Graven-Nielsen (2004). Effect of Experimental Muscle Pain on Motor Unit Firing Rate and Conduction Velocity.

Fitts, R. H. (1994). "Cellular mechanisms of muscle fatigue." Physiological Reviews **74**(1): 49-94.

Forestier, N. and V. Nougier (1998). "The effects of muscular fatigue on the coordination of a multijoint movement in human." Neuroscience Letters **252**(3): 187-190.

Friden, J. and R. L. Lieber (1992). "Structural and mechanical basis of exercise-induced muscle injury." Medicine and Science in Sports and Exercise **24**(5): 521-530.

Fuller, J. R., J. Fung and J. N. Cote (2011). "Time-dependent adaptations to posture and movement characteristics during the development of repetitive reaching induced fatigue." Experimental Brain Research **211**(1): 133-143.

Fuller, J. R., J. Fung and J. N. Côté (2013). "Posture-movement responses to stance perturbations and upper limb fatigue during a repetitive pointing task." Human Movement Science **32**(4): 618-632.

Fuller, J. R., K. V. Lomond, J. Fung and J. N. Cote (2009). "Posture-movement changes following repetitive motion-induced shoulder muscle fatigue." Journal of Electromyography and Kinesiology **19**(6): 1043-1052.

Gandevia, S. C. (2001). "Spinal and supraspinal factors in human muscle fatigue." Physiological Reviews **81**(4): 1725-1789.

Gates, D. H. and J. B. Dingwell (2008). "The effects of neuromuscular fatigue on task performance during repetitive goal-directed movements." Experimental Brain Research **187**(4): 573-585.

Gates, D. H. and J. B. Dingwell (2010). "Muscle fatigue does not lead to increased instability of upper extremity repetitive movements." Journal of Biomechanics **43**(5): 913-919.

Gates, D. H. and J. B. Dingwell (2011). "The effects of muscle fatigue and movement height on movement stability and variability." Experimental Brain Research **209**(4): 525-536.

Gates, D. H., L. S. Walters, J. Cowley, J. M. Wilken and L. Resnik (2016). "Range of Motion Requirements for Upper-Limb Activities of Daily Living." American Journal of Occupational Therapy **70**(1): 7001350010p7001350011-7001350010p7001350010.

George, S. Z., G. C. Dover and R. B. Fillingim (2007). "Fear of pain influences outcomes after exercise-induced delayed onset muscle soreness at the shoulder." Clinical Journal of Pain **23**(1): 76-84.

Gorelick, M., J. M. Brown and H. Groeller (2003). "Short-duration fatigue alters neuromuscular coordination of trunk musculature: implications for injury." Applied Ergonomics **34**(4): 317-325.

Graven-Nielsen, T. and L. Arendt-Nielsen (2010). Reorganized Motor Control Due to Muscle Pain. Muscle Pain: Understanding the Mechanisms. S. Mense and R. D. Gerwin, Springer Berlin Heidelberg**:** 251-268.

Graven-Nielsen, T., H. Lund, L. Arendt-Nielsen, B. Danneskiold-Samsøe and H. Bliddal (2002). "Inhibition of maximal voluntary contraction force by experimental muscle pain: A centrally mediated mechanism." Muscle and Nerve **26**(5): 708-712.

Hamill, J., R. E. van Emmerik, B. C. Heiderscheit and L. Li (1999). "A dynamical systems approach to lower extremity running injuries." Clinical Biomechanics **14**(5): 297-308.

Hausdorff, J. M., C. K. Peng, Z. Ladin, J. Y. Wei and A. L. Goldberger (1995). "Is walking a random walk? Evidence for long-range correlations in stride interval of human gait." Journal of Applied Physiology **78**(1): 349-358.

Hicks, A. L., J. Kent-Braun and D. S. Ditor (2001). "Sex differences in human skeletal muscle fatigue." Exercise and Sport Sciences Reviews **29**(3): 109-112.

Hodges, N. J., S. Hayes, R. R. Horn and A. M. Williams (2005). "Changes in coordination, control and outcome as a result of extended practice on a novel motor skill." Ergonomics **48**(11-14): 1672-1685.

Hodges, P. W. and K. Tucker (2011). "Moving differently in pain: a new theory to explain the adaptation to pain." Pain **152**(3 Suppl): S90-98.

Hooper, A. E. C., A. D. Bryan and M. Eaton (2011). "Menstrual Cycle Effects on Perceived Exertion and Pain During Exercise Among Sedentary Women." Journal of Women's Health **20**(3): 439-446.

Hostens, I., J. Seghers, A. Spaepen and H. Ramon (2004). "Validation of the wavelet spectral estimation technique in biceps brachii and brachioradialis fatigue assessment during prolonged low-level static and dynamic contractions." Journal of Electromyography and Kinesiology **14**(2): 205-215.

Huffenus, A. F., D. Amarantini and N. Forestier (2006). "Effects of distal and proximal arm muscles fatigue on multi-joint movement organization." Experimental Brain Research **170**(4): 438-447.

Hunter, S. K. (2009). "Sex Differences and Mechanisms of Task-Specific Muscle Fatigue." Exercise and Sport Sciences Reviews **37**(3): 113-122.

Hunter, S. K. (2014). "Sex Differences in Human Fatigability: Mechanisms and Insight to Physiological Responses." Acta Physiologica (Oxford, England) **210**(4): 768-789.

Hunter, S. K. (2016). "Sex differences in fatigability of dynamic contractions." Experimental Physiology **101**(2): 250-255.

Huysmans, M. A., M. J. Hoozemans, A. J. van der Beek, M. P. de Looze and J. H. van Dieen (2008). "Fatigue effects on tracking performance and muscle activity." Journal of Electromyography and Kinesiology **18**(3): 410-419.

Iacovides, S., I. Avidon and F. Baker (2015). "Does pain vary across the menstrual cycle? A review." European Journal of Pain.

Jaric, S., S. Blesic, S. Milanovic, S. Radovanovic, M. Ljubisavljevic and R. Anastasijevic (1999). "Changes in movement final position associated with agonist and antagonist muscle fatigue." European Journal of Applied Physiology and Occupational Physiology **80**(5): 467-471.

Julian, R., A. Hecksteden, H. H. K. Fullagar and T. Meyer (2017). "The effects of menstrual cycle phase on physical performance in female soccer players." PloS One **12**(3): e0173951.

Keogh, E., K. Hatton and D. Ellery (2000). "Avoidance versus focused attention and the perception of pain: differential effects for men and women." Pain **85**(1): 225-230.

Lamothe, M., J.-S. Roy, J. Bouffard, M. Gagné, L. J. Bouyer and C. Mercier (2014). "Effect of tonic pain on motor acquisition and retention while learning to reach in a force field." PloS One **9**(6): e99159.

Latko, W. A., T. J. Armstrong, A. Franzblau, S. S. Ulin, R. A. Werner and J. W. Albers (1999). "Cross-sectional study of the relationship between repetitive work and the prevalence of upper limb musculoskeletal disorders." American Journal of Industrial Medicine **36**(2): 248-259.

Leger, A. B. and T. E. Milner (2000). "Passive and active wrist joint stiffness following eccentric exercise." European Journal of Applied Physiology **82**(5-6): 472-479.

Lin, J.-H., R. G. Radwin and T. G. Richard (2001). "Dynamic biomechanical model of the hand and arm in pistol grip power handtool usage." Ergonomics **44**(3): 295-312.

Lin, J.-H., R. G. Radwin and T. G. Richard (2003). "Handle dynamics predictions for selected power hand tool applications." Human Factors: The Journal of the Human Factors and Ergonomics Society **45**(4): 645-656.

Lin, J.-H., R. G. Radwin and T. G. Richard (2003). "A single-degree-of-freedom dynamic model predicts the range of human responses to impulsive forces produced by power hand tools." Journal of Biomechanics **36**(12): 1845-1852.

Loh, P. Y. and S. Muraki (2014). "Effect of wrist deviation on median nerve cross-sectional area at proximal carpal tunnel level." Iranian Journal of Public Health **43**(3): 180-185.

Lorist, M. M., D. Kernell, T. F. Meijman and I. Zijdewind (2002). "Motor fatigue and cognitive task performance in humans." Journal of Physiology **545**(Pt 1): 313-319.

Lyons, M., Y. Al-Nakeeb and A. Nevill (2006). "Performance of soccer passing skills under moderate and high-intensity localized muscle fatigue." The Journal of Strength & Conditioning Research **20**(1): 197-202.

Madeleine, P. (2010). "On functional motor adaptations: from the quantification of motor strategies to the prevention of musculoskeletal disorders in the neck-shoulder region." Acta Physiologica (Oxford, England) **199 Suppl 679**: 1-46.

Madeleine, P. and D. Farina (2008). "Time to task failure in shoulder elevation is associated to increase in amplitude and to spatial heterogeneity of upper trapezius mechanomyographic signals." European Journal of Applied Physiology **102**(3): 325-333.

Madeleine, P., F. Leclerc, L. Arendt-Nielsen, P. Ravier and D. Farina (2006). "Experimental muscle pain changes the spatial distribution of upper trapezius muscle activity during sustained contraction." Clinical Neurophysiology **117**(11): 2436-2445.

Madeleine, P., B. Lundager, M. Voigt and L. Arendt-Nielsen (2003). "Standardized low-load repetitive work: evidence of different motor control strategies between experienced workers and a reference group." Applied Ergonomics **34**(6): 533-542.

Mah, C. D., M. Hulliger, R. G. Lee and I. S. O'Callaghan (1994). "Quantitative analysis of human movement synergies: constructive pattern analysis for gait." Journal of Motor Behavior **26**(2): 83-102.

Mair, S. D., A. V. Seaber, R. R. Glisson and W. E. Garrett (1996). "The role of fatigue in susceptibility to acute muscle strain injury." The American Journal of Sports Medicine **24**(2): 137-143.

Maixner, W. and C. Humphrey (1993). "Gender differences in pain and cardiovascular responses to forearm ischemia." The Clinical journal of pain **9**(1): 16-25.

Marcora, S. (2009). "Perception of effort during exercise is independent of afferent feedback from skeletal muscles, heart, and lungs." Journal of Applied Physiology **106**(6): 2060-2062.

Marcora, S. M. and W. Staiano (2010). "The limit to exercise tolerance in humans: mind over muscle?" European Journal of Applied Physiology **109**(4): 763-770.

Marras, W. S., S. A. Lavender, S. E. Leurgans, S. L. Rajulu, W. G. Allread, F. A. Fathallah and S. A. Ferguson (1993). "The Role of Dynamic Three-Dimensional Trunk Motion in Occupationally-Related Low Back Disorders: The Effects of Workplace Factors, Trunk Position, and Trunk Motion Characteristics on Risk of Injury." Spine **18**(5): 617-628.

Masuda, K., T. Masuda, T. Sadoyama, M. Inaki and S. Katsuta (1999). "Changes in surface EMG parameters during static and dynamic fatiguing contractions." Journal of Electromyography and Kinesiology **9**(1): 39-46.

Mathiassen, S. E. (2006). "Diversity and variation in biomechanical exposure: what is it, and why would we like to know?" Applied Ergonomics **37**(4): 419-427.

Mathiassen, S. E., T. Möller and M. Forsman (2003). "Variability in mechanical exposure within and between individuals performing a highly constrained industrial work task." Ergonomics **46**(8): 800-824.

McDonald, A. C., T. Calvin and P. J. Keir (2015). "Adaptations to isolated shoulder fatigue during simulated repetitive work. Part II: Recovery." Journal of Electromyography and Kinesiology **29**: 42-49.

Mehta, R. and M. Agnew (2012). "Influence of mental workload on muscle endurance, fatigue, and recovery during intermittent static work." European Journal of Applied Physiology **112**(8): 2891-2902.

Missenard, O., D. Mottet and S. Perrey (2008). "The role of cocontraction in the impairment of movement accuracy with fatigue." Experimental Brain Research **185**(1): 151-156.

Mista, C. A., S. W. Christensen and T. Graven-Nielsen (2015). "Modulation of motor variability related to experimental muscle pain during elbow-flexion contractions." Human Movement Science **39**: 222-235.

Monjo, F. and N. Forestier (2014). "Movement unpredictability and temporal constraints affect the integration of muscle fatigue information into forward models." Neuroscience **277**: 584-594.

Monjo, F. and N. Forestier (2014). "Unexperienced mechanical effects of muscular fatigue can be predicted by the Central Nervous System as revealed by anticipatory postural adjustments." Experimental Brain Research **232**(9): 2931-2943.

Monjo, F., R. Terrier and N. Forestier (2015). "Muscle fatigue as an investigative tool in motor control: A review with new insights on internal models and posture–movement coordination." Human Movement Science **44**: 225-233.

Moriarty, O., B. E. McGuire and D. P. Finn (2011). "The effect of pain on cognitive function: a review of clinical and preclinical research." Progress in Neurobiology **93**(3): 385-404.

Moseley, G., D. Sim, M. Henry and T. Souvlis (2005). "Experimental hand pain delays recognition of the contralateral hand—Evidence that acute and chronic pain have opposite effects on information processing?" Cognitive Brain Research **25**(1): 188-194.

Moseley, G. L. (2007). "Reconceptualising pain according to modern pain science." Physical Therapy Reviews **12**(3): 169-178.

Moseley, G. L. and P. W. Hodges (2006). "Reduced variability of postural strategy prevents normalization of motor changes induced by back pain: a risk factor for chronic trouble?" Behavioral Neuroscience **120**(2): 474-476.

Myers, J. B., K. M. Guskiewicz, R. A. Schneider and W. E. Prentice (1999). "Proprioception and neuromuscular control of the shoulder after muscle fatigue." Journal of Athletic Training **34**(4): 362-367.

Nielsen, C. S., R. Staud and D. D. Price (2009). "Individual Differences in Pain Sensitivity: Measurement, Causation, and Consequences." The Journal of Pain **10**(3): 231-237.

Noakes, T. D. (2004). "Linear relationship between the perception of effort and the duration of constant load exercise that remains." Journal of Applied Physiology **96**(4): 1571-1573.

Noakes, T. D. (2008). "Rating of perceived exertion as a predictor of the duration of exercise that remains until exhaustion." British Journal of Sports Medicine **42**(7): 623-624.

Oldfield, R. C. (1971). "The assessment and analysis of handedness: the Edinburgh inventory." Neuropsychologia **9**(1): 97-113.

Osman, A., F. X. Barrios, P. M. Gutierrez, B. A. Kopper, T. Merrifield and L. Grittmann (2000). "The Pain Catastrophizing Scale: further psychometric evaluation with adult samples." Journal of Behavioral Medicine **23**(4): 351-365.

Paas, F. G. W. C., J. J. G. Van Merrienboer and J. J. Adam (1994). "Measurement of Cognitive Load in Instructional Research." Perceptual and Motor Skills **79**(1): 419-430.

Parr, J. J., P. A. Borsa, R. B. Fillingim, M. D. Tillman, T. M. Manini, C. M. Gregory and S. Z. George (2012). "Pain Related Fear and Catastrophizing Predict Pain Intensity and Disability Independently Using an Induced Muscle Injury Model." Journal of Pain **13**(4): 370-378.

Peng, C. K., S. Havlin, H. E. Stanley and A. L. Goldberger (1995). "Quantification of scaling exponents and crossover phenomena in nonstationary heartbeat time series." Chaos **5**(1): 82-87.

Qin, J., J.-H. Lin, G. S. Faber, B. Buchholz and X. Xu (2014). "Upper extremity kinematic and kinetic adaptations during a fatiguing repetitive task." Journal of Electromyography and Kinesiology **24**(3): 404-411.

Rempel, D. M., R. J. Harrison and S. Barnhart (1992). "Work-related cumulative trauma disorders of the upper extremity." JAMA **267**(6): 838-842.

Roy, J.-S. (2014). "Handbook of Musculoskeletal Pain and Disability Disorders in the Workplace Upper Extremity Pain." Handbook of Musculoskeletal Pain and Disability Disorders in the Workplace: 55-79.

Sanger, T. D. (2000). "Human arm movements described by a low-dimensional superposition of principal components." The Journal of Neuroscience **20**(3): 1066-1072.

Sarwar, R., B. B. Niclos and O. M. Rutherford (1996). "Changes in muscle strength, relaxation rate and fatiguability during the human menstrual cycle." Journal of Physiology **493 (Pt 1)**: 267-272.

Seeley, M. K., J. Park, D. King and J. T. Hopkins (2013). "A novel experimental knee-pain model affects perceived pain and movement biomechanics." Journal of athletic training **48**(3): 337.

Selen, L., P. Beek and J. van Dieën (2007). "Fatigue-induced changes of impedance and performance in target tracking." Experimental Brain Research **181**(1): 99-108.

Selen, L. P., P. J. Beek and J. H. van Dieen (2007). "Fatigue-induced changes of impedance and performance in target tracking." Experimental Brain Research **181**(1): 99-108.

Sesto, M., R. Radwin and T. Richard (2005). "Short-term changes in upper extremity dynamic mechanical response parameters following power hand tool use." Ergonomics **48**(7): 807-820.

Sesto, M. E., R. G. Radwin, T. M. Best and T. G. Richard (2004). "Upper limb mechanical changes following short duration repetitive eccentric exertions." Clinical Biomechanics **19**(9): 921-928.

Severeijns, R., J. W. Vlaeyen, M. A. van den Hout and W. E. Weber (2001). "Pain catastrophizing predicts pain intensity, disability, and psychological distress independent of the level of physical impairment." The Clinical Journal of Pain **17**(2): 165-172.

Sjøgaard, G. (1998). "Muscle injury in repetitive motion disorders." Clinical Orthopaedics and Related Research **351**: 21.

Smith, R., S. L. Pearce and T. S. Miles (2006). "Experimental muscle pain does not affect fine motor control of the human hand." Experimental Brain Research **174**(3): 397-402.

Sparto, P. J., M. Parnianpour, T. E. Reinsel and S. Simon (1997). "The effect of fatigue on multijoint kinematics and load sharing during a repetitive lifting test." Spine **22**(22): 2647-2654.

Srinivasan, D. and S. E. Mathiassen (2012). "Motor variability in occupational health and performance." Clinical Biomechanics **27**(10): 979-993.

Srinivasan, D., A. Samani, S. E. Mathiassen and P. Madeleine (2014). "The size and structure of arm movement variability decreased with work pace in a standardised repetitive precision task." Ergonomics **58**(1): 128-139.

Steele, K. M., A. Rozumalski and M. H. Schwartz (2015). "Muscle synergies and complexity of neuromuscular control during gait in cerebral palsy." Developmental Medicine and Child Neurology **57**(12): 1176-1182.

Stergiou, N., R. T. Harbourne and J. T. Cavanaugh (2006). "Optimal Movement Variability: A New Theoretical Perspective for Neurologic Physical Therapy." Journal of Neurologic Physical Therapy **30**(3): 120-129.

Sullivan, M. J. (2009). "The pain catastrophizing Scale User Manual." Montreal: McGill University.

Sullivan, M. J., S. R. Bishop and J. Pivik (1995). The pain catastrophizing scale: development and validation. Psychological Assessment. M. M. University. **7:** 524.

Sullivan, M. J., W. Stanish, H. Waite, M. Sullivan and D. A. Tripp (1998). "Catastrophizing, pain, and disability in patients with soft-tissue injuries." Pain **77**(3): 253-260.

Sundström Poromaa, I. and M. Gingnell (2014). "Menstrual cycle influence on cognitive function and emotion processing—from a reproductive perspective." Frontiers in Neuroscience **8**: 380.

Tenan, M. S., A. C. Hackney and L. Griffin (2015). "Maximal force and tremor changes across the menstrual cycle." European Journal of Applied Physiology.

Terrier, R. and N. Forestier (2009). "Cognitive cost of motor reorganizations associated with muscular fatigue during a repetitive pointing task." Journal of Electromyography and Kinesiology **19**(6): e487-e493.

Tse, C. T. F., A. C. McDonald and P. J. Keir (2015). "Adaptations to isolated shoulder fatigue during simulated repetitive work. Part I: Fatigue." Journal of Electromyography and Kinesiology **29**: 34-41.

van Dieën, J. H., H. H. O. Vrielink and H. M. Toussaint (1993). "An investigation into the relevance of the pattern of temporal activation with respect to erector spinae muscle endurance." European Journal of Applied Physiology and Occupational Physiology **66**(1): 70-75.

Verrel, J., S. Pologe, W. Manselle, U. Lindenberger and M. Woollacott (2013). "Coordination of degrees of freedom and stabilization of task variables in a complex motor skill: expertise-related differences in cello bowing." Experimental Brain Research **224**(3): 323-334.

Vigil, J. M., C. Strenth, T. Trujillo and S. W. Gangestad (2014). "Fluctuating Experimental Pain Sensitivities across the Menstrual Cycle Are Contingent on Women's Romantic Relationship Status." PloS One **9**(3): e91993.

Vlaeyen, J. W. and S. J. Linton (2000). "Fear-avoidance and its consequences in chronic musculoskeletal pain: a state of the art." Pain **85**(3): 317-332.

Waddell, G., M. Newton, I. Henderson, D. Somerville and C. J. Main (1993). "A Fear-Avoidance Beliefs Questionnaire (FABQ) and the role of fear-avoidance beliefs in chronic low back pain and disability." Pain **52**(2): 157-168.

Wakeling, J., O. Blake and H. Chan (2010). "Muscle coordination is key to the power output and mechanical efficiency of limb movements." Journal of Experimental Biology **213**(3): 487-492.

Wallbom, A. S., M. E. Geisser, A. J. Haig, K. Yamakawa and D. Montgomery (2002). "Concordance between rating of perceived exertion and function in persons with chronic, disabling back pain." Journal of Occupational Rehabilitation **12**(2): 93-98.

Wang, Y., C. Zhao, S. M. Passe, A. Filius, A. R. Thoreson, K.-N. An and P. C. Amadio (2014). "Transverse ultrasound assessment of median nerve deformation and displacement in the human carpal tunnel during wrist movements." Ultrasound in Medicine and Biology **40**(1): 53-61.

Wilder, D. G., A. R. Aleksiev, M. L. Magnusson, M. H. Pope, K. F. Spratt and V. K. Goel (1996). "Muscular response to sudden load. A tool to evaluate fatigue and rehabilitation." Spine **21**(22): 2628-2639.

Williamson, A. and B. Hoggart (2005). "Pain: a review of three commonly used pain rating scales." Journal of Clinical Nursing **14**(7): 798-804.

Winter, D. A. (1992). "Foot trajectory in human gait: a precise and multifactorial motor control task." Physical Therapy **72**(1): 45-53; discussion 54-46.

Wolpert, D. M., R. C. Miall and M. Kawato (1998). "Internal models in the cerebellum." Trends in Cognitive Sciences **2**(9): 338-347.

Wu, G., F. C. van der Helm, H. E. Veeger, M. Makhsous, P. Van Roy, C. Anglin, J. Nagels, A. R. Karduna, K. McQuade, X. Wang, F. W. Werner and B. Buchholz (2005). "ISB recommendation on definitions of joint coordinate systems of various joints for the reporting of human joint motion--Part II: shoulder, elbow, wrist and hand." Journal of Biomechanics **38**(5): 981-992.

Yoshikawa, T., S. Mori, A. J. Santiesteban, T. C. Sun, E. Hafstad, J. Chen and D. B. Burr (1994). "The effects of muscle fatigue on bone strain." Journal of Experimental Biology **188**: 217-233.

Zijdewind, I., H. van Duinen, R. Zielman and M. M. Lorist (2006). "Interaction between force production and cognitive performance in humans." Clinical Neurophysiology **117**(3): 660-667.

Zoghi, M., B. Vaseghi, A. Bastani, S. Jaberzadeh and M. P. Galea (2015). "The Effects of Sex Hormonal Fluctuations during Menstrual Cycle on Cortical Excitability and Manual Dexterity (a Pilot Study)." PloS One **10**(8): e0136081.