The effect of muscle fatigue on proprioception in an upper limb multijoint task

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<tr>
<td>CNS</td>
<td>Central Nervous System</td>
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<td>EMG</td>
<td>Electromyography</td>
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<td>MVC</td>
<td>Maximal voluntary Contraction</td>
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<td>MPF</td>
<td>Mean Power Frequency</td>
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CONTRIBUTION OF AUTHORS

The work contained within this thesis is presented in manuscript format and consists of one paper that will be submitted for publication in a peer reviewed journal. This paper will be co-authored with Dr. Archambault and Dr. Cote. In accordance with the guidelines of the Faculty of Graduate and Postdoctoral Studies at McGill University I would like to declare the contribution of all co-authors. The experimental protocol was designed and piloted by all three individuals (Vafadar, Archambault and Cote). I was responsible for subject recruitment, data collection, data processing and statistical analyses. I was responsible for the preparation of the text and figures for the manuscript, receiving comments on drafts from both co-authors.
ABSTRACT

Proprioception is the awareness of joint position in the space. Any disturbance in performance of this sense, such as that caused by muscular fatigue, may cause instability in the joint and make it susceptible to injury. Therefore our objective was to estimate the extent to which muscular fatigue alters the proprioception of the upper extremity in healthy adult subjects. Eighteen healthy subjects participated in this study. Twelve subjects were assigned to a fatigue group who were asked to do a reaching task while grasping a wooden block. They had to match the block with its corresponding target displayed on a flat screen, in one of three different orientations (vertical and ±30°, 10 repetitions each) with blocked vision. Following this reaching task, the subjects performed a series of resistive movements against an elastic band in order to induce muscular fatigue. The reaching task was then repeated, immediately after the fatiguing exercise. Six other subjects were assigned to the non fatigue group, who performed exactly the same protocol, but without the fatiguing phase. An independent t-test showed a significant difference both in the distribution and in the mean change of endpoint position in the fatigue group compared to the non fatigue group. However, a repeated measure ANOVA revealed no significant change in orientation. In this study, we found that position reproduction ability was greatly changed in the presence of muscular fatigue whereas no difference was found in orientation. The result of this study could serve as a basis for further research on upper limb proprioception and neuromuscular control.
Résumé

La Proprioception est la perception de la position d’une articulation dans l’espace. Tout trouble au niveau de cette modalité, tel que celui causé par la fatigue musculaire, peut causer de l'instabilité dans l’articulation et la rendre susceptible à une blessure. Par conséquent, notre objectif était d'estimer l'étendue avec laquelle la fatigue musculaire modifie la proprioception du membre supérieur chez des sujets adultes. Douze sujets en bonne santé ont été assignés à un groupe avec fatigue, auquel on avait demandé d’effectuer une tâche d'atteinte en saisissant un bloc de bois. Ils devaient toucher, avec le bloc, une cible de même forme affichée sur un écran plat, dans l'une de trois différentes orientations (vertical et ±30°, 10 répétitions chaque), sans vision. Puis, les sujets devaient exécuter une série de mouvements avec résistance contre un ruban élastique, de façon à induire la fatigue musculaire. Finalement, les sujets répétaient la tâche d'atteinte. Six autres sujets ont été assignés au groupe sans fatigue, qui a suivi le même protocole, mais sans la phase de fatigue. Un test de t a démontré une différence significative dans la distribution et dans le changement moyen de la position finale dans le groupe fatigue comparé au groupe sans fatigue. Cependant, une mesure ANOVA répétée n’a révélé aucun changement significatif pour l'orientation. Dans cette étude, nous avons trouvé que l'habilité de reproduction de la position a été grandement changée en présence de fatigue musculaire alors qu'aucune différence n’a été trouvée pour l'orientation. Le résultat de cette étude pourrait servir de base à des recherches plus approfondies sur la proprioception et le contrôle neuromusculaire du membre supérieur.
Preface

There were many steps involved in the development of this manuscript-based thesis. The thesis protocol was written by Amirhossein K. Vafadar, under the guidance of Dr. Philippe Archambault and other supervisory committee members, Dr. Robert Dykes and Dr Julie Cote. Then the experimental setup was built, followed by data collection and analysis. The thesis was written by Amirhossein K. Vafadar with guidance from Dr. Philippe Archambault.

Organization of thesis

The purpose of this project was to investigate the effects of muscular fatigue on proprioception of the upper extremity. This objective is addressed in one manuscript. This manuscript will later be submitted to a scientific journal for publication (Experimental Brain Research). Additional chapters have been incorporated in this thesis in order to comply with the regulation of the Graduate and Postdoctoral Studies (GPS). It is required by the GPS to include a literature review and a conclusion that is separate from the manuscript. Thus, it is unavoidable to have duplication of some of the material in this thesis.

Chapter 1 is an introduction and a review of the literature on proprioception and muscle fatigue. First the anatomical structure of the shoulder joint as well as its stabilizing components is explained. Then the role of the Central Nervous System (CNS) in the coordination of joint movements and the relationship between injury and the malfunction of this central coordination is discussed. The different types
of fatigue and their relationship with instability and injury are presented afterward. Lastly, reviews of experiments which have investigated the effect of fatigue on proprioception are presented.

Chapter 2 states a general rationale for conducting an experiment to study the effects of fatigue on proprioception. It also outlines the main objective of the manuscript.

Chapter 3 consists of the manuscript. It includes the text, figures and tables. The format of this manuscript follows the style of the journal “Experimental brain research”.

Chapter 4 includes a summary of the findings and a conclusion of the thesis.

The appendices contain information that is not normally included in a manuscript. A complete list of appendices is presented in the table of contents.
Chapter 1-Introduction

1.1 Fatigue, instability and musculoskeletal injury

1.1.1 Association between fatigue and injury

The relationship between fatigue and injury has been well documented in a number of experiments (Lorentzon, Wedren et al. 1988; Pinto, Kuhn et al. 1999). These studies suggest that fatigue may have a role in the process leading to injury (Figure 3). Pinto et al, (Pinto, Kuhn et al. 1999) investigated the time, frequency and type of injuries for a junior hockey team throughout a season. They found that the frequency of injury increased as the game progressed, with a higher chance of injury observed during the third period compared to the first. More specifically, 45% of the injuries occurred in the last 5 minutes of each 20-minute period when players were fatigued. A similar experiment (Gabbett 2000) on rugby players over three consecutive seasons also showed that the incidence of injury is much higher in the second half of the matches suggesting the role of muscular fatigue or accumulative micro traumas as a cause. On the other hand, the rate of such injuries is believed to be decreased throughout the season. Smith et al. (Smith and Brunolli 1989) have shown that both injury rates and fatigue scores decrease as the season progresses and the players become better conditioned. This finding obviously shows that a good conditioning exercise that delays muscular fatigue can decrease the chance of injury among athletes. Therefore fatigue can be considered as an important factor in production of injury.
The above mentioned studies in athletes are all predicting the effect of fatigue on injury indirectly. Due to the limitations in human subjects, it’s not possible to see the direct effect of fatigue on the production of injury. However, in an animal study, Mair et al (Mair, Seaber et al. 1996) fatigued the extensor digitorum longus muscle of rabbits to 25% or 50% of the force of the contralateral control. The muscle was activated while being stretched to failure. Similar data were collected on the unfatigued contralateral control muscle. Normally, when muscles are controlling and regulating limb movements, they are under intermittent stretch. During these stretches, muscles absorb energy. It was shown that the fatigued muscle was unable to absorb energy before reaching the amount of stretch that causes injury. This means that fatigued muscles were reaching their failure point more quickly.

Figure 3: Neuromuscular control model. Relationship between muscle fatigue and injury; Adapted from the models of Lephart et al. (Lephart and Henry 1996) and Tripp et al. (Tripp, Yochem et al. 2007)
1.1.2 Possible mechanisms of fatigue leading to injury

The exact mechanism under which muscular fatigue can increase the chance of injury is not well known. According to the biomechanical view, loads that are exerted to the body through different activities are normally absorbed by the muscles. In fact, the periarticular muscles work as a major shock-absorber for the joints (Radin, Martin et al. 1984). Therefore it is predictable that when a muscle is fatigued, it wouldn’t have the same load absorbing capacity, thereby putting joints and ligaments under excessive force which can lead to the injury of these structures.

Another mechanism that is discussed more in the literature by different authors is the change in sensory motor integration and neuromuscular control. Voigt et al. (Voight, Hardin et al. 1996) suggest that mechanoreceptors in the muscles around the shoulder become inefficient and dysfunctional as the direct cause of fatigue. Tripp et al (Tripp, Boswell et al. 2004) believe that fatigue can play the same role as injury and hamper the upper extremity sensory motor integration. They suggest that muscular fatigue, in a way similar to the injury, can cause deficit in the afferent proprioceptive information and eventually cause instability in the joint which itself is a predisposing factor for injury.

1.1.3 Association between joint instability and injury

The biomechanical formation of the shoulder joint is mainly designed for mobility rather than stability. In fact, the glenohumeral joint is inherently unstable and exhibits the greatest amount of motion found in any joint in the human body
In spite of this freedom of movement, the joint still needs some sort of stability to function well. This stability is mostly provided by both static and dynamic stabilizers (Wilk, Arrigo et al. 1997). Bony geometry of the shoulder, the joint capsule, the glenoid labrum as well as the acromio-clavicular and gleno-humeral ligaments all play a role in providing static stability to the joint (Wilk, Arrigo et al. 1997).

Dynamic stability of the gleno-humeral joint is mainly provided by muscles around the joint. The rotator cuff muscles as well as the long head of the biceps keep the humeral head in the glenoid fossa and prevent it from excessive translations (Bassett, Browne et al. 1990).

The good function of these dynamic stabilizers is highly dependent on the quality of motor commands sent from higher levels of nervous system (Wilk and Arrigo 1993). Sensory information (proprioception) travels thorough afferent pathways to the Central Nervous System (CNS) where it is integrated with other information leading to efferent motor response. This sensory and motor synergy is defined as neuromuscular control (Myers and Lephart 2000).

Dynamic stabilizers in the shoulder joint need to be coordinated in order to function optimally. The process of sensory-motor integration is responsible for this coordination. The relationship between stability and neuromuscular control in the shoulder joint has been investigated by several authors. In a study by Smith et al. (Smith and Brunolli 1989), the investigators compared the proprioception of dislocated shoulders with normal ones. They found that proprioception is
significantly decreased in dislocated shoulders. They concluded that instability in the shoulder can cause deficits in proprioception and consequently alter the neuromuscular coordination. Other authors have explained these relations in the other way around. They believe that at first an injury to the joint causes proprioceptive deficit, then this deficit leads to an instability in the joint (Freeman, Dean et al. 1965; Barrack, Skinner et al. 1983; Barrack, Skinner et al. 1989).

Whether the instability causes deficit in proprioception or vice versa, the relationship between these two is well accepted by investigators.

It is believed that a proper neuromuscular control as well as a good stability in the shoulder is essential for the prevention of injury (Bjorklund, Crenshaw et al. 2000). Glousman et al, (Glousman, Jobe et al. 1988) measured the EMG activity of several muscles around the shoulder during pitching in subjects with anterior shoulder instability. They showed that the activity of the supraspinatus and biceps muscles is increased in order to compensate for the lack of anterior glenohumeral instability. On the other hand, they reported an unusual decrease in the activity of the subscapularis, pectoralis major, latissimus dorsi and serratus anterior muscles which are vital in providing anterior stability during the cocking phase of pitching. Alteration in muscle activity has also been reported for the deltoid muscle during the same task (Kronberg, Brostrom et al. 1991). These changes in the pattern of muscle recruitment during functional activities in unstable joints might act as a predisposing factor for injuries in the long term. Additionally, in two longitudinal studies, Robinson et al. (Robinson, Kelly et al. 2002; Robinson,
Howes et al. (2006) showed that 55.7% of patients with shoulder instability are likely to develop injuries in their joint within two years of the primary instability. Lephart et al. (Lephart and Henry 1996) also suggests that people with functional instability who also have neuromuscular deficit are more prone to further injuries.

Based on the mentioned studies, it is obvious that in the presence of instability, the normal function of the joint is compromised by abnormal movement patterns that might make it susceptible to further injury.

1.2 Proprioception

As mentioned above, appropriate sensory information (proprioception) is essential in providing stability to the shoulder joint. Proprioception is the ability to detect, without the visual input, the spatial position and/or movement of limbs in relation to the rest of the body (Pedersen, Lonn et al. 1999). In fact, it is a set of sensory information sent from mechanoreceptors to the CNS contributing to stability and motor control (Lephart and Jari 2002). These specialized mechanoreceptors are located in muscles, tendons, capsules, ligaments and skin throughout the body.

Proprioception is generally composed of three submodalities: kinesthesia, position sense and sense of resistance. Position sense is the awareness of the joint position whereas kinesthesia (movement sense) is the conscious awareness of movement (Voight, Hardin et al. 1996) or detection of movement speed (Pedersen, Lonn et al. 1999). The sense of resistance is the minimum threshold of force detection in the joint (Myers and Lephart 2000). Together these modalities are termed proprioception. Distinction in submodalities of proprioception arises from the
difference in signals that each type of receptor produces. For example the current view is that muscle spindles are responsible for the sense of position and movement whereas Golgi tendon organs provide the sense of resistance (Gandevia 1998). However Proske (Proske 2005) believes that beside the muscle spindles, joint and skin receptors have also a contributory role in producing signals for position sense. Further research is still needed to clarify the contribution of each receptor in the production of the different submodalities of proprioception.

1.2.1 Muscle receptors

Two distinct mechanoreceptors (proprioceptors) are located in muscles, each of which responsible for providing a different type of sensory information; muscle spindles and Golgi Tendon Organs (Carpenter 2003).

Muscle spindles are specialized muscle cells containing sensory organs that monitor the length of the muscle. They are very sensitive to the rate of change in the length of the muscle. This means that a sudden and rapid change in muscle length will activate more spindles compared to a slow one. These properties make spindles important for proprioception (Macintosh 2006).
Golgi tendon organs are small sensory receptors, located at the junction between a muscle and tendon that monitor tension. Each Golgi tendon organ consists of small bundles of tendon fibres enclosed in a layered capsule with dendrites (fine branches of neurones) coiling between and around the fibres. They are responsible for responding to tension in the fibres with which they are associated in the tendon. In fact they consistently send feedback information about the force levels in the muscle to the CNS (Brooks, Fahey et al. 2000).

### 1.2.2 Joint receptors

Another important source of information about the movement and the position of the limbs originate from the mechanoreceptors in the ligaments and joint capsules. These receptors are: Pacinian corpuscles, Golgi-like endings, Ruffini endings and
small nerve fibre with unencapsulated endings. The pattern of firing of these receptors is different. Each of them fires at a special joint range of motion but generally most of them fire at the end range to signal the nervous system that the joint is reaching its maximal amplitude (Janwantanakul, Magarey et al. 2001).

The exact contribution of each of the joint, muscle or skin receptors in sending proprioceptive information is not known. When there is no movement in the joint and muscles are not working, joint receptors are expected to be responsible for sending proprioceptive information, rather than the muscle receptors which seem to be inactive. However Goodwin et al (Goodwin, McCloskey et al. 1972) applied vibration on elbow muscle tendons which can produce an illusion that the muscle is shortening even though it is held stationary. It was shown that in this condition, where there is no movement, the sense of position is compromised. Such experiments can clearly show that both joint and muscle receptors play a role in providing proprioceptive feedback.

1.2.3 Proprioception measurement

The proprioception in the upper limb has been measured in different ways in the literature. Generally in most of these methods, a reference position is assigned and subjects are asked to reproduce the reference either actively or passively with eyes closed. Isokinetic dynamometers are one of the devices that have been commonly used to measure proprioception especially in the shoulder joint. An *isokinetic contraction* is a type of contraction where the limb moves at a constant speed. An isokinetic dynamometer can induce this type of contraction by applying an
appropriate level of force against the limb movement and keep the velocity constant at all times. Beside the training purposes, isokinetic dynamometers were also designed for the measurement of mechanical forces, speed, power and joint angle (www.biodex.com). As mentioned earlier, proprioception has three submodalities. In previous experiments, isokinetic dynamometers have been used to measure both position sense (Voight, Hardin et al. 1996; Sterner, Pincivero et al. 1998; Lee, Liau et al. 2003; Ulkar, Kunduracioglu et al. 2004) and kinesthesia or movement sense (Carpenter, Blasier et al. 1998; Pedersen, Lonn et al. 1999). The procedure of proprioception measurement with these dynamometers was as follows:

The upper limb is usually connected to the device while the subject is either seated or in supine position. For the measurement of position sense, after assigning a shoulder reference angle, the subject is asked to reproduce this angle actively or passively. In the passive repositioning test, the investigator or the device itself moves the arm passively and the subject is asked to click a button and stop the movement when the reference is assumed to be reached. For the measurement of kinesthesia, the device starts moving the arm and the subject should notify the experimenter as soon as he/she feels any movement in the arm. A dynamometer reports the angle difference between the starting and the reported positions. During all these procedures, the subject is kept blindfolded.

Motion capture devices have also been used in proprioception measurement of the upper limb (Tripp, Boswell et al. 2004; Tripp, Yochem et al. 2007). Sandlund et al (Sandlund, Djupsjobacka et al. 2006) used a magnetic tracking system in
conjunction with a manipulandum-like device to measure the proprioception in the shoulder. The arm was mounted on a manipulandum while the magnetic markers where attached to it. The ability of subjects to reproduce a reference arm position was recorded by the magnetic tracking system. Suprak et al (Suprak, Osternig et al. 2006) used the same magnetic system but they used a head-mounted display to show the target to the subjects and asked them to move their arm freely in space and try to reach to the target that was seen.

Use of a matching task is another method for the measurement of proprioception, especially in the elbow (Sharpe and Miles 1993; Walsh, Hesse et al. 2004; Proske 2005; Allen and Proske 2006). The position of one forearm is assigned as a reference and the subject should match the other forearm with the reference.

Finally Dover et al (Dover and Powers 2003) used an inclinometer to measure the shoulder proprioception. They attached an inclinometer to the subjects’ arm and asked them to reproduce a reference angle. Inclinometers are able to show the angle difference.

Among the aforementioned measurement techniques, only the inclinometer has been shown to be a valid and reliable tool for measuring the proprioception of the shoulder joint. Although motion capture systems have been shown to be a reliable measurement tool, their reliability, specifically in the measurement of proprioception, has not been documented.
1.3 Muscle fatigue

In simple terms, fatigue may be described as a sensation of weakness or muscle pain, or as a decrement of performance. The physiological site of fatigue in the neuromuscular system varies greatly but it can be grouped under the headings of central fatigue, fatigue of the neuromuscular junction and muscle fatigue (Merletti, Rainoldi et al. 2004). Fatigue of the CNS (central fatigue) includes neurobiological mechanisms of change in subjective effort, motivation, mood and pain tolerance as well as the mechanisms that inhibit motor drive in upper regions of the brain (Gandevia 1998). Fatigue of the neuromuscular junction is defined as the failure in transmission of neural signals to the muscles or failure of the muscles to respond to neural excitations (Bigland-Ritchie, Jones et al. 1978). Localized muscle fatigue is the inability of the muscle fibers to sustain a given intensity (Brooks, Fahey et al. 2000).

1.3.1 Measurement of fatigue

There are different methods to quantify muscle fatigue. Before describing these methods, we should first know the definition of fatigue in different approaches. A quantitative approach to fatigue is often associated to an event, or to the time instant corresponding to an event, such as the inability to further perform a task or sustain an effort, and therefore is somehow related to mechanical performance. Another description deals with the inability to reach the same initial level of Maximal Voluntary Contraction (MVC) force (the force generation capacity), again related to an event or time instant associated with the inability to produce a
specified mechanical performance. These definitions indirectly imply that there is no fatigue before a specific point in time, and just after that specific time, fatigue begins (Merletti, Rainoldi et al. 2004).

1.3.2 Physiological measurements of fatigue

A physiological approach looks at the muscle changes at cellular level during fatigue. Myoelectrical studies have enabled investigators to figure out the function of motor units during muscle contractions and fatigue. The recruitment and firing rate of motor units depend greatly on the type of contraction and the amount of force produced by the muscle. It has been shown that the number of motor unit action potentials increases progressively as soon as the contraction is started (Scherrer and Bourguignon 1959; Maton 1981). But as the contraction continues, the behaviour of motor units depends on the amount of force produced by the muscle. In a submaximal contraction leading to fatigue (30-75% of MVC), the electromyographic (EMG) amplitude is increased which is due to the progressive recruitment of additional motor units (Moritani, Muro et al. 1986). Furthermore, at this level of force, the firing frequency of each active motor unit also increases as a function of time (Maton 1981). Conversely, during a sustained 100% MVC, the motor unit firing rate decreases progressively (Bigland-Ritchie, Jones et al. 1978; Bigland-Ritchie, Johansson et al. 1983). Now how can we quantify these changes?
1.3.3 Quantitative measurement of fatigue

Muscle fatigue can be seen in the EMG signals as a progressive “slowing”. This change in signal can be quantified both in the frequency domain and in the time domain. In order to show the amount of fatigue in the frequency domain, one can calculate the Mean Power Frequency (MPF) of the signals in a specific period of time from the beginning to the end of an isometric contraction and then compare them together. In repeated contractions, the comparison of the first and the last contractions will reveal possible decrease in MPF and the presence of muscle fatigue (Merletti, Rainoldi et al. 2004). The correlation between MPF and fatigue in isometric contraction was first shown by Lindstrom et al (Lindstrom, Magnusson et al. 1970). They showed that the EMG power spectrum decreases in the presence of fatigue. Later on, Gerdle et al. (Gerdle, Elert et al. 1989) reported the same decrease in power frequency under repeated isokinetic shoulder flexions leading to fatigue. They concluded that changes in MPF are parallel to mechanical fatigue.

The presence of fatigue can also be quantified in the time domain. In this situation we are dealing with signal amplitude rather than frequency. Unlike the MPF, the signal amplitude increases with fatigue induced by submaximal contractions (Kramer, Hagg et al. 1987). In order to quantify the progression in the amplitude of EMG signals and detection of muscle fatigue we may calculate the surface area under the EMG signals in an isometric contraction and compare an episode in the beginning with an episode at the end. For repeated contractions, we can detect each peak of EMG signal which corresponds to an individual
contraction and then calculate the surface area under each peak (Figure 2). Comparing the surface area under the first and the last contractions will reveal a possible increase in the signal amplitude, which can be interpreted as a sign of muscular fatigue.

The analysis of the surface EMG signal may provide an objective tool for the assessment of muscle fatigue, although the relationships between EMG variable changes and the underlying physiological phenomena are very complex and not yet fully understood (Merletti, Rainoldi et al. 2004).

1.3.4 Qualitative measurements of fatigue

Beside the quantitative tools, there are also some qualitative measurements of muscle fatigue. Borg scales (Borg 1970; Borg, Hassmen et al. 1987) are commonly used to assess task difficulty, as perceived locally (e.g. upper limb region) or globally. The global scale (1970) consists in a 6-20 point scale, with 7 corresponding to a “very, very light” task and 19 to a “very, very hard” task. In fatigue experiments, a rating of 15-17 or above is usually considered as an indicator of muscular fatigue (Cote, Mathieu et al. 2002; Tripp, Uhl et al. 2006).
The local scale (1987) consists in a 0-10 point scale, where 0 is “nothing” and 10 is “cannot continue”. The rating of 8 usually corresponds to a “very difficult task” and has been considered as an indicator of fatigue in previous studies (Cote, Mathieu et al. 2002).

Both scales for global and local perception of task difficulty show well-documented psychometric properties. The localized Borg CR-10 scale has been widely used to measure perceived task difficulty in both healthy and clinical populations (Noble 1982). The Borg CR-10 scale has demonstrated good reproducibility and sensitivity to change (Grant, Aitchison et al. 1999), acceptable reliability (Lagally and Costigan 2004) as well as good validity with respect to physiological markers of fatigue, including cardiovascular (Chen, Fan et al. 2002), heart rate (Borg, 1987), aerobic power (Eston, Faulkner et al. 2006), oxygen consumption (Goss, Robertson et al. 2003) and blood and muscle lactate (Borg, 1987; Noble et al., 1982). Further, a good correlation (0.68 – 0.76) between Borg ratings and mean power frequency of the EMG signal has previously been shown in tasks that target upper trapezius muscle fatigue (Hummel, Laubli et al. 2005). In a recent study, Borg CR-10 ratings have been shown to be good predictors of endurance time in trapezius isometric contraction efforts (Troiano, Naddeo et al. 2008).

1.3.5 Pros and cons of fatigue measurements

Each of the qualitative and quantitative measurements of fatigue has its own advantages and limitations. For example, EMG recording as a quantitative tool,
gives us accurate information about the fatigue status of the muscle being measured; however, this method can’t determine the fatigue in the other sites of the neuromuscular system like CNS or neuromuscular junctions. On the other hand, a qualitative measurement like the Borg scale, unlike the EMG, is not confined to the individual muscles and can report the overall status of fatigue, whether at the muscular or central level or both. Nevertheless, this type of measurement is based upon the perception of task difficulty, which can vary among different subjects.

Therefore, depending on the area and type of fatigued muscles, each of the methods or a combination of both can be employed for determination of fatigue level.

**1.4 Effects of fatigue on proprioception**

Investigating the effect of muscular fatigue on proprioception and neuromuscular control has been the interest of several researchers especially in the upper extremity where an intact proprioception is vital for function and stability in the joint. Two submodalities of proprioception such as movement and position sense have been studied separately in the context of muscular fatigue.

Generally, these experiments can be divided into two groups; single joint and multi-joint experiments.
1.4.1 Single joint experiments

The single joint experiments have mostly focused on the shoulder joint in the upper extremity and only a few studies have looked at the elbow. Myers et al. (Myers, Guskiewicz et al. 1999) investigated the effects of fatigue on the shoulder position sense by means of an isokinetic dynamometer. Subjects lay down on their backs and their arm was connected to the device. The experiment was based on an active angle reproduction test, where subjects were asked to actively reproduce a specific shoulder angle, either in external or internal rotation, while being blindfolded and using headphones to eliminate visual and auditory feedback. After the initial testing, the subjects performed a series of exercises with the isokinetic device until they got fatigued and continued with the active repositioning assessment, identical to the first set.

The results of the study showed that the amount of error made by the subjects was significantly different before and after fatigue, compared to the control group who did the same protocol without fatiguing exercises and showed no significant difference between the two tests.

Isokinetic dynamometers are useful devices in providing distinctive information about the position of the limb, together with the forces produced during contractions. Therefore they have been widely used by different investigators in the assessment of proprioception. Voigt et al (Voight, Hardin et al. 1996) did a similar study with the help of a dynamometer. They tested the subjects in a sitting position and used both active and passive repositioning tests to determine the acuity of proprioception. In an active repositioning test, subjects actively
reproduced a reference limb position while in a passive one, the dynometer device or the experimenter passively moved the arm until the subject announced that the intended position was reached. The investigators in this experiment found that position sense error was significantly increased after fatigue, both during active and passive repositioning. They also compared the dominant and non dominant arm and found no difference between these two in terms of position sense acuity.

Beside position sense, the movement sense has also been investigated as another submodality of proprioception. Carpenter et al. (Carpenter, Blasier et al. 1998) looked at the passive movement detection threshold before and after fatigue. Using an isokinetic dynamometer, they recorded the shoulder rotational angle in which the subjects could detect the initiation of the movement. By comparing these angles before and after fatigue, they found that the threshold of movement detection is significantly increased after fatigue. Although this increase was significant for both internal and external rotations, internal rotation was found to be more affected by muscular fatigue. The results also showed no difference between dominant and non dominant arm in the detection of movement, similar to the study of Voight et al (Voight, Hardin et al. 1996). Distinguishing different movement velocities is considered to be another aspect of movement sense. Pederson et al. (Pedersen, Lonn et al. 1999) worked exclusively on this ability by asking the subjects to report the speed of the movement in respect to a reference. After initial testing, the experimental group did a series of hard exercises leading to fatigue while the control group did a series of light exercises. Then the same testing procedure was performed. The investigators found that the rate of false
responses was significantly increased after fatigue for the experimental group with hard exercise whereas no difference was seen in control group with light exercise. They also found that women had a lower acuity in the velocity sense than men.

All the single joint experiments are not exclusively in favour of an alteration in proprioception after fatigue. Sterner et al. (Sterner, Pincivero et al. 1998) reported that fatigue does not have any effect on proprioception, neither in active nor in passive repositioning tests. Lee et al (Lee, Liau et al. 2003) also studied active and passive repositioning before and after fatigue for both shoulder internal and external rotation. They found that only active positioning in internal rotation was significantly changed after fatigue whereas active positioning in external rotation as well as passive positioning in internal and external rotation remained unchanged. These two experiments revealed a controversy in the findings of proprioception studies in the shoulder joint.

Single joint experiments are not confined only to the shoulder joint. There are a few experiments which have studied the proprioception acuity in the elbow. Traditionally, testing the proprioception of the elbow has been done by means of matching tasks. In this method, subjects were asked to match the position of their elbow with that of the other one. Sharp et al. (Sharpe and Miles 1993) reported no difference in the ability of subjects to match their elbow position after fatigue. This finding is in controversy with the results of two other similar experiments. Walsh et al. (Walsh, Hesse et al. 2004) employed a series of eccentric exercises as their fatiguing protocol. They found that the matching error was significantly
increased after fatigue. They also found that when muscle force was maximally decreased, the amount of error increased even more. It is well known that the eccentric exercise used in this experiment can cause muscle damage. It was thought that this damage could be extended to the intrafusal fibers of muscle spindles as well, and therefore cause the observed changes in proprioception (Allen and Proske 2006). But Gregory et al. (Gregory, Brockett et al. 2002) reported that the damage and fatigue from a severe eccentric exercise does not change the performance of muscle spindles. Allen et al. (Allen and Proske 2006) confirmed this finding by showing that even after a non damaging concentric exercise, the matching error was still significantly increased. Therefore they hypothesized that another factor called the sense of effort can be a cause for the error.

We judge the muscle forces we generate and the heaviness of objects by means of a sense of effort (McCloskey 1981). The exact origin of the effort signal is not known yet, however it is hypothesized that it arises somewhere upstream (Carson, Riek et al. 2002). It is believed that the sense of effort is linked to the sense of fatigue. During exercise, as muscle force declines, the CNS compensates by increasing activation of motoneurons, leading to a progressive increase in the perceived effort, until the point of exhaustion is reached (Proske 2005).

1.4.2 Multi-joint experiments

There are a few experiments which have looked at the effects of fatigue on proprioception in a multi-joint upper extremity task. In two different studies Tripp
et al. (Tripp, Boswell et al. 2004; Tripp, Yochem et al. 2007) studied baseball players who are more prone to injuries of upper extremity. In these experiments, the subjects were asked to reproduce a throwing movement before and after muscle fatigue. The movements were recorded using an electromagnetic tracking device. The accuracy of subjects was measured in two specific points in the movement trajectory: the arm-cocked and the ball-release positions. In a throwing motion, ball-cocked is a position at which the forward acceleration of the arm would begin whereas the ball-release position is the position at which subject releases the ball. Subjects in these experiments were asked to initiate a throwing movement, stop for one second whenever they felt that they had reached each of the intended positions and then continue the movement to the end. After the initial set, subjects performed repetitive throwing tasks until they got fatigued. The status of muscle fatigue in this experiment was determined through subjects’ rating of the Borg scale of perceived exertion (Borg 1970).

The same testing procedure was then performed after muscle fatigue. The investigators in these experiments found that for both positions in the movement trajectory, the acuity was significantly decreased after fatigue. They also found that this effect could be seen in all of the upper extremity joints including scapulothoracic, glenohumeral, elbow and wrist. In these experiments, the position sense was measured both in the middle and end range of shoulder joint motion. In the end range of joint motion, the capsules, ligaments and surrounding structures are tight, thus more joint receptors are recruited in this position and higher levels of accuracy in proprioception is expected (Allegrucci, Whitney et al.
The investigators found that in the presence of muscle fatigue, the position sense was significantly affected even in the end range of joint motion. Therefore they concluded that muscle mechanoreceptors are playing a major role in providing proprioceptive feedbacks to the CNS.

1.4.3 Limitations of previous studies

Many of the experiments quoted above used an isokinetic dynamometer to measure position sense. In most of the cases, these devices would provide external body support and some movement restrictions which is believed to affect sensory motor system acuity by providing additional proprioceptive feedbacks (Tripp, Yochem et al. 2007). Moreover, in these experiments, usually one joint is moving and other adjacent joints are strapped to the equipment. Obviously it is not possible to extend the results of a single joint to a functional multi-joint task. Therefore the measurement of the position reproduction acuity in a multi-joint functional task should include an unsupported body and an unconstrained multi-joint motion without any external proprioceptive stimulus.

The only two studies that have measured multi-joint position sense in a three dimensional space have eliminated the above mentioned problems to avoid possible measurement biases (Tripp, Boswell et al. 2004; Tripp, Yochem et al. 2007). However, there still seems to be some limitations in these studies. In the experiments by Tripp et al (Tripp, Boswell et al. 2004; Tripp, Yochem et al. 2007), the findings are limited to baseball pitchers. Although the task employed in
these studies (flexion, abduction, and external rotation) is a functional movement in many throwing activities, it is seldom used by ordinary people in their daily activities. On the other hand, the actual throwing motion is continuous and performed with the highest speed possible, whereas in these studies, the subjects are asked to perform the task intermittently and stop at some points during the movement trajectory for the position measurements. This is not representative of an actual task since it is not a continuous motion.

1.5 Summary and conclusions from the literature review

Based on the existing literature, muscular fatigue, joint instability and injury are strongly associated with each other. Finding the exact mechanism of this relation can greatly improve the current knowledge in the prevention and management of musculoskeletal injuries. On the other hand, there are only a few studies that have looked at the effect of fatigue in a functional task. When two or more joints contribute to a task, the sensory-motor integration and neuromuscular control become more complicated. In the presence of fatigue, the CNS may employ different strategies (like movement compensations) to maintain the body in its normal position and achieve the pre-defined movement goal. These processes can only be investigated in the context of a functional task rather than a single joint, non functional movement.

Another factor that emphasizes the importance of extensive research in this area is the controversy in the role of receptors in providing proprioceptive feedbacks. It is not well understood yet that either muscle or joint receptors elicit information
about the position of the limb or which of them is dominant in different situations. This becomes more complicated when we see that in the presence of fatigue, they are not the only factors that can change the movement acuity but another factor called the sense of effort may also contribute to this change. The sense of effort is something more central that its mechanism is not well understood yet (Allen and Proske 2006).

Finally, restoration of proprioception and neuromuscular control trainings are two important aspects of rehabilitation programs in the management and prevention of musculoskeletal injuries. A good understanding of functional mechanism of these two concepts can greatly improve the current approaches in the treatment of musculoskeletal disorders.
Chapter 2- Rationale and objective

The human Central Nervous System (CNS) is responsible for the control of the body movements. Sensory information from all parts of the body is constantly sent to the CNS. The brain interprets this information and elicits appropriate motor responses to the limbs. This central processing can be called sensory-motor integration.

There are several internal factors that may interfere in sensory motor integration, thereby changing the properties of motor commands (e.g. injuries to the peripheral nervous system or brain lesions). Improper motor commands may disturb the movement coordination, thereby producing functional instability and further injuries. Muscle fatigue is a peripheral factor that may play a role in disturbing sensory motor integration. This hypothesis is supported by the fact that the risk of muscular and ligamentous injury increases in the presence of fatigue. Therefore the main objective of this study was:

“To estimate the extent to which muscular fatigue impacts on the proprioception of upper extremity in healthy adult subjects”

We measured the ability of subjects to reproduce an arm reaching task after fatigue, as an indicator of position sense which is one the submodalities of proprioception. The reaching task, a common functional motion in most daily activates, occupational tasks and sports, has not been studied before in the context of fatigue. To avoid the problems of single joint assessment studies, we controlled for any external proprioceptive feedback by letting the subjects perform the task
freely without any limb support. We also added three different hand orientations to our reaching task in order to have more movements in the elbow and wrist as well as requiring more precision from the part of the subjects. We hypothesized a significant change in the subjects’ mean arm position as well as change in their orientation angle after muscle fatigue.

Studying the consequences of fatigue will lead us to investigate the mechanisms by which sensory motor processing is changed in the presence of fatigue. This understanding is vital in the prevention and rehabilitation of musculoskeletal injuries.
Chapter 3- Manuscript

3.1 The effect of muscle fatigue on proprioception in an upper limb multijoint task

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3.1 Abstract

Proprioception is the awareness of joint position in space. Any disturbance in this modality, such as that caused by muscular fatigue, may cause instability in the joint and make it susceptible to injury. Therefore our objective was to estimate the extent to which muscular fatigue alters the proprioception of the upper extremity in healthy adult subjects. Twelve healthy subjects were assigned to a fatigue group and were asked to do a reaching task while grasping a wooden block. They had to match the block with its corresponding target displayed on a flat screen, in one of three different orientations (vertical and ±30°, 10 repetitions each), without vision. Following this reaching task, the subjects performed a series of resistive movements against an elastic band in order to induce muscular fatigue. The reaching task was then repeated. Six other subjects were assigned to a non-fatigue group; these performed exactly the same protocol, but without the fatiguing phase. An independent t-test showed a significant difference both in the distribution and in the mean change in endpoint position in the fatigue group compared to the non-fatigue group. However, repeated measures ANOVA revealed no significant change in orientation. In this study, we found that position reproduction ability was greatly changed in the presence of muscular fatigue whereas no difference was found in orientation. Therefore fatigue is an important factor that should be taken into consideration during the treatment of musculoskeletal injuries as well as athletic training.
3.2 Introduction

The glenohumeral joint is the most mobile joint in the human body, and is inherently unstable (Williams 1986). However, static (ligament and capsule) and dynamic (muscle) stabilizers around this joint can partly compensate for the lack of stability (Wilk, Arrigo et al. 1997). For stability to be achieved, muscles around the joint should function in a coordinated manner. This is fully dependent on the quality of commands sent from spinal and higher levels of the nervous system (Wilk and Arrigo 1993). Proprioception is the ability to detect, without the visual input, the spatial position and/or movement of limbs in relation to the rest of the body (Pedersen, Lonn et al. 1999). It is mainly composed of sensory information from mechanoreceptors located in the muscles, tendons, ligaments and skin around the joint which is sent to the Central Nervous System (CNS) where it is integrated with other sensory modalities, as a basis for an appropriate motor response (Myers and Lephart 2000). Therefore, the quality of proprioception can directly affect the descending motor responses necessary for the coordination of joint movements and stability.

The relationship between proprioception and stability has been demonstrated by several authors (Freeman, Dean et al. 1965; Barrack, Skinner et al. 1983; Barrack, Skinner et al. 1989; Smith and Brunolli 1989). When the shoulder joint becomes unstable, it is prone to muscular and ligamentous injuries. In two longitudinal studies, Robinson et al. (Robinson, Kelly et al. 2002; Robinson, Howes et al. 2006) showed that 55.7% of patients with shoulder instability are likely to develop injuries in their joint within two years of the primary instability. Lephart
et al. (Lephart and Henry 1996) also suggested that people with functional instability who also suffer from a deficit in proprioception are more likely to develop subsequent injuries.

On the other hand, it has been shown that muscle fatigue can also play a role in the incidence of musculoskeletal injury. Pinto et al. (Pinto, Kuhn et al. 1999) and Gabbett et al. (Gabbett 2000) reported that in athletes, the frequency of injury increased as the game progressed, with a higher chance of injury observed during the last period of games compared to the first, suggesting the role of muscular fatigue or accumulative micro traumas as a cause. Finally Smith et al. (Smith and Brunolli 1989) reported that the injury rate and fatigue scores decrease as the players become better conditioned. Based on these studies, fatigue can be considered as an important factor in the development of injuries. The exact mechanism under which muscular fatigue can increase the chance of injury is not well known yet; however, Tripp et al (Tripp, Boswell et al. 2004) suggest that muscular fatigue, can cause a deficit in proprioceptive information and eventually cause instability in the joint, which itself is a predisposing factor for injury. Voight et al. (Voight, Hardin et al. 1996) suggest that the deficit in proprioception happens when the mechanoreceptors in the muscles around the shoulder become inefficient and dysfunctional as the direct cause of fatigue.

The effect of muscle fatigue on shoulder joint proprioception has been investigated by several authors. Proprioception is generally divided in three distinct submodalities: kinaesthesia (movement sense), position sense and sense of resistance. Among these three, position sense has received the greatest
attention, in the context of fatigue. Voight et al (Voight, Hardin et al. 1996) measured the repositioning ability of the subjects with an isokinetic dynamometer. They reported a significant increase in the position sense error after muscular fatigue. Other similar studies on the shoulder also reported the same findings (Carpenter, Blasier et al. 1998; Myers, Guskiewicz et al. 1999). In such single joint experiments, the upper limb was usually strapped and fixed to the measurement device and only one joint was free to move. Such strapping and fixation is believed to affect the proprioceptive signals by providing additional sensory feedback (Tripp, Boswell et al. 2004). To avoid these confounding factors, Trip et al. (Tripp, Boswell et al. 2004; Tripp, Yochem et al. 2007) investigated the effect of fatigue on position sense acuity in an unsupported, functional multi joint task. They tested the acuity of baseball pitchers in reproducing a throwing movement. The result showed a significant difference in the position sense of upper extremity after fatigue.

To date there have been only a few experiments that have investigated the effects of fatigue on proprioception in a functional multijoint task. Specifically the reaching task, as a common daily activity, has not been studied in the context of fatigue. Accordingly, the purpose of this study was to estimate the extent to which muscular fatigue alters the proprioception of upper extremity in healthy adult subjects. In the present study, we hypothesized that muscle fatigue would significantly affect the ability of subjects to reproduce an arm reaching task after fatigue, which would indicate a disruption in the sense of proprioception.
3.3 Method

3.3.1 Subjects

Eighteen healthy, right-handed subjects (five females, thirteen males) with a mean age of 26 years were recruited for the experiment. No subject reported any history of musculoskeletal disease in the upper extremity or in the cervical spine. After the investigators explained the experimental procedure, all subjects provided their informed consent, as approved by the local ethics committee guidelines.

3.3.2 Experimental protocol

The subjects were divided into two groups: fatigue (n = 12) and non fatigue (n = 6). Subjects in the fatigue group performed a proprioception measurement task, followed by a series of intensive fatiguing exercises, and then repeating the proprioception measurement task. For the non fatigue group, the same experimental procedure was followed, except for the fatiguing phase. Instead of performing the fatiguing exercise, these subjects sat quietly for an equivalent amount of time (10 min). The non fatigue experiment served to confirm that the possible changes observed in this experiment were indeed due to muscle fatigue.

3.3.3 Proprioception task

We measured the proprioception of the upper limb by asking the subjects to produce a reaching and orientation task in the standing position. Subjects grasped a light wooden block (15×3×1.5cm) and stood in front of a computer screen. The center of the screen was adjusted at the subject’s shoulder level, and set at a
distance corresponding to 90% of their complete arm length. At the start of a trial, a rectangular target appeared on the screen in one of three different orientations \((125^\circ, 90^\circ, 55^\circ)\) (Figure 4B). After a fixed \((3 \text{ s})\) delay, vision was blocked by means of LCD glasses. Two seconds later, at the sound of a beep, subjects had to reach forward and match the block to the remembered location and orientation of the target. Finally, subjects had to maintain their final arm position until they heard another beep, signaling the end of the trial; they then had to bring back their arm alongside their body. Vision was restored and the next trial was initiated. Thus, subjects never received visual feedback about their performance. Target orientations were presented in a random order \((10 \text{ trials/condition, for a total of 30 trials})\). The control of the experiment and the presentation of the targets were done using custom software developed in Matlab (The Mathworks, USA).

![Figure 4: The experimental setup. A) A subject reaches to the target, while his vision is blocked by LCD glasses. B) The three different target orientations](image)

Precautions were taken to avoid other sources of proprioceptive or tactile feedback. First, the screen was placed behind a large Plexiglas plate to provide a
uniform surface. Also, by selecting a 90% reach distance, the feedback that a fully extended elbow could provide was avoided (figure 4A).

3.3.4 Muscle fatiguing exercises

The independent variable in this study was muscular fatigue. Since the reaching movement involved multiple joints, several muscles in the arm including both prime movers and stabilizers were active during the task. Thus, a comprehensive protocol was developed, in order to fatigue most of these muscles at the same time. The fatiguing exercises consisted in a series of resistive arm movements using an elastic band (Thera-Band USA, blue color, medium resistance). One end of the band was tied to a fixed anchor, located near the floor behind the subject’s standing position. The subjects were asked to grasp the other end with the arm along the body and then reach out completely, once while supinating and once while pronating the hand (Figure 5). The length of the elastic band was set at 60 cm. This length was neither too tight to produce maximum contraction nor too loose to create low resistance. Each set of exercise lasted for one minute followed by a 30s rest period. The speed of the movements was controlled by a metronome which was set at 60 beats per minute; subjects had to reach forward, then back, on the beat (30 reaches per set). Thus, for all subjects, the number of movements in each set was identical. Participants were asked to rate their perceived exertion on the Borg CR-10 scale (see below) during the 30 seconds rest period between each set. They continued the fatiguing exercises until one of the following conditions were met: they reported a Borg scale rating of 8 or higher, or they could no longer fully extend the arm for three consecutive movements.
Following the fatiguing exercise, subjects repeated the initial proprioception testing for 10 reaches to each of the three target orientations, as described above. It has been shown that the changes in EMG activity and metabolic environment accompanying fatigue are restored within 10 minutes (Tripp, Yochem et al. 2007). Therefore we completed the second proprioception testing of all subjects within 4 to 6 minutes after the fatiguing protocol. In the non fatigue group, the re-testing was done after 10 minutes of rest.

3.3.5 Measures

3.3.5.1 Kinematics

We used a motion analysis system (Vicon, Oxford Metrics ltd., Oxford, UK) to record movement kinematics and to measure the endpoint position. The reliability
and validity of the Vicon system have been well established before (Henmi, Yonenobu et al. 2006). Vicon has a distance accuracy of 0.42 mm (measurement between two points) and an angle accuracy of 0.16 deg (The comparison meeting of motion analysis systems 2002, Tokyo, Japan). In addition, we calibrated the system before each session to eliminate errors due to accidental changes in the position of the cameras. Seven markers were used on the right upper extremity. Two markers were also placed at both ends of the block in order to measure hand orientation. Marker position was captured (120 Hz) using six high-resolution infra-red cameras.

3.3.5.2 Borg scale

Both quantitative and qualitative measurements were used to measure muscular fatigue in this study. Borg scales (Borg 1970; Borg, Hassmen et al. 1987) are commonly used to assess task difficulty, as perceived locally (e.g. in the neck-shoulder region) or globally. Both scales for global (1970) and local (1987) perception of task difficulty show well-documented psychometric properties. The localized Borg CR-10 scale has been widely used to measure perceived task difficulty in both healthy and clinical populations (Noble 1982). More specifically to our study, the Borg CR-10 scale has demonstrated good reproducibility and sensitivity to change (Grant, Aitchison et al. 1999) and acceptable reliability (Lagally and Costigan 2004). The CR-10 scale consists in a 0-10 point scale where 0 is “nothing” and 10 “cannot continue”. A rating of 8 usually corresponds
to a “very difficult task” and has been considered as an indicator of fatigue (Cote, Mathieu et al. 2002).

3.3.5.3 EMG

The presence of fatigue was also evaluated offline through a detailed electromyographic (EMG) analysis. The EMG data of five shoulder and arm muscles (anterior, middle and posterior deltoid, pectoralis major and biceps) were recorded throughout the fatiguing exercises (sampled at 1080 Hz) using bipolar, Ag-AgCl surface electrodes (Noraxon, USA). A significant increase in the mean signal amplitude during a reaching cycle (t-test) was considered as a sign of muscular fatigue.

3.3.6 Data analysis

In order to find the difference in the arm position reproduced by each subject before and after fatigue, the mean and standard deviation of the endpoint positions pre and post fatigue (pre-test and post-test in non fatigue group) were calculated. The distance between the means was considered as the overall change in the endpoint positions. An independent t-test was used to compare the mean position change between the fatigue and non fatigue groups.

Additionally, we used a two-dimensional implementation of the Kolmogorov-Smirnov test (Fasano 1987) to find the difference in the distribution of the endpoint position after fatigue. This non-parametric test indicates whether two samples come from the same two-dimensional distribution or not, in the form of a
d-value. D-values close to 1 represent a complete mismatch in the distributions of the two samples while values close to 0 shows that the two samples have overlapping distributions. We computed the d-value for each subject and compared the fatigue and non fatigue group with an independent t-test. Finally, for each group, we used repeated measures ANOVA to detect the significant change in the variability of endpoint positions after fatigue.

We were also interested in the effects of fatigue on hand orientation. For each of the three target orientations, we averaged the angles of the wooden block produced before and after fatigue. Then we used a repeated measure ANOVA to compare the changes in orientation within subjects and groups (3 orientations × 2 conditions (before and after) × 2 groups (fatigue and non fatigue).

The purpose of the EMG recording in this study was to confirm the fatigue status of the muscles. When a muscle is fatigued, its EMG signal amplitude increases (Kramer, Hagg et al. 1987). At first, the absolute value of EMG signals was calculated and signals were filtered using a low pass filter with a cut off frequency of 5Hz. Then the peak of each EMG signal was identified and the surface area under each peak was calculated. In each set of fatiguing exercise, subjects performed approximately 30 movements. Therefore 30 peaks were expected in each set of EMG signal. In order to determine the fatigue status of each muscle, the surface areas of the first and the last set of exercises were compared with each other using an independent t-test.
3.4 Results

The ability of subjects in the reproduction of an arm position was measured by computing both the change in endpoint position and in hand orientation. We considered the position of the middle point of the wooden block as the endpoint position. Also, as shown in figure 4B, the middle points of all three target orientations were at a same point. Therefore reproduction of hand orientation and endpoint position were not two separate tasks. Subjects reproduced an orientation while ending the task in a certain point.

3.4.1 Endpoint position

The endpoint position for each subject in both the fatigue and non fatigue groups were compared before and after fatigue. Figure 6 shows the endpoint positions in all trials, for one subject from each group. In the fatigue subject (figure 6A), an obvious displacement of the mean endpoint position can be seen after muscle fatigue. The two ellipses on the figure make this observation more clear. The ellipses were drawn for each condition before and after fatigue based on 95% confidence interval, which clearly define the distribution of endpoints in each condition.

Conversely, the subject in the non fatigue group (figure 6B) shows no change in the mean endpoint position after re-test. For this subject, the two mean positions as well as the ellipses are approximately in the same position. Furthermore, the d-value and mean changes are shown for both subjects on the figure. D-values close to one represent a large difference in the distribution of the two samples while
values close to zero show that the two samples have almost the same distribution. The mean change shown on the figure is the distance between the centers of the two ellipses. This value was remarkably larger for the subject in fatigue group compared to the subject in the non fatigue group (figure 6A, B).

**Figure 6: Final endpoint position before and after fatigue.** This figure illustrates the change in the distribution and in the mean endpoint position after re-test in two individual subjects in the A) fatigue and B) non fatigue groups.
In a subject-by-subject analysis, we found a significant difference in the endpoint position for 11 out of 12 subjects in the fatigue group using a two dimensional Kolmogorov-Smirnov test (Fasano 1987). However, in none of the subjects in the non fatigue group this difference was significant.

A trial-by-trial analysis showed that the movement trajectory from the starting to the end position in the fatigue group was changed after fatigue, whereas no difference was seen in the non fatigue group. Figure 7A illustrates two movement trajectories before and after fatigue in the fatigue group. Both trajectories start from the same initial position and begin to diverge gradually right after the starting position. Finally each of them ends up at a different point. Therefore, difference in the endpoint position was the resultant of a gradual change in the movement trajectory. Such a difference was not seen in the subjects of non fatigue group (Figure 7B).

![Figure 7: Side-view of the hand trajectories](image)

In the fatigue subject (panel A), a typical trial illustrates the gradual change in the hand trajectory, from the initial to the final position. This was not seen in the non fatigue subject (panel B).
By comparing the direction of change for all subjects in the fatigue group we found that 75% of the subjects (9 out of 12) had a trend to move up in the vertical plane after fatigue (figure 8).

**Figure 8: Mean change in hand position.** The figure shows the mean change in hand position for all subjects in the fatigue group, with respect to their mean position before fatigue (0, 0). Error bars indicate standard error.
This finding was surprising as we expected the subjects to move down in the direction of gravity when their muscles got fatigued. Further, we didn’t find any constant pattern of displacement in the horizontal plane, as some subjects tended to move to the left and some to the right after muscle fatigue, with respect to their performance before fatigue (66% to the left, 44% to the right).

A group analysis using an independent t-test showed that the mean change in the endpoint position in the fatigue group was significantly different from that of the non fatigue group (p=0.02). Furthermore, a comparison of the d-values, using an independent t-test, showed a significant difference between the two groups (p=0.0004). This means that the change in the distribution of endpoint positions after re-test was more important in the fatigue group compared to the non fatigue group. Figure 9 shows the group means for the change in endpoint position and in endpoint distribution. Both of these were significantly higher in the fatigue group.

![Figure 9: Changes in endpoint distribution and mean position. Both endpoint distribution and mean position sense is greater in fatigue group compared to the non fatigue.](image)

We also compared the variability of the endpoint positions in the two groups. For each individual subject, we defined the variability as the inter-trial standard
deviation of endpoint positions. We observed that most subjects in the fatigue group displayed a higher variability after fatigue whereas no difference was seen for subjects in the non fatigue group. However when we compared both groups with a repeated measures ANOVA (variability× 2 conditions (pre and post) × 2 groups (fatigue & non fatigue)) we didn’t find any significant difference between the two groups (P=0.68). Figure 10 shows the variability of endpoints in each group before and after fatigue.

![Image of endpoint variability](image.png)

**Figure 10: Endpoint variability.** Comparisons of endpoint variability before and after fatigue in the fatigue and non fatigue groups. Error bars indicate standard error.

### 3.4.2 Orientation

The mean angle for all trials to each target orientation before and after fatigue was calculated for subjects of both groups (Table 1). A repeated measures ANOVA showed no significant difference between the two groups ($p=0.795$) and between the subjects.
Table 1: Effects of fatigue on hand orientation. Mean angle (± SD) for each target orientation in each group. There was no significant difference between the two groups.

<table>
<thead>
<tr>
<th>Orientation</th>
<th>Fatigue Before (°)</th>
<th>Fatigue After (°)</th>
<th>Non fatigue Before (°)</th>
<th>Non fatigue After (°)</th>
</tr>
</thead>
<tbody>
<tr>
<td>125°</td>
<td>124.75 ± 4.36</td>
<td>124.8 ± 4.25</td>
<td>124.5 ± 4.17</td>
<td>124.18 ± 4.09</td>
</tr>
<tr>
<td>90°</td>
<td>90.6 ± 2.8</td>
<td>91.3 ± 1.83</td>
<td>90.78 ± 2.46</td>
<td>90.92 ± 3.08</td>
</tr>
<tr>
<td>55°</td>
<td>56.03 ± 4.91</td>
<td>56 ± 5.97</td>
<td>55.06 ± 5.97</td>
<td>55.82 ± 6.91</td>
</tr>
</tbody>
</table>

3.4.3 EMG

For each subject, we compared the EMG signals of all recorded muscles during the first and the last set of fatiguing exercises. Figure 11 shows the EMG signals of the medial deltoid in one subject. An obvious increase in the signal amplitude can be seen by the end of exercise, which confirms the presence of fatigue in the muscle. The analysis of all muscle in the same way for subjects in the fatigue group showed that in each subject, the EMG signal amplitudes of at least four muscles were significantly increased by the end of the fatiguing exercises. Figure 12 illustrates the difference in the signal amplitude of 5 muscles in one subject by the end of fatiguing exercise. The fact that a majority of muscles in all subjects displayed a significant increase in activity confirmed that the stretching exercise did induce fatigue.

We also analyzed the fatigue status of each target muscle and its relation to the direction of change in the endpoint. For example we examined if the excessive fatigue of anterior deltoid could result in more errors in the direction of horizontal adduction of the arm. By analysing all involved muscles, we couldn’t find any
relationship between the level of muscle fatigue and change in the position of the arm.

**Figure 11: Results of the fatiguing exercise on EMG activity.** The EMG activity of the medial deltoid increased between the first and the last set of fatiguing exercises. The mean signal amplitude (dotted line) increased at the end of the exercise.

**Figure 12: Mean increase in EMG after fatigue.** In this subject, the EMG signals of the five recorded muscles significantly increased between the first and last set of exercises. Error bars indicate standard error.
3.5 Discussion

The purpose of this experiment was to estimate the extent to which muscle fatigue alters the proprioception of the upper limb in healthy adult subjects. We measured the proprioception of the right upper limb by examining the ability of subjects to reproduce an arm position after fatigue. Since the subjects did not have any visual or useful tactile feedback about their performance, we considered that the change in endpoint position as an indicator of an alteration in proprioception.

There are different hypotheses regarding the underlying causes of change in proprioception in the presence of fatigue. Some authors believe that the malfunction of joint and muscle receptors may contribute to the change in proprioception (Voight, Hardin et al. 1996). But other authors (Proske 2005) believe that another factor, which they term the sense of effort, could play a role in providing feedback to the CNS. The sense of effort is our perception of the heaviness of objects and the muscle forces we generate (McCloskey 1981), which is linked to the sense of fatigue in a way that the decline in muscle force due to fatigue is compensated centrally by an increase in the motoneurons activity which eventually leads to a progressive increase in the perceived effort (Proske 2005).

The exact origin of the sense of effort is controversial. Traditionally, the perception of effort is believed to arise from a "corollary discharge," a neurological discharge from the motor to the sensory cortex (McCloskey 1981). However recent studies suggest that the sense of effort arises somewhere upstream and not simply from the motor cortex (Carson, Riek et al. 2002; Proske, Gregory et al. 2004)
It has been shown that fatigue from exercise has not changed the responsiveness of muscle receptors (Gregory, Brockett et al. 2002). Walsh et al (Walsh, Hesse et al. 2004) also reported that the change seen in proprioception in the presence of fatigue may not be due to the function of muscle receptors alone. They suggested that an alteration in the amount of effort required for maintaining the limb position could play an important role in proprioception change and subsequent movement errors. In this experiment, we found that the direction of change in the endpoint positions was not identical for all subjects. Nevertheless, the majority of subjects (75%) tended to move upwards in respect to their pre-fatigue position. Allen et al (Allen and Proske 2006) reported that in an elbow matching task when the forearm is fatigued, the muscles produce less force, thereby requiring more effort to maintain a given arm position against the gravity. Therefore the shifting of the endpoints to an upper position in our experiment could be due to the extra effort that subjects made to move their arm to the target against the gravity which caused them to overestimate the target position. This extra effort and overestimation of target was at the presence of gravity, therefore future research should be done in conditions were the effects of gravity is eliminated (e.g horizontal arm movements on flat surfaces or with arm supports that can bear the weight of the arm.

Although the amount of change in proprioception was significant for all subjects of fatigue group, the change was not so big in a few subjects (around 1cm). Due to the multijoint nature of the task employed in this study, a big change in position was not expected, because several joints and muscles were involved which could
reduce the rate of position error. Therefore even the slightest change in position could have had future consequences.

The target in this study was presented in three different orientations. We added these orientations to make our reaching task more precise. Overall, we did not find any significant effect of fatigue on hand orientation. This could be due to the unconstrained, multi-joint nature of our reaching task where subjects were able to employ different strategies to reach the targets. For example, if the shoulder proprioception became less accurate due to fatigue, subjects could compensate with other joints like elbow and wrist and employ a different reaching pattern. On the other hand, as one of the limitations of this experiment, we couldn’t fatigue all the muscles of the upper limb simultaneously. Therefore the lack of sensory information could have been compensated by other muscle receptors, especially the ones in the wrist and fingers. These factors might have helped subjects to align their hand correctly with each orientation. Finally, orienting the hand to a before-seen target could be effected by some CNS mappings. Gosselin-Kessiby et al. (Gosselin-Kessiby, Messier et al. 2008) suggest the existence of an automatic error correction mechanism for hand orientation during reaching movements to stationary target with closed eyes. They believe that this mechanism accompanies the proprioception and corrects the errors of hand orientation. Therefore in our experiment, this central mapping could have helped subjects to align their hands correctly to the target.

In this experiment, we were interested in the effects of fatigue at the level of muscles. We did not differentiate between central and peripheral fatigue. Central
fatigue may include mechanisms that inhibit motor drive in upper regions of the brain (Gandevia 1998). Although our EMG analysis showed that all subjects were fatigued at the level of muscles, we shouldn’t overlook the role of fatigue at the upper levels of nervous system. Future research should be focused on differentiation between these two types of fatigue and the role of each type in distortion of proprioception.

3.6 Conclusion

The result of this study showed that the proprioception of the upper extremity can be changed in the presence of fatigue. When proprioception is altered in a joint, the likelihood of instability is increased (Lephart and Henry 1996). An instable joint is more susceptible to muscular and ligamentous injuries (Robinson, Kelly et al. 2002; Robinson, Howes et al. 2006). Therefore fatigue should be considered as an important factor in the rehabilitation of musculoskeletal injuries, particularly in exercise therapy. Clinicians may use fatigue measurement tools to assess the fatigue level of the patients during the treatments. Furthermore, increasing the muscular endurance and fatigue threshold in athletes should be considered as an important factor in athletic trainings.
Chapter 4- Summary and Conclusion

The stability of the shoulder, as the most mobile joint in the body, is provided by static and dynamic stabilizers (Wilk, Arrigo et al. 1997). The proper function and coordination of dynamic stabilizers (muscles) is determined by a neural process called neuromuscular control (Myers and Lephart 2000). The afferent signals from mechanoreceptors, known as proprioception, travel to the CNS where they are integrated with other sensory information and consequently an efferent response is elicited (Myers and Lephart 2000). Therefore, deficit in proprioception or any component involved in neuromuscular control may cause instability in the joint (Smith and Brunolli 1989) which itself is a predisposing factor for joint and muscular injury (Robinson, Kelly et al. 2002; Robinson, Howes et al. 2006). It is believed that muscle fatigue can cause a deficit in proprioception, thus changing the neuromuscular control and eventually causing an injury to the muscular and ligamentous structures (Voight, Hardin et al. 1996; Tripp, Boswell et al. 2004).

To date a number of studies have investigated the effects of fatigue on proprioception. The majority of these experiments have been single-joint studies investigating mostly the shoulder (Voight, Hardin et al. 1996; Carpenter, Blasier et al. 1998; Sterner, Pincivero et al. 1998; Myers, Guskiewicz et al. 1999) and a few have been multi-joint experiments (Tripp, Boswell et al. 2004; Tripp, Yochem et al. 2007). However, the effect of fatigue on proprioception in an unconstrained, functional and multi-joint task such as reaching has not been studied before.
The objective of this study was to estimate the extent to which muscular fatigue alters the proprioception of upper extremity in healthy adult subjects. To achieve this goal, the ability of subjects in the reproduction of an arm position after muscular fatigue was investigated. Since subjects did not have any visual or tactile feedback, the change in arm position was considered as a change in the proprioception. The result of the study showed that the proprioception of the upper limb was significantly changed in the presence of muscle fatigue.

Lephart et al (Lephart and Henry 1996) showed that the deficit in proprioception can cause functional instability in a joint, which itself may lead to subsequent injuries. We found that fatigue can indeed cause a deficit in proprioception. Therefore fatigue should be considered as an important factor in the management and treatment of musculoskeletal injuries. Musculoskeletal injuries in the shoulder are usually accompanied by a deficit in proprioception (Smith and Brunolli 1989; Lephart and Henry 1996). The goal of physiotherapy treatments in such patients is to restore proprioception with the help of neuromuscular training exercises (Lephart and Henry 1996). The goal of these exercises is to ameliorate the proprioception, however as for any type of exercise, development of muscular fatigue is inevitable. Therefore precautions should be taken by therapists about the fatigue status of patients during any strengthening or neuromuscular training exercises as these may have adverse effects. More research is required to determine the level of fatigue at which the exercise should be stopped.

As with any study, there were limitations with this project. The task employed in this experiment was a multijoint task where several muscles were involved. We
were not able to fatigue all of the involved muscles at a same time. As well, the result of this experiment was limited to healthy adult subjects. Specific populations like throwing athletes or shoulder injured patients may show different results.

Over all, this study can serve as a basis for further research on the proprioception and neuromuscular control of the upper extremity. It can also be used by researchers and clinicians in developing new techniques in the treatment of musculoskeletal injuries.
References


1 - Title of project
Effects of muscular fatigue on position reproduction acuity

2 - Researchers in charge of project
Philippe Archambault, Ph.D. Assistant professor, School of Physical and Occupational Therapy, McGill University, (450) 688-9550, ext. 4832
Amirhossein Khazraiyanvafadar, MSc. student, School of Physical and Occupational Therapy, McGill University, (450) 688-9550, ext. 4834

3 - Project description and objectives
The objective of this project is to better understand the effects of repetitive motion-induced fatigue on arm position sense. We want to study how fatigue affects a person’s ability to perceive where their body is in space. Results will contribute to our understanding of the mechanisms of repetitive motion disorders and will help us to treat and prevent this type of injury.

4 - Nature and duration of participation
The research project to which I am invited to participate aims at understanding how position sense in healthy people is affected by repetitive movements with their dominant arm. This research is conducted in two experimental sessions, spaced 48 hours at least, with each testing session lasting approximately two hours. The tests will be performed at the research center of the Jewish Rehabilitation Hospital. During each testing session, the preparation will last approximately one hour. Using adhesive tape, surface electrodes will be fixed on the skin over muscles of my dominant arm and trunk, and reflective markers will be fixed on the skin over my spine, legs and arms in order to record their positions. I will stand on two force plates that will record the stability of my posture. None of these procedures is invasive.
During each experimental session, I will perform a simple task where I will be asked to reach between two targets. I will then perform the fatiguing protocol. It consists of repeated arm movements either in the air or against a long elastic band. I will perform this movement at a rate of one per second by following the beat of a metronome. The protocol will be terminated when 1) I will no longer be able to maintain the movement rhythm; or 2) administrators will deem that the task has become too difficult for me. Although the objective is to reach fatigue, I will be able to stop anytime if I feel abnormal discomfort or pain. The fatiguing protocol will be followed by another series of reaching movements.

5 - Advantages associated with my participation

I will not personally benefit from advantages by participating in this study. However, I will contribute to the fundamental science of motor control and the applied science of occupational health.

6 - Risks associated with my participation

None of the techniques used are invasive. My participation in this project does not put me at any medical risk. It is understood that I will be allowed to terminate the session anytime I wish. Although the electrodes and the adhesive tape used to fix the markers on the body are hypo-allergen, they may induce slight redness or cutaneous irritation during the few minutes following the end of the protocol. Should this happen, lotion will be applied on the irritated site. Also, some individuals may feel a sensation of fatigue or discomfort at the shoulder during the 48 hours following participation.

7 - Personal inconvenience

The duration of each session (approximately two hours) may represent an inconvenience for some individuals.

8 - Access to my medical file

No access to my medical file is required for this study.

9 - Confidentiality

All the personal information collected for this study will be codified to insure confidentiality. Information will be kept under locking key at the research center of the Jewish Rehabilitation Hospital by one of the persons responsible for the study for a period of five years. Only the people involved in the project will have access to this information. If the results of this research project are presented or published, nothing will allow my identification. After this five-year period, data will be destroyed.
10 - Questions concerning the study
The researchers present during the session should answer my questions concerning the project in a satisfactory manner.

11 - Withdrawal of subject from study
Participation in the research project described above is completely voluntary. I have the right to withdraw from the study at any moment. Should I withdraw from the study, all documents concerning myself will be destroyed.

12 - Responsibility
By accepting to enter this study, I do not surrender to my rights and do not free the researchers, sponsor or the institutions involved from their legal and professional obligations.

13 - Monetary compensation
No monetary compensation will be given to me for participation in this protocol. Transportation fees (maximum 15$ per visit) can be reimbursed.

14 - Contact persons
If I need to ask questions about the project, signal an adverse effect and/or an incident, I can contact at any time either one of the researchers in charge of this project at the coordinates indicated on the first page. I may also contact M. Michael Greenberg, local commissioner for the quality of services at the JRH, at (450) 688-9550, extension 232.

Also, if I have any questions concerning my rights regarding my participation to this research project, I can contact Mme. Anik Nolet, Research ethics co-ordinator of CRIR at (514) 527-4527 ext. 2643 or by email at anolet.crir@ssss.gouv.qc.ca
CONSENT

I have read and understand this study, the nature and extent of my participation, as well as the benefits and risks/ inconveniences to which I will be exposed as presented in this form. I have been given the opportunity to ask any questions concerning any aspect of the study and have received answers to my satisfaction.

I, the undersigned, voluntarily agree to take part in this study, I can withdraw from the study at any time without prejudice of any kind. A copy of this consent form will be put into my medical file.

A signed copy of this consent form will be given to me.

NAME OF SUBJECT (print)  
SIGNATURE OF SUBJECT

________________________
________________________

Date:
COMMITMENT OF RESEARCHER

I, undersigned, ________________________________ , certify

(a) having explained to the signatory the terms of the present form ;

(b) having answered all questions he/she asked concerning the study ;

(c) having clearly told him/her that he/she is at any moment free to withdraw from
the research project described above ;

and (d) that I will give him/her a signed and dated copy of the present document.

______________________________
Signature of person in charge of the project
or representative

Signed in __________________, ____________ 20__.
Vicon plug-in gait model - upper limb
Par la présente, le comité d’éthique de la recherche des établissements du CRIR (CÉR) atteste qu’il a évalué, lors de sa réunion du 16 juin 2008, le projet de recherche CRIR-357-0508 intitulé :

«Effects of Repetitive Motion-induced Arm Fatigue on Local and Global Aspects of Upper Limb Position Sense».

Présenté par: Asha Mathew, Julie Côté, Philippe Archambault, Amirhossein Khazraiyanvafadar.

Le présent projet répond aux exigences éthiques de notre CÉR. Le Comité autorise donc sa mise en œuvre sur la foi des documents suivants :

- Formulaire A daté du 3 juin 2008 ;
- Preuve d'octroi de fonds de l'Université McGill ;
- Lettre et formulaire de l'Hôpital juif de réadaptation, datés respectivement du 22 et du 1er mai 2008, mentionnant que le projet est acceptable sur le plan de la convenance institutionnelle ;
- Document intitulé « Summary » ;
- Protocole de recherche intitulé «Effects of Repetitive Motion-induced Arm Fatigue on Local and Global Aspects of Upper Limb Position Sense » ;
- Formulaires de consentement, en versions française et anglaise (version du 29 juillet 2008, telle que datée et approuvée par le CÉR) ;
- Affiches de recrutement, en versions française et anglaise (version du 29 juillet 2008, telle que datée et approuvée par le CÉR) ;
- Questionnaires « Échelle de Borg modifiée », en versions française et anglaise.

Ce projet se déroulera dans le site du CRIR suivant : Hôpital juif de réadaptation.

Ce certificat est valable pour un an. En acceptant le présent certificat d’éthique, le chercheur s’engage à :

1. Informer, dès que possible, le CÉR de tout changement qui pourrait être apporté à la présente recherche ou aux documents qui en découlent (Formulaire M) ;
2. Notifier, dès que possible, le CÉR de tout incident ou accident lié à la procédure du projet ;
3. Notifier, dès que possible, le CÉR de tout nouveau renseignement susceptible d’affecter l’intégrité ou l’éthique du projet de recherche, ou encore, d’influer sur la décision d’un sujet de recherche quant à sa participation au projet ;
4. Notifier, dès que possible, le CÉR de toute suspension ou annulation d'autorisation relative au projet qu'aura formulée un organisme de subvention ou de réglementation ;

5. Notifier, dès que possible, le CÉR de tout problème constaté par un tiers au cours d'une activité de surveillance ou de vérification, interne ou externe, qui est susceptible de remettre en question l'intégrité ou l'éthique du projet ainsi que la décision du CÉR ;

6. Notifier, dès que possible, le CÉR de l'interruption prématurée, temporaire ou définitive du projet. Cette modification doit être accompagnée d'un rapport faisant état des motifs à la base de cette interruption et des répercussions sur celles-ci sur les sujets de recherche ;

7. Fournir annuellement au CÉR un rapport d'étape l'informant de l'avancement des travaux de recherche (formulaire R) ;

8. Demander le renouvellement annuel de son certificat d'éthique ;

9. Tenir et conserver, selon la procédure prévue dans la Politique portant sur la conservation d'une liste des sujets de recherche, incluse dans le cadre réglementaire des établissements du CRIR, une liste des personnes qui ont accepté de prendre part à la présente étude ;

10. Envoyer au CÉR une copie de son rapport de fin de projet / publication.

Me Michel T. Giroux
Président du CÉR

Date d'émission
29 juillet 2008